Supplementary Information

Synthesis and multifaceted exploration of dibenzoxepinones: in-vitro antimicrobial and ct-DNA binding, DFT/TD-DFT, molecular docking and simulation studies

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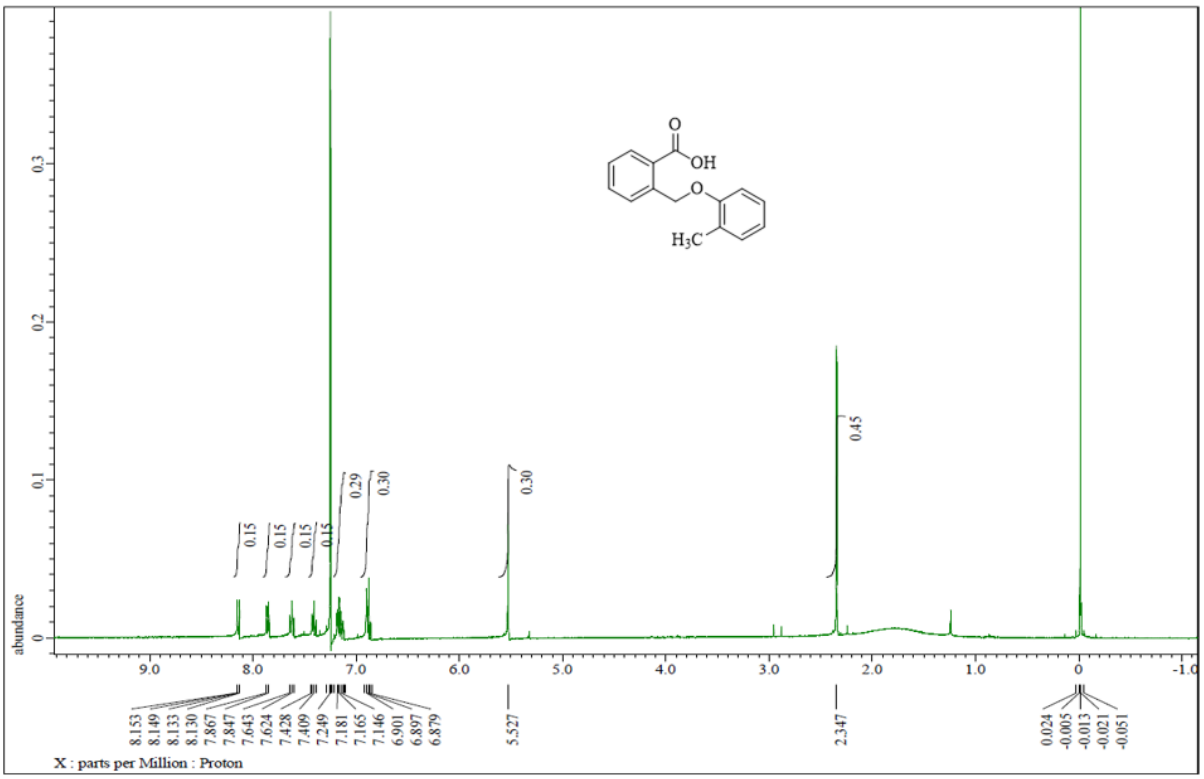
Contents

1. Proton NMR Spectra
2. Carbon NMR Spectra
3. High-Resolution Mass Spectra
4. Binding energy of all compounds with antibacterial, antifungal, and ct-DNA activity.
5. Molecular Docking Images for Antibacterial Activity
6. Molecular Docking Images for Antifungal Activity
7. Molecular Docking Images for ct-DNA Activity
8. Physicochemical Properties Values
9. DFT coordinates for UV-vis
10. DFT coordinates for FTIR
11. DFT coordinates for ESP
12. In-vitro antibacterial photos

1. Proton NMR Spectra

3



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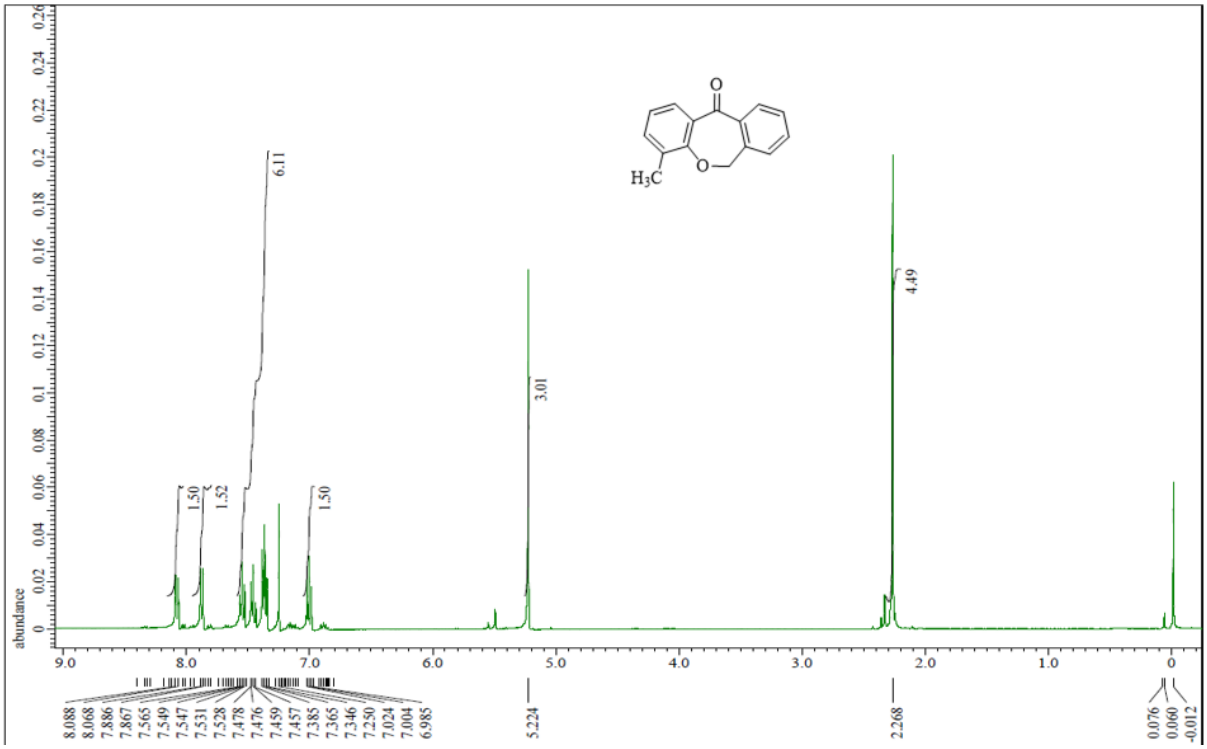

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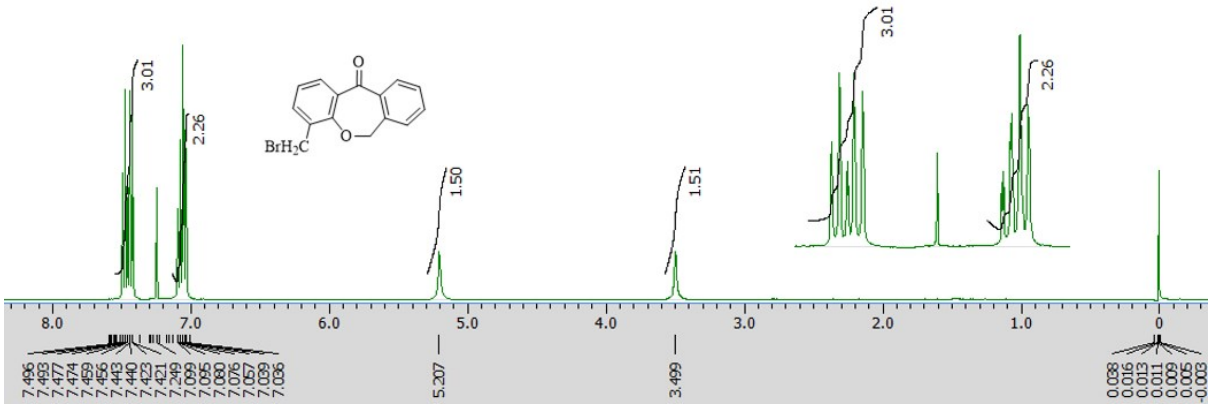
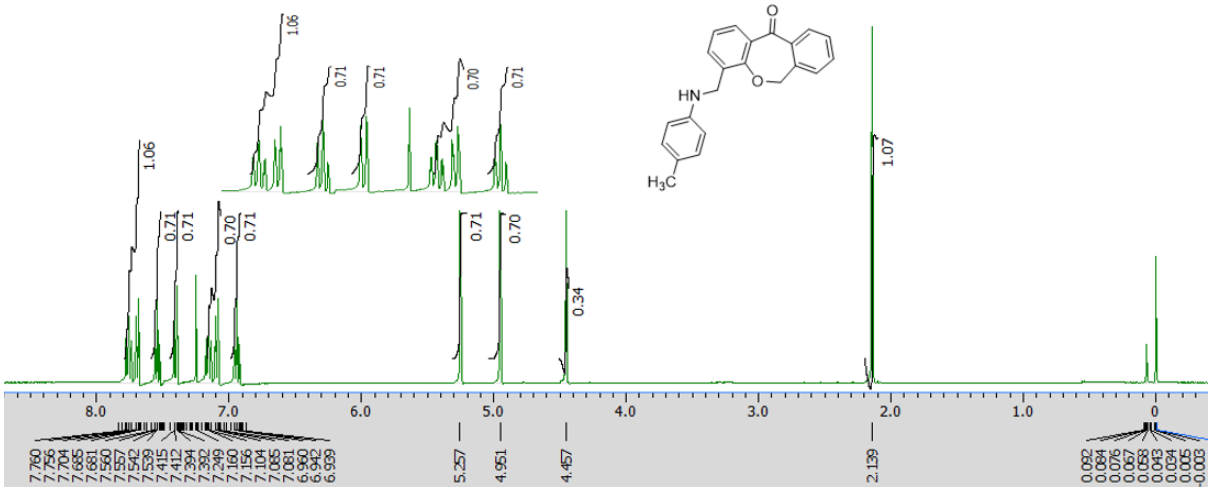
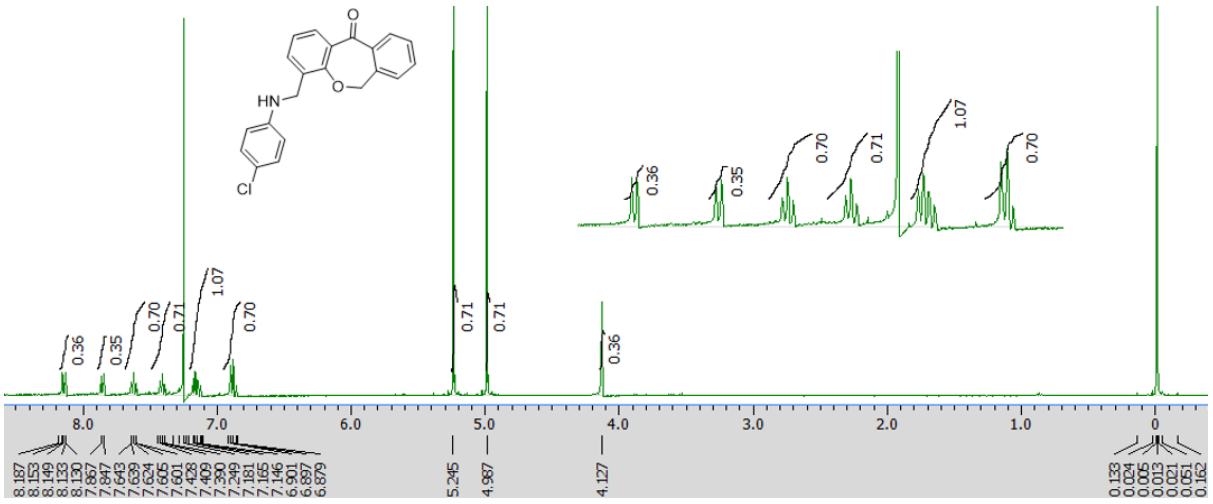

3.01
2.26
1.50
1.51
3.01
2.26
BrH2C
O
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
5.207
3.499

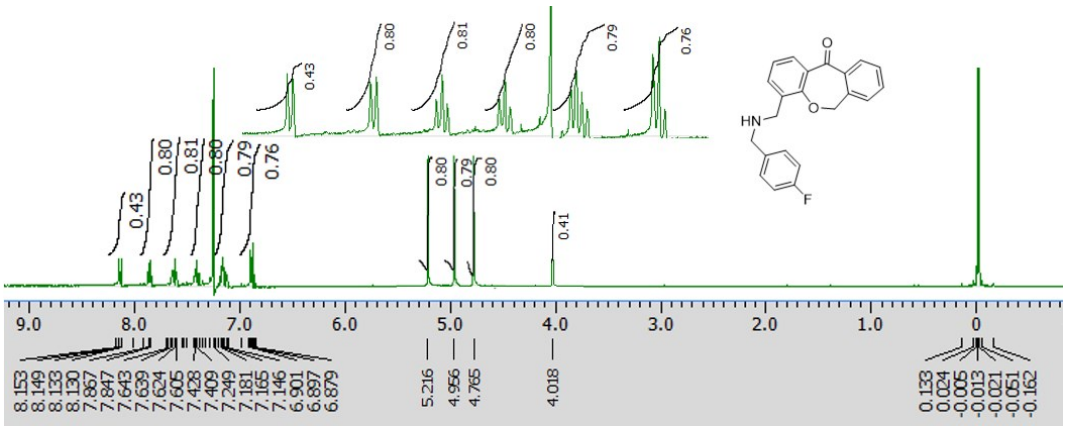
7a


1.06
0.71
0.71
0.70
0.71
1.06
0.71
0.71
0.70
0.71
0.71
0.70
0.34
1.07
HN
H3C
O
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
5.257
4.951
4.457
2.139

7b


0.36
0.35
0.70
0.71
1.07
0.70
0.71
0.71
0.36
0.36
0.35
0.70
0.71
1.07
0.70
HN
Cl
O
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
5.245
4.987
4.127

7c



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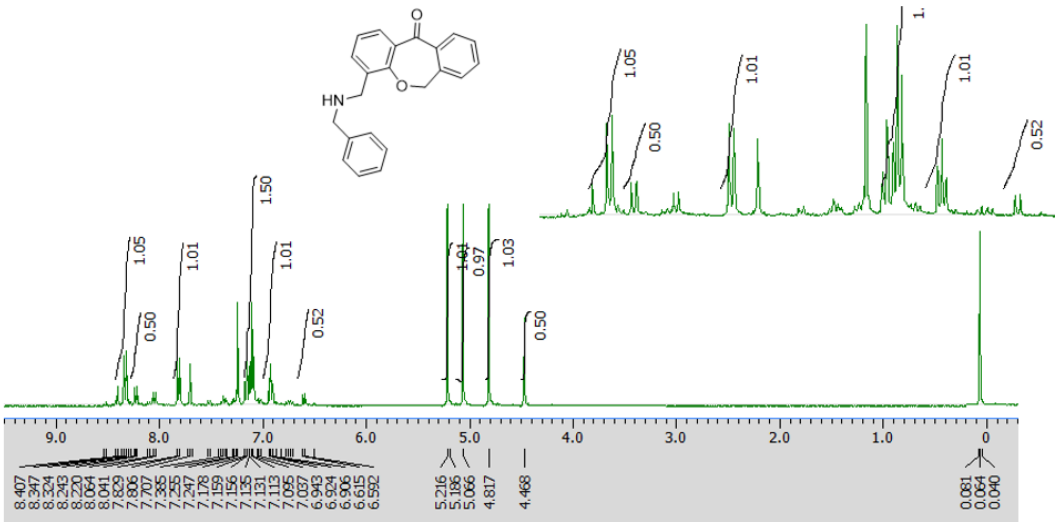

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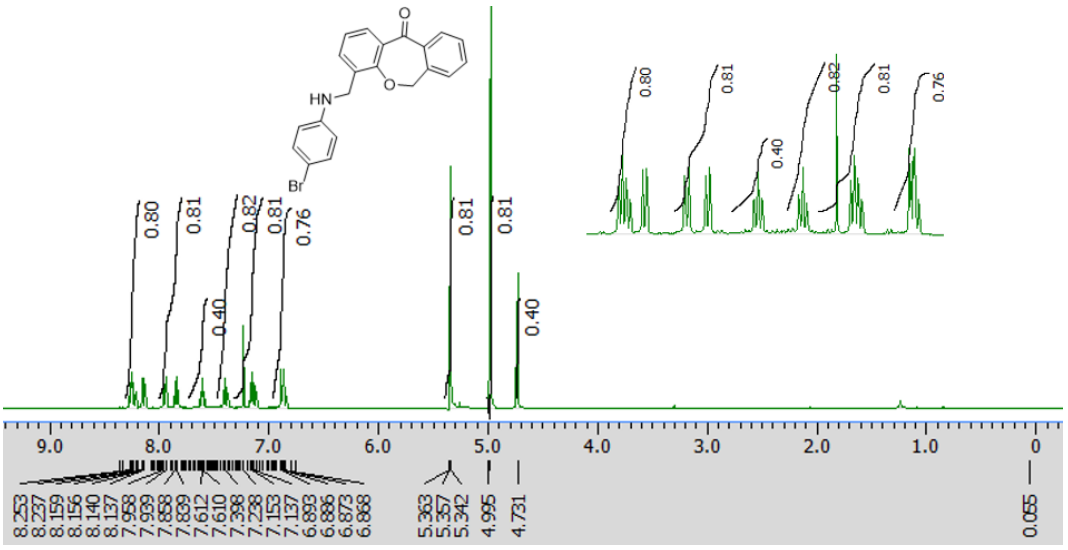

