

Synthesis of in-silico designed plasmepsin X inhibitors and evaluation of their anti-plasmodial effects

Prem Prakash Sharma,^{1,2} Monika Kumari,^{1,2} Ravindra Kumar,^{3*} Geeta Singh^{1*}

¹Department of Biomedical Engineering, Deenbandhu Chhotu Ram, University of Science & Technology, Murthal, Sonapat Haryana 131039 India. ²Laboratory for Translational Chemistry and Drug Discovery, Department of Chemistry, Hansraj College, University of Delhi, Delhi-110007 India. ³Department of Botany, Hindu College, University of Delhi, Delhi-110007 India.

Supplementary Information

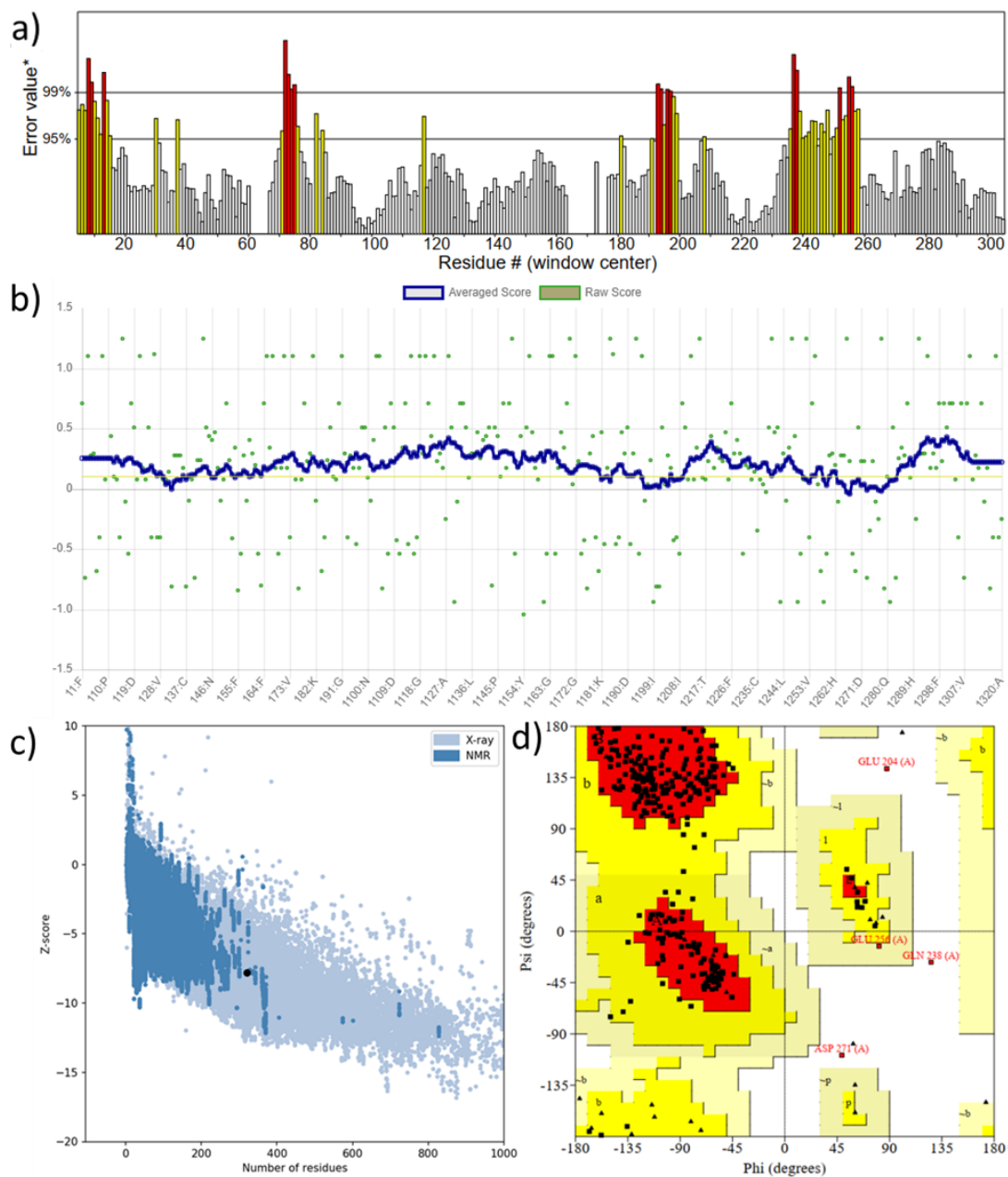


Figure S1. Model structure quality analysis: a) ERRAT, b) Verify3D, c) PROSA, and d) Procheck

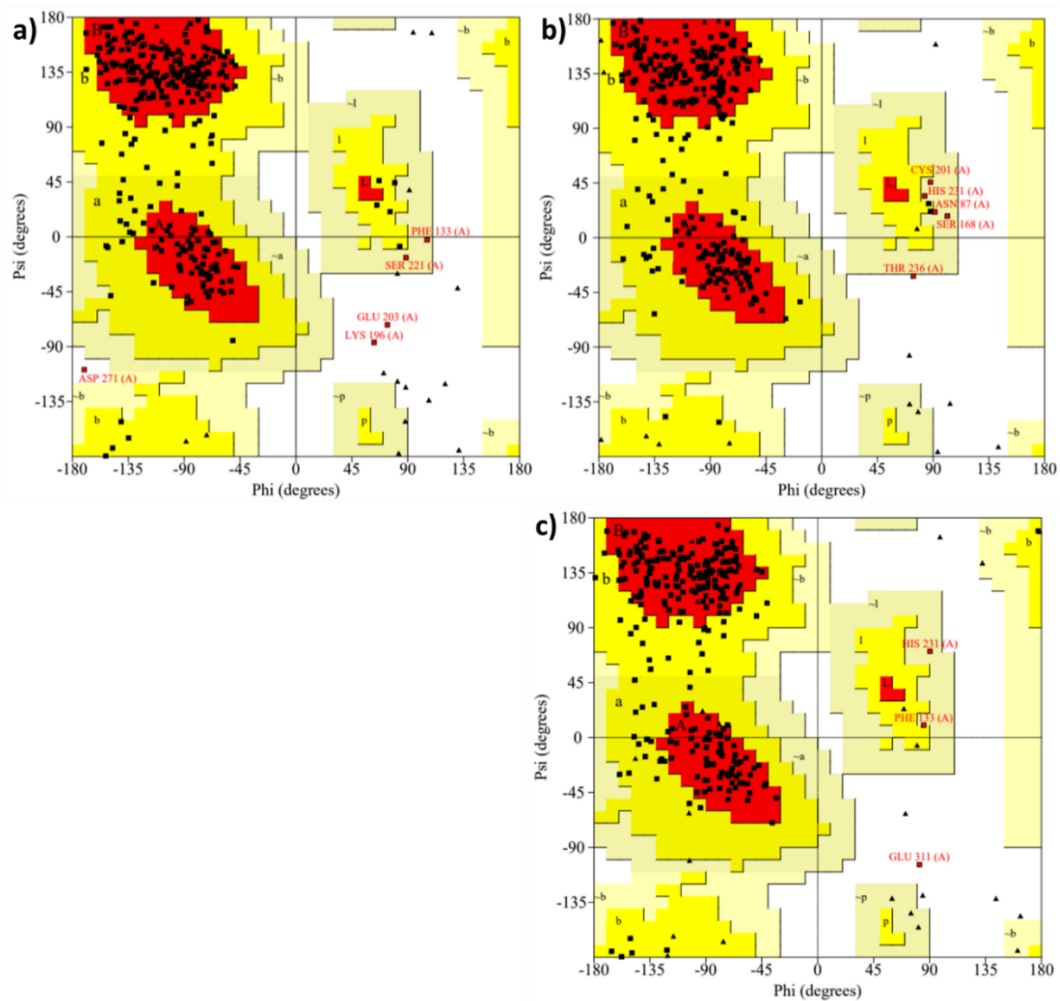


Figure S2. Ramachandran plot: **a)** *PfPlmX-22* complex, **b)** *PfPlmX-49c* complex, and **c)** unligated *PfPlmX*

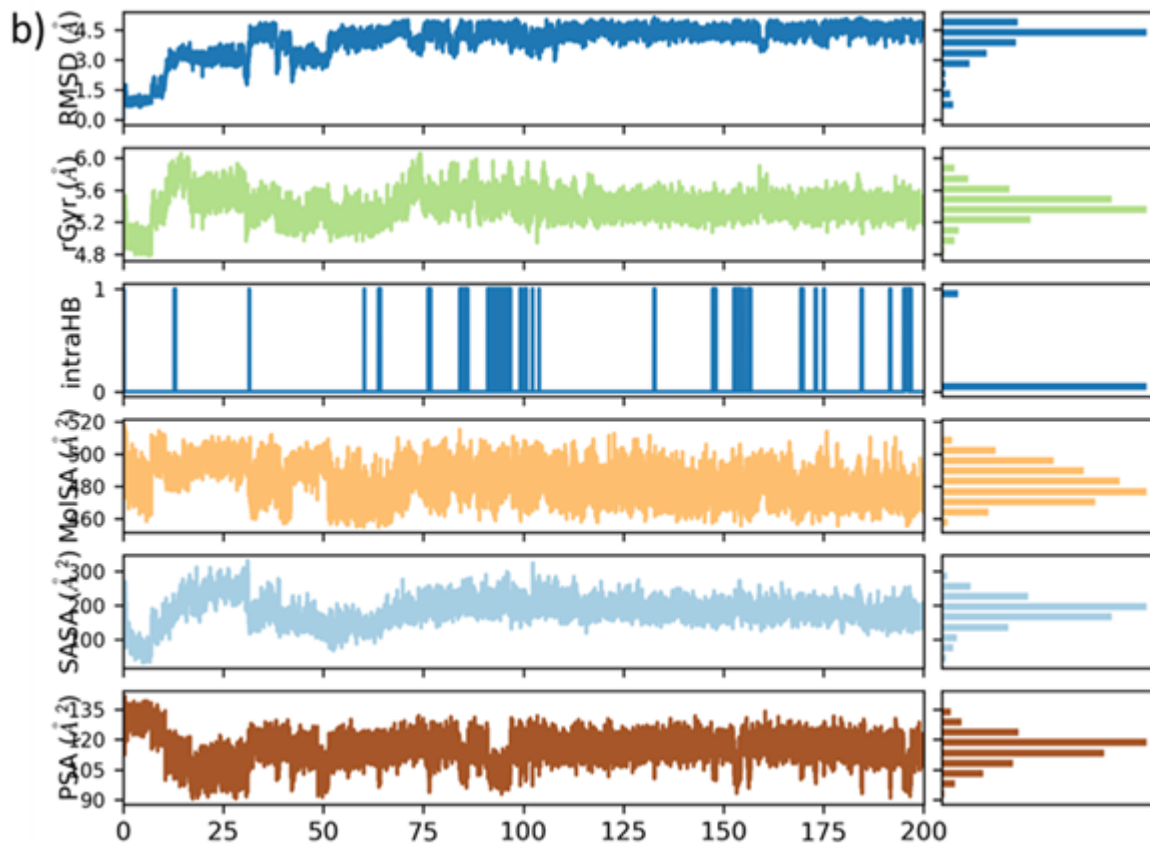


Figure S3. Ligand properties during the 200-ns simulations: (b) *PfPlmX-49c* complex

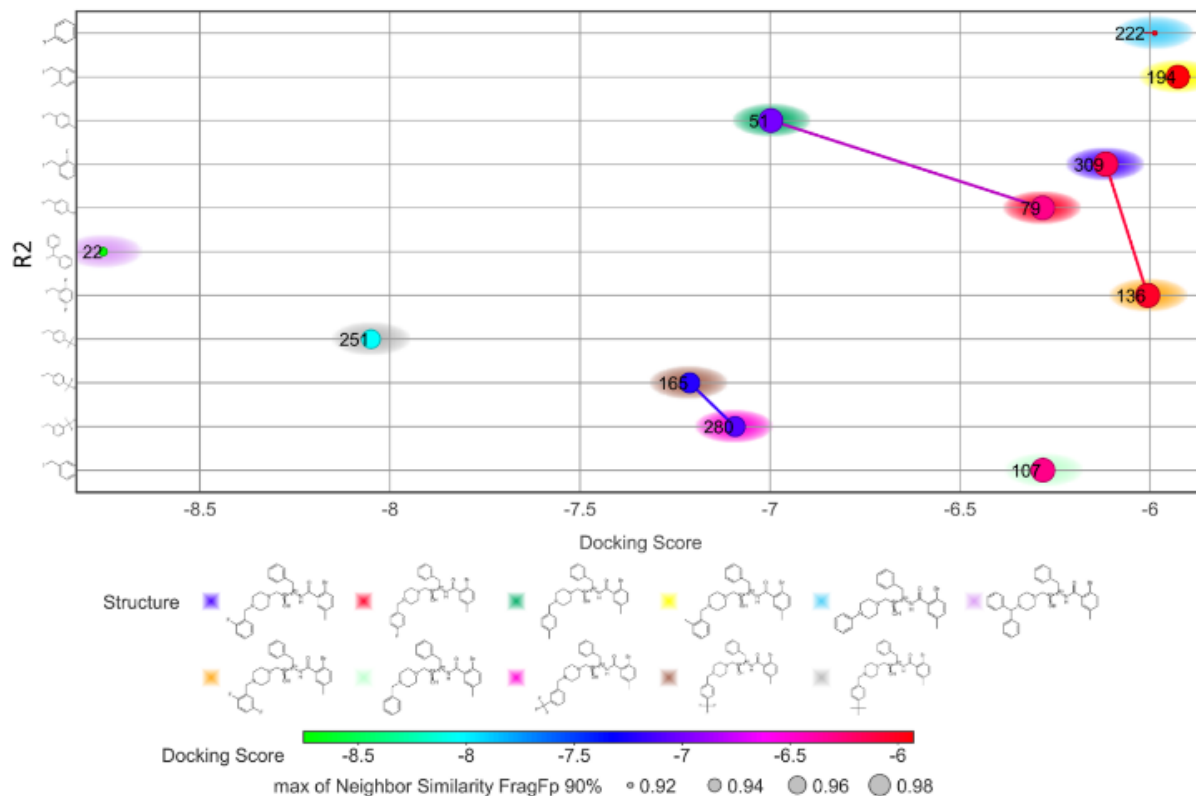


Figure S4. SALI of antiplasmodial compounds having same 2-bromo-5-methylbenzoic acid at pocket I and different substitutions made at pocket II. Compounds arranged according to their docking score and different substitutions at R2. The node size variation symbolizes the structurally similar compounds connected through edge.

