Electronic Supplementary Material (ESI) for Physical Chemistry Chemical Physics.

Supporting information

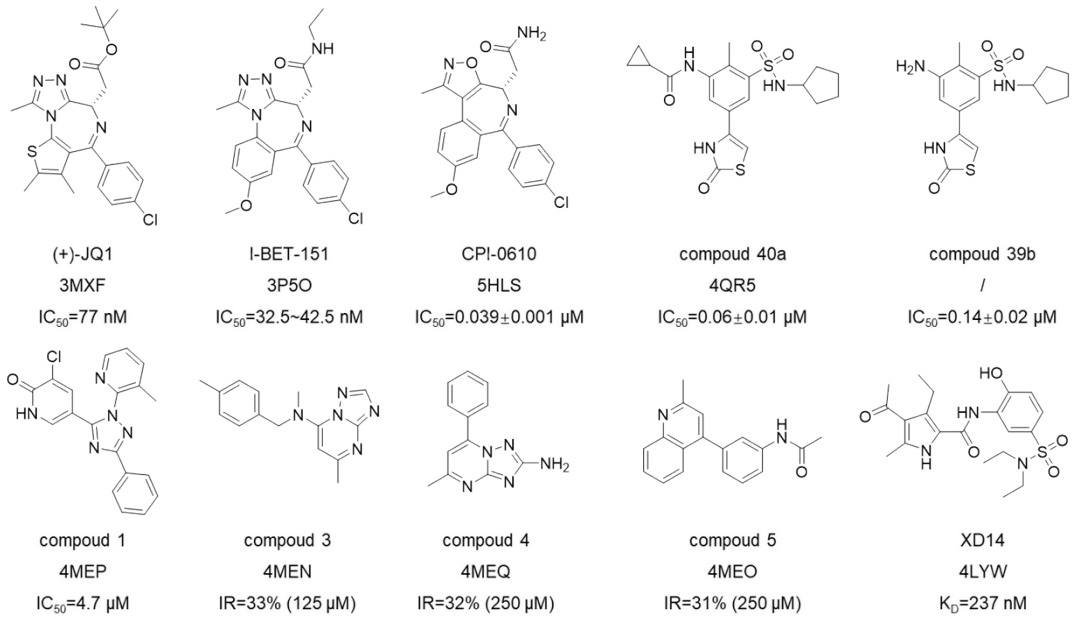

Figure S1. The structures and activities of representative BRD4-BD1 inhibitors used in the performance evaluation of docking-based VS. Except for compound 39b, the remaining nine compounds with crystal structures were used in the docking power test. During the screening power test, all ten compounds and the corresponding decoys were used.

