

Identification of Novel Bromodomain-Containing Protein 4 (BRD4) Binders through 3D Pharmacophore-Based Repositioning Screening Campaign

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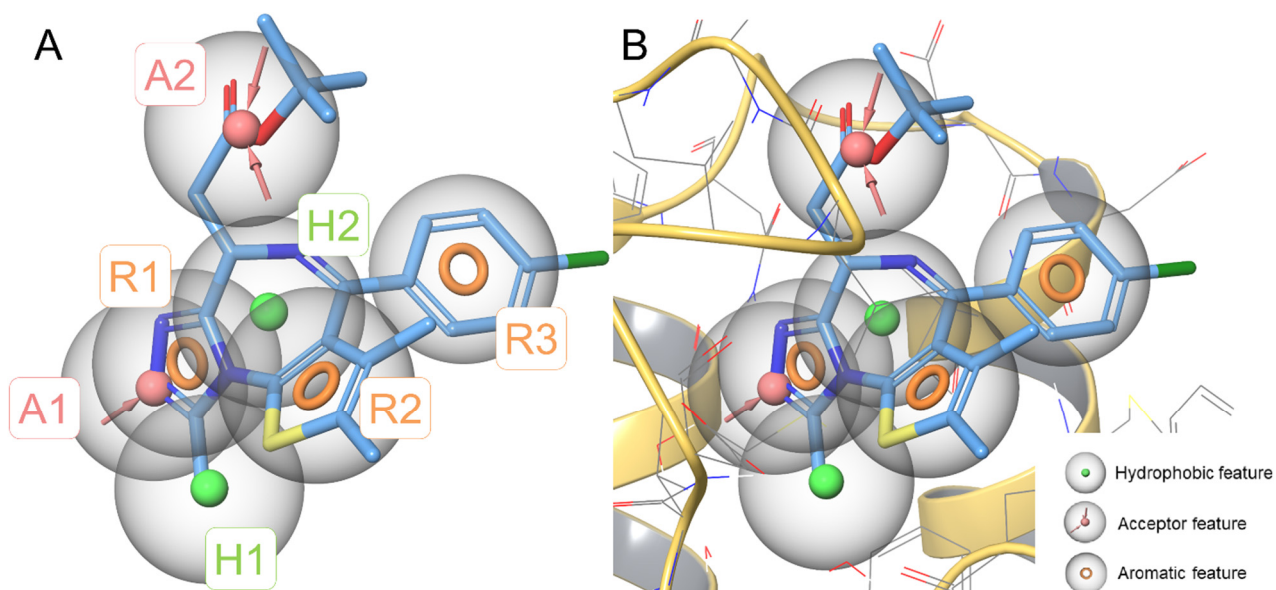


Figure S1. A) Representation of the AAHHRRR-7 point BRD4 pharmacophore model, featuring the specified features (“A” = acceptor, “H” = hydrophobic, and “R” aromatic ring groups). B) Representation of the AAHHRRR-7 point BRD4 pharmacophore model in the BRD4 binding site.

Table S1. SMILES of the compounds belonging to the investigated in-house library.

Compound	Smile
1	<chem>c1cccc(n(c2=O)CC)c1n(c23)nc(c3)C(=O)NCCOc4c(OC)cccc4</chem>
2	<chem>CCOc(ccc1)c(c12)oc(=O)c(c2)C(=O)OCCn3c([N+])([O-])=O)cnc3C</chem>
3	<chem>CCOC(=O)c1ccc(cc1)Nc2ncnc(c23)n(mn3)CC</chem>
4	<chem>CC(=O)c1cc(ccc1)NC(=O)c2cc(C3CC3)nc(c24)n(C(C)C)nc4</chem>
5	<chem>COC(OC)CNC(=O)c(c1)ccc(c12)n(c(n2)C)-c3cc(F)ccc3</chem>
6	<chem>CCCN(c1=O)c(cccc2)c2n(c13)nc(c3)C(=O)NCCc4c[nH]c(c45)ccc(c5)OC</chem>
7	<chem>C1CCCCc(c12)sc(c2C(=O)OCC)NC(=O)CSc(nn3)n(c34)c5c(c(C)c4)cccc5</chem>
8	<chem>CCOc(cc1)ccc1[C@@H]2C(C#N)=C(N)Oc3c2ccc(=O)c(c34)c(C)oc4C</chem>
9	<chem>CCc1nnc(s1)NC(=O)c(c2N)sc(c23)nc(C)cc3COC</chem>
10	<chem>O=c(o1)cc(CC)c(c2)c1c(C)c(c23)oc(C)c3C</chem>
11	<chem>c1cccc(c1OC)Oc(c2C)c(n[nH]2)-c3c(O)cc(O)cc3</chem>
12	<chem>Cc1ccc(cc1)S(=O)(=O)NCCC(=O)Oc(cc2)cc(c23)oc(=O)c(Cl)c3C</chem>
13	<chem>n1cccc1NC(=O)CNC(=O)c(c2)[nH]c(c23)c(OC)ccc3OC</chem>
14	<chem>Cc1cc(C)cc(c12)occ2CC(=O)Nc(sc(c34)CCC4)c3C(=O)NCCCOC</chem>
15	<chem>COc1ccc(OC)c(c12)[nH]c(c2)C(=O)N(C3)CCC[C@H]3c(nn4)n(c45)cccc5</chem>
16	<chem>COc1c(Cl)cc(cc1)NC(=O)CCNC(=O)c(c2)n(C)c(c23)cc(OC)cc3OC</chem>
17	<chem>Cc(n1)sc(c12)c(n[nH]c2=O)-c3cc(OC)ccc3</chem>
18	<chem>O=S1(=O)C[C@H](CC1)NC(=O)c(c2[O-])cnc(c23)c(Cl)ccc3</chem>
19	<chem>O=S1(=O)C[C@H](CC1)NC(=O)c(c2[O-])cnc(c23)c(OC(F)(F)F)ccc3</chem>