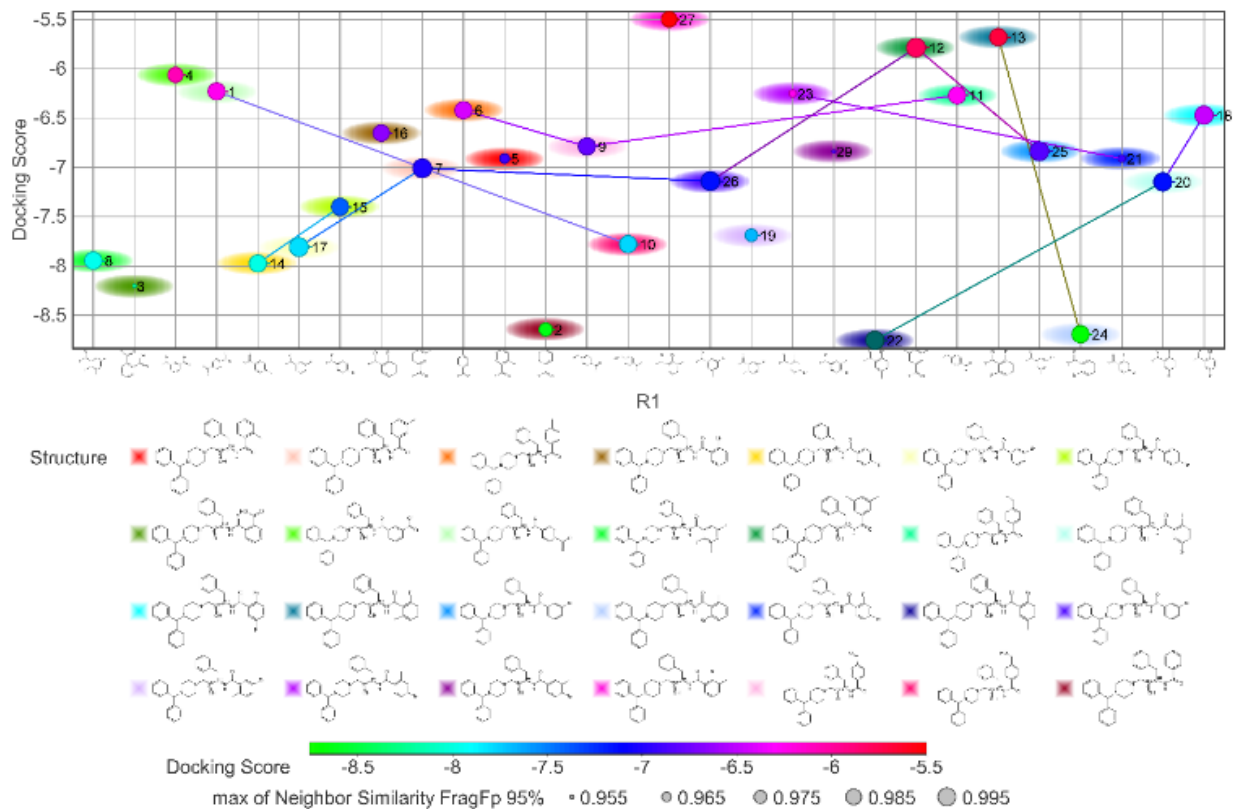


Figure S5. SALI of antiplasmodial compounds having same 1-benzhydrylpiperazine at pocket II and different substitutions made at pocket I. Compounds arranged according to their docking score and different substitutions at R1. The node size variation symbolizes the structurally similar compounds connected through edge.

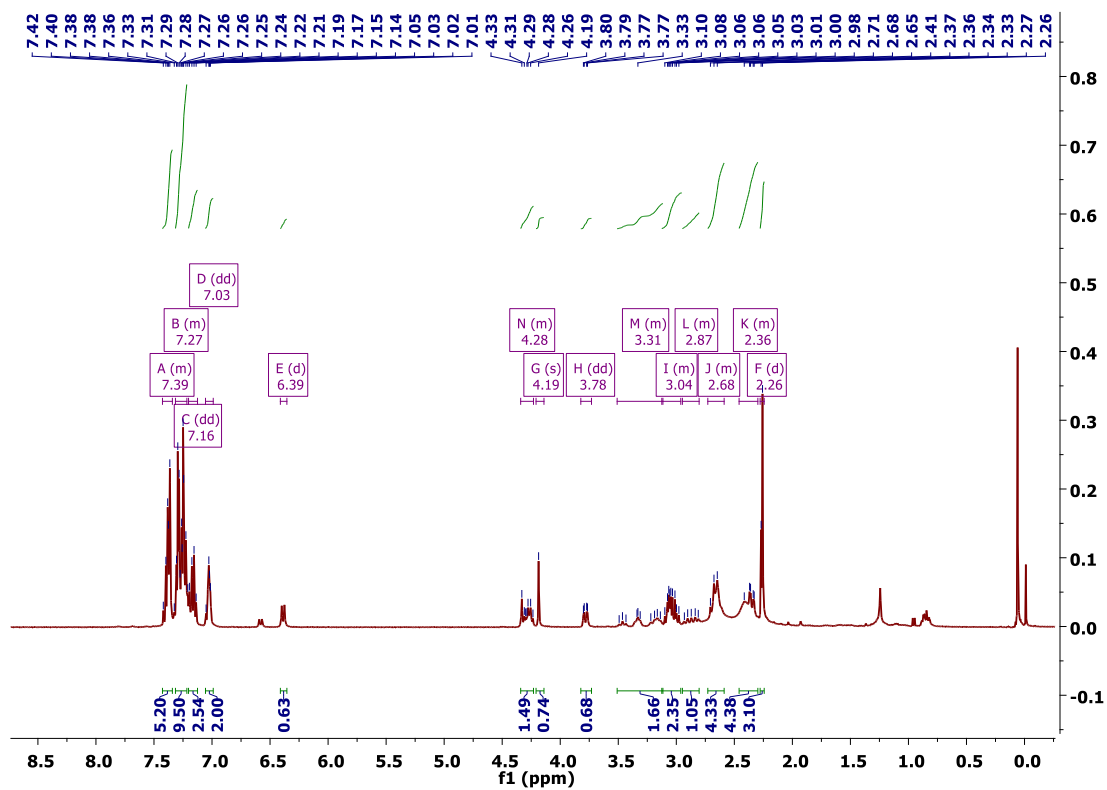


Figure S6. ^1H NMR spectra of **22**, in CDCl_3

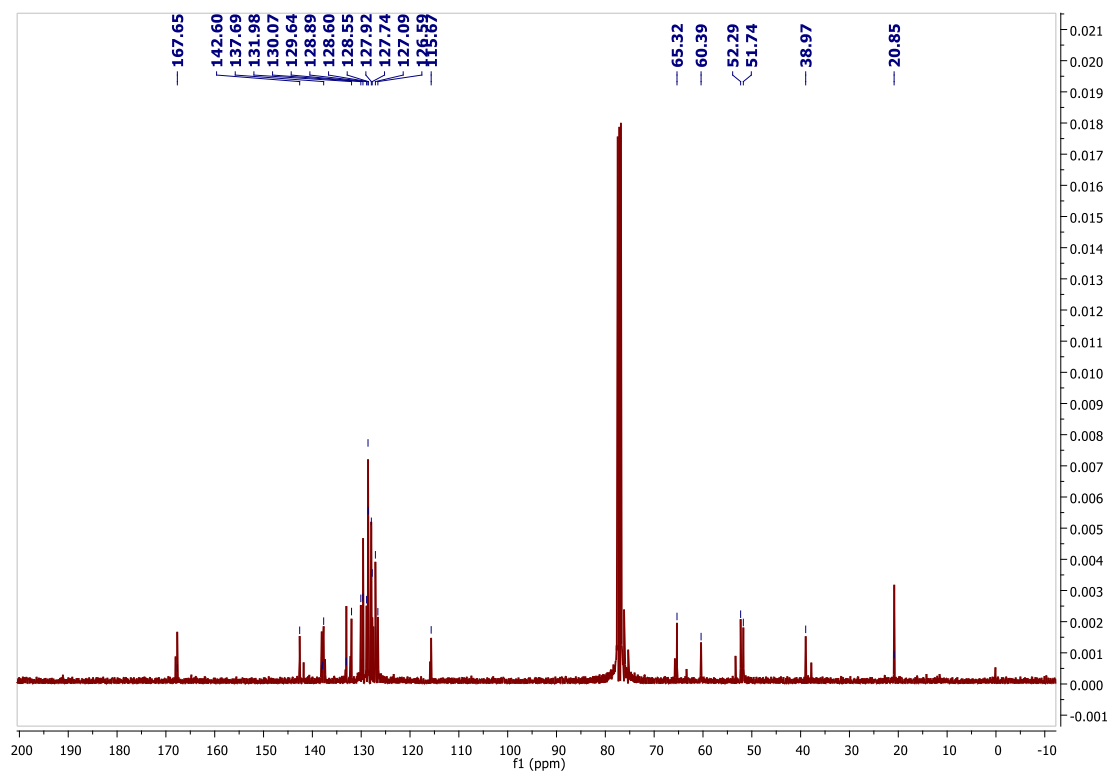


Figure S7. ^{13}C NMR spectra of **22**, in CDCl_3

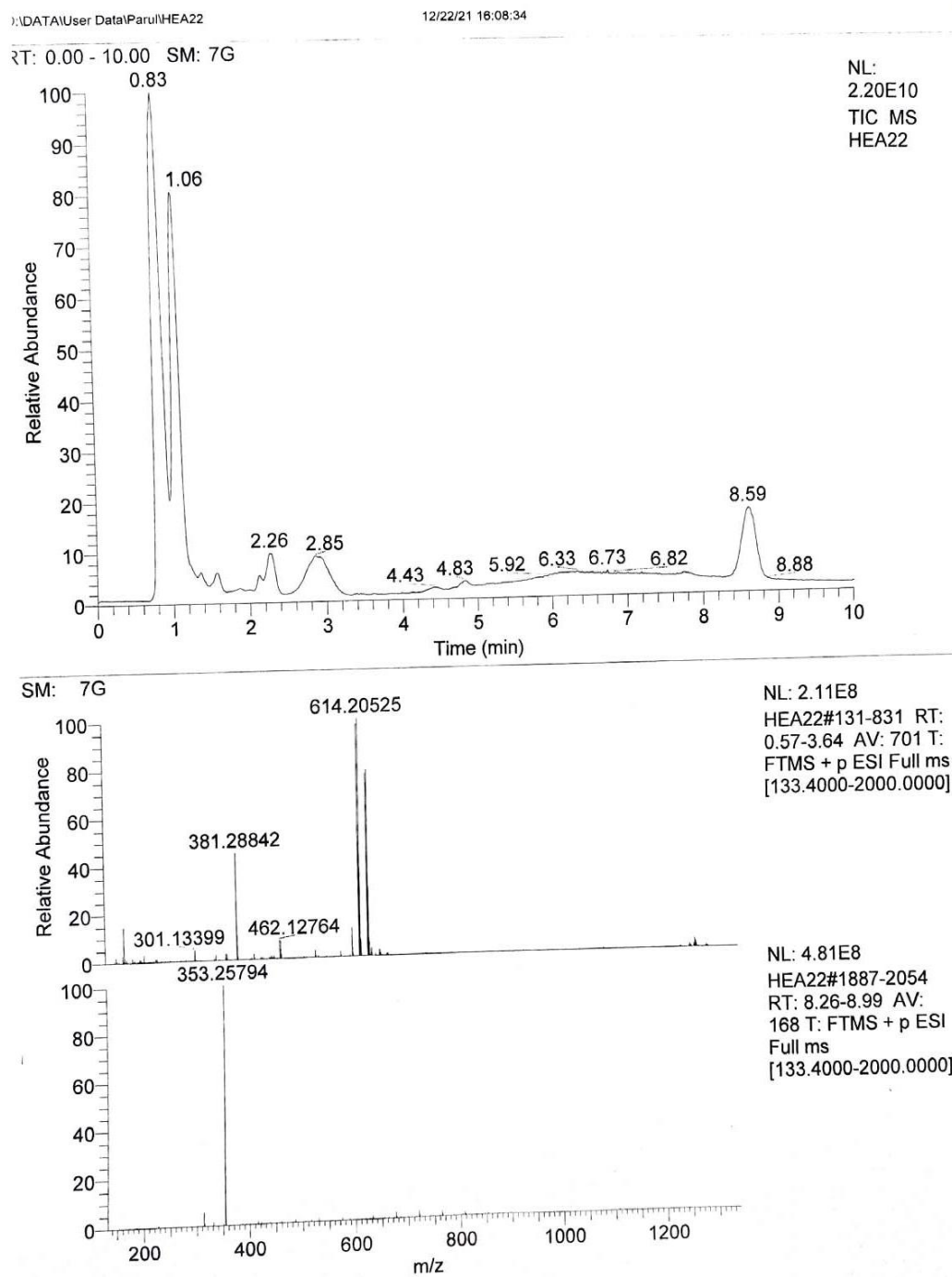
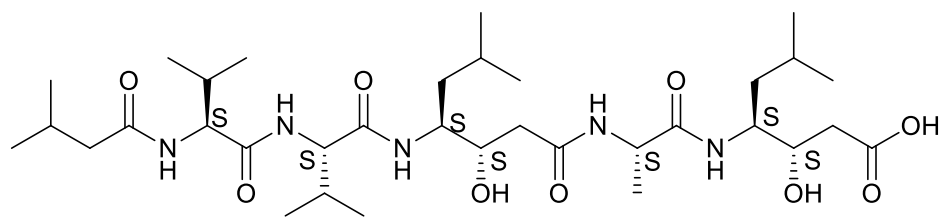
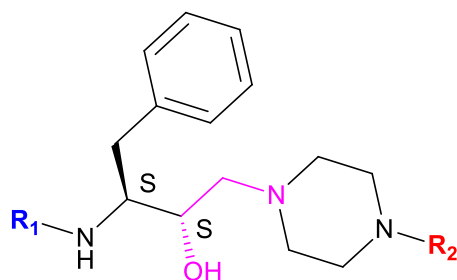