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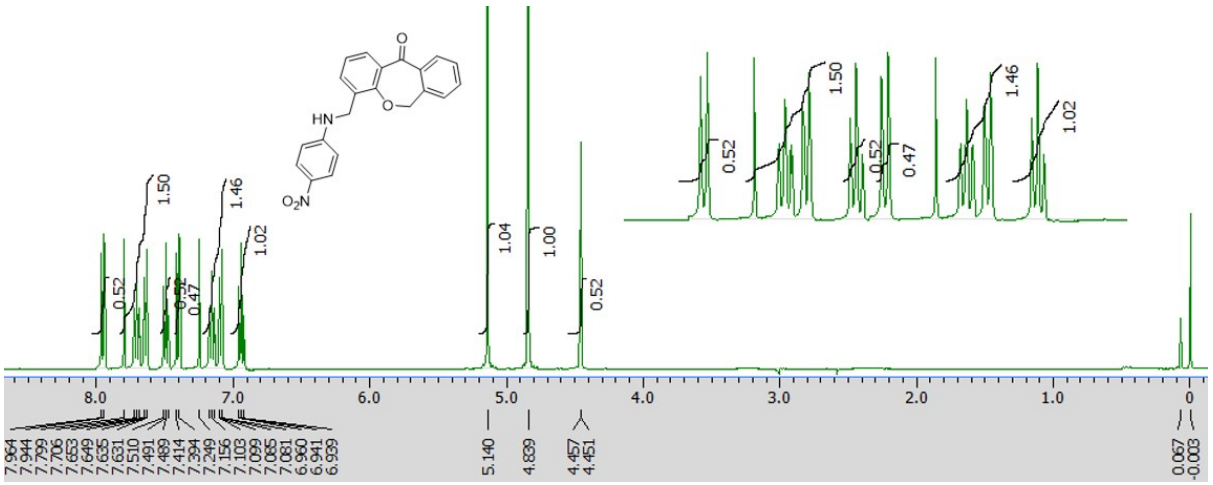
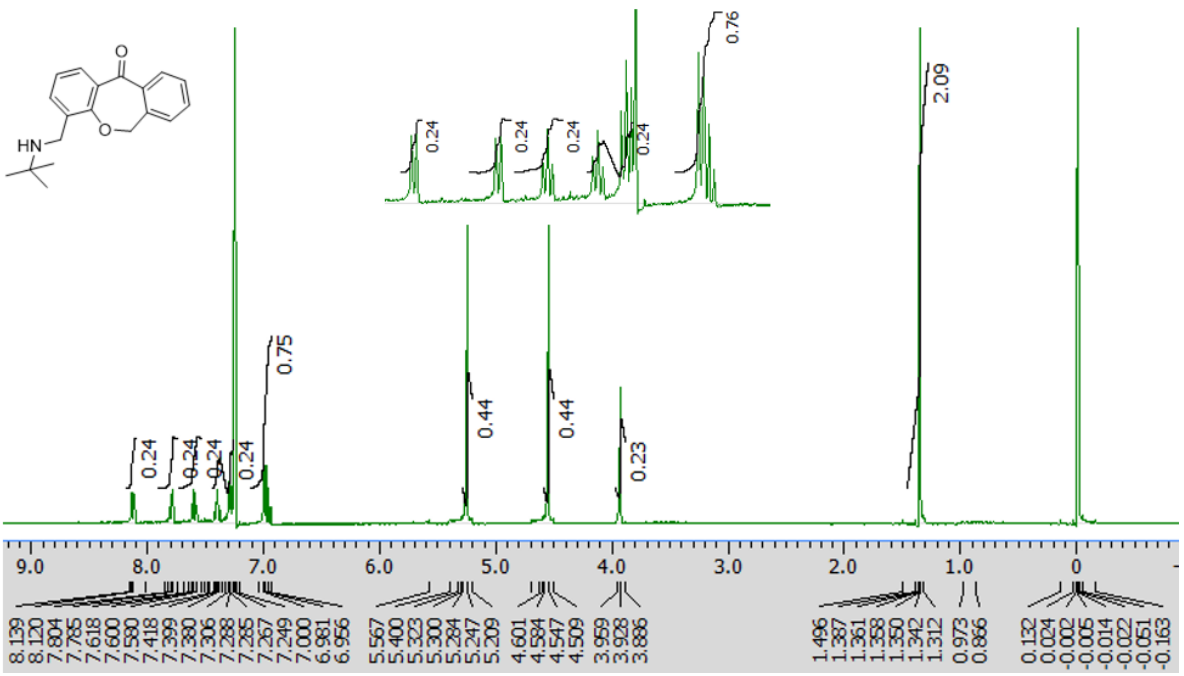
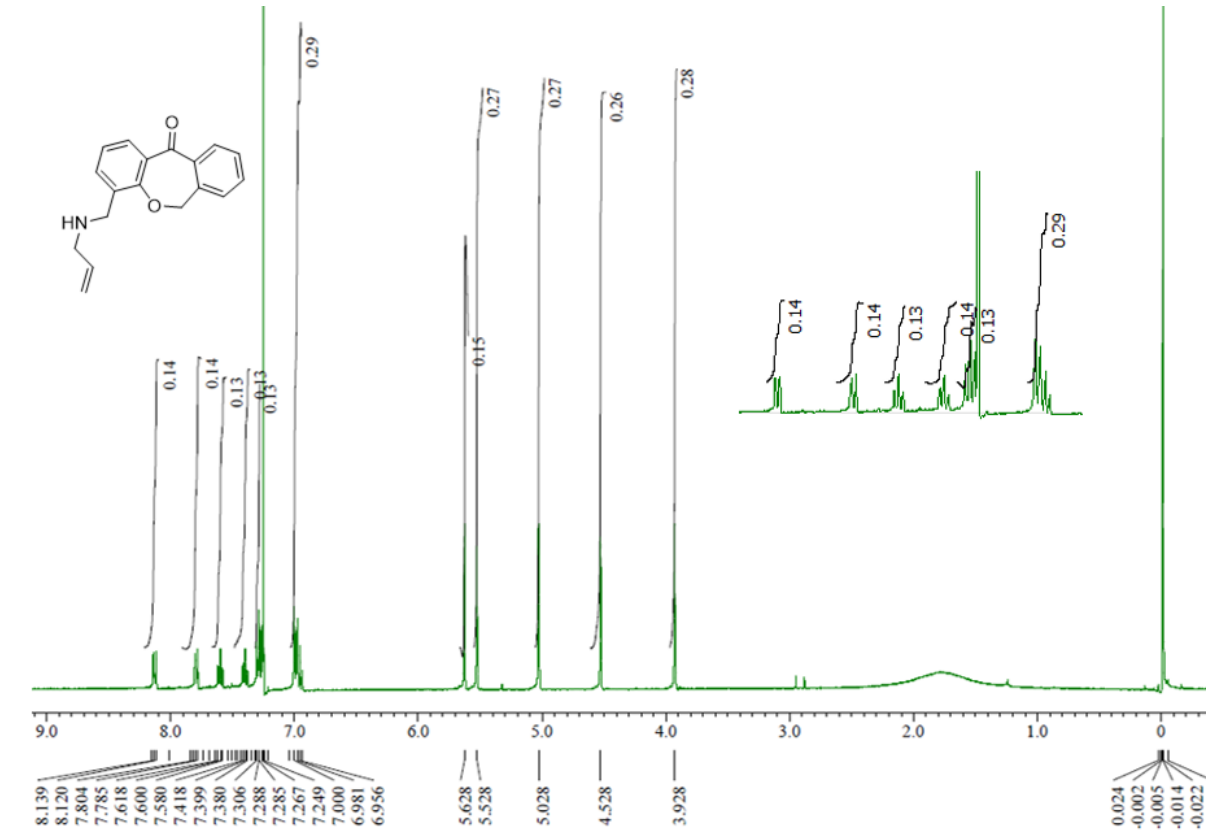

HN
O2N
O
0.52
1.50
0.52
0.47
1.46
1.02
1.04
1.00
0.52
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0

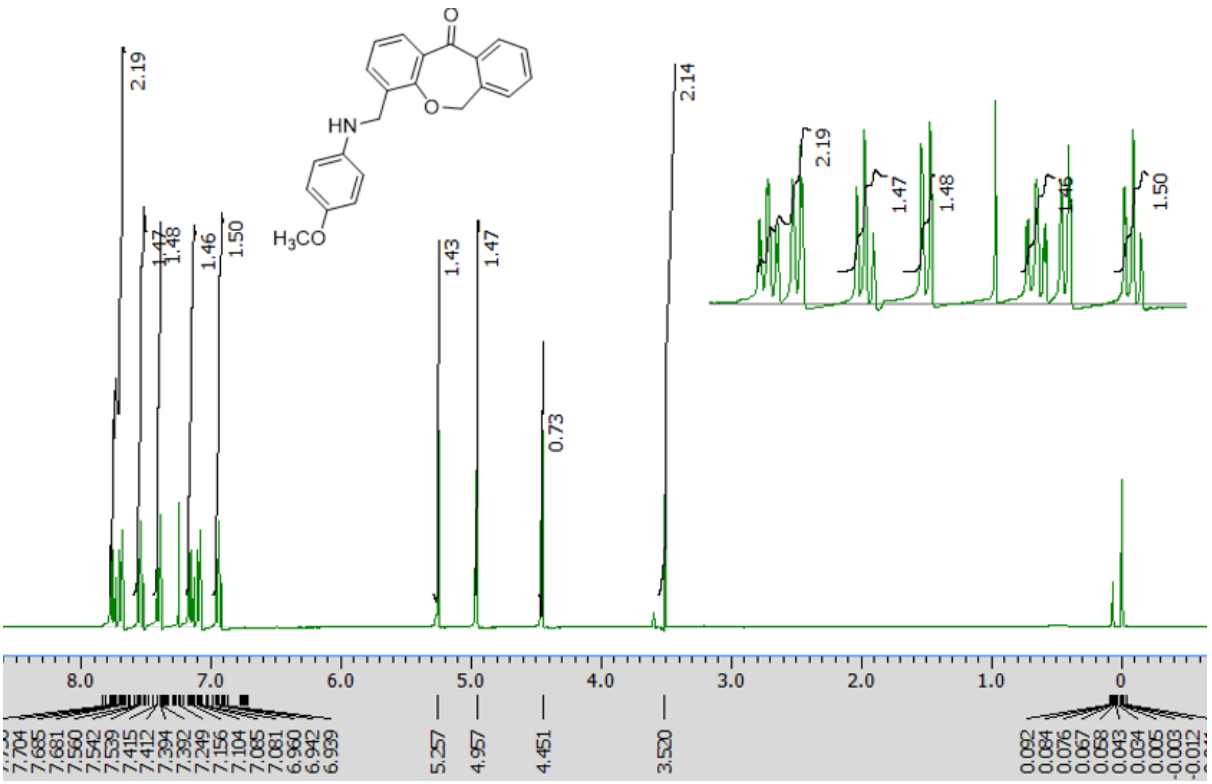
7g


HN
O
0.24
0.24
0.24
0.24
0.75
0.44
0.44
0.23
0.24
0.24
0.24
0.24
0.76
2.09
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0

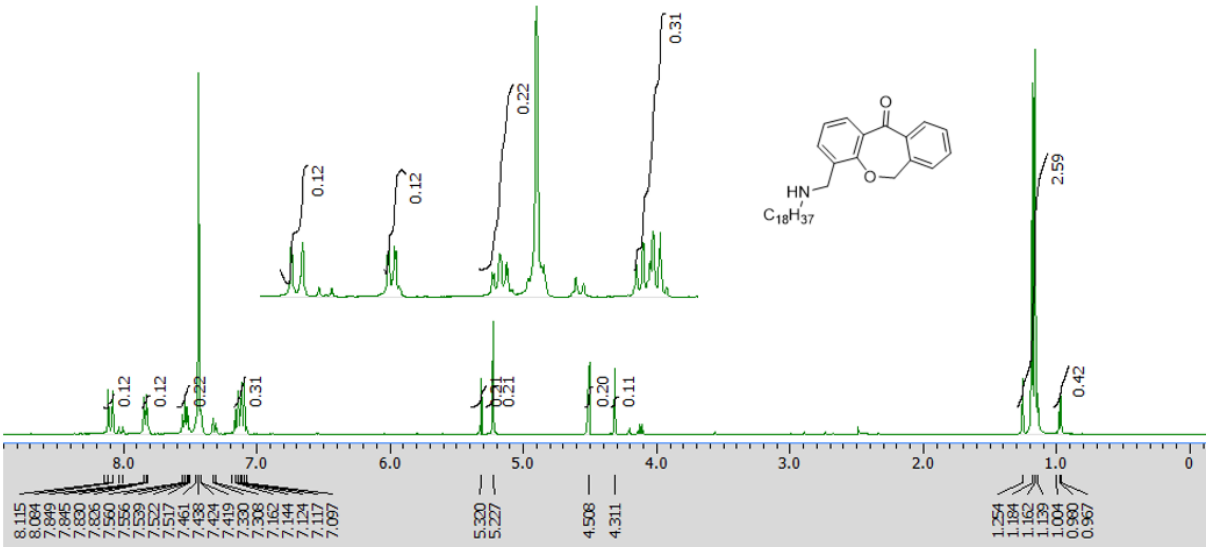
7h


HN
O
0.14
0.14
0.13
0.13
0.15
0.29
0.27
0.27
0.26
0.28
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
8.139
8.120
7.804
7.785
7.618
7.600
7.580
7.418
7.399
7.380
7.306
7.288
7.285
7.267
7.249
7.000
6.981
6.956
5.628
5.528
5.028
4.528
3.928
0.024
-0.002
-0.005
-0.014
-0.022

7i

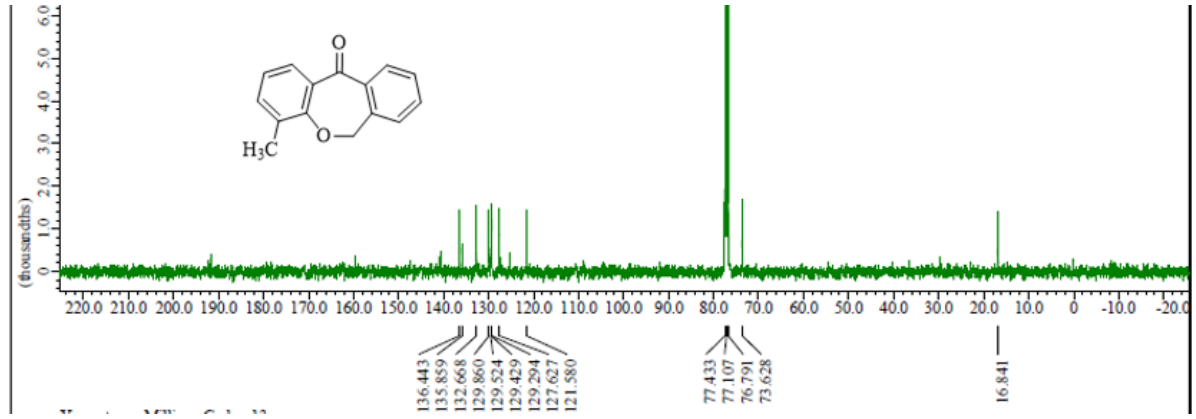

HN
O
H3CO
2.19
1.47
1.48
1.46
1.50
1.43
1.47
0.73
2.14
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
7.704
7.685
7.681
7.560
7.542
7.539
7.415
7.412
7.394
7.392
7.249
7.156
7.104
7.085
7.081
6.960
6.942
6.939
5.257
4.957
4.451
3.520
0.092
0.084
0.076
0.067
0.058
0.043
0.034
0.005
-0.003
-0.012

7j



2. Carbon NMR Spectra

4



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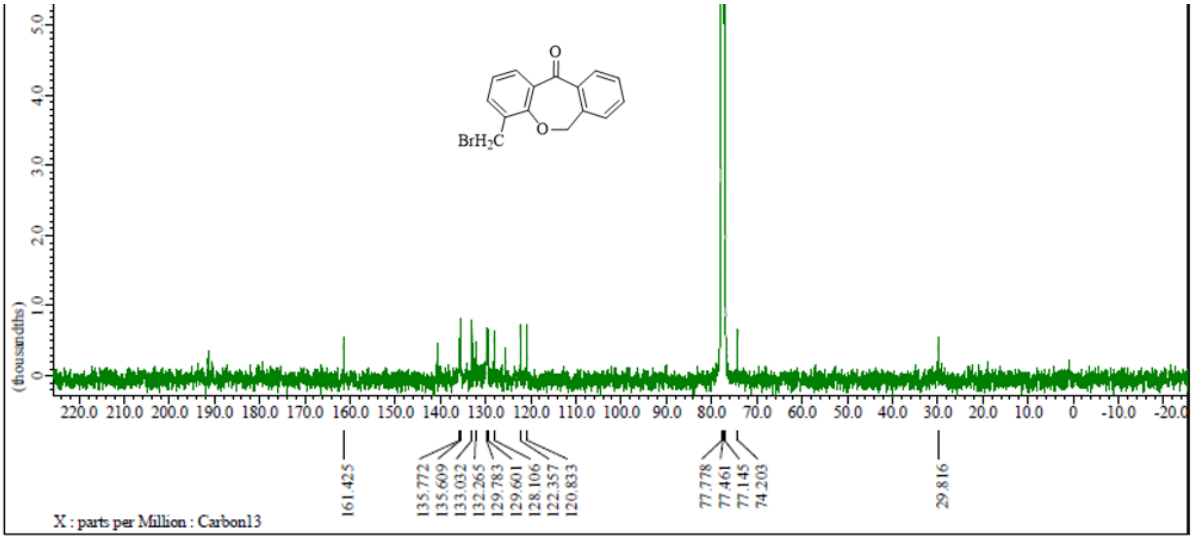

