Supporting Information

Protein binding of benzofuran derivatives: A CD spectroscopic and in silico comparative study of the effects of 4-nitrophenyl functionalized benzofurans and benzodifurans on BSA protein structure.

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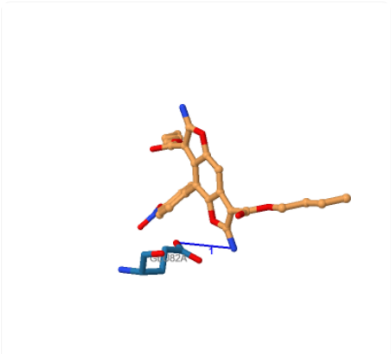
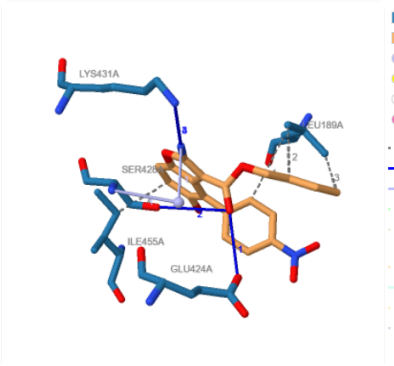


Hydrogen Bonds

Index	Residue	AA	Distance H-A	Distance D-A	Donor Angle	Protein donor?	Side chain	Donor Atom	Acceptor Atom
1	82A	GLU	3.66	4.02	103.99	×	✓	4865 [Npl]	654 [O2]



Hydrophobic Interactions

Index	Residue	AA	Distance	Ligand Atom	Protein Atom
1	189A	LEU	3.90	4851	1535
2	189A	LEU	3.05	4848	1537
3	189A	LEU	2.91	4856	1538
4	455A	ILE	3.22	4846	3652

Hydrogen Bonds

Index	Residue	AA	Distance H-A	Distance D-A	Donor Angle	Protein donor?	Side chain	Donor Atom	Acceptor Atom
1	424A	GLU	2.66	3.33	128.77	✓	✓	3416 [O3]	4833 [O2]
2	428A	SER	3.25	3.63	105.62	✓	✓	3446 [O3]	4833 [O2]
3	431A	LYS	2.89	3.45	115.57	✓	✓	3467 [N3]	4836 [Npl]
4	431A	LYS	3.01	3.45	108.66	×	✓	4836 [Npl]	3467 [N3]

Water Bridges

Index	Residue	AA	Dist. A-W	Dist. D-W	Donor Angle	Water Angle	Protein donor?	Donor Atom	Acceptor Atom	Water Atom
1	428A	SER	3.22	3.46	121.54	92.94	✓	3441 [Nam]	4836 [Npl]	4680

Figure S1. 3D interaction diagrams for BDF1 (up) and BF1 (bottom) in complex with monomeric BSA (PDB ID: 4f5s, chain: A) obtained by PLIP (Protein–Ligand Interaction Profiler, https://plip-tool.biotec.tu-dresden.de/, accessed on 31 December 2021).