Figure S8. ESI-HRMS spectra of **22**



Papstatin A



HEA-Piperazine analogs

Figure S9. Stereo geometry of pepstatin A and HEA-piperazine analogs

Table S1. Docking results of compounds having docking score more than cut off value

Entry no	Compounds	Structure	Docking score	XP Gcore
1	24		-8.693	-8.718
2	2		-8.644	-8.668
3	180		-8.542	-8.732

4	153		-8.380	-8.869
5	37		-8.358	-10.530
6	213		-8.279	-8.279
7	261		-8.211	-10.300
8	3		-8.204	-8.226
9	313		-8.108	-10.280
10	152		-8.097	-8.287
11	151		-8.064	-10.236

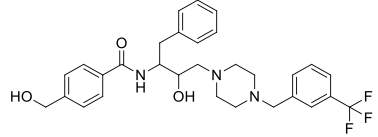
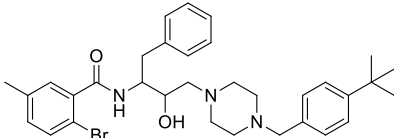
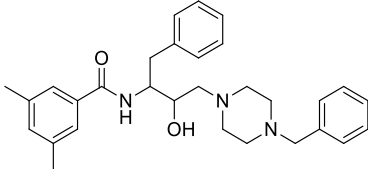
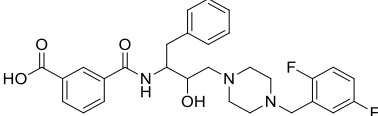
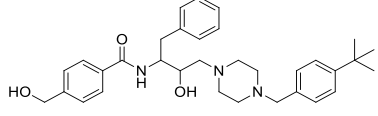
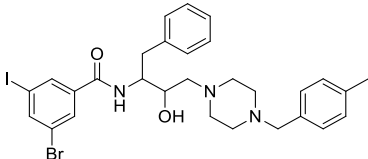
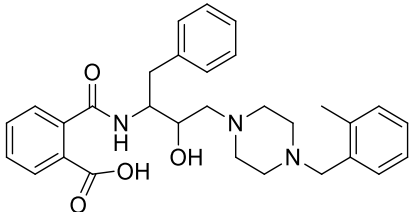
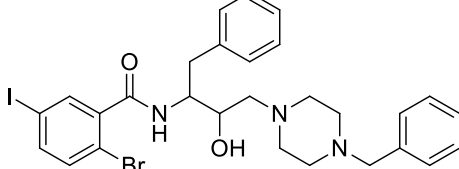
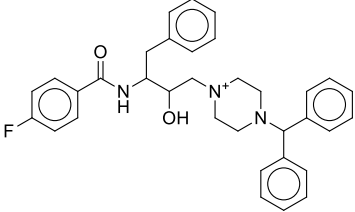
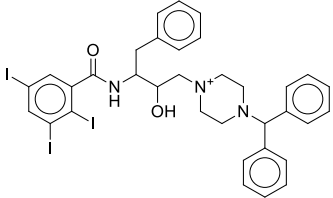
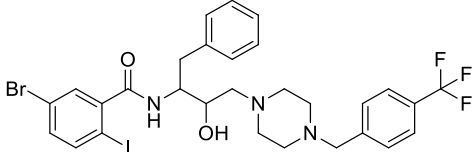
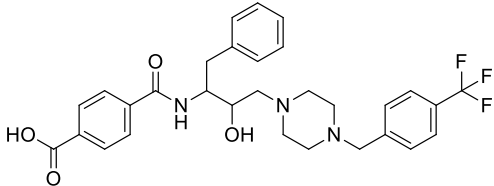
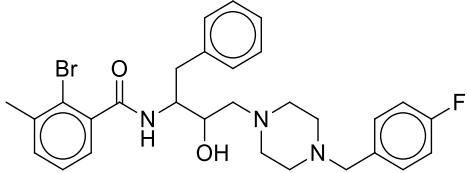
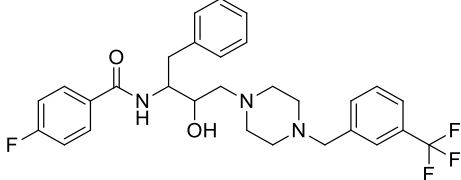
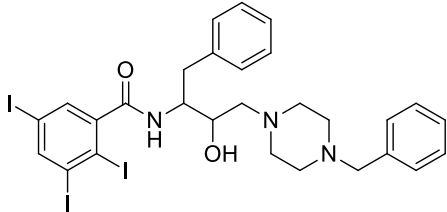
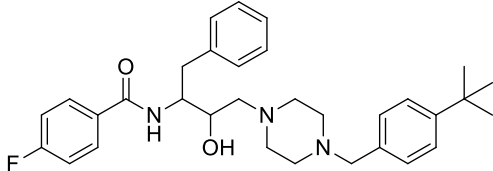
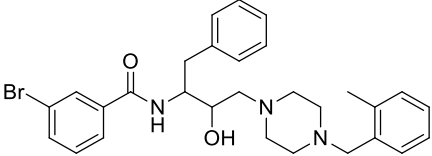
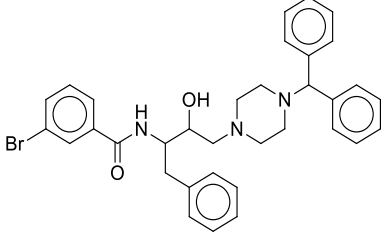
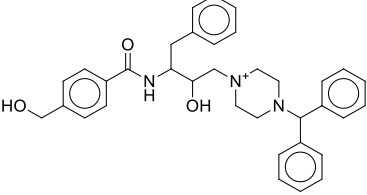
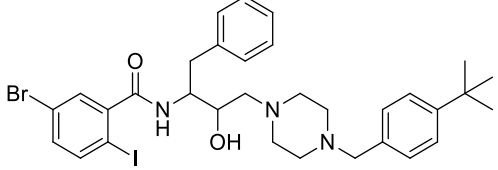
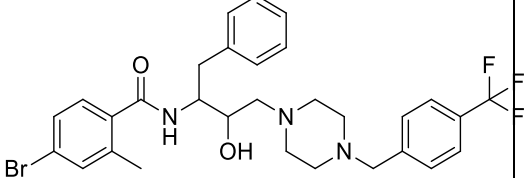
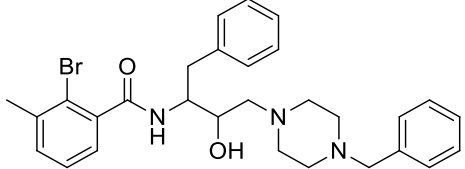
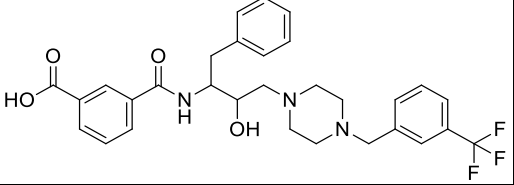
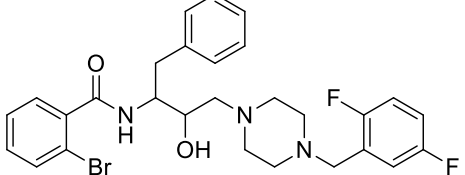
12	268		-8.064	-10.237
13	251		-8.050	-8.239
14	98		-8.031	-8.221
15	118		-8.028	-10.116
16	239		-8.023	-8.212
17	54		-8.003	-10.175

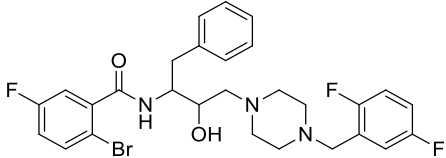
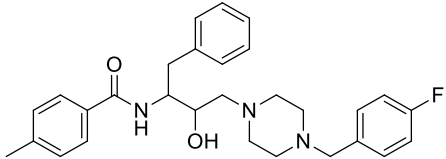
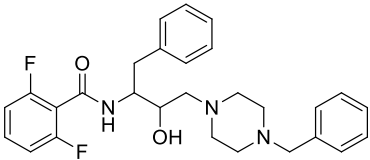
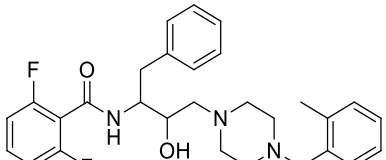
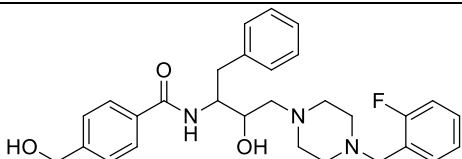
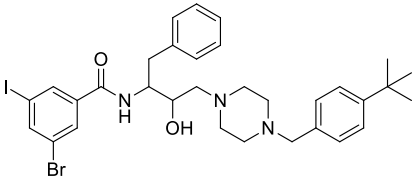
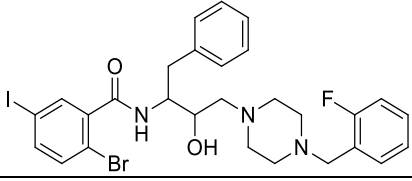
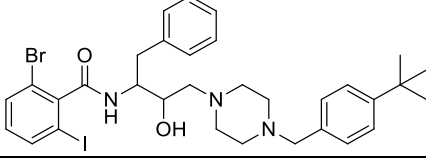
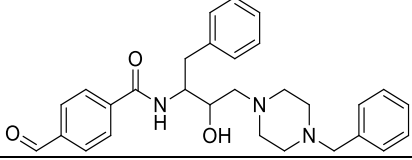
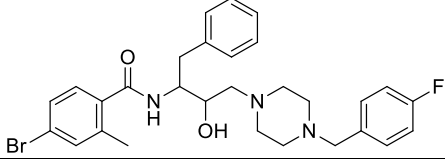
Table S2. Docking results of compounds having docking score lower than cut off value

Entry	Compound	Structures	Docking score	XP GScore
1	175		-7.994	-8.435
2	113		-7.988	-10.160

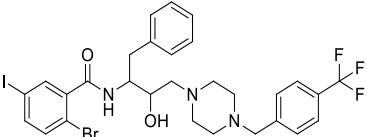
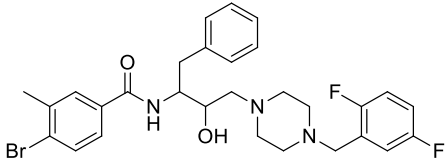
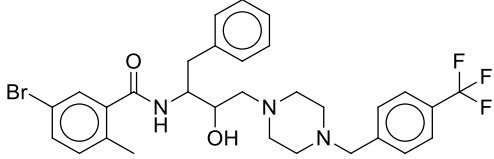
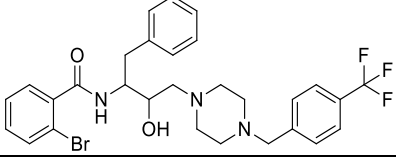
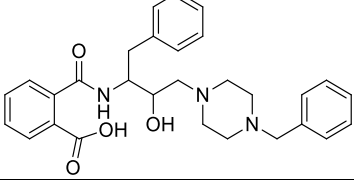
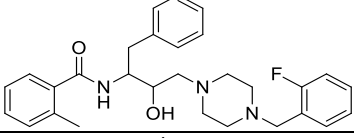
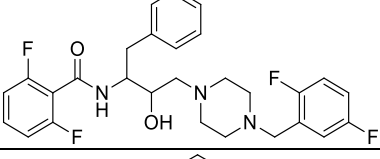
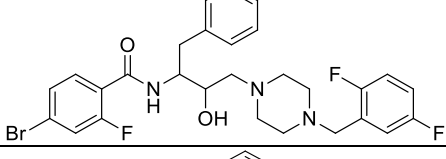
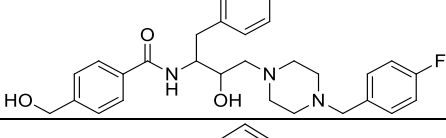
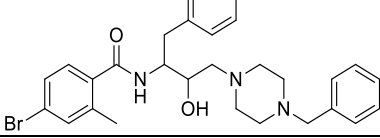
3	14		-7.975	-7.999
4	8		-7.947	-7.971
5	163		-7.864	-8.053
6	144		-7.858	-8.299
7	84		-7.834	-8.024
8	272		-7.827	-9.999
9	94		-7.820	-8.010
10	243		-7.820	-8.010