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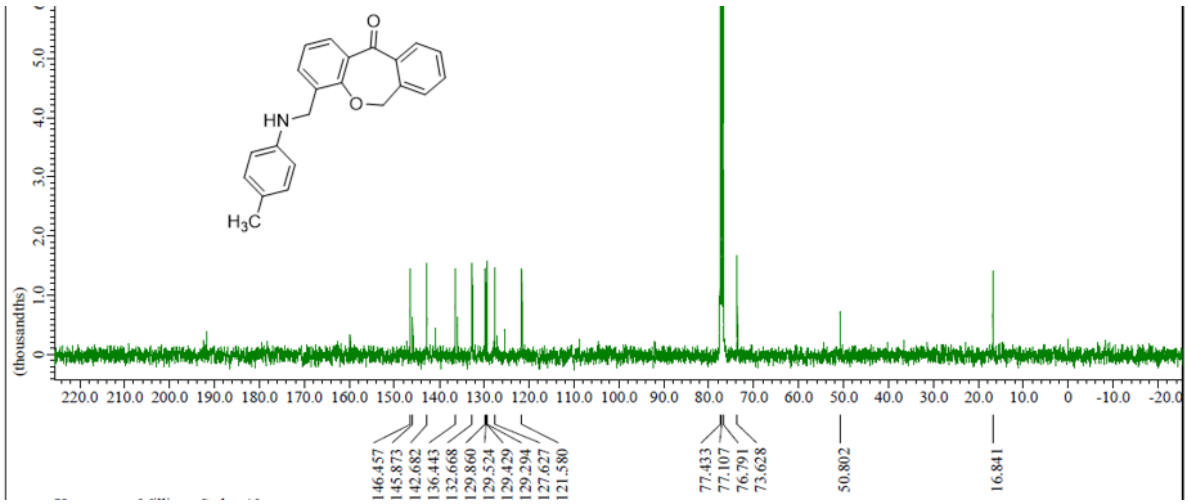
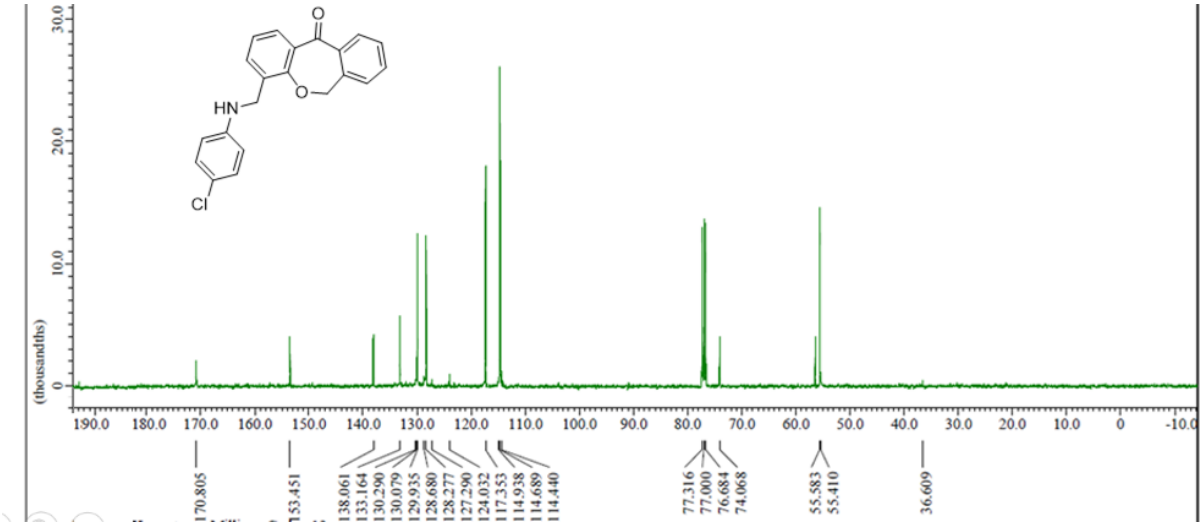
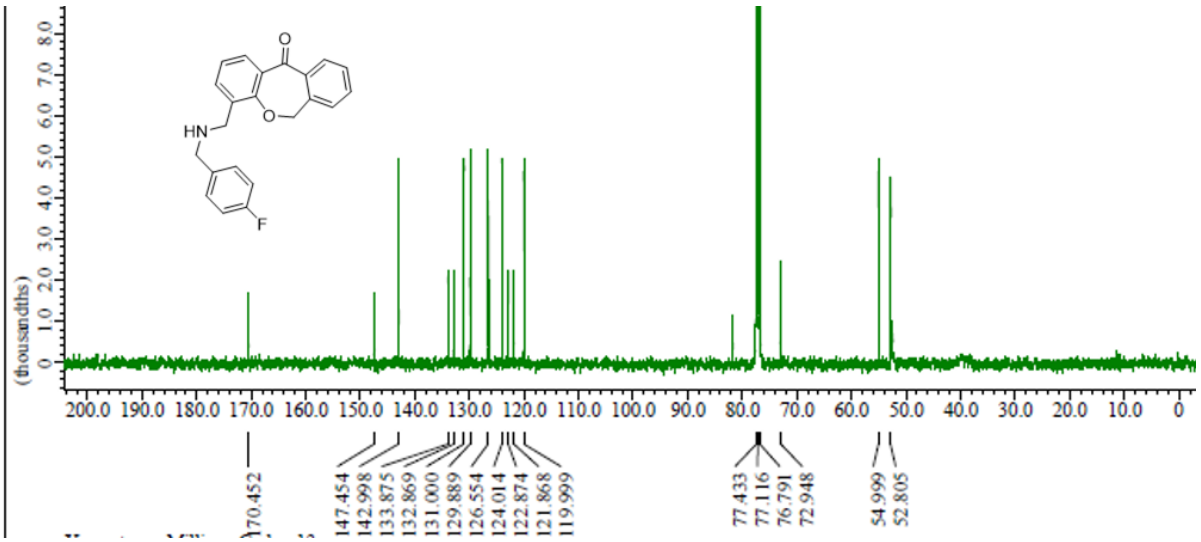

O
HN
H3C
(thousandths)
146.457
145.873
142.682
136.443
132.668
129.860
129.524
129.429
129.294
127.627
121.580
77.433
77.107
76.791
73.628
50.802
16.841

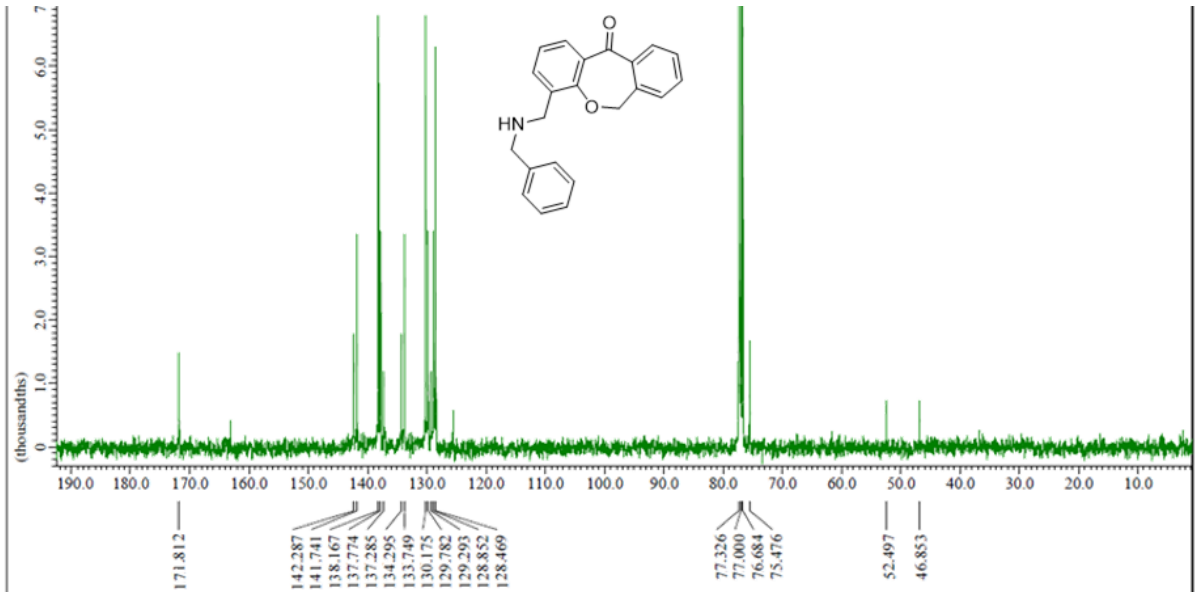
7b


O
HN
Cl
(thousandths)
170.805
153.451
138.061
133.164
130.290
130.079
129.935
128.680
128.277
127.290
124.032
117.353
114.938
114.689
114.440
77.316
77.000
76.684
74.068
55.583
55.410
36.609

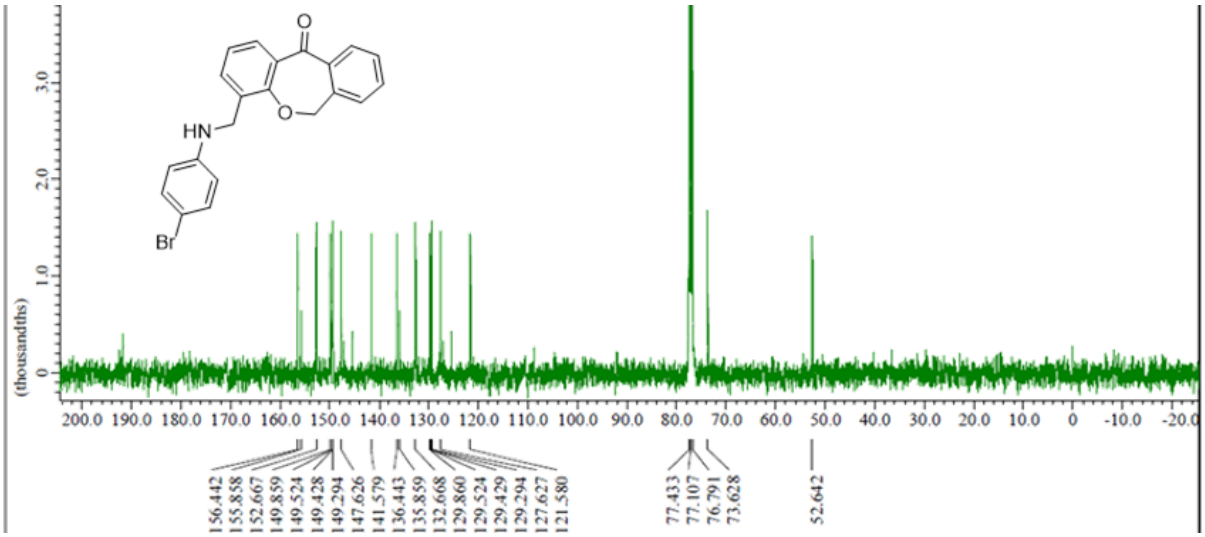
7c


O
HN
F
(thousandths)
170.452
147.454
142.998
133.875
132.869
131.000
129.889
126.554
124.014
122.874
121.868
119.999
77.433
77.116
76.791
72.948
54.999
52.805

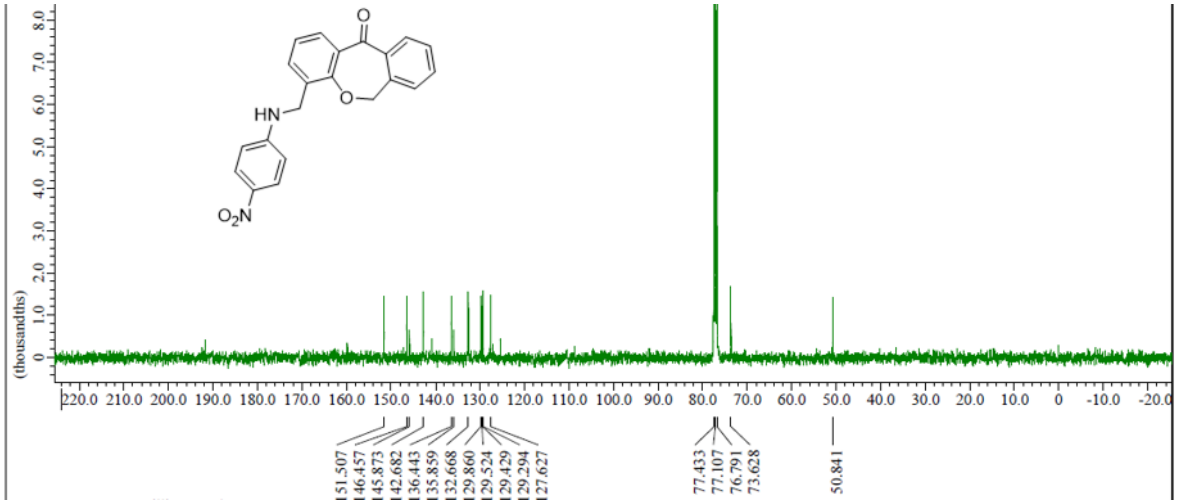
7d


O
HN
O
(thousandths)
171.812
142.287
141.741
138.167
137.774
137.285
134.295
133.749
130.175
129.782
129.293
128.852
128.469
77.326
77.000
76.684
75.476
52.497
46.853

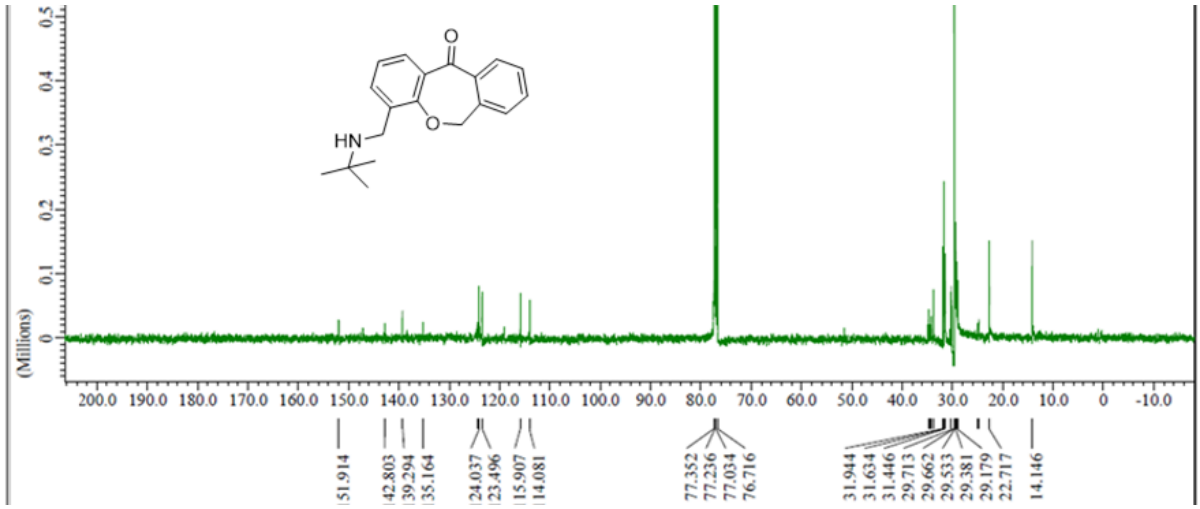
7e


O
HN
O
Br
(thousandths)
156.442
155.858
152.667
149.859
149.524
149.428
149.294
147.626
141.579
136.443
135.859
132.668
129.860
129.524
129.429
129.294
127.627
121.580
77.433
77.107
76.791
73.628
52.642

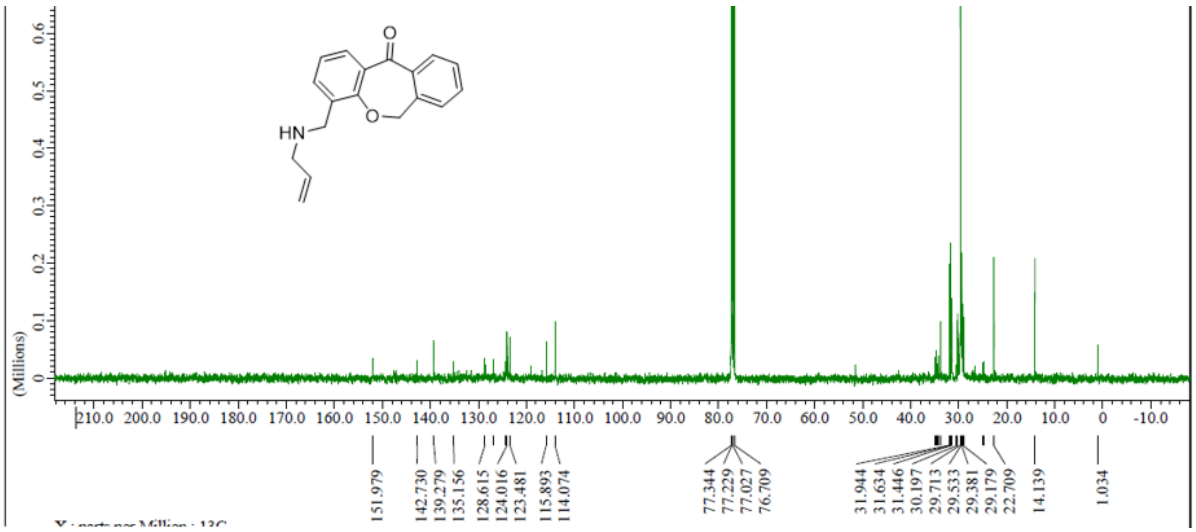
7f


O
HN
O
O2N
(thousandths)
151.507
146.457
145.873
142.682
136.443
135.859
132.668
129.860
129.524
129.429
129.294
127.627
77.433
77.107
76.791
73.628
50.841