20	<chem>c1ccc(OC(F)(F)F)c(c12)[nH]cc(c2=O)C(=O)N3CCN(CC3)C(=O)OCC</chem>
21	<chem>COc1ccc(OC)c(c12)[nH]c(c2)C(=O)NCCNC(=O)[C@H]3CCCO3</chem>
22	<chem>COc1ccc(OC)c(c12)[nH]c(c2)C(=O)NCCNC(=O)c3cccnc3</chem>
23	<chem>c1ccc(OC)c(c12)oc(c2)C(=O)Nc(c3)ccc(c34)OCO4</chem>
24	<chem>CCc(n1)nn(c12)c(ccn2)-c3ccc(Br)cc3</chem>
25	<chem>FC(F)(F)c1cc(ccc1)Nc(cc2C)nc(n2)Nc(cc3C(F)(F)F)ccc3</chem>
26	<chem>c1cc(F)cc(OC)c1-c(ccn2)n(c23)nc(n3)C4CCC4</chem>
27	<chem>c1cc(F)cc(OC)c1-c(ccn2)n(c23)nc(n3)[C@@H]4CCCO4</chem>
28	<chem>O=c1[nH]c(C)nc(c12)sc(c2C)C(=O)NCCc3c[nH]c(c34)ccc(Cl)c4</chem>
29	<chem>Cc1[nH]nc(C)c1CCC(=O)Nc(c2)ccc(c23)ncn(c3=O)C4CCC4</chem>
30	<chem>CS(=O)(=O)N(CC1)CCN1C(=O)c(c2=O)c[nH]c(c23)c(OC)ccc3</chem>
31	<chem>CSCC[C@@H](CO)NC(=O)Cn(c1=O)nc(c12)ccc(OC)c2OC</chem>
32	<chem>COC(=O)c1c(cccc1)NC(=O)c(c2N)sc(c23)nc(C)cc3C(F)(F)F</chem>
33	<chem>c1cccc(c12)n3c(n2)c(C#N)c(C)cc3-n4ccnc4</chem>
34	<chem>c1cccc(c12)n(c(n2)[C@@H](C)O)CCOc(cc3)ccc3C</chem>
35	<chem>CC(=O)c1c(=O)[nH]c2ccc(Cl)c(c2c13)C(=O)c4c3cccc4</chem>
36	<chem>COCCNC(=O)c1c(sc(c12)CCCC2)NC(=O)c3cc(n[nH]3)-c(cc4)c(O)cc4C</chem>
37	<chem>COc(c1)ccc(OC)c1NC(=O)c2cc(n[nH]2)-c(c3C)c(O)cc(C)c3</chem>
38	<chem>CCNc1c(=O)n(C)c2cccc(c2c13)C(=O)c4c3cccc4</chem>
39	<chem>COc1c(Cl)cc(cc1)NC(=O)c(c2N)sc(c23)nc(C)cc3C</chem>
40	<chem>CCOc(c1)ccc(c12)nc(C(=O)OCC)c2Nc(ccc3)cc3C(=O)OCC</chem>
41	<chem>CCOC(=O)c(c1)ccc(c12)nc(C)cc2Nc3c(OC)ccc(Cl)c3</chem>
42	<chem>CCOC(=O)c(c1)ccc(c12)nc(C)cc2Nc(c3CC)cccc3</chem>
43	<chem>CCOC(=O)C1=C(C)N(c2ccccc2)C(=O)N[C@@H]1c3c(Br)ccc(c3)O</chem>
44	<chem>CCOC(=O)C1=C(C)N(c2ccccc2)C(=O)N[C@H]1c3c(Br)ccc(c3)O</chem>
45	<chem>CC(=O)c1cc(ccc1)Nc(cc(n2)C)n(c23)nc(n3)-c4ccccc4</chem>
46	<chem>c1ccc(Cl)cc1Nc(cc(n2)C)n(c23)nc(c3)-c4cc(OC)c(cc4)OC</chem>
47	<chem>c1ccc(OC)cc1C(=O)N(c2ccc(Cl)cc2)Cc(n3)nn(c34)c([O-])cc(n4)C</chem>
48	<chem>c1cccc(F)c1Nc(cc(n2)C(C)C)n(c23)nc(n3)-c4ccnc4</chem>
49	<chem>o1cccc1CNC(=O)CNC(=O)c(c2)[nH]c(c23)c(OC)c(OC)c(c3)OC</chem>
50	<chem>FC(F)(F)c1cc(ccc1)N(C2=O)N=C(CC)C2=C\c3c([O-])ccc(c3)[N+](([O-])=O</chem>
51	<chem>c1ncccc1CNC(=O)c(c2-n3ccccc3)sc(c24)nc(C)cc4C</chem>
52	<chem>Cc(n1)ccc(cc2)c1c(c23)[nH]c(c3)C(=O)N4CCN(CC4)c5ccccc5</chem>
53	<chem>N#CCSc(nn1)n(c12)c3c(c(=O)n2CCC)ccc(c3)C(=O)NCC(C)C</chem>
54	<chem>CC(C)Cn(c(n1)CO)c(c12)cccc2</chem>
55	<chem>O=C1C[C@H](C#N)CN1c(c2)ccc(OC)c2OC</chem>
56	<chem>COc(cc1)c(OC)cc1[C@@H]2NCCc(c23)[nH+][c[nH]3</chem>
57	<chem>CCCN(C(=O)C1=O)c(c12)ccc(Br)c2</chem>
58	<chem>CCNc(n1CC)nc(c12)n(C)c(=O)[nH]c2=O</chem>
59	<chem>ClC1(Cl)[C@H](C1)Cn(c(n2)CO)c(c23)cccc3</chem>
60	<chem>CC(=O)c1cc(F)c(O)cc1</chem>
61	<chem>c1cc(F)ccc1-n(c2C)nc(c23)c(=O)n(C)nc3C</chem>
62	<chem>CC(C)c1nc(C2CC2)nc(n1)N</chem>
63	<chem>c1cccc2n(CCC)c(=O)c(c3c12)NC(=O)[C@H](O3)C</chem>
64	<chem>COCCc([nH]1)nc(c12)n(C)c(=O)n(C)c2=O</chem>
65	<chem>OCc(n1)[nH]c(c12)cccc2</chem>