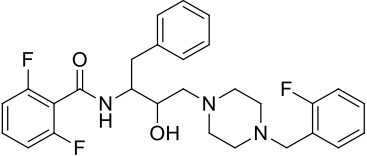
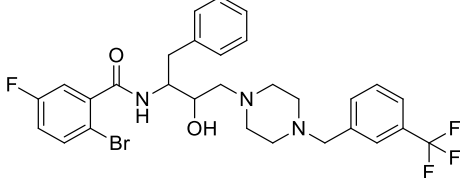
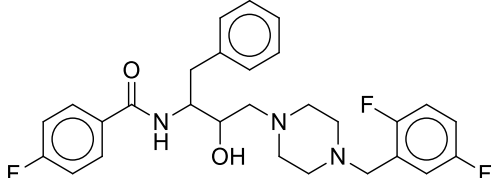
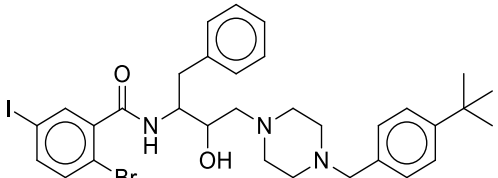
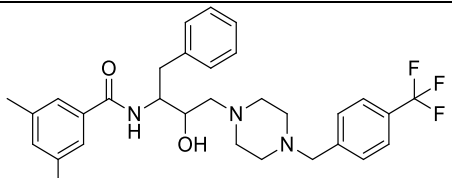
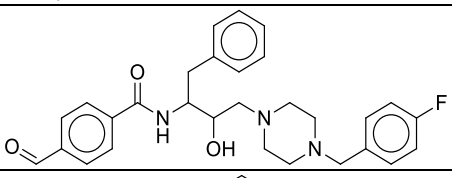
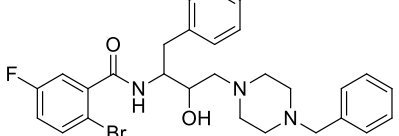
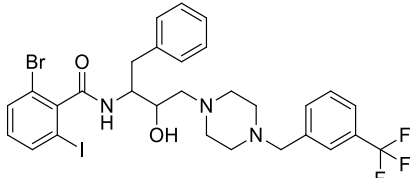
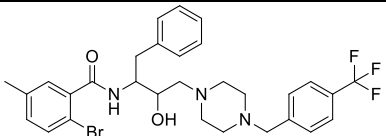
11	189		-7.809	-8.644
12	17		-7.809	-7.833
13	10		-7.779	-7.803
14	249		-7.777	-9.949
15	166		-7.776	-7.966
16	112		-7.760	-7.949
17	262		-7.756	-8.196
18	130		-7.736	-9.908

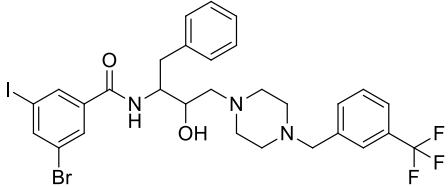
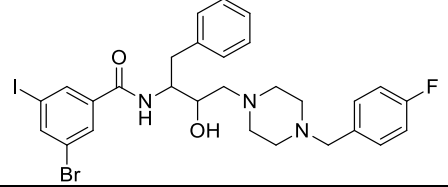
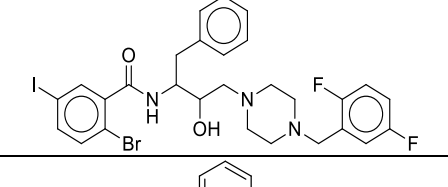
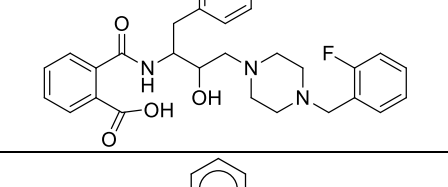
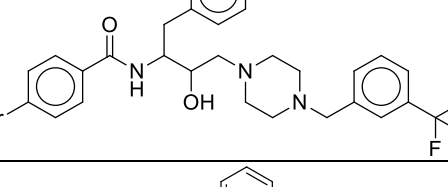
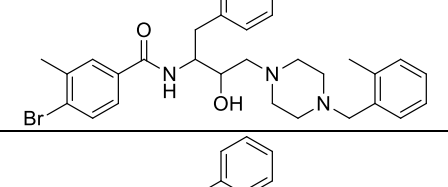
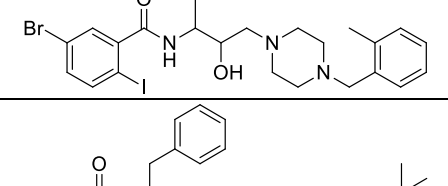
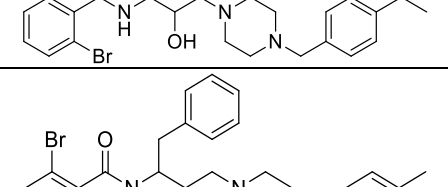
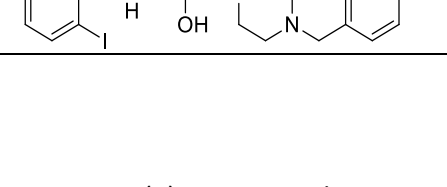
19	19		-7.689	-7.713
20	285		-7.684	-9.856
21	311		-7.671	-7.861
22	178		-7.623	-8.458
23	141		-7.605	-9.777
24	169		-7.594	-9.766
25	264		-7.592	-7.782
26	83		-7.583	-8.418
27	259		-7.578	-9.666

28	132		-7.573	-9.763
29	64		-7.566	-9.738
30	99		-7.544	-9.716
31	185		-7.542	-9.714
32	297		-7.513	-9.703
33	254		-7.501	-7.69
34	315		-7.489	-7.678
35	253		-7.48	-7.67
36	95		-7.428	-7.617
37	80		-7.418	-7.608

38	15		-7.401	-7.426
39	93		-7.391	-7.58
40	238		-7.369	-7.558
41	248		-7.360	-7.550
42	241		-7.347	-7.537
43	87		-7.344	-9.432
44	197		-7.344	-7.534
45	230		-7.332	-9.42
46	49		-7.326	-7.515

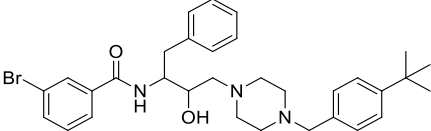
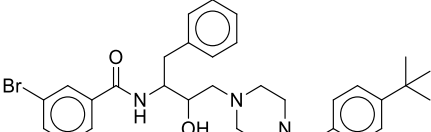
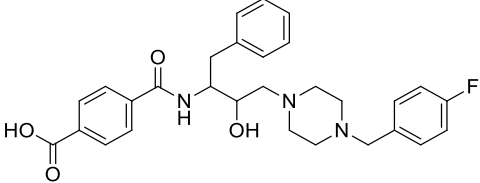
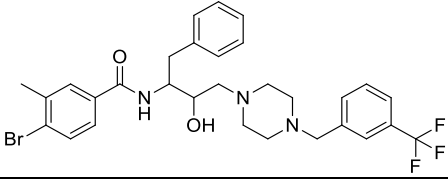
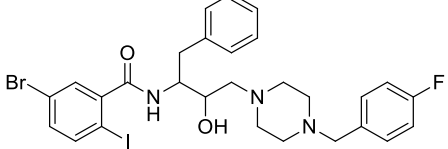
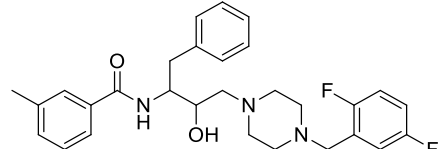
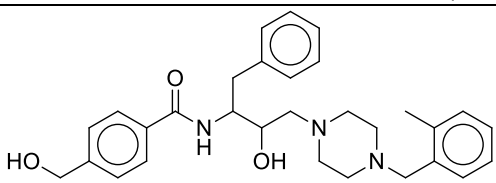
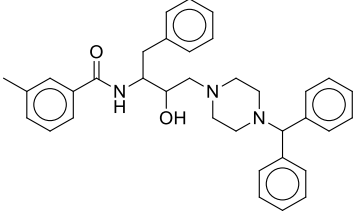
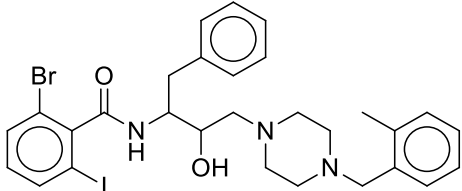
47	171		-7.32	-7.51
48	143		-7.315	-7.504
49	162		-7.313	-9.485
50	159		-7.305	-9.477
51	89		-7.296	-9.384
52	292		-7.292	-7.482
53	127		-7.29	-9.462
54	135		-7.281	-9.453
55	68		-7.28	-7.47
56	108		-7.276	-9.448

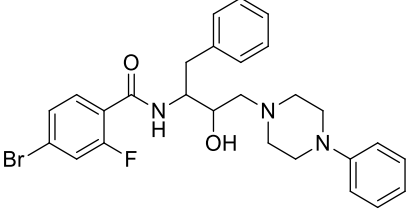
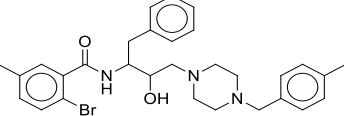
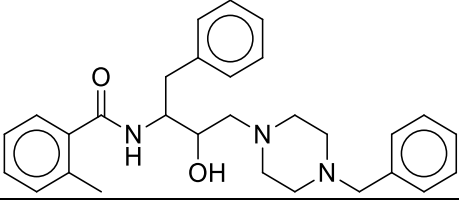
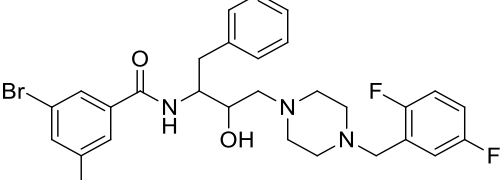
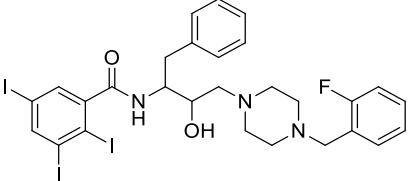
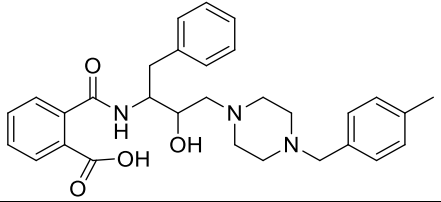
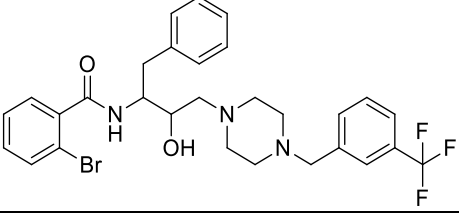
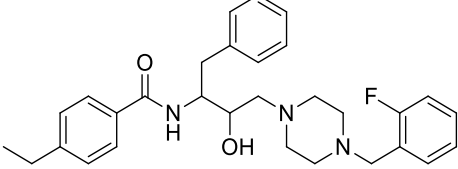
57	300		-7.276	-9.448
58	276		-7.255	-9.427
59	128		-7.248	-7.438
60	257		-7.246	-8.081
61	155		-7.24	-9.412
62	67		-7.239	-7.429
63	104		-7.228	-9.4
64	282		-7.227	-7.416
65	165		-7.211	-9.383

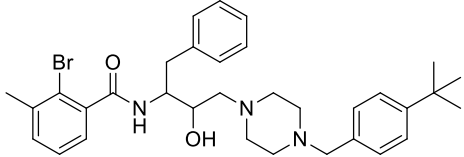
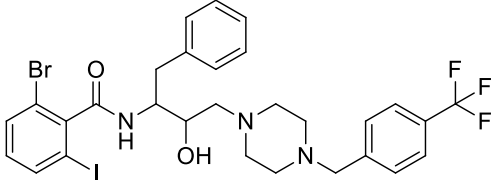
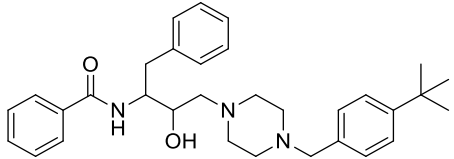
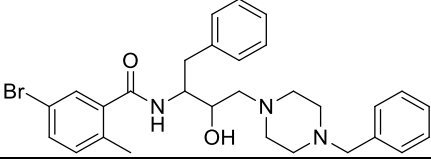
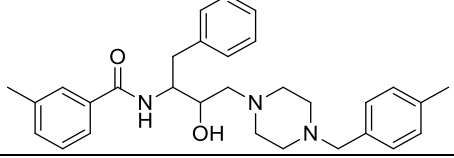
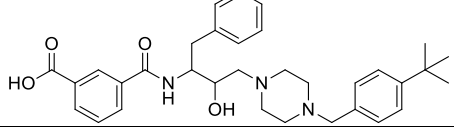
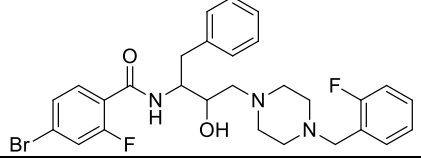
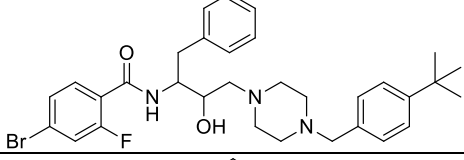
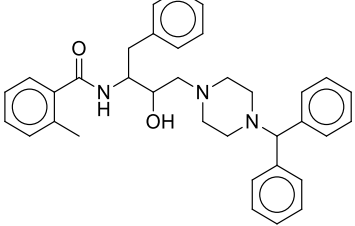
66	283		-7.21	-9.382
67	82		-7.21	-9.382
68	142		-7.202	-9.374
69	290		-7.202	-7.642
70	273		-7.196	-7.386
71	201		-7.172	-7.361
72	192		-7.159	-7.348
73	245		-7.159	-7.348
74	53		-7.158	-7.347

75	20		-7.147	-7.172
76	26		-7.140	-7.164
77	252		-7.132	-7.322
78	168		-7.128	-7.318
79	284		-7.118	-7.307
80	306		-7.11	-9.282
81	302		-7.105	-9.277
82	90		-7.095	-9.183
83	280		-7.092	-7.281

