Discovery of New Hydroxyethylamine Analogs Against 3CL^{pro} Protein Target of SARS-CoV-2: Molecular Docking, Molecular Dynamics Simulation and Structure-Activity Relationship Studies

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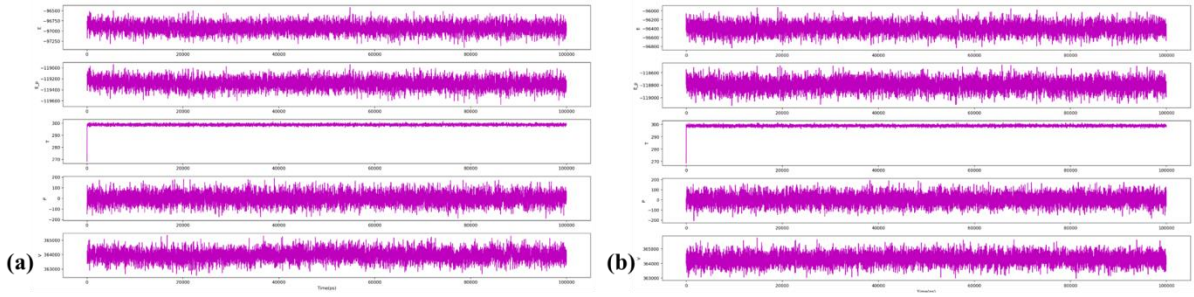


Fig. S1. Simulation Quality parameters for 100 ns simulation in terms of total energy (E), potential energy (E_p), pressure (P), temperature (T), and volume (V): (a) Un-ligated-3CL^{pro}; and (b) Indianvir-3CL^{pro} complex.

Table S1. Average value of total energy (E), potential energy (E_p), pressure (P), temperature (T), and volume (V) for Compound **16**-3CL^{pro} complex for 100 ns simulation.

Parameter	**Average**	**Standard Deviation**	**Slope(ps^{-1})**
Total Energy (E, kcal/mol)	-96750.358	120.442	-0.000
Potential Energy (E_p, kcal/mol)	-119153.595	91.814	-0.000
Temperature (K)	298.726	0.719	0.000
Pressure (P, bar)	0.600	53.376	0.000
Volume (V, $Å^3$)	364445.325	383.354	0.000

Table S2. Average value of total energy (E), potential energy (E p), pressure (P), temperature (T), and volume (V) for indinavir-3CL^{pro} complex for 100 ns simulation.

Parameters	**Average**	**Standard Deviation**	**Slope(ps^{-1})**
Total Energy (E, kcal/mol)	-96398.559	120.977	-0.000
Potential Energy (E_p, kcal/mol)	-118801.852	92.135	-0.000
Temperature (K)	298.739	0.729	0.000
Pressure (P, bar)	0.785	53.623	0.000
Volume (V, $Å^3$)	364300.344	378.896	0.001

Table S3. The average RMSD for backbone, Cα, and side-chain of Indinavir-3CL^{pro} and un-ligated-3CL^{pro} complex.

System	**$RMSD_{Backbone}$**	**$RMSD_{Cα}$**	**$RMSD_{side-chain}$**
Indinavir-3CL^{pro} complex	0.873	0.641	1.390
Un-ligated-3CL^{pro}	0.691	0.594	1.214

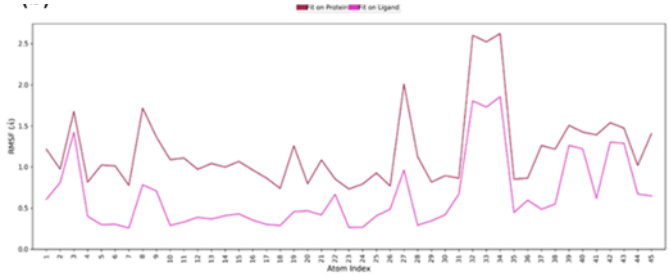


Fig. S2. RMSF plot for Indinavir-3CL^{pro} complex.