66	<chem>O=c1n(C)cnc2sc(c3c12)CCCC3</chem>
67	<chem>CCn(c1=O)cnc2sc(c3c12)C[C@H](C)CC3</chem>
68	<chem>CCn(c1=O)cnc2sc(c3c12)CCCC3</chem>
69	<chem>CC(C)n(c1=O)cnc(c12)sc(C)c2C</chem>
70	<chem>CC(C)Cn(c1=O)cnc(c12)sc(c2)CC</chem>
71	<chem>Cc1cc(C)nc(n1)Nc2ccc(F)cc2</chem>
72	<chem>CNC(=O)Cc(c1C(=O)NC)n(C)cc1C</chem>
73	<chem>OCc(n1)n(CC)c(c12)cccc2</chem>
74	<chem>CCCNc(c1C)nc(=O)[nH]n1</chem>
75	<chem>n1[nH]c(=O)nc(c1C)N[C@@H](C)c2cccc2</chem>
76	<chem>CC[C@H](C)Nc(c1C)nc(=O)[nH]n1</chem>
77	<chem>CCNc(c1C)nc(=O)[nH]n1</chem>
78	<chem>CCCNc(c1C)nc(=S)[nH]n1</chem>
79	<chem>n1[nH]c(=O)nc(c1C)N[C@@H]([C@@H]2C)CCCC2</chem>
80	<chem>Cc1c(Cl)cc(OC)c(c1)Nc(cc(n2)C)n(c23)nc(n3)-c4cccc4</chem>
81	<chem>s1cc(C)n(c12)c(=O)cc(n2)C[N@@H+](CCC)Cc3cc(OC)c(OC)c(c3)OC</chem>
82	<chem>c1cc(F)cc(OC)c1-c(ccn2)n(c23)nc(n3)C4CCC4</chem>
83	<chem>O1COc(c12)ccc(c2)CNC(=O)CC3CCN(CC3)C(=O)c(c4)ccc(c45)oc(n5)C6CC6</chem>
84	<chem>c1cc(F)ccc1CNC(=O)CC2CCN(CC2)C(=O)c(c3)ccc(c34)oc(n4)C5CC5</chem>
85	<chem>CC[C@H](C)NC(=O)CSc(n1)n(CC)c(=O)c(c1c23)n(C)c2ccc(c3)OC</chem>
86	<chem>c1cccc1CNC(=O)CN(C(=O)S2)C(=O)\C2=C\c3ccc(cc3)OC</chem>
87	<chem>n1nc(C)n(c12)c3c(cccn3)n(c2=O)CC(=O)N[C@@H](CC)c4ccc(cc4)OC</chem>
88	<chem>O1CCOc(c12)ccc(c2)NC(=O)CCCCn(c3=O)c(=O)[nH]c(c34)cccc4</chem>
89	<chem>O1CCOc(c12)ccc(c2)NC(=O)CCCCn(c3=O)c(=O)[nH]c(c34)cccc4</chem>
90	<chem>c1ncc(Br)cc1NC(=O)CCCCn(c2=O)c(=O)[nH]c(c23)cccc3</chem>
91	<chem>c1ncc(Br)cc1NC(=O)CCCCCn(c2=O)c(=O)[nH]c(c23)cccc3</chem>
92	<chem>c1nc(I)ccc1NC(=O)CCCCCn(c2=O)c(=O)[nH]c(c23)cccc3</chem>
93	<chem>n1csc(c12)cc(cc2)NC(=O)CCCCCn(c3=O)c(=O)[nH]c(c34)cccc4</chem>
94	<chem>c1cc(F)ccc1/C=C/C(NC(C)=C2C(=O)OCC)=N[C@@H]2c3c(Br)ccc(c3)O</chem>
95	<chem>c1cc(F)ccc1/C=C/C(NC(C)=C2C(=O)OCC)=N[C@H]2c3c(Br)ccc(c3)O</chem>
96	<chem>O1CCOC12CCN(CC2)C(=O)c3snc(c34)c(=O)n(c([n-]4)=O)CCC</chem>
97	<chem>c1cc(Cl)ccc1/C=C2/C(C)=NN(C2=O)c(cc3)ccc3[N+](O-)=O</chem>
98	<chem>COc(c1)cc(OC)cc1COc(ccc2)cc2-c3nc(N)nc(c34)[nH]cn4</chem>
99	<chem>c1cccc1COc(ccc2)cc2-c3nc(N)nc(c34)[nH]cn4</chem>
100	<chem>FC(F)(F)c1cc(c(Cl)cc1)OCc2ccc(cc2)-c3nc(N)nc(c34)[nH]cn4</chem>
101	<chem>COC(=O)[C@@H]1CCCN1C(=O)c(c2)nn(c23)c4c(cccc4)n(c3=O)CC(C)C</chem>
102	<chem>c1cccc1C(=O)c2ccc(cc2)Cn(nn3)cc3-c4cc(O)ccc4</chem>
103	<chem>c1cc(O)c(O)cc1/C=C2/C(=O)N(C(=O)S2)Cc3nnc(o3)-c4ccccn4</chem>
104	<chem>CCOC(=O)C1=C(C)N(CCC([O-])=O)C(=O)N[C@@H]1c2ccc([N+](O-)=O)cc2</chem>
105	<chem>CCOC(=O)C1=C(C)N(CCC([O-])=O)C(=O)N[C@H]1c2ccc([N+](O-)=O)cc2</chem>
106	<chem>CCOC(=O)C1=C(C)N(c2cccc2)C(=O)N[C@@H]1c3c(Br)cc(c(c3)O)OC</chem>
107	<chem>CCOC(=O)C1=C(C)N(c2cccc2)C(=O)N[C@@H]1c3c(O)ccc(c3)OC</chem>
108	<chem>CCOC(=O)C1=C(C)N(c2cccc2)C(=O)N[C@@H]1c3c([N+](O-)=O)ccc([O-])c3</chem>
109	<chem>CCOC(=O)C1=C(C)N(c2cccc2)C(=O)N[C@@H]1c3c([N+](O-)=O)cccc3</chem>
110	<chem>CCOC(=O)C1=C(C)N(c2cccc2)C(=O)N[C@@H]1c3cc(Br)ccc3</chem>
111	<chem>CCOC(=O)C1=C(C)N(c2cccc2)C(=O)N[C@@H]1c3cc([N+](O-)=O)ccc3</chem>

