

Small Heterocyclic G-quadruplex Ligands as Anticancer Agents: a QSAR

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Table S1. Computed electronic energies with the 6-31G(d,p) basis set, in *a.u.*, and ligand affinities, in *kcal.mol⁻¹*, against experimentally determined IC₅₀ values, *mol*. The model quadruplex energy at wB97XD is E_{Q2} = -4939.424743 *a.u.*; E_{Q3} = -7709.073670 *a.u.*; E_L – ligand energy; Q_{L2} – the complex ligand-quadruplex energy; A_{QL2}: ligand affinity. Top row: wB97XD/6-31G(d,p); bottom row: RI-MP2/6-31G(d,p)//wB97XD; E_{Q2} = -4927.803098 *a.u.* For some of the ligands and the respective complexes, more than one minimum has been located due to low-energy tautomerization or rotation processes.

	Ligands	E _L - wB97XD/ 6-31G(d,p)	Q _{L2} - wB97XD/ 6-31G(d,p)	A _{QL2}	IC ₅₀
1		-1221.484259	-6160.971211	-39.04	1.43 x 10⁻⁵
		-1218.157251	-6146.025961	-43.30	
2		-1104.982776	-6044.467535	-37.66	2.9 x 10⁻⁵
		-1104.983076	-6044.468157		
		-1102.014583	-6029.884273	-41.79	
3		-1069.087694	-6008.596043	-37.63	3.19 x 10⁻⁵
		-1069.108354			
		-1069.113637			
		-1066.179220		-44.42	
		-1066.184832			
4		-933.966342	-5873.446834	-34.98	4.47 x 10⁻⁵
				-41.04	
5		-860.183549	-5799.660935	-33.03	5.8 x 10⁻⁵
		-857.811416	-5785.667800	-33.44	
		-857.810868			

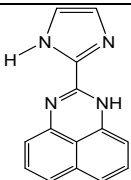
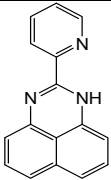
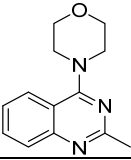
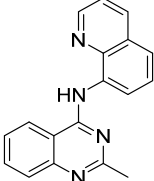
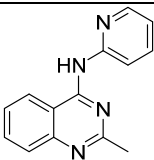
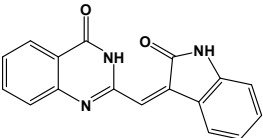
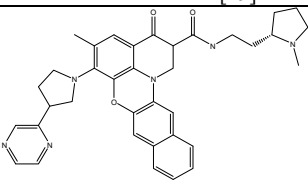
6		-758.318366	-5697.793309	-31.50 -35.71	6.05 x 10⁻⁵
7		-780.369285	-5719.845155	-32.08 -38.74	9.37 x 10⁻⁵
8		-743.685384 -741.672301	-5683.152521 -5683.151177 -5669.521223	-26.60 -28.76	1.28 x 10⁻⁴
9		-913.106098 -913.293027 -913.115572 -910.653425	-5852.581625 -5852.568090 -5838.500144 -5838.493578	-35.20 -45.02	9.8 x 10⁻⁵
10		-759.521386 √ -757.479491	-5698.995996 -5698.995265	-31.29 -37.96	1.61 x 10⁻⁴
11	 Schizocommunis [29]	-968.888943	-5908.369172	-34.82 -40.74	> 5 x 10⁻⁴
12	 Quarfloxin CX3543 [42]	-2007.047343	-6946.563341	-57.30 -70.67	

Table S2. Q2.Ligand 1—atomic coordinates of the two-layered G4-quadruplex complex, Gaussian format, wB97XD/6-31G(d,p).