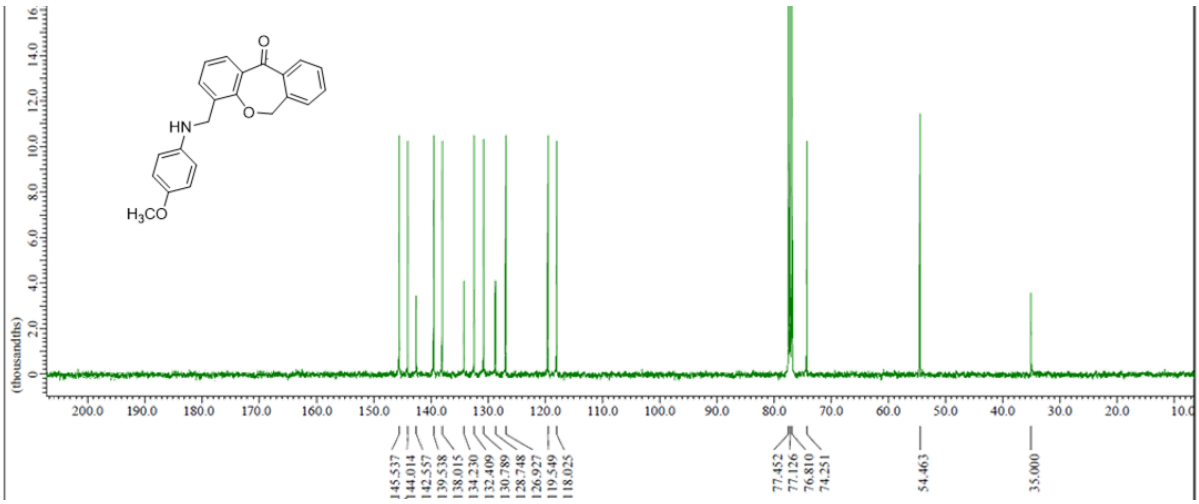
7g


O
HN
(Millions)
51.914
42.803
39.294
35.164
24.037
23.496
15.907
14.081
77.352
77.236
77.034
76.716
31.944
31.634
31.446
29.713
29.662
29.533
29.381
29.179
22.717
14.146

7h


O
HN
(Millions)
151.979
142.730
139.279
135.156
128.615
124.016
123.481
115.893
114.074
77.344
77.229
77.027
76.709
31.944
31.634
31.446
30.197
29.713
29.533
29.381
29.179
22.709
14.139
1.034

7i



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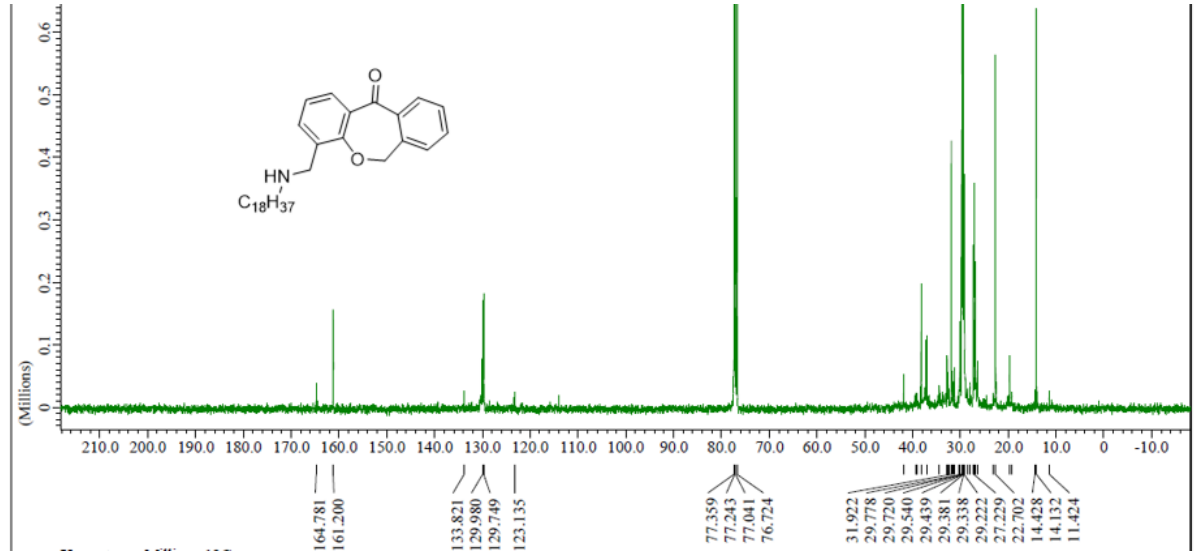
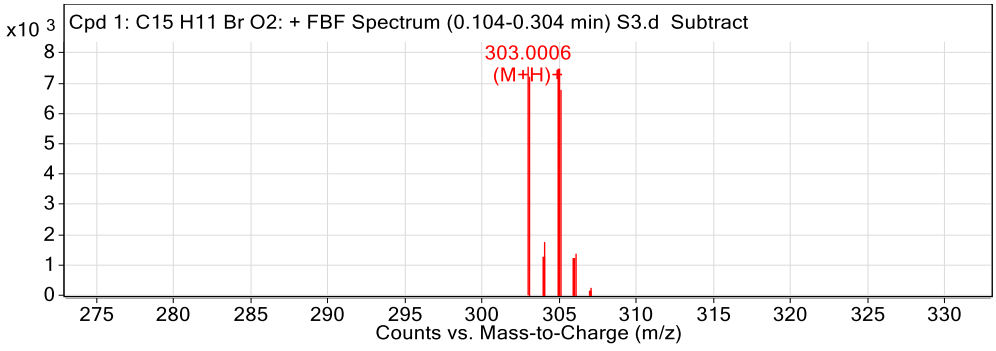


3. High-Resolution Mass Spectra

5



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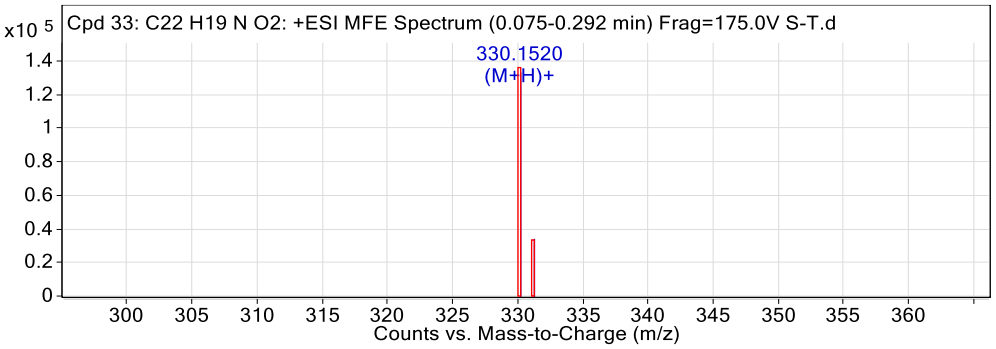
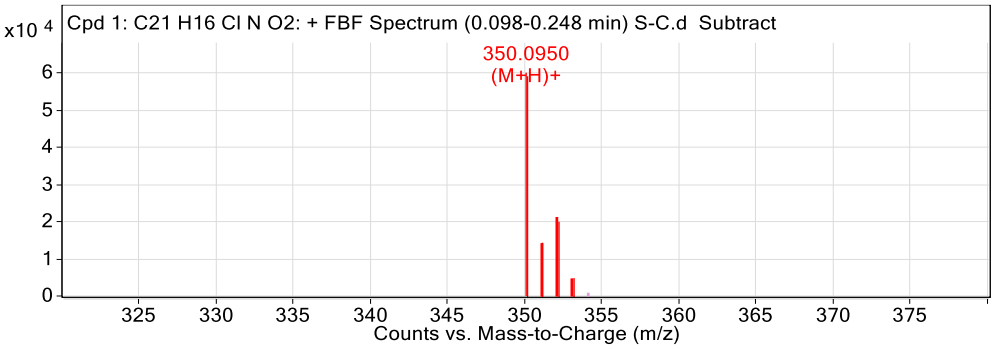
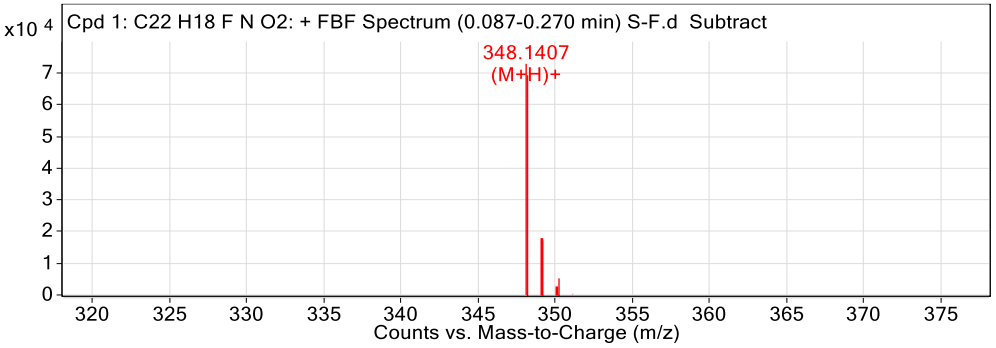

Cpd 33: C22 H19 N O2: +ESI MFE Spectrum (0.075-0.292 min) Frag=175.0V S-T.d
x10 5
330.1520
(M+H)+
Counts vs. Mass-to-Charge (m/z)

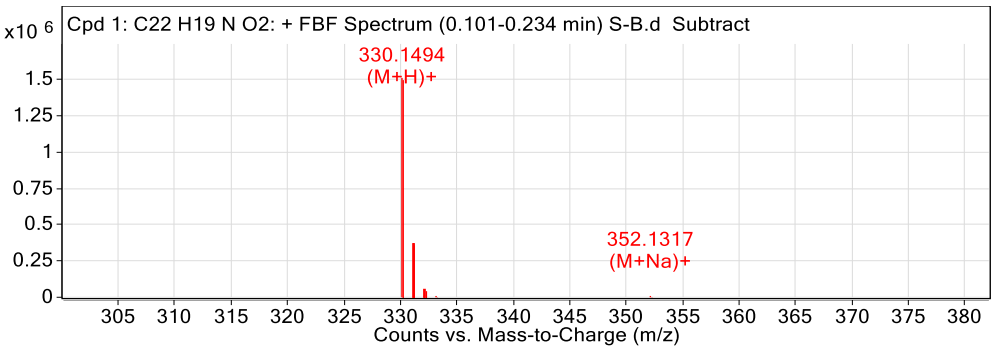
7b


Cpd 1: C21 H16 Cl N O2: + FBF Spectrum (0.098-0.248 min) S-C.d Subtract
x10 4
350.0950
(M+H)+
Counts vs. Mass-to-Charge (m/z)

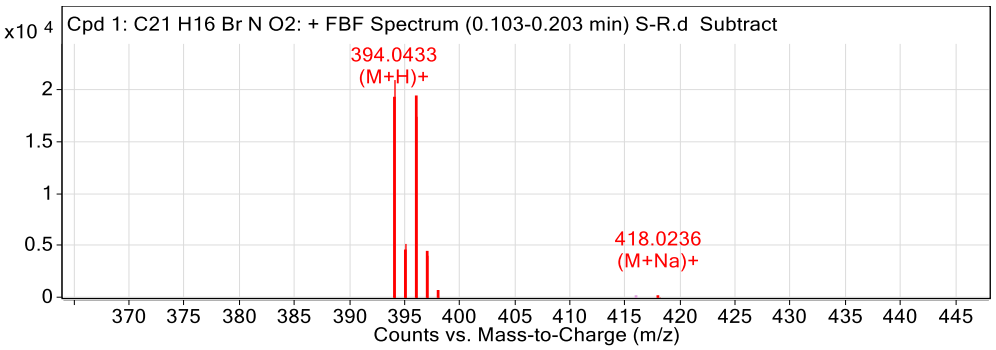
7c


Cpd 1: C22 H18 F N O2: + FBF Spectrum (0.087-0.270 min) S-F.d Subtract
x10 4
348.1407
(M+H)+
Counts vs. Mass-to-Charge (m/z)

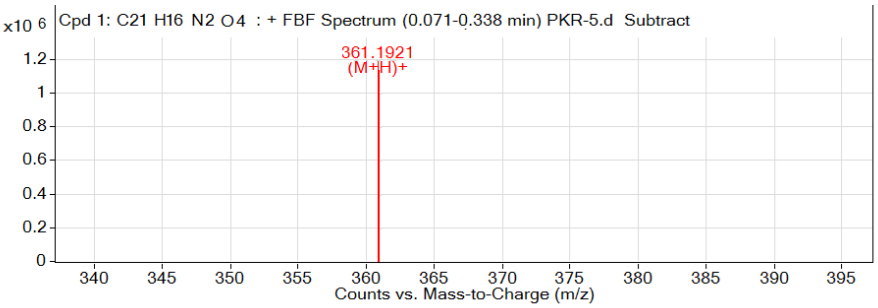
7d


Cpd 1: C22 H19 N O2: + FBF Spectrum (0.101-0.234 min) S-B.d Subtract
x10 6
330.1494
(M+H)+
352.1317
(M+Na)+
Counts vs. Mass-to-Charge (m/z)

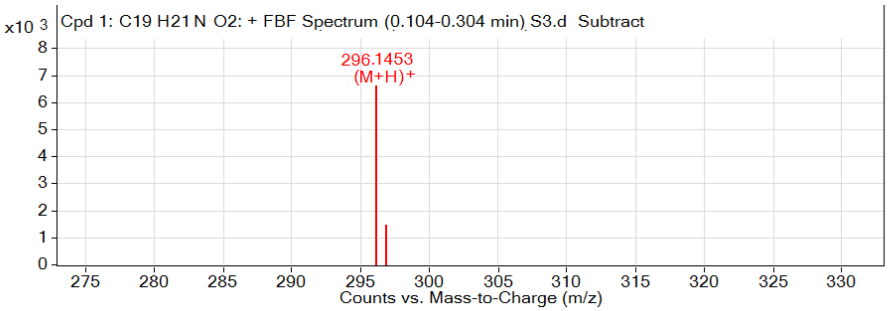
7e


Cpd 1: C21 H16 Br N O2: + FBF Spectrum (0.103-0.203 min) S-R.d Subtract
x10 4
394.0433
(M+H)+
418.0236
(M+Na)+
Counts vs. Mass-to-Charge (m/z)

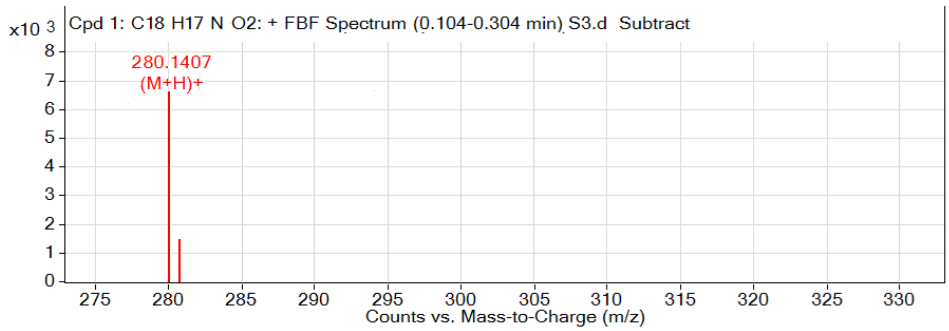
7f


Cpd 1: C21 H16 N2 O4 : + FBF Spectrum (0.071-0.338 min) PKR-5.d Subtract
x10 6
361.1921
(M+H)+
Counts vs. Mass-to-Charge (m/z)

7g


Cpd 1: C19 H21 N O2: + FBF Spectrum (0.104-0.304 min) S3.d Subtract
x10 3
296.1453
(M+H)+
Counts vs. Mass-to-Charge (m/z)

7h



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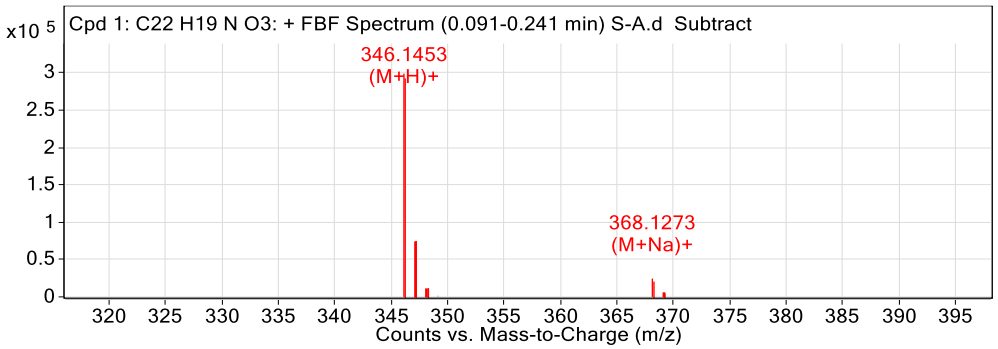
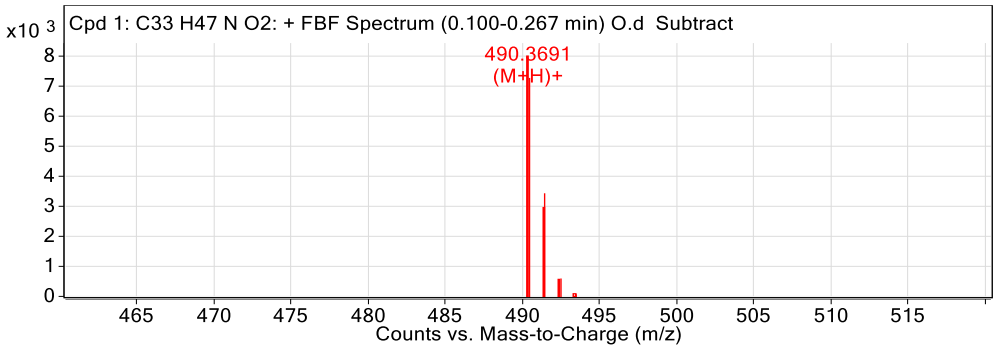