112	<chem>CCOC(=O)C1=C(C)N(c2ccccc2)C(=O)N[C@@H]1c3ccc(Br)cc3</chem>
113	<chem>CCOC(=O)C1=C(C)N(c2ccccc2)C(=O)N[C@@H]1c3ccc(Cl)cc3</chem>
114	<chem>CCOC(=O)C1=C(C)N(c2ccccc2)C(=O)N[C@@H]1c3ccc(O)cc3</chem>
115	<chem>CCOC(=O)C1=C(C)N(c2ccccc2)C(=O)N[C@@H]1c3ccc([N+])([O-])=O)cc3</chem>
116	<chem>CCOC(=O)C1=C(C)N(c2ccccc2)C(=O)N[C@@H]1c3ccc(cc3)OC</chem>
117	<chem>CCOC(=O)C1=C(C)N(c2ccccc2)C(=O)N[C@@H]1c(c3C(F)(F)F)cccc3</chem>
118	<chem>CCOC(=O)C1=C(C)N(c2ccccc2)C(=O)N[C@@H]1c(c(Br)cc3)cc3C(F)(F)F</chem>
119	<chem>CCOC(=O)C1=C(C)N(c2ccccc2)C(=O)N[C@@H]1c(c(Cl)cc3)cc3C(F)(F)F</chem>
120	<chem>CCOC(=O)C1=C(C)N(c2ccccc2)C(=O)N[C@@H]1c(cc3)ccc3C</chem>
121	<chem>CCOC(=O)C1=C(C)N(c2ccccc2)C(=O)N[C@H]1c3c(Br)cc(c(c3)O)OC</chem>
122	<chem>CCOC(=O)C1=C(C)N(c2ccccc2)C(=O)N[C@H]1c3c(O)ccc(c3)OC</chem>
123	<chem>CCOC(=O)C1=C(C)N(c2ccccc2)C(=O)N[C@H]1c3c([N+])([O-])=O)ccc([O-])c3</chem>
124	<chem>CCOC(=O)C1=C(C)N(c2ccccc2)C(=O)N[C@H]1c3c([N+])([O-])=O)cccc3</chem>
125	<chem>CCOC(=O)C1=C(C)N(c2ccccc2)C(=O)N[C@H]1c3cc(Br)ccc3</chem>
126	<chem>CCOC(=O)C1=C(C)N(c2ccccc2)C(=O)N[C@H]1c3cc([N+])([O-])=O)ccc3</chem>
127	<chem>CCOC(=O)C1=C(C)N(c2ccccc2)C(=O)N[C@H]1c3ccc(Br)cc3</chem>
128	<chem>CCOC(=O)C1=C(C)N(c2ccccc2)C(=O)N[C@H]1c3ccc(Cl)cc3</chem>
129	<chem>CCOC(=O)C1=C(C)N(c2ccccc2)C(=O)N[C@H]1c3ccc(O)cc3</chem>
130	<chem>CCOC(=O)C1=C(C)N(c2ccccc2)C(=O)N[C@H]1c3ccc([N+])([O-])=O)cc3</chem>
131	<chem>CCOC(=O)C1=C(C)N(c2ccccc2)C(=O)N[C@H]1c3ccc(cc3)OC</chem>
132	<chem>CCOC(=O)C1=C(C)N(c2ccccc2)C(=O)N[C@H]1c(c3C(F)(F)F)cccc3</chem>
133	<chem>CCOC(=O)C1=C(C)N(c2ccccc2)C(=O)N[C@H]1c(c(Br)cc3)cc3C(F)(F)F</chem>
134	<chem>CCOC(=O)C1=C(C)N(c2ccccc2)C(=O)N[C@H]1c(c(Cl)cc3)cc3C(F)(F)F</chem>
135	<chem>CCOC(=O)C1=C(C)N(c2ccccc2)C(=O)N[C@H]1c(cc3)ccc3C</chem>
136	<chem>[O-]C(=O)c1cc(ccc1)[C@@H]2NC(=O)N(C(C)=C2C(=O)OCC)c3ccccc3</chem>
137	<chem>[O-]C(=O)c1cc(ccc1)[C@H]2NC(=O)N(C(C)=C2C(=O)OCC)c3ccccc3</chem>
138	<chem>COc(c(c1)O)cc(Br)c1/C=C2/C(C)=NN(C2=O)c(cc3)ccc3[N+])([O-])=O</chem>
139	<chem>FC(F)(F)c1cc(c(Cl)cc1)/C=C2/C(C)=NN(C2=O)c(cc3)ccc3[N+])([O-])=O</chem>
140	<chem>N#Cc1cc(ccc1)-c(n2)cccc2/C=C3/C(C)=NN(C3=O)c(cc4)ccc4[N+])([O-])=O</chem>
141	<chem>[O-]C(=O)c1cc(ccc1)/C=C2/C(C)=NN(C2=O)c(cc3)ccc3[N+])([O-])=O</chem>
142	<chem>c1c(O)ccc(Br)c1/C=C2/C(C)=NN(C2=O)c(cc3)ccc3[N+])([O-])=O</chem>
143	<chem>CCOc(ccc1)c([O-])c1/C=C2/C(C(C)C)=NN(C2=O)c3cncnc3</chem>
144	<chem>CCOc(ccc1)c([O-])c1/C=C2/C(CC)=NN(C2=O)c3c(F)cc(F)cc3</chem>
145	<chem>CCOc(ccc1)c([O-])c1/C=C2/C(CC)=NN(C2=O)c3cncnc3</chem>
146	<chem>FC(F)(F)c1cc(ccc1)-c(o2)ccc2/C=C3/C(CC)=NN(C3=O)c(cc4C(F)(F)F)ccc4</chem>
147	<chem>FC(F)(F)c1cc(ccc1)N(C2=O)N=C(C(C)C)\C2=C\c3cc([O-])c([N+])([O-])=O)cc3</chem>
148	<chem>FC(F)(F)c1cc(ccc1)N(C2=O)N=C(CC)\C2=C\c3c([O-])c(ccc3)OCC</chem>
149	<chem>N#Cc1ccc(cc1)N(C2=O)N=C(C)\C2=C\c3c([O-])ccc(c3)[N+])([O-])=O</chem>
150	<chem>[O-][N+](=O)c(c1)ccc([O-])c1/C=C2/C(C)=NN(C2=O)c3c(F)cc(Br)cc3</chem>
151	<chem>[O-][N+](=O)c(c1)ccc([O-])c1/C=C2/C(C)=NN(C2=O)c(cc3[N+])([O-])=O)ccc3</chem>
152	<chem>[O-][N+](=O)c(c1)ccc([O-])c1/C=C2/C(CC)=NN(C2=O)c3c(F)cc(F)cc3</chem>
153	<chem>[O-][N+](=O)c(c1)ccc([O-])c1/C=C2/C(CC)=NN(C2=O)c3cncnc3</chem>
154	<chem>c1ccc(OC)c([O-])c1/C=C2/C(CC)=NN(C2=O)c3c(F)cc(F)cc3</chem>
155	<chem>c1ccc(OC)c([O-])c1/C=C2/C(CC)=NN(C2=O)c3cncnc3</chem>
156	<chem>n1ccncc1N(C2=O)N=C(C)\C2=C\c3cc(ccc3)Oc4ccccc4</chem>
157	<chem>CCOC(=O)CN(C(=O)S1)C(=O)\C1=C\c2c([O-])ccc(c2)[N+])([O-])=O</chem>

