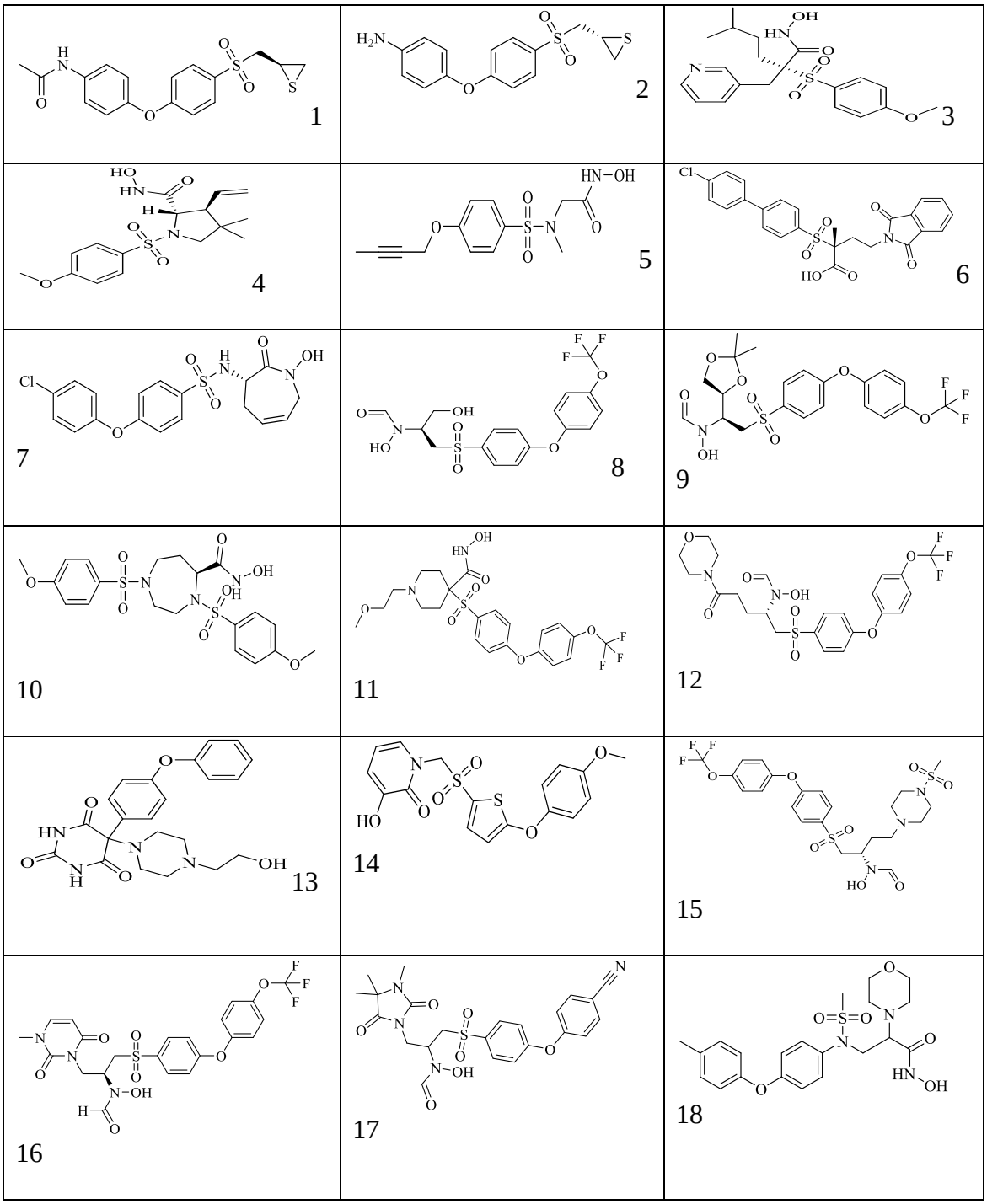
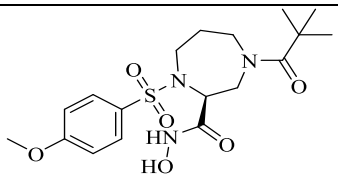
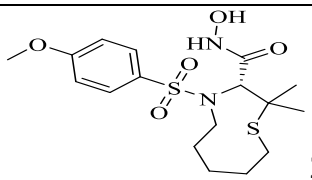
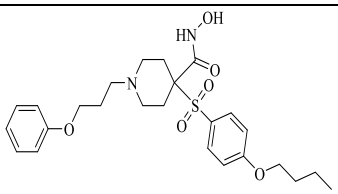
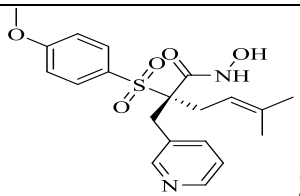
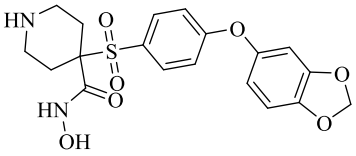
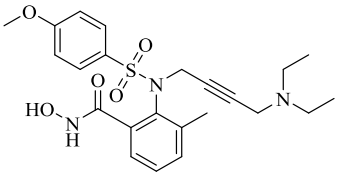
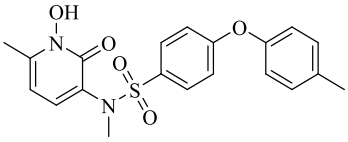
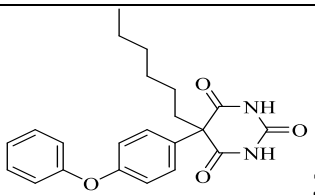
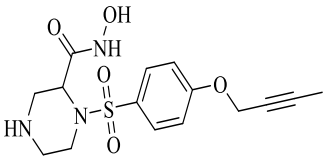
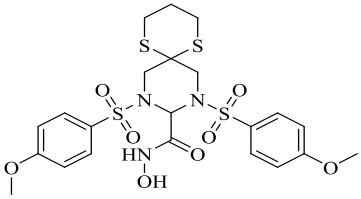
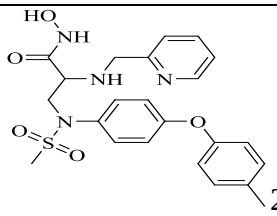
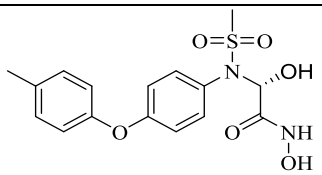
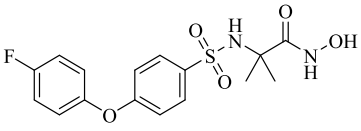
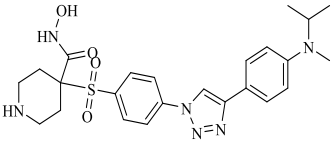
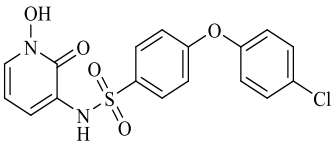
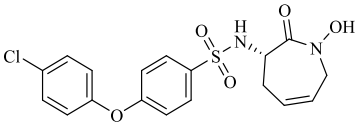
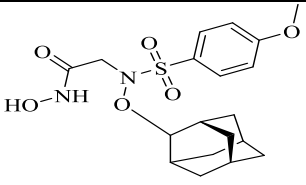
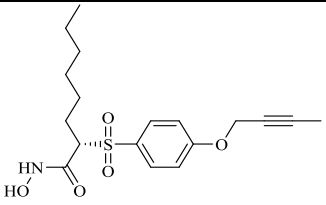
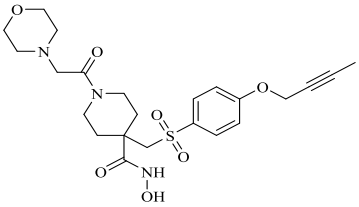
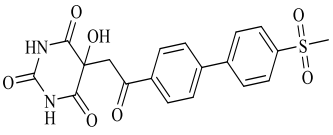
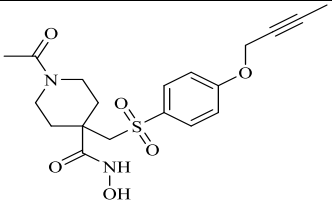
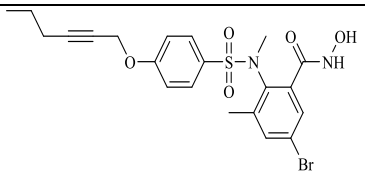
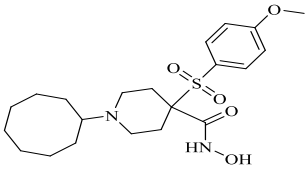
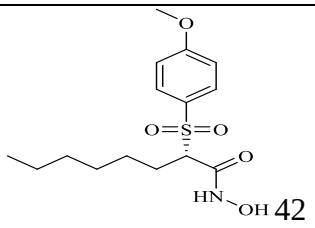
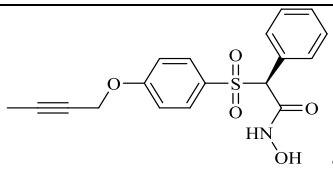
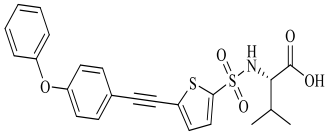
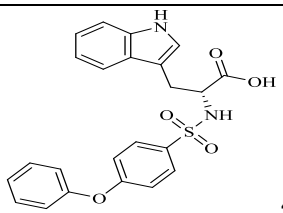
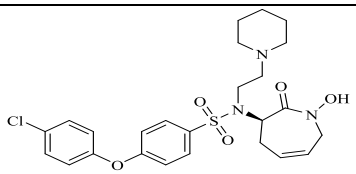
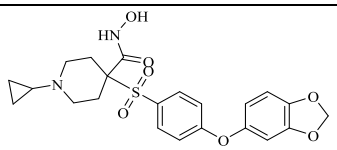
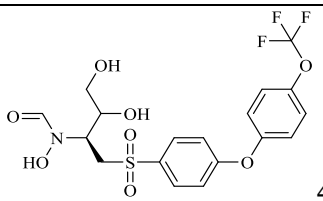
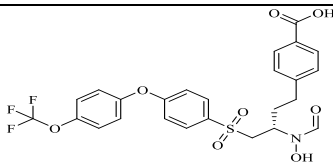
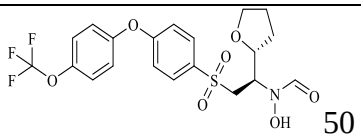
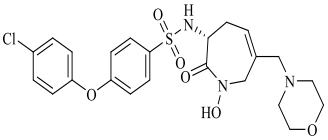
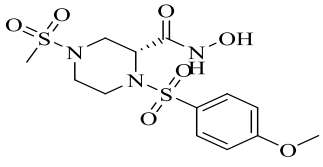
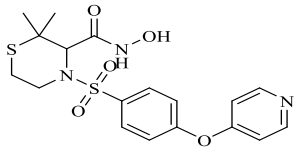
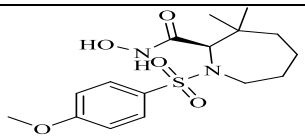
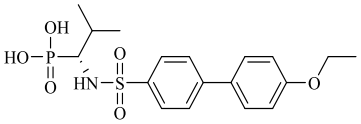
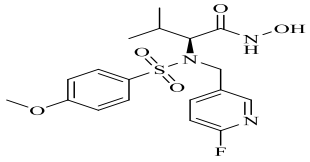
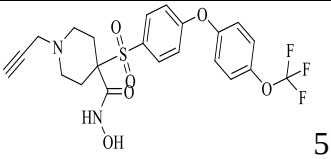
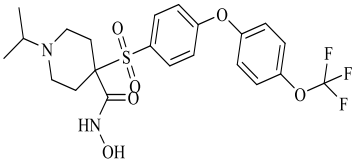
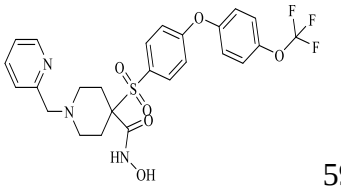
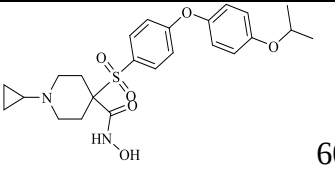
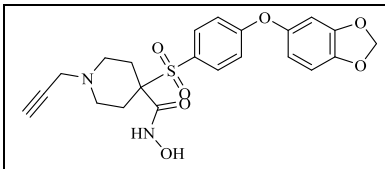
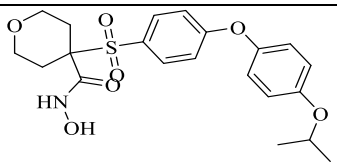
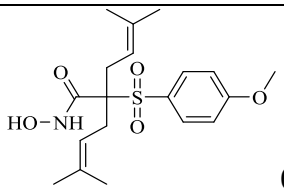
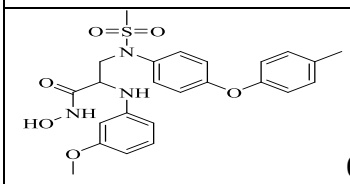
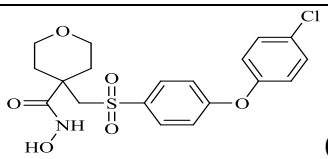
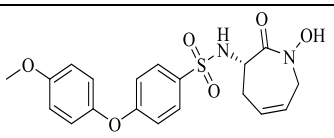
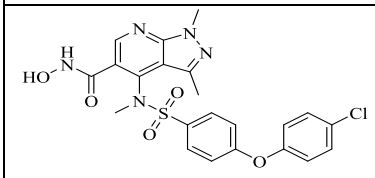
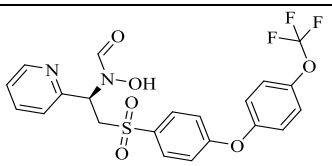
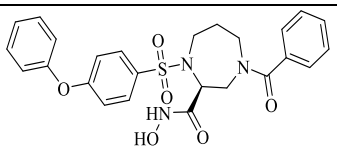
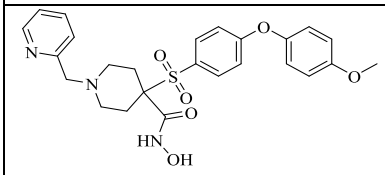
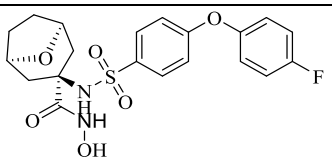
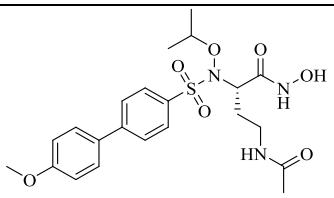
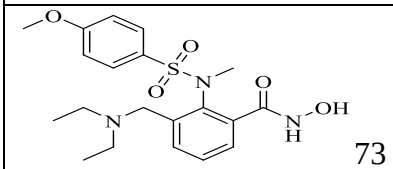
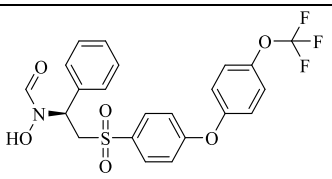
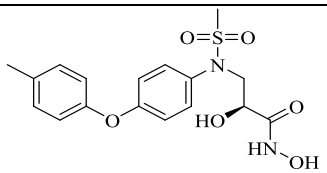
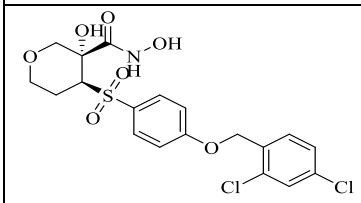
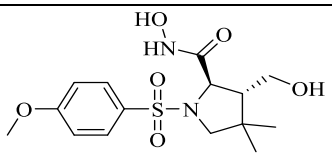
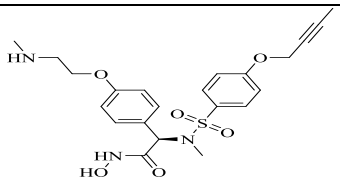
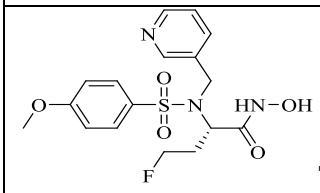
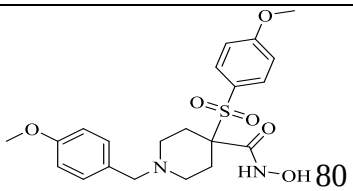
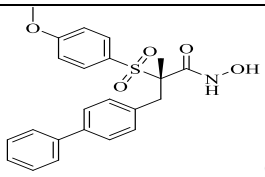
Appendix