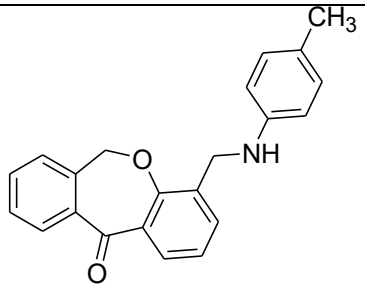
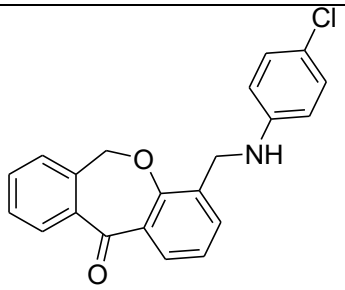
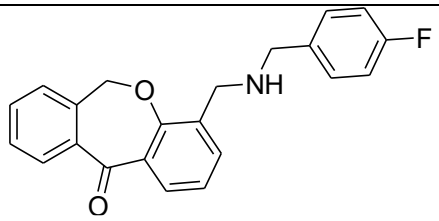
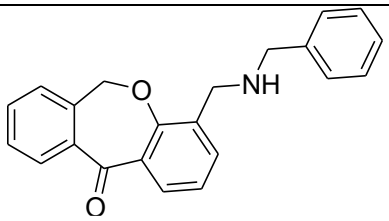
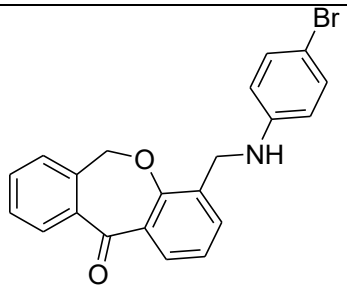
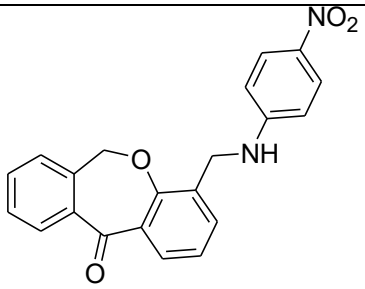
7j

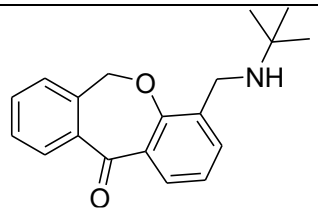
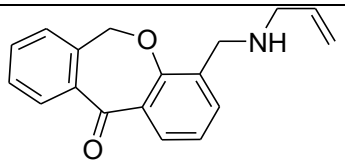
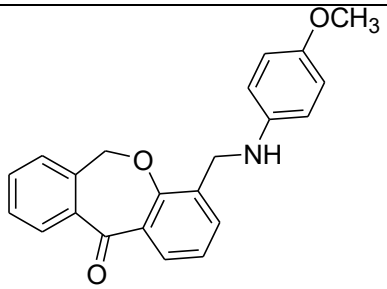
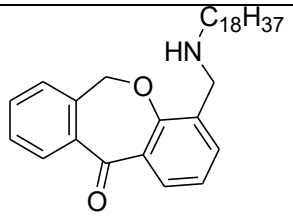


3. **Binding Energy of all compounds with antibacterial, antifungal and ct-DNA activity proteins.**

Table S1. Details of Binding Energy (kcal/mol) and types of interactions between ligands and proteins.

Ligands	Ligand Structure	1KZN	1IYL	1BNA

7a		-9.2	-11.0	-8.1
7b		-9.1	-11.0	-7.8
7c		-8.2	-10.9	-6.8
7d		-8.0	-10.9	-7.0
7e		-7.9	-10.6	-8.3
7f		-7.8	-10.2	-7.7

7g		-7.7	-9.3	-6.8
7h		-7.6	-9.2	-7.2
7i		-7.2	-10.2	-7.4
7j		-6.0	-8.5	-5.3

4. Molecular Docking Images for Antibacterial Activity (PDB ID : 1KZN)

7b

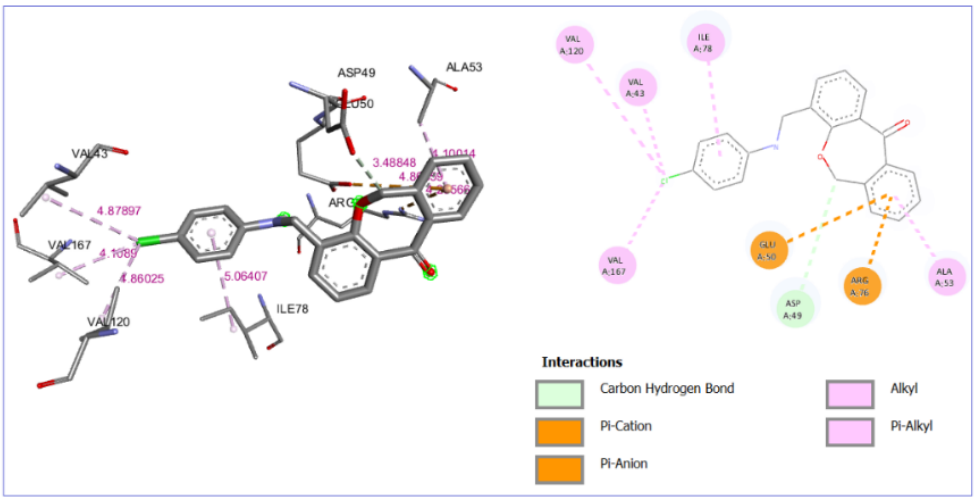


Figure S1. 3D and 2D interaction diagram of compound **7b** with E. Coli bacterial protein.

7c

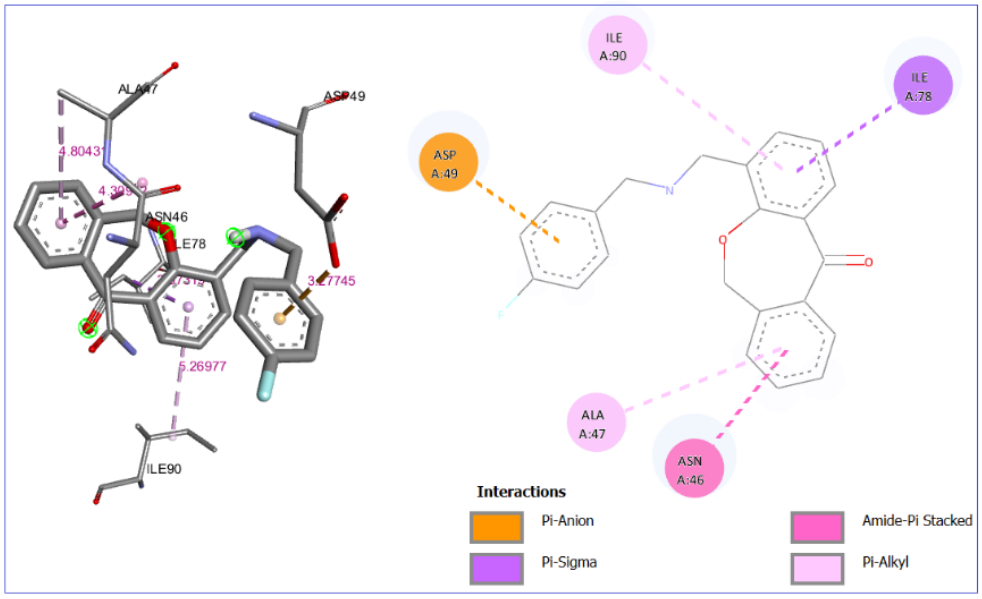


Figure S2. 3D and 2D interaction diagram of compound **7c** with E. Coli bacterial protein.

7d

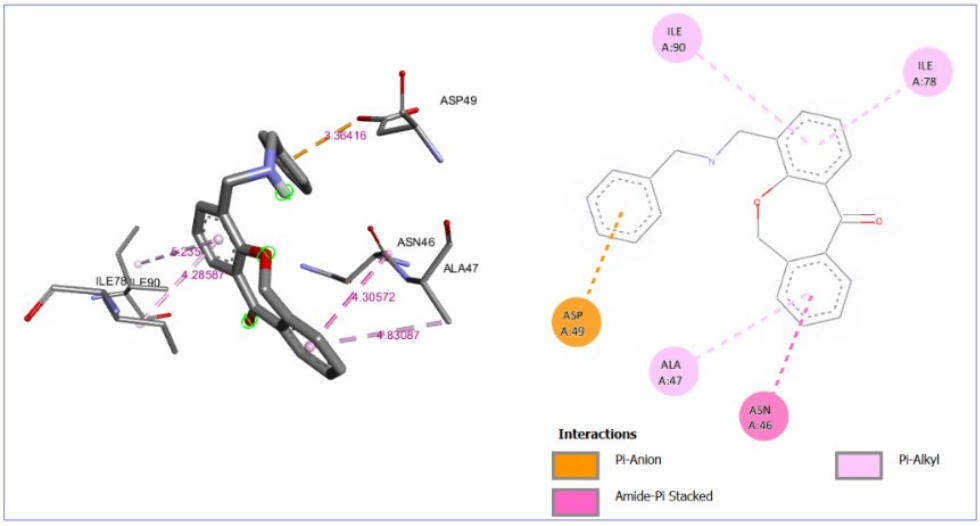


Figure S3. 3D and 2D interaction diagram of compound **7d** with E. Coli bacterial protein.

7e

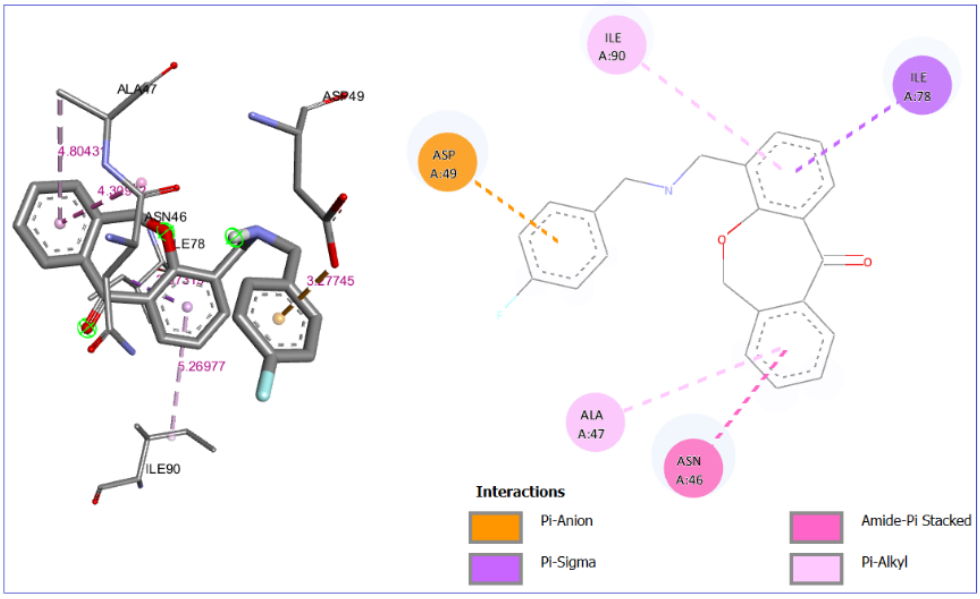


Figure S4. 3D and 2D interaction diagram of compound **7d** with E. Coli bacterial protein.

7f

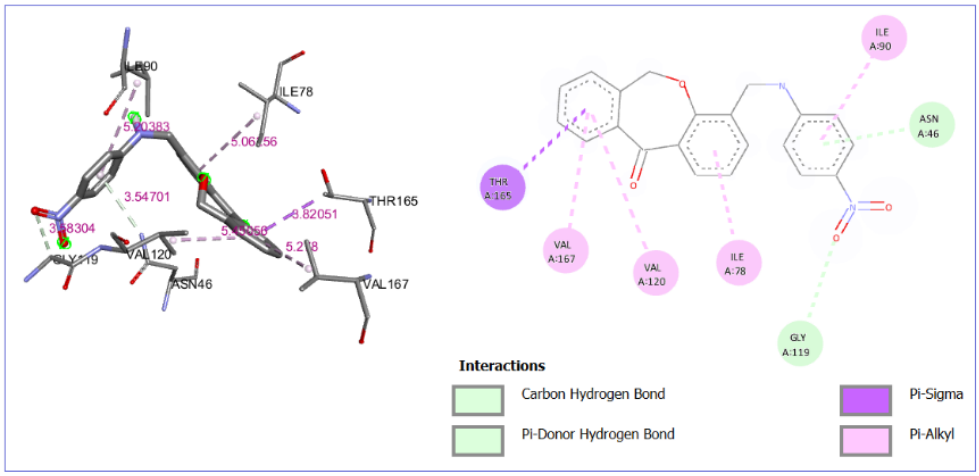


Figure S5. 3D and 2D interaction diagram of compound **7f** with E. Coli bacterial protein.

7g

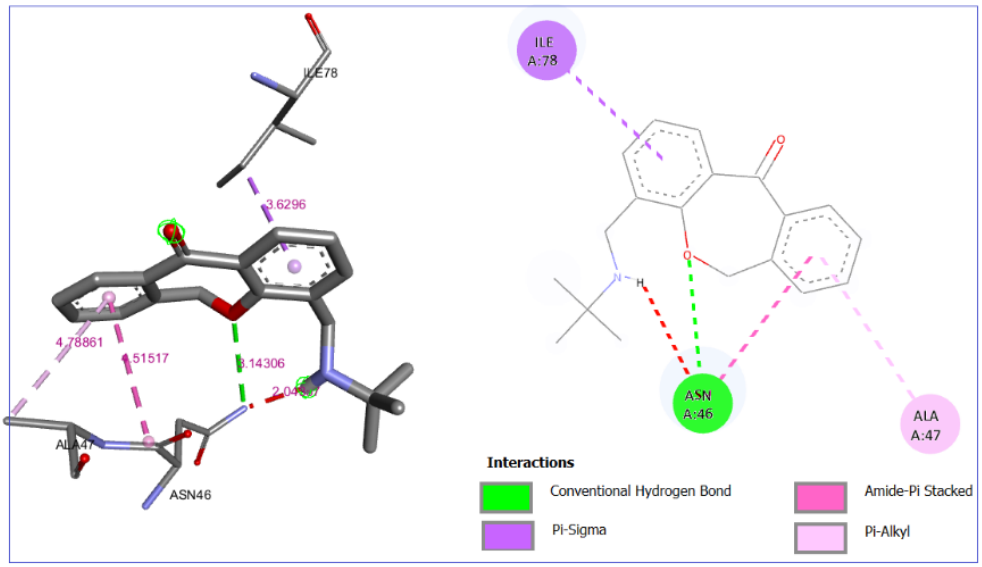


Figure S6. 3D and 2D interaction diagram of compound **7g** with E. Coli bacterial protein.

7h

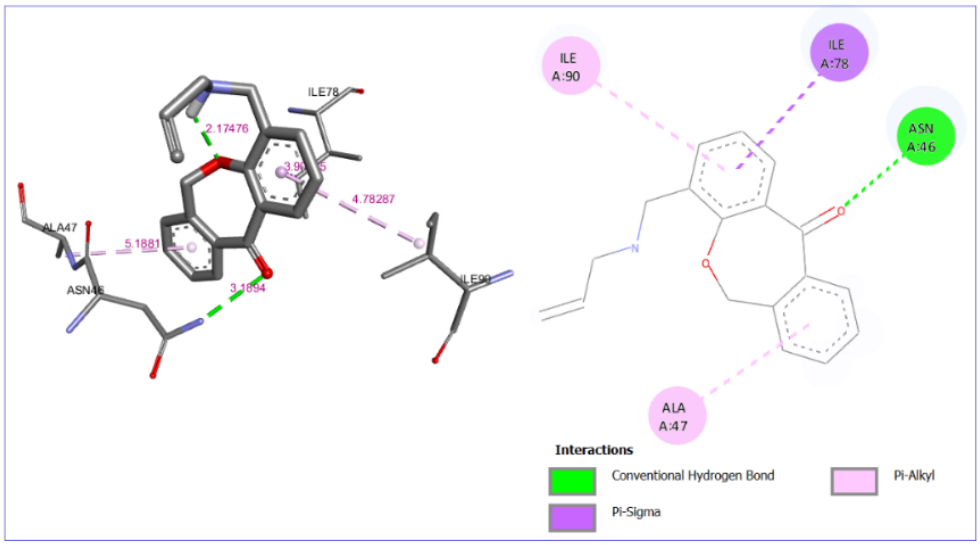


Figure S7. 3D and 2D interaction diagram of compound **7h** with E. Coli bacterial protein.

7i

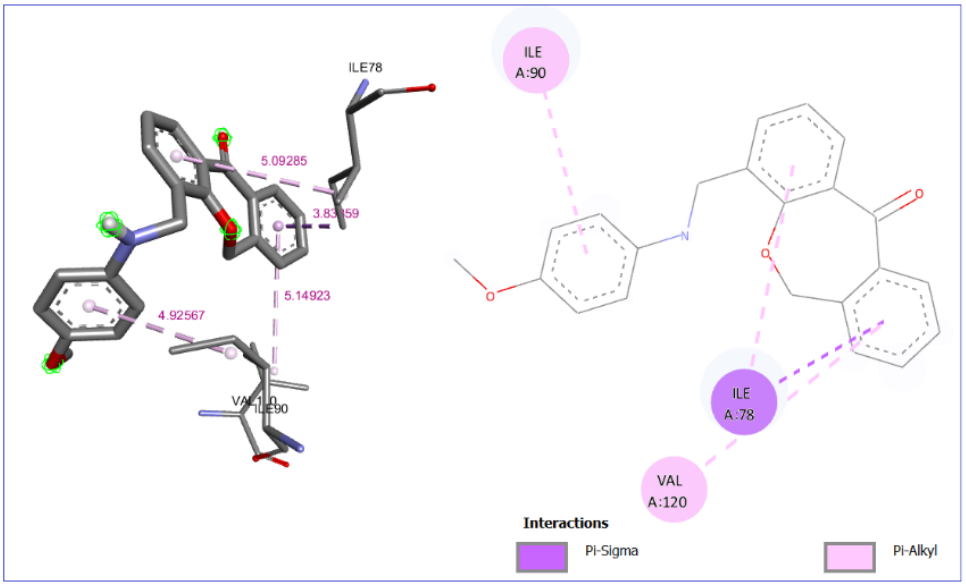


Figure S8. 3D and 2D interaction diagram of compound **7i** with E. Coli bacterial protein.