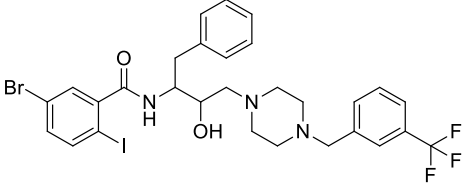
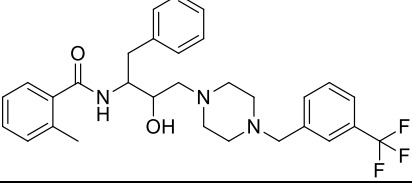
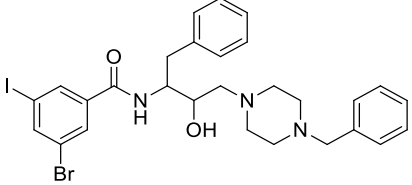
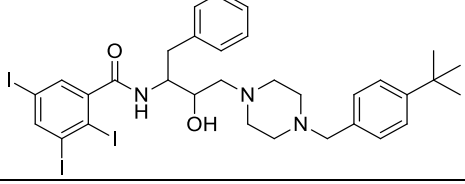
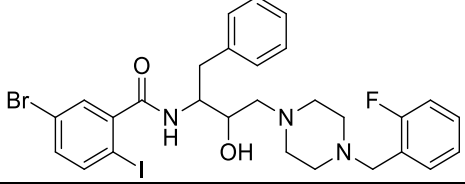
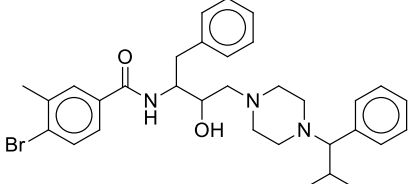
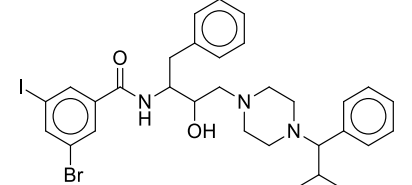
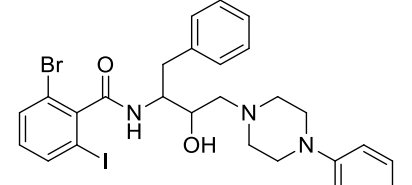
84	312		-7.083	-9.255
85	138		-7.077	-7.267
86	106		-7.076	-7.265
87	97		-7.059	-7.249
88	117		-7.058	-7.499
89	148		-7.058	-9.23
90	275		-7.057	-7.246
91	42		-7.048	-7.237
92	210		-7.046	-7.046

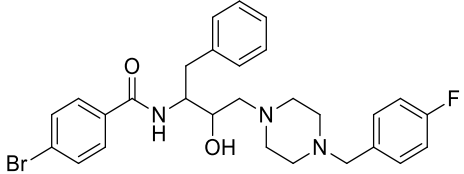
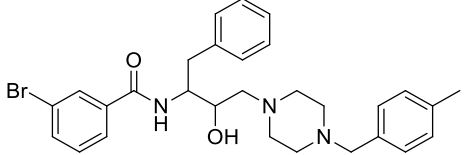
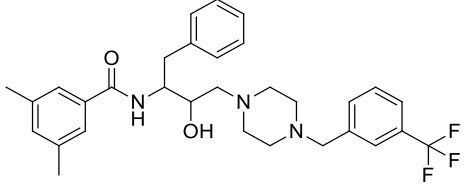
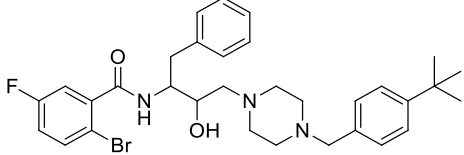
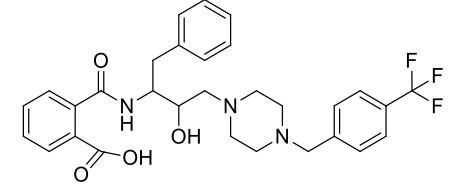
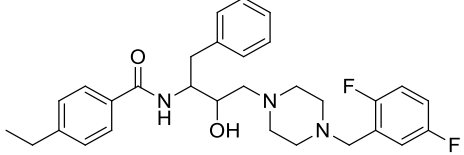
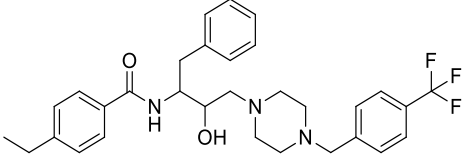
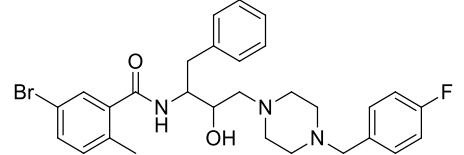
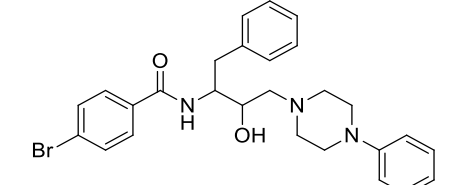
93	246		-7.044	-9.216
94	255		-7.04	-9.212
95	59		-7.037	-9.125
96	287		-7.036	-7.226
97	77		-7.03	-7.22
98	121		-7.029	-7.864
99	182		-7.018	-7.208
100	7		-7.010	-7.034
101	196		-7.001	-7.19

102	221		-7	-7
103	51		-6.997	-7.187
104	91		-6.991	-9.163
105	140		-6.989	-7.824
106	295		-6.982	-7.172
107	32		-6.98	-7.421
108	274		-6.956	-7.145
109	298		-6.949	-7.139

110	256		-6.937	-9.109
111	167		-6.937	-7.126
112	231		-6.934	-7.124
113	105		-6.933	-9.105
114	36		-6.925	-7.114
115	233		-6.924	-9.012
116	308		-6.921	-9.094
117	250		-6.919	-7.108
118	5		-6.912	-6.936

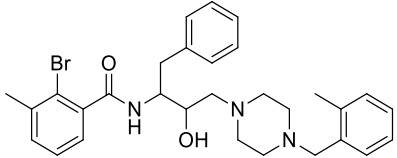
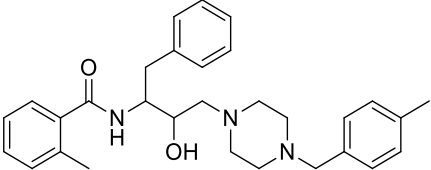
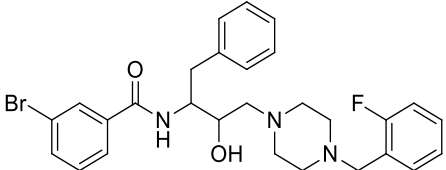
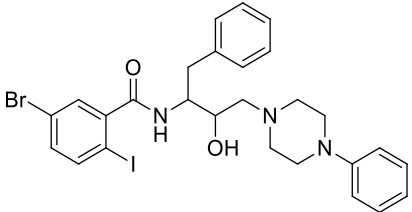
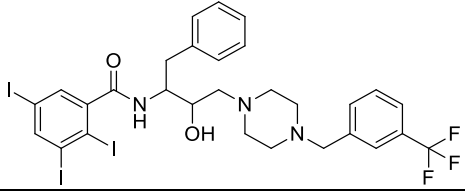
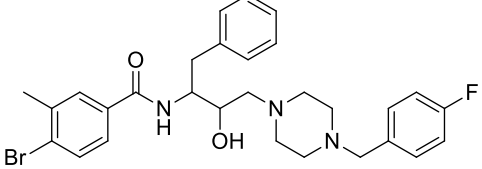
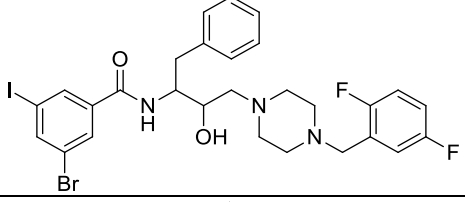
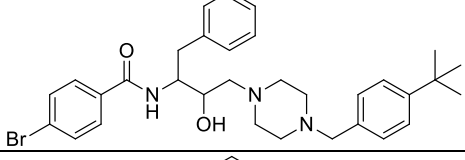
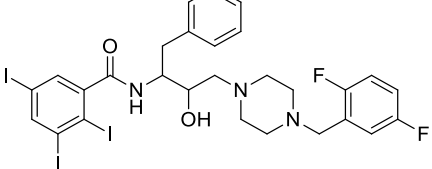
119	21		-6.911	-6.935
120	124		-6.895	-9.068
121	187		-6.891	-7.08
122	203		-6.891	-6.891
123	61		-6.883	-7.324
124	137		-6.874	-9.046
125	156		-6.874	-9.046
126	242		-6.869	-9.041

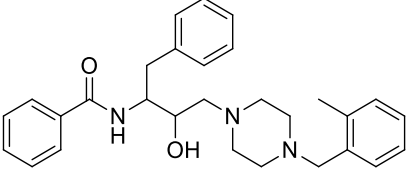
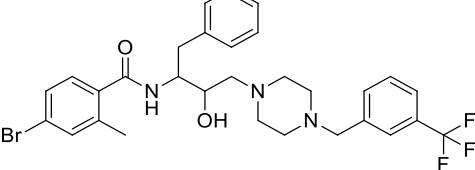
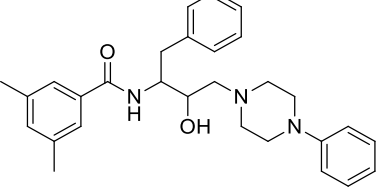
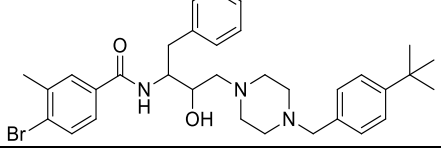
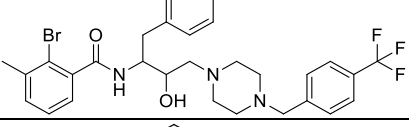
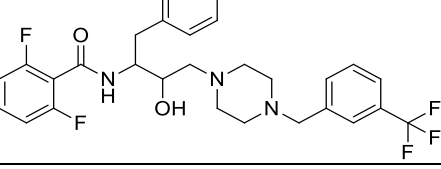
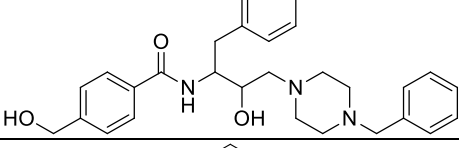
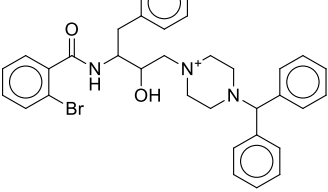
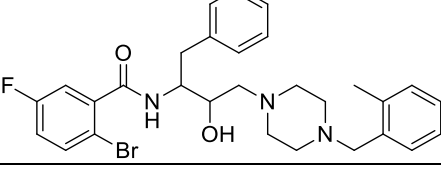
127	278		-6.864	-7.054
128	263		-6.863	-7.053
129	110		-6.85	-7.04
130	237		-6.848	-7.038
131	307		-6.845	-7.034
132	29		-6.839	-6.864
133	25		-6.838	-6.862
134	224		-6.819	-6.819

135	72		-6.818	-7.653
136	46		-6.815	-8.987
137	270		-6.812	-8.984
138	247		-6.81	-6.999
139	146		-6.801	-7.242
140	125		-6.8	-6.989
141	154		-6.798	-6.988
142	76		-6.793	-8.965
143	215		-6.793	-6.793

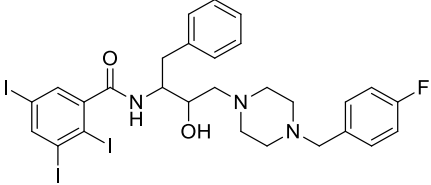
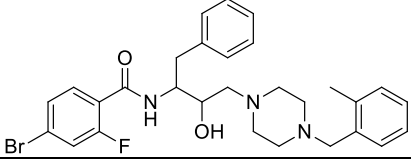
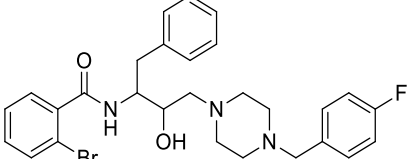
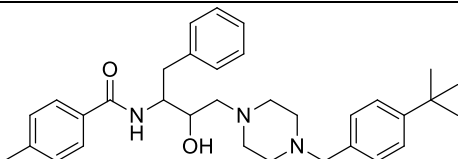
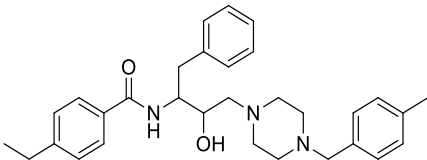
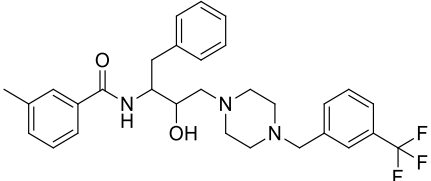
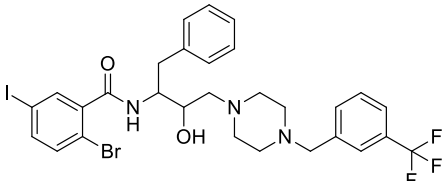
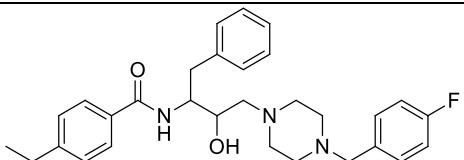
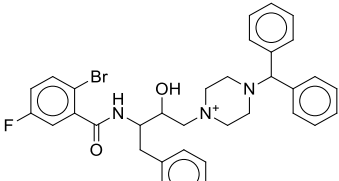
144	57		-6.792	-6.981
145	39		-6.791	-6.981
146	147		-6.79	-8.878
147	9		-6.789	-6.813
148	183		-6.787	-8.959
149	74		-6.786	-6.975
150	44		-6.785	-6.975
151	31		-6.78	-6.969
152	310		-6.779	-8.951