158	<chem>CCOC(=O)CN(C(=O)S1)C(=O)\C1=C\c2cc(O)c(O)cc2</chem>
159	<chem>CCOC(=O)CN(C(=O)S1)C(=O)\C1=C\c2cc(OCc3ccccc3)c(cc2)OCc4ccccc4</chem>
160	<chem>c1ccccc1OC(=O)CN(C(=O)S2)C(=O)\C2=C\c3cc([O-])c([NH+])([O-])=O)cc3</chem>
161	<chem>c1cc(F)ccc1/C=C/C(N=C(C)/C2=C\[O-])OCC)=[NH+][C@@H]2c3ccc(cc3)OCC=C</chem>
162	<chem>c1cc(F)ccc1/C=C/C(N=C(C)/C2=C\[O-])OCC)=[NH+][C@H]2c3ccc(cc3)OCC=C</chem>
163	<chem>c1cc([NH+])([O-])=O)ccc1[C@@H]2[NH+]=C(N=C(C)/C2=C\[O-])OCC)\C=C\c3ccc(F)cc3</chem>
164	<chem>c1cc([NH+])([O-])=O)ccc1[C@H]2[NH+]=C(N=C(C)/C2=C\[O-])OCC)\C=C\c3ccc(F)cc3</chem>
165	<chem>c1cc(Cl)ccc1C(=O)NC(S2)=N[C@@H](c3ccc(F)cc3)C=C2c4ccccc4</chem>
166	<chem>c1cc(Cl)ccc1C(=O)NC(S2)=N[C@@H](c3ccccc3)C=C2c4ccccc4</chem>
167	<chem>c1cc(Cl)ccc1C(=O)NC(S2)=N[C@H](c3ccc(F)cc3)C=C2c4ccccc4</chem>
168	<chem>c1cc(Cl)ccc1C(=O)NC(S2)=N[C@H](c3ccccc3)C=C2c4ccccc4</chem>
169	<chem>c1ccccc1C2=C[C@@H](N=C(S2)N)c3ccc(F)cc3</chem>
170	<chem>c1ccccc1C2=C[C@H](N=C(S2)N)c3ccc(F)cc3</chem>
171	<chem>c1ccccc1C(=O)NC(S2)=N[C@@H](c3ccc(F)cc3)C=C2c4ccccc4</chem>
172	<chem>c1ccccc1C(=O)NC(S2)=N[C@@H](c3ccccc3)C=C2c4ccccc4</chem>
173	<chem>c1ccccc1C(=O)NC(S2)=N[C@H](c3ccc(F)cc3)C=C2c4ccccc4</chem>
174	<chem>c1ccccc1C(=O)NC(S2)=N[C@H](c3ccccc3)C=C2c4ccccc4</chem>
175	<chem>COc(cc1)ccc1C(=O)NC(S2)=N[C@@H](c3ccccc3)C=C2c4ccccc4</chem>
176	<chem>COc(cc1)ccc1C(=O)NC(S2)=N[C@H](c3ccccc3)C=C2c4ccccc4</chem>
177	<chem>c1cc(C)ccc1C(=O)NC(S2)=N[C@@H](c3ccccc3)C=C2c4ccccc4</chem>
178	<chem>c1cc(C)ccc1C(=O)NC(S2)=N[C@H](c3ccccc3)C=C2c4ccccc4</chem>
179	<chem>c1cc(F)ccc1C(=O)NC(S2)=N[C@@H](c3ccccc3)C=C2c4ccccc4</chem>
180	<chem>c1cc(F)ccc1C(=O)NC(S2)=N[C@H](c3ccccc3)C=C2c4ccccc4</chem>
181	<chem>c1cc([NH+])([O-])=O)ccc1C(=O)NC(S2)=N[C@@H](c3ccccc3)C=C2c4ccccc4</chem>
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188	<chem>c1cc(F)ccc1C(=O)NC(S2)=N[C@H](c3ccc(F)cc3)C=C2c4ccccc4</chem>
189	<chem>c1cc([NH+])([O-])=O)ccc1C(=O)NC(S2)=N[C@@H](c3ccc(F)cc3)C=C2c4ccccc4</chem>
190	<chem>c1cc([NH+])([O-])=O)ccc1C(=O)NC(S2)=N[C@H](c3ccc(F)cc3)C=C2c4ccccc4</chem>
191	<chem>FC(F)(F)c1cc(c(Cl)cc1)OCc2cc(ccc2)-c3nc(N)nc(c34)[nH]cn4</chem>
192	<chem>c1cc(C)cc(c1C(C)C)OCc2ccc(cc2)-c3nc(N)nc(c34)[nH]cn4</chem>
193	<chem>c1ccc(Cl)cc1COc(ccc2)cc2-c3nc(N)nc(c34)[nH]cn4</chem>
194	<chem>c1ccc(F)cc1COc(ccc2)cc2-c3nc(N)nc(c34)[nH]cn4</chem>
195	<chem>c1ccc(OC)cc1COc(ccc2)cc2-c3nc(N)nc(c34)[nH]cn4</chem>
196	<chem>c1ccccc12)cccc2OCc3cc(ccc3)-c4nc(N)nc(c45)[nH]en5</chem>
197	<chem>c1ccccc1COc(c2C)cc(cc2)-c3nc(N)nc(c34)[nH]cn4</chem>
198	<chem>n1c[nH]c(c12)nc(N)nc2-c3cc(ccc3)Oe4ccccc4</chem>
199	<chem>CC(C)Oc(cc1)ccc1-c(cc2)ccc2-c3nc(N)nc(c34)[nH]cn4</chem>
200	<chem>COe1c(OC)cc(cc1OC)-c2nc(N)nc(c23)[nH]cn3</chem>
201	<chem>FC(F)(F)Oe1ccc(cc1)OCc2cc(ccc2)-c3nc(N)nc(c34)[nH]cn4</chem>
202	<chem>FC(F)(F)c1cc(ccc1)COc(ccc2)cc2-c3nc(N)nc(c34)[nH]cn4</chem>
203	<chem>c1cc(F)ccc1COc(ccc2)cc2-c3nc(N)nc(c34)[nH]cn4</chem>