1	7	0	-6.998881	-0.528519	-1.146479
2	6	0	-6.706627	0.764359	-1.343028
3	6	0	-5.487695	1.334703	-1.673569
4	6	0	-4.353361	0.487503	-1.800931
5	7	0	-4.681373	-0.850984	-1.592501
6	6	0	-5.941179	-1.313536	-1.293625
7	7	0	-7.571843	1.822026	-1.254280
8	6	0	-6.851961	2.958665	-1.536506
9	7	0	-5.599285	2.705124	-1.792795
10	8	0	-3.189199	0.818799	-2.054698
11	7	0	-6.087061	-2.635588	-1.136603
12	7	0	-1.748103	3.137772	-2.781453
13	6	0	-0.407820	2.790311	-2.940251
14	6	0	0.393494	3.917630	-3.270127
15	6	0	-0.219173	5.155744	-3.381606
16	7	0	-1.516130	5.462880	-3.241113
17	6	0	-2.254575	4.406420	-2.934199
18	7	0	1.753380	4.017562	-3.481510
19	6	0	1.960604	5.284023	-3.710145
20	7	0	0.802437	6.024172	-3.660679
21	8	0	-0.037428	1.620808	-2.789200
22	7	0	-3.574374	4.562646	-2.764778
23	7	0	2.296180	0.078649	-3.243245
24	6	0	3.556364	0.531689	-3.554208
25	7	0	4.620670	-0.250052	-3.633497
26	6	0	4.337106	-1.530000	-3.353540
27	6	0	3.107304	-2.097658	-3.059707
28	6	0	1.968808	-1.251415	-2.987231
29	7	0	3.232826	-3.451542	-2.819874
30	6	0	4.507051	-3.693071	-2.959355
31	7	0	5.222471	-2.571061	-3.294684
32	7	0	3.690382	1.844528	-3.795145
33	8	0	0.802714	-1.569549	-2.721964
34	7	0	-0.719341	-3.914108	-2.361464
35	6	0	-2.023652	-3.558955	-2.033871
36	6	0	-2.843963	-4.700142	-1.820768
37	6	0	-2.269024	-5.956884	-1.928592
38	7	0	-1.005035	-6.274428	-2.233582
39	6	0	-0.250752	-5.203609	-2.439782
40	7	0	-4.173540	-4.794464	-1.462391
41	6	0	-4.398561	-6.074450	-1.355816
42	7	0	-3.281675	-6.828708	-1.625798
43	8	0	-2.353899	-2.368814	-1.949916
44	7	0	1.039436	-5.368259	-2.761578
45	1	0	-0.070565	-3.125170	-2.516335
46	1	0	1.738067	-4.616115	-2.748048

47	1	0	1.363587	-6.320156	-2.742943
48	1	0	1.514415	0.745888	-3.163287
49	1	0	4.630826	2.159196	-3.958641
50	1	0	2.951964	2.538597	-3.644662
51	1	0	0.701798	7.009700	-3.841709
52	1	0	-2.381166	2.360334	-2.536451
53	1	0	-3.915401	5.502620	-2.866468
54	1	0	-4.210091	3.835548	-2.419122
55	1	0	-3.901561	-1.520793	-1.705539
56	1	0	-7.026326	-2.950500	-0.966782
57	1	0	-5.341260	-3.329819	-1.265824
58	1	0	-7.306822	3.937801	-1.530852
59	1	0	-5.341292	-6.526524	-1.085811
60	1	0	4.981073	-4.653928	-2.827036
61	1	0	2.919107	5.736971	-3.915245
62	1	0	-8.558281	1.758595	-1.062052
63	1	0	-3.214533	-7.833390	-1.643641
64	1	0	6.218777	-2.500941	-3.420117
65	19	0	-0.887573	-0.250586	-0.980137
66	7	0	-4.336242	-4.434176	1.879209
67	6	0	-5.033892	-3.294051	1.960876
68	6	0	-4.598727	-1.995335	1.745851
69	6	0	-3.251477	-1.789448	1.342486
70	7	0	-2.553580	-2.990909	1.238167
71	6	0	-3.079950	-4.232025	1.510226
72	7	0	-6.359873	-3.169736	2.276647
73	6	0	-6.661523	-1.829901	2.235271
74	7	0	-5.630195	-1.095978	1.923806
75	8	0	-2.691669	-0.713192	1.094045
76	7	0	-2.255300	-5.282393	1.411716
77	7	0	-3.433244	2.022590	1.013822
78	6	0	-2.314243	2.712527	0.562473
79	6	0	-2.574204	4.100609	0.408690
80	6	0	-3.839879	4.574702	0.710490
81	7	0	-4.902068	3.893114	1.155748
82	6	0	-4.648025	2.599495	1.296703
83	7	0	-1.737118	5.128830	0.030285
84	6	0	-2.480154	6.199349	0.086804
85	7	0	-3.765355	5.924720	0.491315
86	8	0	-1.250844	2.119029	0.344721
87	7	0	-5.619853	1.791382	1.736340
88	7	0	1.451378	2.733118	-0.138881
89	6	0	2.000350	3.984308	-0.293087
90	7	0	3.284965	4.204143	-0.517094
91	6	0	3.991652	3.065582	-0.595378
92	6	0	3.545881	1.764282	-0.436504
93	6	0	2.166321	1.537382	-0.192758
94	7	0	4.572763	0.865478	-0.613558
95	6	0	5.616835	1.598159	-0.876600
96	7	0	5.324089	2.942561	-0.881678
97	7	0	1.169653	5.035061	-0.185066