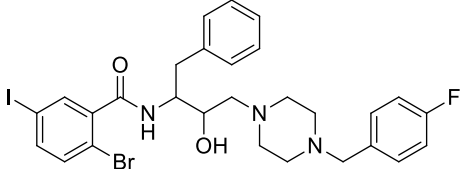
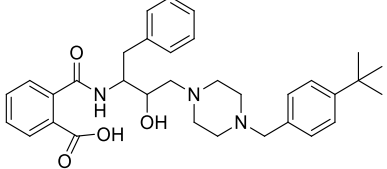
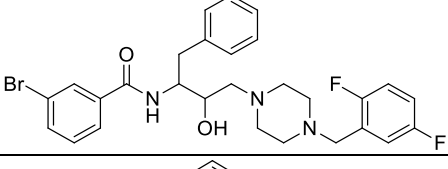
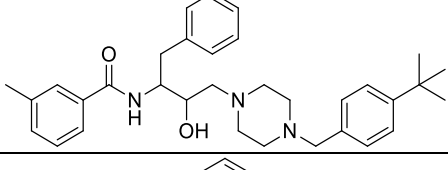
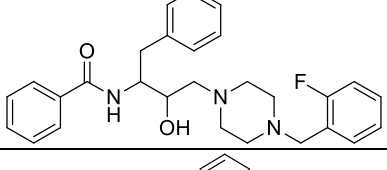
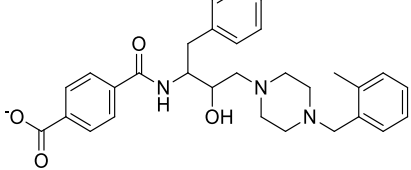
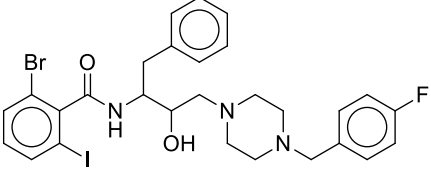
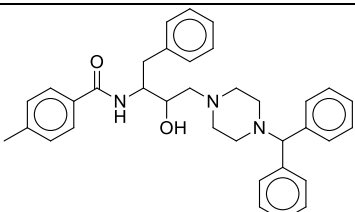
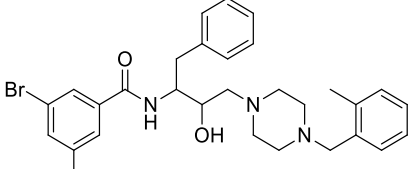
153	296		-6.771	-6.961
154	279		-6.768	-6.958
155	75		-6.765	-6.955
156	38		-6.759	-6.949
157	269		-6.752	-6.941
158	92		-6.733	-8.905
159	277		-6.733	-6.923
160	126		-6.727	-6.917
161	62		-6.71	-7.127

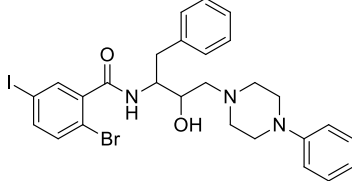
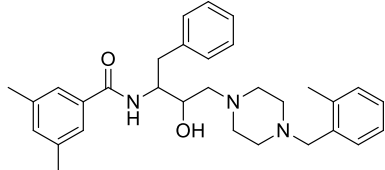
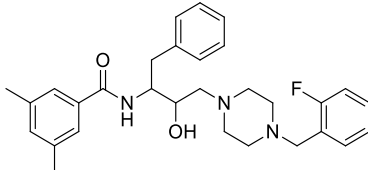
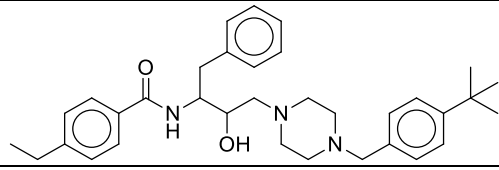
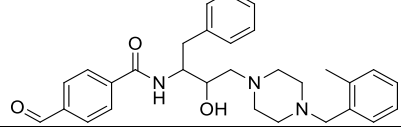
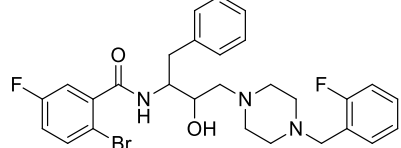
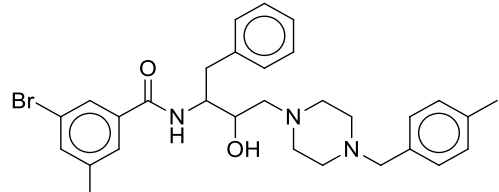
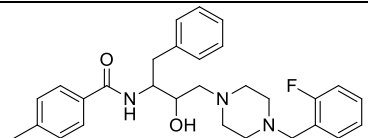
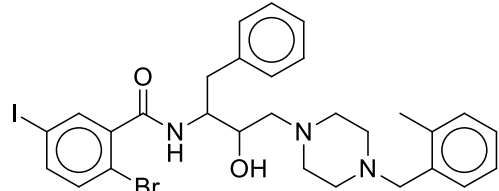
162	199		-6.71	-6.899
163	34		-6.705	-6.895
164	304		-6.704	-6.893
165	220		-6.704	-6.704
166	266		-6.7	-7.535
167	86		-6.696	-6.886
168	139		-6.691	-7.527
169	244		-6.683	-6.873
170	122		-6.681	-6.871

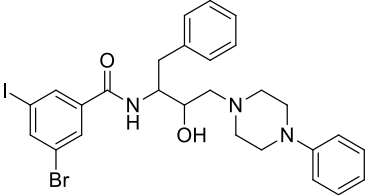
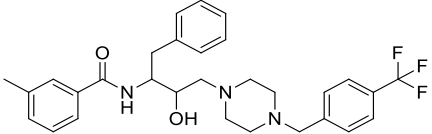
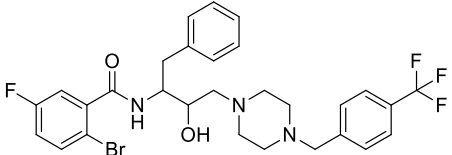
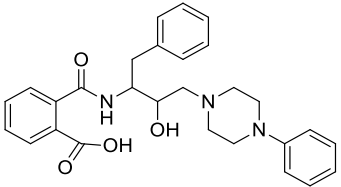
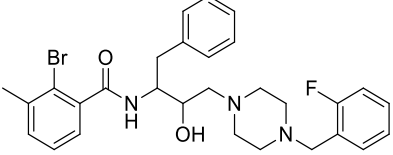
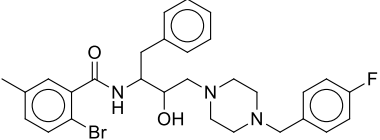
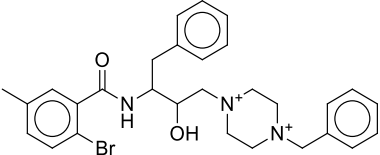
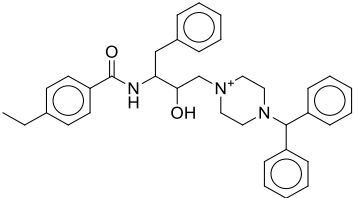
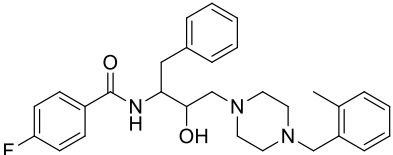
171	174		-6.678	-6.868
172	281		-6.675	-6.864
173	212		-6.67	-6.67
174	258		-6.668	-6.858
175	170		-6.667	-6.856
176	271		-6.667	-6.857
177	96		-6.656	-6.845
178	16		-6.652	-6.676
179	190		-6.65	-6.84

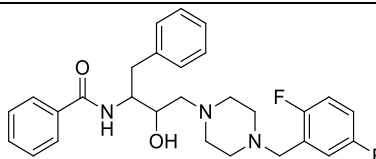
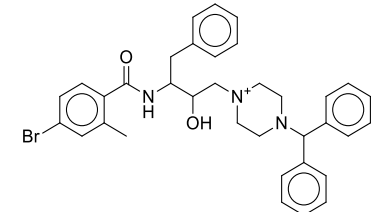
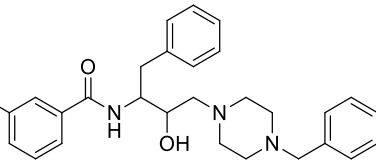
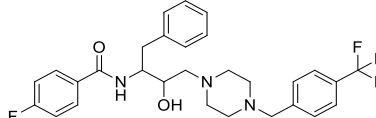
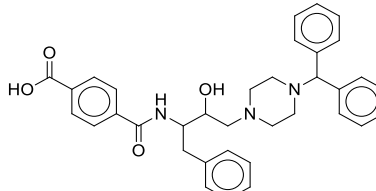
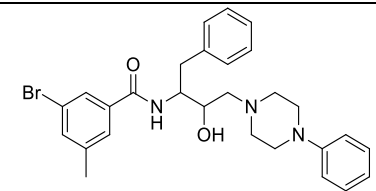
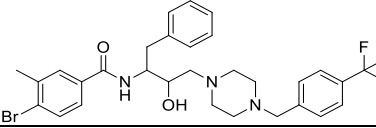
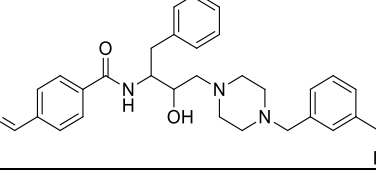
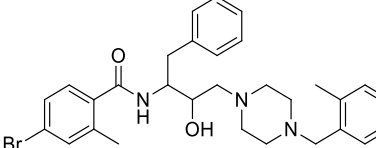
180	33		-6.633	-7.05
181	58		-6.629	-8.801
182	123		-6.624	-6.813
183	260		-6.6	-7.435
184	41		-6.597	-6.787
185	145		-6.586	-6.776
186	133		-6.58	-6.77
187	158		-6.58	-6.77
188	209		-6.57	-6.57

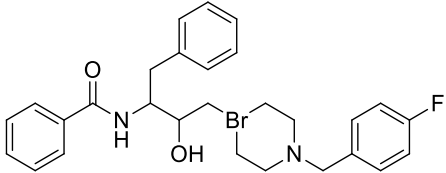
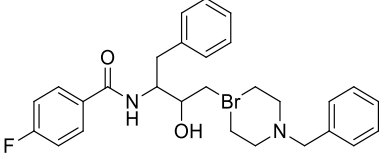
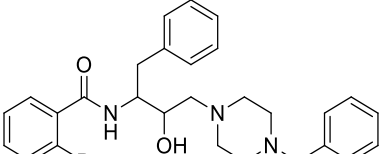
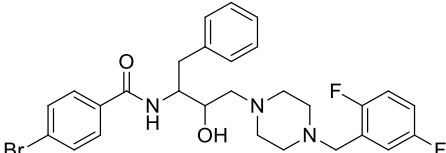
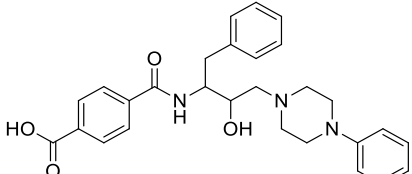
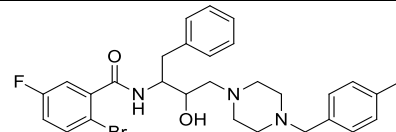
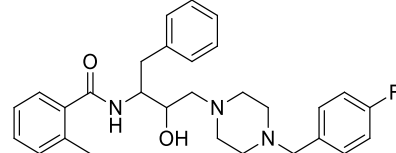
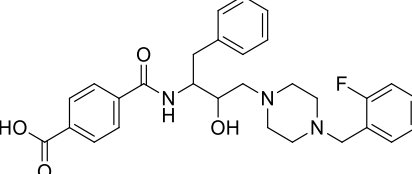
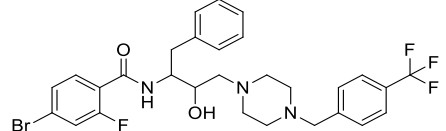
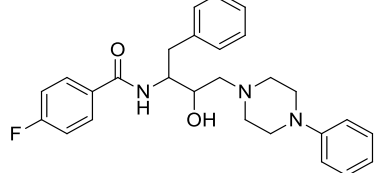
189	66		-6.568	-6.758
190	193		-6.54	-6.73
191	73		-6.539	-8.711
192	235		-6.529	-6.718
193	40		-6.521	-6.711
194	265		-6.494	-6.684
195	286		-6.472	-8.644
196	69		-6.471	-6.66
197	18		-6.471	-6.495