204	<chem>c1cccc1COc(c2C)cc(cc2)-c3nc(Cl)nc(c34)[nH]cn4</chem>
205	<chem>n1c[nH]c(c12)nc(N)nc2-c(cc3C(F)(F)F)cc(c3)OCc4ccc(cc4)OC</chem>
206	<chem>n1c[nH]c(c12)nc(N)nc2-c3ccc(I)cc3</chem>
207	<chem>O1COc(c12)ccc(c2)C(=O)OCc3c(C)n(nn3)-c4nccs4</chem>
208	<chem>O1COc(c12)ccc(c2)C(=O)OCc3cn(nn3)-c(cc4)cc(c45)scn5</chem>
209	<chem>O1COc(c12)ccc(c2)C(=O)OCc3cn(nn3)Cc4nc(no4)-c5ccenc5</chem>
210	<chem>O1COc(c12)ccc(c2)C(=O)OCc3cn(nn3)Cc4nnc(o4)-c5ccenc5</chem>
211	<chem>c1cc(O)cc(O)c1C(=O)OCc2c(C)n(nn2)-c3nccs3</chem>
212	<chem>c1ccc(OC)cc1C(=O)OCc2c(C)n(nn2)-c3nccs3</chem>
213	<chem>c1ccc(OC)cc1C(=O)OCc2cn(nn2)-c(cc3)cc(c34)scn4</chem>
214	<chem>c1ccc([N+])([O-])=O)cc1C(=O)OCc2c(C)n(nn2)-c3nccs3</chem>
215	<chem>c1ccc([N+])([O-])=O)cc1C(=O)OCc2cn(nn2)-c(cc3)cc(c34)scn4</chem>
216	<chem>c1ccc([N+])([O-])=O)cc1C(=O)OCc2cn(nn2)C[C@@H](O3)COc(c34)cccc4</chem>
217	<chem>c1ccc([N+])([O-])=O)cc1C(=O)OCc2cn(nn2)C[C@H](O3)COc(c34)cccc4</chem>
218	<chem>c1ccc([N+])([O-])=O)cc1C(=O)OCc2cn(nn2)Cc3ccc(cc3)-c4cccc4</chem>
219	<chem>c1ccc([N+])([O-])=O)cc1C(=O)OCc2cn(nn2)Cc3nc(no3)-c4ccenc4</chem>
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221	<chem>c1cccc(c12)nc2C(=O)OCc3cn(nn3)-c(cc4)cc(c45)scn5</chem>
222	<chem>c1cccc1C(=O)c2ccc(cc2)Cn(nn3)cc3COC(=O)c4cc([N+])([O-])=O)ccc4</chem>
223	<chem>c1cccc1C(=O)c2ccc(cc2)Cn(nn3)cc3COC(=O)c(c4)ccc(c45)OCO5</chem>
224	<chem>c1cnccc1C(=O)OCc2c(C)n(nn2)-c3nccs3</chem>
225	<chem>FC(F)(F)c1cc(ccc1)CCn(nn2)cc2-c3cc(O)ccc3</chem>
226	<chem>FC(F)(F)c1cc(ccc1)CCn(nn2)cc2-c3cccn3</chem>
227	<chem>[O-]C(=O)c1cc([N+])([O-])=O)c(cc1)Cn(nn2)cc2-c3cc(O)ccc3</chem>
228	<chem>[O-]C(=O)c1cc([N+])([O-])=O)c(cc1)Cn(nn2)cc2-c3cccn3</chem>
229	<chem>c1ccc(O)cc1-c2cn(nn2)Cc3ccc(cc3)-c4cccc4</chem>
230	<chem>c1ccc(O)cc1-c2cn(nn2)Cc3nnc(o3)-c4ccenc4</chem>
231	<chem>c1cccc(c12)OC[C@@H](O2)Cn(nn3)cc3-c4cc(O)ccc4</chem>
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235	<chem>c1cccc(c12)[nH]cc2CCn(nn3)cc3-c4cc(O)ccc4</chem>
236	<chem>c1cccc(c12)[nH]cc2CCn(nn3)cc3-c4cccn4</chem>
237	<chem>c1cccc1C(=O)c2ccc(cc2)Cn(nn3)cc3-c4cccn4</chem>
238	<chem>c1ncccc1-c(no2)nc2Cn(nn3)cc3-c4cc(O)ccc4</chem>
239	<chem>n1cccc1-c2cn(nn2)Cc3ccc(cc3)-c4cccc4</chem>
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241	<chem>n1cccc1-c2cn(nn2)Cc3nnc(o3)-c4ccenc4</chem>
242	<chem>FC(F)(F)c1cc(ccc1)NC(=O)CN(C(=O)S2)C(=O)\C2=C\c3c([O-])cc(OC)cc3OC</chem>
243	<chem>[O-][N+](=O)c1c(Cl)ccc(c1)NC(=O)CN(C(=O)S2)C(=O)\C2=C\c(n3)ccc(c34)cccc4[O-]</chem>
244	<chem>c1cc(O)c(O)cc1/C=C2/C(=O)N(C(=O)S2)CCc3c[nH]c(c34)cccc4</chem>
245	<chem>c1ccc(Cl)c([O-])c1/C=C2/C(=O)N(C(=O)S2)Cc3nc(no3)-c4cccn4</chem>
246	<chem>c1ccc(F)cc1CCNC(=O)CN(C(=O)S2)C(=O)\C2=C\c3c([O-])c([N+])([O-])=O)cc(c3)OC</chem>
247	<chem>c1ccc(O)c(Cl)c1/C=C2/C(=O)N(C(=O)S2)Cc3nnc(o3)-c4cccn4</chem>
248	<chem>c1cccc1OC(=O)CN(C(=O)S2)C(=O)\C2=C\c3c([O-])c([N+])([O-])=O)cc(Br)c3</chem>
249	<chem>c1cccc1OC(=O)CN(C(=O)S2)C(=O)\C2=C\c3cc(O)c(O)cc3</chem>

