Supplementary material

Lipophilicity and ADMET analysis of quinoline-1,4-quinone hybrids

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Table of contents

Figure S1. The optimalization structure of compounds **1-24**.

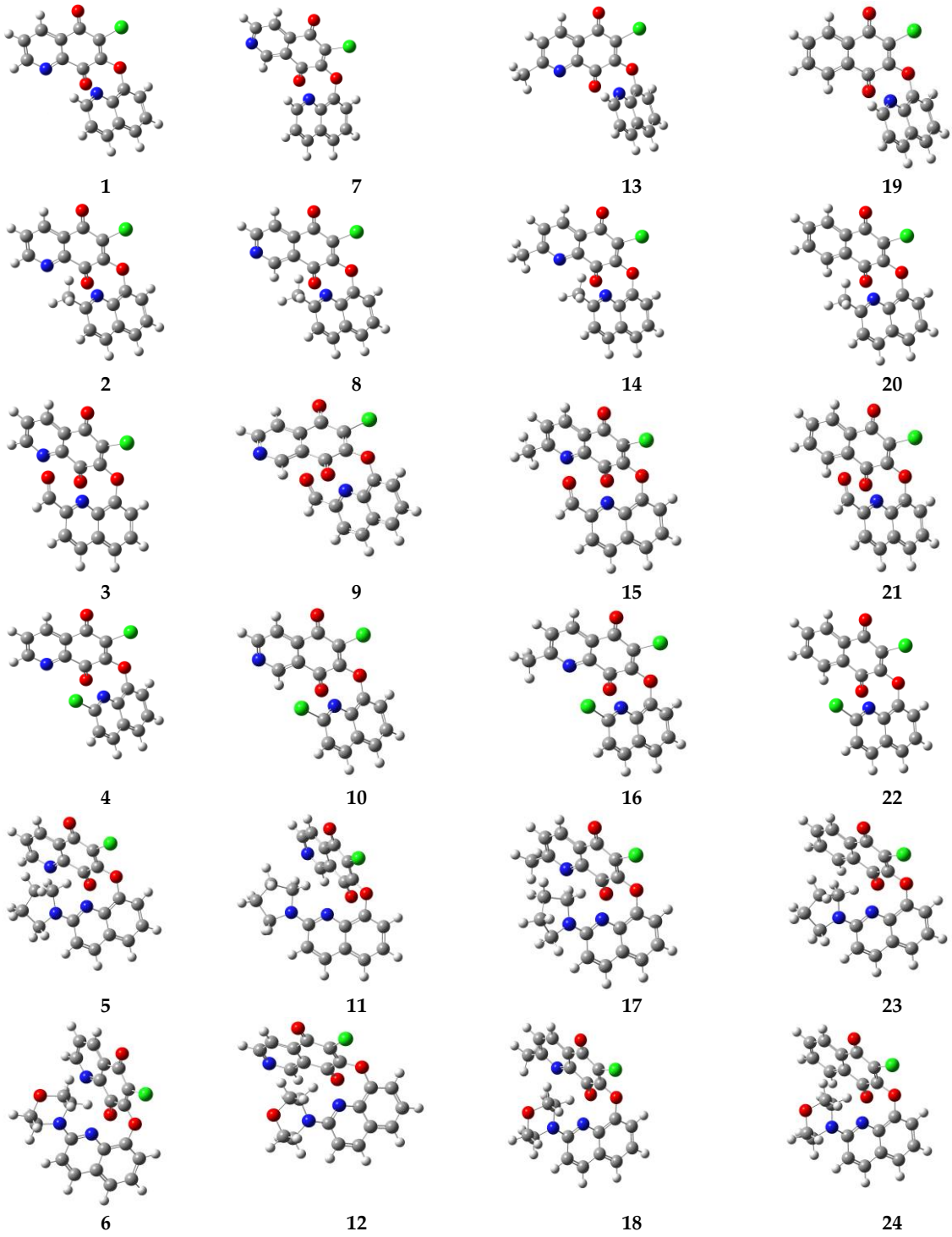

Figure S2. Docking pose of the BCL-2 protein complex with Venetoclax.