7j

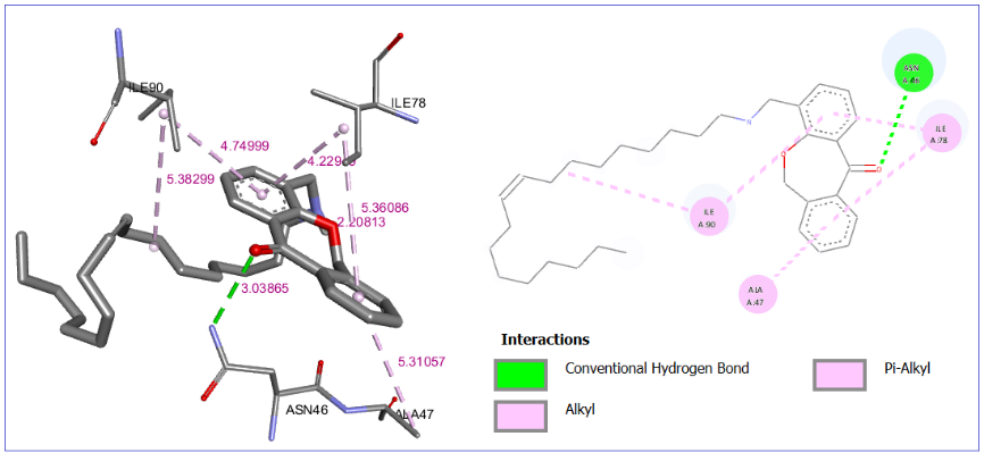


Figure S9. 3D and 2D interaction diagram of compound **7j** with E. Coli bacterial protein.

5. Molecular Docking Images for Antifungal Activity.

7b

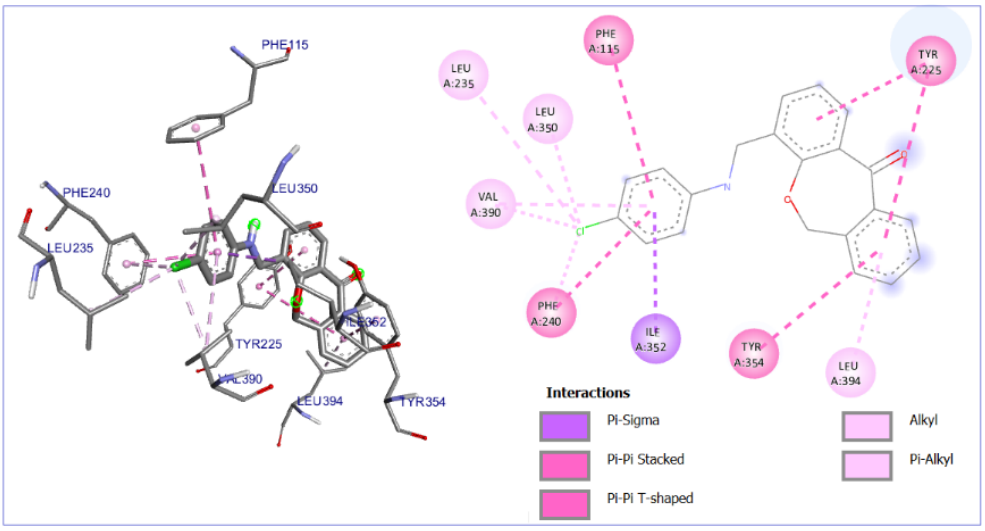


Figure S10. 3D and 2D interaction diagram of compound **7b** with antifungal protein.

7c

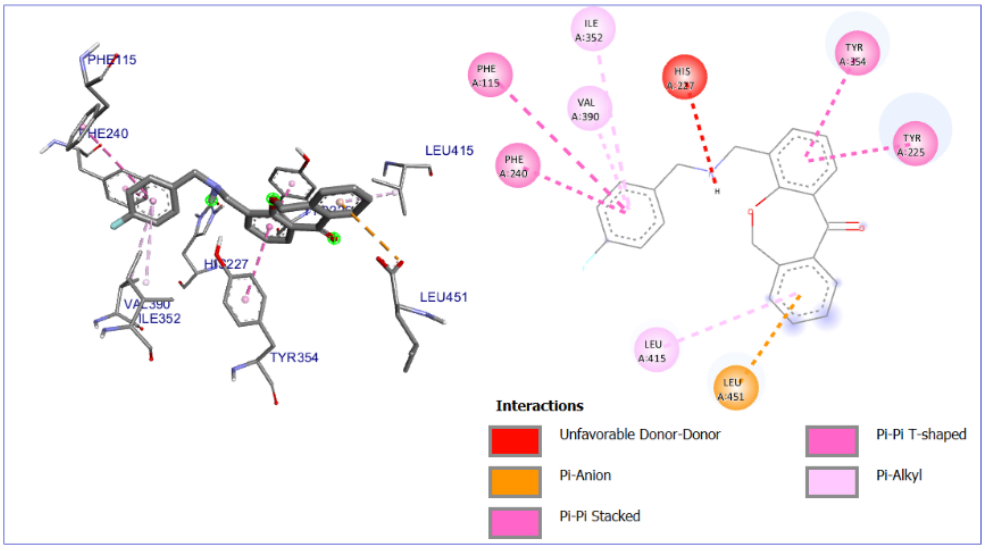


Figure S11. 3D and 2D interaction diagram of compound **7c** with antifungal protein.

7d

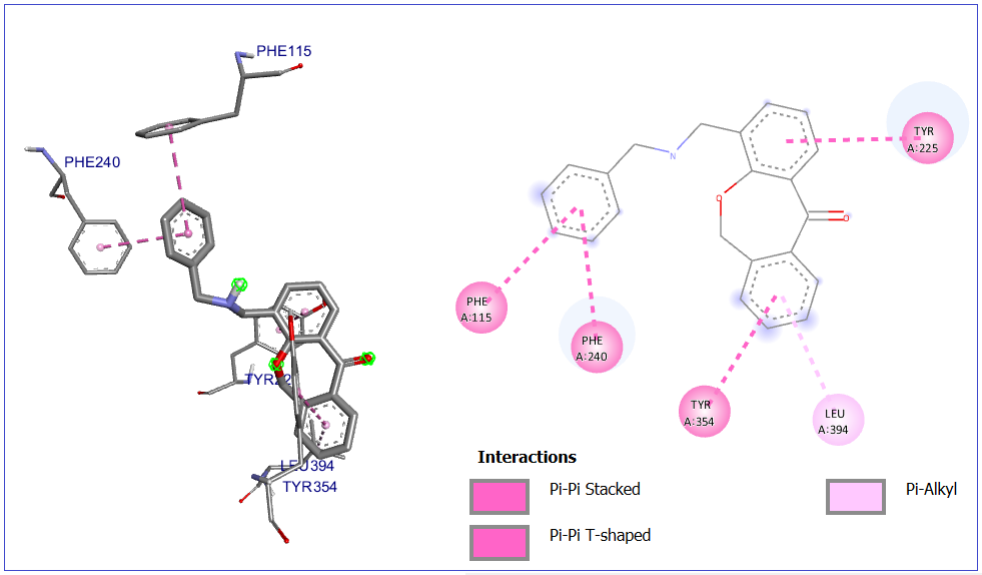


Figure S12. 3D and 2D interaction diagram of compound **7d** with antifungal protein.

7e

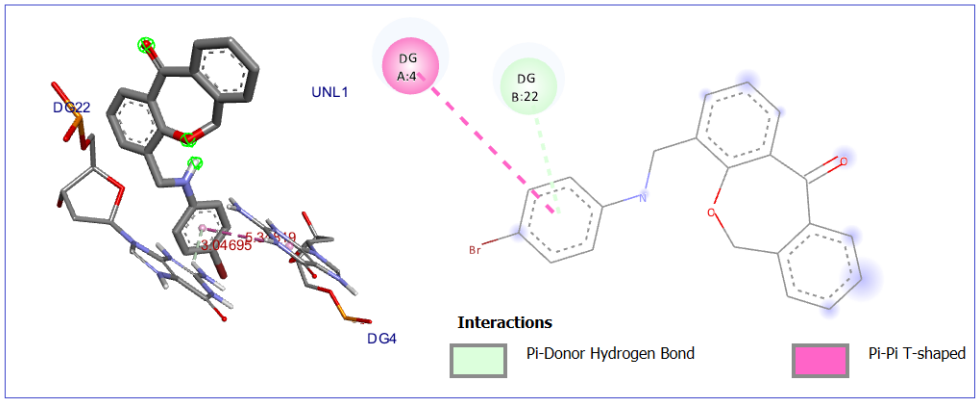


Figure S13. 3D and 2D interaction diagram of compound **7e** with antifungal protein.

7f

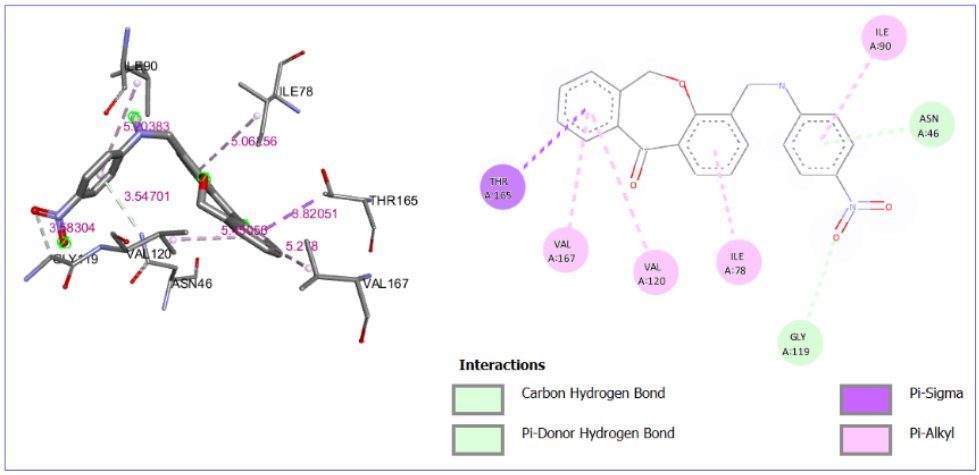


Figure S14. 3D and 2D interaction diagram of compound **7f** with antifungal protein.

7g

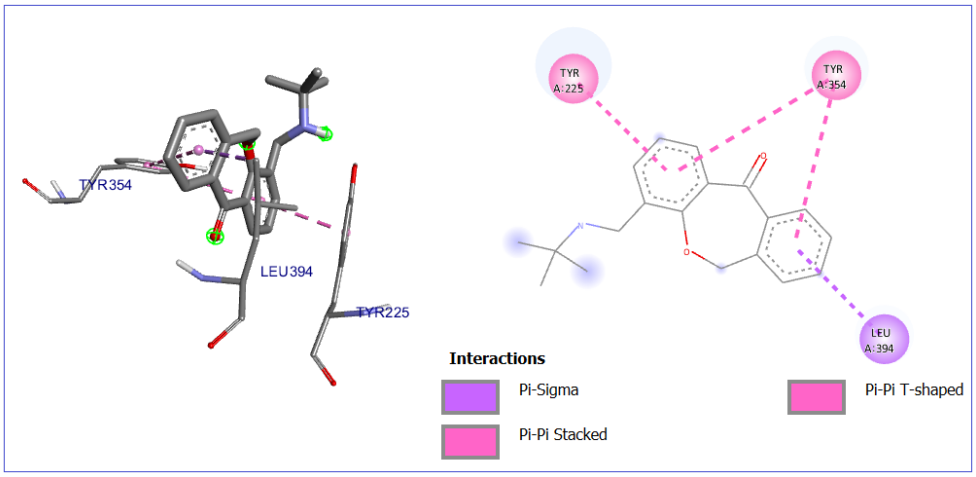


Figure S15. 3D and 2D interaction diagram of compound **7g** with antifungal protein.

7h

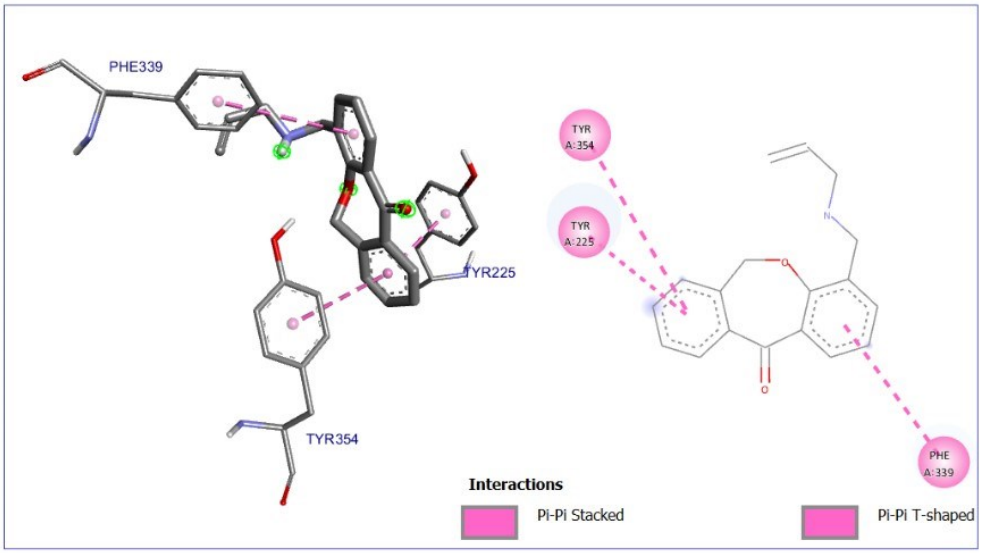


Figure S16. 3D and 2D interaction diagram of compound **7h** with antifungal protein

7i

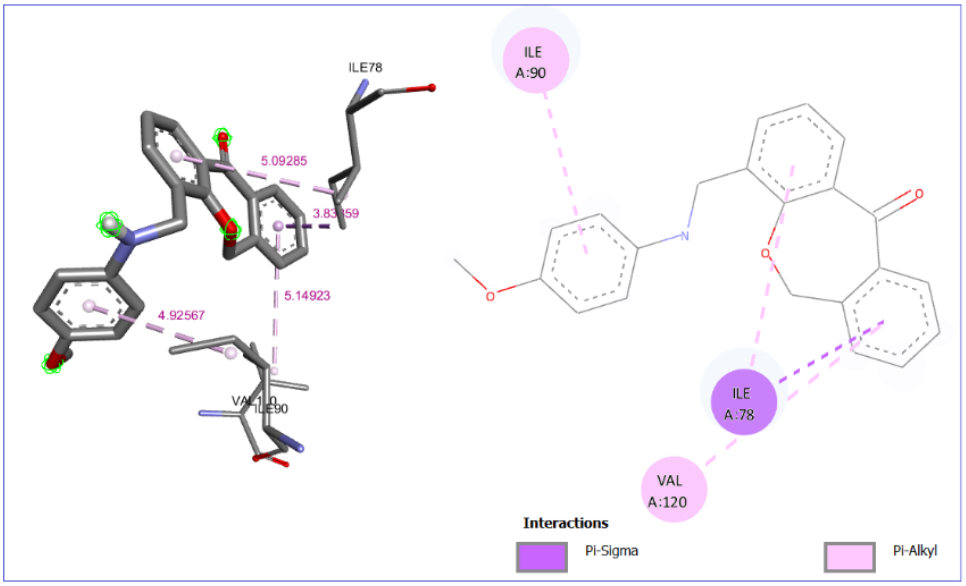


Figure S17. 3D and 2D interaction diagram of compound **7i** with antifungal protein.

7j

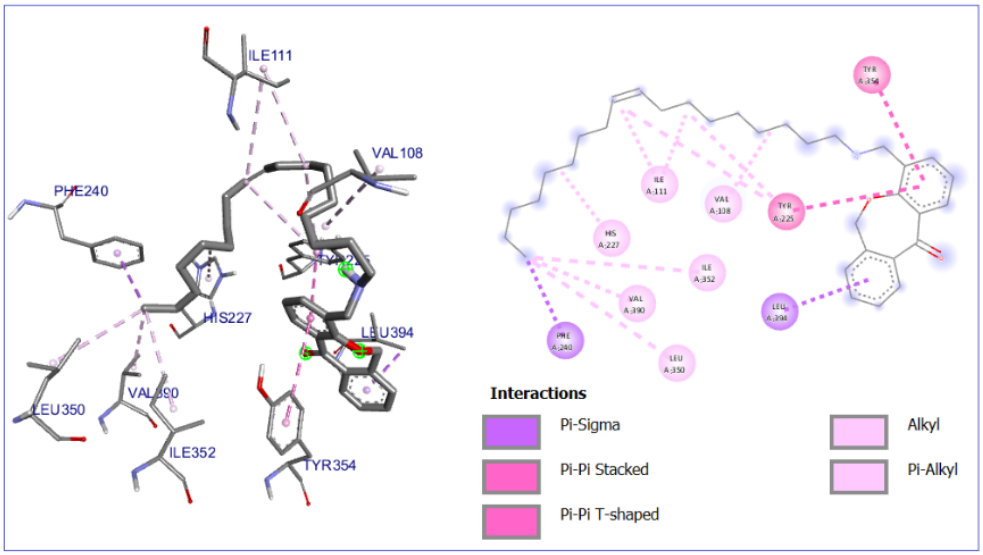


Figure S18. 3D and 2D interaction diagram of compound **7j** with antifungal protein.