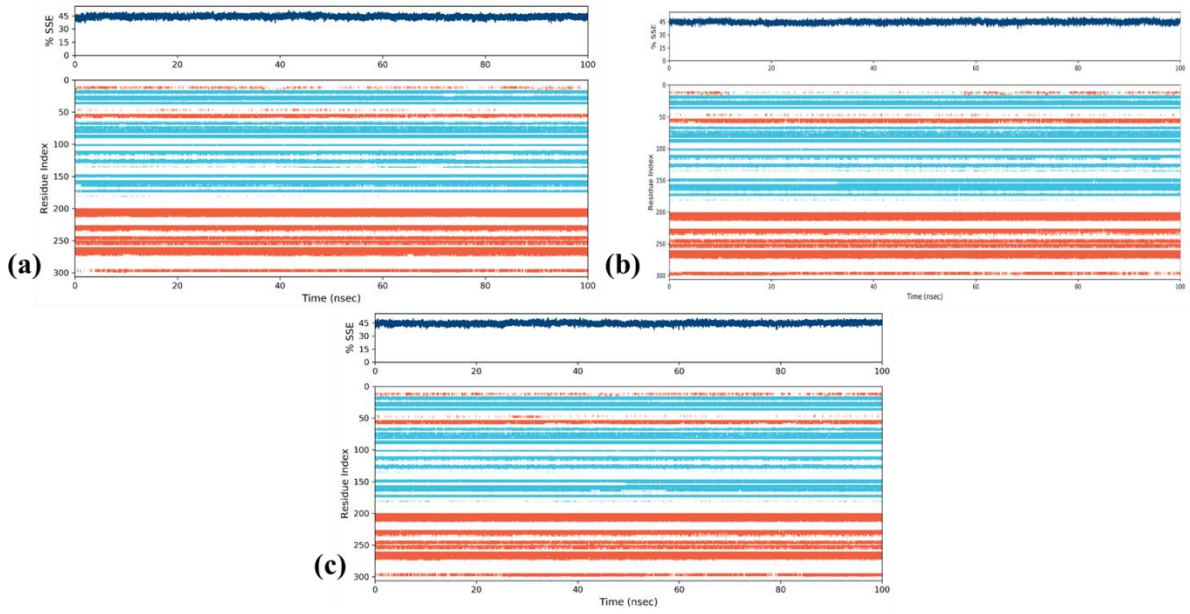
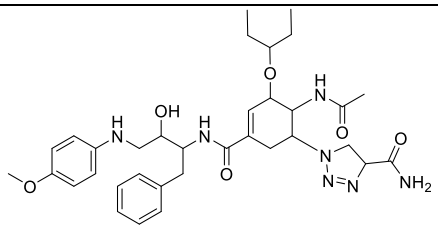
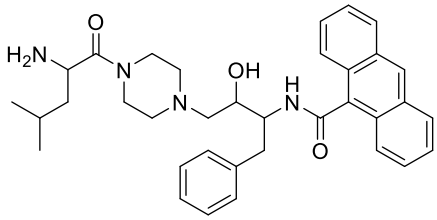
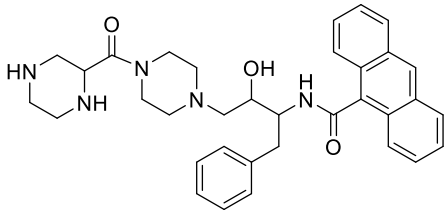
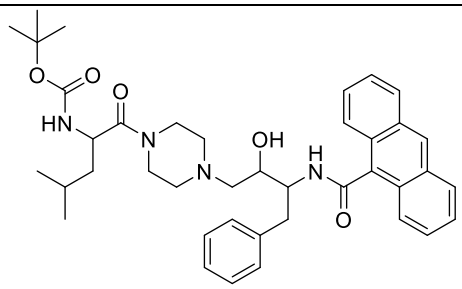
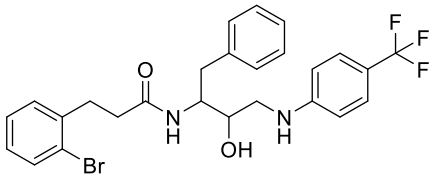