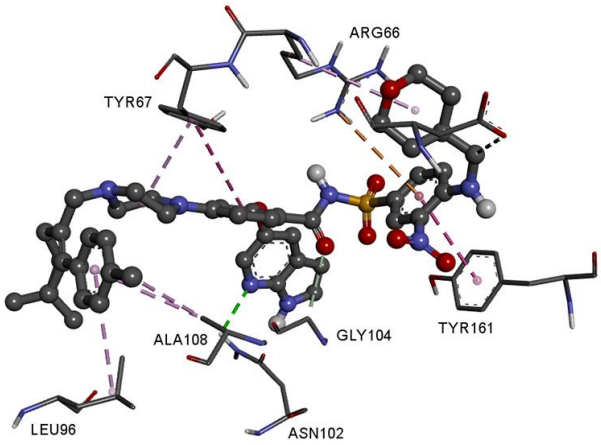

Table S1. Theoretical value of lipophilicity of compounds **1-24**.

Compound	ILOGP	XLOGP3	WLOGP	MLOGP	SILICOS-IT	milogP
1	1.87	3.56	3.54	0.80	3.85	2.17
2	2.18	3.96	3.85	1.03	4.36	2.22
3	1.55	3.35	3.35	0.14	4.05	2.03
4	2.10	4.52	4.19	1.30	4.49	3.19
5	2.30	4.50	3.76	1.55	4.14	3.02
6	2.45	3.64	2.99	0.75	3.73	2.46
7	2.23	3.22	3.54	0.80	3.85	2.82
8	2.39	3.62	3.85	1.03	4.36	2.87
9	1.65	3.02	3.35	0.14	4.05	2.68
10	2.24	4.18	4.19	1.30	4.49	3.84
11	2.49	4.17	3.76	1.55	4.14	3.66
12	2.37	3.31	2.99	0.75	3.73	3.11
13	2.15	3.96	3.85	1.03	4.36	2.22
14	2.43	4.36	4.16	1.25	4.87	2.28
15	1.65	3.75	3.66	0.37	4.57	2.08
16	2.43	4.92	4.5	1.52	5.00	3.24
17	2.81	4.90	4.07	1.76	4.66	3.07
18	2.72	4.04	3.30	0.96	4.25	2.51
19	2.32	4.29	4.14	1.86	4.41	3.91
20	2.69	4.69	4.45	2.08	4.92	3.97
21	2.02	4.09	3.96	1.18	4.61	3.77
22	2.68	5.25	4.8	2.35	5.04	4.93
23	2.88	5.24	4.36	2.57	4.71	4.76
24	2.62	4.38	3.60	1.76	4.30	4.20

Table S2. Experimental ($logP_{TLC}$) and calculated by the multilinear regression (MLR) equation (5) ($logP_{calc}$) value of lipophilicity and absolute error.

Compound	$logP_{TLC}$	$logP_{calc}$	Error	Compound	$logP_{TLC}$	$logP_{calc}$	Error
1	1.65	2.47	0.50	**13**	2.31	2.54	0.10
2	1.84	2.54	0.38	**14**	2.00	2.61	0.30
3	1.75	2.24	0.28	**15**	2.26	2.31	0.02
4	2.55	2.64	0.03	**16**	3.30	2.71	0.18
5	2.60	3.66	0.41	**17**	3.79	3.72	0.02
6	2.72	3.07	0.13	**18**	2.98	3.14	0.05
7	2.40	2.47	0.03	**19**	3.23	3.57	0.11
8	2.85	2.54	0.11	**20**	3.73	3.64	0.03
9	2.72	2.24	0.18	**21**	4.61	3.74	0.19
10	3.63	2.64	0.27	**22**	5.06	3.34	0.34
11	3.15	3.66	0.16	**23**	4.16	4.75	0.14
12	3.68	3.07	0.17	**24**	4.50	4.17	0.07

Table S3. Experimental (logNQO1) and calculated by the multilinear regression (MLR) equation (5) ($logNQO1_{calc}$) value of lipophilicity and absolute error.