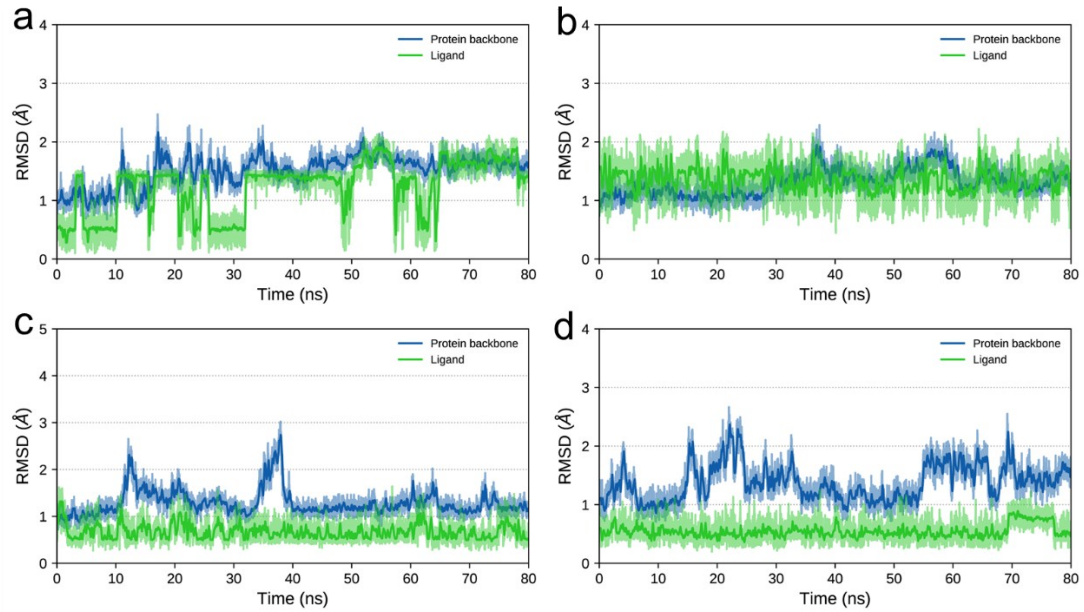

Figure S2. The RMSDs of the (a) compound 31, (b) compound 31, (c) compound 64 and (d) compound 65 systems as a function of time.

Table S1. Results of the cross-docking by Glide with the SP scoring mode without the crystalline water molecules.

Structure	**RMSD (Å)**								
	3MXF	3P5O	5HLS	4QR5	4MEP	4MEN	4MEQ	4MEO	4LYW
3P5O	1.74	0.45	0.53	2.87	6.64	4.74	1.27	3.23	3.36
5HLS	1.86	0.41	0.37	6.65	6.65	4.61	1.09	3.23	3.27

Table S2. The 85 compounds chosen for experimental validation.

Index	ID	Smiles	Inhibition
1	AE-473/30684053	O=C1Cn3c4CCCCc4(c2cccc(N1)c23)	42.02
2	AE-848/30695031	COC(=O)C(O)(c1ccc(O)c(c1)C(C)(C)C)C(F)(F)F	42.83
3	AG-690/12243070	Cc1cccc(c1)Cn3c(nc2c3(C(=O)NC(=O)N2(C)))S	81.43
4	AJ-292/40763118	COc1cc(cc(c1)C(=O)N=C(N)Nc3nc2ccccc2s3)OC	45.17
5	AK-918/43446338	Cc1ccc(cc1)NS(=O)(=O)c3ccc2c(CCN2(C(C)=O))c3	-0.54
6	AQ-390/41639145	CC(=O)Oc1ccc(c2ccccc12)N(C(C)=O)S(=O)(=O)c3ccc(cc3)Br	20.82
7	AP-124/43383081	CC(=O)c2c(C)nn(CC(=O)Nc1cc(cc(c1)Cl)Cl)c2(C)	7.21
8	AM-807/42003520	CCOc1cc(ccc1(OC))C4C(C#N)=C(N)Oc3n[nH]c(c2cccs2)c34	22.74
9	AK-968/41470055	O=C2CNC(N2(Cc1ccccc1))=S	11.96
10	AI-204/31723045	O=C1C=CC=CN1S(=O)(=O)c2cc(ccc2Cl)Cl	27.40
11	AE-562/12222340	CC1CC(CC1(=O))c2ccc3ccccc3(c2)	-0.10
12	AH-262/31953006	O=C1CCCc2c3cc(ccc3([nH]c12))Br	12.00
13	AO-801/41077232	COc1ccc2C(=O)CCN(c2(c1))S(=O)(=O)c3ccccc3	-54.91
14	AP-853/43405633	Cc3ccc(cc3(NC(=O)CC1=NN(C)C(=O)c2ccccc12))Cl	31.03
15	AR-434/42808176	COc3ccccc3(NCC=1NC(=O)c2ccccc2(N=1))	3.75
16	AO-476/43380324	N#CC=3C(=O)NC=1c4ccccc4(OCC=1C=3(c2cccnc2))	14.78
17	AF-399/15032361	CCc2n[nH]c3OC(N)=C(C#N)C(c1cccc(c1)Cl)c23	12.33
18	AN-907/14236007	CCC(=O)c1cccc(c1)C(=O)c2ccccc2	29.74
19	AC-907/34128009	CC(=O)Nc1ccc2c(O)ncnc2(c1)	0.12
20	AA-504/32629046	CC(=O)c1c(C)[nH]c(c1(C))c2ccccc2	25.74
21	AP-836/41220133	O=C3CNC(=O)C23(CCCc1ccccc12)	16.64
22	AK-778/43114837	O=C(Cc1ccccc1)CC3(O)(C(=O)Nc2ccccc23)	17.28
23	AN-974/42099356	CCOC2C(=O)NC(=O)N2(Cc1ccccc1)	34.94
24	AO-476/43380494	N#CC=2C(=O)NC(=CC=2(c1ccco1))c3ccco3	18.87
25	AP-048/15613078	O=C(CSc1nnc([nH]1)c2ccncc2)c4c[nH]c3ccccc34	31.41
26	AB-323/25048023	CN2C(=O)C=C(NCCc1ccccc1)N(C)C2(=O)	-4.27
27	AN-789/13334001	NN2C(=O)c3cnn(c1ccccc1)c3(N=C2S)	28.28
28	AK-125/11586030	Cc2cc(C)c3c1N=CNC(=O)c1sc3(n2)	23.53
29	AC-509/25001342	[H]C3(O)(C(=O)Nc1ccccc1SC3([H])(c2ccc(cc2)OC))	13.92
30	AK-968/41922851	O=C1CNC(N1c3cccc2ccccc23)=S	33.39
31	AM-879/41890720	CN2C(=O)N(C)c1cc(ccc12)C=NNC(NCc3ccccc3)=S	86.55
32	AN-988/40889716	COc1ccccc1N(CC(=O)NCc2ccccn2)S(C)(=O)=O	33.39
33	AO-289/42804229	COc1ccc3c(c1)C(=O)c2cccc(OC)c23	2.20

