

# Dopamine Receptor Ligand Selectivity – An In Silico/In Vitro Insight – Supplementary information

Lukas Zell, Alina Bretl, Veronika Temml and Daniela Schuster

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## 1. Dataset assembly

### 2.1 Dataset of D<sub>1</sub>R-selective compounds (ChEMBL)

**Table S1.** D<sub>1</sub>R-selective compounds extracted from ChEMBL with in vitro determined biological activities for all investigated DR subtypes.

ID	SMILES	Ki [nM] <sup>a</sup>			Ref
		D <sub>1</sub> R	D <sub>2</sub> R	D <sub>3</sub> R	
SC1	<chem>O=C(C=1C([H])=C([H])C([F])=C([H])C=1[H])N([H])C([H])([H])C([H])([H])N2C([H])([H])C([H])([H])N(C([H])([H])C2([H])[H])[C@@]4([H])C=3C([H])=C([H])C([H])=C([H])C=3C([H])([H])C([H])([H])C4([H])[H]</chem>	70	3090	1570	[46]
SC2	<chem>N#CC=1C([H])=C([H])C2=C(C=1[H])C(=C([H])N2[H])C([H])([H])N4C([H])([H])C([H])([H])N(C=3C([H])=C([H])C([Cl])=C([H])C=3[H])C([H])([H])C4([H])[H]</chem>	550	4300	6400	[47]
SC3	<chem>N#CC=2C([H])=C([H])C=1C([H])=C(N([H])C=1C=2[H])C([H])([H])N4C([H])([H])C([H])([H])N(C=3C([H])=C([H])C([Cl])=C([Cl])C=3[H])C([H])([H])C4([H])[H]</chem>	880	2000	33000	
SC4	<chem>[Br]C=1C([H])=C([H])C(OC([H])([H])[H])=C(C=1[H])C2=N[C@]([H])([C@]([H])(O2)C([H])([H])[H])C([H])([H])N4C([H])([H])C([H])([H])N(C=3C([H])=C([H])C([H])=C([H])C=3[H])C([H])([H])C4([H])[H]</chem>	480	21000	10000	[48]
SC5	<chem>[Cl]C=1C([H])=C([H])C(=C([H])C=1[H])N2C([H])([H])C([H])([H])N(C([H])([H])C2([H])[H])C([H])([H])C=3C([H])=NN4C=3C([H])=C([H])C([H])=C4C#C[H]</chem>	810	3700	4600	[49]
SC6	<chem>[H]C=1C([H])=C([H])C(=C([H])C=1[H])C([H])([H])C=2C([H])=C([H])C([H])=C([H])C=2OC([H])([H])C([H])([H])N(C([H])([H])[H])C([H])([H])[H]</chem>	343	2740	10000	[50]
SC7	<chem>[H]C=1C([H])=C([H])C(=C([H])C=1[H])C([H])([H])C=2C([H])=C([H])C([H])=C([H])C=2OC([H])([H])C([H])([H])C([H])([H])N3C([H])([H])C([H])([H])C([H])([H])C3([H])[H]</chem>	113	1006	2923	
SC8	<chem>[H]C=1C([H])=C([H])C(=C([H])C=1[H])C([H])([H])C=2C([H])=C([H])C([H])=C([H])C=2OC([H])([H])C([H])([H])N3C([H])([H])C([H])([H])C([H])([H])C3([H])[H]</chem>	33.7	1015	7804	
SC9	<chem>[H]C=1C([H])=C([H])C(=C([H])C=1[H])C([H])([H])C=2C([H])=C([H])C([H])=C([H])C=2OC([H])([H])C([H])([H])N3C([H])([H])C([H])([H])OC([H])([H])C3([H])[H]</chem>	201	10000	10000	
SC10	<chem>[H]C=1C([H])=C([H])C(=C([H])C=1[H])C([H])([H])C=2C([H])=C([H])C([H])=C([H])C=2OC([H])([H])C([H])([H])N3C([H])([H])C([H])([H])C([H])([H])C3([H])[H]</chem>	379	10000	1818	
SC11	<chem>O=C2C1=C(C([H])=C([Cl])C([H])=C1[Cl])N([H])C(=O)[C@@]2(C=4C([H])=C([H])C([H])=C(OC([H])([H])C=3C([H])=C([H])C([H])=C([H])C=3[H])C=4[H])C([H])([H])[H]</chem>	120	10000	10000	[51]
SC12	<chem>[H]C=1C([H])=C([H])C3=C(C=1[H])C([H])([H])C=2C([H])=C(OC([H])([H])[H])C([H])=C([H])C=2C([H])([H])C([H])([H])N(C([H])([H])C([H])([H])C3([H])[H])C([H])([H])[H]</chem>	137	1396	23903	[52]
SC13	<chem>[H]C=1C([H])=C([H])C3=C(C=1[H])C([H])([H])C2=C([H])C(OC([H])([H])[H])=C(OC([H])([H])[H])C([H])=C2C([H])([H])C([H])([H])N(C([H])([H])C([H])([H])C3([H])[H])C([H])([H])[H]</chem>	579	1028	14830	
SC14	<chem>O=C1C3=C(N=C(N1C([H])([H])[H])N2C([H])([H])C([H])([H])OC([H])([H])C2([H])[H])C=C([H])N3[H])C([H])([H])N5C([H])([H])C([H])([H])</chem>	520	1100	2700	[53]

ID	SMILES	Ki [nM] <sup>a</sup>			Ref ·
		D <sub>1</sub> R	D <sub>2</sub> R	D <sub>3</sub> R	
	<chem>[H])([H])N(C=4C([H])=C([H])C([H])=C([H])C=4[H])C([H])([H])C5([H])[H]</chem>				
SC15	<chem>O=C(C=1C([H])=C([H])C([F])=C([H])C=1[H])C([H])([H])C([H])([H])C([H])([H])N5[C@@]3([H])[C@]7([H])[C@@]2([H])C([H])([H])[C@]6([H])[C@]4([H])[C@@]2([H])[C@@]3([H])[C@]4([H])[C@@]5(O[H])[C@]67[H]</chem>	209	1724	1958	[54]
SC16	<chem>[H]C=1C([H])=C([H])C2=C(C=1[H])C4=C(N2[H])C([H])([H])C=3C([H])=C([H])C([H])=C([H])C=3C([H])([H])C([H])([H])N([C@@]([H])(C4([H])[H])C([H])([H])C([H])([H])[H]</chem>	640	10000	10000	[55]
SC17	<chem>[H]C=1C([H])=C([H])C2=C(C=1[H])C4=C(N2[H])C([H])([H])C=3C([H])=C([H])C([H])=C([H])C=3C([H])([H])C([H])([H])O[H]C([H])([H])[H]</chem>	114	2923	4676	
SC18	<chem>O=C2C=1C([H])=C([H])C([H])=C([H])C=1C([H])([H])[C@@]2([H])C([H])([H])C([H])([H])N4C([H])([H])C([H])([H])N(C=3C([H])=C([H])C([Cl])=C([H])C=3[H])C([H])([H])C4([H])[H]</chem>	389.05	10000	4534	[56]
SC19	<chem>[Cl]C=1C([H])=C([H])C(=C([H])C=1[H])N2C([H])([H])C([H])([H])C([H])([H])N(C([H])([H])C2([H])[H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])C=4OC=3C([H])=C([H])C([H])=C([H])C=3C=4[H]</chem>	274	2507	1462	
SC20	<chem>[H]C=1C([H])=C([H])C(=C([H])C=1[H])[C@@]3([H])C=2C([H])=C(O[H])C([H])=C([H])C=2C([H])([H])C([H])([H])N(C3([H])[H])C([H])([H])[H]</chem>	207	1000	1000	[57]
SC21	<chem>[H]C=1C([H])=C([H])C(=C([H])C=1[H])[C@@]3([H])C=2C([H])=C(O[H])C(=C([H])C=2C([H])([H])C([H])([H])N(C3([H])[H])C([H])([H])[H])N([H])[H]</chem>	334	1000	1000	
SC22	<chem>[H]C=1C([H])=C([H])C(=C([H])C=1[H])[C@]3([H])C2=C([H])C(O[H])=C(C([H])=C2C([H])([H])C([H])([H])N(C3([H])[H])C([H])([H])[H])C4=C([H])C([H])=C([H])C(=C4[H])C([H])([H])[H]</chem>	216	1000	1000	
SC23	<chem>[H]C=1C([H])=C([H])C(=C([H])C=1[H])[C@@]3([H])C=2C([H])=C(O[H])C(=C([H])C=2C([H])([H])C([H])([H])N(C3([H])[H])C([H])([H])[H])C=4C([H])=C([H])C(O[H])=C([H])C=4[H]</chem>	349	1000	1000	
SC24	<chem>[H]/C4=C3\C1=C2/C(=C(/[H])C(OC([H])([H])[H])=C1OC([H])([H])[H])C([H])([H])C([H])([H])N([C@@]2([H])C([H])([H])C3=C([H])C(O[H])=C4OC([H])([H])[H])C([H])([H])[H]</chem>	373	inactive	>950	[58]
SC25	<chem>[H]/C1=C(\[H])C(OC([H])([H])[H])=C(OC([H])([H])[H])C4=C1C([H])([H])[C@@]3([H])C2=C([H])C(OC([H])([H])[H])=C(OC([H])([H])[H])C([H])=C2C([H])([H])C([H])([H])N3C4([H])[H]</chem>	153	1125	1371	[59]
SC26	<chem>[H]/C3=C(\[H])C(O/C2=N/C([H])=C([H])C=1OC([H])=C([H])C=12)C([H])C(=C3/C5=C(/N=C(/[H])C4=NC([H])=C([H])N45)C([H])([H])[H])C([H])([H])[H]</chem>	110	8300	7900	[60]
SC27	<chem>[F]C([F])([F])C=3C([H])=C(O/C2=N/C([H])=C([H])C=1C([H])=C([H])[S]C=12)C([H])=C([H])C=3/C5=C(\[H])C([H])=C([H])C4=NC([H])=C([H])N45</chem>	130	8700	6200	
SC28	<chem>[F]C([F])([F])C=3C([H])=C(O/C2=N/C([H])=C([H])C=1OC([H])=C([H])C=12)C([H])=C([H])C=3/C5=C(\[H])C([H])=C([H])C4=NC([H])=C([H])N45</chem>	150	7600	10000	

ID	SMILES	Ki [nM] <sup>a</sup>			Ref
		D <sub>1</sub> R	D <sub>2</sub> R	D <sub>3</sub> R	
SC29	<chem>[F]C([F])([F])C=3C([H])=C(O/C2=N/C([H])=C([H])C=1OC([H])=C([H])C=12)C([H])=C([H])C=3/C5=C(/N=C(/[H])C4=NC([H])=C([H])N45)C([H])([H])[H]</chem>	140	9600	8100	

<sup>a</sup>All KI values retrieved from ChEMBL were determined in vitro utilizing radio-ligand binding assays.

## 2.2 Dataset of D<sub>2</sub>R-selective compounds (ChEMBL)

**Table S2.** D2R-selective compounds extracted from ChEMBL with in vitro determined biological activities for all investigated DR subtypes.

ID	SMILES	Ki [nM] <sup>a</sup>			Ref.
		D <sub>1</sub> R	D <sub>2</sub> R	D <sub>3</sub> R	
SC30	[H]C=3C([H])=C2C1=C(/N=C(/[H])N1C([H])([H])[C@]([H])(N([H])C([H])([H])[H])C2([H])[H])C=3[H]	low affinity	355	2459	[61]
SC31	O=C(/C1=C(\[H])C([Cl])=C(C([H])=C1OC([H])([H])[H])N([H])C([H])([H])[H])N([H])[C@@]2([H])C([H])([H])C([H])([H])C([H])([H])N(C2([H])[H])C([H])([H])C=3C([H])=C([H])C([H])=C([H])C=3[H]	low affinity	12	1929	
SC32	O=C(C=1C([H])=C([Cl])C(=C([H])C=1OC([H])([H])[H])N(C(=O)C([H])([H])[H])C([H])([H])[H])N([H])C([H])([H])[C@]2([H])C([H])([H])C([H])([H])N(C2([H])[H])C([H])([H])C=3C([H])=C([H])C([H])=C([H])C=3[H]	5100	110	7200	
SC33	O=C(C=1C([H])=C([Cl])C(=C([H])C=1OC([H])([H])[H])N([H])[H])N([H])C([H])([H])[C@@]2([H])C([H])([H])C([H])([H])N(C2([H])[H])C([H])([H])C=3C([H])=C([H])C([H])=C([H])C=3[H]	11000	820	2200	
SC34	O=C1OC([H])([H])C([H])([H])N1C([H])([H])C([H])([H])N6C([H])([H])C([H])([H])C([H])(C2=C([H])N(C=3C([H])=C([H])C(=C([H])C2=3)C=4N=NN(N=4)C([H])([H])[H])C=5C([H])=C([H])C([F])=C([H])C=5[H])C([H])([H])C6([H])[H]	1250	610	1190	[63]
SC35	[H]C=1/C(=C(/[H])N2C=1C([H])([H])[C@]([H])(N(C([H])([H])C([H])([H])C([H])([H])[H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])C2([H])[H])C([H])([H])[H]	83000	800	1300	[64]
SC36	O=C(C=1C([H])=C([Cl])C(=C([H])C=1OC([H])([H])[H])N([H])[H])N([H])[C@@]2([H])C([H])([H])C([H])([H])N(C([H])([H])[C@]2([H])C([H])([H])[H])C([H])([H])C=3C([H])=C([H])C([H])=C([H])C=3[H]	19000	470	2200	[65]
SC37	[H]C=1C([H])=C([H])C(OC([H])([H])[H])=C(C=1[H])N2C([H])([H])C([H])([H])N(C([H])([H])C2([H])[H])C([H])([H])C=4C=3C([H])=NC(=NC=3N([H])C=4C([H])([H])[H])N(C([H])([H])[H])C([H])([H])[H]	5600	250	1500	
SC38	[H]C=1C([H])=C([H])C(OC([H])([H])[H])=C(C=1[H])N2C([H])([H])C([H])([H])N(C([H])([H])C2([H])[H])C([H])([H])C=4N=C3/C(=C(/[H])C(=C([H])N3C=4[H])C([H])([H])[H])N5/N=C(/[H])C([H])=C5[H]	8700	530	2400	
SC39	[H]C=1C([H])=C([H])C(OC([H])([H])[H])=C(C=1[H])N2C([H])([H])C([H])([H])N(C([H])([H])C2([H])[H])C([H])([H])C=4N=C3/C(=C(/[H])C(=C([H])N3C=4[H])C([H])([H])[H])N5C([H])([H])C([H])([H])OC([H])([H])C5([H])[H]	6400	210	2100	

ID	SMILES	Ki [nM] <sup>a</sup>			Ref.
		D <sub>1</sub> R	D <sub>2</sub> R	D <sub>3</sub> R	
SC40	<chem>[H]C=1C([H])=C([H])C(OC([H])([H])[H])=C(C=1[H])N2C([H])([H])C([H])([H])N(C([H])([H])C2([H])[H])C([H])([H])C=4N=C3C([H])=C([H])C([H])=C(N3C=4[H])N5/N=C/[H])C([H])=C5[H]</chem>	27000	590	1000	
SC41	<chem>[H]C=1C([H])=C([H])C(OC([H])([H])[H])=C(C=1[H])N2C([H])([H])C([H])([H])N(C([H])([H])C2([H])[H])C([H])([H])C=4N=C3C([H])=C([H])C([H])=C([H])N3C=4[H]</chem>	20000	990	3900	
SC42	<chem>[Cl]/C2=N/N1C([H])=C(N=C1C([H])=C2[H])C([H])([H])N4C([H])([H])C([H])([H])N(C=3C([H])=C([H])C([H])=C([H])C=3OC([H])([H])[H])C([H])([H])C4([H])[H]</chem>	7700	96	1400	
SC43	<chem>[F]C([H])([H])C([H])([H])OC=1C([H])=C([H])C([H])=C(C=1[H])C([H])([H])N3C([H])([H])C([H])([H])N(C=2C([H])=C([H])C([Cl])=C([H])C=2[H])C([H])([H])C3([H])[H]</chem>	5100	590	1100	
SC44	<chem>[F]C([H])([H])C([H])([H])OC=1C([H])=C([H])C(=C([H])C=1OC([H])([H])[H])C([H])([H])N3C([H])([H])C([H])([H])N(C=2C([H])=C([H])C([H])=C([H])C=2OC([H])([H])[H])C([H])([H])C3([H])[H]</chem>	5400	310	1100	[67]
SC45	<chem>[F]C([H])([H])C([H])([H])O/C1=C(\[H])C(OC([H])([H])[H])=C(O C([H])([H])[H])C([H])=C1C([H])([H])N3C([H])([H])C([H])([H])N(C=2C([H])=C([H])C([Cl])=C([H])C=2[H])C([H])([H])C3([H])[H]</chem>	3500	760	3900	
SC46	<chem>O=C1N([H])C([H])([H])C([H])([H])N1C([H])([H])C([H])([H])N6C([H])([H])C([H])([H])C([H])(C2=C([H])N(C=3C([H])=C([H])C(=C([H])C2=3)C=4/N=C/[H])N(N=4)C([H])([H])[H])C=5C([H])=C([H])C([F])=C([H])C=5[H])C([H])([H])C6([H])[H]</chem>	4100	660	2900	
SC47	<chem>O=C1N(C([H])([H])C([H])([H])[C@]1([H])C([H])([H])C([H])([H])N6C([H])([H])C([H])([H])[C@@]([H])(C2=C([H])N(C=3C([H])=C([H])C(=C([H])C2=3)C=4/N=C/[H])N(N=4)C([H])([H])[H])C=5C([H])=C([H])C([F])=C([H])C=5[H])C([H])([H])C6([H])[H])C([H])([H])[H]</chem>	2600	190	1400	[68]
SC48	<chem>[Br]C=1C([H])=C([H])C(OC([H])([H])[H])=C(C=1[H])C2=N/C(=C/[H])[S]2)C([H])([H])N4C([H])([H])C([H])([H])N(C=3C([H])=C([H])C([H])=C([H])C=3[H])C([H])([H])C4([H])[H]</chem>	6400	190	20000	[53]
SC49	<chem>[H]C=3C([H])=C2C1=C(/N=C(/O[H])N1C([H])([H])[C@]([H])(N(C([H])([H])[H])C([H])([H])[H])C2([H])[H])C=3[H]</chem>	5000	20	10000	[69]
SC50	<chem>[F]C([H])([H])C([H])([H])C([H])([H])OC=1C([H])=C([H])C(=C([H])C=1[H])N2N=N/C(=C2/[H])C([H])([H])N4C([H])([H])C([H])([H])N(C=3C([H])=C([H])C([H])=C([H])C=3OC([H])([H])[H])C([H])([H])C4([H])[H]</chem>	38000	340	2800	
SC51	<chem>[F]C([H])([H])C([H])([H])OC([H])([H])C([H])([H])C([H])([H])OC=1C([H])=C([H])C(=C([H])C=1[H])N2N=N/C(=C2/[H])C([H])([H])N4C([H])([H])C([H])([H])N(C=3C([H])=C([H])C([H])=C([H])C=3OC([H])([H])[H])C([H])([H])C4([H])[H]</chem>	3600	440	2900	[70]
SC52	<chem>O=C(C=1C([H])=C([H])C([F])=C([H])C=1[H])C([H])([H])C([H])([H])C(=O)N3C([H])([H])C([H])([H])C(O[H])(C=2C([H])=C([H])C([Cl])=C([H])C=2[H])C([H])([H])C3([H])[H]</chem>	19000	860	1700	[71]
SC53	<chem>[H]C=1C([H])=C([H])C2=C(C=1[H])C([H])([H])C([H])(C2([H])[H])C([H])([H])N5C([H])([H])C([H])([H])N(C=4C([H])=C([H])C=3OC([H])([H])C([H])([H])OC=3C=4[H])C([H])([H])C5([H])[H]</chem>	3000	738	2840	[72]

ID	SMILES	Ki [nM] <sup>a</sup>			Ref.
		D <sub>1</sub> R	D <sub>2</sub> R	D <sub>3</sub> R	
SC54	<chem>[Cl]C=1C([H])=C([H])C(=C([H])C=1[H])N2C([H])([H])C([H])([H])N(C([H])([H])C2([H])[H])C([H])([H])C3=C([H])N([H])C=4/N=C([H])C([H])=C([H])C3=4</chem>	10000	960	2310	

<sup>a</sup>All KI values retrieved from ChEMBL were determined in vitro utilizing radio-ligand binding assays.

### 2.3 Dataset of D<sub>2</sub>-like-selective compounds (ChEMBL)

**Table S3.** D<sub>2</sub>-like-selective compounds extracted from ChEMBL with in vitro determined biological activities for all investigated DR subtypes.