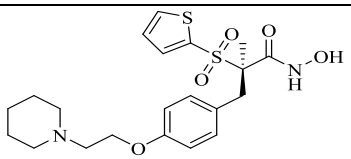
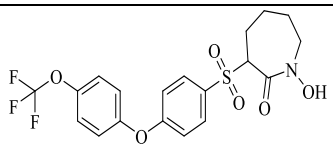
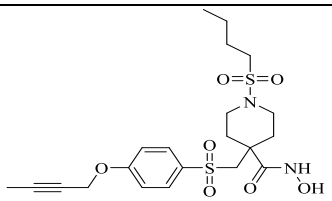
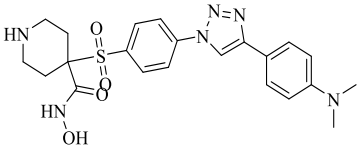
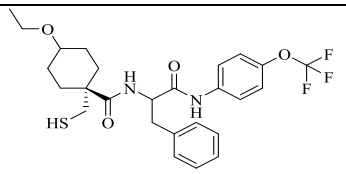
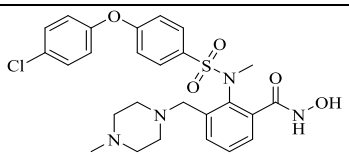
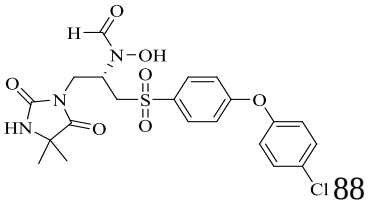
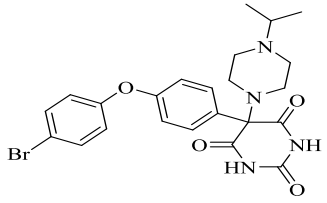
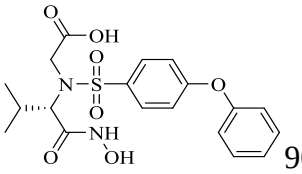
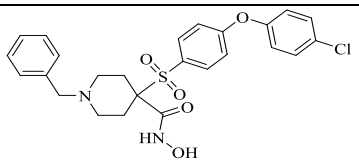
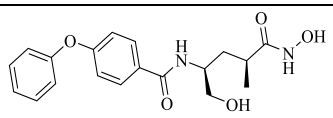
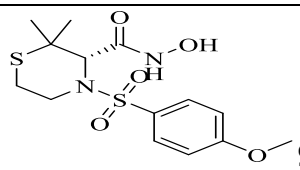
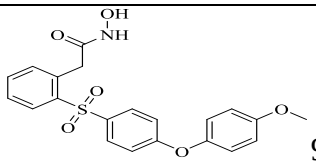
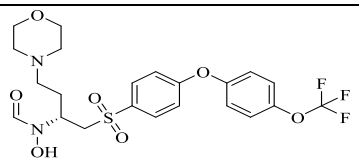
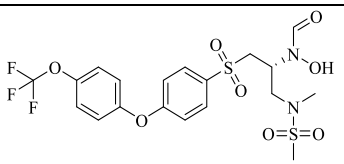
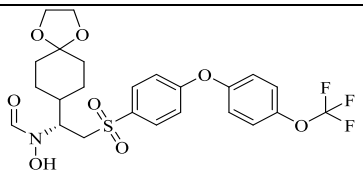
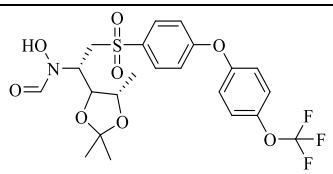
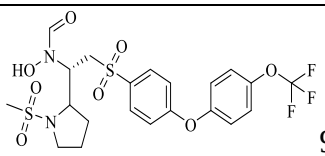
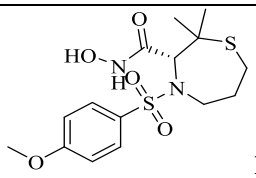
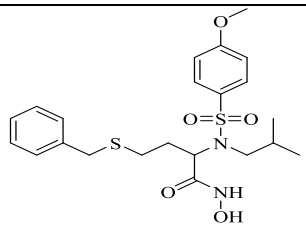
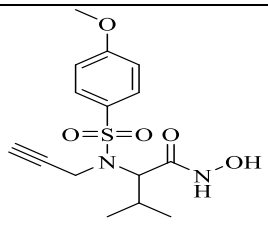
Figure A.1 Known MMP-9 inhibitors for development of 3D-QSAR models.

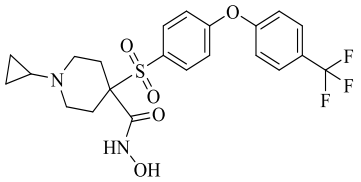
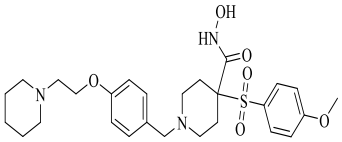
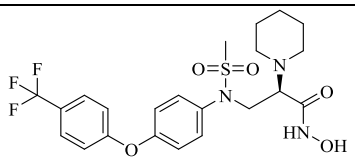
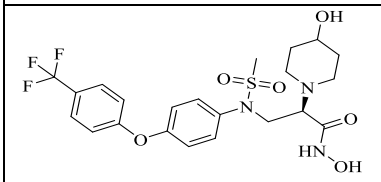
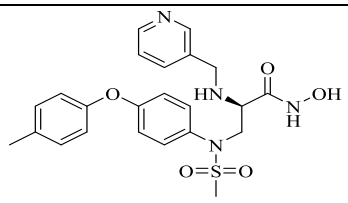
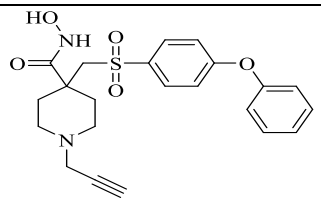
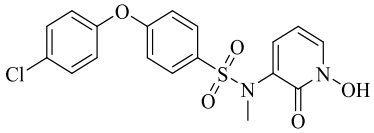
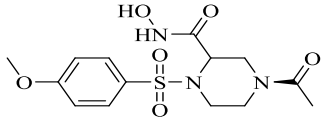
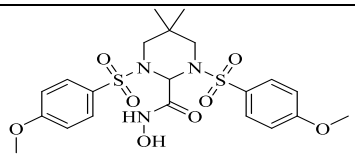
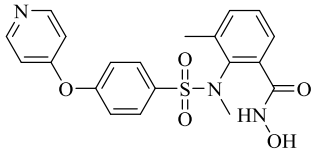
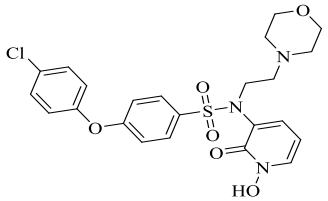
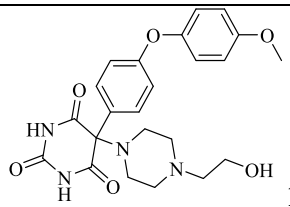
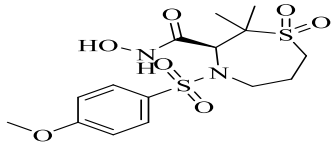
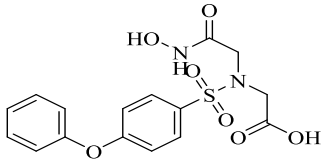
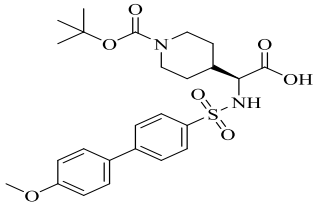
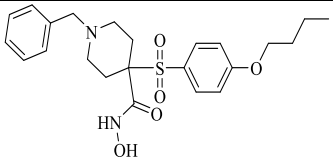
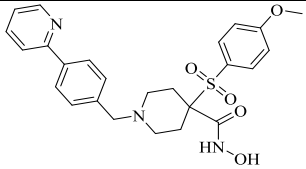
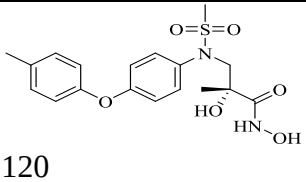
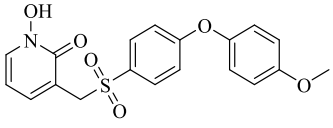
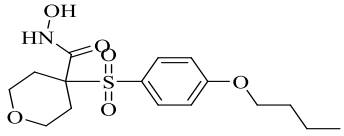
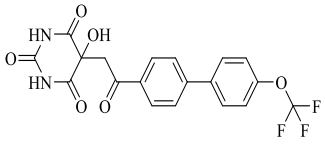


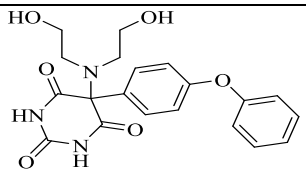
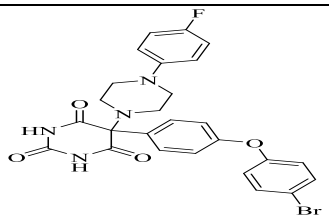
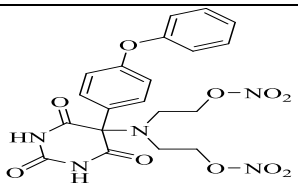
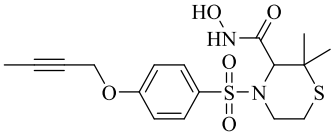
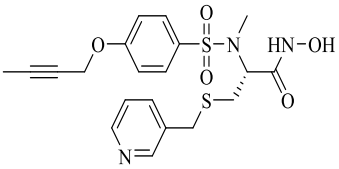
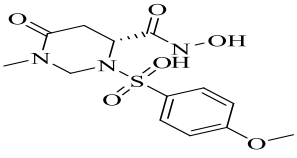
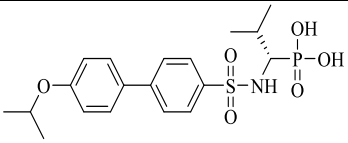
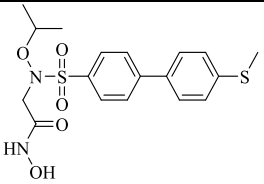
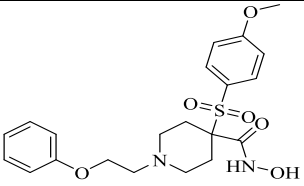
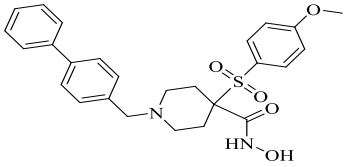
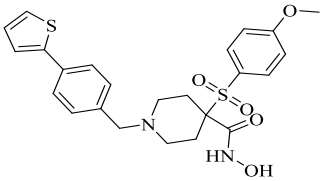
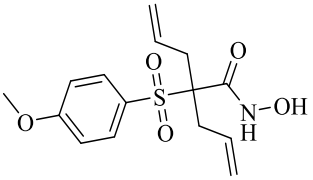
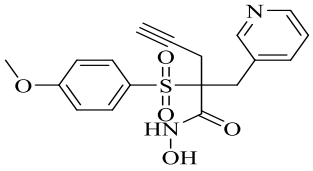
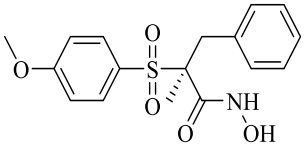
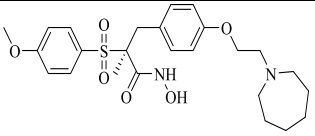
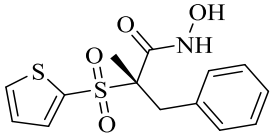
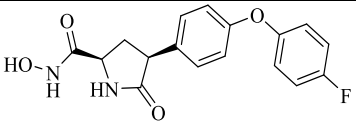
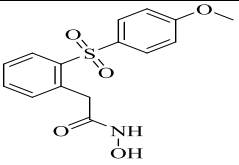
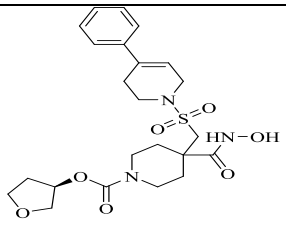
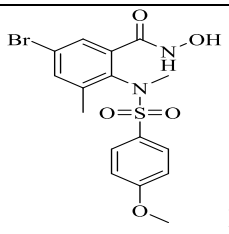
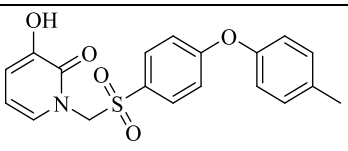
 19	 20	 21
 22	 23	 24
 25	 26	 27
 28	 29	 30
 31	 32	 33
 34	 35	 36
 37	 38	 39

 40	 41	 42
 43	 44	 45
 46	 47	 48
 49	 50	 51
 52	 53	 54
 55	 56	 57
 58	 59	 60

 61	 62	 63
 64	 65	 66
 67	 68	 69
 70	 71	 72
 73	 74	 75
 76	 77	 78
 79	 80	 81

 82	 83	 84
 85	 86	 87
 88	 89	 90
 91	 92	 93
 94	 95	 96
 97	 98	 99
 100	 101	 102

 103	 104	 105
 106	 107	 108
 109	 110	 111
 112	 113	 114
 115	 116	 117
 118	 119	 120
 121	 122	 123

 124	 125	 126
 127	 128	 129
 130	 131	 132
 133	 134	 135
 136	 137	 138
 139	 140	 141
 142	 143	 144

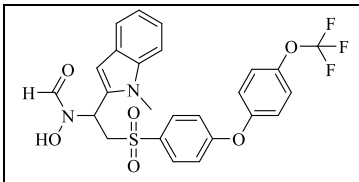
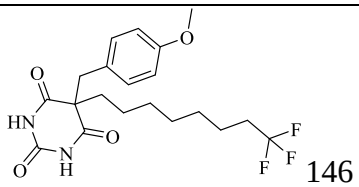
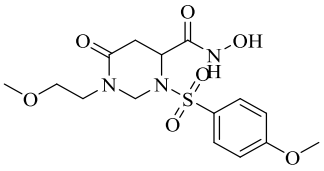
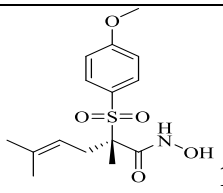
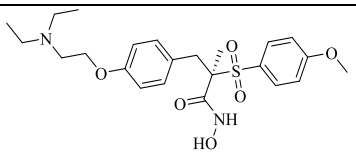
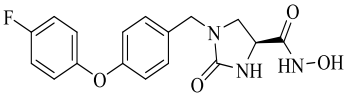
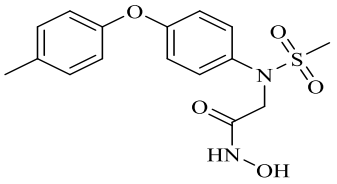
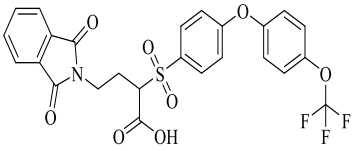
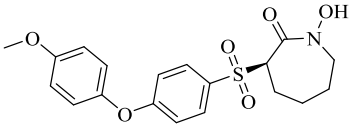
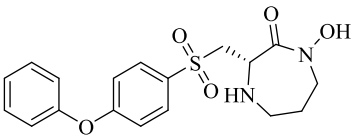
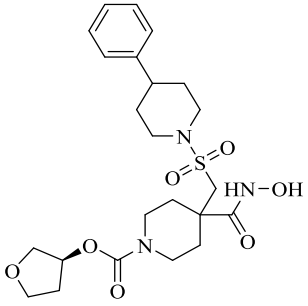
 145	 146	 147
 148	 149	 150
 151	 152	 153
 154	 155	

Table A.1 3D-QSAR data set of 155 MMP-9 inhibitors with their activity (pIC_{50}), predicted activity, error (the difference between their predicted and actual activity) and fitness to the best pharmacophore selected.