34	AI-204/31701021	O=C3OCCN3(N=Cc1ccnc2ccccc12)	-12.03
35	AJ-333/13050040	O=C2N=CN(c1ccccc1C(F)(F)F)c3ncccc23	19.89
36	AA-504/34234033	COc3cc(C=Cc1noc2C(=O)C=CC=Cc12)cc(OC)c3(OC)	45.15
37	AA-516/25012264	[O-][N+](=Cc1ccc2OCOc2(c1))c3ccccc3	-4.65
38	AS-662/43412983	Cc2[nH]c1ccccc1c2C3c4ccccc4(C(=O)N3(CC(O)=O))	-6.22
39	AO-989/42007867	CC(=O)CN2C(=O)CCN(C(C)=O)c1ccccc12	-4.76
40	AE-411/41415562	CC(=O)C2=C(C=C(C)N(Cc1ccccc1)C2=S)SC	3.46
41	AG-690/11203364	CC(=CCn1c3C(=O)NC(=O)N(C)c3(nc1SCc2ccccc2))Cl	44.38
42	AH-262/31958015	CN1CCN(CC1)C3=C(N)C(=O)Oc2ccccc23	44.09
43	AI-211/09901014	COc1ccc(cc1)C(CC(=O)c2ccc(cc2)Cl)C(C#N)C#N	-9.55
44	AG-690/36518054	C=CCn3c(NN=Cc1ccccc1)nc2c3(C(=O)NC(=O)N2(C))	-9.02
45	AB-131/42301019	OCc2ccc3ccc1ccccc1c3(c2)	9.33
46	AO-476/43305930	c1ccc(cc1)N2CCN(CC2)C4=C5CCCCC5(=Nc3ncnn34)	-258.79
47	AK-080/41967500	Cc1cccc(n1)NC(=O)c3cccc4C(=O)c2ccccc2c34	2.57
48	AI-204/31683007	O=C3NC(CCSc1nc2ccccc2(o1))Oc4ccccc34	13.76
49	AG-690/09403010	CCCCCCCCCCn1c2C(=O)NC(=O)N(C)c2(nc1SCC(N)=O)	7.31
50	AJ-292/13893232	CC(NC(=O)COc1ccccc1)C2COc3ccccc3(O2)	38.55
51	AG-690/13701136	Cc1ccc(cc1)CSc3nc2c(C(=O)NC(=O)N2(C))n3(CC(N)=O)	-4.46
52	AJ-030/12105154	CCCCCCC(C)N1C=C(C(C)=O)C(=O)NC1(=O)	10.45
53	AB-016/41252640	OC(=O)CC1Cc3cccc2cccc1c23	17.18
54	AP-853/43416355	Cc1ccc(cc1)S(=O)(=O)CC2=Nc3cc(C)c(C)cc3(NC2(=O))	18.15
55	AI-031/43090786	Oc1cc3c(coc3(c2ccccc12))C(=O)c4ccco4	21.59
56	AN-023/41021002	Cc3cccc(C)c3(NC(=O)Cn2c(C)c(C#N)c1ccccc12)	23.92
57	AJ-916/15344019	O=C(c1cccnc1)c3conc3(C(=O)c2ccc(cc2)Cl)	10.97
58	AE-641/30153058	Cc3nnc4CCC(c1ccc(F)cc1)c2ccc(F)cc2n34	21.68
59	AE-641/14413031	COc1ccc(cc1)c2csc3N=CN(N)C(=O)c23	34.61
60	AG-690/11665750	COC(=O)CN3C(=O)C1(OCCO1)c2cc(ccc23)Br	29.94
61	AR-527/43363312	COc1ccc(cc1)C=C2CCCNC2(=O)	31.48
62	AP-853/43416357	Cc1nnc(n1c2ccccc2)SCC3=NNC(=O)c4ccccc4(O3)	15.32
63	AQ-344/43100409	O=C2CCC(c1ccccc1)=C(N2)c3ccccc3	-0.54
64	AQ-390/42869159	CCN3C(=O)c1cccc2c(ccc3(c12))S(=O)(=O)NCCCO	97.30
65	AQ-390/42869172	CCCNS(=O)(=O)c1ccc3c2c(cccc12)C(=O)N3(CC)	/
66	AO-476/43305888	Nc2[nH]nc(N)c2(Cc1cccc(c1)Br)	4.23
67	AR-685/43306363	COc1cc(cc(OC)c1(OC))C3N(Cc2ccco2)C(=O)CS3	9.65
68	AO-362/15059013	COc3ccccc3(C=CC2=C(C#N)C(=O)Oc1ccc(C)cc12)	5.36