ID	SMILES	Ki [nM] <sup>a</sup>			Ref.
		D <sub>1</sub> R	D <sub>2</sub> R	D <sub>3</sub> R	
SC55	<chem>[H]C=1C([H])=C([H])C(=C([H])C=1[H])C2=C([H])C([H])([H])N(C([H])([H])C2([H])[H])C([H])([H])C([H])([H])C#CC=3C([H])=C([H])C([H])=NC=3[H]</chem>	5004	3.3	20	
SC56	<chem>[H]C=1C([H])=C([H])C(=C([H])C=1[H])C2=C([H])C([H])([H])N(C([H])([H])C2([H])[H])C([H])([H])C([H])([H])C#CC=3C([H])=C([H])C([H])=C([H])C=3[H]N([H])[H]</chem>	10000	0.67	24	[73]
SC57	<chem>[H]C=1C([H])=C([H])C(=C([H])C=1[H])C2=C([H])C([H])([H])N(C([H])([H])C2([H])[H])C([H])([H])C([H])([H])C#CC=3C([H])=C([H])C([H])=NC=3[H]N([H])[H]</chem>	10000	19	7	
SC58	<chem>[H]C=1C([H])=C([H])C(=C([H])C=1[H])C2=C([H])C([H])([H])N(C([H])([H])C2([H])[H])C([H])([H])C([H])([H])C#C/C3=N/C([H])=C(C([H])=C3[H])N([H])[H]</chem>	10000	1.9	2.6	
SC59	<chem>O=C(C=3C([H])=C([H])C=2C=1C([H])=C([H])C([H])=C([H])C=1C([H])([H])C=2C=3[H]N([H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])N5C([H])([H])C([H])([H])N(C=4C([H])=C([H])C([H])=C([Cl])C=4[Cl])C([H])([H])C5([H])[H]</chem>	10000	217	1.4	[74]
SC60	<chem>O=C(C=3C([H])=C([H])C=2C=1C([H])=C([H])C([H])=C([H])C=1C=2C=3[H]N([H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])N5C([H])([H])C([H])([H])N(C=4C([H])=C([H])C([H])=C([Cl])C=4[Cl])C([H])([H])C5([H])[H]</chem>	10000	262	0.9	
SC61	<chem>[Cl]C=2C([H])=C([H])C=1OC([H])([H])[C@@]([H])(OC=1C=2[H])C([H])([H])N([H])C([H])([H])[C@@]4([H])C([H])([H])C([H])([H])N(C=3C([H])=C([H])C([H])=C([H])C=3OC([H])([H])[H])C([H])([H])C4([H])[H]</chem>	1000	13.2	1.6	[75]
SC62	<chem>[Cl]C=1C([H])=C([H])C(=C([H])C=1[H])[C@@]3(O[H])C([H])([H])[C@@]2([H])N([C@]([H])(C([H])([H])C2([H])[H])C3([H])[H])C([H])([H])C4=C([H])N([H])C=5C([H])=C([H])C([H])=C([H])C4=5</chem>	1220	33.4	15.5	
SC63	<chem>[Cl]C=1C([H])=C([H])C(=C([H])C=1[H])[C@@]3(O[H])C([H])([H])[C@@]2([H])N([C@]([H])(C([H])([H])C2([H])[H])C3([H])[H])C([H])([H])C4=C([H])[S]C=5C([H])=C([H])C([H])=C([H])C4=5</chem>	3000	12.9	3.62	[76]
SC64	<chem>[Cl]C=1C([H])=C([H])C(=C([H])C=1[H])[C@@]3(O[H])C([H])([H])[C@@]2([H])N([C@]([H])(C([H])([H])C2([H])[H])C3([H])[H])C([H])([H])C4=C([H])OC=5C([H])=C([H])C([H])=C([H])C4=5</chem>	3930	1.06	0.71	
SC65	<chem>O=C1C([H])=NN(C(=O)N1C([H])([H])[H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])N4C([H])([H])C([H])([H])N(/C3=C([H])C([H])=C([H])C=2C([H])=C([H])C(OC([H])([H])[H])=C([H])C=23)C([H])([H])C4([H])[H]</chem>	7396	22.01	62.8	[77]

ID	SMILES	Ki [nM] <sup>a</sup>			Ref.
		D <sub>1</sub> R	D <sub>2</sub> R	D <sub>3</sub> R	
SC66	<chem>O=C(C=1C([H])=C3C([H])=C([H])C=1C([H])([H])C([H])C=2C([H])=C([H])C(=C([H])C=2[H])C([H])([H])C3([H])([H])N([H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])N5C([H])([H])C([H])([H])N(C=4C([H])=C([H])C([H])=C([Cl])C=4[Cl])C([H])([H])C5([H])[H])</chem>	2800	220	3.6	[78]
SC67	<chem>O=C(C=2OC=1C([H])=C([H])C([H])=C([H])C=1C=2[H])N([H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])N4C([H])([H])C([H])([H])N(C=3C([H])=C([H])C([H])=C([H])C=3OC([H])([H])[H])C([H])([H])C4([H])[H]</chem>	2000	36.5	0.92	
SC68	<chem>O=C(C=2OC=1C([H])=C([H])C([H])=C([H])C=1C=2[H])N([H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])N4C([H])([H])C([H])([H])N(C=3C([H])=C([H])C([H])=C([Cl])C=3[Cl])C([H])([H])C4([H])[H]</chem>	2100	44.8	0.81	
SC69	<chem>O=C(/C2=C([H])C=1C([H])=C([H])C([H])=C([H])C=1N2[H])N([H])C([H])([H])C([H])([H])C([H])([H])[C@@]([H])(O[H])C([H])([H])N4C([H])([H])C([H])([H])N(C=3C([H])=C([H])C([H])=C([Cl])C=3[Cl])C([H])([H])C4([H])[H]</chem>	4630	502	1.39	
SC70	<chem>O=C(/C2=C([H])C=1C([H])=C([H])C([H])=C([H])C=1N2[H])N([H])C([H])([H])C([H])([H])C([H])([H])[C@@]([H])(O[H])C([H])([H])N4C([H])([H])C([H])([H])N(C=3C([H])=C([H])C([H])=C([Cl])C=3[Cl])C([H])([H])C4([H])[H]</chem>	10000	433	1.12	
SC71	<chem>O=C(/C2=C([H])C=1C([H])=C([H])C([H])=C([H])C=1N2[H])N([H])C([H])([H])C([H])([H])C([H])([H])[C@]([H])(O[H])C([H])([H])N4C([H])([H])C([H])([H])N(C=3C([H])=C([H])C([H])=C([Cl])C=3[Cl])C([H])([H])C4([H])[H]</chem>	10000	715	16.6	
SC72	<chem>O=C(/C2=C([H])C=1C([H])=C([H])C([H])=C([H])C=1N2[H])N([H])C([H])([H])C([H])([H])C([H])([H])[C@@]([H])(O[H])C([H])([H])N4C([H])([H])C([H])([H])N(C=3C([H])=C([H])C([H])=C([H])C=3OC([H])([H])[H])C([H])([H])C4([H])[H]</chem>	10000	249	1.4	[79]
SC73	<chem>O=C(/C2=C([H])C=1C([H])=C([H])C([H])=C([H])C=1N2[H])N([H])C([H])([H])C([H])([H])C([H])([H])[C@@]([H])(O[H])C([H])([H])N4C([H])([H])C([H])([H])N(C=3C([H])=C([H])C([H])=C([H])C=3OC([H])([H])C([H])([H])C([H])([H])[H])C([H])([H])C4([H])[H]</chem>	4960	47.1	62.1	
SC74	<chem>O=C(/C2=C([H])C=1C([H])=C([F])C([H])=C([H])C=1N2[H])N([H])C([H])([H])C([H])([H])C([H])([H])[C@]([H])(O[H])C([H])([H])N4C([H])([H])C([H])([H])N(C=3C([H])=C([H])C([H])=C([Cl])C=3[Cl])C([H])([H])C4([H])[H]</chem>	10000	293	1.61	
SC75	<chem>O=C(/C2=C([H])C=1C([H])=C([F])C([H])=C([H])C=1N2[H])N([H])C([H])([H])C([H])([H])C([H])([H])[C@@]([H])(O[H])C([H])([H])N4C([H])([H])C([H])([H])N(C=3C([H])=C([H])C([H])=C([H])C=3OC([H])([H])[H])C([H])([H])C4([H])[H]</chem>	5060	244	2.41	
SC76	<chem>O=C(/C2=C([H])C=1C([H])=C([I])C([H])=C([H])C=1N2[H])N([H])C([H])([H])C([H])([H])C([H])([H])[C@@]([H])(O[H])C([H])([H])N4C([H])([H])C([H])([H])N(C=3C([H])=C([H])C([H])=C([H])C=3OC([H])([H])[H])C([H])([H])C4([H])[H]</chem>	10000	520	3.6	
SC77	<chem>O=C(/C2=C([H])C=1C([H])=C(OC([H])([H])[H])C([H])=C([H])C=1N2[H])N([H])C([H])([H])C([H])([H])[C@@]([H])(O[H])C([H])([H])N4C([H])([H])C([H])([H])N(C=3C([H])=C([H])C([H])=C([Cl])C=3[Cl])C([H])([H])C4([H])[H]</chem>	10000	489	1.2	

ID	SMILES	Ki [nM] <sup>a</sup>			Ref.
		D <sub>1</sub> R	D <sub>2</sub> R	D <sub>3</sub> R	
SC78	<chem>O=C(/C2=C(\ [H])C=1C([H])=C(OC([H])([H])[H])C([H])=C([H])C=1N2[H])N([H])C([H])([H])C([H])([H])[C@@]([H])(O[H])C([H])([H])N4C([H])([H])C([H])([H])N(C=3C([H])=C([H])C([H])=C([H])C=3OC([H])([H])[H])C4([H])[H])</chem>	10000	390	2.32	
SC79	<chem>O=C(C=2OC=1C([H])=C([H])C([H])=C([H])C=1C=2[H])N([H])C([H])([H])C([H])([H])[C@@]([H])(O[H])C([H])([H])N4C([H])([H])C([H])([H])N(C=3C([H])=C([H])C([H])=C([Cl])C=3[Cl])C([H])([H])C4([H])[H])</chem>	10000	622	6.11	
SC80	<chem>O=C(C=2OC=1C([H])=C([H])C([H])=C([H])C=1C=2[H])N([H])C([H])([H])C([H])([H])[C@@]([H])(O[H])C([H])([H])N4C([H])([H])C([H])([H])N(C=3C([H])=C([H])C([H])=C([H])C=3OC([H])([H])[H])C4([H])[H])</chem>	10000	507	7.51	
SC81	<chem>O=C(C=2OC=1C([H])=C([H])C([H])=C([H])C=1C=2[H])N([H])C([H])([H])C([H])([H])[C@@]([H])(O[H])C([H])([H])N4C([H])([H])C([H])([H])N(C=3C([H])=C([H])C([H])=C([Cl])C=3[Cl])C([H])([H])C4([H])[H])</chem>	10000	581	7.71	
SC82	<chem>O=C(C=2OC=1C([H])=C([H])C([H])=C([H])C=1C=2[H])N([H])C([H])([H])C([H])([H])[C@@]([H])(O[H])C([H])([H])N4C([H])([H])C([H])([H])N(C=3C([H])=C([H])C([H])=C([H])C=3OC([H])([H])[H])C4([H])[H])</chem>	3690	430	7.5	
SC83	<chem>O=C(C=2[S]C=1C([H])=C([H])C([H])=C([H])C=1C=2[H])N([H])C([H])([H])C([H])([H])[C@@]([H])(O[H])C([H])([H])N4C([H])([H])C([H])([H])N(C=3C([H])=C([H])C([H])=C([H])C=3OC([H])([H])[H])C4([H])[H])</chem>	6650	337	4.6	
SC84	<chem>O=C(/C2=C(\ [H])C=1C([H])=C([H])C([H])=C([H])C=1N2[H])N([H])C([H])([H])C([H])([H])[C@@]([H])(O[H])C([H])([H])C([H])([H])N4C([H])([H])C([H])([H])N(C=3C([H])=C([H])C([H])=C([Cl])C=3[Cl])C([H])([H])C4([H])[H])</chem>	10000	28.4	0.26	
SC85	<chem>O=C(C=2[S]C=1C([H])=C([H])C([H])=C([H])C=1C=2[H])N([H])C([H])([H])C([H])=C([H])C([H])([H])N4C([H])([H])C([H])([H])N(C=3C([H])=C([H])C([H])=C([Cl])C=3[Cl])C([H])([H])C4([H])[H])</chem>	1730	149	1.11	
SC86	<chem>O=C(C=2OC=1C([H])=C([H])C([H])=C([H])C=1C=2[H])N([H])C([H])([H])C([H])=C([H])C([H])([H])N4C([H])([H])C([H])([H])N(C=3C([H])=C([H])C([H])=C([Cl])C=3[Cl])C([H])([H])C4([H])[H])</chem>	1460	76.5	2.11	
SC87	<chem>O=C2C=1C([H])=C([H])C([H])=C([H])C=1C([H])([H])C([H])([H])C([H])([H])N2C([H])([H])C([H])([H])C([H])([H])C([H])([H])N4C([H])([H])C([H])([H])N(C=3C([H])=C([H])C([H])=C([Cl])C=3[Cl])C([H])([H])C4([H])[H])</chem>	1737.8	36.3078	14.45	[80]
SC88	<chem>O=C2C=1C([H])=C([H])C([H])=C([H])C=1C([H])([H])C([H])([H])C([H])([H])N2C([H])([H])C([H])([H])C([H])([H])C([H])([H])N4C([H])([H])C([H])([H])N(C=3C([H])=C([H])C([H])=C([H])C=3OC([H])([H])[H])C4([H])[H])</chem>	2691.53	3.63078	1.585	
SC89	<chem>O=C(C=1C([H])=C3C([H])=C([H])C=1C([H])([H])C([H])([H])C=2C([H])=C([H])C=C([H])C=2[H])C([H])([H])C3([H])[H])C([H])([H])C([H])([H])C([H])([H])N5C([H])([H])C([H])([H])C(O[H])(C=4C([H])=C([H])C([Cl])=C([H])C=4[H])C([H])([H])C5([H])[H])</chem>	9800	21	17	[81]



ID	SMILES	Ki [nM] <sup>a</sup>			Ref.
		D <sub>1</sub> R	D <sub>2</sub> R	D <sub>3</sub> R	
SC90	<chem>O=C(C=2[S]C=1C([H])=C([H])C([H])=C([H])C=1C=2[H])N([H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])N6C([H])([H])C([H])([H])N(C=3C([H])=C5C([H])=C([H])C=3C([H])([H])C([H])([H])C=4C([H])=C([H])C(=C([H])C=4[H])C([H])([H])C5([H])[H])C([H])([H])C6([H])[H]</chem>	4000	83	1.6	
SC91	<chem>O=C(C=2[S]C=1C([H])=C([H])C([H])=C([H])C=1C=2[H])N([H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])N4C([H])([H])C([H])([H])N(C=3C([H])=C(C([H])=C([H])C=3C([H])([H])[H])C([H])([H])[H])C([H])([H])C4([H])[H]</chem>	2400	84	2.5	
SC92	<chem>O=C(C=1C([H])=C(C([H])=C([H])C=1C([H])([H])[H])C([H])([H])[H])N([H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])N3C([H])([H])C([H])([H])N(C=2C([H])=C([H])C([H])=C([H])C=2OC([H])([H])[H])C([H])([H])C3([H])[H]</chem>	2100	22	4.7	
SC93	<chem>O=C(C([H])=C([H])C=1C([H])=C([H])C([H])=C([H])C=1[H])N([H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])N3C([H])([H])C([H])([H])N(C=2C([H])=C([H])C([H])=C([H])C=2OC([H])([H])[H])C([H])([H])C3([H])[H]</chem>	1100	27	0.34	[82]
SC94	<chem>[F]C([H])([H])C([H])([H])C([H])([H])OC=3C([H])=C2C1=C(C([H])=C([H])C(O[H])=C1O[H])C([H])([H])[C@]4([H])C2=C(C=3[H])C([H])([H])C([H])([H])N4C([H])([H])C([H])([H])C([H])([H])[H]</chem>	5000	28	430	
SC95	<chem>[F]C([H])([H])C([H])([H])C([H])([H])OC=3C([H])=C2C1=C(C([H])=C([H])C([H])=C1O[H])C([H])([H])[C@]4([H])C2=C(C=3[H])C([H])([H])C([H])([H])N4C([H])([H])C([H])([H])C([H])([H])[H]</chem>	5000	0.54	100	
SC96	<chem>[F]C([H])([H])C([H])([H])OC=3C([H])=C2C1=C(C([H])=C([H])C([H])=C1O[H])C([H])([H])[C@]4([H])C2=C(C=3[H])C([H])([H])C([H])([H])N4C([H])([H])C([H])([H])C([H])([H])[H]</chem>	5000	3.5	410	[69]
SC97	<chem>[F]C([H])([H])C([H])([H])C([H])([H])OC=3C([H])=C2C1=C(C([H])=C([H])C([H])=C1O[H])C([H])([H])[C@]4([H])C2=C(C=3[H])C([H])([H])C([H])([H])N4C([H])([H])C([H])([H])[H]</chem>	5000	3.2	240	
SC98	<chem>[F]C([H])([H])C([H])([H])OC=3C([H])=C2C1=C(C([H])=C([H])C([H])=C1O[H])C([H])([H])[C@]4([H])C2=C(C=3[H])C([H])([H])C([H])([H])N4C([H])([H])C([H])([H])[H]</chem>	5000	0.83	550	
SC99	<chem>[H]C=1C([H])=C([H])C(OC([H])([H])[H])=C(C=1[H])N2C([H])([H])C([H])([H])N(C([H])([H])C2([H])[H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])N3N=N/C(=C3/[H])C([H])([H])O/C4=C(\[H])C([H])=C([H])C7=C4/C5=C(\[H])C([H])=C([H])C6=C5[C@@([H])(N(C([H])([H])C6([H])[H])C([H])([H])C([H])([H])C([H])([H])C7([H])[H])</chem>	2700	661	2.67	
SC100	<chem>[H]C=1C([H])=C([H])C(OC([H])([H])[H])=C(C=1[H])N2C([H])([H])C([H])([H])N(C([H])([H])C2([H])[H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])C=3N=NN(C=3[H])C([H])([H])C([H])([H])C([H])([H])O/C4=C(\[H])C([H])=C([H])C7=C4/C5=C(\[H])C([H])=C([H])C6=C5[C@@([H])(N(C([H])([H])C6([H])[H])C([H])([H])C([H])([H])C7([H])[H])</chem>	1900	206	8.14	[83]
SC101	<chem>[H]C=1C([H])=C([H])C(OC([H])([H])[H])=C(C=1[H])N2C([H])([H])C([H])([H])N(C([H])([H])C2([H])[H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])O/C3=C(\[H])C([H])=C([H])C6=C3/C4</chem>	1174	174	189	