Compound ID	Fitness	pIC_{50}	Phase predicted pIC_{50}	Error	Phase QSAR set
1	1.683	6.277	6.99	−0.713	Test
2	1.142	6.214	5.97	0.244	Test
3	0.109	6.921	6.75	0.171	Test
4	1.732	6.86	7.68	−0.82	Test
5	1.637	6.51	7.18	−0.67	Test
6	1.433	6.943	6.72	0.223	Test
7	1.978	9.237	8.49	0.747	Test
8	3.000	9.585	8.41	1.175	Test
9	2.715	9.301	8.64	0.661	Test
10	1.653	9.301	8.81	0.491	Test
11	2.356	9.745	8.92	0.825	Test
12	2.321	8.699	8.99	−0.291	Test
13	1.668	8.092	8.52	−0.428	Test
14	0.960	7.857	8.19	−0.333	Test
15	2.479	9.102	8.73	0.372	Test
16	1.377	8.854	9.04	−0.186	Test
17	1.644	8.745	8.85	−0.105	Test
18	1.831	8.721	8.33	0.391	Test
19	1.624	8.319	8.42	−0.101	Test
20	1.664	8.432	8.56	−0.128	Test
21	1.724	8.301	8.0	0.301	Test
22	1.755	8.046	8.28	−0.234	Test
23	2.068	8.42	8.89	−0.47	Test
24	1.182	7.959	8.29	−0.331	Test
25	0.560	7.457	7.84	−0.383	Test
26	1.586	7.745	7.15	0.595	Test
27	0.764	7.854	8.03	−0.176	Test
28	0.341	7.796	7.46	0.336	Test
29	1.666	7.638	8.39	−0.752	Test
30	1.974	7.921	8.31	−0.389	Test
31	1.934	7.886	8.65	−0.764	Test
32	1.176	6.461	6.53	−0.069	Training
33	1.999	6.502	7.08	−0.578	Training
34	1.604	5.952	6.25	−0.298	Training
35	0.879	5.699	5.53	0.169	Training
36	0.276	5.602	5.94	−0.338	Training
37	1.556	6.056	6.03	0.026	Training
38	1.113	6.187	6.13	0.057	Training
39	1.615	6.228	5.93	0.298	Training
40	0.848	6.635	6.57	0.065	Training
41	0.353	6.86	6.77	0.09	Training

42	0.611	6.924	6.99	−0.066	Training
43	1.761	6.907	6.93	−0.023	Training
44	1.740	6.585	6.87	−0.285	Training
45	1.321	6.602	6.48	0.122	Training
46	1.559	9.678	9.83	−0.152	Training
47	2.017	10.0	9.65	0.35	Training
48	2.240	10.036	9.6	0.436	Training
49	2.548	9.276	8.73	0.546	Training
50	2.231	9.495	8.83	0.665	Training
51	1.708	9.337	9.37	−0.033	Training
52	1.657	9.222	9.3	−0.078	Training
53	1.714	9.699	9.47	0.229	Training
54	1.586	9.301	8.89	0.411	Training
55	1.163	9.252	9.25	0.002	Training
56	0.677	9.301	9.45	−0.149	Training
57	2.304	10.0	9.79	0.21	Training
58	2.137	10.0	10.14	−0.14	Training
59	1.837	9.699	9.87	−0.171	Training
60	1.757	9.678	9.96	−0.282	Training
61	0.492	9.523	9.65	−0.127	Training
62	2.115	10.0	9.93	0.07	Training
63	1.705	9.301	9.02	0.281	Training
64	1.842	9.208	9.45	−0.242	Training
65	2.361	9.959	9.51	0.449	Training
66	1.649	9.0	8.74	0.26	Training
67	1.790	9.0	9.01	−0.01	Training
68	2.797	8.658	8.43	0.228	Training
69	1.643	8.921	9.11	−0.189	Training
70	1.571	8.959	9.57	−0.611	Training
71	1.579	8.854	9.17	−0.316	Training
72	0.679	8.699	8.6	0.099	Training
73	0.781	8.097	8.34	−0.243	Training
74	1.853	8.387	8.34	0.047	Training
75	1.871	8.108	7.92	0.188	Training
76	1.450	8.276	8.13	0.146	Training
77	1.729	7.301	7.39	−0.089	Training
78	1.494	7.959	7.88	0.079	Training
79	0.291	7.921	7.92	0.001	Training
80	1.057	7.921	8.06	−0.139	Training
81	1.653	7.638	7.51	0.128	Training
82	1.138	7.102	7.2	−0.098	Training
83	1.926	7.668	7.97	−0.302	Training
84	1.589	7.721	7.57	0.151	Training
85	1.097	7.357	6.9	0.457	Training
86	0.395	7.092	7.35	−0.258	Training
87	1.924	9.0	9.18	−0.18	Training

88	1.928	9.018	8.95	0.068	Training
89	1.802	9.0	8.65	0.35	Training
90	1.987	9.114	9.19	−0.076	Training
91	1.839	9.0	8.88	0.12	Training
92	1.766	9.097	9.08	0.017	Training
93	1.574	9.046	9.1	−0.054	Training
94	1.989	9.097	8.7	0.397	Training
95	2.167	8.77	8.86	−0.09	Training
96	2.293	8.77	8.7	0.07	Training
97	2.148	8.699	8.94	−0.241	Training
98	2.208	8.959	9.38	−0.421	Training
99	2.063	8.699	8.93	−0.231	Training
100	1.680	8.721	8.56	0.161	Training
101	1.738	8.602	8.74	−0.138	Training
102	1.697	8.699	8.65	0.049	Training
103	1.698	8.638	8.63	0.008	Training
104	1.615	8.523	8.39	0.133	Training
105	1.989	8.638	8.59	0.048	Training
106	1.683	8.721	8.58	0.141	Training
107	1.837	8.553	8.43	0.123	Training
108	1.684	8.824	8.39	0.434	Training
109	1.949	8.62	8.64	−0.02	Training
110	1.715	8.745	8.44	0.305	Training
111	0.128	8.745	8.53	0.215	Training
112	1.762	8.155	8.3	−0.145	Training
113	1.169	8.377	8.34	0.037	Training
114	1.859	8.222	8.39	−0.168	Training
115	1.649	8.444	8.53	−0.086	Training
116	1.787	8.495	8.46	0.035	Training
117	1.275	8.268	8.16	0.108	Training
118	1.750	8.398	8.51	−0.112	Training
119	1.629	8.222	8.5	−0.278	Training
120	1.848	8.26	8.26	0	Training
121	1.829	8.137	8.05	0.087	Training
122	1.799	8.036	7.88	0.156	Training
123	1.236	7.678	7.76	−0.082	Training
124	1.687	7.585	7.57	0.015	Training
125	1.757	7.721	7.83	−0.109	Training
126	0.801	7.041	7.33	−0.289	Training
127	1.570	7.921	8.05	−0.129	Training
128	1.803	7.854	7.73	0.124	Training
129	1.876	7.618	7.88	−0.262	Training
130	1.094	7.62	7.67	−0.05	Training
131	1.626	7.114	6.74	0.374	Training
132	1.743	7.585	7.69	−0.105	Training
133	1.702	7.886	7.99	−0.104	Training

134	1.637	7.959	8.37	−0.411	Training
135	1.760	7.456	7.73	−0.274	Training
136	1.802	7.081	7.29	−0.209	Training
137	1.704	7.959	8.09	−0.131	Training
138	1.626	7.721	7.69	0.031	Training
139	0.351	7.31	7.51	−0.2	Training
140	0.537	7.086	7.1	−0.014	Training
141	0.199	7.009	6.79	0.219	Training
142	0.322	7.602	7.45	0.152	Training
143	0.065	7.959	7.86	0.099	Training
144	1.745	7.339	7.6	−0.261	Training
145	2.741	7.921	8.25	−0.329	Training
146	0.510	7.658	7.28	0.378	Training
147	1.559	7.28	7.36	−0.08	Training
148	1.729	7.959	7.97	−0.011	Training
149	0.910	7.886	8.19	−0.304	Training
150	1.324	7.208	7.36	−0.152	Training
151	1.599	7.509	7.25	0.259	Training
152	2.184	7.638	7.61	0.028	Training
153	1.250	7.509	7.52	−0.011	Training
154	1.425	7.676	7.72	−0.044	Training
155	0.242	7.658	7.69	−0.032	Training

Figure A.2. Total 24 hits from Zinc15 database as MMP-9 inhibitor (selective and non-selective).

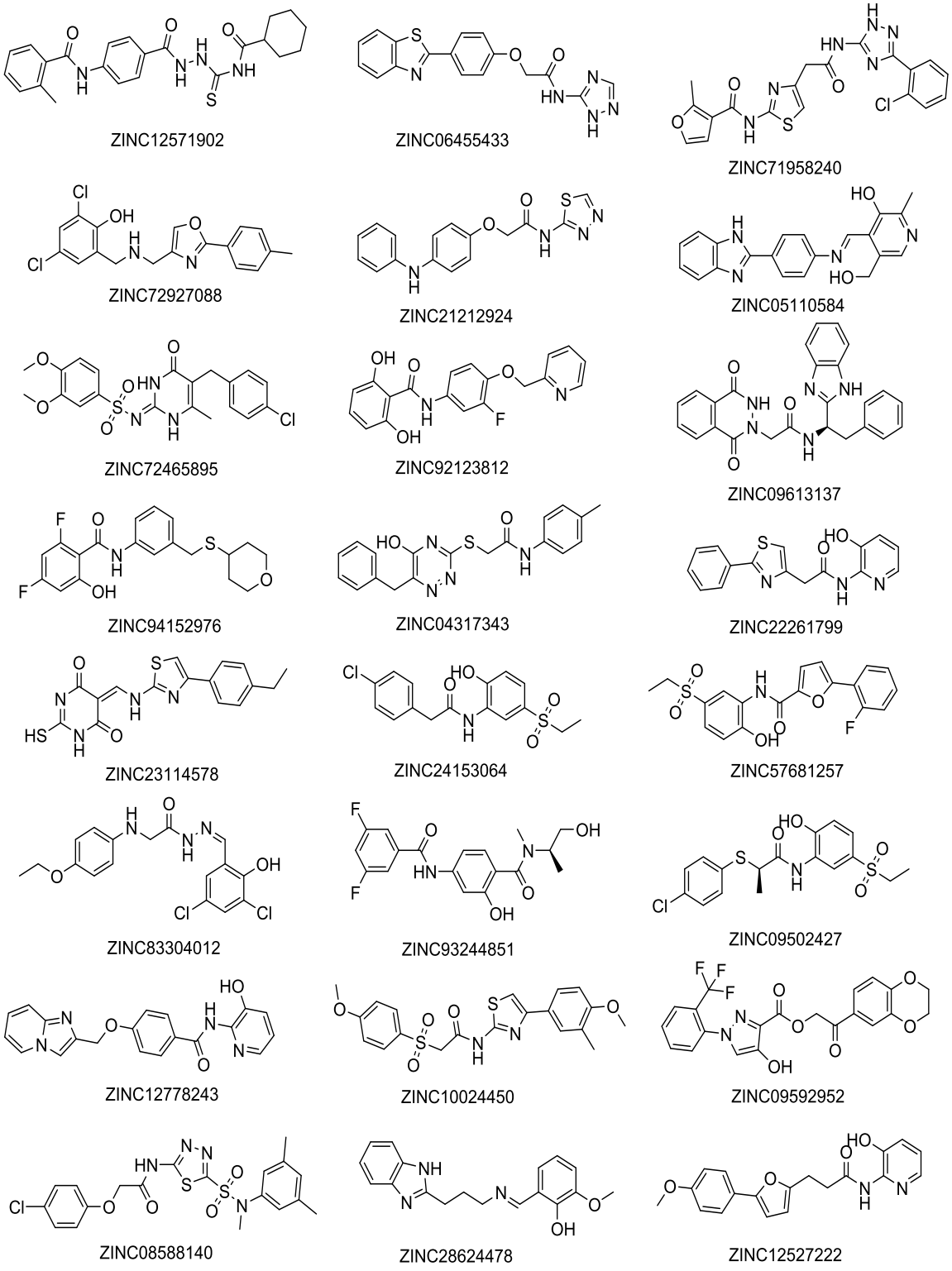


Figure A.3. Binding pose of H-1 to H-12 in the active site pocket of MMP-9.

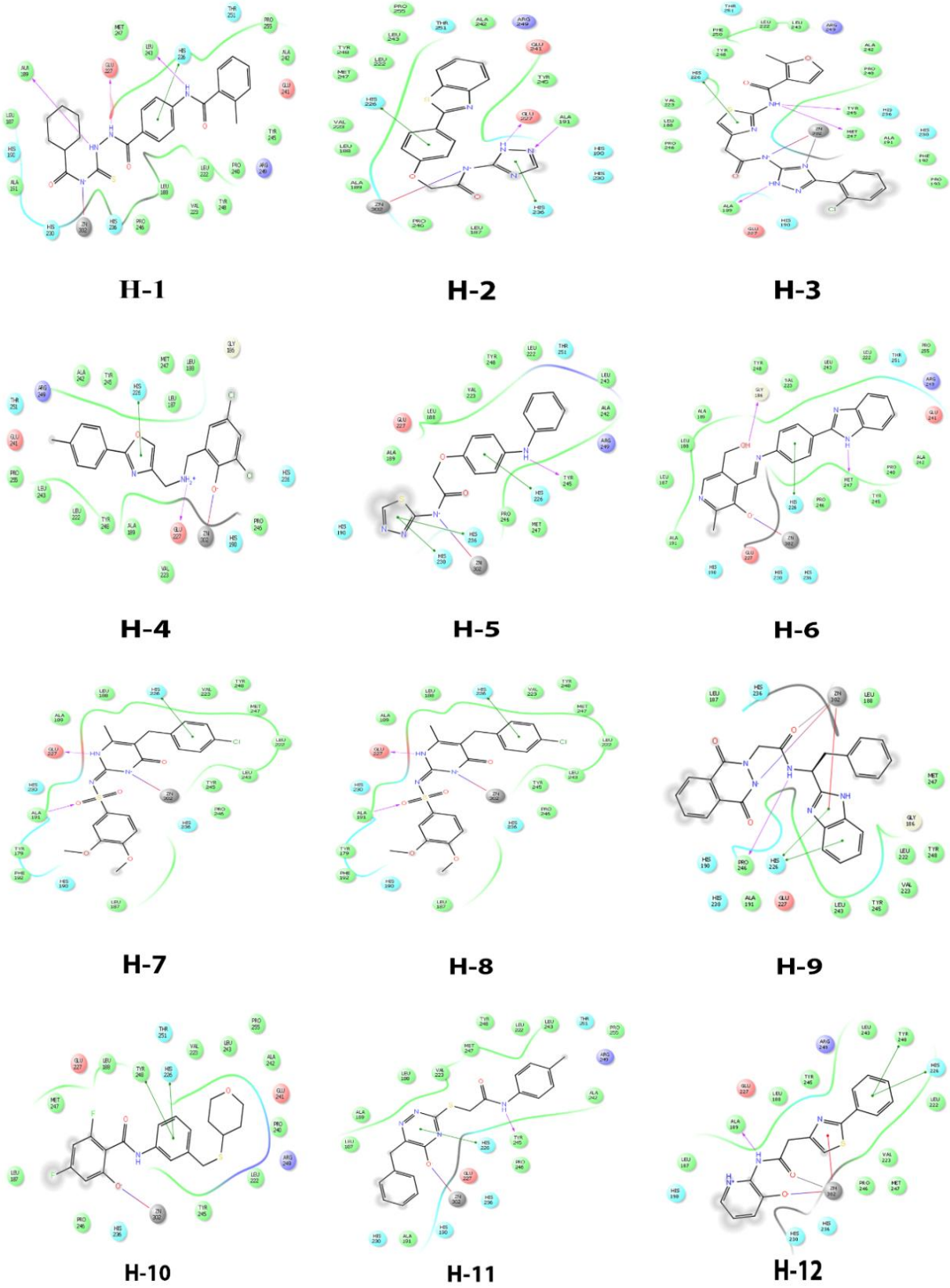


Figure A.4. Binding pose of H-13 to H-24 at the active site pocket of MMP-9.