6. Molecular Docking Images for ct-DNA activity (PDB ID : 1BNA).

7b

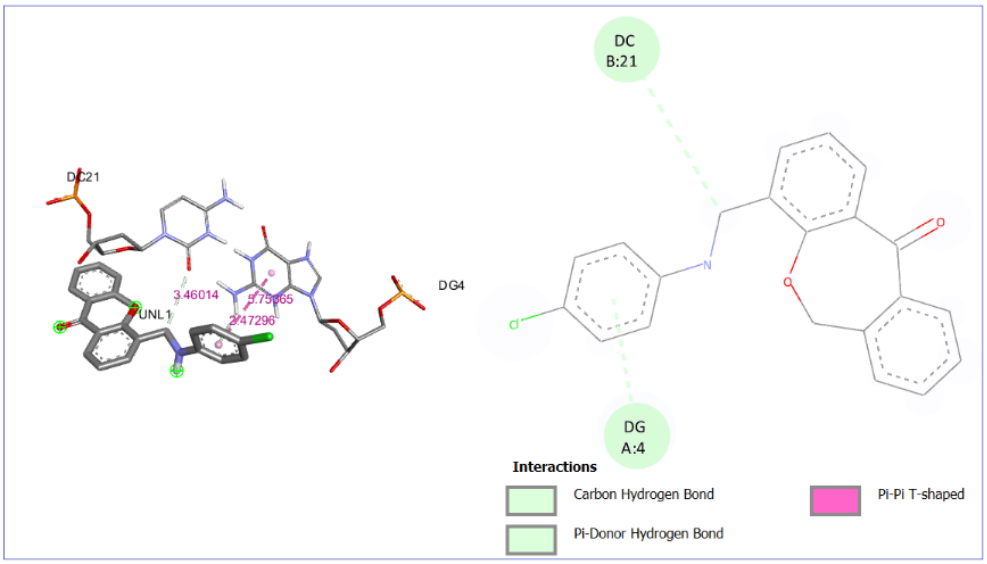


Figure S19. 3D and 2D interaction diagram of compound **7b** with ct-DNA .

7c

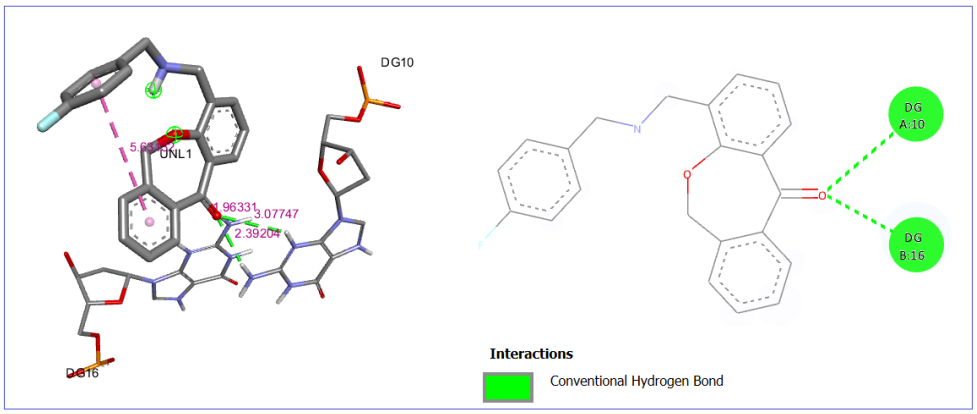


Figure S20. 3D and 2D interaction diagram of compound **7c** with ct-DNA.

7d

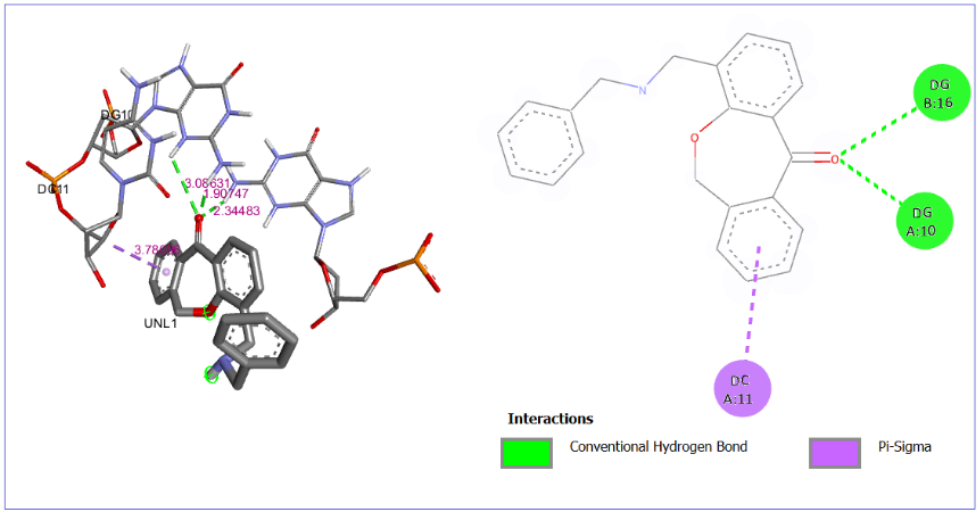


Figure S21. 3D and 2D interaction diagram of compound **7d** with ct-DNA.

7e

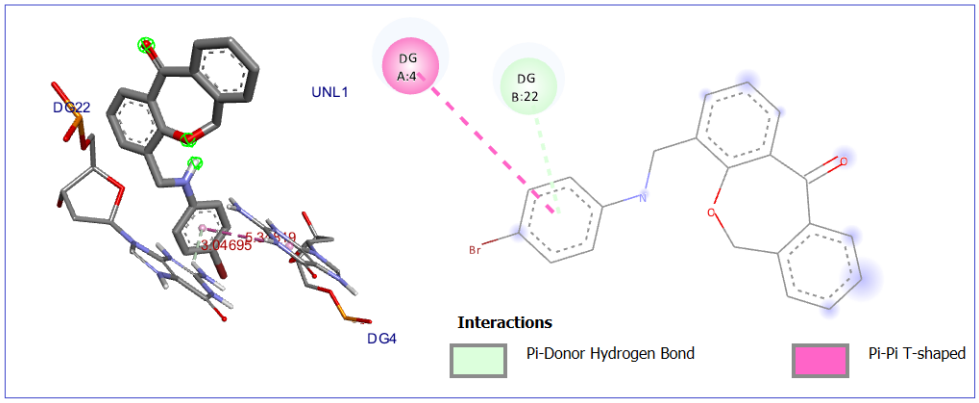


Figure S22. 3D and 2D interaction diagram of compound **7e** with ct-DNA.

7f

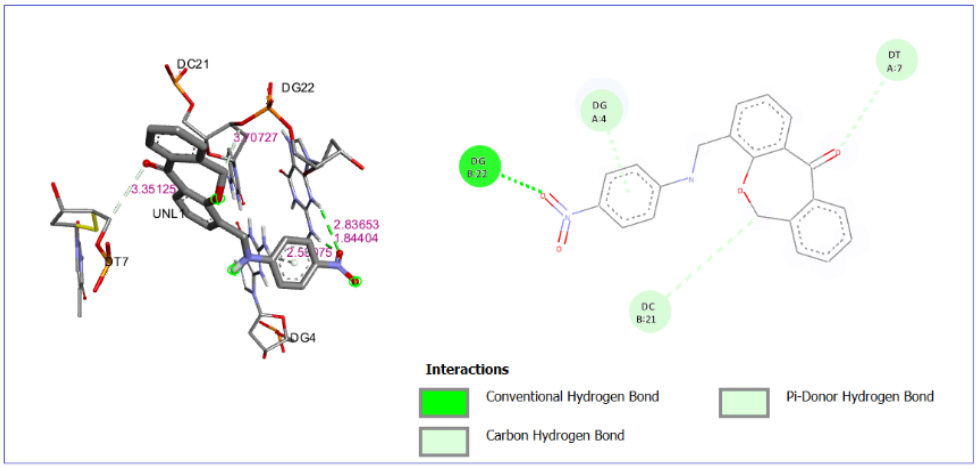


Figure S23. 3D and 2D interaction diagram of compound **7f** with ct-DNA.

7g

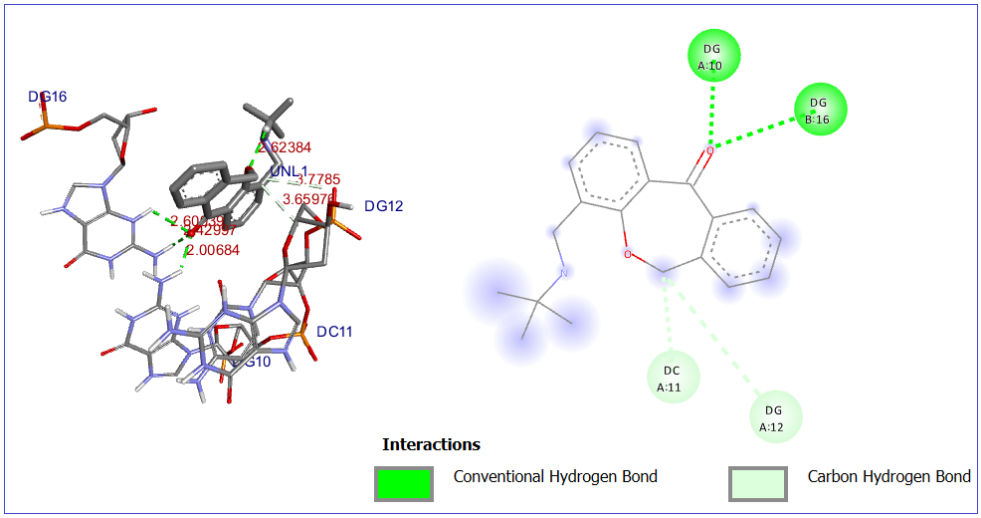


Figure S24. 3D and 2D interaction diagram of compound **7g** with ct-DNA.

7h

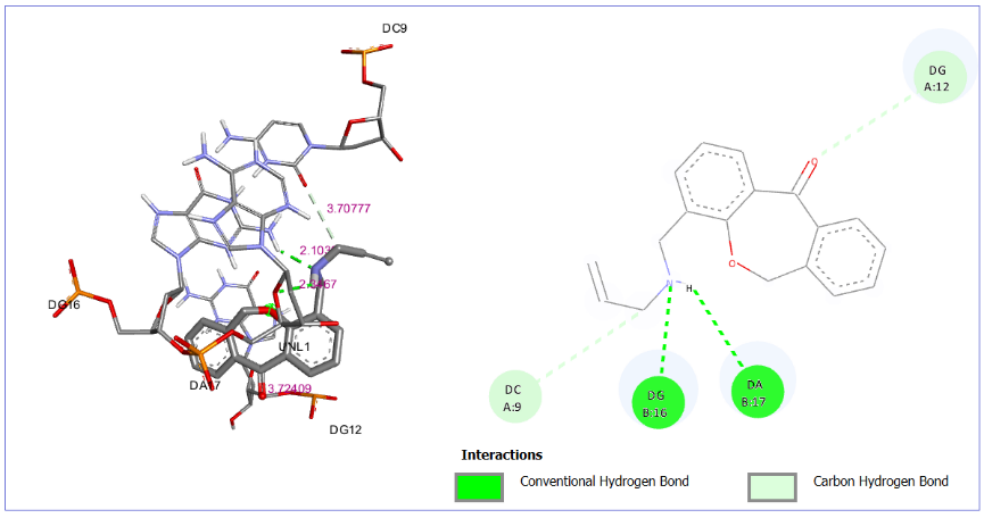


Figure S25. 3D and 2D interaction diagram of compound **7h** with ct-DNA.

7i

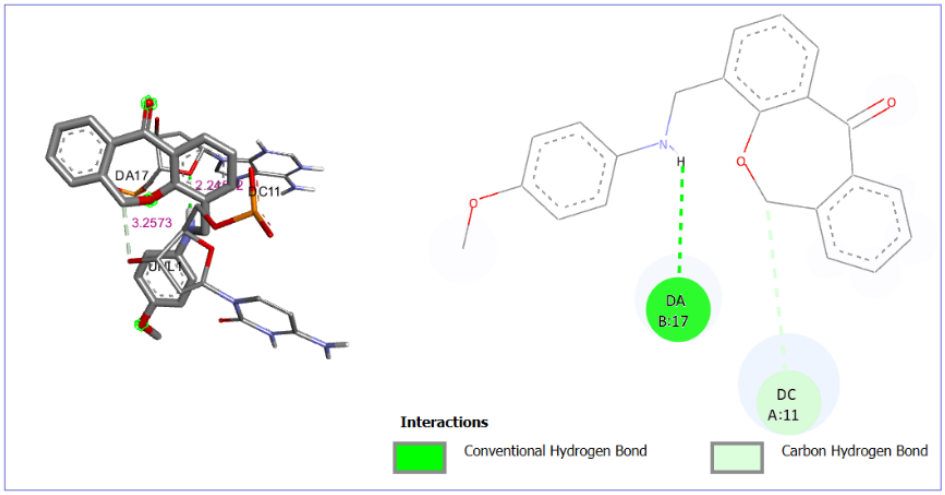


Figure S26. 3D and 2D interaction diagram of compound **7i** with ct-DNA.

7j

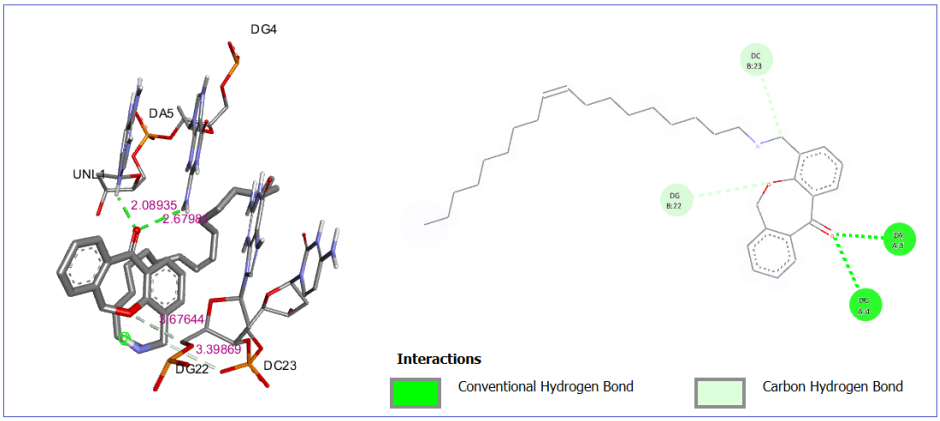


Figure S27. 3D and 2D interaction diagram of compound **7j** with ct-DNA.

8. Physicochemical Properties Values

Table S2. ADME and Physicochemical parameters

Ligands	Log P	TPSA	nOH	nOHNH	Nvio.	Nrot	BBB	Caco2	HIA	MDCK	SP	PPB
7a	4.84	38.33	3	1	0	3	2.06	52.04	96.73	1.34	-2.54	97.34
7b	5.07	38.33	3	1	1	3	2.34	42.67	96.92	0.96	-2.66	100
7c	4.26	38.33	3	1	0	4	0.504	51.66	96.56	0.096	-2.94	96.24
7d	4.09	38.33	3	1	0	4	0.37	53.35	96.56	0.77	-2.64	87.79
7e	5.20	38.33	3	1	1	3	2.59	42.67	97.03	0.03	-2.54	100

7f	4.35	38.33	6	1	0	4	0.02	8.98	97.03	0.18	-2.68	98.99
7g	3.88	38.33	3	1	0	3	0.53	48.31	95.94	3.66	-2.37	84.67
7h	3.34	38.33	3	1	0	4	0.86	47.51	95.99	26.63	-2.89	84.47
7i	4.45	38.33	4	1	0	4	0.39	49.63	96.34	0.86	-2.78	97.39
7j	9.31	38.33	3	1	1	18	16.48	52.18	97.05	65.00	-1.03	97.92

Table S3. Bioactivity Score Parameters

Ligand	**GPCR Ligand**	**Ion channel modulator**	**Kinase Inhibitor**	**Nuclear Receptor Ligand**	**Protease Inhibitor**	**Enzyme Inhibitor**
7a	0.08	-0.31	0.08	0.11	-0.09	0.06
7b	0.12	-0.25	0.10	0.12	-0.07	0.08
7c	0.14	-0.24	0.06	0.15	0.00	0.10
7d	0.14	-0.24	0.04	0.14	0.03	0.12
7e	0.02	-0.32	0.07	0.03	-0.14	0.04
7f	-0.02	-0.27	-0.04	0.04	-0.15	0.01
7g	0.19	-0.33	0.01	0.07	0.09	0.06
7h	0.11	-0.26	-0.12	0.00	-0.09	0.09
7i	0.08	-0.28	0.09	0.10	-0.06	0.07
7j	0.21	-0.14	0.00	0.13	0.10	0.16