ID	SMILES	Ki [nM] <sup>a</sup>			Ref.
		D <sub>1</sub> R	D <sub>2</sub> R	D <sub>3</sub> R	
	<chem>=C([H])C([H])=C([H])C5=C4[C@@]([H])(N(C([H])([H])C5([H])</chem> <chem>[H])C([H])([H])C([H])([H])C([H])([H])[H])C6([H])[H]</chem>				
SC102	<chem>[H]C=1C([H])=C([H])C(OC([H])([H])[H])=C(C=1[H])N2C([H])(</chem> <chem>[H])C([H])([H])N(C([H])([H])C2([H])[H])C([H])([H])C([H])([H]</chem> <chem>)C([H])([H])C([H])([H])O/C3=C([H])C([H])=C([H])C6=C3/C4</chem> <chem>=C([H])C([H])=C([H])C5=C4[C@]([H])(N(C([H])([H])C5([H])</chem> <chem>[H])C([H])([H])C([H])([H])C([H])([H])[H])C6([H])[H]</chem>	1307	141	23.4	
SC103	<chem>[H]C=1C([H])=C([H])C(=C([H])C=1[H])[C@]2([H])N(C([H])([H]</chem> <chem>)[C@]4([H])[C@@]2([H])[C@@]([H])(N3C([H])([H])C([H])([H])</chem> <chem>C([H])([H])C3([H])[H])[C@]4([H])C([H])([H])O[H])C([H])([H])</chem> <chem>C=5C([H])=C([H])C([H])=C([H])C=5[H]</chem>	22000	250	280	[84]
SC104	<chem>[H]C=1C([H])=C([H])C(=C([H])C=1[H])C([H])([H])C([H])([H])</chem> <chem>N(C([H])([H])C([H])([H])C=2C([H])=C([H])C([H])=C(O[H])C=2</chem> <chem>[H])C([H])([H])C([H])([H])C([H])([H])[H]</chem>	10000	64.4	21.8	
SC105	<chem>[H]C=1C([H])=C([H])C(=C([H])C=1[H])C([H])([H])C([H])([H])</chem> <chem>N(C([H])([H])C2([H])C([H])([H])C2([H])[H])C([H])([H])C([H])</chem> <chem>([H])C3=C([H])C([H])=C([H])C(O[H])=C3[H]</chem>	10000	118	168	[85]
SC106	<chem>[H]C=1C([H])=C([H])C(=C([H])C=1[H])C([H])([H])C([H])([H])</chem> <chem>N(C([H])([H])C2([H])C([H])([H])C([H])([H])C2([H])[H])C([H])</chem> <chem>([H])C([H])([H])C3=C([H])C([H])=C([H])C(O[H])=C3[H]</chem>	10000	450	282	
SC107	<chem>O=C1C([H])=NN(C(=O)N1C([H])([H])[H])C([H])([H])C([H])([</chem> <chem>H])C([H])([H])C([H])([H])N3C([H])([H])C([H])([H])N(C=2C([</chem> <chem>H])=C([H])C([H])=C([H])C=2OC([H])([H])C([H])([H])[H])C([H]</chem> <chem>)([H])C3([H])[H]</chem>	10000	37.1	22	[86]
SC108	<chem>[H]C=1C([H])=C([H])C(OC([H])([H])C([H])([H])[H])=C(C=1[H]</chem> <chem>)N2C([H])([H])C([H])([H])N(C([H])([H])C2([H])[H])C([H])([H]</chem> <chem>)C=3[S]C([H])=C([H])C=3[H]</chem>	10000	162	112	
SC109	<chem>[H]C=1C([H])=C([H])C(OC([H])([H])C([H])([H])[H])=C(C=1[H]</chem> <chem>)N2C([H])([H])C([H])([H])N(C([H])([H])C2([H])[H])C([H])([H]</chem> <chem>)C=3C([H])=C([H])C([H])=NC=3[H]</chem>	10000	255	42	
SC110	<chem>[Cl]C=1C([H])=C([H])C([H])=C(C=1[Cl])N2C([H])([H])C([H])([</chem> <chem>H])N(C([H])([H])C2([H])[H])C([H])([H])C=3C([H])=C([H])C([</chem> <chem>H])=NC=3[H]</chem>	10000	327	41	
SC111	<chem>[H]C=1C([H])=C([H])C2=C(C=1[H])C([H])=C([H])C([H])=C2C([</chem> <chem>H])([H])N4C([H])([H])C([H])([H])N(C=3C([H])=C([H])C([H])=</chem> <chem>C([H])C=3OC([H])([H])C([H])([H])[H])C([H])([H])C4([H])[H]</chem>	10000	264	59	[87]
SC112	<chem>[Cl]C=1C([H])=C([H])C([H])=C(C=1[Cl])N2C([H])([H])C([H])([</chem> <chem>H])N(C([H])([H])C2([H])[H])C([H])([H])C4=C([H])C([H])=C([</chem> <chem>H])C=3C([H])=C([H])C([H])=C([H])C=34</chem>	10000	351	92	
SC113	<chem>[H]C=2C([H])=C([H])C=1[S]C([H])=C(C=1C=2[H])C([H])([H])N</chem> <chem>4C([H])([H])C([H])([H])N(C=3C([H])=C([H])C([H])=C([H])C=3</chem> <chem>OC([H])([H])C([H])([H])[H])C([H])([H])C4([H])[H]</chem>	10000	219	45.1	
SC114	<chem>[Cl]C=1C([H])=C([H])C([H])=C(C=1[Cl])N2C([H])([H])C([H])([</chem> <chem>H])N(C([H])([H])C2([H])[H])C([H])([H])C3=C([H])[S]C=4C([H]</chem> <chem>)=C([H])C([H])=C([H])C3=4</chem>	10000	383	52.5	
SC115	<chem>[H]C=1C([H])=C([H])C(=C([H])C=1[H])C([H])([H])N3C([H])([</chem> <chem>H])C([H])([H])N(C=2C([H])=C([H])C([H])=C([H])C=2OC([H])([</chem> <chem>H])C([H])([H])[H])C([H])([H])C3([H])[H]</chem>	10000	217	42.7	

ID	SMILES	Ki [nM] <sup>a</sup>			Ref.
		D <sub>1</sub> R	D <sub>2</sub> R	D <sub>3</sub> R	
SC116	<chem>[Cl]C=1C([H])=C([H])C([H])=C(C=1[Cl])N2C([H])([H])C([H])([H])N(C([H])([H])C2([H])[H])C([H])([H])C=3C([H])=C([H])C([H])=C([H])C=3[H]</chem>	10000	242	41	
SC117	<chem>[H]C=1C([H])=C([H])C2=C(C=1[H])C(=C([H])N2[H])C([H])([H])N4C([H])([H])C([H])([H])N(C=3C([H])=C([H])C([H])=C([H])C=3OC([H])([H])C([H])([H])[H])C([H])([H])C4([H])[H]</chem>	10000	473	103	
SC118	<chem>[Cl]C=1C([H])=C([H])C([H])=C(C=1[Cl])N2C([H])([H])C([H])([H])N(C([H])([H])C2([H])[H])C([H])([H])C3=C([H])N([H])C=4C([H])=C([H])C([H])=C([H])C3=4</chem>	10000	502	123	
SC119	<chem>[H]C=1C([H])=C([H])C(OC([H])([H])[H])=C(C=1[H])N2C([H])([H])C([H])([H])N(C([H])([H])C2([H])[H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])N3N=N/C(=C3/[H])C=4C([H])=C([H])C(=C([H])C=4[H])N([H])[H]</chem>	38430	198.8	2.7	[88]
SC120	<chem>[I]C=1C([H])=C([H])C(=C([H])C=1[H])N2C([H])([H])C([H])([H])N(C([H])([H])C2([H])[H])C([H])([H])C([H])([H])N([H])C([H])([H])[C@]4([H])OC=3C([H])=C(O[H])C([H])=C([H])C=3C([H])([H])C4([H])[H]</chem>	3960	80.5	23	[89]
SC121	<chem>[H]/C1=C([H])C(O[H])=C([H])C=2O[C@]([H])(C([H])([H])C([H])([H])C1=2)C([H])([H])N([H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])[H]</chem>	10900	8.19	547	
SC122	<chem>[Cl]C=1C([H])=C([H])C(=C([H])C=1[H])N2C([H])([H])C([H])([H])N(C([H])([H])C2([H])[H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])C4=NC=3C([H])=C([H])C([H])=C([H])C=3[S]4</chem>	1897	219	31	[56]
SC123	<chem>O=C(N([H])[C@@]1([H])C([H])([H])C([H])([H])[C@]([H])(C([H])([H])C1([H])[H])C([H])([H])C([H])([H])N3C([H])([H])C([H])([H])N(C=2C([H])=C([H])C([H])=C([Cl])C=2[Cl])C([H])([H])C3([H])[H])N(C([H])([H])[H])C([H])([H])[H]</chem>	2100	0.47	0.27	
SC124	<chem>[Cl]C=1C([H])=C([H])C([H])=C(C=1[Cl])N2C([H])([H])C([H])([H])N(C([H])([H])C2([H])[H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])O/C4=C([H])C3=C([H])C([H])=NN3C([H])=C4[H]</chem>	2900	34	7	
SC125	<chem>[Cl]C=1C([H])=C([H])C([H])=C(C=1[Cl])N2C([H])([H])C([H])([H])N(C([H])([H])C2([H])[H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])OC=4/C3=C([H])C([H])=NN3C([H])=C([H])C=4[H]</chem>	1800	25	10	
SC126	<chem>[Cl]C=1C([H])=C([H])C([H])=C(C=1[Cl])N2C([H])([H])C([H])([H])N(C([H])([H])C2([H])[H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])OC=4C([H])=C([H])C3=C([H])C([H])=NN3C=4[H]</chem>	1200	4.2	2.3	[90]
SC127	<chem>[Cl]C=1C([H])=C([H])C([H])=C(C=1[Cl])N2C([H])([H])C([H])([H])N(C([H])([H])C2([H])[H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])O/C3=N/N4/C(=C3/[H])C([H])=C([H])C([H])=C4[H]</chem>	1100	9.4	3.5	
SC128	<chem>O=C([H])C=1C([H])=NN2C=1C([H])=C([H])C([H])=C2OC([H])([H])C([H])([H])C([H])([H])C([H])([H])N4C([H])([H])C([H])([H])N(C=3C([H])=C([H])C([H])=C([Cl])C=3[Cl])C([H])([H])C4([H])[H]</chem>	1600	51	6.4	
SC129	<chem>[Cl]/C1=C([H])C([H])=C([H])C(=C1[Cl])N2C([H])([H])C([H])([H])N(C([H])([H])C2([H])[H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])[H]</chem>	4300	1.8	2.3	

ID	SMILES	Ki [nM] <sup>a</sup>			Ref.
		D <sub>1</sub> R	D <sub>2</sub> R	D <sub>3</sub> R	
	<chem>CC([H])([H])O/C4=C([H])C3=C(C([H])=NN3C([H])=C4[H])C([H])=NO[H]</chem>				
SC130	<chem>N#C/C1=N/N4/C(=C1/[H])C([H])=C(OC([H])([H])C([H])([H])C([H])([H])C([H])([H])N3C([H])([H])C([H])([H])N(C=2C([H])=C([H])C([H])=C([Cl])C=2[Cl])C([H])([H])C3([H])[H])C([H])=C4[H])</chem>	3500	8.9	1.9	
SC131	<chem>[F]C=1C([H])=C([H])C(=C([H])C=1[H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])N2[C@@]4([H])C([H])([H])C([H])([H])[C@]2([H])C([H])([H])[C@@](O[H])(C=3C([H])=C([H])C([Cl])=C([H])C=3[H])C4([H])[H]</chem>	10000	33	9.7	
SC132	<chem>[F]C=4C([H])=C([H])C(OC([H])([H])C([H])([H])C([H])([H])N1[C@@]3([H])C([H])([H])C([H])([H])[C@]1([H])C([H])([H])[C@@](O[H])(C=2C([H])=C([H])C([Cl])=C([H])C=2[H])C3([H])[H])=C([H])C=4[H]</chem>	10000	22	4.1	
SC133	<chem>[F]C=1C([H])=C([H])C([H])=C([H])C=1[S]C([H])([H])C([H])([H])C([H])([H])N2[C@@]4([H])C([H])([H])C([H])([H])[C@]2([H])C([H])([H])[C@@](O[H])(C=3C([H])=C([H])C([Cl])=C([H])C=3[H])C4([H])[H]</chem>	4093	4.8	1.3	[91]
SC134	<chem>O=C(C=1C([H])=C([H])C([H])=C([H])C=1OC([H])([H])C([H])([H])C([H])([H])N5C([H])([H])C([H])([H])N(C=2C([H])=C([H])C([H])=C3C=2C([H])=C([H])N3[S](=O)(=O)C=4C([H])=C([H])C([H])=C([H])C=4[H])C([H])([H])C5([H])[H])N([H])[H]</chem>	1000	6.3	0.1	
SC135	<chem>O=C(C=1C([H])=C([H])C(=C([H])C=1[H])C=2C([H])=C([H])C([H])=C([H])C=2[H])N([H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])N([C@]3([H])C([H])([H])C([H])=C(C#C[H])C([H])([H])C3([H])[H])C([H])([H])C([H])([H])C([H])([H])[H]</chem>	13000	9.4	1	
SC136	<chem>O=C(C=1C([H])=C([H])C(=C([H])C=1[H])C=2C([H])=C([H])C([H])=C([H])C=2[H])N([H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])N([C@@]3([H])C([H])([H])C([H])=C(C#C[H])C([H])([H])C3([H])[H])C([H])([H])C([H])([H])C([H])([H])[H]</chem>	18000	14	4.3	
SC137	<chem>O=C(C=2C([H])=C([H])C(OC([H])([H])C([H])([H])C([H])([H])C=1N=NN(C=1[H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])N([C@]3([H])C([H])([H])C([H])=C(C#C[H])OC3([H])[H])C([H])([H])C([H])([H])C([H])([H])[H]</chem>	2600	1.6	0.63	
SC138	<chem>O=C(C=2C([H])=C([H])C(OC([H])([H])C([H])([H])C([H])([H])C=1N=NN(C=1[H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])N([C@@]3([H])C([H])([H])C([H])=C(C#C[H])OC3([H])[H])C([H])([H])C([H])([H])C([H])([H])[H]</chem>	3900	4.9	2.2	[92]
SC139	<chem>O=C2C([H])=C([H])C=1/C(=C/[H])C([H])=C(O[H])C=1N2[H])C([H])([H])C([H])([H])N(C([H])([H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])N([H])C(=O)C=4C([H])=C([H])C(OC([H])([H])C([H])([H])C([H])([H])C=3N=NN(C=3[H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])=C(OC([H])([H])[H])C=4[H]</chem>	4600	24	1.6	
SC140	<chem>O=C(C=2C([H])=C([H])C(OC([H])([H])C([H])([H])C([H])([H])C=1N=NN(C=1[H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])N([C@@]3([H])C([H])([H])C([H])=C(C#C[H])OC3([H])[H])C([H])([H])C([H])([H])C([H])([H])[H]</chem>	23000	18	1.2	

[illegible]

ID	SMILES	Ki [nM] <sup>a</sup>			Ref.
		D <sub>1</sub> R	D <sub>2</sub> R	D <sub>3</sub> R	
	<chem>=C([H])C(OC([H])([H])C([H])([H])C([H])([H])C=3C([H])=C([H])C([H])=C([H])C=3[H])=C(OC([H])([H])([H])C=4[H])</chem>				
SC153	<chem>O=C(N([H])C2=C([H])C1=C([H])C([H])=NN1C([H])=C2[H])C([H])([H])C([H])([H])C([H])([H])N4C([H])([H])C([H])([H])N(C=3C([H])=C([H])C([H])=C([H])C=3OC([H])([H])([H])C([H])([H])C4([H])[H])</chem>	1700	46	97	
SC154	<chem>O=C([H])C=1C([H])=NN4C=1C([H])=C([H])C(OC([H])([H])C([H])([H])C([H])([H])C([H])([H])N3C([H])([H])C([H])([H])N(C=2C([H])=C([H])C([H])=C([H])C=2OC([H])([H])([H])C([H])([H])C3([H])([H])=C4[H])</chem>	1400	7.8	17	
SC155	<chem>O=C(N([H])C2=C([H])C1=C([H])=NN1C([H])=C2[H])C([H])=NO([H])C([H])([H])C([H])([H])C([H])([H])N4C([H])([H])C([H])([H])N(C=3C([H])=C([H])C([H])=C([Cl])C=3[Cl])C([H])([H])C4([H])([H])</chem>	2900	0.57	2.2	
SC156	<chem>[H]C=1C([H])=C([H])C(OC([H])([H])([H])=C(C=1[H])N2C([H])([H])C([H])([H])N(C([H])([H])C2([H])([H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])OC=4C([H])=C([H])C3=C(C([H])=NN3C=4[H])C([H])=NO[H])</chem>	1000	4.2	2.3	
SC157	<chem>O=C([H])C=1C([H])=NN4C=1C([H])=C([H])C(OC([H])([H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])N([C@]3([H])C([H])([H])C=2C([H])=C([H])C([H])=C(O[H])C=2C([H])([H])C3([H])([H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])=C4[H])</chem>	1400	2.4	1.6	
SC158	<chem>[H]C=1C([H])=C([H])C(OC([H])([H])([H])=C(C=1[H])N2C([H])([H])C([H])([H])N(C([H])([H])C2([H])([H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])O/C4=C([H])C3=C([H])C([H])=NN3C([H])=C4[H])</chem>	2800	18	20	[97]
SC159	<chem>O=C([H])C=1C([H])=NN2C=1C([H])=C(C([H])=C2[H])N([H])C(=O)C([H])([H])C([H])([H])C([H])([H])N4C([H])([H])C([H])([H])N(C=3C([H])=C([H])C([H])=C([H])C=3OC([H])([H])([H])C([H])([H])C4([H])([H])</chem>	1200	1.4	70	
SC160	<chem>O=C([H])C=1C([H])=NN4C=1C([H])=C(OC([H])([H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])N([C@]3([H])C([H])([H])C=2C([H])=C([H])C([H])=C(O[H])C=2C([H])([H])C3([H])([H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])=C4[H])</chem>	1300	2.3	1.1	
SC161	<chem>[H]/C1=C([H])C4=C(C(O[H])=C1[H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])N(C([H])([H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])O/C3=C([H])C2=C([H])C([H])=NN2C([H])=C3[H])C4([H])([H])</chem>	3700	96	13	
SC162	<chem>[H]/C1=C([H])C4=C(C(O[H])=C1[H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])N(C([H])([H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])OC=3C([H])=C([H])C2=C([H])C([H])=NN2C=3[H])C4([H])([H])</chem>	2100	0.63	0.71	
SC163	<chem>[H]C=1C([H])=C([H])C(OC([H])([H])([H])=C(C=1[H])N2C([H])([H])C([H])([H])N(C([H])([H])C2([H])([H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])OC=4C([H])=C([H])C3=C([H])C([H])=NN3C=4[H])</chem>	1100	1.8	5	
SC164	<chem>[H]/C1=C([H])C4=C(C(O[H])=C1[H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])N(C([H])([H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])=C4[H])</chem>	1800	2.2	0.59	

[illegible]

[illegible]



ID	SMILES	Ki [nM] <sup>a</sup>			Ref.
		D <sub>1</sub> R	D <sub>2</sub> R	D <sub>3</sub> R	
	<chem>C([H])([H])C([H])([H])C([H])([H])O/C5=C([H])C4=C(C([H])=NN4C([H])=C5[H])C([H])=NO[H]</chem>				
SC188	<chem>O=C1N([H])C=2C(OC1([H])[H])=C(C([H])=C([H])C=2O[H])N3C([H])([H])C([H])([H])N(C([H])([H])C3([H])[H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])[H]</chem>	20000	120	5.9	
SC189	<chem>O=C2C([H])=C([H])C=1/C(=C([H])C([H])=C(O[H])C=1N2[H])N3C([H])([H])C([H])([H])N(C([H])([H])C3([H])[H])C([H])([H])[H]</chem>	20000	780	380	
SC190	<chem>O=C([H])C=1C([H])=NN5C=1C([H])=C(OC([H])([H])C([H])([H])C([H])([H])C([H])([H])N4C([H])([H])C([H])([H])N(C=2C([H])=C([H])C(O[H])=C3OC([H])([H])C([H])([H])OC=23C([H])([H])C4([H])[H])C([H])=C5[H]</chem>	11000	5.7	24	
SC191	<chem>O=C1N([H])C=2C(OC1([H])[H])=C(C([H])=C([H])C=2O[H])N3C([H])([H])C([H])([H])N(C([H])([H])C3([H])[H])C([H])([H])[H]</chem>	20000	630	48	
SC192	<chem>O=C2C([H])=C([H])C=1/C(=C([H])C([H])=C(O[H])C=1N2[H])N3C([H])([H])C([H])([H])N(C([H])([H])C3([H])[H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])O/C5=C([H])C4=C(C([H])=NN4C([H])=C5[H])C(=O)[H]</chem>	15000	1	2.3	
SC193	<chem>O=C/C1=N/N2/C(=C1/[H])C([H])=C([H])C([H])=C2[H])N([H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])N4C([H])([H])C([H])([H])N(C=3C([H])=C([H])C([H])=C([H])C=3OC([H])([H])[H])C([H])([H])C4([H])[H]</chem>	1600	270	3.5	[100]
SC194	<chem>O=C/C1=N/N2/C(=C1/[H])C([H])=C([H])C([H])=C2[H])N([H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])N4C([H])([H])C([H])([H])N/C3=N/C(=N/C(=C3/[H])C([F])([F])[F])C(C([H])([H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])C4([H])[H]</chem>	7500	430	1.2	
SC195	<chem>O=C(C=1C([H])=C([H])C=C([H])C=1[H])N(C([H])([H])C([H])([H])C([H])([H])N([H])C([H])([H])C([H])([H])C([H])([H])N3C([H])([H])C([H])([H])C@([H])(C=2C([H])=C([H])C([H])=C(O[H])C=2[H])C3([H])[H]</chem>	10000	345	27	[101]
SC196	<chem>[F]C([F])([F])C=1C([H])=C(C([H])=C([H])C=1[Cl])C2(O[H])C([H])([H])C([H])([H])N(C([H])([H])C2([H])[H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])N(C=3C([H])=C([H])C(OC([H])([H])[H])=C([H])C=3[H])C=4C([H])=C([H])C(OC([H])([H])[H])=C([H])C=4[H]</chem>	10000	417	437	[102]
SC197	<chem>N#CC=1C([H])=C([H])C([H])=C(C=1[H])N2C([H])([H])C([H])([H])N(C([H])([H])C2([H])[H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])N([H])C(=O)C=3C([H])=C([H])C(=C([H])C=3[H])C=4C([H])=C([H])[S]C=4[H]</chem>	10000	743	0.5	[103]
SC198	<chem>[F]C=1C([H])=C([H])C(OC([H])([H])[H])=C(C=1[H])[C@@]2([H])C([H])([H])[C@]2([H])C([H])([H])N(C([H])([H])C([H])([H])C([H])([H])[S]/C4=N/N=C(/C=3C([H])=C([H])C([H])=C([H])C=3[H])N4C([H])([H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])[H]</chem>	5000	512.9	104.7	[104]
SC199	<chem>O=C(C=2C([H])=C([H])C=1C([H])=C([H])C([H])=C([H])C=1C=2[H])N([H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])N(C([H])([H])[C@]3([H])C([H])([H])[C@@]3([H])C=4C([H])=C([Cl])C([H])=C([H])C=4OC([H])([H])[H])C([H])([H])C([H])([H])[H]</chem>	1981	408	23.4	