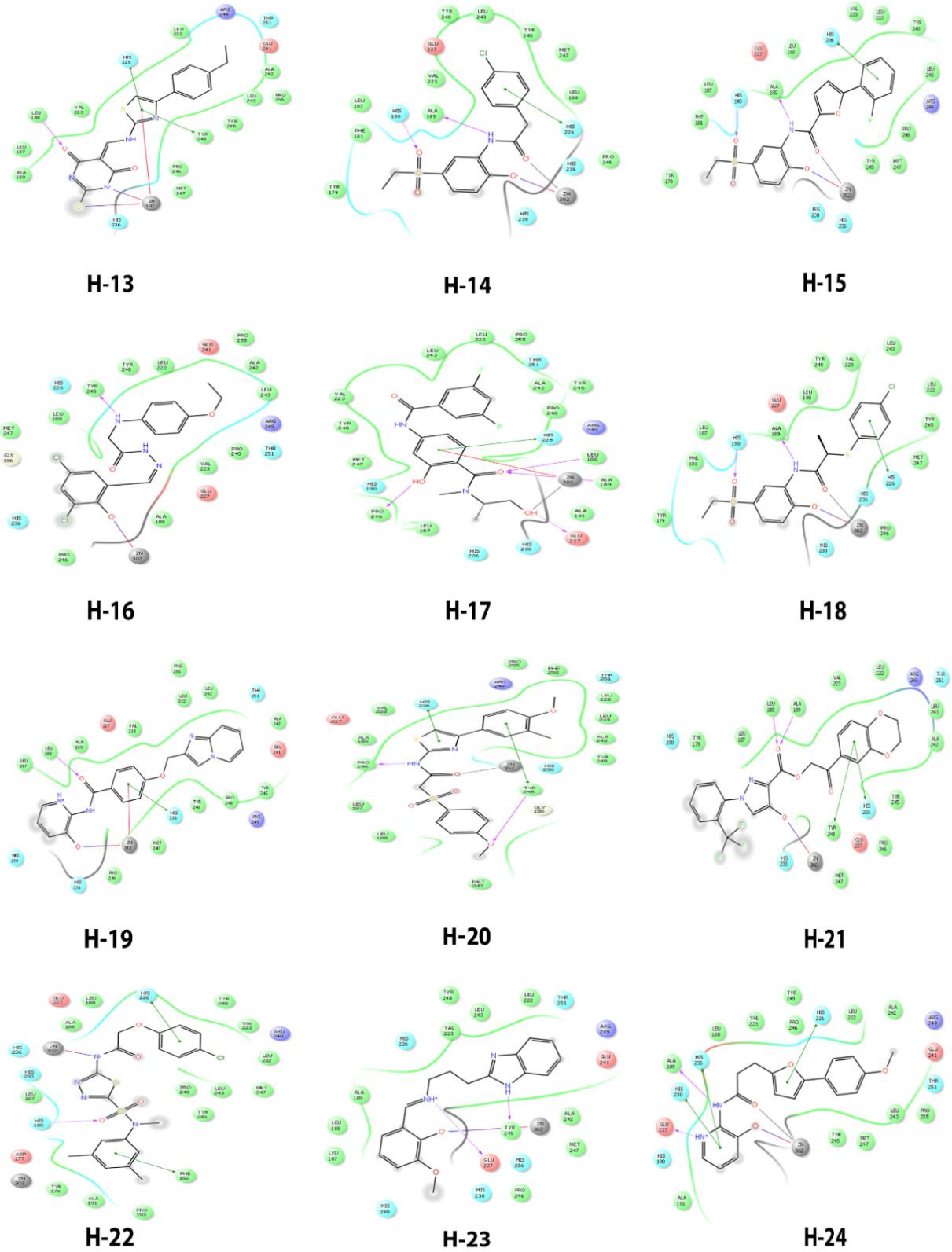
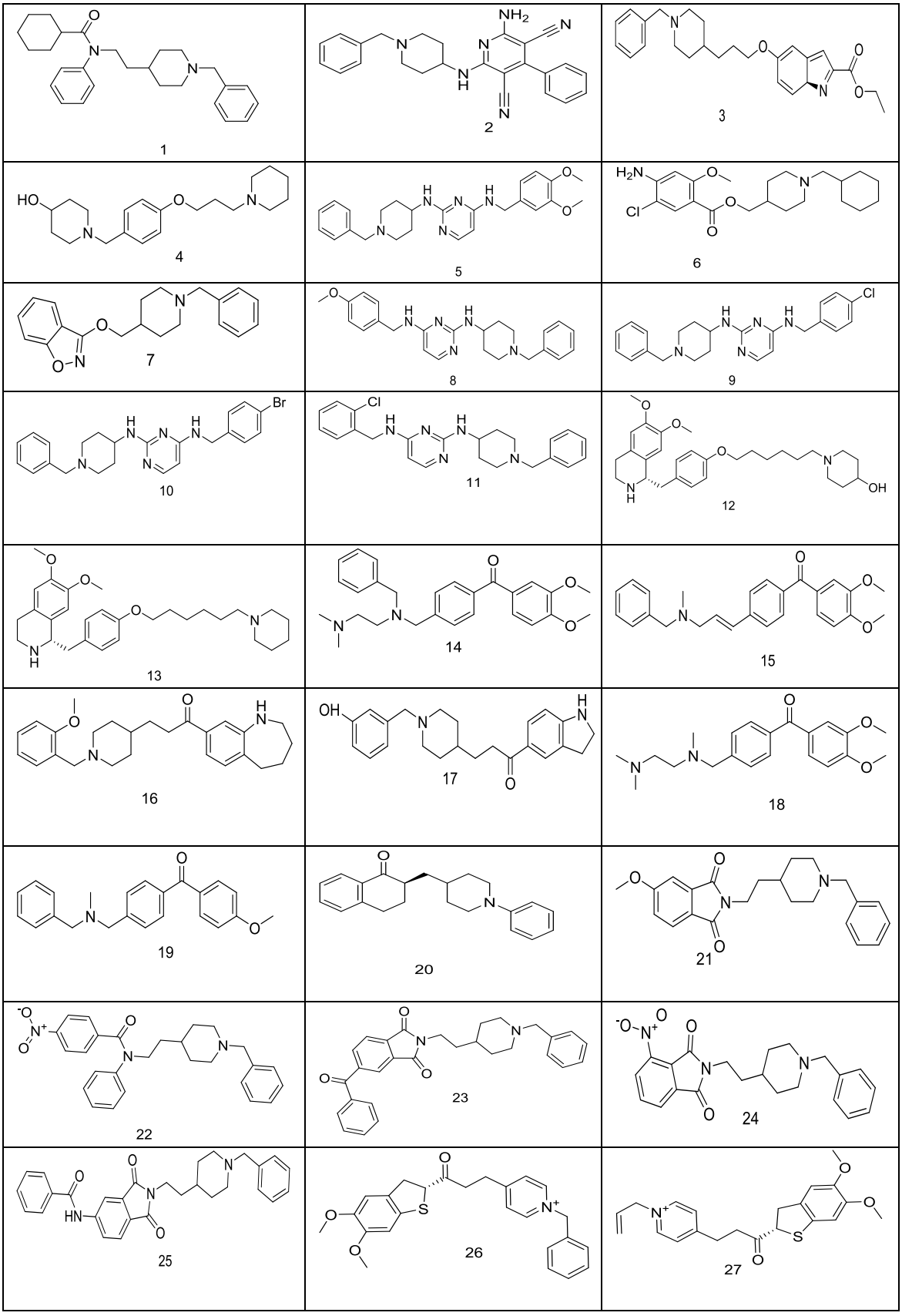
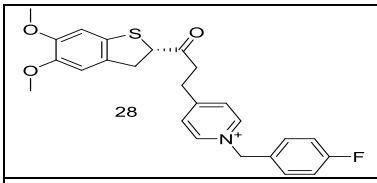
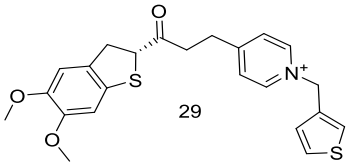
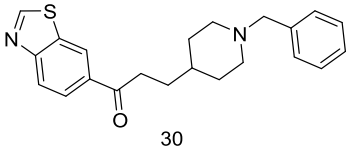
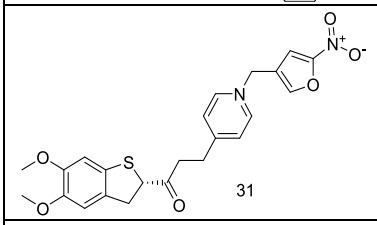
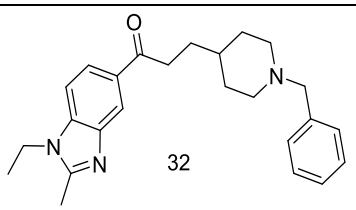
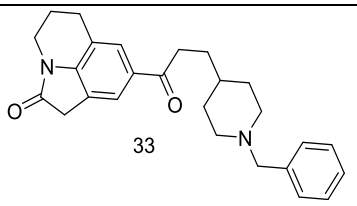
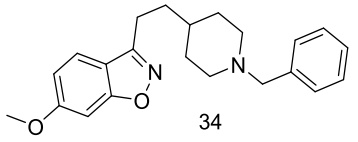
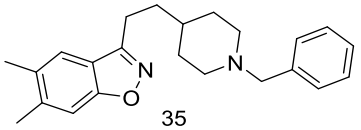
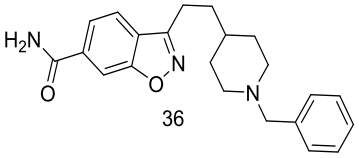
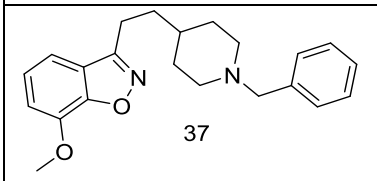
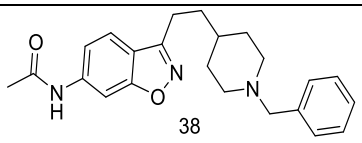
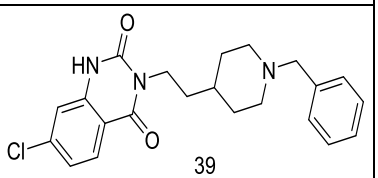
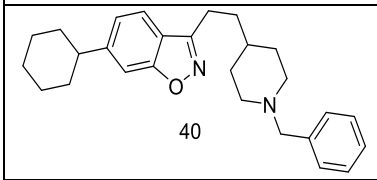
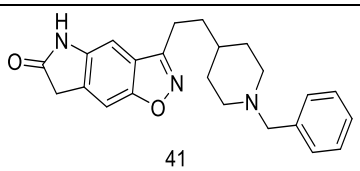
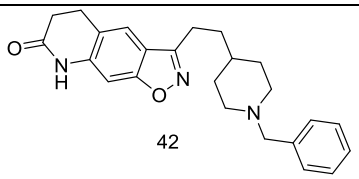
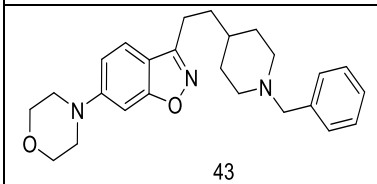
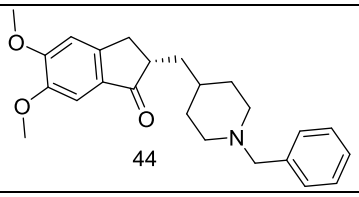
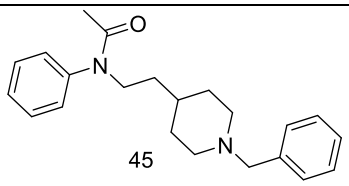
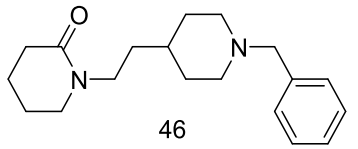
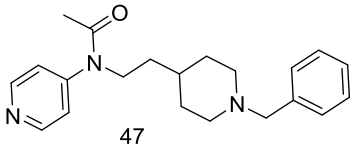
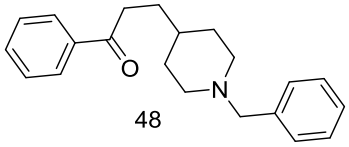
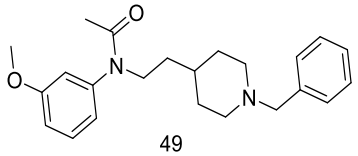
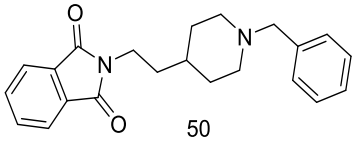
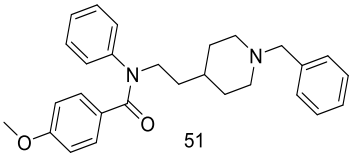
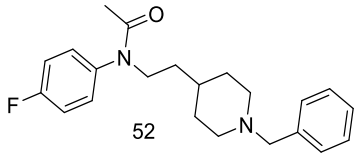
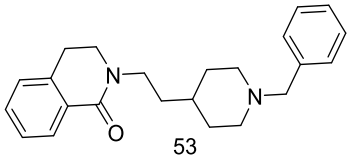
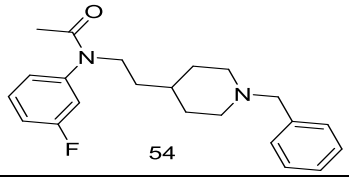
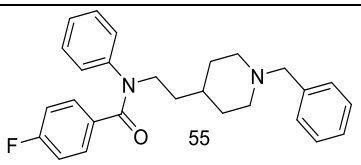
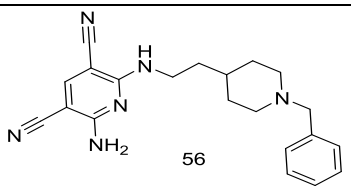
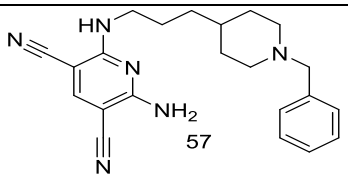
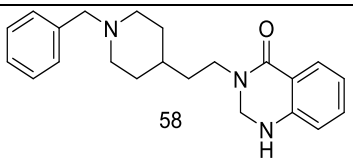
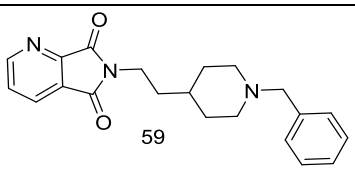
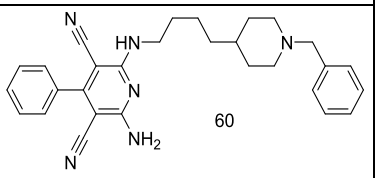
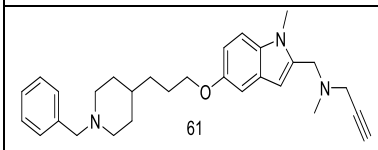
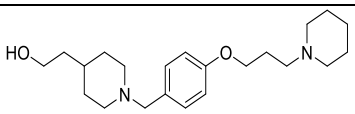
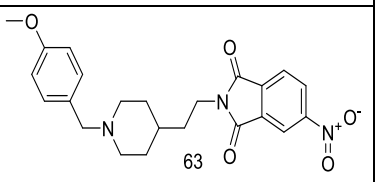
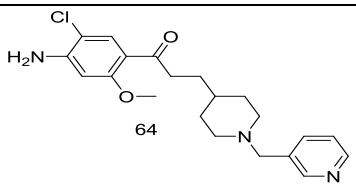
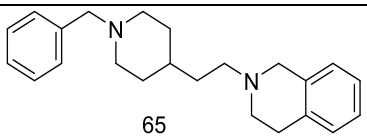
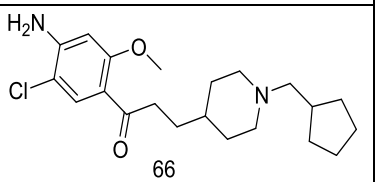
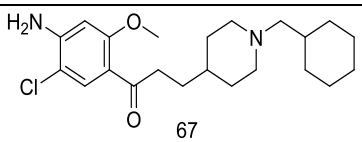
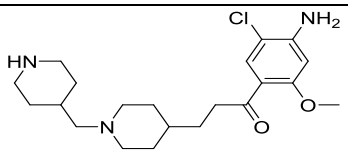
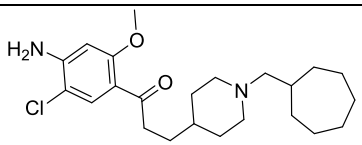
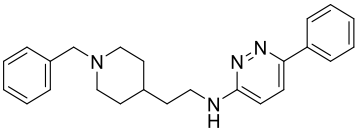
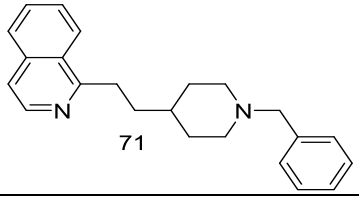
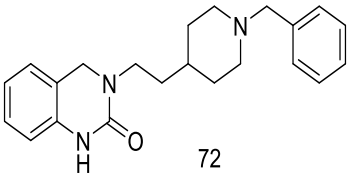
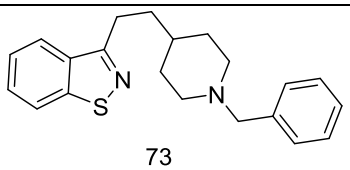
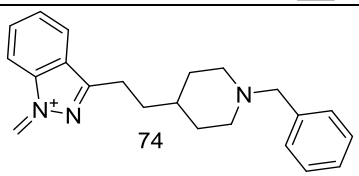
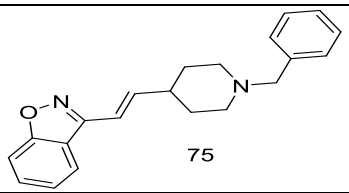
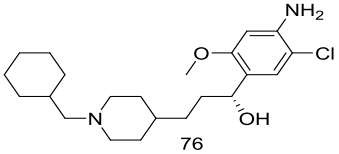
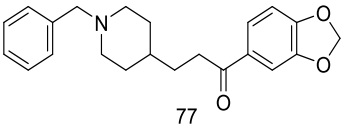
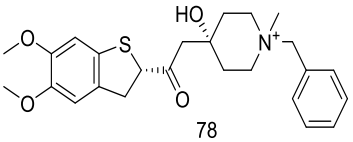
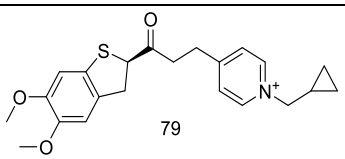
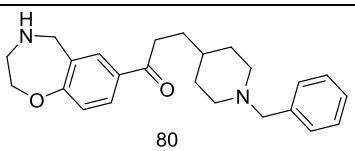
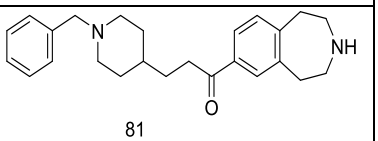
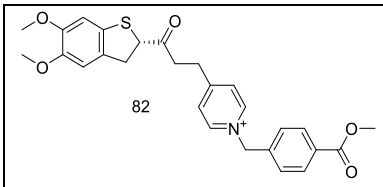
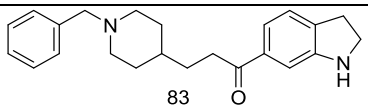
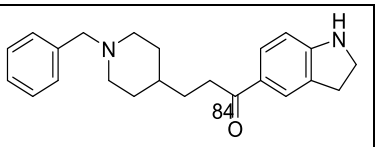
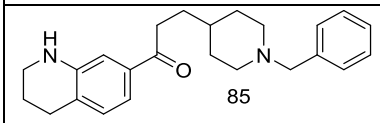
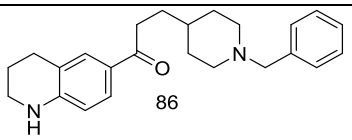
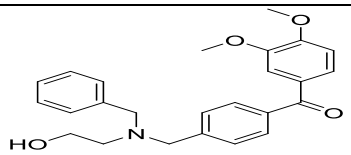
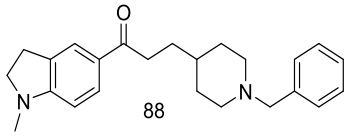
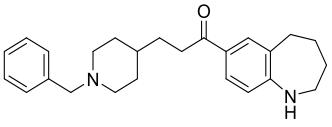
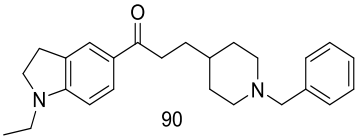
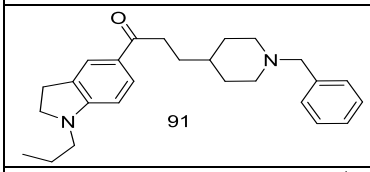
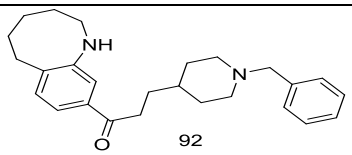
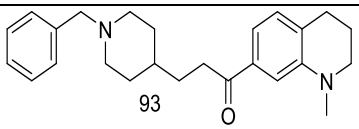
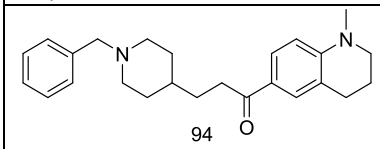
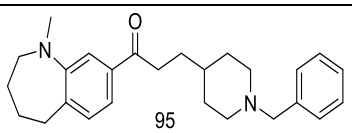
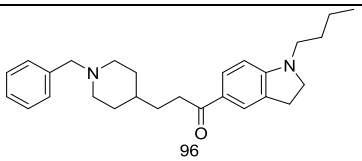
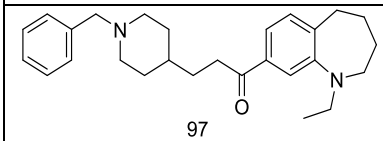
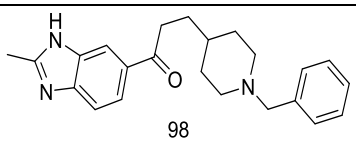
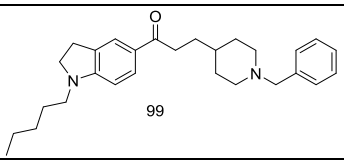
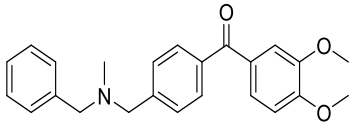
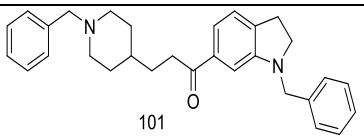
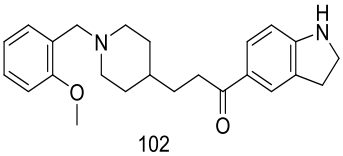
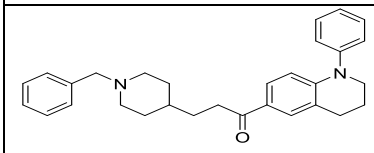
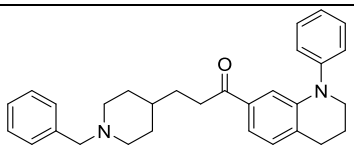
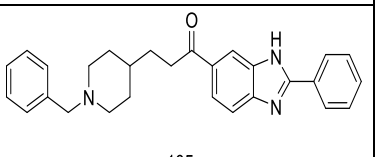
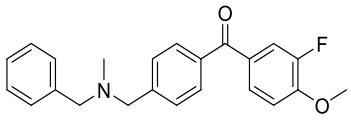
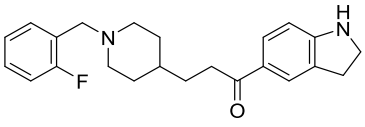
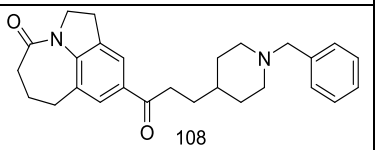
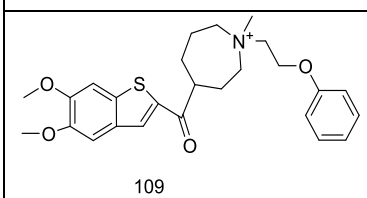
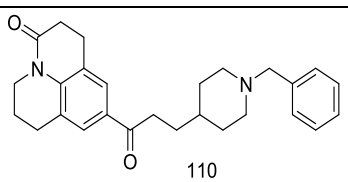
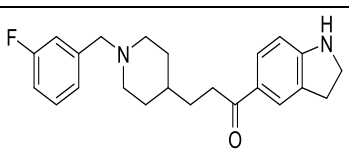