69	AR-685/43306311	COc1ccc2cc(ccc2(c1))C3N(C(=O)CS3)C4CC4	13.82
70	AE-842/33004010	[H]C2(NN=C(C(=O)OC)C2([H])(c1ccccc1))(C(=O)OC(C)(C)C)	0.75
71	AK-245/12665006	N#Cc1c(N)nc(cc1c2cccs2)c3cccs3	14.22
72	AR-685/43306294	O=C2CSC(c1ccccc1Cl)N2C3CC3	9.63
73	AH-487/42193825	O=C(CSC=1NC(=O)c2ccccc2(N=1))Nc3ccc(cc3(F))Br	24.78
74	AN-329/43197468	CCC2C(=O)NCCN2(C(=O)c1ccc(o1)Br)	-1.94
75	AB-131/42300791	O=S=C(Cc1ccccc1)S(=O)(=O)c2ccccc2	22.47
76	AQ-917/42754261	C=CCN1c2nccnc2(C(=O)N(C)C1=S)	12.45
77	AE-842/31986052	COc2ccc1C(C)=CC(=O)Oc1c2(C(C)=O)	22.62
78	AN-829/25042021	CC=1c2ccc(O)c(O)c2(OC(=O)C=1Cl)	34.94
79	AN-970/40920413	N#Cc1cnn(c1(N))c2ccc(cc2)[N+](=O)[O-]	10.38
80	AP-842/40874612	CCC(C(O)=O)c1ccc(OC)c(c1)OC	25.59
81	AR-683/43306494	Oc1ccc2OC(=CC(=O)c2(c1(O)))c3ccccc3	32.53
82	AE-411/41415621	Cc1cc(C)c(C#N)c(n1)SC(C)(C)C	11.51
83	AE-848/08360045	CC(=O)N2C(N)=C(C#N)C=1CCCCC=12	/
84	AG-205/05254028	Nc1ncnc3c1c2CCCCc2s3	/
85	AE-562/12222280	OC(=O)c2nc1ccc(cc1c(n2)c3ccccc3)Cl	/