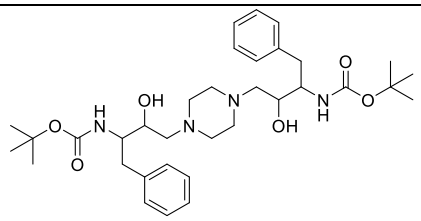
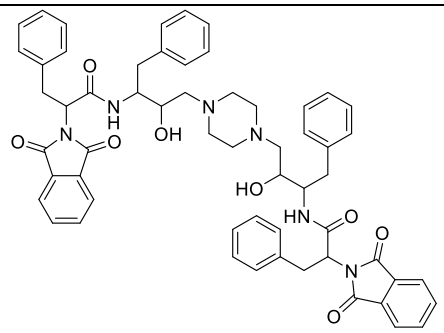
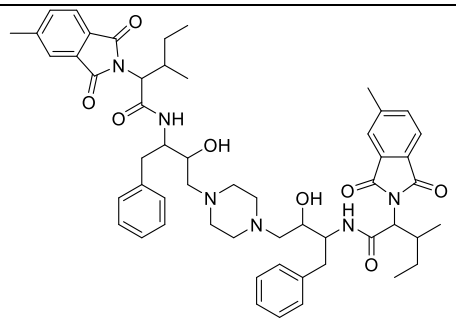
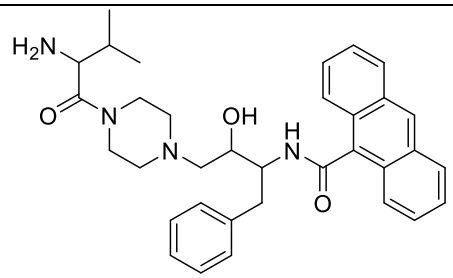
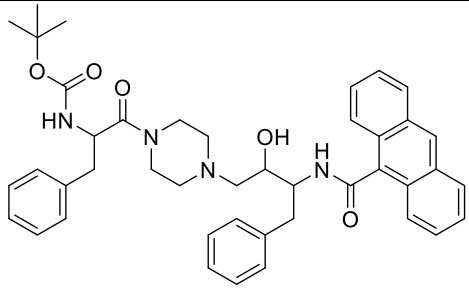
Fig. S3. Residues involved in secondary structure of 3CL^{pro} during 100ns simulation for: a) compound **16**-3CL^{pro} complex; b) Indinavir-3CL^{pro} complex and c) un-ligated-3CL^{pro} complex.

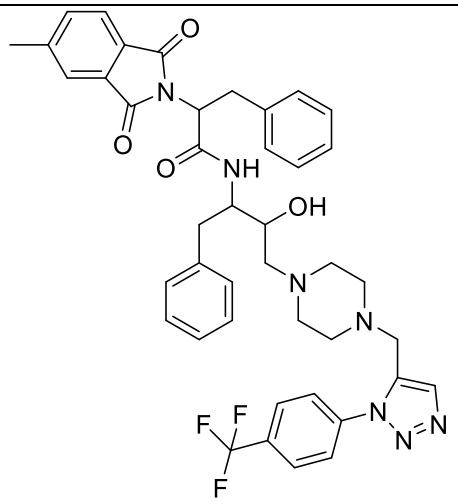
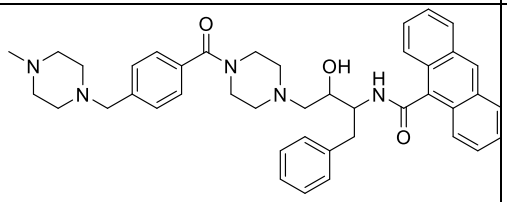
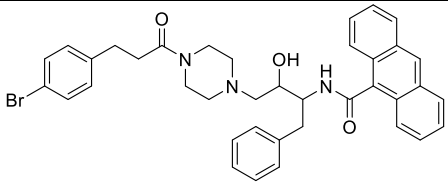
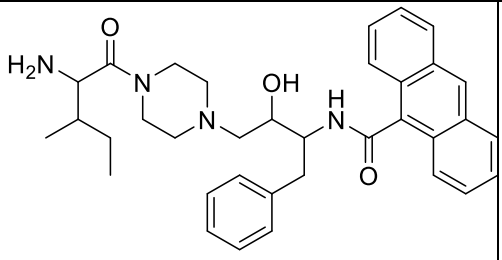
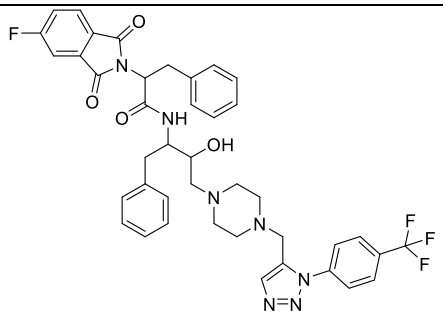
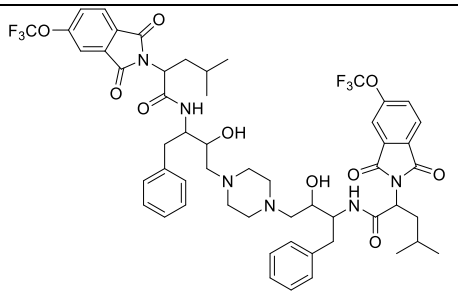
Table S4. Percentage composition of secondary structure element (SSE) in $3CL^{pro}$ complex systems.