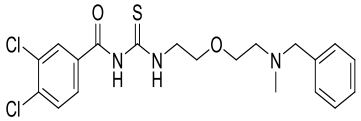
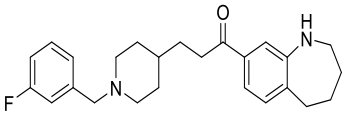
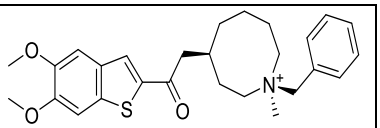
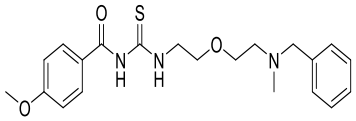
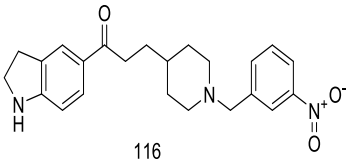
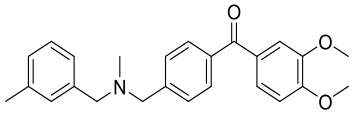
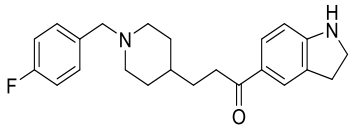
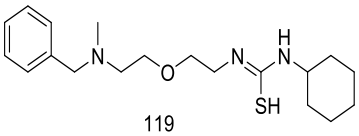
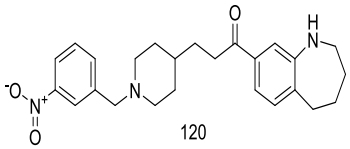
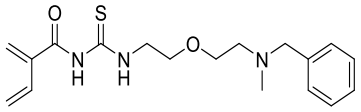
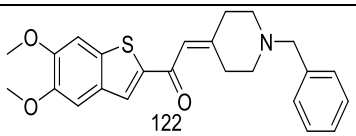
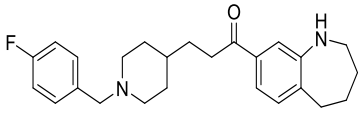
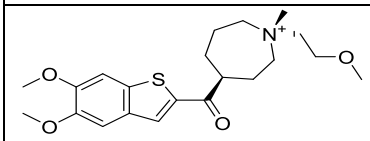
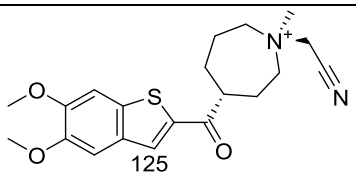
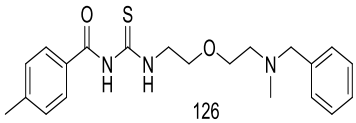
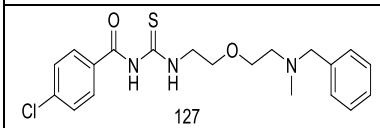
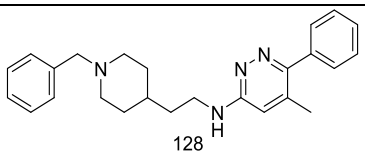
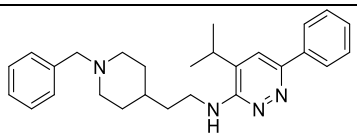
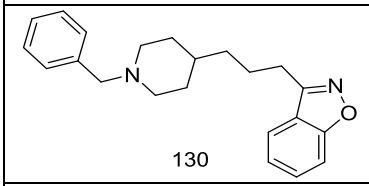
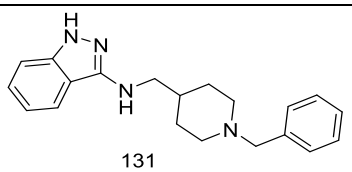
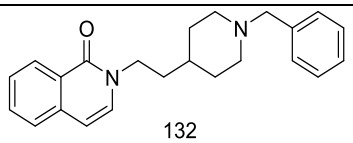
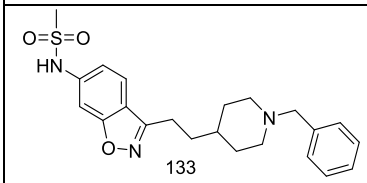
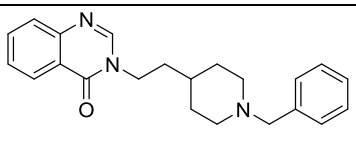
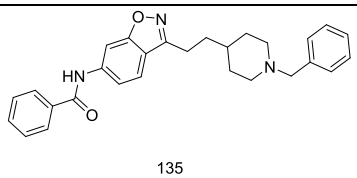
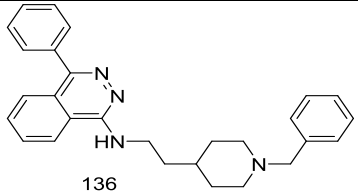
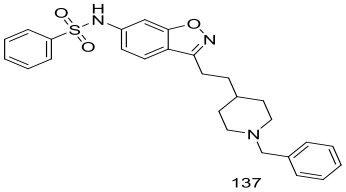
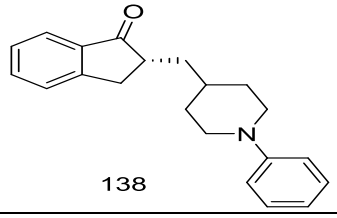
Figure A.5 List of AChE Inhibitors used for development of 3D-QSAR model.