9. DFT coordinates of UV-vis

1	6	0	-3.868148	0.044386	0.462946
2	6	0	-3.721170	-0.954560	-0.513745

3	6	0	-2.746574	-0.757355	-1.638711
4	6	0	-1.683788	1.446192	-0.027148
5	6	0	-0.911435	0.458312	-0.678388
6	1	0	-2.958009	0.166744	-2.193748
7	1	0	-2.787774	-1.596340	-2.337291
8	8	0	-1.391547	-0.720546	-1.176838
9	6	0	0.476268	0.629547	-0.881557
10	6	0	1.074854	1.815273	-0.476404
11	6	0	0.321445	2.833585	0.120708
12	6	0	-1.029568	2.643699	0.341158
13	6	0	-4.505831	-2.108320	-0.444249
14	6	0	-5.430299	-2.280422	0.585604
15	6	0	-5.581430	-1.286826	1.554594
16	6	0	-4.812261	-0.128875	1.485389
17	1	0	-4.394078	-2.874489	-1.206893
18	1	0	-6.030155	-3.184572	0.629951
19	1	0	-6.299389	-1.413049	2.359288
20	1	0	-4.926854	0.664501	2.215490
21	1	0	-1.631062	3.397881	0.834634
22	1	0	0.800573	3.758638	0.425180
23	1	0	2.139596	1.946250	-0.638216
24	6	0	1.251340	-0.483467	-1.585892
25	1	0	1.111637	-1.424407	-1.041841
26	1	0	0.797253	-0.659530	-2.567547
27	7	0	2.664804	-0.262857	-1.783665
28	1	0	2.922028	0.307948	-2.574188
29	6	0	3.632634	-0.387517	-0.790982
30	6	0	3.344418	-0.866236	0.498244
31	6	0	4.968999	-0.050415	-1.084455
32	6	0	4.363761	-1.013642	1.439470

33	1	0	2.325352	-1.107582	0.779042
34	6	0	5.967766	-0.197114	-0.130336
35	1	0	5.218314	0.323503	-2.075304
36	6	0	5.692870	-0.688216	1.154620
37	1	0	4.107277	-1.384255	2.429293
38	1	0	6.987822	0.075321	-0.392208
39	6	0	-3.103879	1.338150	0.458031
40	8	0	-3.637821	2.318535	0.970565
41	6	0	6.790934	-0.869738	2.175927
42	1	0	6.381506	-0.983637	3.184108
43	1	0	7.396576	-1.761190	1.967767
44	1	0	7.475266	-0.014307	2.189398

10. DFT coordinates of FTIR

1	6	0	-3.868148	0.044386	0.462946
2	6	0	-3.721170	-0.954560	-0.513745
3	6	0	-2.746574	-0.757355	-1.638711
4	6	0	-1.683788	1.446192	-0.027148
5	6	0	-0.911435	0.458312	-0.678388
6	1	0	-2.958009	0.166744	-2.193748
7	1	0	-2.787774	-1.596340	-2.337291
8	8	0	-1.391547	-0.720546	-1.176838
9	6	0	0.476268	0.629547	-0.881557
10	6	0	1.074854	1.815273	-0.476404
11	6	0	0.321445	2.833585	0.120708
12	6	0	-1.029568	2.643699	0.341158
13	6	0	-4.505831	-2.108320	-0.444249
14	6	0	-5.430299	-2.280422	0.585604
15	6	0	-5.581430	-1.286826	1.554594
16	6	0	-4.812261	-0.128875	1.485389
17	1	0	-4.394078	-2.874489	-1.206893
18	1	0	-6.030155	-3.184572	0.629951
19	1	0	-6.299389	-1.413049	2.359288

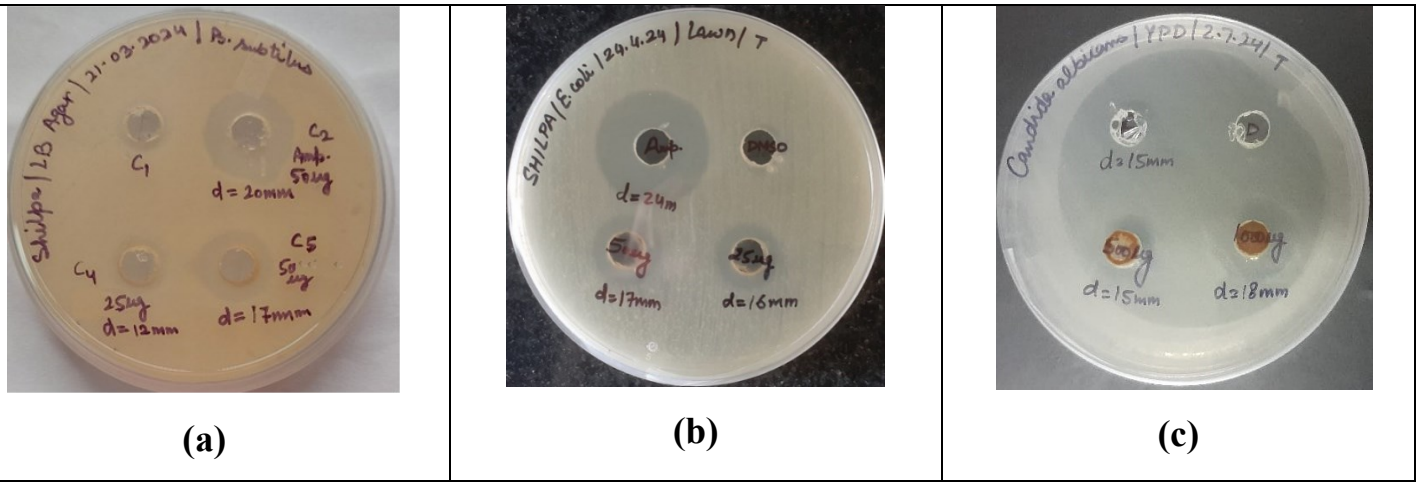
20	1	0	-4.926854	0.664501	2.215490
21	1	0	-1.631062	3.397881	0.834634
22	1	0	0.800573	3.758638	0.425180
23	1	0	2.139596	1.946250	-0.638216
24	6	0	1.251340	-0.483467	-1.585892
25	1	0	1.111637	-1.424407	-1.041841
26	1	0	0.797253	-0.659530	-2.567547
27	7	0	2.664804	-0.262857	-1.783665
28	1	0	2.922028	0.307948	-2.574188
29	6	0	3.632634	-0.387517	-0.790982
30	6	0	3.344418	-0.866236	0.498244
31	6	0	4.968999	-0.050415	-1.084455
32	6	0	4.363761	-1.013642	1.439470
33	1	0	2.325352	-1.107582	0.779042
34	6	0	5.967766	-0.197114	-0.130336
35	1	0	5.218314	0.323503	-2.075304
36	6	0	5.692870	-0.688216	1.154620
37	1	0	4.107277	-1.384255	2.429293
38	1	0	6.987822	0.075321	-0.392208
39	6	0	-3.103879	1.338150	0.458031
40	8	0	-3.637821	2.318535	0.970565
41	6	0	6.790934	-0.869738	2.175927
42	1	0	6.381506	-0.983637	3.184108
43	1	0	7.396576	-1.761190	1.967767
44	1	0	7.475266	-0.014307	2.189398

11. DFT coordinates of ESP

1	6	0	-3.451329	0.434352	0.392740
2	6	0	-3.363411	-0.976164	0.200582
3	6	0	-2.125794	-1.753149	-0.307919
4	6	0	-1.010988	1.173078	-0.627811
5	6	0	-0.426268	-0.094398	-0.614999
6	1	0	-2.112775	-1.781649	-1.377460

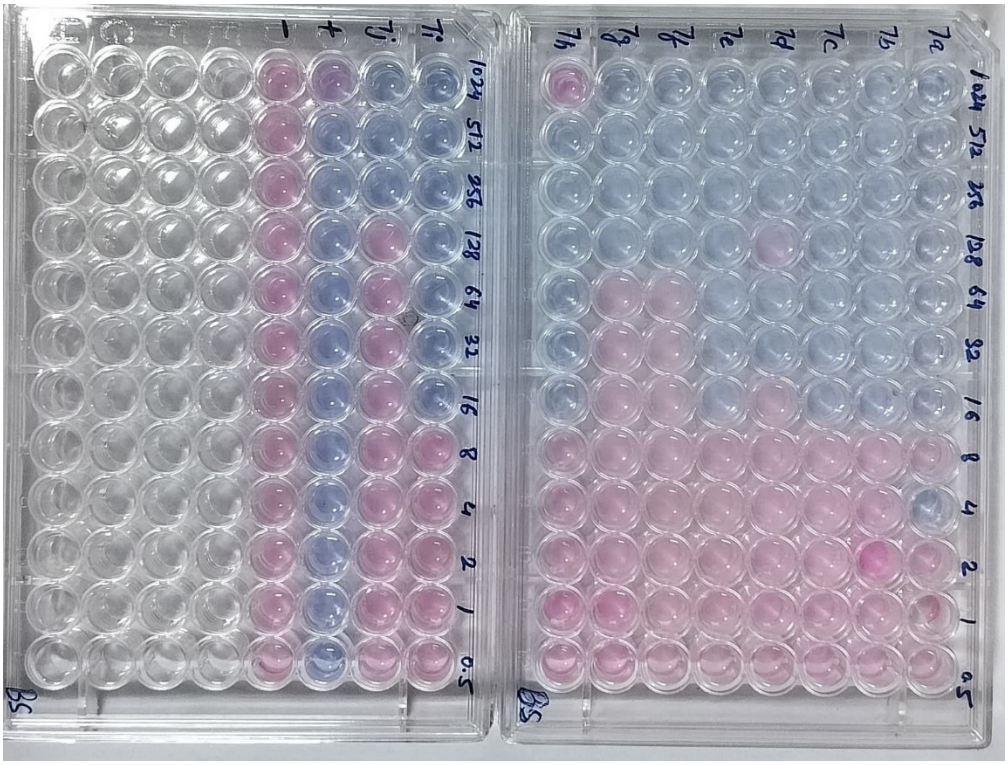
7	1	0	-2.190740	-2.748873	0.078366
8	8	0	-0.926811	-1.168970	0.172374
9	6	0	0.723181	-0.336128	-1.383522
10	6	0	1.355411	0.711065	-2.061201
11	6	0	0.841161	2.005757	-1.969023
12	6	0	-0.338745	2.235182	-1.253489
13	6	0	-4.482600	-1.772853	0.499289
14	6	0	-5.644325	-1.215328	1.037835
15	6	0	-5.706322	0.152835	1.286329
16	6	0	-4.619338	0.968724	0.964587
17	1	0	-4.441810	-2.826148	0.315424
18	1	0	-6.484407	-1.839212	1.261290
19	1	0	-6.586355	0.579242	1.720633
20	1	0	-4.678531	2.020503	1.152091
21	1	0	-0.737160	3.226246	-1.190582
22	1	0	1.345293	2.819007	-2.447955
23	1	0	2.232584	0.521688	-2.643956
24	6	0	1.299303	-1.761644	-1.470644
25	1	0	1.135459	-2.157244	-0.794880
26	1	0	0.858543	-2.274405	-2.299924
27	7	0	2.755828	-1.691000	-1.656227
28	1	0	2.709607	-1.181239	-2.515301
29	6	0	3.361357	-0.986548	-0.516936
30	6	0	3.775818	-1.706226	0.611872
31	6	0	3.524166	0.404708	-0.559621
32	6	0	4.353088	-1.034648	1.697995
33	1	0	3.651509	-2.768481	0.644463
34	6	0	4.101432	1.076286	0.526505
35	1	0	3.207716	0.954198	-1.421491
36	6	0	4.515888	0.356609	1.655315

37	1	0	4.669538	-1.584138	2.559866
38	1	0	4.225737	2.138542	0.493916
39	6	0	-2.377956	1.482156	0.002371
40	8	0	-2.661984	2.693063	0.193694
41	6	0	5.150246	1.094607	2.848859
42	1	0	5.844377	0.445996	3.341186
43	1	0	5.663227	1.965563	2.497879
44	1	0	4.383890	1.385029	3.53679

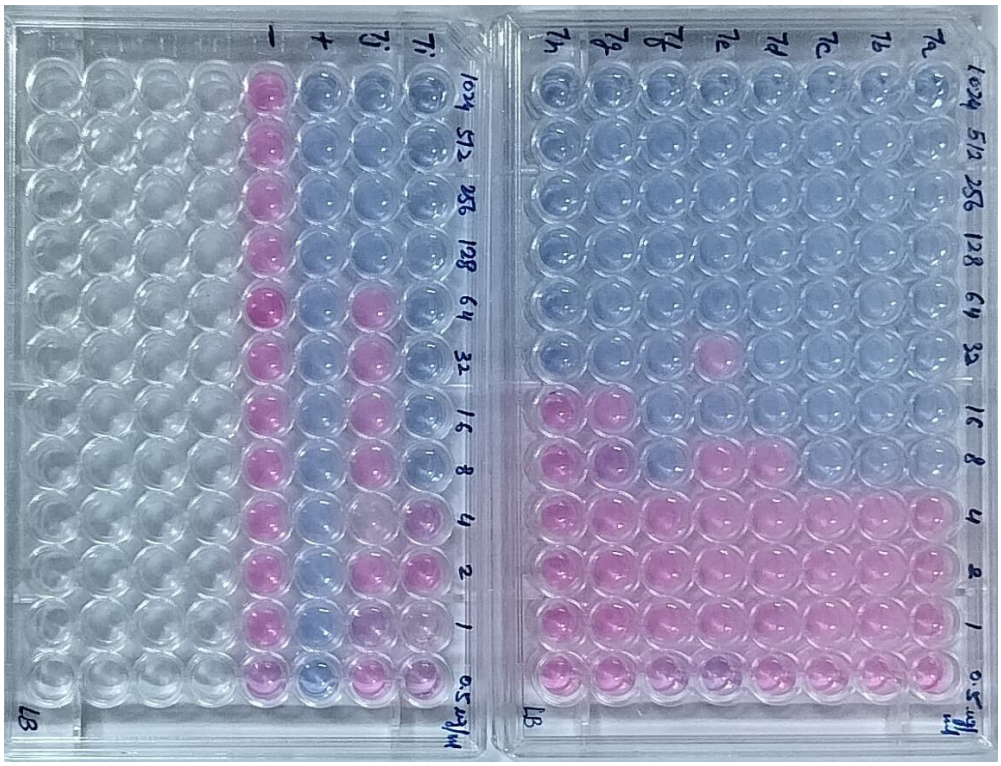


(a) **(b)** **(c)**

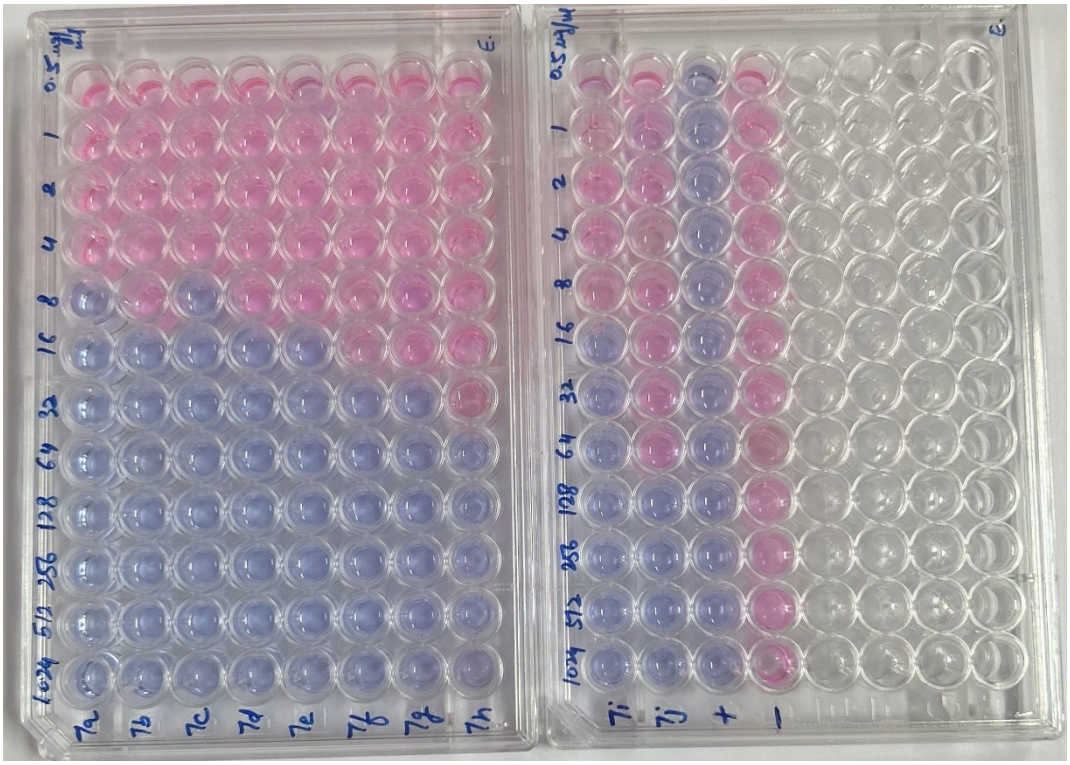
Figure S28. Antimicrobial activity of compound 7a against (a) Gram-positive *B. subtilis*: Pure DMSO (C1), Positive Control (C2), Conc. of 7a (C4) 25 µg, (C5) 50 µg, loaded onto 7-mm wells on agar plates, incubated at 37 ℃ for 24 h. (b) Gram-negative *E. coli*: concentrations of 7a as 25 µg and 50 µg, Positive control (Amp) loaded onto 7-mm wells on agar plates, incubated overnight at 37 ℃. (c) *C. albicans*: concentrations 25 µg and 50 µg of 7a, positive control (Fluconazole) loaded onto 7-mm wells on agar plates, incubated at 30 ℃ for 16-20 h.



(a) *B. subtilis* gram-positive antibacterial strain



(b) *Lb. rhamnosus* gram-positive antibacterial strain



(c) *E.coli* gram-negative antibacterial strain

Figure S28. Minimum Inhibitory Concentration (MIC) values of compounds 7(a-j) against tested bacterial strains **a**(*LB. rhamnosus*), **b**(*B. subtilis*), **c**(E. coli). MIC values were determined using the broth microdilution method, with results expressed in µg/mL. Lower MIC values indicate higher antibacterial potency.