98	8	0	1.590912	0.451572	-0.048934
99	7	0	2.277641	-2.308604	0.113167
100	6	0	1.112219	-3.048760	0.253126
101	6	0	1.381879	-4.425144	0.470594
102	6	0	2.702628	-4.826932	0.586045
103	7	0	3.812608	-4.089605	0.482892
104	6	0	3.553636	-2.815325	0.224403
105	7	0	0.522581	-5.482323	0.684128
106	6	0	1.302298	-6.505222	0.903628
107	7	0	2.633641	-6.168998	0.856312
108	8	0	0.002005	-2.501116	0.204088
109	7	0	4.570536	-1.963664	0.030849
110	1	0	2.148461	-1.289753	0.025648
111	1	0	4.412770	-0.967757	-0.143136
112	1	0	5.407188	-2.160751	0.561774
113	1	0	0.436526	2.632039	0.017446
114	1	0	1.585819	5.929448	-0.379530
115	1	0	0.147346	4.962620	-0.164082
116	1	0	-4.511097	6.585436	0.637463
117	1	0	-3.296560	1.008608	1.145348
118	1	0	-6.507016	2.231564	1.906686
119	1	0	-5.542699	0.769051	1.790508
120	1	0	-1.577644	-2.913474	0.901746
121	1	0	-2.682342	-6.180255	1.561525
122	1	0	-1.287413	-5.245964	1.067758
123	1	0	-7.655334	-1.461448	2.441507
124	1	0	0.974147	-7.515197	1.100275
125	1	0	6.613190	1.227176	-1.064985
126	1	0	-2.159885	7.200131	-0.161519
127	1	0	-6.978863	-3.926642	2.517507
128	1	0	3.421956	-6.775364	1.015135
129	1	0	5.971939	3.702070	-1.010645
130	6	0	4.028207	0.016177	2.846026
131	6	0	2.636396	-1.705743	3.310738
132	6	0	1.511127	-0.846717	3.256482
133	6	0	1.824990	0.561387	3.213366
134	7	0	3.910247	-1.261807	3.095752
135	6	0	2.440183	-3.088773	3.531530
136	6	0	1.169180	-3.600837	3.611117
137	1	0	1.019608	-4.665347	3.761806
138	6	0	0.215077	-1.412705	3.229956
139	6	0	0.050041	-2.763960	3.423044
140	1	0	-0.943710	-3.197340	3.397626
141	1	0	-0.643186	-0.790322	2.998232
142	7	0	3.057538	0.954043	2.953016
143	1	0	3.322029	-3.716681	3.590553
144	6	0	-0.066130	1.367924	4.553146
145	6	0	1.291371	2.931427	3.336043
146	6	0	-2.302223	4.274560	3.615551
147	6	0	-1.290683	2.226479	4.366618
148	6	0	0.097076	3.816510	2.985754