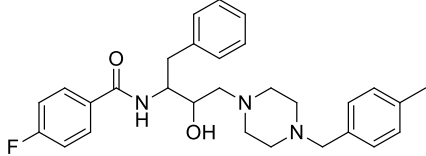
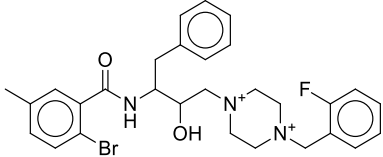
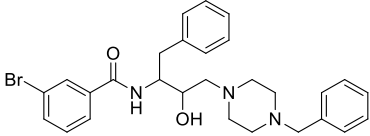
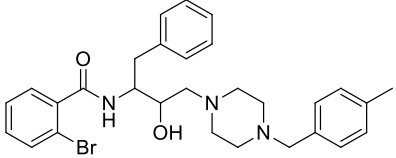
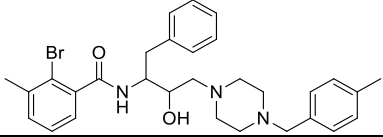
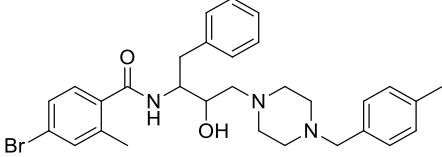
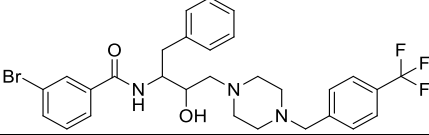
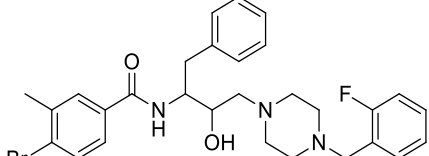
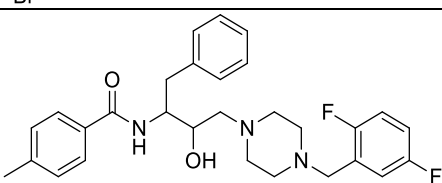
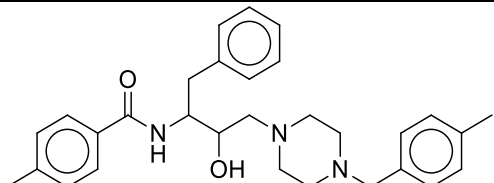
198	85		-6.468	-8.64
199	232		-6.464	-6.905
200	131		-6.461	-6.65
201	236		-6.456	-6.646
202	289		-6.456	-6.646
203	173		-6.455	-6.896
204	81		-6.445	6.634
205	6		-6.421	-6.445
206	198		-6.42	-6.61

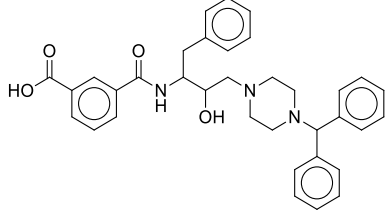
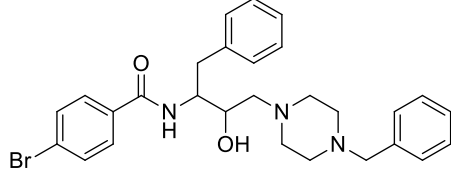
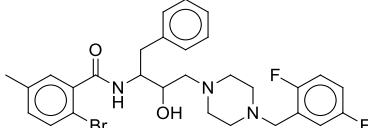
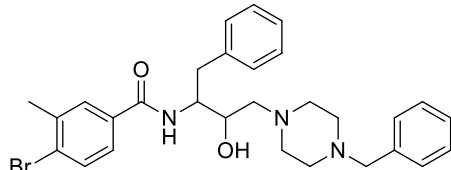
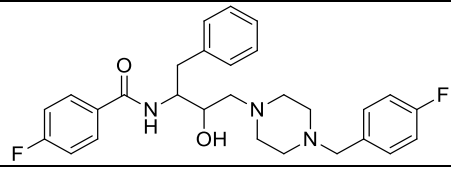
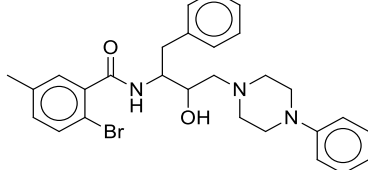
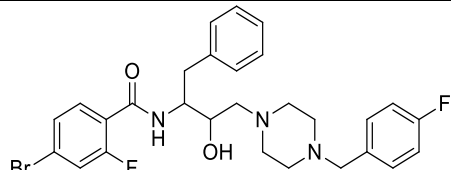
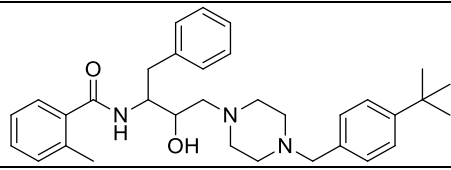
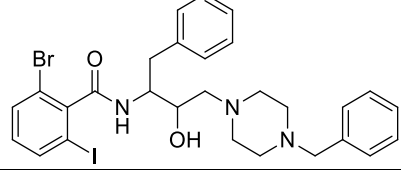
207	228		-6.41	-6.41
208	184		-6.401	-8.573
209	299		-6.364	-6.554
210	240		-6.361	-6.551
211	181		-6.357	-6.547
212	305		-6.337	-7.172
213	55		-6.329	-7.164
214	293		-6.329	-6.519
215	200		-6.321	-6.511

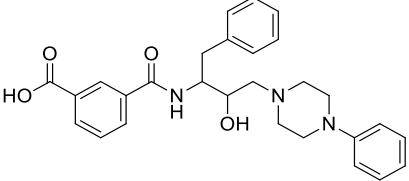
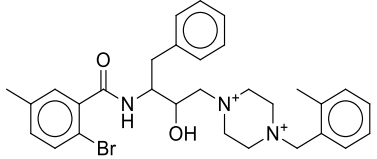
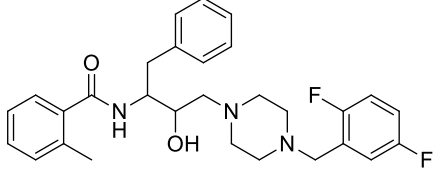
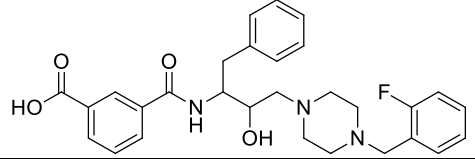
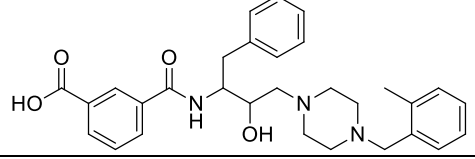
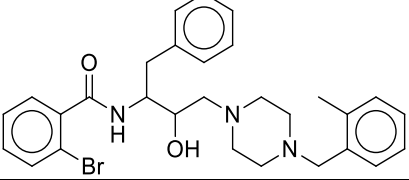
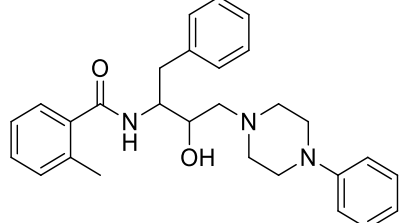
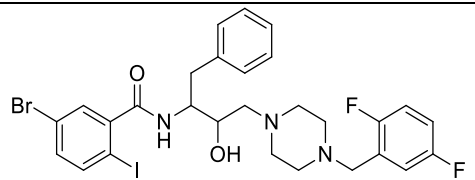
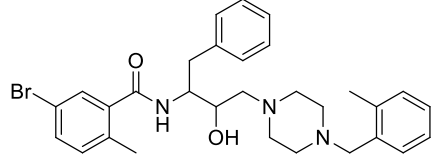
216	225		-6.311	-6.311
217	150		-6.308	-6.498
218	161		-6.307	-6.496
219	204		-6.302	-6.302
220	314		-6.285	-8.457
221	79		-6.282	-8.455
222	107		-6.281	-8.454
223	11		-6.269	-6.294
224	186		-6.266	-7.101

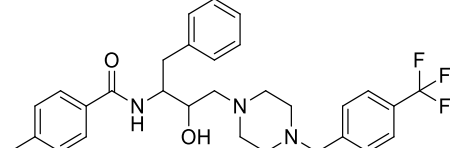
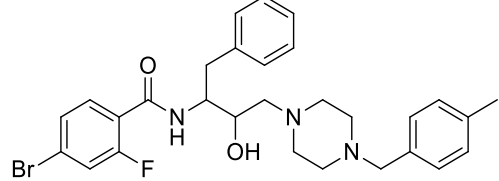
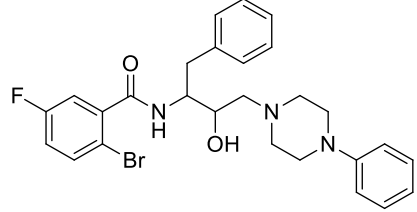
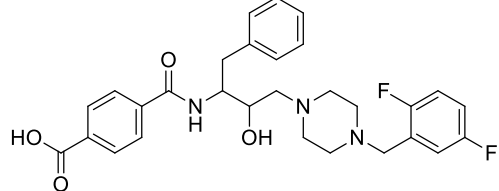
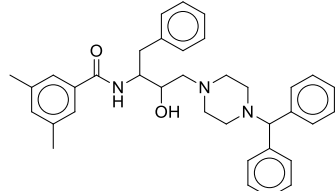
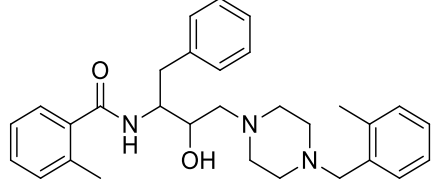
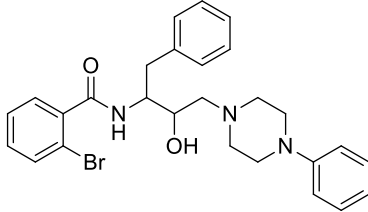
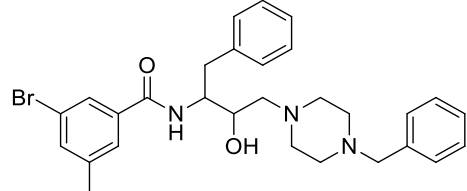
225	116		-6.259	-8.431
226	23		-6.252	-6.276
227	65		-6.242	-7.077
228	157		-6.242	-6.432
229	1		-6.231	-6.253
230	226		-6.226	-6.226
231	172		-6.223	-6.412
232	267		-6.217	-6.407
233	195		-6.205	-6.395

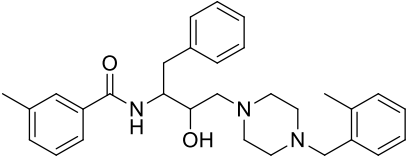
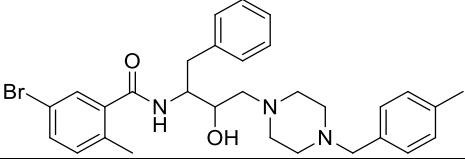
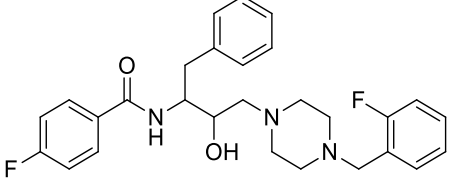
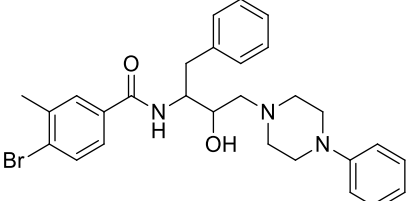
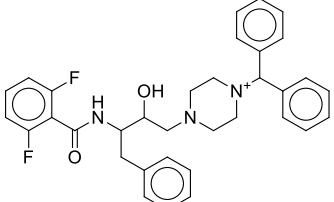
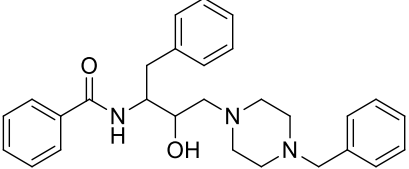
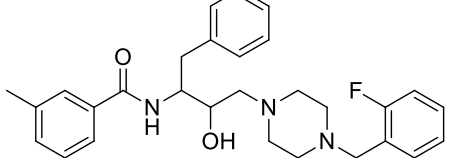
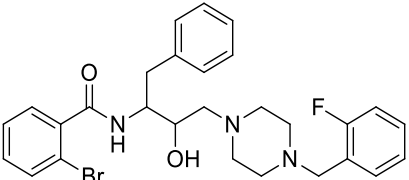
234	60		-6.204	-6.394
235	100		-6.201	-6.39
236	102		-6.201	-8.373
237	129		-6.179	-8.351
238	202		-6.174	-6.174
239	47		-6.169	-6.358
240	63		-6.162	-8.334
241	288		-6.142	-6.583
242	164		-6.136	-8.308
243	214		-6.136	-6.136

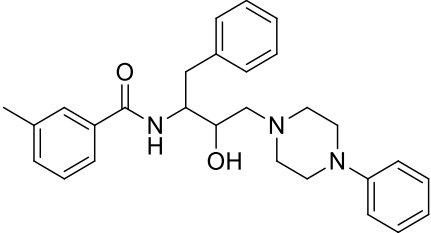
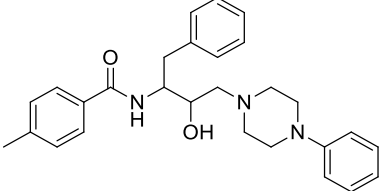
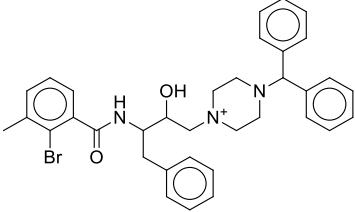
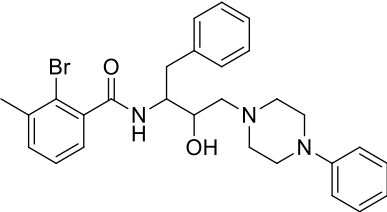
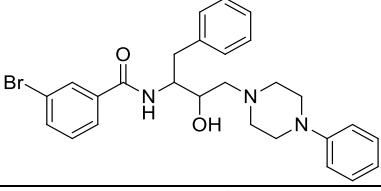
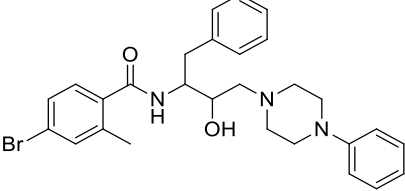
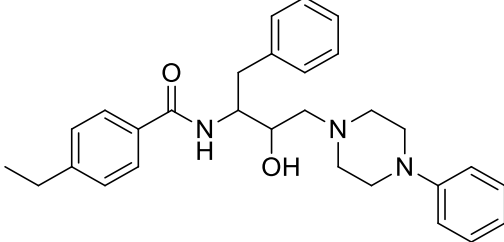
244	43		-6.133	-8.305
245	309		-6.116	-8.288
246	103		-6.11	-6.3
247	45		-6.1	-6.29
248	56		-6.094	-6.284
249	52		-6.079	-6.269
250	160		-6.079	-8.251
251	316		-6.076	-8.248
252	120		-6.074	-8.246
253	35		-6.071	-6.261