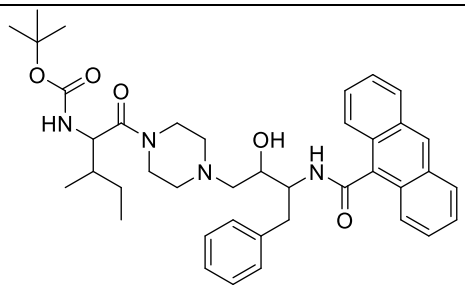
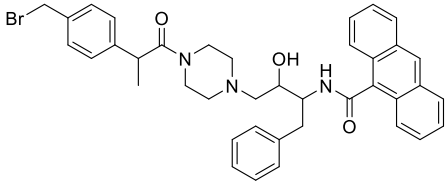
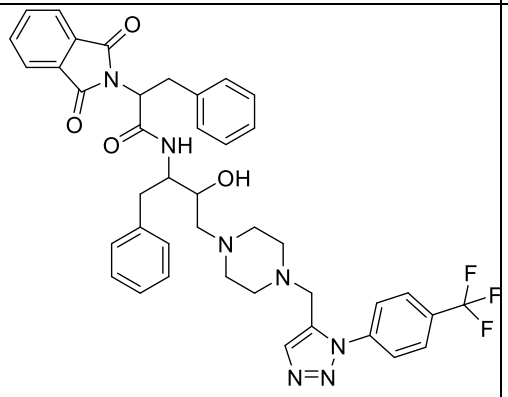
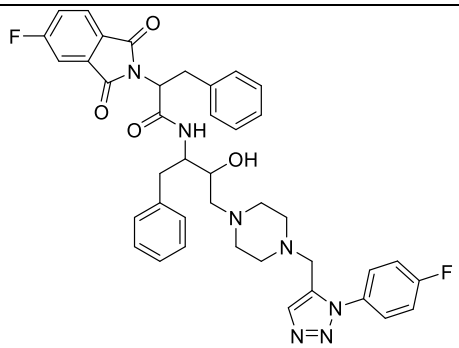
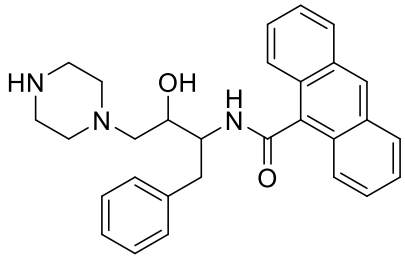
System	α-helix (%)	β-strand (%)	Total SSE (%)
Unligated-$3CL^{pro}$	20.18	24.27	44.45
Compound **16**	19.83	24.37	44.20
Indinavir	19.94	24.80	44.74