ID	SMILES	Ki [nM] <sup>a</sup>			Ref.
		D <sub>1</sub> R	D <sub>2</sub> R	D <sub>3</sub> R	
SC200	<chem>[Cl]C=1C([H])=C([H])C(OC([H])([H])[H])=C(C=1[H])[C@]2([H])C([H])([H])[C@]2([H])C([H])([H])N(C([H])([H])C([H])([H])[H])C([H])([H])C([H])([H])C([H])([H])[S]/C4=N/N=C(/C=3C([H])=C([H])C([H])=C([H])C=3[H])N4C([H])([H])[H]</chem>	1509	238	31.6	
SC201	<chem>[Cl]C=1C([H])=C([H])C(OC([H])([H])[H])=C(C=1[H])[C@]2([H])C([H])([H])[C@@]2([H])C([H])([H])N(C([H])([H])C([H])([H])C([H])([H])[H])C([H])([H])C([H])([H])C([H])([H])[S]/C4=N/N=C(/C=3C([H])=C([H])C([H])=C([H])C=3[H])N4C([H])([H])[H]</chem>	1918	233	36.7	
SC202	<chem>[F]C=1C([H])=C([H])C(OC([H])([H])[H])=C(C=1[H])[C@@]2([H])C([H])([H])[C@]2([H])C([H])([H])N(C([H])([H])C([H])([H])[H])C([H])([H])C([H])([H])C([H])([H])[S]/C4=N/N=C(/C=3C([H])=C([H])C([H])=C([H])C=3[H])N4C([H])([H])[H]</chem>	1724.6	275.4	44	
SC203	<chem>[H]C2([H])C=1N=C([S]C=1C([H])([H])[C@@]([H])(N([H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])C2([H])[H])N([H])[H]</chem>	10000	743.5	0.9	[105]
SC204	<chem>O=C(/C2=C(\ [H])C=1C([H])=C([H])C([H])=C([H])C=1N2[H])N([H])C([H])([H])C([H])([H])[C@@]3([H])C([H])([H])[C@]3([H])C([H])([H])N4C([H])([H])[C@@]([H])(OC([H])([H])[C@]4([H])C([H])([H])[H])C=5C([H])=C([H])C(=NC=5[H])N([H])[H]</chem>	5630	87.8	1.85	
SC205	<chem>O=C(/C2=C(\ [H])C=1C([H])=C([H])C([H])=C([H])C=1N2[H])N([H])[C@@]3([H])C([H])([H])C([H])([H])[C@]([H])(C([H])([H])C3([H])[H])C([H])([H])C([H])([H])N4C([H])([H])[C@@]([H])(OC([H])([H])[C@]4([H])C([H])([H])[H])C=5C([H])=C([H])C(=NC=5[H])N([H])[H]</chem>	100000	104	21.6	[106]
SC206	<chem>[H]/C1=C(\ [H])C(O[H])=C([H])C2=C1OC([H])([H])[C@]3([H])N(C([H])([H])C([H])([H])O[C@]23[H])C([H])([H])C([H])([H])C([H])([H])[H]</chem>	100000	28	1.67	

<sup>a</sup>All KI values retrieved from ChEMBL were determined in vitro utilizing radio-ligand binding assays.

## 2.4 Dataset of D<sub>3</sub>R-selective compounds (ChEMBL)

**Table S4.** D<sub>3</sub>R-selective compounds extracted from ChEMBL with in vitro determined biological activities for all investigated DR subtypes.

ID	SMILES	Ki [nM] <sup>a</sup>			Ref.
		D <sub>1</sub> R	D <sub>2</sub> R	D <sub>3</sub> R	
SC207	<chem>O=C(C=1C([H])=C([Cl])C(=C([H])C=1OC([H])([H])[H])N([H])[H])N([H])C([H])([H])[C@]2([H])C([H])([H])C([H])([H])N(C2([H])([H])C([H])([H])C=3C([H])=C([H])C([H])=C([H])C=3[H]</chem>	11000	1400	570	[62]
SC208	<chem>[H]C=1C([H])=C([H])C(=C([H])C=1[H])C2=N/C(=C(/[H])[S]2)C([H])([H])N([H])C([H])([H])[C@]3([H])C([H])([H])C([H])([H])N(C3([H])[H])C([H])([H])C=4C([H])=C([H])C([H])=C([H])C=4[H]</chem>	8850	7900	660	
SC209	<chem>[Br]C=1C([H])=C([H])C(OC([H])([H])[H])=C(C=1[H])C2=N/C(=C(/[H])O2)C([H])([H])N([H])C([H])([H])C([H])([H])[C@]3([H])C([H])([H])C([H])([H])N(C3([H])[H])C([H])([H])C=4C([H])=C([H])C([H])=C([H])C=4[H]</chem>	8950	1070	120	[63]
SC210	<chem>[H]C=1C([H])=C([H])C(=C([H])C=1[H])N2C([H])([H])C([H])([H])N(C([H])([H])C2([H])[H])C([H])([H])C3=C([H])C([H])=C([H])N3[H]</chem>	5400	3000	570	[107]

ID	SMILES	Ki [nM] <sup>a</sup>			Ref.
		D <sub>1</sub> R	D <sub>2</sub> R	D <sub>3</sub> R	
SC211	<chem>O=C(C=2[S]C=1C([H])=C([H])C([H])=C([H])C=1C=2[H])N([H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])N4C([H])([H])C([H])([H])N(C=3C([H])=C([H])C([H])=C([Cl])C=3[Cl])C([H])([H])C4([H])[H])</chem>	8800	3600	0.5	[108]
SC212	<chem>O=C(C=2C([H])=C([Br])C=1C([H])=C([H])C([H])=C([H])C=1C=2OC([H])([H])[H])N([H])C([H])([H])C([H])([H])[C@]3([H])C([H])([H])C([H])([H])N(C3([H])[H])C([H])([H])C=4C([H])=C([H])C([H])=C([H])C=4[H])</chem>	1700	2000	580	[65]
SC213	<chem>O=C(C=2OC=1C([H])=C([H])C([I])=C([H])C=1C=2[H])N([H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])N4C([H])([H])C([H])([H])([H])N(C=3C([H])=C([H])C([H])=C([Cl])C=3[Cl])C([H])([H])C4([H])[H])</chem>	3300	3200	5.7	[109]
SC214	<chem>O=C(C=2C([H])=C([H])C(C#CC=1C([H])=C([H])C([H])=C([H])C=1[H])=C([H])C=2[H])N([H])C([H])([H])C([H])([H])N4C([H])([H])C([H])([H])N(C=3C([H])=C([H])C([H])=C([Cl])C=3[Cl])C([H])([H])C4([H])[H])</chem>	5500	4700	29	[110]
SC215	<chem>O=C(C=2C([H])=C([H])C([H])=C(C#CC=1C([H])=C([H])C([H])=C([H])C=1[H])C=2[H])N([H])C([H])([H])C([H])([H])N4C([H])([H])C([H])([H])N(C=3C([H])=C([H])C([H])=C([Cl])C=3[Cl])C([H])([H])C4([H])[H])</chem>	3100	1200	68	
SC216	<chem>O=C(C=2C([H])=C([H])C(C#CC=1C([H])=C([H])C([H])=C([H])C=1[H])=C([H])C=2[H])N([H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])N4C([H])([H])C([H])([H])N(C=3C([H])=C([H])C([H])=C([H])C=3OC([H])([H])[H])C([H])([H])C4([H])[H])</chem>	16000	1400	10	
SC217	<chem>O=C(C=2C([H])=C([H])C([H])=C(C#CC=1C([H])=C([H])C([H])=C([H])C=1[H])C=2[H])N([H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])N4C([H])([H])C([H])([H])N(C=3C([H])=C([H])C([H])=C([H])C=3OC([H])([H])[H])C([H])([H])C4([H])[H])</chem>	5900	1200	22	[66]
SC218	<chem>[Cl]C=1C([H])=C([H])C(=C([H])C=1[Cl])N2C([H])([H])C([H])([H])N(C([H])([H])C2([H])[H])C([H])([H])C=4N=C3C([H])=C([H])C(=NN3C=4[H])N5C([H])([H])C([H])([H])N(C([H])([H])C5([H])[H])C([H])([H])[H])</chem>	13000	8000	880	
SC219	<chem>O=C(/C2=C(\ [H])C=1C([H])=C([H])C([H])=C([H])C=1C([H])([H])N2[H])N([H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])N5C([H])([H])C4=C([H])C=3C([H])=C([H])C([H])=C(OC([H])([H])[H])C=3N4C([H])([H])C5([H])[H])</chem>	10000	1012	33.5	
SC220	<chem>O=C(/C2=N/C([H])=C1C([H])=C([H])C([H])=C([H])C1=C2[H])N([H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])N4C([H])([H])C([H])([H])N(C=3C([H])=C([H])C([H])=C([Cl])C=3[H])C([H])([H])C4([H])[H])</chem>	5500	1039	0.27	[111]
SC221	<chem>O=C3/C2=C(\ [H])C=1C([H])=C([H])C([H])=C([H])C=1N2C([H])([H])C([H])([H])N3C([H])([H])C([H])([H])C([H])([H])C([H])([H])N6C([H])([H])C5=C([H])C=4C([H])=C([H])C([H])=C(OC([H])([H])[H])C=4N5C([H])([H])C6([H])[H])</chem>	10000	3530	8.6	
SC222	<chem>O=C(/C2=C(\ [H])C=1C([H])=C([H])C([H])=C([H])C=1C([H])([H])N2[H])N([H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])N5C([H])([H])C4=N/C3=C(\ [H])C([H])=C([H])C(OC([H])([H])[H])=C3[C@]4([H])C([H])([H])C5([H])[H])</chem>	10000	6475	6	

[illegible]

ID	SMILES	Ki [nM] <sup>a</sup>			Ref.
		D <sub>1</sub> R	D <sub>2</sub> R	D <sub>3</sub> R	
			-ful activity		
SC236	<chem>[Cl]C=1C([H])=C([H])C=C([H])C=1[H]N2C([H])([H])C([H])([H])N(C([H])([H])C2([H])[H])C([H])([H])C([H])([H])C([H])([H])C4=NC=3C([H])=C([H])C([H])=C([H])C=3[S]4</chem>	1273	2321	214	[56]
SC237	<chem>[Cl]C=1C([H])=C([H])C=C([H])C=1[H]N2C([H])([H])C([H])([H])N(C([H])([H])C2([H])[H])C([H])([H])C([H])([H])C([H])([H])C4=NC=3C([H])=C([H])C([H])=C([H])C=3O4</chem>	1172	3962	180	
SC238	<chem>[F]C([F])([F])C=3C([H])=C([H])C(OC([H])([H])C([H])([H])C([H])([H])N2C([H])([H])C([H])([H])N(/C1=N/C([H])=C([H])C([H])=C1[H])C([H])([H])C2([H])[H])=C([H])C=3[H]</chem>	2344	1092	355	
SC239	<chem>[Cl]C=1C([H])=C([H])C=C([H])C=1[H]N2C([H])([H])C([H])([H])N(C([H])([H])C2([H])[H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])C4=NC=3C([H])=C([H])C([H])=C([H])C=3O4</chem>	7939	3108	119	
SC240	<chem>[H]C=1C([H])=C([H])C=C([H])C=1[H]C([H])([H])C([H])([H])C@@]2([H])OC([H])([H])C([H])([H])N(C2([H])[H])C([H])([H])C4=NC=3C([H])=C([H])C([H])=C([H])C=3N4[H]</chem>	100000	100000	10.8	[115]
SC241	<chem>[H]C=1C([H])=C([H])C=C([H])C=1[H]C([H])([H])C([H])([H])C@]2([H])OC([H])([H])C([H])([H])N(C2([H])[H])C([H])([H])C4=NC=3C([H])=C([H])C([H])=C([H])C=3N4[H]</chem>	100000	100000	25.9	
SC242	<chem>[H]C=1C([H])=C([H])C=C([H])C=1[H]C([H])([H])C([H])([H])C@@]2([H])OC([H])([H])C([H])([H])N(C2([H])[H])C([H])([H])C4=NC=3C([H])=C([H])C([H])=C([H])C=3N4[H]</chem>	100000	100000	15.7	
SC243	<chem>[H]C=1C([H])=C([H])C=C([H])C=1[H]C([H])([H])C([H])([H])C([H])([H])N(C([H])([H])C([H])([H])C=3C([H])=C([H])C=2OC([H])([H])OC=2C=3[H])C([H])([H])C([H])([H])C=4C([H])=C([H])C(OC([H])([H])C([H])=C(OC([H])([H])C([H])C=4[H]</chem>	1682	1729	498	
SC244	<chem>[H]C=1C([H])=C([H])C=C([H])C=1[H]C([H])([H])C([H])([H])C([H])([H])OC=2C([H])=C([H])C=C([H])C=2OC([H])([H])C([H])([H])C([H])([H])C([H])N([H])C([H])([H])C@@]([H])(O[H])C=3C([H])=C([H])C(O[H])=C(O[H])C=3[H]</chem>	2900	1900	660	[96]
SC245	<chem>O=C2C([H])=C([H])C=1/C=C(/[H])C([H])=C(O[H])C=1N2[H])(C@]([H])(O[H])C([H])([H])N([H])C([H])([H])C([H])([H])C=4C([H])=C([H])C(OC([H])([H])C([H])([H])C([H])([H])C=3C([H])=C([H])C([H])=C([H])C=3[H])=C(OC([H])([H])C([H])C=4[H]</chem>	6800	2900	790	
SC246	<chem>[H]/C2=C(\[H])C(O[H])=C1OC([H])([H])C([H])([H])O/C1=C2\N3C([H])([H])C([H])([H])N(C([H])([H])C3([H])[H])C([H])([H])[H]</chem>	7700	3200	790	[99]
SC247	<chem>[H]/C2=C(\[H])C(O[H])=C1OC([H])([H])C([H])([H])O/C1=C2\N3C([H])([H])C([H])([H])N([H])C([H])([H])C3([H])[H]</chem>	6000	6900	110	
SC248	<chem>O=C1N([H])C2=C(OC1([H])[H])C=C([H])C([H])=C2O[H])N3C([H])([H])C([H])([H])C([H])([H])N([H])C([H])([H])C3([H])[H]</chem>	20000	14000	510	
SC249	<chem>O=C1N([H])C=2C(OC1([H])[H])=C(C([H])=C([H])C=2O[H])N3C([H])([H])C([H])([H])C([H])([H])N(C([H])([H])C3([H])[H])C([H])([H])[H]</chem>	20000	6400	42	

ID	SMILES	Ki [nM] <sup>a</sup>			Ref.
		D <sub>1</sub> R	D <sub>2</sub> R	D <sub>3</sub> R	
SC250	<chem>O=C2C([H])=C([H])C=1/C(=C/[H])C([H])=C(O[H])C=1N2([H])N3C([H])([H])C([H])([H])N(C([H])([H])C3([H])([H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])[H])</chem>	20000	1900	420	[100]
SC251	<chem>O=C1N([H])C2=C(OC1([H])([H])C(=C([H])C([H])=C2O[H])N3C([H])([H])C([H])([H])N([H])C([H])([H])C3([H])([H])[H])</chem>	20000	8300	160	
SC252	<chem>O=C(/C1=N/N2/C(=C1/[H])C([H])=C([H])C([H])=C2[H])N([H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])N5C([H])([H])C([H])([H])([H])N+4(C=3C([H])=C([H])C([H])=C([H])C=3OC([H])([H])C4([H])([H])C([H])([H])C5([H])([H])[H])</chem>	5700	6300	200	
SC253	<chem>O=C(C=2[S]C=1C([H])=C([H])C([H])=C([H])C=1C=2[H])N([H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])N4C([H])([H])C([H])([H])N/C3=N/C(=N/C(=C3/[H])C([F])([F])[F])C(C([H])([H])C([H])([H])([H])C([H])([H])C([H])([H])C4([H])([H])[H])</chem>	10000	4000	2.4	[101]
SC254	<chem>[H]/C1=C(\[H])C(=C([H])C(O[H])=C1[H])[C@@]2([H])C([H])([H])C([H])([H])N(C2([H])([H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])[H])</chem>	1278	3555	162	
SC255	<chem>O=C(/C1=C(\[H])C([H])=NC=2C([H])=C([H])C([H])=C([H])C1=2)N([H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])N4C([H])([H])C3=C([H])C(O[H])=C(OC([H])([H])([H])C([H])=C3C([H])([H])C4([H])([H])[H])</chem>	1810	inactive	22	
SC256	<chem>O=C(C=1C([H])=C([H])C([H])=C([H])C=1[H])N([H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])N3C([H])([H])C2=C([H])C(O[H])=C(OC([H])([H])([H])C([H])=C2C([H])([H])C3([H])([H])[H])</chem>	1600	inactive	10	[103]
SC257	<chem>O=C(C=1C([H])=C([H])C(=C([H])C=1[H])C=2C([H])=C([H])([S])C=2[H])N([H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])N4C([H])([H])C([H])([H])N(C=3C([H])=C([Cl])C([H])=C([Cl])C=3[H])C([H])([H])C4([H])([H])[H])</chem>	10000	2049	0.44	
SC258	<chem>O=C(C=2C([H])=C([H])C=1C([H])=C([H])C([H])=C([H])C=1C=2[H])N([H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])N(C([H])([H])[C@]3([H])C([H])([H])[C@@]3([H])C=4C([H])=C([H])C([H])=C([F])C=4[H])C([H])([H])C([H])([H])C([H])([H])[H])</chem>	1308	4823	26.7	
SC259	<chem>[F]C=1C([H])=C([H])C(OC([H])([H])[H])=C(C=1[H])[C@@]2([H])C([H])([H])[C@@]2([H])C([H])([H])N(C([H])([H])[C@]3([H])C([H])([H])C3([H])([H])C([H])([H])C([H])([H])[S]/C5=N/N=C(/C=4C([H])=C([H])C([H])=C([H])C=4[H])N5C([H])([H])[H])</chem>	1078	5000	64.6	[104]
SC260	<chem>O=C(C=1C([H])=C([H])C(=C([H])C=1[H])C2=NC([H])=C([H])C([H])=C2[H])N([H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])N(C([H])([H])[C@]3([H])C([H])([H])[C@@]3([H])C=4C([H])=C([F])C([H])=C([H])C=4OC([H])([H])[H])C([H])([H])C([H])([H])C([H])([H])[H])</chem>	1758	3144	4	
SC261	<chem>[F]C=1C([H])=C([H])C(OC([H])([H])[H])=C(C=1[H])[C@@]2([H])C([H])([H])[C@]2([H])C([H])([H])N(C([H])([H])C([H])([H])C([H])([H])[H])C([H])([H])C([H])([H])C([H])([H])[S]/C4=N/N=C(/C=3C([H])=C([H])C([H])=C([H])C=3[H])N4C([H])([H])[H])</chem>	1668	1161.4	87.1	
SC262	<chem>O=C(C=2C([H])=C([H])C=1C([H])=C([H])C([H])=C([H])C=1C=2[H])N([H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])N(C([H])([H])[C@]3([H])C([H])([H])[C@@]3([H])C=4C([H])=C([H])C([H])([H])C([H])([H])[H])</chem>	1711	5000	43	