 28	 29	 30
 31	 32	 33
 34	 35	 36
 37	 38	 39
 40	 41	 42
 43	 44	 45
 46	 47	 48
 49	 50	 51
 52	 53	 54

 55	 56	 57
 58	 59	 60
 61	 62	 63
 64	 65	 66
 67	 68	 69
 70	 71	 72
 73	 74	 75
 76	 77	 78
 79	 80	 81

 82	 83	 84
 85	 86	 87
 88	 89	 90
 91	 92	 93
 94	 95	 96
 97	 98	 99
 100	 101	 102
 103	 104	 105
 106	 107	 108
 109	 110	 111

 112	 113	 114
 115	 116	 117
 118	 119	 120
 121	 122	 123
 124	 125	 126
 127	 128	 129
 130	 131	 132
 133	 134	 135
 136	 137	 138

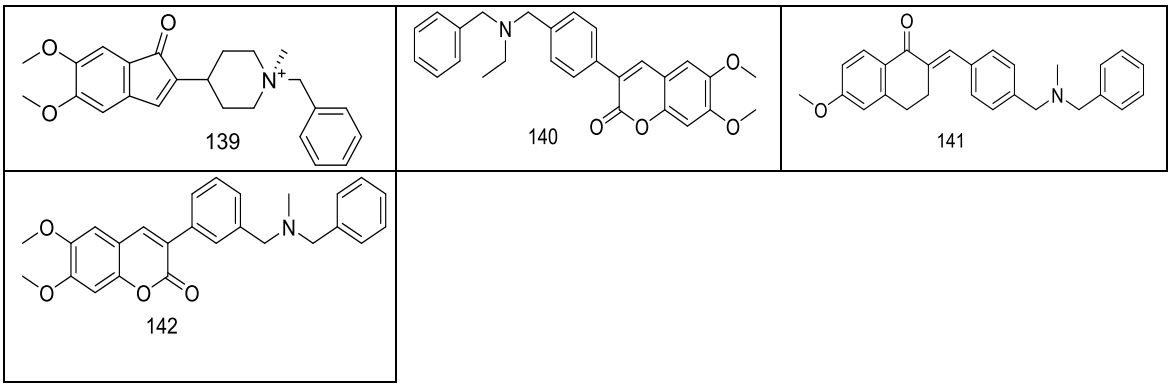

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Table A.2 AChE inhibitors with observed and predicted pIC_{50}, Canvas similarity, molecular weight, fitness, and errors

Sl. No.	Mol. Wt.	Canvas Similarity	Fitness	Phase QSAR set	Observed pIC_{50}	Predicted pIC_{50}	Error
1	433.56	0.155	1.365	test	5.00	5.93	0.93
2	322.41	0.134	2.078	test	5.59	5.99	0.40
3	467.57	0.125	1.986	test	8.92	8.44	−0.48
4	426.58	0.153	1.503	test	8.22	8.38	0.16
5	350.47	0.146	2.915	test	8.08	8.09	0.01
6	348.49	0.14	3	test	8.24	8.01	−0.23
7	363.46	0.139	2.787	test	8.06	7.96	−0.10
8	377.49	0.124	2.805	test	8.55	8.27	−0.28
9	300.45	0.162	2.106	test	6.57	6.39	−0.18
10	348.45	0.161	2.12	test	7.10	7.67	0.57
11	428.58	0.161	1.869	test	6.23	6.41	0.18
12	354.47	0.16	1.996	test	6.69	6.98	0.29
13	354.47	0.151	2.105	test	7.19	6.51	−0.68
14	416.54	0.151	1.699	test	7.74	6.97	−0.77
15	360.47	0.144	1.456	test	6.66	6.58	−0.08
16	387.91	0.195	1.561	test	7.35	7.14	−0.21
17	393.96	0.146	1.793	test	6.93	7.27	0.34
18	407.00	0.146	1.674	test	7.24	6.7	−0.54
19	336.50	0.133	2.85	test	7.01	7.25	0.24
20	318.42	0.123	1.541	test	6.68	7.15	0.47
21	376.55	0.156	1.88	test	7.60	6.76	−0.84
22	362.52	0.151	2.167	test	7.27	7.32	0.05
23	362.52	0.149	0.83	test	8.00	7.33	−0.67
24	390.57	0.146	0.67	test	6.90	6.68	−0.22
25	376.55	0.146	1.515	test	7.44	7.08	−0.36
26	390.57	0.144	1.085	test	7.09	7.05	−0.04
27	375.47	0.136	1.569	test	6.34	6.48	0.14
28	438.62	0.129	1.053	test	7.27	7.27	0.00

29	363.44	0.122	1.758	test	5.80	5.69	−0.11
30	366.48	0.117	0.961	test	7.37	6.83	−0.54
31	454.61	0.113	1.295	test	6.41	6.3	−0.11
32	416.57	0.113	1.845	test	7.80	7.28	−0.52
33	401.53	0.108	1.516	test	7.59	7.52	−0.07
34	366.48	0.105	2.167	test	7.05	7.08	0.03
35	421.54	0.103	2.088	test	6.41	6.49	0.08
36	422.57	0.102	1.952	test	6.28	6.58	0.30
37	394.54	0.101	1.872	test	6.41	7.07	0.66
38	405.95	0.1	1.758	test	7.52	7.01	−0.51
39	386.55	0.144	2.122	test	7.68	7.58	−0.10
40	320.44	0.128	2.078	test	6.92	6.27	−0.65
41	305.42	0.286	1.772	test	6.82	6.19	−0.63
42	378.50	0.144	1.243	test	6.60	6.59	−0.01
43	404.60	0.153	1.686	training	5.03	5.09	0.06
44	408.51	0.121	1.75	training	5.06	5.02	−0.04
45	420.5	0.115	1.942	training	5.02	4.58	−0.44
46	332.49	0.1	1.065	training	5.64	5.68	0.04
47	394.95	0.143	1.49	training	5.57	5.41	−0.16
48	403.53	0.134	1.191	training	5.03	4.95	−0.08
49	407.95	0.124	0.876	training	5.06	4.96	−0.10
50	452.41	0.124	0.862	training	5.00	4.78	−0.22
51	407.95	0.124	1.543	training	5.11	5.02	−0.09
52	482.67	0.122	1.698	training	5.02	5.22	0.20
53	466.67	0.106	1.699	training	5.67	5.48	−0.19
54	432.57	0.148	0.803	training	5.06	5.02	−0.04
55	401.51	0.131	1.197	training	5.68	5.74	0.06
56	406.57	0.126	2.111	training	5.58	5.86	0.28
57	378.52	0.125	2.156	training	5.57	6.13	0.56
58	356.47	0.113	1.076	training	5.63	5.6	−0.03
59	345.45	0.1	1.76	training	5.74	5.72	−0.02

60	319.45	0.176	1.229	training	5.68	5.56	−0.12
61	378.48	0.176	2.06	training	8.10	7.66	−0.44
62	443.55	0.144	1.951	training	8.27	8.16	−0.11
63	452.56	0.132	1.965	training	8.62	8.8	0.18
64	393.45	0.127	2.121	training	8.05	8.14	0.09
65	420.56	0.178	1.551	training	8.34	8.5	0.16
66	370.49	0.164	1.625	training	8.20	8.25	0.05
67	438.55	0.155	1.693	training	8.59	8.38	−0.21
68	378.54	0.143	1.43	training	8.17	8.2	0.03
69	455.51	0.142	1.537	training	8.35	8.42	0.07
70	389.55	0.132	1.367	training	8.37	8.72	0.35
71	402.54	0.11	2.127	training	8.44	7.92	−0.52
72	350.47	0.138	2.757	training	8.15	7.92	−0.23
73	397.91	0.117	1.875	training	8.35	7.96	−0.39
74	402.59	0.116	2.71	training	9.10	8.59	−0.51
75	375.49	0.116	2.825	training	9.02	8.56	−0.46
76	389.50	0.115	2.892	training	9.24	9.02	−0.22
77	405.55	0.114	2.732	training	9.10	8.75	−0.35
78	379.50	1	1.774	training	8.24	8.18	−0.06
79	336.48	0.166	2.005	training	7.28	6.89	−0.39
80	337.47	0.162	2.006	training	6.97	6.97	0.00
81	307.44	0.179	2.188	training	6.52	6.35	−0.17
82	366.51	0.161	1.952	training	7.34	7.22	−0.12
83	348.49	0.153	1.923	training	6.00	6.07	0.07
84	374.49	0.144	1.987	training	8.03	8.21	0.18
85	349.48	0.142	1.988	training	6.10	6.17	0.07
86	349.44	0.137	1.778	training	7.89	7.98	0.09
87	464.62	0.126	0.889	training	6.92	7.04	0.12
88	443.64	0.125	0.73	training	6.42	6.51	0.09
89	360.54	0.103	1.355	training	6.46	6.45	−0.01
90	423.47	0.101	2.046	training	6.36	6.5	0.14

91	334.51	0.151	1.958	training	5.80	5.96	0.16
92	378.95	0.147	1.665	training	7.16	7.28	0.12
93	392.97	0.146	1.677	training	7.80	7.61	−0.19
94	372.52	0.139	1.738	training	6.92	6.63	−0.29
95	330.48	0.137	2.686	training	6.66	6.78	0.12
96	349.48	0.136	1.707	training	7.89	8.04	0.15
97	332.47	0.128	1.863	training	6.47	6.3	−0.17
98	394.99	0.103	1.767	training	5.99	5.95	−0.04
99	351.45	0.172	2.176	training	7.52	7.02	−0.50
100	442.60	0.169	1.624	training	7.05	7.1	0.05
101	384.52	0.163	1.653	training	6.96	7.14	0.18
102	378.52	0.161	2.145	training	7.40	7.3	−0.10
103	478.59	0.155	1.69	training	6.00	5.83	−0.17
104	348.49	0.154	2.187	training	6.95	6.79	−0.16
105	348.49	0.154	0.732	training	7.28	6.89	−0.39
106	362.52	0.151	2.167	training	6.79	6.8	0.01
107	405.50	0.149	1.696	training	5.85	6.05	0.20
108	376.55	0.148	2.14	training	6.90	7.06	0.16
109	376.55	0.148	0.757	training	7.96	8.06	0.10
110	390.57	0.147	1.057	training	7.66	7.49	−0.17
111	376.55	0.146	0.524	training	7.62	7.67	0.05
112	404.60	0.144	0.354	training	7.54	7.31	−0.23
113	404.60	0.143	0.348	training	6.42	6.39	−0.03
114	361.49	0.143	2.112	training	7.92	7.6	−0.32
115	418.69	0.141	1.102	training	7.33	7.33	0.00
116	438.62	0.135	0.084	training	6.07	5.64	−0.43
117	378.52	0.131	0.79	training	6.09	6.41	0.32
118	438.62	0.128	2.025	training	5.83	5.93	0.10
119	423.56	0.123	1.815	training	7.48	7.85	0.37
120	416.57	0.113	0.045	training	7.28	7.02	−0.26
121	366.48	0.111	1.929	training	7.80	7.7	−0.10

122	440.40	0.111	1.738	training	7.26	7.16	−0.10
123	394.54	0.108	2.116	training	6.84	6.63	−0.21
124	452.64	0.108	0.855	training	6.96	6.88	−0.08
125	393.49	0.106	2.13	training	7.19	6.81	−0.38
126	389.50	0.105	1.754	training	5.78	5.71	−0.07
127	349.54	0.103	1.569	training	5.85	5.73	−0.12
128	371.51	0.103	1.007	training	6.92	7.08	0.16
129	392.54	0.101	1.578	training	7.28	7.18	−0.10
130	373.50	0.1	1.616	training	6.00	5.78	−0.22
131	385.53	0.1	1.525	training	7.11	7.11	0.00
132	414.60	0.139	1.986	training	6.37	6.4	0.03
133	334.47	0.133	1.777	training	6.05	5.88	−0.17
134	346.48	0.128	2.302	training	5.96	6.24	0.28
135	413.54	0.122	2.735	training	7.85	8.02	0.17
136	347.46	0.122	2.27	training	5.92	6.39	0.47
137	439.56	0.119	2.669	training	8.03	8.23	0.20
138	422.58	0.117	1.667	training	6.36	6.19	−0.17
139	475.61	0.111	2.669	training	7.85	7.88	0.03
140	429.52	0.11	1.217	training	7.74	7.95	0.21
141	397.52	0.105	1.087	training	6.96	6.94	−0.02
142	415.49	0.101	1.916	training	6.69	6.86	0.17

Table A.3. PAINS assessment of THVS retrieves as AChE inhibitor by utilizing FAF-Drugs4 server

SMILES	ZINC id	PAINS
Cc1nc(nc2sc3c(ncn(CCN4CCOCC4)c3=O)c12)-c1ccc(Cl)cc1	ZINC20649934	Accepted
CCN1CCC[C@H]1CNC(=O)c1ccc([nH]c1=O)-c1ccc(C)cc1	ZINC72451013	Accepted
CN1CCC[C@H]1CNC(=O)c1ccc([nH]c1=O)-c1cccc(C)c1	ZINC75124044	Accepted
CCN1CCC[C@@H]1CNC(=O)c1ccc([nH]c1=O)-c1ccccc1	ZINC72451248	Accepted
CN1CCC[C@H]1CNC(=O)c1ccc([nH]c1=O)-c1ccccc1	ZINC75124041	Accepted
CCN(Cc1cc(=O)n2ccsc2n1)Cc1nc2ccccc2c(=O)[nH]1	ZINC13597919	Accepted
C[C@@H](C1CC1)N(Cc1cc(=O)n2cc(C)ccc2n1)Cc1cc(=O)n2cc(C)ccc2n1	ZINC12815113	Accepted
COCCN1COc2c(C)c3oc(=O)c4CCCc4c3cc2C1	ZINC05354646	Accepted
Fc1ccc(CN[C@@H]2CCc3c(C2)sc2ncn(CCCc4ccncc4)c(=O)c32)cc1	ZINC19770760	Accepted
Cc1c2OCN(Cc2cc2c3CCCc3c(=O)oc12)C(C)(C)CO	ZINC09184462	Accepted
Cc1c2OCN(Cc2cc2c3CCCCc3c(=O)oc12)C1CC1	ZINC06661592	Accepted
CC(C)N1COc2c(C1)cc1c3CCCCc3c(=O)oc1c2C	ZINC06669765	Accepted
COCCCN1COc2c(C)c3oc(=O)c4CCCc4c3cc2C1	ZINC13681872	Accepted
O[C@@H](COc1ccc2c3CCCc3c(=O)oc2c1)CN1CCCC1	ZINC01811023	Accepted
Oc1ccc2c3CCCc3c(=O)oc2c1CNC[C@H]1CCCO1	ZINC06661394	Intermediate
COC[C@@H](C)N(Cc1cc(=O)n2ccccc2n1)Cc1cc(=O)n2ccccc2n1	ZINC12889927	Accepted
C\N=C(\NCCn1c(C)nc2ccccc12)NCc1ccc2OCOc2c1	ZINC79331983	Accepted
CCCN1CCc2cc(O)cc-3c2[C@H]1Cc1ccc(O)c(O)c-31	ZINC00011665	Intermediate
Fc1ccccc1CCN1COc2c(Cl)cc3c4CCCc4c(=O)oc3c2C1	ZINC20412308	Accepted
Oc1ccc2c3CCCc3c(=O)oc2c1CNCCc1cccc(F)c1	ZINC20592007	Intermediate
Cc1c2OCN(CC=C)Cc2cc2c3CCCc3c(=O)oc12	ZINC57151337	Accepted
CN1CCO[C@H](CN2CCC(=O)NC2=O)C1	ZINC92079957	Accepted
COc1cc2CCN(C)[C@@H](Cc3ccc(O)cc3)c2cc1O	ZINC00895668	Accepted
CC(C)c1nccn1CCN1CCN(CC1)C(=O)CN1C(=O)c2ccccc2C1=O	ZINC77161317	Accepted
O=c1cc(CN2CCCC[C@@H]2c2nc3ccccc3s2)nc2sccn12	ZINC58160603	Accepted
O=C(COc1ccc2c3CCCc3c(=O)oc2c1)N1CCCC1	ZINC00250014	Accepted
COc1cc2CCN(C)[C@H](Cc3ccc(O)cc3)c2cc1O	ZINC00895617	Accepted
O=c1oc2c3CN(Cc4ccncc4)COc3ccc2c2CCCc12	ZINC05345942	Accepted
Cn1c(CCCNCc2cccc(c2)C(N)=O)nc2ccccc12	ZINC76901024	Accepted
O=C(OCCCN1NC2CCCCN2C1=O)c1cnn(n1)-c1ccccc1	ZINC77877910	Accepted
COc1ccc(cc1)[C@H]1N=NC(NCCc2c[nH]c3ccc(C)cc23)=NC1=O	ZINC39154782	Accepted