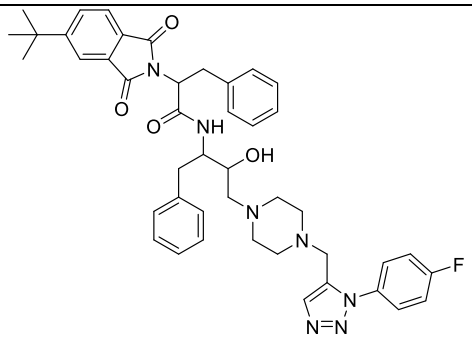
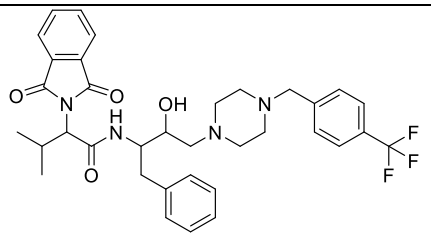
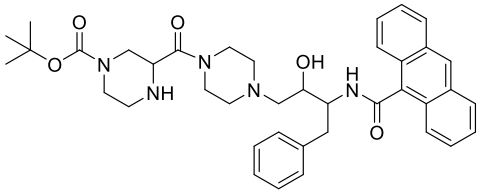
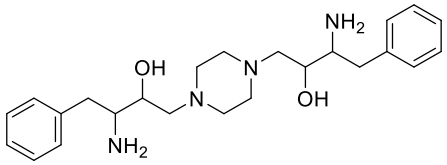
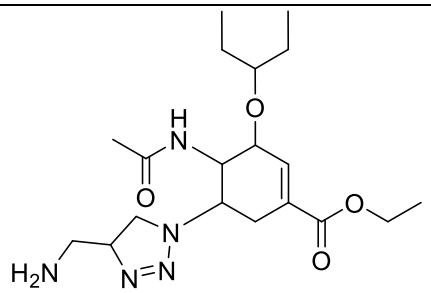
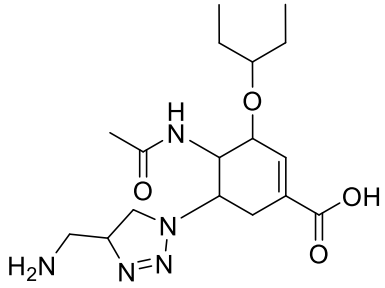
Table S5. Molecules ranked on the basis of docking score and XP Gscore (kcal/mol) against target protein ($3CL^{pro}$ of SARS-CoV2).

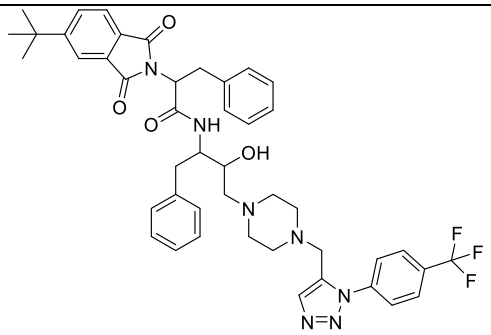
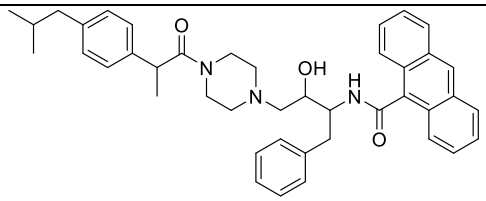
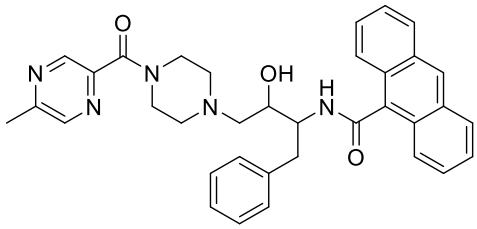
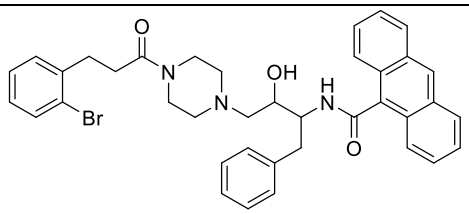
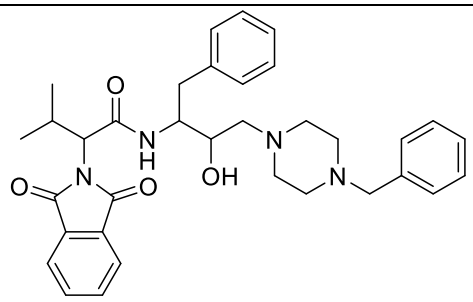
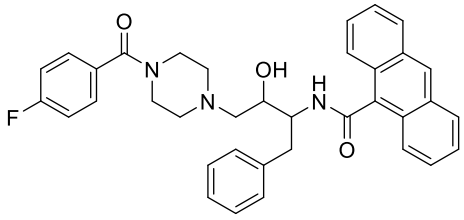
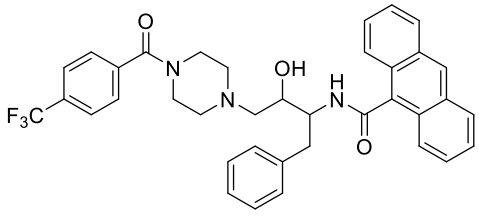
Entry No	Molecule	docking score	XP GScore
1		-8.695	-8.699
2		-8.656	-8.802
3		-8.637	-8.744
4		-8.591	-8.6
5		-8.523	-8.523