149	1	0	1.749565	3.253496	4.284530
150	6	0	-3.518756	3.891288	4.166974
151	1	0	-2.215130	5.228418	3.100731
152	6	0	-2.514272	1.837129	4.910344
153	6	0	-1.183119	3.444928	3.693455
154	1	0	-0.091883	3.743940	1.911776
155	6	0	-3.629864	2.659009	4.805665
156	1	0	-4.382422	4.541858	4.079913
157	1	0	-2.591534	0.880548	5.421066
158	1	0	-4.580042	2.341907	5.222294
159	1	0	-0.348550	0.326441	4.672640
160	7	0	0.879764	1.533035	3.448047
161	1	0	2.058909	3.010449	2.568415
162	1	0	0.357067	4.861863	3.182313
163	1	0	0.436847	1.663472	5.490248
164	6	0	5.372460	0.547848	2.457266
165	6	0	5.620978	1.942370	2.586593
166	6	0	9.069710	1.992664	1.188024
167	6	0	7.462852	0.184118	1.578932
168	6	0	6.832132	2.438509	2.199175
169	1	0	4.839496	2.575551	2.985207
170	6	0	9.953087	1.093238	0.648314
171	1	0	9.327685	3.045665	1.261724
172	6	0	8.401096	-0.724724	1.024322
173	6	0	7.805624	1.560776	1.661626
174	1	0	7.056605	3.497882	2.290801
175	6	0	9.614186	-0.278923	0.567095
176	1	0	10.919681	1.428551	0.287131
177	1	0	8.126405	-1.773547	0.982255
178	1	0	10.327038	-0.979998	0.145311
179	7	0	6.258202	-0.300766	1.983539

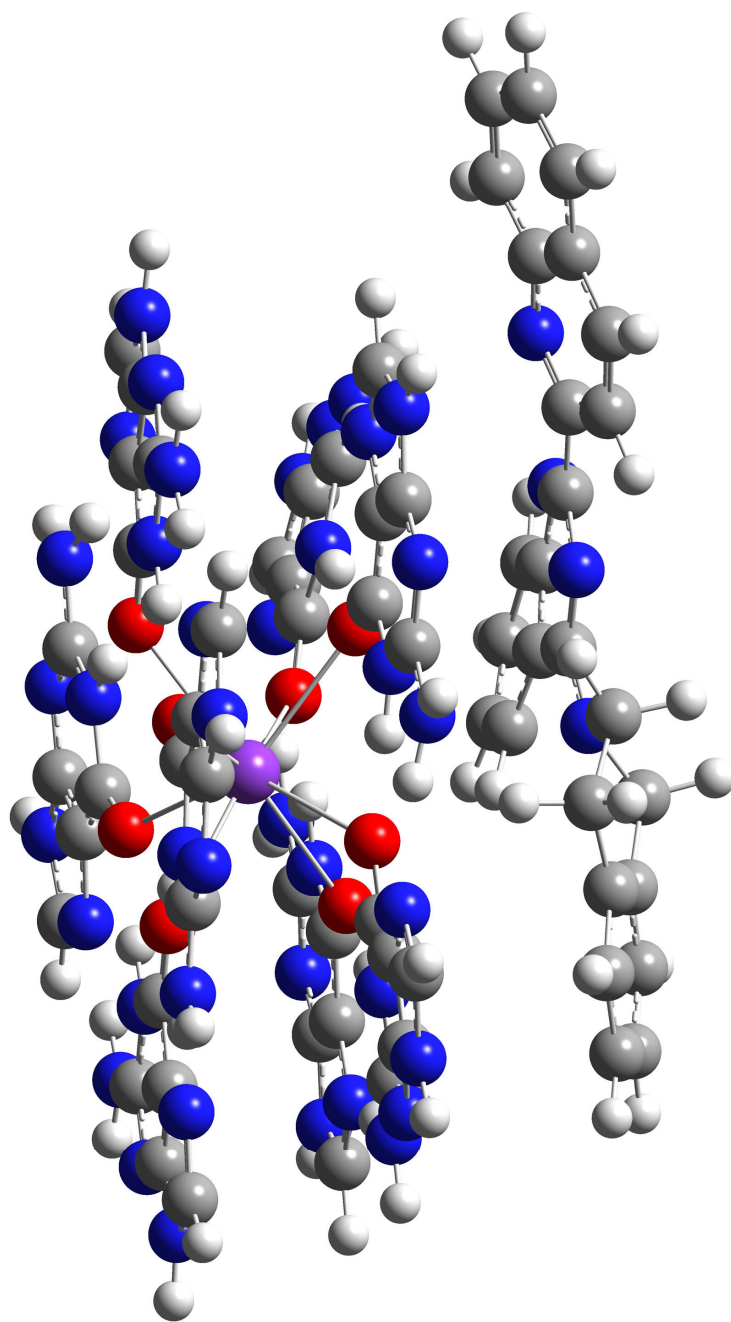


Figure S1. The optimized complex of the most active ligand **1**, having the lowest IC_{50} , “concave” form, with the model two-layered G-quadruplex. The computed stabilization energy at wB97XD/6-31G(d,p) is 39.04 kcal mol⁻¹.