COc1ccc(C[C@H]2N(C)CCc3cc(OC)c(O)cc23)cc1O	ZINC00901258	Accepted
Cc1cccn2c1nc(CN1CCCC[C@@H]1c1nc3ccccc3s1)cc2=O	ZINC58160594	Accepted
Fc1ccc(COc2cc3oc(=O)c4CCCc4c3cc2Cl)cc1	ZINC00123048	Accepted
O=C(NCCCN[C@@H]1CCCc2[nH]c(=O)ccc12)c1cccs1	ZINC89641280	Accepted
CCN1CCc2c(C1)c(O)[nH]c(=O)c2C#N	ZINC02260762	Accepted
Clc1ccc(CN2COc3ccc4c5CCCc5c(=O)oc4c3C2)cc1	ZINC57120589	Accepted
CCn1c2cccc3c(CN)ccc(c23)c1=O	ZINC04698637	Accepted
NC(=O)Cn1c2cc(Cl)ccc2c2=NCCn2c1=O	ZINC72373666	Accepted
Cc1coc2c1c(C)cc1o\c(=N\N)c3CCCCc3c21	ZINC11867378	Accepted
Cc1ccc2nc(CN3CCCC[C@@H]3c3nc4ccccc4s3)cc(=O)n2c1	ZINC58160583	Accepted
CN(Cc1cnc2ccc(C)cn12)Cc1cc2OCOc2cc1OC(F)F	ZINC93614597	Accepted
CCn1c(SC[C@H](O)CN2CCc3ccccc3C2)nc2ccccc2c1=O	ZINC66476884	Accepted
O[C@H]1C=C[C@@H]2[C@H]3Cc4ccc(O)c5O[C@@H]1[C@]2(CCN3)c45	ZINC13831510	Accepted
Cc1[nH]c(=O)[nH]c(=O)c1CN1CCC[C@@H](CCc2ccccc2)C1	ZINC72171674	Accepted
NC(=O)Cn1c2cc(Cl)ccc2c2=NCCCn2c1=O	ZINC72373687	Accepted
O=C(Cn1c(=O)c2cccc3cccc(c23)c1=O)N1CCN(Cc2ccccc2)CC1	ZINC20295069	Accepted
C=C1N(CC(=O)N2CCN(Cc3ccccc3)CC2)C(=O)c2ccccc12	ZINC14051880	Accepted
Oc1cccc(c1)C(=O)N1CCN(CCn2nc3ccccn3c2=O)CC1	ZINC81012067	Accepted
CCc1nccn1CC1CCN(CCN2C(=O)c3ccccc3C2=O)CC1	ZINC90470430	Accepted
Cc1cccc(c1)C(=O)N1CCN(CCN2C(=O)c3ccccc3C2=O)CC1	ZINC12462726	Accepted
Fc1cccc(COc2ccc3c4CCCc4c(=O)oc3c2)c1	ZINC00316719	Accepted
C[C@@H](NCc1c(F)cccc1OC(F)F)c1c[nH]c2cc(F)ccc12	ZINC90177501	Accepted
O=c1[nH]nc(CN2CCC[C@@H]2c2ccc3OCCOc3c2)[nH]1	ZINC92617175	Accepted
O=C1Nc2ccccc2\C1=N/c1ccc2[nH]c3ccccc3c2c1	ZINC17425356	Accepted
O=C1N(CCN2CCC(Cn3ccnc3)CC2)C(=O)c2ccccc12	ZINC90470199	Accepted
CCN[C@@]1(CCCc2ccc(OC)cc12)C(N)=O	ZINC92384915	Accepted

Table A.4 PAINS results for HTVS retrieves as TTBK-1 inhibitors by using FAF-Drugs4

SMILE structures of HTVS retrive	Molecule No.	PAINS
CC(C(O)=O)c1cccc(Oc2ccccc2)c1	DB00573_1	Accepted
CCNC(C)Cc1cccc(c1)C(F)(F)F	DB00574_2	Accepted
Cc1nnc(NS(=O)(=O)c2ccc(N)cc2)s1	DB00576_3	Accepted
CC(C)[C@H](N)C(=O)OCCOCn1cnc2c1[nH]c(N)nc2=O	DB00577_4	Accepted
Oc1c(Cl)cc(Cl)c(Cl)c1Cc1c(O)c(Cl)cc(Cl)c1Cl	DB00756_5	Accepted
CCn1cc(C(O)=O)c(=O)c2cc(F)c(N3CCNC(C)C3)c(F)c12	DB00978_6	Accepted
CN(C)CCOC(=O)C(c1ccccc1)C1(O)CCCC1	DB00979_7	Accepted
CC1(C)SC2C(NC(=O)C3(N)CCCCC3)C(=O)N2C1C(O)=O	DB01000_8	Accepted
C[C@]12CCC3C(CCC4CC(=O)C=C[C@]34C)C1CC[C@@H]2O	DB01481_9	Accepted
CC(Cc1ccccc1)NCCn1cnc2n(C)c(=O)n(C)c(=O)c12	DB01482_10	Accepted
CN(C)C(=O)OC1N=C(c2ccccc2)c2cc(Cl)ccc2N(C)C1=O	DB01489_11	Accepted
CCC(C)(C)C(=O)C(=O)N1CCCC1C(=O)OCCCc1cccnc1	DB01951_12	Accepted
COc1ccc(cc1OC1CCCC1)C1CNC(=O)C1	DB01954_13	Accepted
NCCS(O)(=O)=O	DB01956_14	Accepted
CC(C)(C)c1ccc(Sc2cccc3nc(N)nc(N)c23)cc1	DB01958_15	Accepted
CCOC(=O)c1c(C)nn(c1C)-c1cccc(c1)[N+]([O-])=O	DB01959_16	Accepted
CN(CC(O)=O)C(N)N	DB02490_17	Accepted
OCC(OS(O)(O)O)C(O)CN1CC(O)C(O)C1CO	DB02492_18	Accepted
N[C@@H](CO[P@](O)(=O)OC[C@@H](O)CO)C(O)=O	DB02497_19	Accepted
N[C@@H](C\N=C(/N)NO)C(O)=O	DB02499_20	Accepted
CNC(=O)C(Cc1ccccc1)NC(=O)C(CC(C)C)C(CSc1cccs1)C(=O)NO	DB03880_21	Accepted
C[C@]12CCC3C(CCC4C[C@@H](O)CC[C@]34C)C1CC[C@@H]2O	DB03882_22	Accepted
OC[C@@H](O)[C@H](O)[C@@H](O)Cn1c2[nH]c(=O)[nH]c(=O)c2nc(CCC(O)=O)c1=O	DB03883_23	Accepted
OC(=O)C(=O)Cc1ccccc1	DB03884_24	Accepted
NC(CCC(=O)NC(CSCc1cccc2ccccc12)C(=O)NCC(O)=O)C(O)=O	DB03885_25	Accepted
C[C@@H](O)[C@@H](O)c1cnc2nc(N)[nH]c(=O)c2n1	DB03886_26	Accepted
Nc1ncnc2ncn([C@@H]3O[C@@H](COP(O)(O)=O)[C@H](O)[C@H]3O)c12	DB03887_27	Accepted
CN(CCCCCCOc1ccc2c(nn(C)c2c1)-c1ccc(Br)cc1)CC=C	DB03888_28	Accepted

NC(CCC(=O)NC(CSC(O)N(O)c1ccc(Br)cc1)C(=O)NCC(O)=O)C(O)=O	DB03889_29	Accepted
CC(=O)NC1C(O)C(F)C(OC1C(O)C(O)CO)C(O)=O	DB04211_30	Accepted
Nc1ccnc2n(cnc12)[C@@H]1O[C@@H](CO)[C@H](O)[C@H]1O	DB04218_31	Accepted
COc1cc(OC)cc(c1)C(=O)NC1C(O)C(CO)OC1n1cnc2c(NC3CCCc4ccccc34)ncnc12	DB04477_32	Accepted
CC(C)(c1ccccc1)c1ccc(O)cc1	DB06902_33	Accepted
CO[C@@H](Cc1ccccc1)[C@@H](C)\C=C(/C)\C=C\[C@H](N)[C@H](C)C(=O)O	DB06905_34	Accepted
CCOC(=O)c1cnc(N)nc1O	DB06906_35	Accepted
CCO[C@@H](Cc1ccc2n(Cc3nc(oc3C)-c3ccccc3Cl)ccc2c1)C(O)=O	DB06908_36	Accepted
CCn1ncc2c(NC3CCOCC3)c(cnc12)C(=O)NCc1ccccc1	DB06909_37	Accepted
NC(Cc1ccccc1)C(=O)N1CCCC1C(=O)NCCNc1ccncc1	DB08422_38	Accepted
Nc1c(cnn1-c1ccc(F)cc1)C(=O)c1cccc(OC2CCNCC2)c1	DB08423_39	Accepted
Nc1c(cnn1-c1ccc(F)cc1)C(=O)c1cccc(OC[C@@H](O)CO)c1	DB08424_40	Accepted
O=C1C(CCN1Cc1cc2ccncc2[nH]1)NS(=O)(=O)c1cc2ncccc2s1	DB08426_41	Accepted
O[C@H]1C=C[C@@](CC(=O)C(O)=O)(C=C1)C(O)=O	DB08427_42	Accepted
OC(=O)[C@H](Cc1ccccc1)Oc1ccc(Cl)cc1	DB08760_43	Accepted
Oc1ccc(CC2NC(=O)C(Cc3ccc(O)cc3)NC2=O)cc1	DB08761_44	Accepted
CC(NC(=O)OCc1ccccc1)C(=O)NC(C)P(O)(=O)OC(Cc1ccccc1)C(O)=O	DB08762_45	Accepted
NC(=N)c1ccc(cc1)C(NC(=O)OCc1ccccc1)P(O)(O)=O	DB08763_46	Accepted
COc1cc2c(cc1OCC1CCN(C)CC1)[nH]cn\c2=N/c1ccc(Br)cc1F	DB08764_47	Accepted
NS(=O)(=O)c1nc2ccc(O)cc2s1	DB08765_48	Accepted
CC(CS)C(=O)N1CC(CC1C(O)=O)Sc1ccccc1	DB08766_49	Accepted
CC(C)=CCNc1ncnc2nc[nH]c12	DB08768_50	Accepted
CC(=O)NCC1CN(C(=O)O1)c1ccc(N2CCOCC2)c(F)c1	DB08769_51	Accepted
C[N+]1(C)CCC(CC1)=C(c1ccccc1)c1ccccc1	DB00729_59	Accepted

Figure A.6 ^{1}H NMR spectrum of compound **6C** in DMSO-d_6.

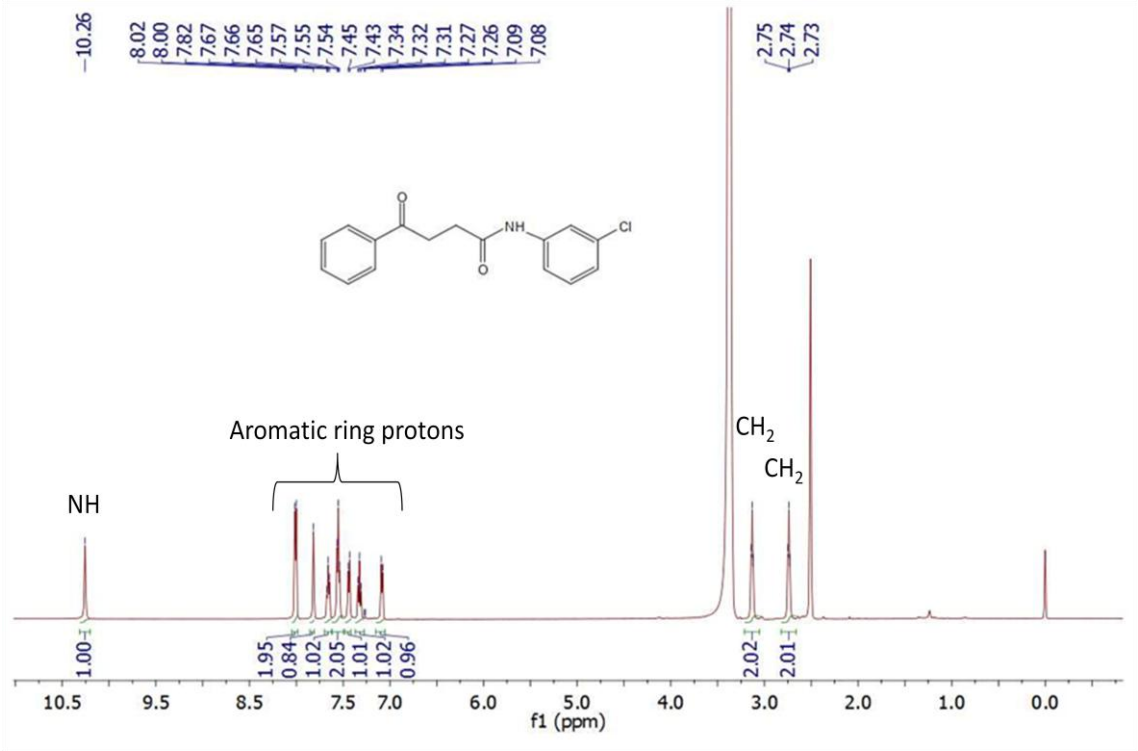


Figure A.7 ^{13}C NMR spectrum of compound **6C** in DMSO-d_6.

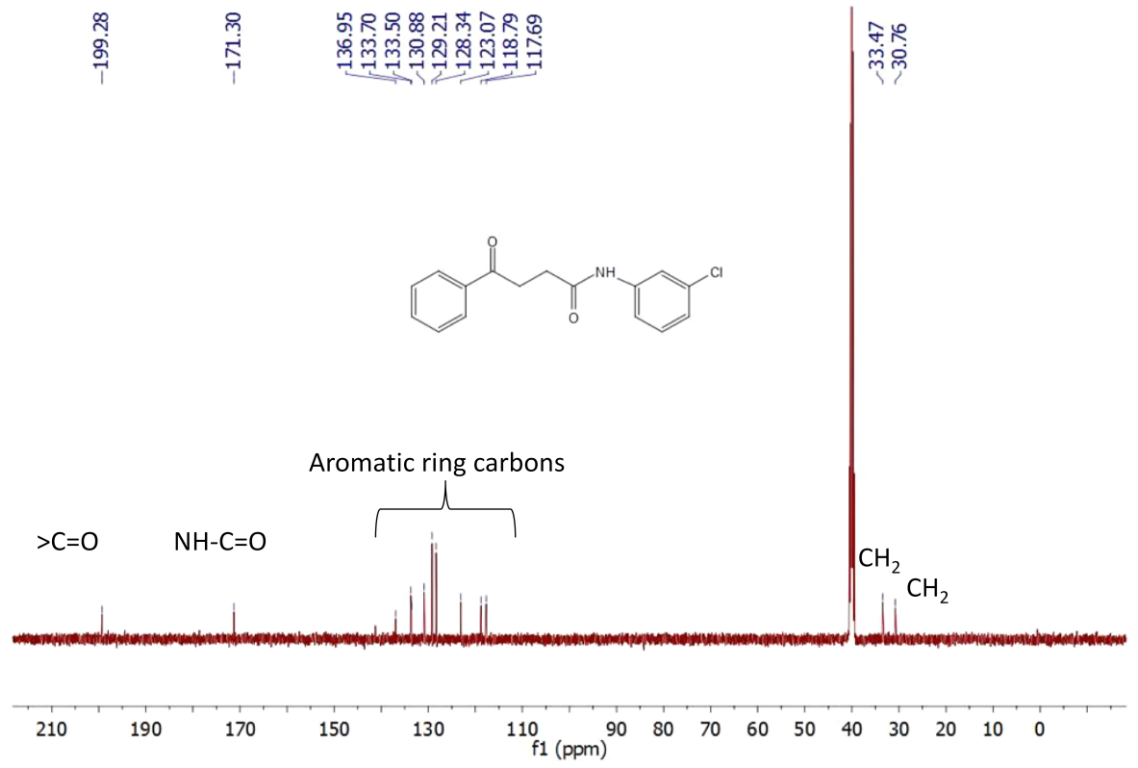


Figure A.8 ^{1}H NMR spectrum of compound **7k** in DMSO-d_6.