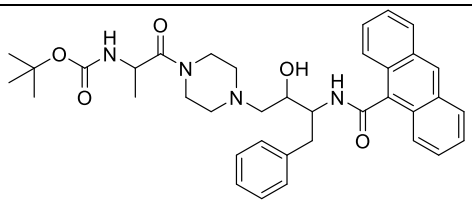
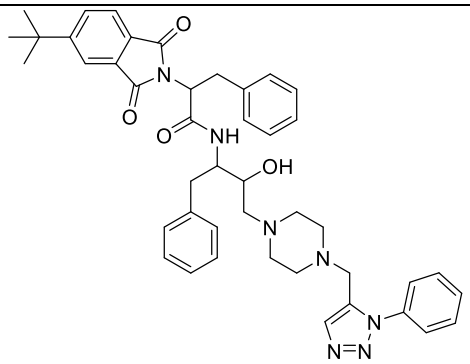
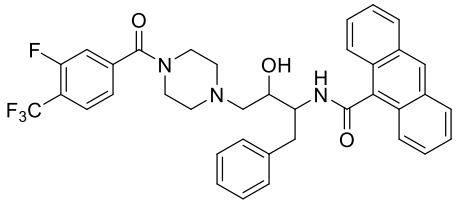
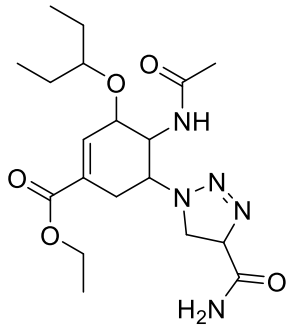
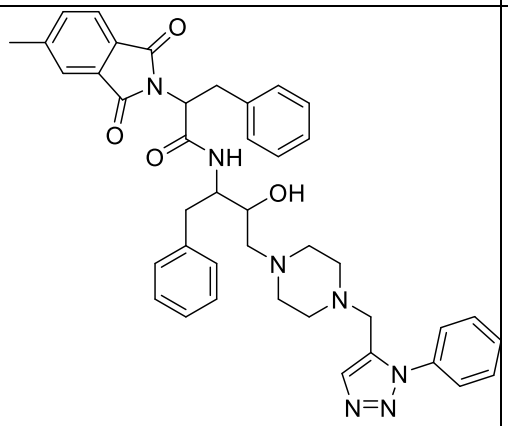
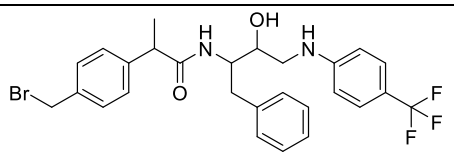
6		-8.431	-8.45
7		-8.424	-8.443
8		-8.416	-8.435
9		-8.403	-8.541
10		-8.362	-8.373