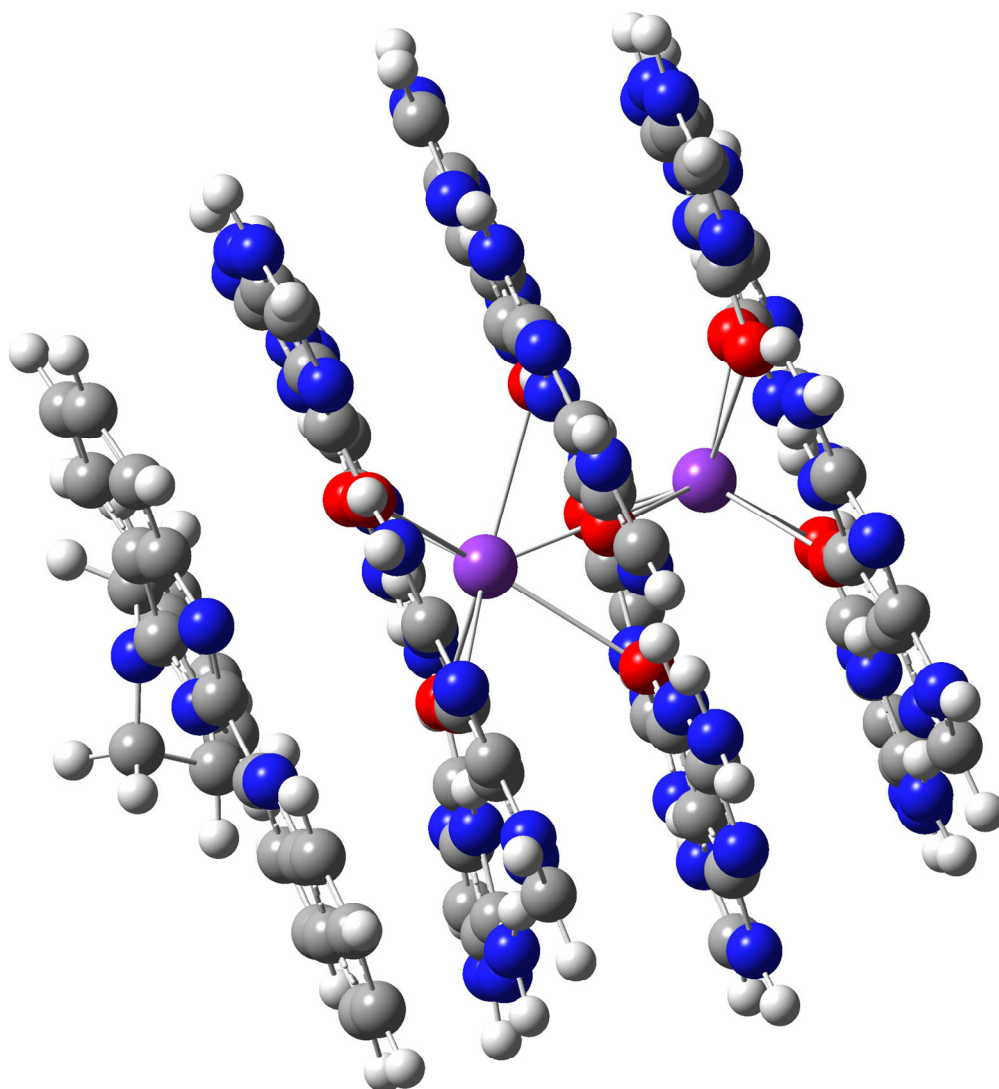


Figure S2. The optimized complex with the most active ligand **1**, having the lowest IC_{50} , “concave” form, with the model three-layered G-quadruplex. The computed stabilization energy at wB97XD/6-31G(d,p) is 41.53 kcal mol⁻¹.