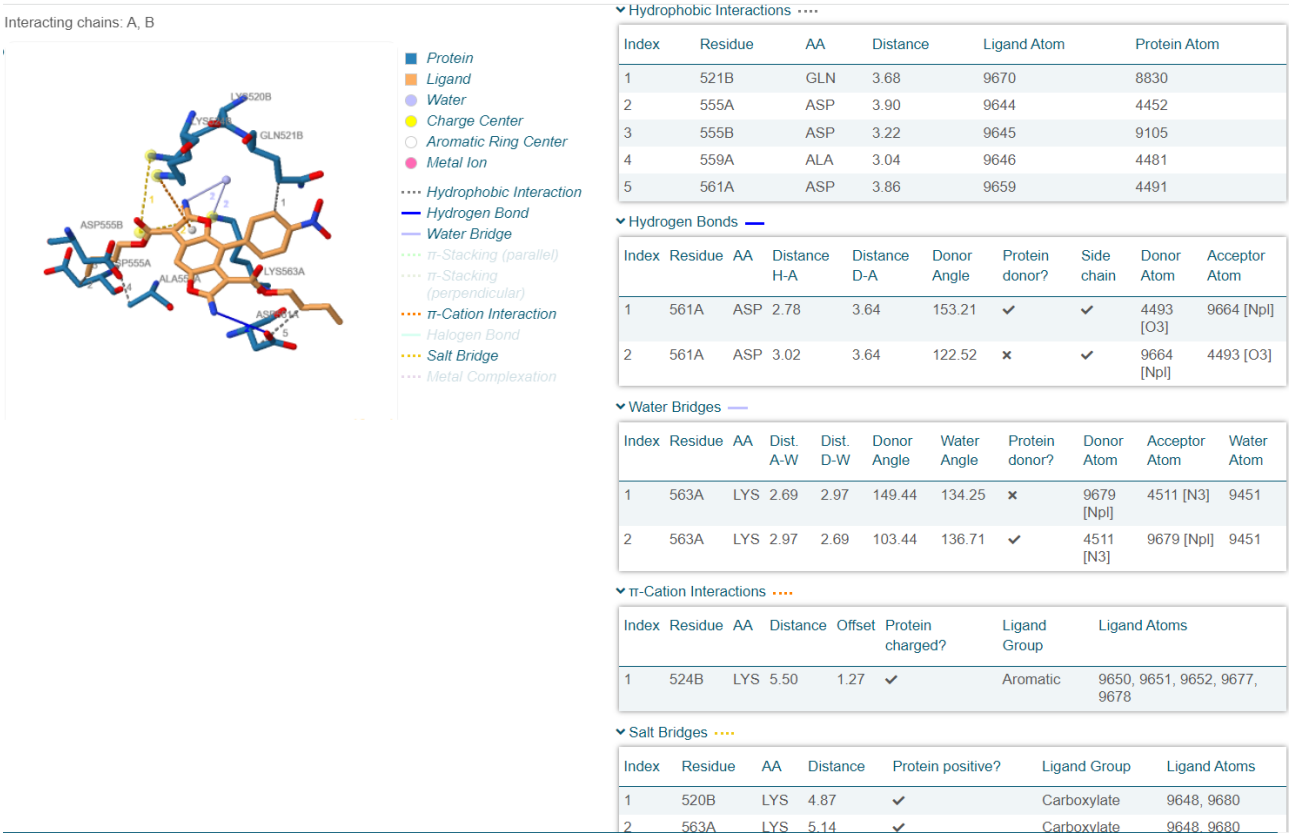
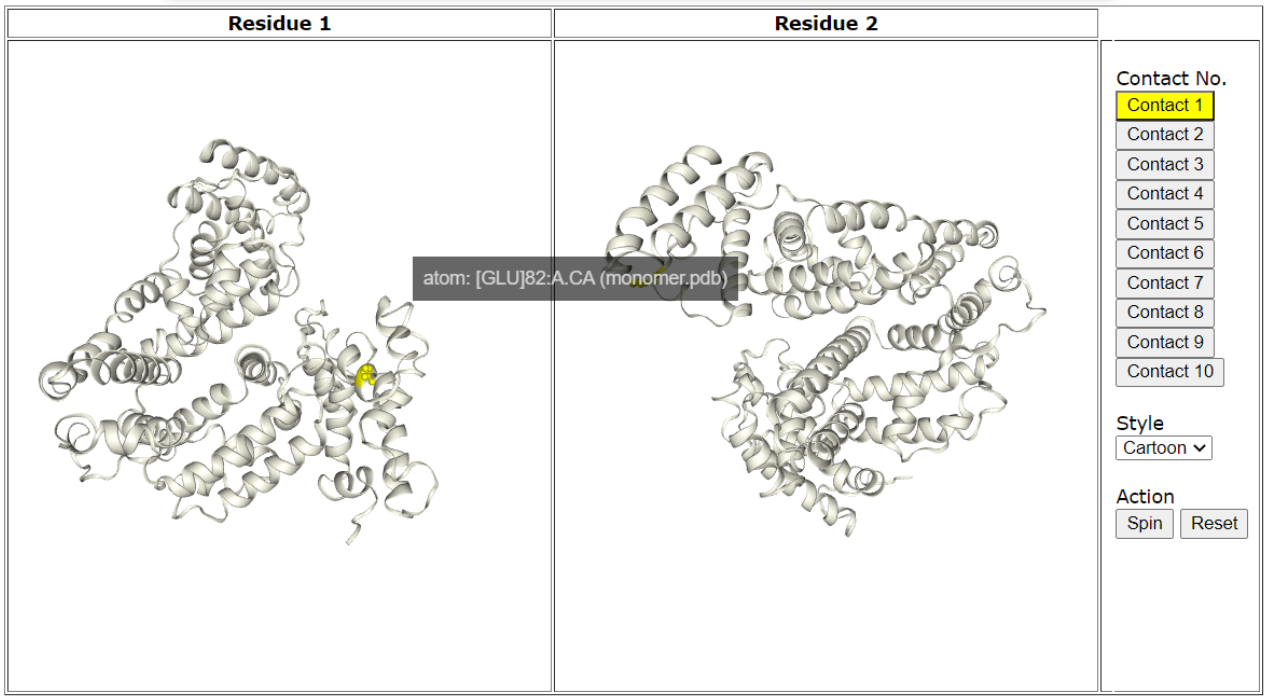


Figure S2. 3D interaction diagrams for BDF1 (up) and BF1 (bottom) in complex with dimeric BSA (PDB ID: 4f5s, chains: A,B) obtained by PLIP (Protein–Ligand Interaction Profiler, https://plip-tool.biotec.tu-dresden.de/, accessed on 31 December 2021).