Compound	logNQO1	$logNQO1_{cal}$	Error	Compound	logNQO1	$logNQO1_{cal}$	Error
1	3.146	2.933	0.07	**13**	3.178	2.926	0.08
2	3.112	2.900	0.07	**14**	3.157	2.897	0.08
3	3.041	3.010	0.01	**15**	2.672	2.993	0.12
4	2.903	3.014	0.04	**16**	2.949	3.007	0.02
5	3.034	2.422	0.20	**17**	2.778	2.446	0.12
6	2.053	2.464	0.20	**18**	2.322	2.500	0.08
7	3.083	2.930	0.05	**19**	3.108	2.929	0.06
8	3.058	2.888	0.06	**20**	3.100	2.899	0.06
9	2.502	2.967	0.19	**21**	2.740	2.986	0.09
10	2.801	2.956	0.06	**22**	3.000	3.008	0.01
11	2.330	2.307	0.01	**23**	2.549	2.492	0.02
12	2.155	2.323	0.08	**24**	1.940	2.521	0.30

Table S4. Interaction of 2-methyl-5,8-quinolinedione hybrids **7-12** with BCL-2 protein.

Ligand	2-methylo-5,8-quinolinedione moiety			Quinoline scaffold		
	Residue	Type	Distance	Residue	Type	Distance
7	Phe63	Pi-alkyl	4.972	Ala59	Pi-alkyl	4.476 4.788
	Gly104	Amide-Pi Stacked	4.406 3.868	Val107	Pi-alkyl	5.136
	Arg105	Pi-Alkyl	4.896	Tyr161	Pi-Pi Stacked	4.081 5.058
	Ala108	Alkyl	3.787			
8	Phe63	Pi-alkyl	5.015	Ala59	Pi-alkyl	4.468 4.651
	Gly104	Amide-Pi Stacked	4.393 3.394	Val107	Pi-alkyl	5.091
	Arg105	Pi-Alkyl	4.852	Tyr161	Pi-Pi Stacked	4.099 5.088
	Ala108	Pi-Alkyl	3.728 5.418			
9	Phe63	Pi-alkyl	4.986	Ala59	Pi-alkyl	4.459 4.668
	Gly104	Amide-Pi Stacked	4.361 3.850	Val107	Pi-alkyl	5.074
	Arg105	Pi-Alkyl	4.865	Tyr161	Pi-Pi Stacked	4.082 5.002
	Ala108	Alkyl	3.765 5.410			
10	Phe63	Pi-alkyl	5.004	Ala59	Pi-alkyl	4.460 4.633
	Gly104	Amide-Pi Stacked	4.386 3.833	Val107	Pi-alkyl	5.072
	Arg105	Pi-Alkyl	4.852	Tyr161	Pi-Pi Stacked	4.086 5.048
	Ala108	Alkyl	3.721 5.818			
11	Phe63	Pi-Alkyl	5.257	Ala59	Pi-Alkyl	4.573 4.387
	Leu96	Alkyl	5.322	Arg66	Alkyl	5.441
	Arg105	Alkyl Pi-Alkyl	4.616 4.821	Val107	Pi-Alkyl	5.020
	Ala108	Alkyl Pi-Alkyl	3.686 5.426	Tyr161	Pi-Pi Stacked	4.098 5.034
12	Phe63	Pi-Alkyl	4.899	Ala59	Pi-Alkyl	4.694 4.381
	Tyr67	Pi-Sigma	3.820	Arg66	H-bond	2.527
				Val107	Pi-Alkyl	4.987
				Tyr161	Pi-Pi Stacked	3.841 4.702