ID	SMILES	Ki [nM] <sup>a</sup>			Ref.
		D <sub>1</sub> R	D <sub>2</sub> R	D <sub>3</sub> R	
	<chem>=C([H])C=4[H]C([F])([F])[F]C([H])([H])C([H])([H])C([H])([H])[H]</chem>				
SC263	<chem>O=C(C=1C([H])=C([H])C(=C([H])C=1[H])C2=NC([H])=C([H])C([H])=C2[H])N([H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])N(C([H])([H])[C@]3([H])C([H])([H])[C@@]3([H])C=4C([H])=C([H])C([H])=C([F])C=4[H]C([H])([H])C([H])([H])C([H])([H])[H]</chem>	2906	5000	45.4	
SC264	<chem>O=C(/C2=C(\ [H])C=1C([H])=C([H])C([H])=C([H])C=1N2[H])N([H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])N(C([H])([H])[C@]3([H])C([H])([H])[C@@]3([H])C=4C([H])=C([H])C([H])=C([Cl])C=4[H]C([H])([H])C([H])([H])C([H])([H])[H]</chem>	992	3494	11.1	
SC265	<chem>O=C(C=2C([H])=C([H])C=1C([H])=C([H])C([H])=C([H])C=1C=2[H])N([H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])N(C([H])([H])[C@]3([H])C([H])([H])[C@@]3([H])C=4C([H])=C([F])C([H])=C([H])C=4OC([H])([H])[H])C([H])([H])C([H])([H])C([H])([H])[H]</chem>	967	1083.9	14.5	
SC266	<chem>O=C(C=1C([H])=C([H])C(=C([H])C=1[H])C2=NC([H])=C([H])C([H])=C2[H])N([H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])N(C([H])([H])[C@]3([H])C([H])([H])[C@@]3([H])C=4C([H])=C([Cl])C([H])=C([H])C=4OC([H])([H])[H])C([H])([H])C([H])([H])C([H])([H])[H]</chem>	5000	2105	39.4	
SC267	<chem>O=C(C=2C([H])=C([H])C=1C([H])=C([H])C([H])=C([H])C=1C=2[H])N([H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])N(C([H])([H])[C@]3([H])C([H])([H])[C@@]3([H])C=4C([H])=C([Cl])C([H])=C([H])C=4OC([H])([H])[H])C([H])([H])C([H])([H])C([H])([H])[H]</chem>	930	1116	26.9	
SC268	<chem>O=C(C=1C([H])=C([H])C(=C([H])C=1[H])C2=NC([H])=C([H])C([H])=C2[H])N([H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])N(C([H])([H])[C@]3([H])C([H])([H])[C@@]3([H])C=4C([H])=C([H])C([F])=C([H])C=4[H]C([H])([H])C([H])([H])C([H])([H])[H]</chem>	3631	5000	106.3	
SC269	<chem>O=C(C=1C([H])=C([H])C(=C([H])C=1[H])C2=NC([H])=C([H])C([H])=C2[H])N([H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])N(C([H])([H])[C@]3([H])C([H])([H])[C@@]3([H])C=4C([H])=C([H])C(=C([H])C=4[H]C([F])([F])[F]C([H])([H])C([H])([H])C([H])([H])[H]</chem>	1423	5000	23.4	
SC270	<chem>O=C(C=1C([H])=C([H])C(=C([H])C=1[H])C2=NC([H])=C([H])C([H])=C2[H])N([H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])N(C([H])([H])[C@]3([H])C([H])([H])[C@@]3([H])C=4C([H])=C([F])C([H])=C([H])C=4OC([H])([H])[H])C([H])([H])C([H])([H])C([H])([H])[H]</chem>	4898	1349	4.1	
SC271	<chem>O=C(C=1C([H])=C([H])C(=C([H])C=1[H])C2=NC([H])=C([H])C([H])=C2[H])N([H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])N(C([H])([H])[C@@]3([H])C([H])([H])[C@]3([H])C=4C([H])=C([H])C([H])=C([Cl])C=4[Cl]C([H])([H])C([H])([H])C([H])([H])[H]</chem>	2344	1023	5.3	
SC272	<chem>O=C(C=2C([H])=C([H])C=1C([H])=C([H])C([H])=C([H])C=1C=2[H])N([H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])N(C([H])([H])[C@]3([H])C([H])([H])[C@@]3([H])C=4C([H])=C([H])C([H])=C([H])C=4OC([H])([H])[H])C([H])([H])C([H])([H])C([H])([H])[H]</chem>	940	4012	15.5	

ID	SMILES	Ki [nM] <sup>a</sup>			Ref.
		D <sub>1</sub> R	D <sub>2</sub> R	D <sub>3</sub> R	
	<chem>H])([H])[C@]3([H])C([H])([H])[C@@]3([H])C=4C([H])=C([H])C([H])=C([Cl])C=4[H])C([H])([H])C([H])([H])C([H])([H])[H]</chem>				
SC273	<chem>O=C(C=1C([H])=C([H])C(=C([H])C=1[H])C2=NC([H])=C([H])C([H])=C2[H])N([H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])N(C([H])([H])[C@]3([H])C([H])([H])[C@@]3([H])C=4C([H])=C([H])C([H])=C([Cl])C=4[Cl])C([H])([H])C([H])([H])C([H])([H])[H]</chem>	1647	2362	1.2	
SC274	<chem>O=C(C=1C([H])=C([H])C(=C([H])C=1[H])C2=NC([H])=C([H])C([H])=C2[H])N([H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])N(C([H])([H])[C@]3([H])C([H])([H])[C@@]3([H])C=4C([H])=C([H])C([Cl])=C([H])C=4[H])C([H])([H])C([H])([H])C([H])([H])[H]</chem>	1308	5000	17.6	
SC275	<chem>O=C(C=2C([H])=C([H])C=1C([H])=C([H])C([H])=C([H])C=1C=2[H])N([H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])N(C([H])([H])[C@]3([H])C([H])([H])[C@@]3([H])C=4C([H])=C([H])C([F])=C([H])C=4[H])C([H])([H])C([H])([H])C([H])([H])[H]</chem>	992	5623	55.8	
SC276	<chem>O=C(/C2=C([H])C=1C([H])=C([H])C([H])=C([H])C=1N2[H])N([H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])N(C([H])([H])[C@]3([H])C([H])([H])[C@@]3([H])C=4C([H])=C([H])C([F])=C([H])C=4[H])C([H])([H])C([H])([H])C([H])([H])[H]</chem>	1457	5934	45.7	
SC277	<chem>O=C(C=2C([H])=C([H])C=1C([H])=C([H])C([H])=C([H])C=1C=2[H])N([H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])N(C([H])([H])[C@@]3([H])C([H])([H])[C@]3([H])C=4C([H])=C([H])C([H])=C([Cl])C=4[Cl])C([H])([H])C([H])([H])C([H])([H])[H]</chem>	1047	1148	20.8	
SC278	<chem>O=C(/C2=C([H])C=1C([H])=C([H])C([H])=C([H])C=1N2[H])N([H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])N(C([H])([H])[C@]3([H])C([H])([H])[C@@]3([H])C=4C([H])=C([H])C(=C([H])C=4[H])C([F])([F])[F])C([H])([H])C([H])([H])C([H])([H])[H]</chem>	1278	5000	33.1	
SC279	<chem>O=C(/C2=C([H])C=1C([H])=C([H])C([H])=C([H])C=1N2[H])N([H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])N(C([H])([H])[C@]3([H])C([H])([H])[C@@]3([H])C=4C([H])=C([H])C([H])=C([F])C=4[H])C([H])([H])C([H])([H])C([H])([H])[H]</chem>	1105	3494	18.8	
SC280	<chem>O=C(C=1C([H])=C([H])C(=C([H])C=1[H])C2=NC([H])=C([H])C([H])=C2[H])N([H])C([H])([H])C([H])([H])C([H])([H])C([H])([H])N(C([H])([H])[C@@]3([H])C([H])([H])[C@]3([H])C=4C([H])=C([F])C([H])=C([H])C=4OC([H])([H])[H])C([H])([H])C([H])([H])C([H])([H])[H]</chem>	1071	1230	3.8	
SC281	<chem>O=C(C=2C([H])=C([H])C=1C([H])=C([H])C([H])=C([H])C=1C=2[H])N([H])[C@]3([H])C([H])([H])[C@](O[H])(C3([H])[H])C([H])([H])C([H])([H])N([C@]5([H])C([H])([H])C=4[S]C(=NC=4C([H])([H])C5([H])[H])N([H])[H])C([H])([H])C([H])([H])C([H])([H])[H]</chem>	inactive	3902	30	[105]
SC282	<chem>[H]C=4C([H])=C3C1=C(C([H])=C([H])C=2N=C([S]C1=2)N([H])[H])C([H])([H])[C@]5([H])C3=C(C=4[H])C([H])([H])C([H])([H])N5C([H])([H])[H]</chem>	1150	1740	381	[118]
SC283	<chem>[H]/C1=C([H])C(=NC([H])=C1[C@@]2([H])OC([H])([H])[C@@]([H])(N(C2([H])[H])C([H])([H])C([H])([H])C([H])([H])[H])C([H])([H])[H])N([H])[H]</chem>	100000	1740	185	[106]



ID	SMILES	Ki [nM] <sup>a</sup>			Ref.
		D <sub>1</sub> R	D <sub>2</sub> R	D <sub>3</sub> R	
SC284	<chem>O=C(/C2=C(\ [H])C=1C([H])=C([H])C([H])=C([H])C=1N2[H])N([H])C([H])([H])C([H])([H])[C@@]([H])(O[H])C([H])([H])N3C([H])([H])[C@@]([H])(OC([H])([H])[C@]3([H])C([H])([H])[H])C=4C([H])=C([H])C(=NC=4[H])N([H])[H]</chem>	100000	1010	423	

<sup>a</sup>All KI values retrieved from ChEMBL were determined in vitro utilizing radio-ligand binding assays.

## 2. Molecular Dynamics Simulation (MDS) – methodological overview

A summary of the minimization process settings is shown in Table S5. An overview of all parameters is given in Table S6. A summary of the Standard Dynamics Cascade as well as a detailed listing of all parameters is shown in Table S7 and Table S8. A Spherical Cutoff method is used for electrostatics.

**Table S5.** Summary of the Minimization process for the D<sub>2</sub>R structure.

Potential Energy	Van der Waals Energy	Electrostatic Energy	Initial RMS Gradient	Final RMS Gradient	Minimization Criteria
[kcal/mol]	[kcal/mol]	[kcal/mol]	[kcal/mol*Å]	[kcal/mol*Å]	
-73078.46743	-7856.40360	-74320.37289	1.16878	0.47676	CONJUG< Minimization exiting with number of steps limit (200) exceeded

Initial Potential Energy [kcal/mol]	Forcefield	CHARMM	-70950.65436
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**Table S6.** Detailed overview of the settings used during the Minimization process of the D<sub>2</sub>R structure.

Minimization	
Parameter	Setting
Algorithm	Smart Minimizer
Max Steps	200
RMS Gradient	0.1
Energy Change	00
Save Results Frequency	0
Implicit Solvent Model	None
Dielectric Constant	1
Implicit Solvent Dilectric Constant	80
Generalized Born Lambda Constant	-
Minimum Hydrogen Radius	0.8
Use Non-polar surface	True
Non-polar Surface Constant	0.92
Non-Polar Surface Coefficient	0.00542
Salt Concentration	0.0
Input Atomic Radii	van der Waals Radii
Use Molecular Surface	True
Nonbond List Radius	14.0
Nonbond Higher Cutoff Distance	12.0
Nonbond Lower Cutoff Distance	10.0
Electrostatics	Automatic
Kappa	0.34
Order	4
Minimization Constraints	-
Apply SHAKE Constraint	False

Table S7. Summary of the Standard Dynamics Cascade process for the D<sub>2</sub>R structure.

End Time [ps]	Initial Potential Energy [kcal/mol]	Total Energy [kcal/mol]	Potential Energy [kcal/mol]	Kinetic Energy [kcal/mol]	Temperature [K]	Van der Waals Energy [kcal/mol]	Electrostatic Energy [kcal/mol]	Initial RMS Gradient [kcal/mol*Å]	Final RMS Gradient [kcal/mol*Å]
-	-72896.919	-	-72964.947	-	-	-7836.896	-74028.920	0.972	0.650
-	-72964.947	-	-74257.521	-	-	-7843.438	-75322.971	0.650	0.075
4000	-74257.521	-48876.612	-62155.902	13279.289	302.709	-6715.957	-74737.941	3.628	19.257
1004	-62155.902	-54734.887	-67927.536	13192.649	300.734	-6952.978	-80960.394	19.257	19.232
1014	-67927.536	-54865.097	-68117.446	13252.349	302.094	-6758.705	-81034.075	19.232	19.127

Stage	Forcefield	Start Time [ps]
Minimization	CHARMm	-
Minimization 2	CHARMm	-
Heating	CHARMm	0
Equilibration	CHARMm	4
Production	CHARMm	1004

**Table S8.** Detailed overview of the settings used during the Standard Dynamics Cascade process of the D<sub>2</sub>R structure.

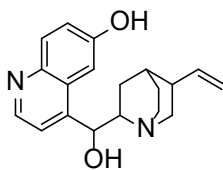
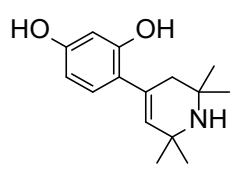
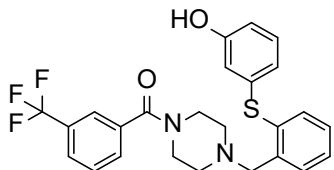
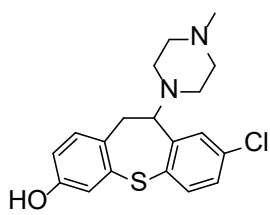
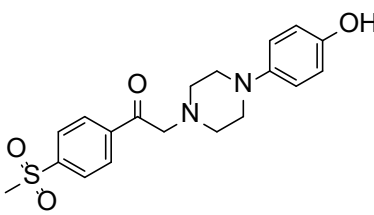
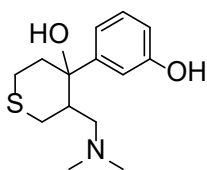
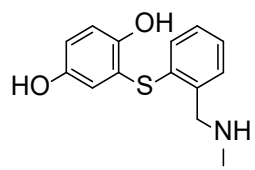
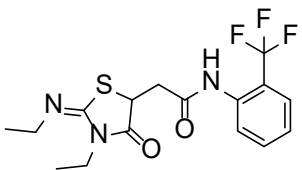
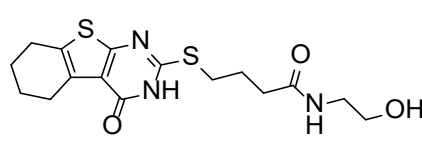
Standard Dynamics Cascade	
Minimization	
Parameter	Setting
Algorithm	Steepest Descent
Max Steps	1000
RMS Gradient	1.0
Constraints	-
Minimization 2	
Parameter	Setting
Algorithm	Adopted Basis NR
Max Steps	2000
RMS Gradient	0.1
Constraints	-
Heating	
Parameter	Setting
Simulation Time [ps]	4
Time Step [fs]	2
Initial Temperature	50.0
Target Temperature	300.0
Adjust Velocity Frequency	50
Save Results Interval [ps]	2
Constraints	-

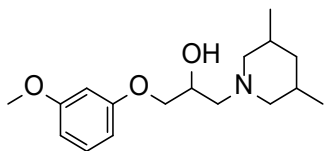
Equilibration	
Parameter	Setting
Simulation Time [ps]	1000
Time Step [fs]	2
Target Temperature	300.0
Adjust Velocity Frequency	50
Save Results Interval [ps]	2
Constraints	-
Production	
Parameter	Setting
Simulation Time [ps]	10
Time Step [fs]	2
Target Temperature	300.0
Temperature Coupling Decay Time	5.0
Save Result Interval [ps]	2
Save Result File	True
Constraints	-
Type	NVT
TMass	1000.0
PMass	1000.0
PGamma	25.0
Reference Pressure	1.0
Implicit Solvent Model	
Parameter	Setting
Implicit Solvent Model	None
Dielectric Constant	1
Implicit Solvent Dielectric Constant	80
Generalized Born Lambda Constant	-
Minimum Hydrogen Radius	0.8
Use Non-polar surface	True
Non-polar Surface Constant	0.92
Non-Polar Surface Coefficient	0.00542
Salt Concentration	0.0
Input Atomic Radii	Van der Waals Radii

Use Molecular Surface	True
Nonbond List Radius	14.0
Nonbond Higher Cutoff Distance	12.0
Nonbond Lower Cutoff Distance	10.0
Electrostatics	Automatic
Kappa	0.34
Order	4
Dynamics Integrator	Leapfrog Verlet
Apply SHAKE Constraint	True
Random Number Seed	314159 314159 314159 314159
Number of Processors	1

### 3. In vitro screening– overview of 2D structures and NDF values of all compounds

**Table S9.** Overview of all compounds selected for further in vitro investigations. 2D structures and NDF  $\pm$  standard deviation (SD) are shown for each compound (n = 4). All NDF values for D<sub>2</sub>R were obtained in the previously published article of Zell et al [42]. NDF, normalized decreased fluorescence.

 <p><b>SC285</b>  NDF (D<sub>1</sub>R) = <math>0.83 \pm 0.06</math>  NDF (D<sub>2</sub>R) = <math>1.13 \pm 0.37</math>  NDF (D<sub>3</sub>R) = <math>1.17 \pm 0.11</math></p>	 <p><b>SC286</b>  NDF (D<sub>1</sub>R) = <math>0.88 \pm 0.20</math>  NDF (D<sub>2</sub>R) = <math>1.05 \pm 0.45</math>  NDF (D<sub>3</sub>R) = <math>1.04 \pm 0.10</math></p>	 <p><b>SC287</b>  NDF (D<sub>1</sub>R) = <math>0.91 \pm 0.21</math>  NDF (D<sub>2</sub>R) = <math>0.90 \pm 0.25</math>  NDF (D<sub>3</sub>R) = <math>1.00 \pm 0.17</math></p>
 <p><b>2</b>  NDF (D<sub>1</sub>R) = <math>5.41 \pm 1.97</math>  NDF (D<sub>2</sub>R) = <math>40.41 \pm 1.39</math>  NDF (D<sub>3</sub>R) = <math>4.16 \pm 1.08</math></p>	 <p><b>SC288</b>  NDF (D<sub>1</sub>R) = <math>3.21 \pm 3.27</math>  NDF (D<sub>2</sub>R) = <math>1.01 \pm 0.38</math>  NDF (D<sub>3</sub>R) = <math>1.58 \pm 0.58</math></p>	 <p><b>SC289</b>  NDF (D<sub>1</sub>R) = <math>1.66 \pm 1.16</math>  NDF (D<sub>2</sub>R) = <math>0.90 \pm 0.30</math>  NDF (D<sub>3</sub>R) = <math>1.24 \pm 0.25</math></p>
 <p><b>SC290</b>  NDF (D<sub>1</sub>R) = <math>3.50 \pm 3.16</math>  NDF (D<sub>2</sub>R) = <math>0.91 \pm 0.36</math>  NDF (D<sub>3</sub>R) = <math>1.81 \pm 1.04</math></p>	 <p><b>SC291</b>  NDF (D<sub>1</sub>R) = <math>0.81 \pm 0.08</math>  NDF (D<sub>2</sub>R) = <math>0.84 \pm 0.23</math>  NDF (D<sub>3</sub>R) = <math>1.02 \pm 0.24</math></p>	 <p><b>SC292</b>  NDF (D<sub>1</sub>R) = <math>0.80 \pm 0.21</math>  NDF (D<sub>2</sub>R) = <math>0.95 \pm 0.43</math>  NDF (D<sub>3</sub>R) = <math>0.92 \pm 0.13</math></p>