Summary of the top 10 contacts

Rank	1	2	3	4	5	6	7	8	9	10
Residue 1	GLU 97	CYS 101	GLU 97	ARG 98	LYS 180	LYS 64	GLU 97	GLU 63	GLU 100	GLU 97
Residue 2	HIS 509	HIS 509	PRO 572	HIS 509	GLU 339	GLU 503	LYS 573	PHE 501	HIS 509	GLY 571
Predicted Score	0.2149	0.2110	0.2052	0.1996	0.1969	0.1819	0.1795	0.1791	0.1790	0.1787

Figure S3. Inter-protein residue-residue contacts for homo-dimeric BSA as predicted by DeepHomo Server (http://huanglab.phys.hust.edu.cn/deephomo/data/61ce50fad2e29/, accessed on 31 December 2021). Note how Glu-82 lies in the vicinity of one of the main residues (Glu-97) involved in the dimerization of BSA as predicted by DeepHomo Server.

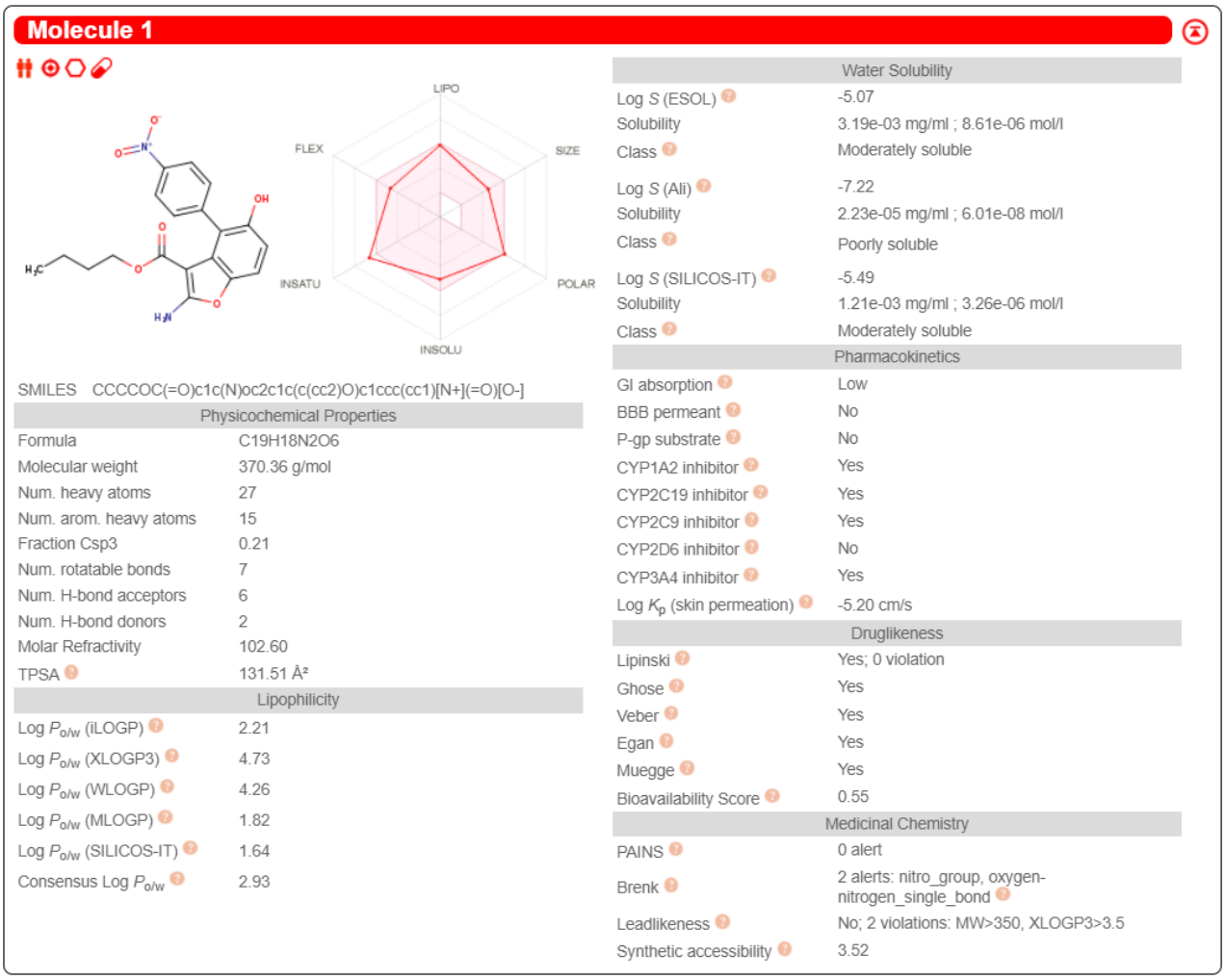


Figure S4. Pharmacokinetic properties, including partition coefficients (cLogP), blood–brain barrier (BBB) permeability, pan-assay interference compounds (PAINS) score, and other druggability properties, predicted by SwissADME (http://www.swissadme.ch/index.php, accessed on 14 December 2021) for BF1.