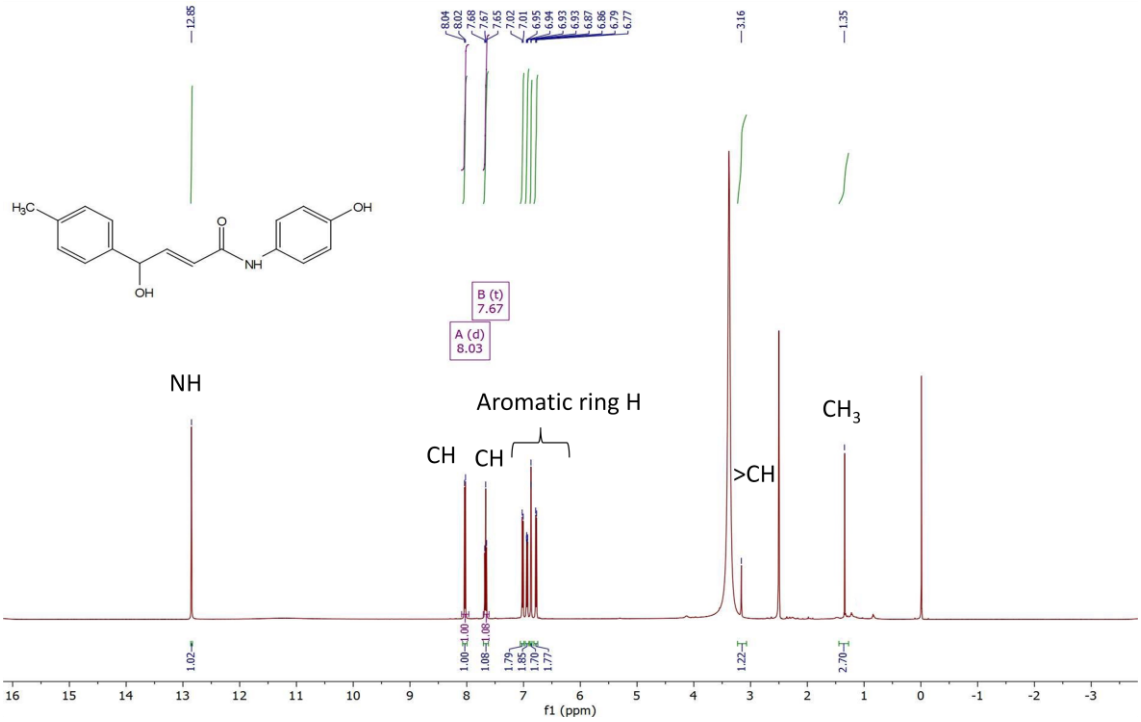


Figure A.9 ^{13}C NMR spectrum of compound **7k** in DMSO-d_6.

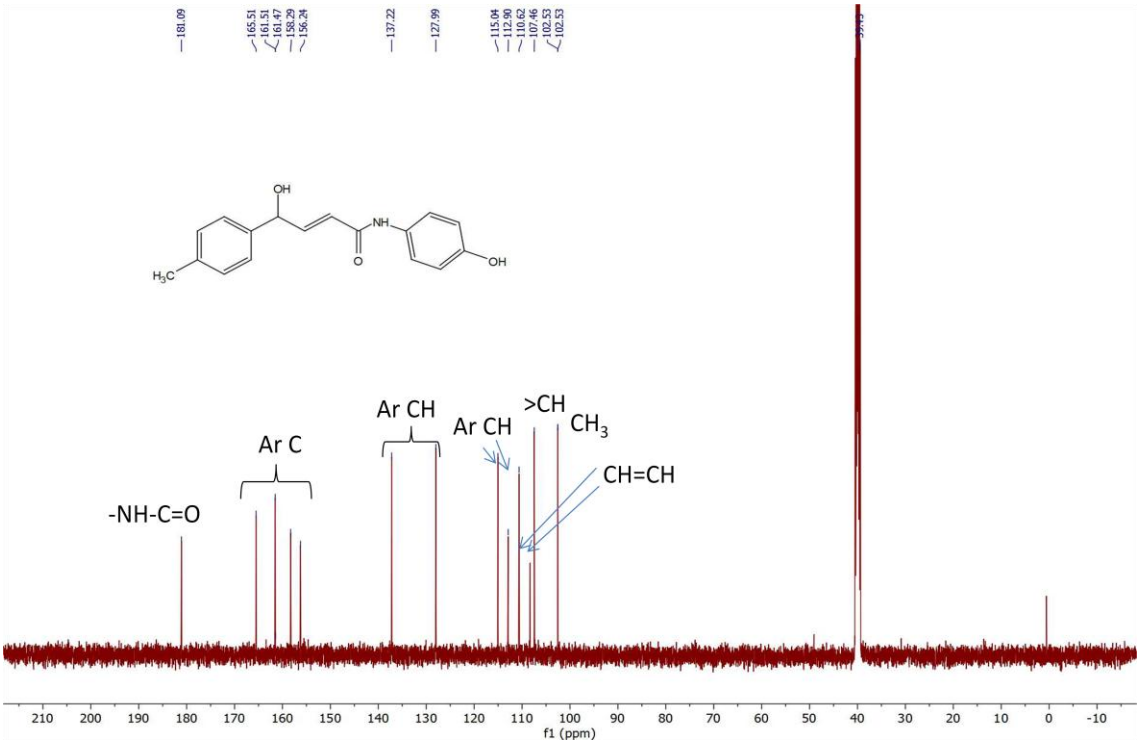


Figure A.10 FTIR spectra of compound **6h**.

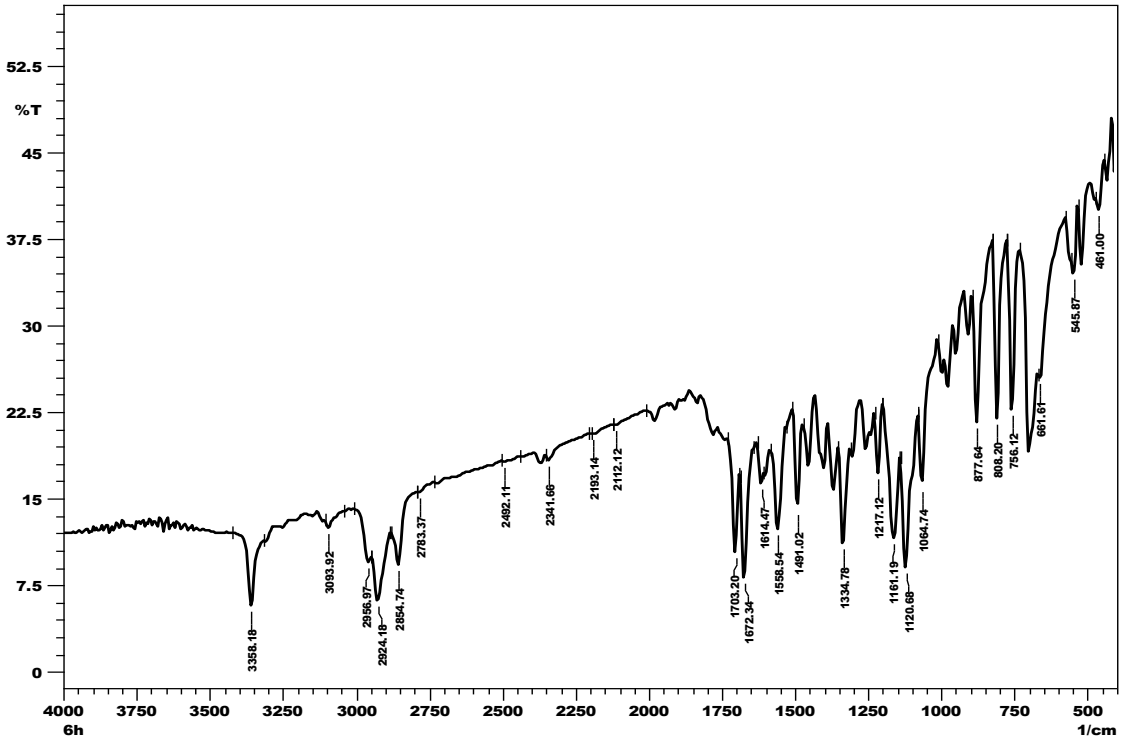


Figure A.11 FTIR spectra of compound **7k**.

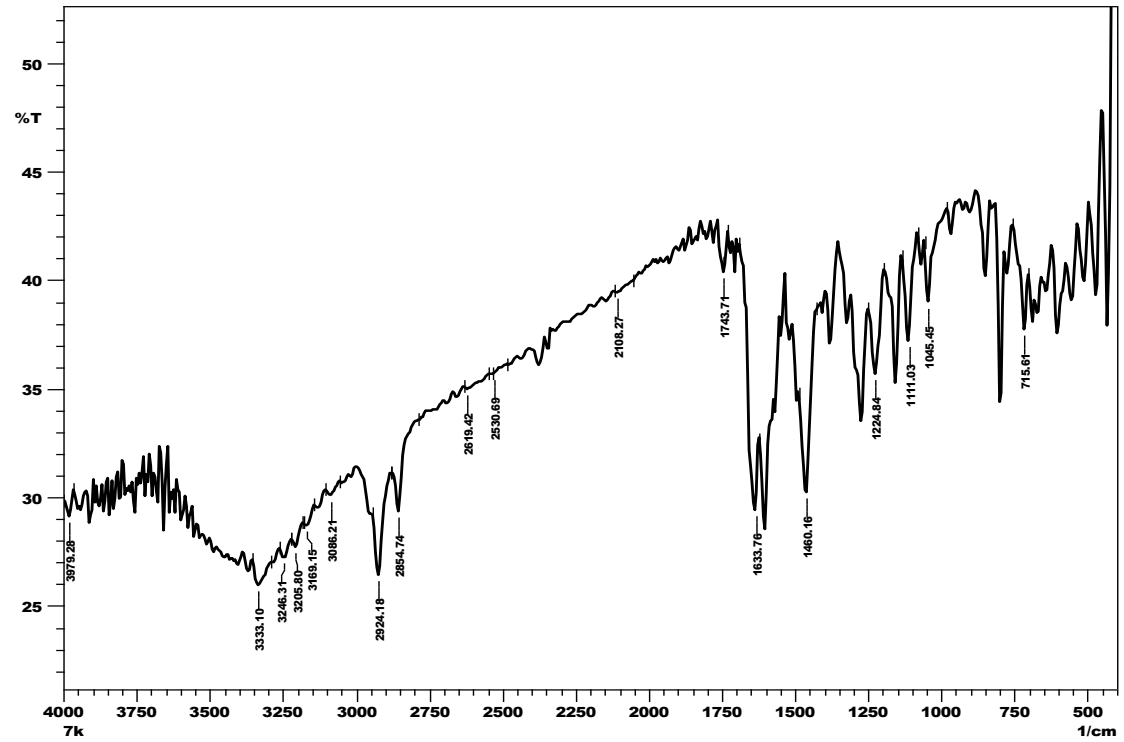
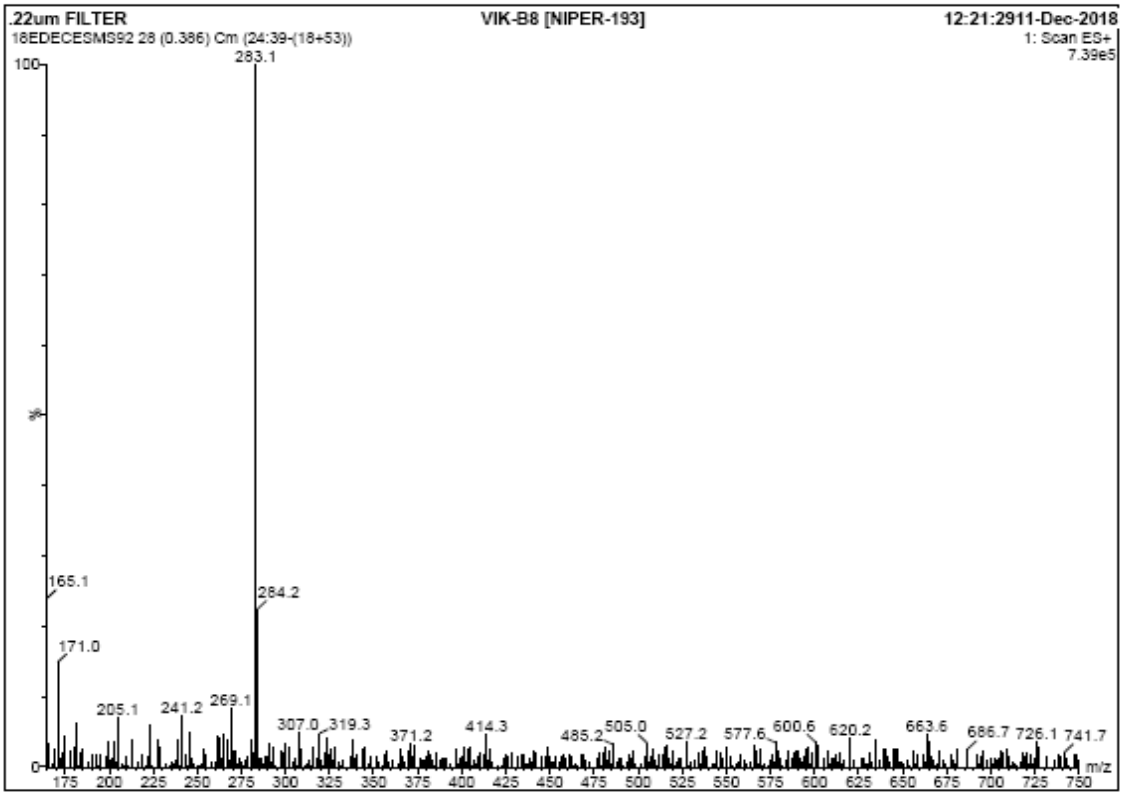


Figure A.12 Mass spectra of Compound **7k**



List of publications from thesis work

1. **S. Jana**, S. K. Singh*, Identification of human tau-tubulin kinase 1 inhibitors: an integrated e-pharmacophore based virtual screening and molecular dynamics simulation, **Journal of Biomolecular Structure and Dynamics**, (2019), doi: 10.1080/07391102.2019. 1590242, (IF 3.107).

2. **S. Jana**, A. Ganeshpurkar, S. K. Singh*, Multiple 3D-QSAR modeling, e-pharmacophore, molecular docking, and *in vitro* study to explore novel AChE inhibitors, **RSC Advances**, (2018), 8(69), 39477-95. (IF 2.936).

3. **S. Jana**, S. K. Singh*, Identification of selective MMP-9 inhibitors through multiple e-pharmacophore, ligand-based pharmacophore, molecular docking, and density functional theory approaches, **Journal of Biomolecular Structure and Dynamics**, (2019), 37(4), 944–965, (IF 3.107).

4. **S. Jana**, T. Nasreen, S. K. Singh*, Synthesis and evaluation of multitargeted anti-Alzheimer's agent derived from 4-oxo-N, 4-diphenyl-butanamides and (E)-N-aryl-4-hydroxy-4-phenylbut-2-enamides (**Under review**).

Other than thesis work

1. A. Ganeshpurkar, R. Swetha, D. Kumar, G. Gangaram, R. Singh, G. Gutti, **S. Jana**, A. Kumar, S. Singh*, Protein-protein interaction and aggregation inhibitors in Alzheimer's disease, **Current topics in medicinal chemistry**, (2019) (IF 3.374).

2. A. Ganeshpurkar, S. Makar, D. Kumar, **S. Jana**, S. K. Singh*, Aspartic Proteases: Potential drug targets for anticancer drug development, Cancer Leading Proteases, **Elsevier book** (**in press**).

Conference presentations

1. 'RICT 2016 Interfacing Chemical Biology and Drug Discovery', Caen, Normandy, France, on July 6–8, 2016, entitled "Design, synthesis, and evaluation of some novel rhodanine derivatives as potent gelatinase inhibitor".

2. 'Emerging Trends in Drug Discovery and Development-2018' (ETDDD-2018), Indian Institute of Technology (BHU), Varanasi, on January 18–20, 2018., entitled "Multiple 3D-QSAR modeling, e-pharmacophore and molecular docking to explore potent AchE inhibitors".

3. 'Trends in Biochemical and Biomedical Research: Advances and Challenges (TBBR-2018)', Department of Biochemistry, Institute of Science, Banaras Hindu University, Varanasi, on February 13–15, 2018 entitled "Identification of selective MMP-9 inhibitors through multiple e-Pharmacophore, ligand-based pharmacophore, molecular docking, and density functional theory approaches".

4. 'The ACS Publications Forum: Expanding Frontiers in Chemical Sciences, in partnership with the Indian Academy of Sciences' on November 1, 2018, Banaras Hindu University, Varanasi.

5. 25th ISCB International Conference (ISCBC-2019), Lucknow, India, on January 12–14, 2019,.entitled "Discovery of N-(4-phenyl)-4-Oxo-4-phenylbutanamides for the treatment of Alzheimer's disease".