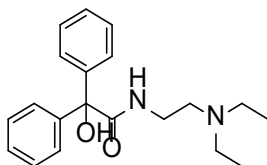


**SC293**

NDF (D<sub>1</sub>R) =  $0.85 \pm 0.14$

NDF (D<sub>2</sub>R) =  $1.02 \pm 0.39$

NDF (D<sub>3</sub>R) =  $1.04 \pm 0.11$

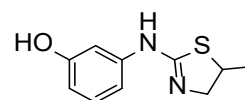


**SC294**

NDF (D<sub>1</sub>R) =  $2.72 \pm 2.66$

NDF (D<sub>2</sub>R) =  $1.01 \pm 0.50$

NDF (D<sub>3</sub>R) =  $1.49 \pm 0.54$

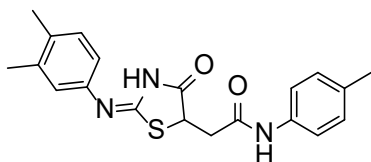


**SC295**

NDF (D<sub>1</sub>R) =  $1.08 \pm 0.42$

NDF (D<sub>2</sub>R) =  $0.95 \pm 0.43$

NDF (D<sub>3</sub>R) =  $1.26 \pm 0.25$

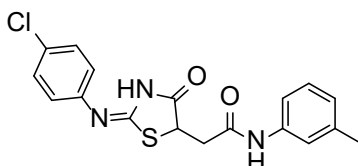


**SC296**

NDF (D<sub>1</sub>R) =  $1.02 \pm 0.36$

NDF (D<sub>2</sub>R) =  $0.94 \pm 0.32$

NDF (D<sub>3</sub>R) =  $0.93 \pm 0.12$

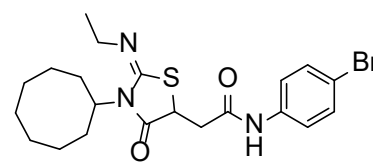


**SC297**

NDF (D<sub>1</sub>R) =  $0.89 \pm 0.24$

NDF (D<sub>2</sub>R) =  $0.96 \pm 0.38$

NDF (D<sub>3</sub>R) =  $1.04 \pm 0.11$

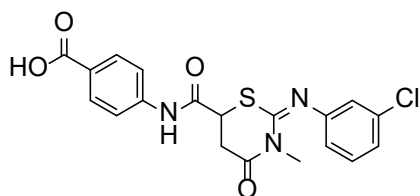


**SC298**

NDF (D<sub>1</sub>R) =  $1.21 \pm 0.43$

NDF (D<sub>2</sub>R) =  $1.00 \pm 0.35$

NDF (D<sub>3</sub>R) =  $0.85 \pm 0.13$

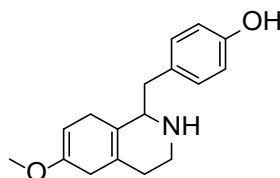


**SC299**

NDF (D<sub>1</sub>R) =  $0.94 \pm 0.13$

NDF (D<sub>2</sub>R) =  $0.82 \pm 0.25$

NDF (D<sub>3</sub>R) =  $1.05 \pm 0.36$

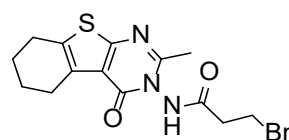


**SC300**

NDF (D<sub>1</sub>R) =  $2.72 \pm 0.84$

NDF (D<sub>2</sub>R) =  $1.14 \pm 0.56$

NDF (D<sub>3</sub>R) =  $2.16 \pm 0.40$

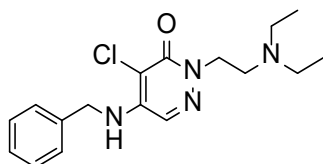


**SC301**

NDF (D<sub>1</sub>R) =  $0.78 \pm 0.22$

NDF (D<sub>2</sub>R) =  $0.99 \pm 0.35$

NDF (D<sub>3</sub>R) =  $0.97 \pm 0.11$

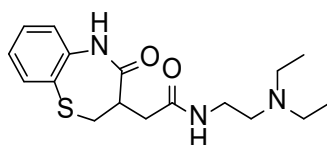


**SC302**

NDF (D<sub>1</sub>R) =  $1.04 \pm 0.28$

NDF (D<sub>2</sub>R) =  $0.99 \pm 0.39$

NDF (D<sub>3</sub>R) =  $1.26 \pm 0.14$

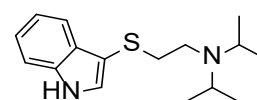


**SC303**

NDF (D<sub>1</sub>R) =  $1.00 \pm 0.33$

NDF (D<sub>2</sub>R) =  $1.02 \pm 0.36$

NDF (D<sub>3</sub>R) =  $1.50 \pm 0.24$

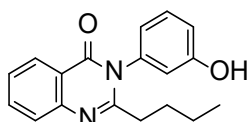


**SC304**

NDF (D<sub>1</sub>R) =  $0.88 \pm 0.17$

NDF (D<sub>2</sub>R) =  $0.98 \pm 0.32$

NDF (D<sub>3</sub>R) =  $1.20 \pm 0.11$

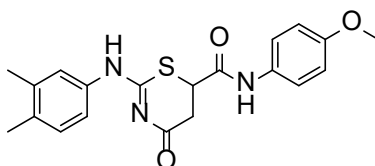


**SC305**

NDF (D<sub>1</sub>R) =  $0.90 \pm 0.26$

NDF (D<sub>2</sub>R) =  $0.93 \pm 0.29$

NDF (D<sub>3</sub>R) =  $1.03 \pm 0.14$

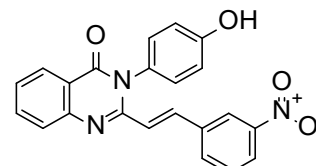


**SC306**

NDF (D<sub>1</sub>R) =  $1.05 \pm 0.44$

NDF (D<sub>2</sub>R) =  $0.94 \pm 0.36$

NDF (D<sub>3</sub>R) =  $1.09 \pm 0.30$

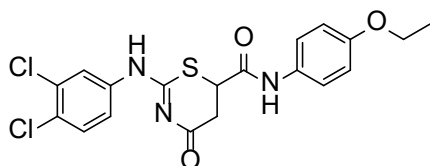


**SC307**

NDF (D<sub>1</sub>R) =  $0.93 \pm 0.16$

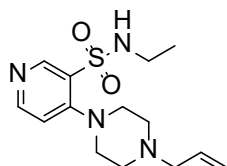
NDF (D<sub>2</sub>R) =  $0.86 \pm 0.24$

NDF (D<sub>3</sub>R) =  $0.93 \pm 0.15$



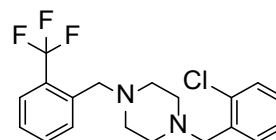
**SC308**

NDF (D<sub>1</sub>R) =  $0.87 \pm 0.20$   
 NDF (D<sub>2</sub>R) =  $2.04 \pm 1.34$   
 NDF (D<sub>3</sub>R) =  $1.64 \pm 0.29$



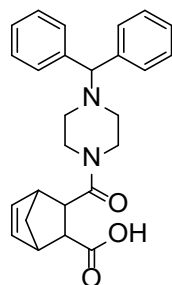
**SC309**

NDF (D<sub>1</sub>R) =  $0.96 \pm 0.34$   
 NDF (D<sub>2</sub>R) =  $1.10 \pm 0.46$   
 NDF (D<sub>3</sub>R) =  $2.03 \pm 0.18$



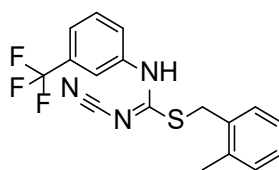
**SC310**

NDF (D<sub>1</sub>R) =  $0.99 \pm 0.34$   
 NDF (D<sub>2</sub>R) =  $1.06 \pm 0.41$   
 NDF (D<sub>3</sub>R) =  $1.54 \pm 0.33$



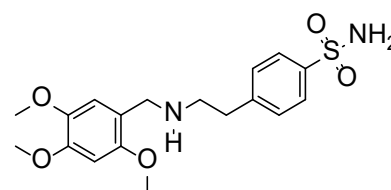
**SC311**

NDF (D<sub>1</sub>R) =  $1.09 \pm 0.43$   
 NDF (D<sub>2</sub>R) =  $1.02 \pm 0.35$   
 NDF (D<sub>3</sub>R) =  $1.67 \pm 0.44$



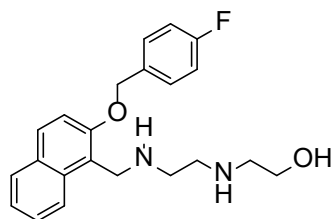
**SC312**

NDF (D<sub>1</sub>R) =  $0.97 \pm 0.40$   
 NDF (D<sub>2</sub>R) =  $1.10 \pm 0.44$   
 NDF (D<sub>3</sub>R) =  $1.23 \pm 0.27$



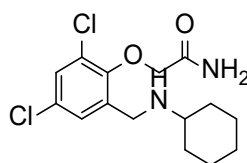
**SC313**

NDF (D<sub>1</sub>R) =  $0.88 \pm 0.33$   
 NDF (D<sub>2</sub>R) =  $0.94 \pm 0.32$   
 NDF (D<sub>3</sub>R) =  $1.12 \pm 0.15$



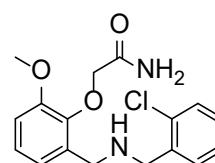
**SC314**

NDF (D<sub>1</sub>R) =  $4.17 \pm 1.08$   
 NDF (D<sub>2</sub>R) =  $1.68 \pm 0.90$   
 NDF (D<sub>3</sub>R) =  $3.00 \pm 0.61$



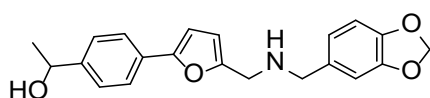
**SC315**

NDF (D<sub>1</sub>R) =  $1.18 \pm 1.01$   
 NDF (D<sub>2</sub>R) =  $0.95 \pm 0.32$   
 NDF (D<sub>3</sub>R) =  $1.06 \pm 0.20$



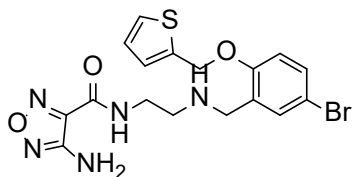
**SC316**

NDF (D<sub>1</sub>R) =  $0.93 \pm 0.30$   
 NDF (D<sub>2</sub>R) =  $1.01 \pm 0.44$   
 NDF (D<sub>3</sub>R) =  $1.16 \pm 0.16$



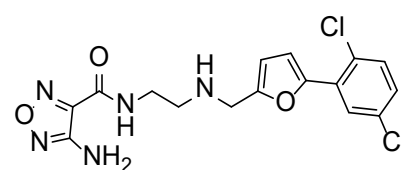
**SC317**

NDF (D<sub>1</sub>R) =  $1.06 \pm 0.47$   
 NDF (D<sub>2</sub>R) =  $0.93 \pm 0.42$   
 NDF (D<sub>3</sub>R) =  $1.07 \pm 0.15$



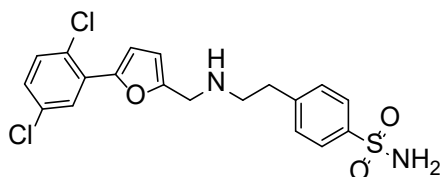
**SC318**

NDF (D<sub>1</sub>R) =  $1.81 \pm 0.42$   
 NDF (D<sub>2</sub>R) =  $1.14 \pm 0.57$   
 NDF (D<sub>3</sub>R) =  $2.39 \pm 0.48$

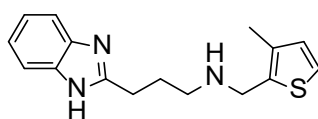


**SC319**

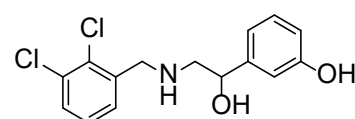
NDF (D<sub>1</sub>R) =  $0.89 \pm 0.26$   
 NDF (D<sub>2</sub>R) =  $2.41 \pm 2.01$   
 NDF (D<sub>3</sub>R) =  $3.64 \pm 1.08$



**3**



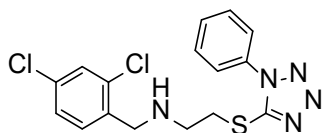
**SC320**



**4**

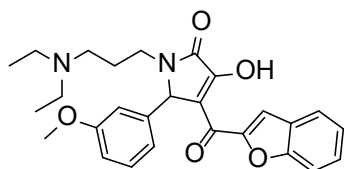


NDF (D<sub>1</sub>R) = 1.78 ± 1.35  
 NDF (D<sub>2</sub>R) = 3.99 ± 2.58  
 NDF (D<sub>3</sub>R) = 3.96 ± 1.10



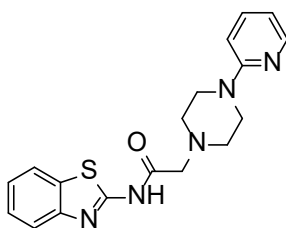
**SC321**

NDF (D<sub>1</sub>R) = 1.00 ± 0.42  
 NDF (D<sub>2</sub>R) = 0.97 ± 0.36  
 NDF (D<sub>3</sub>R) = 1.26 ± 0.24



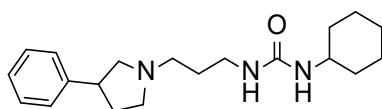
**SC324**

NDF (D<sub>1</sub>R) = -  
 NDF (D<sub>2</sub>R) = -  
 NDF (D<sub>3</sub>R) = -



**SC327**

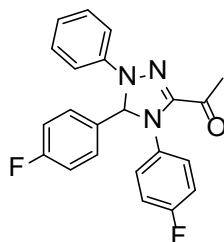
NDF (D<sub>1</sub>R) = 0.92 ± 0.39  
 NDF (D<sub>2</sub>R) = 0.90 ± 0.39  
 NDF (D<sub>3</sub>R) = 1.00 ± 0.20



**SC330**

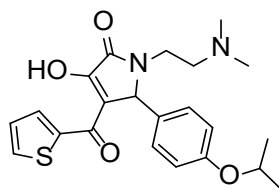
NDF (D<sub>1</sub>R) = 1.88 ± 0.72  
 NDF (D<sub>2</sub>R) = 1.35 ± 0.68  
 NDF (D<sub>3</sub>R) = 3.31 ± 0.92

NDF (D<sub>1</sub>R) = -  
 NDF (D<sub>2</sub>R) = -  
 NDF (D<sub>3</sub>R) = -



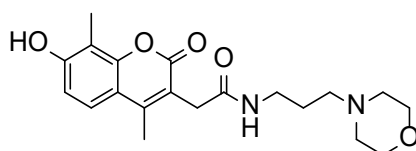
**SC322**

NDF (D<sub>1</sub>R) = 0.86 ± 0.24  
 NDF (D<sub>2</sub>R) = 0.90 ± 0.25  
 NDF (D<sub>3</sub>R) = 1.01 ± 0.23



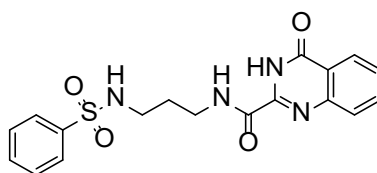
**SC325**

NDF (D<sub>1</sub>R) = 1.02 ± 0.46  
 NDF (D<sub>2</sub>R) = 0.94 ± 0.46  
 NDF (D<sub>3</sub>R) = 1.22 ± 0.27



**SC328**

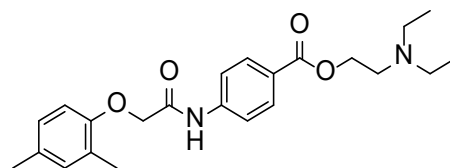
NDF (D<sub>1</sub>R) = 0.43 ± 0.15  
 NDF (D<sub>2</sub>R) = 0.99 ± 0.43  
 NDF (D<sub>3</sub>R) = 1.13 ± 0.31



**SC331**

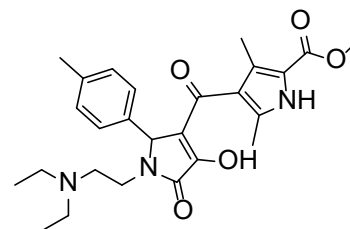
NDF (D<sub>1</sub>R) = 0.95 ± 0.17  
 NDF (D<sub>2</sub>R) = 0.90 ± 0.35  
 NDF (D<sub>3</sub>R) = 1.14 ± 0.40

NDF (D<sub>1</sub>R) = 0.90 ± 0.31  
 NDF (D<sub>2</sub>R) = 0.90 ± 0.38  
 NDF (D<sub>3</sub>R) = 2.75 ± 0.61



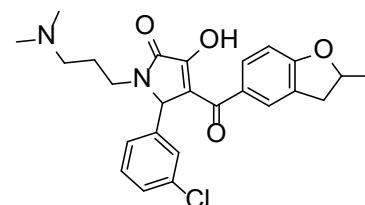
**SC323**

NDF (D<sub>1</sub>R) = 1.43 ± 0.58  
 NDF (D<sub>2</sub>R) = 0.95 ± 0.35  
 NDF (D<sub>3</sub>R) = 1.55 ± 0.23



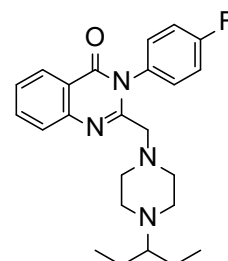
**SC326**

NDF (D<sub>1</sub>R) = 0.87 ± 0.33  
 NDF (D<sub>2</sub>R) = 0.95 ± 0.42  
 NDF (D<sub>3</sub>R) = 1.06 ± 0.36



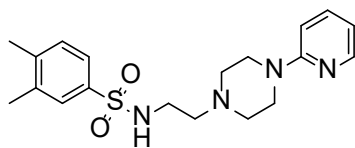
**SC329**

NDF (D<sub>1</sub>R) = -  
 NDF (D<sub>2</sub>R) = -  
 NDF (D<sub>3</sub>R) = -



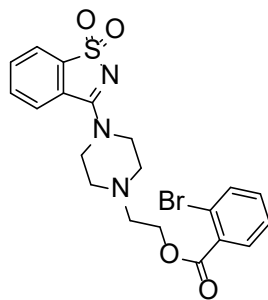
**SC332**

NDF (D<sub>1</sub>R) = 0.97 ± 0.40  
 NDF (D<sub>2</sub>R) = 0.90 ± 0.36  
 NDF (D<sub>3</sub>R) = 1.18 ± 0.28



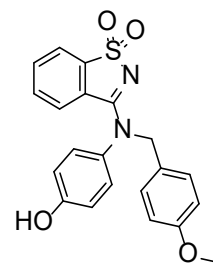
**SC333**

NDF (D<sub>1</sub>R) = 1.13 ± 0.52  
 NDF (D<sub>2</sub>R) = 2.98 ± 1.77  
 NDF (D<sub>3</sub>R) = 2.49 ± 0.47



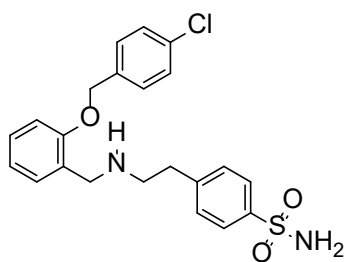
**SC334**

NDF (D<sub>1</sub>R) = 0.95 ± 0.35  
 NDF (D<sub>2</sub>R) = 0.96 ± 0.37  
 NDF (D<sub>3</sub>R) = 1.12 ± 0.30



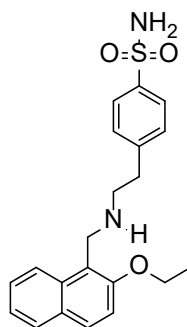
**SC335**

NDF (D<sub>1</sub>R) = 0.93 ± 0.39  
 NDF (D<sub>2</sub>R) = 1.03 ± 0.42  
 NDF (D<sub>3</sub>R) = 1.40 ± 0.54



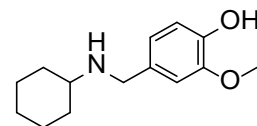
**SC336**

NDF (D<sub>1</sub>R) = 1.46 ± 0.71  
 NDF (D<sub>2</sub>R) = 1.07 ± 0.46  
 NDF (D<sub>3</sub>R) = 2.76 ± 0.63



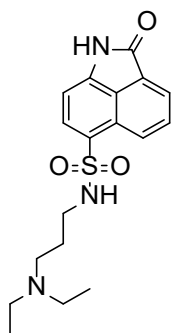
**SC337**

NDF (D<sub>1</sub>R) = 1.12 ± 0.56  
 NDF (D<sub>2</sub>R) = 0.99 ± 0.40  
 NDF (D<sub>3</sub>R) = 1.24 ± 0.22



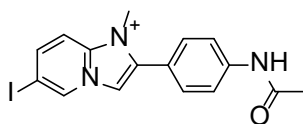
**SC338**

NDF (D<sub>1</sub>R) = 1.14 ± 0.77  
 NDF (D<sub>2</sub>R) = 0.93 ± 0.38  
 NDF (D<sub>3</sub>R) = 1.15 ± 0.35



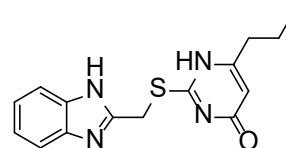
**SC339**

NDF (D<sub>1</sub>R) = 0.59 ± 0.17  
 NDF (D<sub>2</sub>R) = 0.94 ± 0.41  
 NDF (D<sub>3</sub>R) = 1.11 ± 0.48



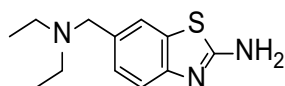
**SC340**

NDF (D<sub>1</sub>R) = 0.83 ± 0.35  
 NDF (D<sub>2</sub>R) = 1.41 ± 1.07  
 NDF (D<sub>3</sub>R) = 1.10 ± 0.29



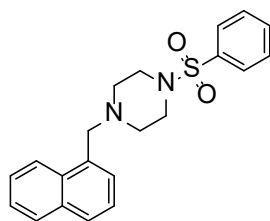
**SC341**

NDF (D<sub>1</sub>R) = 0.83 ± 0.51  
 NDF (D<sub>2</sub>R) = 1.52 ± 1.15  
 NDF (D<sub>3</sub>R) = 0.92 ± 0.14



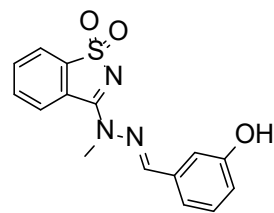
**SC342**

NDF (D<sub>1</sub>R) =  $1.24 \pm 0.51$   
 NDF (D<sub>2</sub>R) =  $1.38 \pm 0.91$   
 NDF (D<sub>3</sub>R) =  $1.24 \pm 0.29$



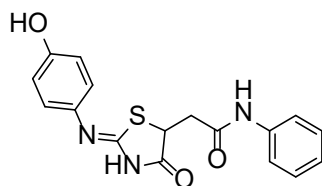
**SC343**

NDF (D<sub>1</sub>R) =  $1.36 \pm 0.89$   
 NDF (D<sub>2</sub>R) =  $1.06 \pm 0.44$   
 NDF (D<sub>3</sub>R) =  $1.15 \pm 0.32$