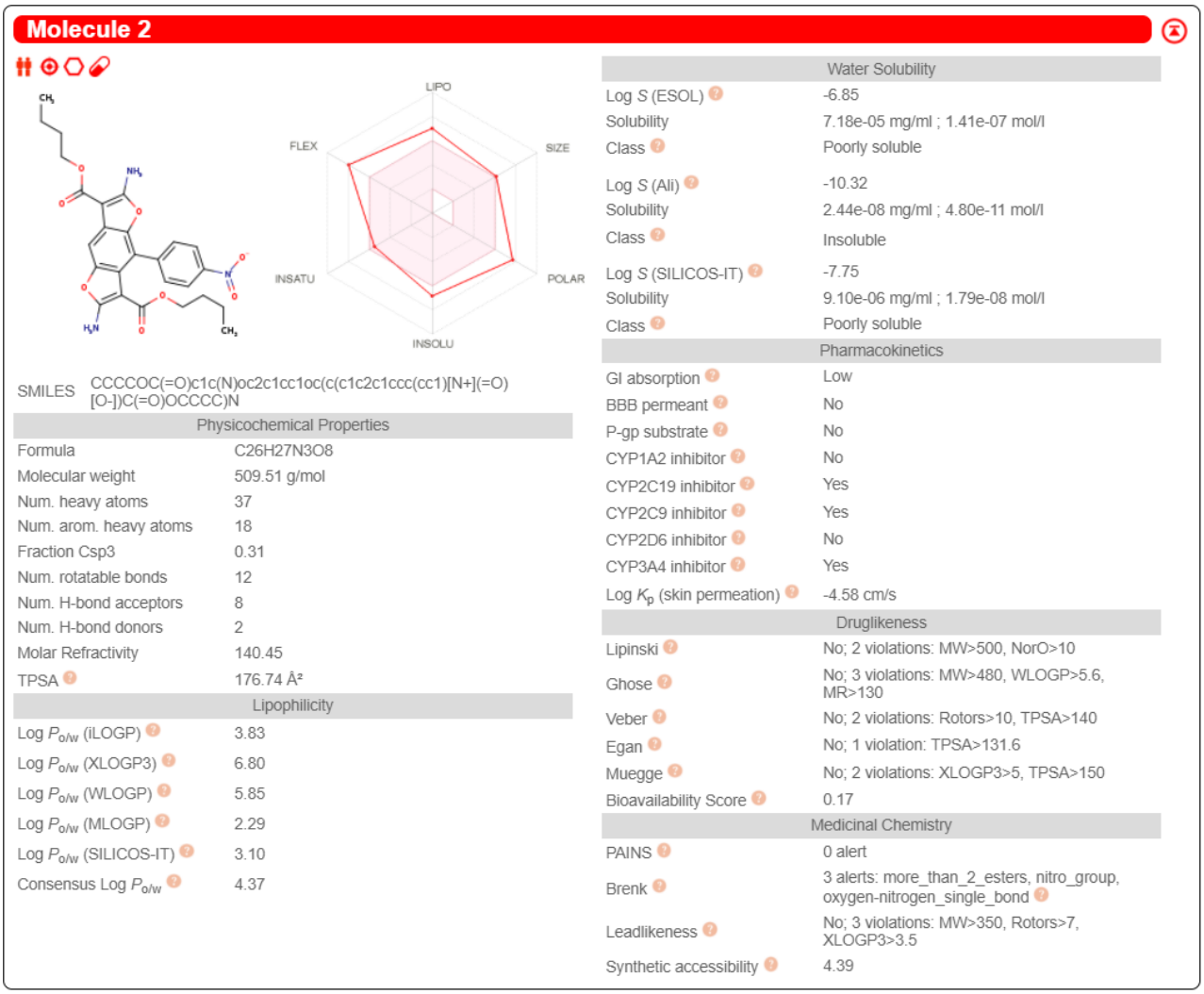


Figure S5. Pharmacokinetic properties, including partition coefficients (cLogP), blood–brain barrier (BBB) permeability, pan-assay interference compounds (PAINS) score, and other druggability properties, predicted by SwissADME (http://www.swissadme.ch/index.php, accessed on 14 December 2021) for BDF1.