254	4		-6.063	-6.085
255	101		-6.036	-6.226
256	136		-6.006	-6.195
257	114		-5.995	-8.167
258	71		-5.993	-6.182
259	222		-5.987	-5.987
260	78		-5.981	-6.171
261	234		-5.974	-6.809
262	109		-5.971	-6.806

263	205		-5.952	-5.952
264	194		-5.927	-8.099
265	119		-5.92	-6.11
266	291		-5.879	-6.32
267	176		-5.871	-7.959
268	188		-5.869	-8.041
269	206		-5.86	-5.86
270	134		-5.847	-8.019
271	191		-5.845	-6.034

272	149		-5.841	-6.031
273	50		-5.83	-6.02
274	218		-5.802	-5.802
275	115		-5.798	-6.238
276	12		-5.788	-5.812
277	177		-5.779	-6.614
278	216		-5.758	-5.758
279	111		-5.751	-6.586

280	179		-5.724	-5.913
281	48		-5.709	-5.899
282	301		-5.688	-5.877
283	229		-5.681	-5.681
284	13		-5.680	-7.641
285	88		-5.673	-5.863
286	294		-5.632	-7.805
287	303		-5.631	-5.82

288	208		-5.585	-5.585
289	207		-5.547	-5.547
290	27		-5.499	-5.523
291	227		-5.312	-5.312
292	217		-5.238	-5.238
293	223		-5.052	-5.052
294	211		-4.693	-4.693

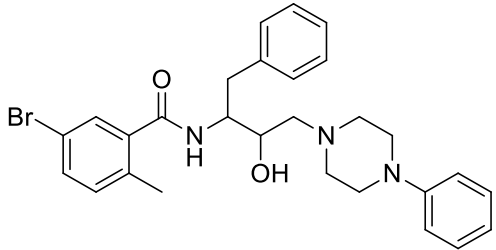
295	219		-4.594	-4.594
-----	-----	--	--------	--------

Table S3. Stereochemical geometry analysis by Ramachandran mapping for residues of *PfPlmX*

Entry no	Complex	Number and percentage of residues in favoured region	Number and percentage of residues in additional allowed region	Number and percentage of residues in additional generously region	Number and percentage of residues in the outlier region
1	<i>PfPlmX-22</i>	219 79.3%	52 18.8%	2 0.7%	3 1.1%
2	<i>PfPlmX-49c</i>	28 82.6%	43 15.6%	4 1.4%	1 0.4%
3	Unligated- <i>PfPlmX</i>	221 80.1%	52 18.8%	2 0.7%	1 0.4%

Table S4. Thermodynamic MM/GBSA results for *PfPlmX-22*, and b) *PfPlmX-49c* for every 2ns after conformational stability of compounds

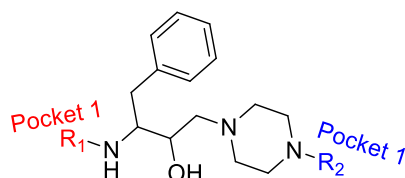
Time (ns)	Compound 22 ΔG°	Time (ns)	49c ΔG°
16	-112.9451712	60	-94.08212114
18	-107.608968	62	-96.34868378
20	-112.4204964	64	-85.27542661
22	-120.2660485	66	-89.92105681
24	-101.9739729	68	-83.1481782
26	-105.0968468	70	-87.72999812

28	-105.3219957	72	-96.18010465
30	-118.8241403	74	-91.31016744
32	-127.7110339	76	-75.81980409
34	-120.0127726	78	-85.27735931
36	-121.0561954	80	-89.56990275
38	-114.1295715	82	-92.5225952
40	-125.3516747	84	-91.98369022
42	-121.8921416	86	-78.20219966
44	-116.1948212	88	-89.11826384
46	-98.27348822	90	-86.24359215
48	-109.9275826	92	-91.51299932
50	-106.1164613	94	-83.15668329
52	-113.0623917	96	-81.65730487
54	-115.1109888	98	-86.23859109
56	-110.3552891	100	-87.09292356
58	-120.4471396	102	-75.87647425
60	-115.0286181	104	-81.4623022
62	-113.9838541	106	-75.2624054
64	-100.037592	108	-77.13110817
66	-113.1035361	110	-71.53834425
68	-101.5695434	112	-85.50847031
70	-104.8698746	114	-86.74602849
72	-120.9796494	116	-79.76494575
74	-115.4588989	118	-87.63757458
76	-106.367114	120	-89.68886305
78	-120.4766904	122	-83.99172466
80	-124.6391891	124	-79.05245114
82	-127.7838957	126	-83.72530847
84	-117.7682019	128	-89.10608553
86	-111.3798073	130	-90.06759486
88	-101.0566971	132	-91.77385572
90	-107.4006004	134	-89.25350583
92	-112.6515284	136	-85.39803017
94	-114.0939816	138	-84.58318529
96	-91.83496937	140	-85.47460989
98	-110.8574064	142	-91.16238998
100	-108.9317284	144	-90.28423908
102	-107.0113055	146	-89.90655473
104	-116.9241778	148	-79.41777365

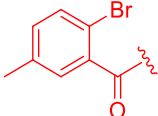
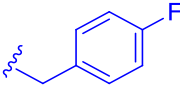

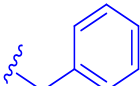
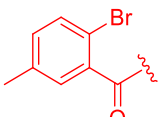
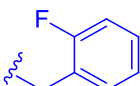
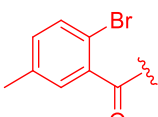
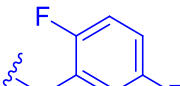
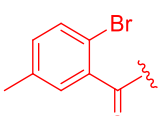
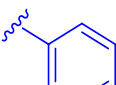
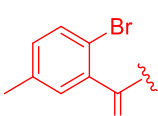
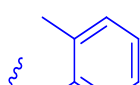
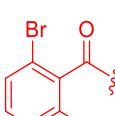
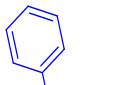
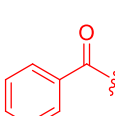
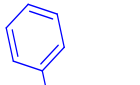
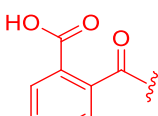
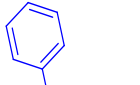
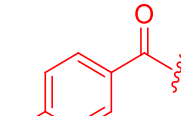
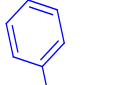
106	-105.2026437	150	-97.14740946
108	-93.9777003	152	-87.84941345
110	-94.26104774	154	-88.42853473
112	-89.88594276	156	-87.61067941
114	-111.6727278	158	-91.29079382
116	-100.9507948	160	-90.26391228
118	-120.7169771	162	-93.11979364
120	-107.1412968	164	-91.41530317
122	-113.583938	166	-93.8082606
124	-107.0637573	168	-86.01779081
126	-104.9489011	170	-89.9406861
128	-100.7614125	172	-89.10945564
130	-109.9466948	174	-83.11745767
132	-103.23587	176	-83.28124824
134	-106.6617241	178	-86.15161591
136	-98.82075868	180	-74.0257986
138	-104.6396008	182	-88.9643951
140	-101.0996999	184	-72.8073516
142	-101.7161565	186	-79.52211421
144	-100.3785669	188	-82.19327068
146	-105.1889275	190	-85.10817021
148	-98.98653689	192	-85.79816119
150	-103.8989911	194	-83.8885444
152	-95.6271897	196	-93.56083253
154	-106.9037775	198	-85.0283496
156	-102.1156481	200	-83.8194894
158	-118.3861493		
160	-74.69116794		
162	-106.1033556		
164	-114.4871012		
166	-110.8808349		
168	-108.0014678		
170	-107.6301746		
172	-99.98945472		
174	-103.4987468		
176	-102.4247683		
178	-107.2165857		
180	-113.7895753		
182	-107.8773005		

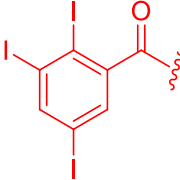
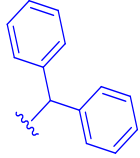
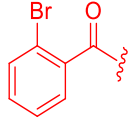
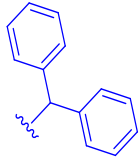
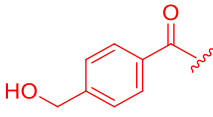
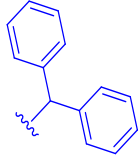
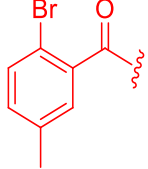
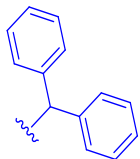
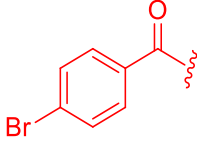
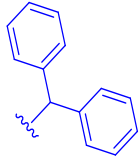
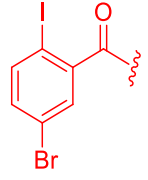
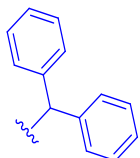
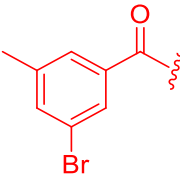
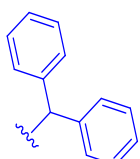
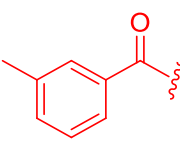
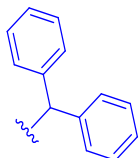
184	-93.76402828
186	-107.1807698
188	-109.0403494
190	-109.5230523
192	-97.9752407
194	-101.4844603
196	-100.33522
198	-100.3229321
200	-82.22233074

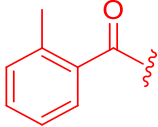
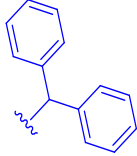
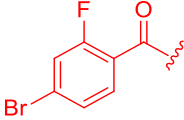
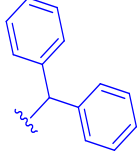
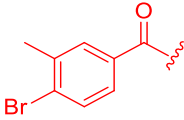
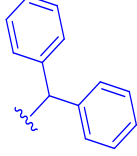
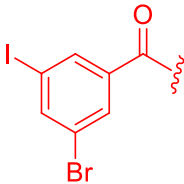
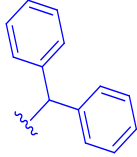
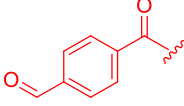
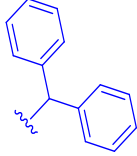
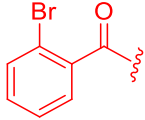
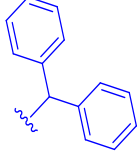
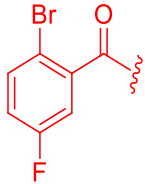
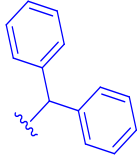
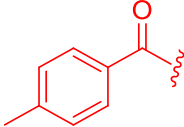
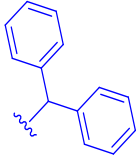
Table S5. Structure activity relationship for *PfPlmX*

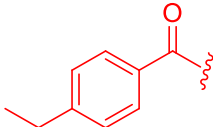
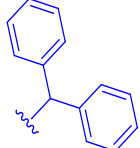
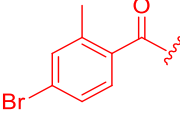
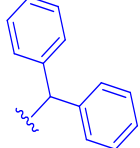
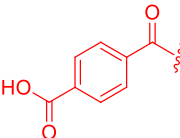
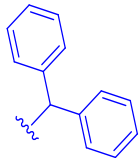
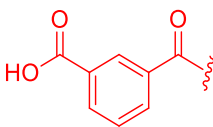
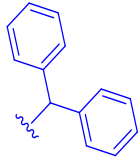
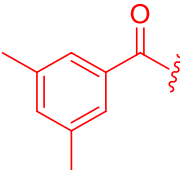
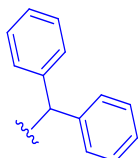
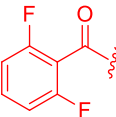
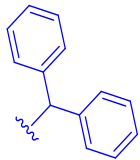
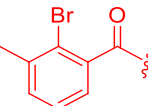
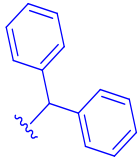


Entry no.	Compounds	R1 (Pocket 1) Acids	R2 (Pocket 2) Amines	Docking Score	XP Gscore
1	22			-8.754	-8.779
2	251			-8.050	-8.239
3	165			-7.211	-9.383
4	280			-7.092	-7.281
5	51			-6.997	-7.187

6	79			-6.282	-8.455
7	107			-6.281	-8.454
8	309			-6.116	-8.288
9	136			-6.006	-6.195
10	222			-5.987	-5.987
11	194			-5.927	-8.099
12	24			-8.693	-8.718
13	2			-8.644	-8.668
14	3			-8.204	-8.226
15	14			-7.975	-7.999

16	8			-7.947	-7.971
17	17			-7.809	-7.833
18	10			-7.779	-7.803
19	19			-7.689	-7.713
20	15			-7.401	-7.426
21	20			-7.147	-7.172
22	26			-7.140	-7.164
23	7			-7.010	-7.034

24	5			-6.912	-6.936
25	21			-6.911	-6.935
26	29			-6.839	-6.864
27	25			-6.838	-6.862
28	9			-6.789	-6.813
29	16			-6.652	-6.676
30	18			-6.471	-6.495
31	6			-6.421	-6.445

32	11			-6.269	-6.294
33	23			-6.252	-6.276
34	1			-6.231	-6.253
35	4			-6.063	-6.085
36	12			-5.788	-5.812
37	13			-5.680	-7.641
38	27			-5.499	-5.523