250	<chem>CCOC(=O)C1=C(C)N(CCC([O-])=O)C(=O)N[C@@H]1c2ccccc2</chem>
251	<chem>CCOC(=O)C1=C(C)N(CCC([O-])=O)C(=O)N[C@@H]1c(c2=O)coc(c23)ccc(Br)c3</chem>
252	<chem>CCOC(=O)C1=C(C)N(CCC([O-])=O)C(=O)N[C@@H]1c(cc2C([O-])=O)ccc2</chem>
253	<chem>CCOC(=O)C1=C(C)N(CCC([O-])=O)C(=O)N[C@@H]1c(n2)cccc2-c(ccc3)cc3C(=O)OC</chem>
254	<chem>CCOC(=O)C1=C(C)N(CCC([O-])=O)C(=O)N[C@H]1c2ccccc2</chem>
255	<chem>CCOC(=O)C1=C(C)N(CCC([O-])=O)C(=O)N[C@H]1c(c2=O)coc(c23)ccc(Br)c3</chem>
256	<chem>CCOC(=O)C1=C(C)N(CCC([O-])=O)C(=O)N[C@H]1c(cc2C([O-])=O)ccc2</chem>
257	<chem>CCOC(=O)C1=C(C)N(CCC([O-])=O)C(=O)N[C@H]1c(n2)cccc2-c(ccc3)cc3C(=O)OC</chem>
258	<chem>CCOC(=O)C1=C(C)NC(=S)N[C@@H]1c2cc(ccc2)OCC</chem>
259	<chem>CCOC(=O)C1=C(C)NC(=S)N[C@H]1c2cc(ccc2)OCC</chem>
260	<chem>COc(cc1)ccc1/C=C/C(N=C(C)/C2=C([O-])OCC)=[NH+][C@@H]2c3cc(ccc3)OCC</chem>
261	<chem>COc(cc1)ccc1/C=C/C(N=C(C)/C2=C([O-])OCC)=[NH+][C@H]2c3cc(ccc3)OCC</chem>
262	<chem>FC(F)(F)c1ccc(cc1)/C=C/C(N=C(C)/C2=C([O-])OCC)=[NH+][C@@H]2c3cc(ccc3)OCC</chem>
263	<chem>FC(F)(F)c1ccc(cc1)/C=C/C(N=C(C)/C2=C([O-])OCC)=[NH+][C@H]2c3cc(ccc3)OCC</chem>
264	<chem>c1cc(Cl)ccc1/C=C/C(N=C(C)/C2=C([O-])OCC)=[NH+][C@@H]2c3cc(ccc3)OCC</chem>
265	<chem>c1cc(Cl)ccc1/C=C/C(N=C(C)/C2=C([O-])OCC)=[NH+][C@H]2c3cc(ccc3)OCC</chem>
266	<chem>c1cc(F)ccc1/C=C/C(N=C(C)/C2=C([O-])OCC)=[NH+][C@@H]2c3cc(ccc3)OCC</chem>
267	<chem>c1cc(F)ccc1/C=C/C(N=C(C)/C2=C([O-])OCC)=[NH+][C@H]2c3cc(ccc3)OCC</chem>
268	<chem>c1ccccc1/C=C/C(N=C(C)/C2=C([O-])OCC)=[NH+][C@@H]2c3cc(ccc3)OCC</chem>
269	<chem>c1ccccc1/C=C/C(N=C(C)/C2=C([O-])OCC)=[NH+][C@H]2c3cc(ccc3)OCC</chem>
270	<chem>c1cc(C)ccc1/C=C/C(N=C(C)/C2=C([O-])OCC)=[NH+][C@@H]2c3cc(ccc3)OCC</chem>
271	<chem>c1cc(C)ccc1/C=C/C(N=C(C)/C2=C([O-])OCC)=[NH+][C@H]2c3cc(ccc3)OCC</chem>
272	<chem>c1ccccc1C2=C[C@@H](N=C(S2)N)c3ccccc3</chem>
273	<chem>c1ccccc1C2=C[C@H](N=C(S2)N)c3ccccc3</chem>