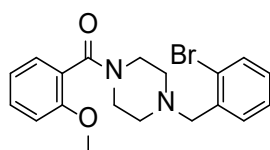
**SC344**

NDF (D<sub>1</sub>R) =  $1.09 \pm 0.58$   
 NDF (D<sub>2</sub>R) =  $1.06 \pm 0.42$   
 NDF (D<sub>3</sub>R) =  $0.99 \pm 0.13$



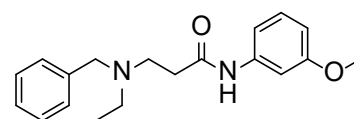
**SC345**

NDF (D<sub>1</sub>R) =  $0.93 \pm 0.32$   
 NDF (D<sub>2</sub>R) =  $0.95 \pm 0.38$   
 NDF (D<sub>3</sub>R) =  $1.11 \pm 0.36$



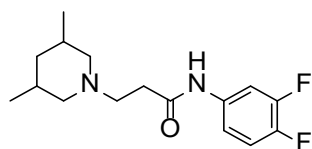
**SC346**

NDF (D<sub>1</sub>R) =  $1.04 \pm 0.54$   
 NDF (D<sub>2</sub>R) =  $0.97 \pm 0.39$   
 NDF (D<sub>3</sub>R) =  $1.15 \pm 0.37$



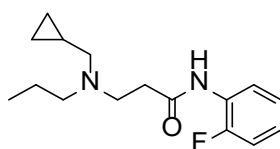
**5**

NDF (D<sub>1</sub>R) =  $1.26 \pm 0.64$   
 NDF (D<sub>2</sub>R) =  $15.74 \pm 18.15$   
 NDF (D<sub>3</sub>R) =  $2.65 \pm 0.64$



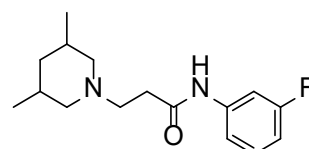
**SC347**

NDF (D<sub>1</sub>R) =  $1.12 \pm 0.60$   
 NDF (D<sub>2</sub>R) =  $1.05 \pm 0.50$   
 NDF (D<sub>3</sub>R) =  $1.40 \pm 0.33$



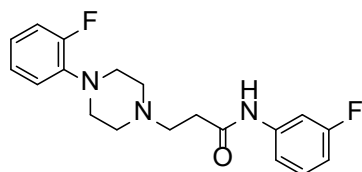
**SC348**

NDF (D<sub>1</sub>R) =  $0.89 \pm 0.31$   
 NDF (D<sub>2</sub>R) =  $1.02 \pm 0.38$   
 NDF (D<sub>3</sub>R) =  $1.36 \pm 0.36$



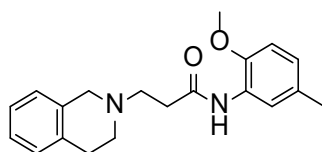
**SC349**

NDF (D<sub>1</sub>R) =  $1.12 \pm 0.59$   
 NDF (D<sub>2</sub>R) =  $1.26 \pm 0.70$   
 NDF (D<sub>3</sub>R) =  $1.95 \pm 0.47$



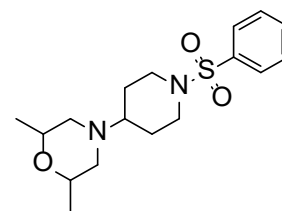
**6**

NDF (D<sub>1</sub>R) =  $2.15 \pm 1.16$   
 NDF (D<sub>2</sub>R) =  $8.18 \pm 3.62$   
 NDF (D<sub>3</sub>R) =  $4.21 \pm 0.79$



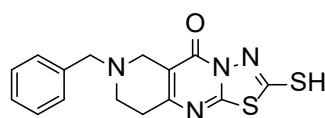
**SC350**

NDF (D<sub>1</sub>R) =  $1.19 \pm 0.57$   
 NDF (D<sub>2</sub>R) =  $1.83 \pm 0.83$   
 NDF (D<sub>3</sub>R) =  $3.25 \pm 0.47$



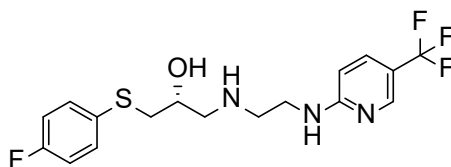
**SC351**

NDF (D<sub>1</sub>R) =  $0.93 \pm 0.39$   
 NDF (D<sub>2</sub>R) =  $0.99 \pm 0.42$   
 NDF (D<sub>3</sub>R) =  $1.19 \pm 0.45$



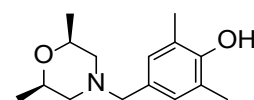
**SC352**

NDF (D<sub>1</sub>R) =  $0.91 \pm 0.42$   
 NDF (D<sub>2</sub>R) =  $1.02 \pm 0.47$   
 NDF (D<sub>3</sub>R) =  $1.22 \pm 0.38$



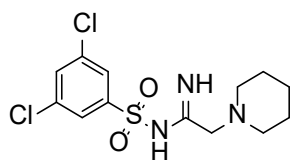
**7**

NDF (D<sub>1</sub>R) =  $1.57 \pm 0.54$   
 NDF (D<sub>2</sub>R) =  $10.85 \pm 4.93$   
 NDF (D<sub>3</sub>R) =  $3.79 \pm 0.70$



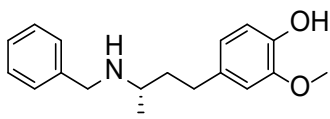
**SC353**

NDF (D<sub>1</sub>R) =  $1.08 \pm 0.61$   
 NDF (D<sub>2</sub>R) =  $1.00 \pm 0.40$   
 NDF (D<sub>3</sub>R) =  $1.20 \pm 0.43$



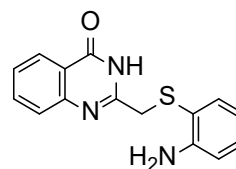
**SC354**

NDF (D<sub>1</sub>R) =  $0.98 \pm 0.52$   
 NDF (D<sub>2</sub>R) =  $0.99 \pm 0.39$   
 NDF (D<sub>3</sub>R) =  $1.06 \pm 0.24$



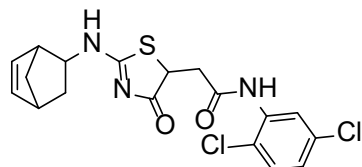
**8**

NDF (D<sub>1</sub>R) =  $1.20 \pm 0.59$   
 NDF (D<sub>2</sub>R) =  $1.10 \pm 0.52$   
 NDF (D<sub>3</sub>R) =  $2.63 \pm 0.52$



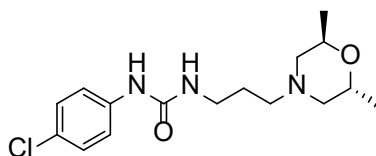
**SC355**

NDF (D<sub>1</sub>R) =  $1.34 \pm 1.14$   
 NDF (D<sub>2</sub>R) =  $1.13 \pm 0.34$   
 NDF (D<sub>3</sub>R) =  $1.22 \pm 0.35$



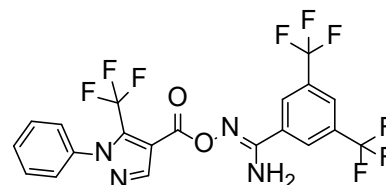
**SC356**

NDF (D<sub>1</sub>R) =  $1.28 \pm 0.99$   
 NDF (D<sub>2</sub>R) =  $2.44 \pm 1.39$   
 NDF (D<sub>3</sub>R) =  $1.23 \pm 0.29$



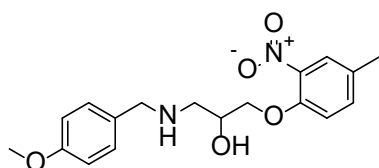
**SC357**

NDF (D<sub>1</sub>R) =  $1.05 \pm 0.57$   
 NDF (D<sub>2</sub>R) =  $1.66 \pm 1.60$   
 NDF (D<sub>3</sub>R) =  $2.02 \pm 0.83$



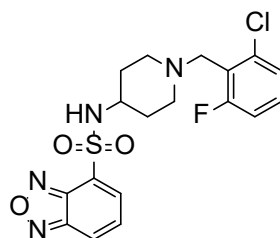
**SC358**

NDF (D<sub>1</sub>R) =  $1.33 \pm 0.55$   
 NDF (D<sub>2</sub>R) =  $1.11 \pm 0.47$   
 NDF (D<sub>3</sub>R) =  $1.22 \pm 0.53$



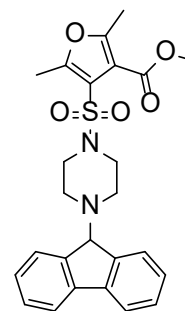
**SC359**

NDF (D<sub>1</sub>R) =  $1.28 \pm 0.73$   
 NDF (D<sub>2</sub>R) =  $2.00 \pm 0.85$   
 NDF (D<sub>3</sub>R) =  $2.49 \pm 0.74$



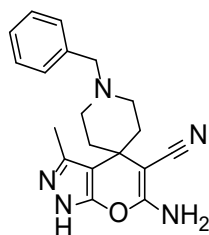
**SC360**

NDF (D<sub>1</sub>R) =  $1.05 \pm 0.56$   
 NDF (D<sub>2</sub>R) =  $0.93 \pm 0.40$   
 NDF (D<sub>3</sub>R) =  $1.35 \pm 0.33$



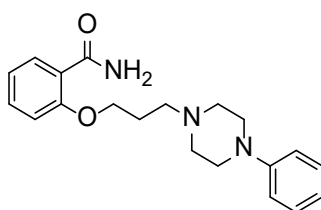
**SC361**

NDF (D<sub>1</sub>R) =  $0.96 \pm 0.52$   
 NDF (D<sub>2</sub>R) =  $1.11 \pm 0.51$   
 NDF (D<sub>3</sub>R) =  $1.10 \pm 0.24$



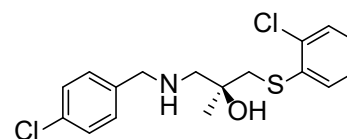
**SC362**

NDF (D<sub>1</sub>R) =  $1.05 \pm 0.36$   
 NDF (D<sub>2</sub>R) =  $1.41 \pm 0.71$   
 NDF (D<sub>3</sub>R) =  $2.03 \pm 0.45$



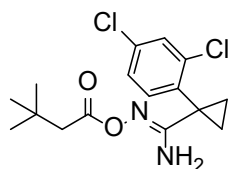
**9**

NDF (D<sub>1</sub>R) =  $1.71 \pm 0.86$   
 NDF (D<sub>2</sub>R) =  $22.08 \pm 6.62$   
 NDF (D<sub>3</sub>R) =  $3.97 \pm 0.78$



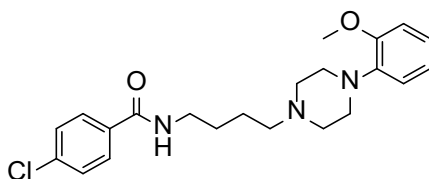
**SC363**

NDF (D<sub>1</sub>R) =  $1.11 \pm 0.70$   
 NDF (D<sub>2</sub>R) =  $1.11 \pm 0.53$   
 NDF (D<sub>3</sub>R) =  $1.53 \pm 0.21$



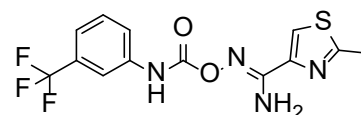
SC364

NDF (D<sub>1</sub>R) =  $0.92 \pm 0.42$   
 NDF (D<sub>2</sub>R) =  $1.08 \pm 0.56$   
 NDF (D<sub>3</sub>R) =  $1.17 \pm 0.37$



10

NDF (D<sub>1</sub>R) =  $2.59 \pm 1.04$   
 NDF (D<sub>2</sub>R) =  $22.89 \pm 8.41$   
 NDF (D<sub>3</sub>R) =  $4.09 \pm 1.07$



SC365

NDF (D<sub>1</sub>R) =  $0.99 \pm 0.38$   
 NDF (D<sub>2</sub>R) =  $1.04 \pm 0.39$   
 NDF (D<sub>3</sub>R) =  $1.12 \pm 0.14$

#### 4. In silico assessment of DR subtype selectivity – a distance-based approach

##### 4.1. ChEMBL validation

**Table S10.** Summary of the validation of the distance-based in silico approach using the described datasets extracted from ChEMBL. Cons. Gly, conserved glycine residue within the respective SBP. COM, center of mass.

Dataset	Distance (cons. Gly – COM) [Å]			Fold-difference (distance-based)		
	D <sub>1</sub> R	D <sub>2</sub> R	D <sub>3</sub> R	D <sub>1</sub> R/D <sub>2</sub> R	D <sub>1</sub> R/D <sub>3</sub> R	D <sub>2</sub> R/D <sub>3</sub> R
D <sub>2</sub> R-selective	17.88	13.59	13.66	1.32	1.31	0.99
D <sub>2</sub> like-selective	17.91	12.31	13.11	1.45	1.37	0.94
D <sub>3</sub> R-selective	17.79	12.44	13.17	1.43	1.35	0.94

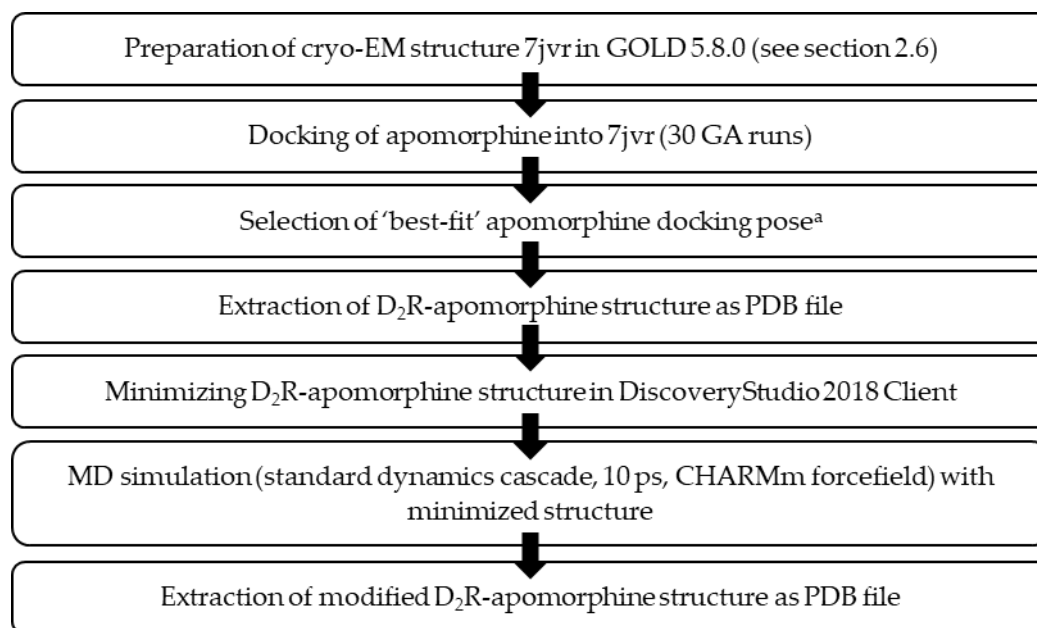
##### 4.2. Retrospective analysis of investigated compounds

**Table S11.** Summary of the distance-based in silico approach used during the investigation of the binding poses of the selected compounds 1 to 10. Cpd., compound. Cons. Gly, conserved glycine residue within the respective SBP. COM, center of mass.

Cpd.	Pose rank (out of 30)			Distance (cons. Gly – COM) [Å]			Fold-difference (distance-based)		
	D <sub>1</sub> R	D <sub>2</sub> R	D <sub>3</sub> R	D <sub>1</sub> R	D <sub>2</sub> R	D <sub>3</sub> R	D <sub>1</sub> R/D <sub>2</sub> R	D <sub>1</sub> R/D <sub>3</sub> R	D <sub>2</sub> R/D <sub>3</sub> R
1	4 <sup>th</sup>	1 <sup>st</sup>	5 <sup>th</sup>	19.96	17.70	16.70	1.13	1.19	1.06
2	1 <sup>st</sup>	4 <sup>th</sup>	1 <sup>st</sup>	19.20	14.47	14.96	1.33	1.28	0.97
3	1 <sup>st</sup>	1 <sup>st</sup>	1 <sup>st</sup>	18.16	13.41	14.15	1.35	1.28	0.95
4	1 <sup>st</sup>	2 <sup>nd</sup>	1 <sup>st</sup>	17.70	15.42	14.06	1.15	1.26	1.10
5	1 <sup>st</sup>	6 <sup>th</sup>	4 <sup>th</sup>	18.73	13.95	14.31	1.34	1.31	0.98
6	1 <sup>st</sup>	1 <sup>st</sup>	2 <sup>nd</sup>	17.12	14.77	15.14	1.16	1.13	0.98
7	1 <sup>st</sup>	2 <sup>nd</sup>	2 <sup>nd</sup>	18.32	12.99	14.05	1.41	1.30	0.93
8	1 <sup>st</sup>	1 <sup>st</sup>	7 <sup>th</sup>	19.27	16.45	15.77	1.17	1.22	1.04
9	2 <sup>nd</sup>	2 <sup>nd</sup>	2 <sup>nd</sup>	19.29	12.83	14.07	1.50	1.37	0.91
10	1 <sup>st</sup>	1 <sup>st</sup>	1 <sup>st</sup>	18.11	12.84	13.50	1.41	1.34	0.95

## 5. Molecular dynamics simulation (MDS) – a workflow for the D<sub>2</sub>R

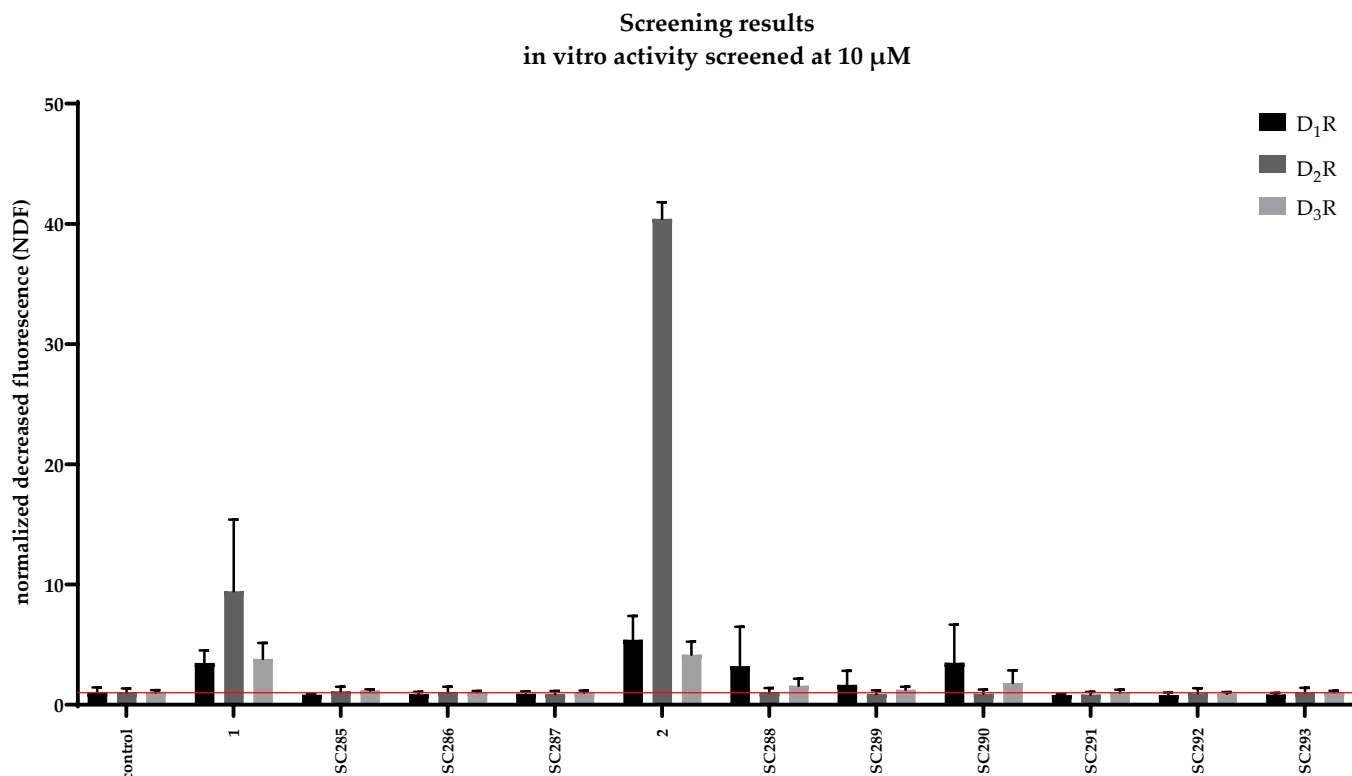
The MDS was performed following the workflow shown in Figure S1.