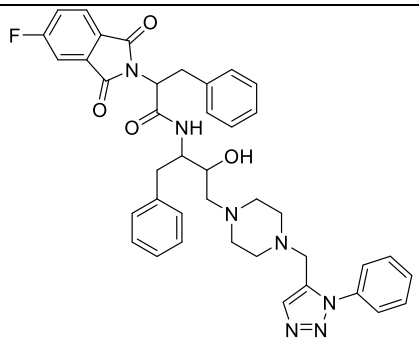
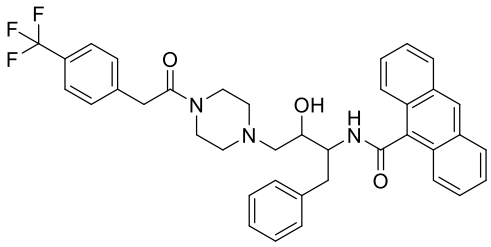
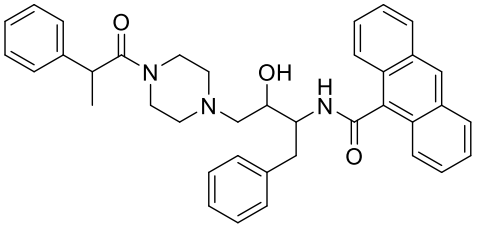
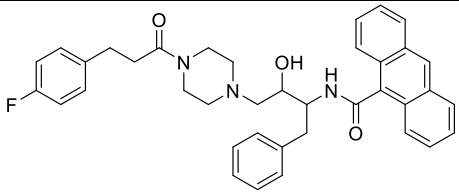
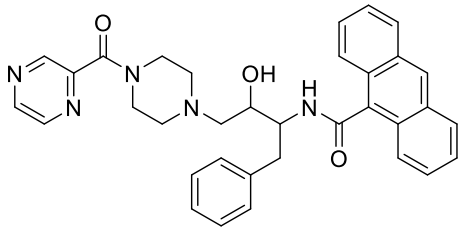
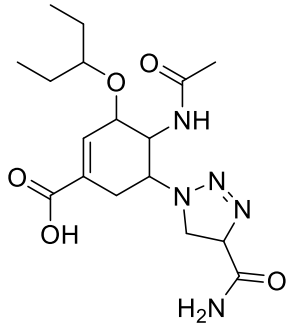
11		-8.361	-8.366
12		-8.289	-9.068
13		-8.241	-8.246
14		-8.233	-8.38
15		-8.181	-8.186
16		-8.127	-8.146

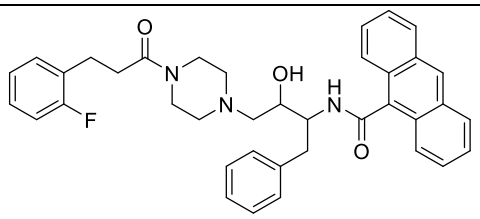
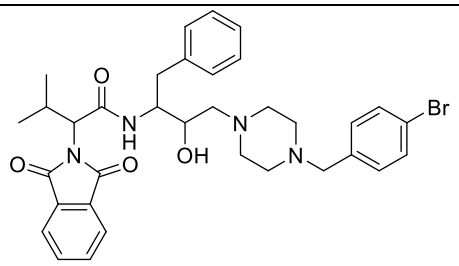
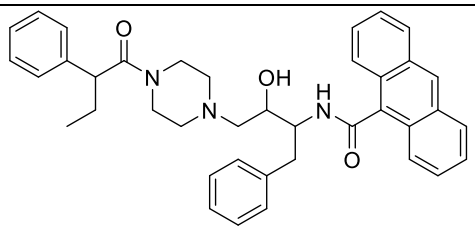
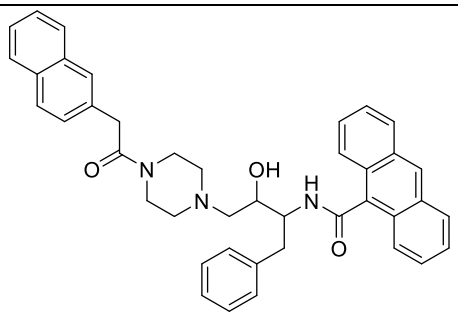
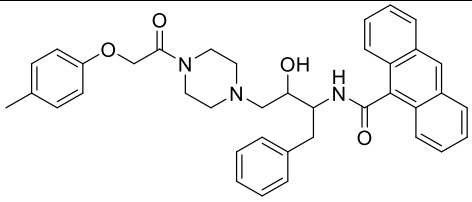
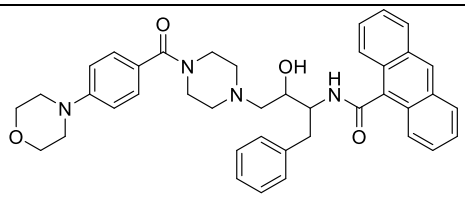
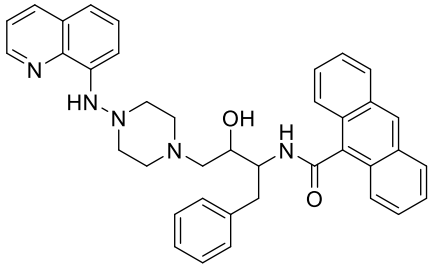
17		-7.98	-7.989
18		-7.963	-7.968
19		-7.926	-7.931
20		-7.916	-7.921
21		-7.855	-8.674