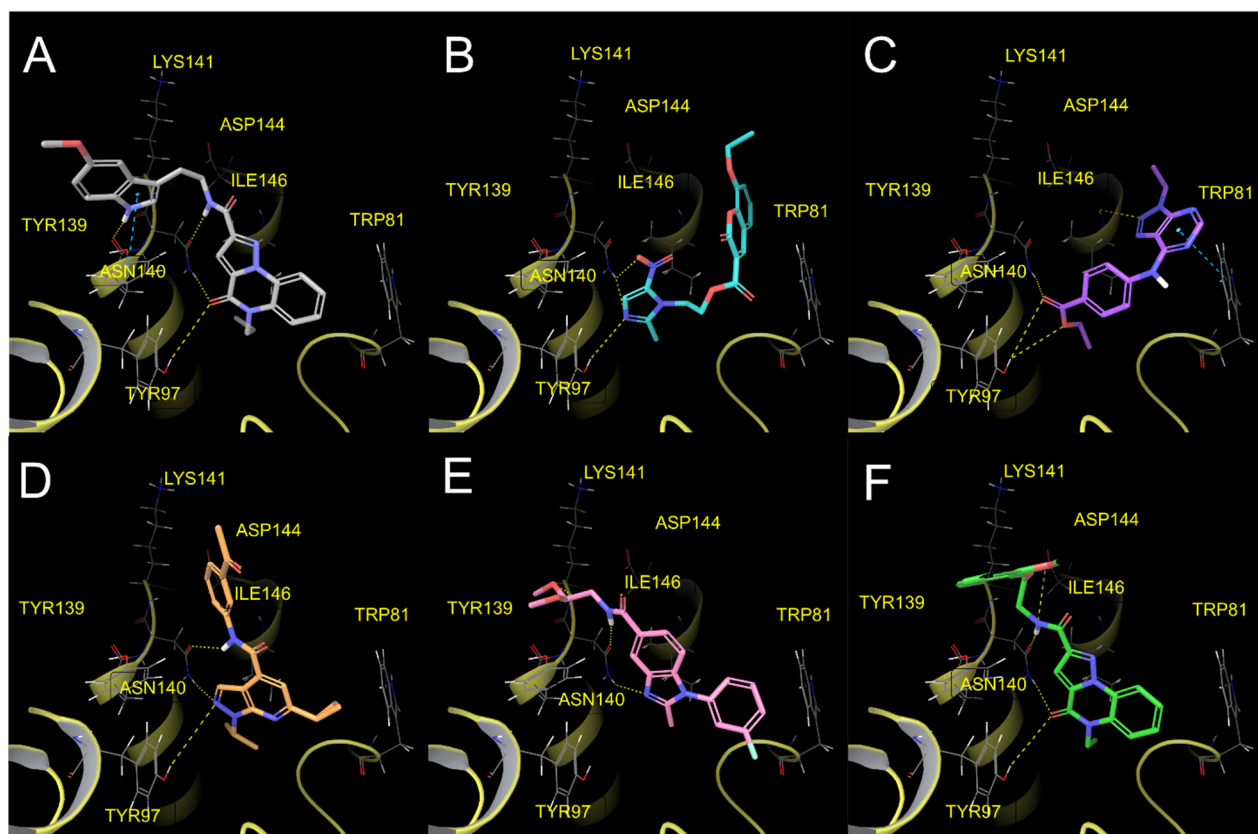


Figure S2. Docking poses of compounds **1** (panel A, colored by atom type: C grey, O red, N blue, S yellow, polar H light grey), **2** (panel B, colored by atom type: C turquoise, O red, N blue, S yellow, polar H light grey), **3** (panel C, colored by atom type: C violet, O red, N blue, S yellow, polar H light grey), **4** (panel D, colored by atom type: C orange, O red, N blue, S yellow, polar H light grey), **5** (panel E, colored by atom type: C pink, O red, N blue, S yellow, polar H light grey), and **6** (panel F, colored by atom type: C green, O red, N blue, S yellow, polar H light grey) in BRD4 binding site (PDB code: 4QB3). H-bonds and π - π interactions are reported in yellow and cyan, respectively.

Table S2. Predicted computational parameters of the 20 BRD4 known ligands respecting the generated 7-point 3D structure-based pharmacophore model “AAHHRRR”.

PDB compound code	Number of matched features	PhaseScreen score
2YEL	7	2.299
3P5O	7	2.401
3ZYU	5	1.433
4F3I	7	2.667
4LRG	7	2.335
4Z1Q	6	2.026
4Z93	5	1.347
5ACY	5	1.433
5FBX	5	1.663
5HLS	7	2.367
5IGK	6	1.599
5JWM	7	2.143
5UOO	5	1.249
5V67	5	1.204
5WMD	7	2.41
5Y8Y	5	1.269
5YOU	5	1.068
6C7R	5	1.502
6Q3Y	5	1.295
6Q3Z	5	1.411

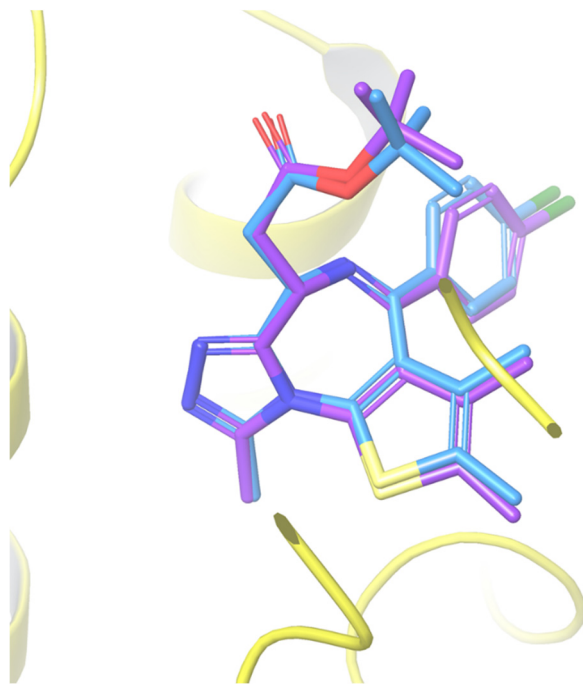


Figure S3. Superposition of co-crystallized (+)-JQ1 (highlighted in light blue) to the reproduced docking pose of (+)-JQ1 (highlighted in violet) in the BRD4 binding site, with an RMSD value of 0.5.