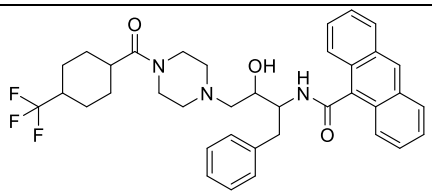
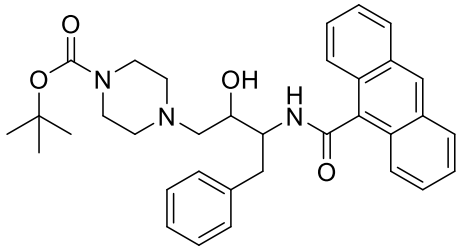
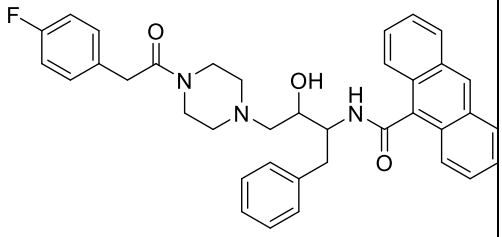
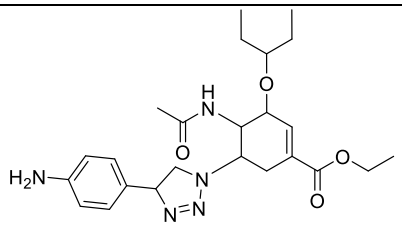
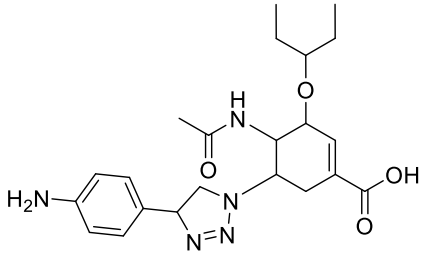
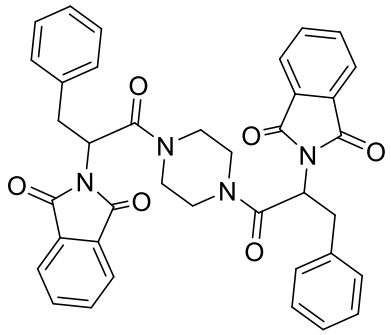
22		-7.821	-7.826
23		-7.74	-8.553
24		-7.701	-7.706
25		-7.676	-8.42
26		-7.672	-7.674
27		-7.604	-7.604

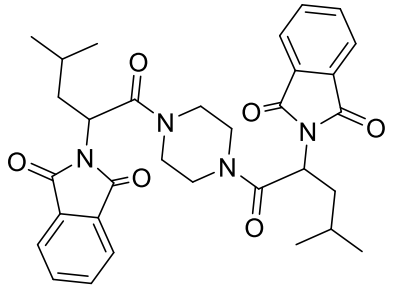
28		-7.595	-7.6
29		-7.574	-7.579
30		-7.545	-7.6
31		-7.451	-7.456
32		-7.449	-7.646
33		-7.426	-7.45
34		-7.42	-7.444

35		-7.4	-7.409
36		-7.359	-7.364
37		-7.337	-7.362
38		-7.263	-7.263
39		-7.248	-7.253
40		-7.223	-7.223

41		-7.217	-7.222
42		-7.199	-7.206
43		-7.188	-7.194
44		-7.175	-7.18
45		-7.171	-8.602
46		-7.163	-7.164

47		-7.103	-7.108
48		-7.074	-7.887
49		-7.051	-7.057
50		-6.994	-7
51		-6.987	-6.999
52		-6.78	-6.804
53		-6.708	-6.715

54		-6.615	-6.619
55		-6.482	-6.509
56		-6.423	-6.43
57		-6.326	-6.329
58		-6.238	-6.238
59		-5.243	-5.243

60		-4.761	-4.761