**Figure S1.** Summary of the utilized approach to modify PDB entry 7jvr [34] using a MDS approach. <sup>a</sup> 'best-fit' docking pose was assessed based on the correct positioning of apomorphine in the related D<sub>1</sub>R structure 7jvq [34] with respect to the orientation of the catechol motif towards the serine triade as well as the formation of a salt-bridge with Asp<sup>3.32</sup>.

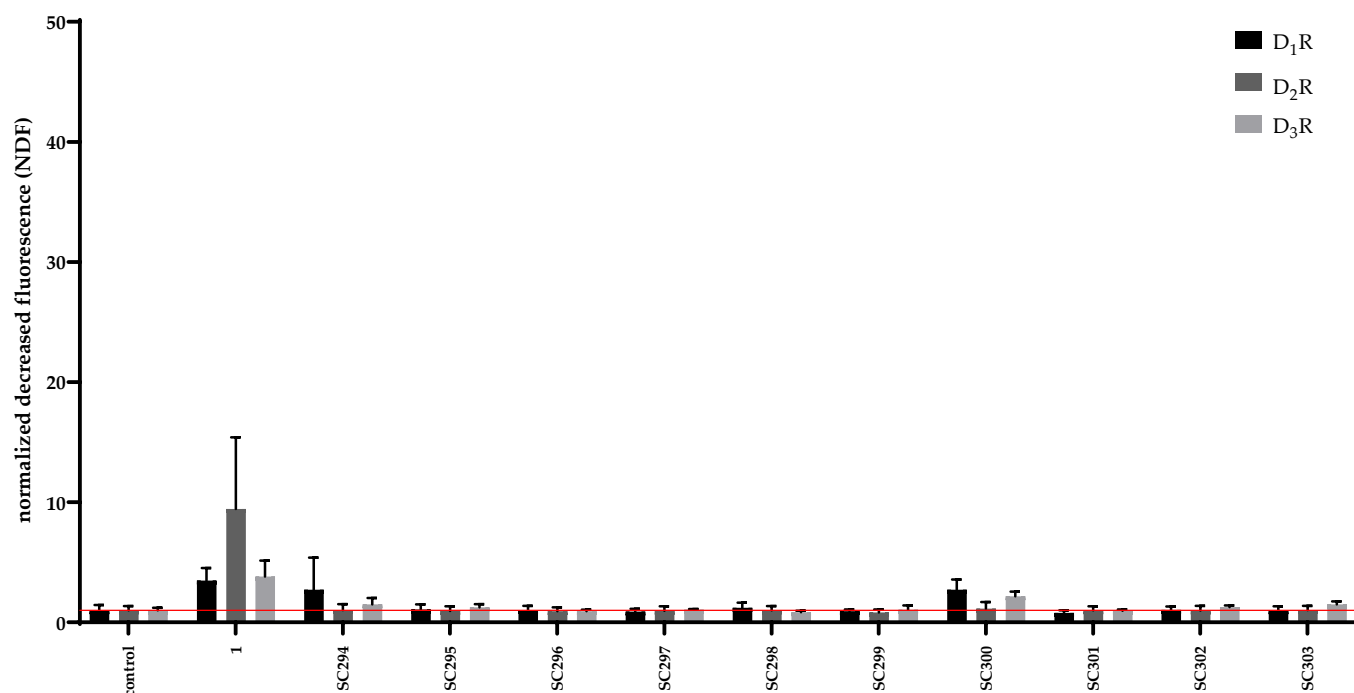
## 6. In vitro careening activity of selected compounds

### 6.1. Summary of in vitro activity (based on NDF values) of control compounds and selected virtual hits



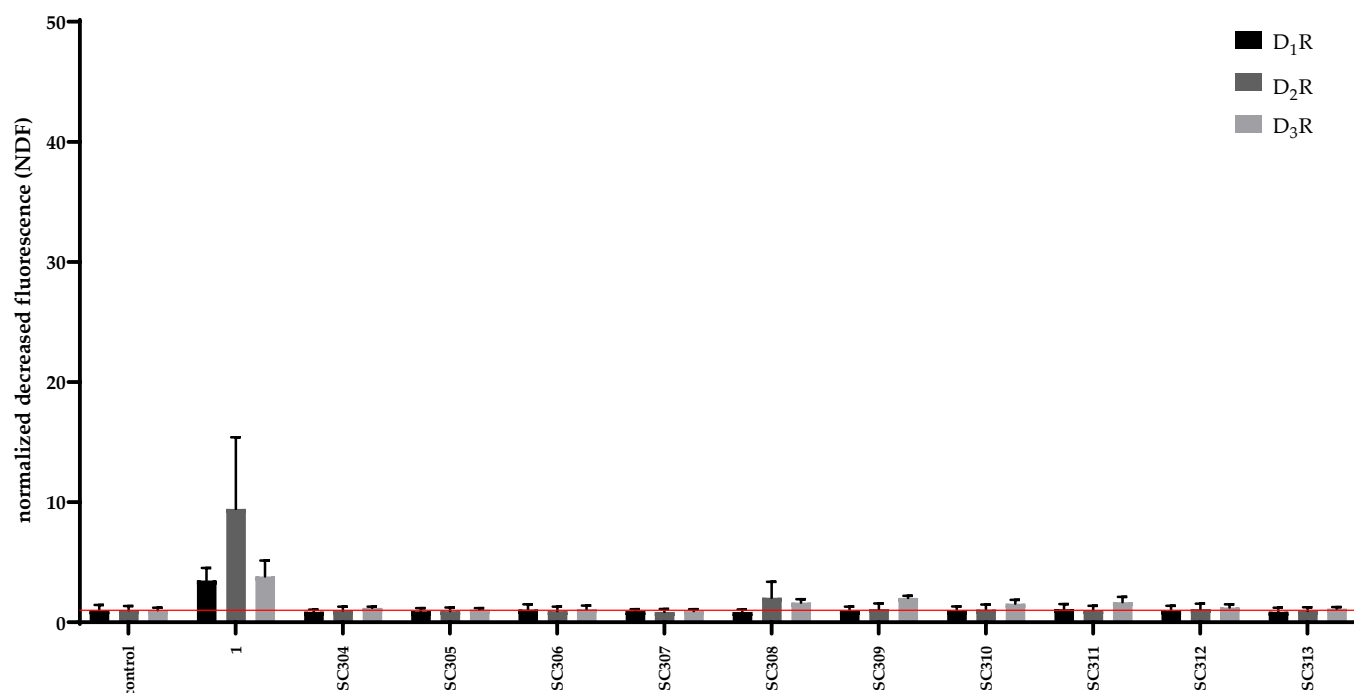
**Figure S2.** Comparison of biological activity of selected compounds at DR subtypes D<sub>1</sub>R (black), D<sub>2</sub>R (dark grey) and D<sub>3</sub>R (light grey). Compound binding is shown as NDF in comparison to the control. Activities were measured in biological duplicates (two technical replicates each). Error bars show standard deviations (SD). The red line indicates a NDF of 1, thus, an inactive ligand at 10  $\mu$ M screening concentration. NDF, normalized decreased fluorescence.

**Screening results**  
**in vitro activity screened at 10  $\mu$ M**



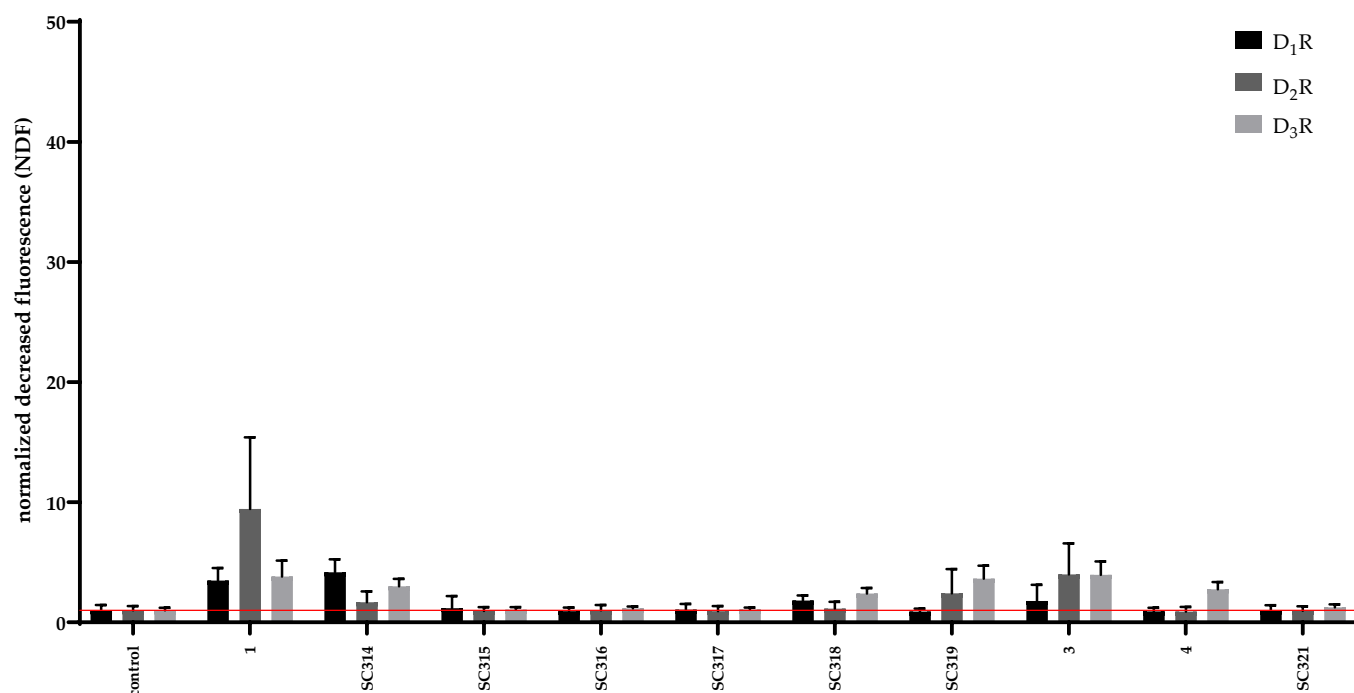
**Figure S3.** Comparison of biological activity of selected compounds at DR subtypes D<sub>1</sub>R (black), D<sub>2</sub>R (dark grey) and D<sub>3</sub>R (light grey). Compound binding is shown as NDF in comparison to the control. Activities were measured in biological duplicates (two technical replicates each). Error bars show standard deviations (SD). The red line indicates a NDF of 1, thus, an inactive ligand at 10  $\mu$ M screening concentration. NDF, normalized decreased fluorescence.

**Screening results**  
**in vitro activity screened at 10  $\mu$ M**



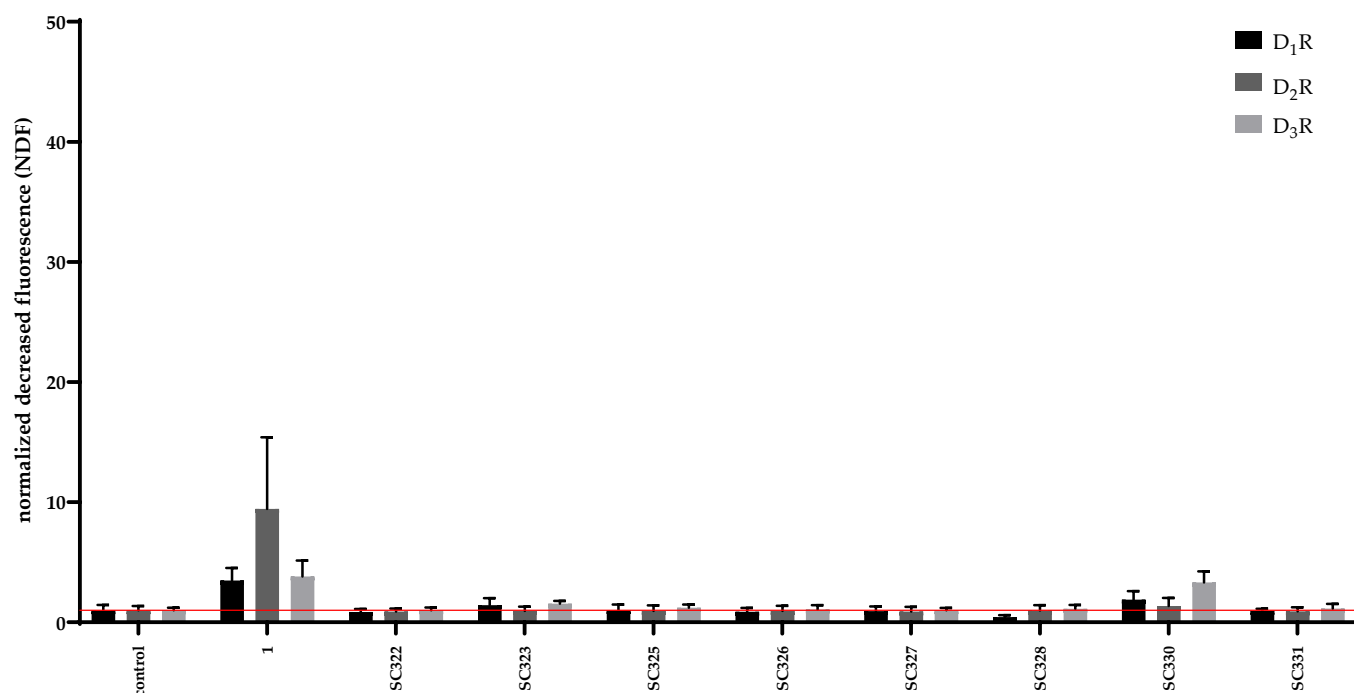
**Figure S4.** Comparison of biological activity of selected compounds at DR subtypes D<sub>1</sub>R (black), D<sub>2</sub>R (dark grey) and D<sub>3</sub>R (light grey). Compound binding is shown as NDF in comparison to the control. Activities were measured in biological duplicates (two technical replicates each). Error bars show standard deviations (SD). The red line indicates a NDF of 1, thus, an inactive ligand at 10  $\mu$ M screening concentration. NDF, normalized decreased fluorescence.

**Screening results**  
**in vitro activity screened at 10  $\mu$ M**



**Figure S5.** Comparison of biological activity of selected compounds at DR subtypes D<sub>1</sub>R (black), D<sub>2</sub>R (dark grey) and D<sub>3</sub>R (light grey). Compound binding is shown as NDF in comparison to the control. Activities were measured in biological duplicates (two technical replicates each). Error bars show standard deviations (SD). The red line indicates a NDF of 1, thus, an inactive ligand at 10  $\mu$ M screening concentration. NDF, normalized decreased fluorescence.

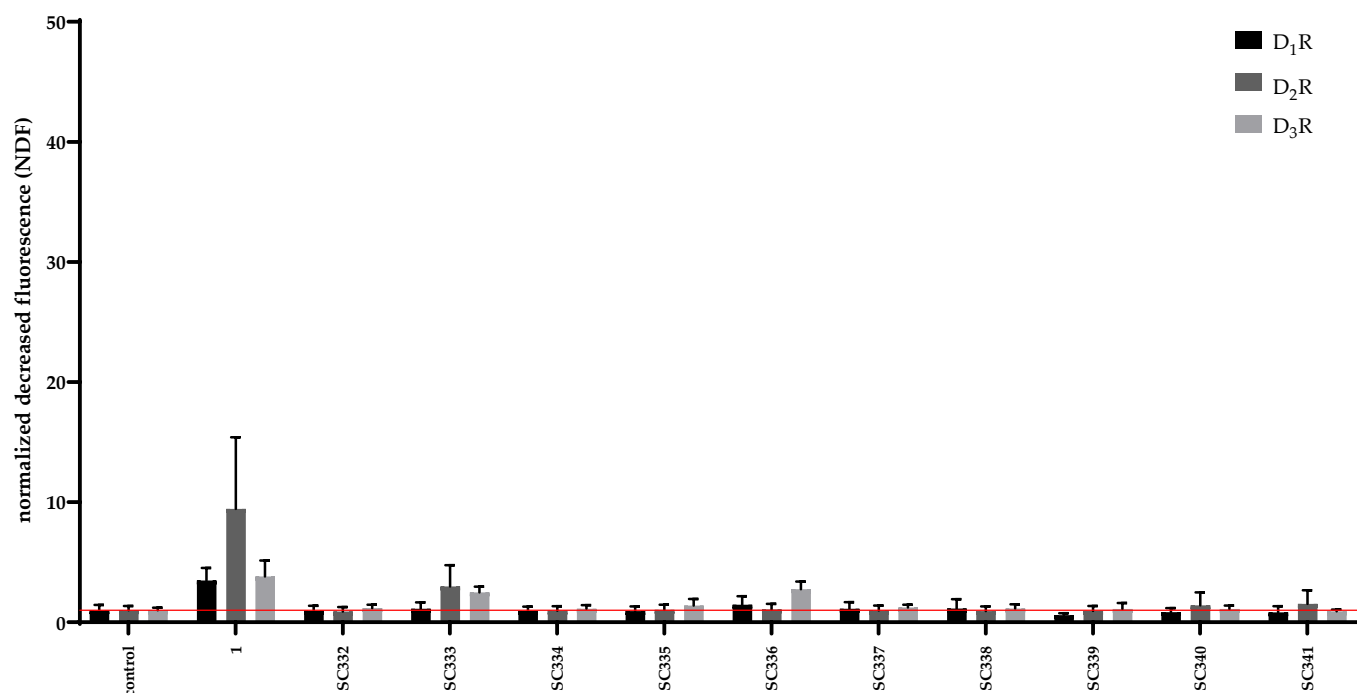
**Screening results**  
**in vitro activity screened at 10  $\mu$ M**



**Figure S6.** Comparison of biological activity of selected compounds at DR subtypes D<sub>1</sub>R (black), D<sub>2</sub>R (dark grey) and D<sub>3</sub>R (light grey). Compound binding is shown as NDF in comparison to the control. Activities were measured in biological duplicates (two technical replicates each). Error bars show standard deviations (SD). The red line indicates a NDF of 1, thus, an inactive ligand at 10  $\mu$ M screening concentration. NDF, normalized decreased fluorescence.

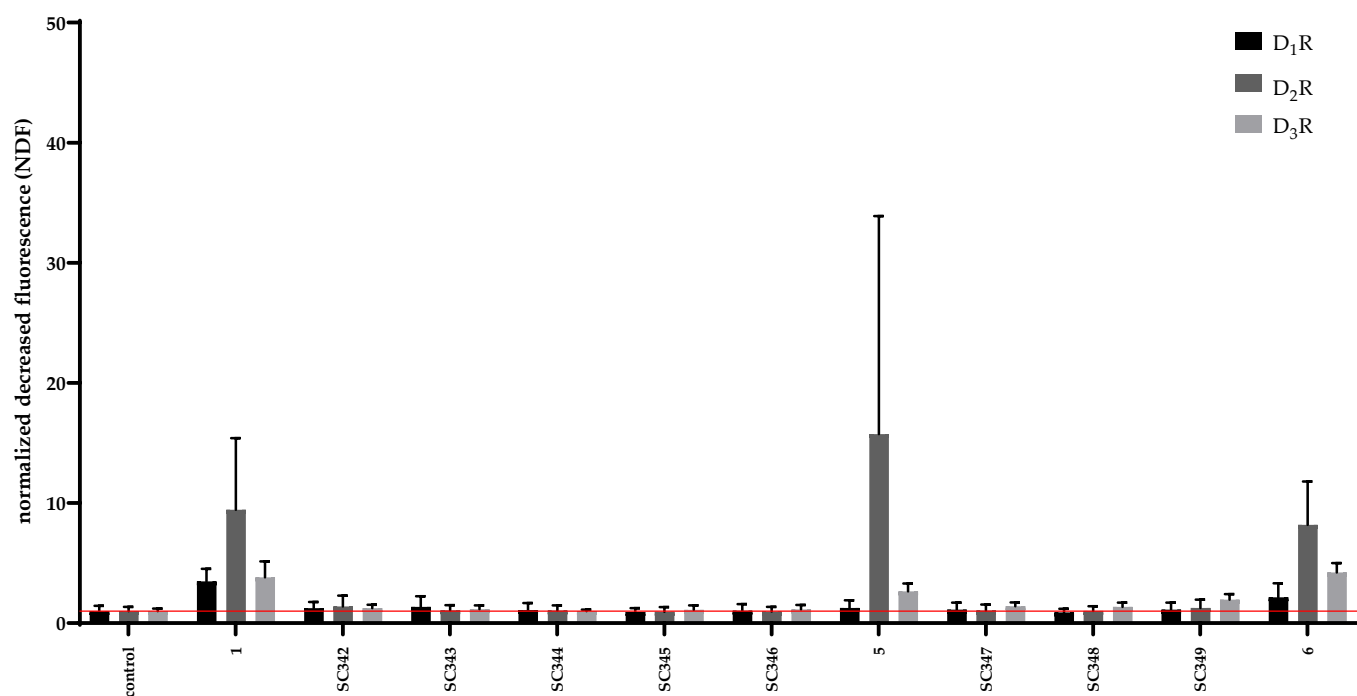


**Screening results**  
**in vitro activity screened at 10  $\mu$ M**



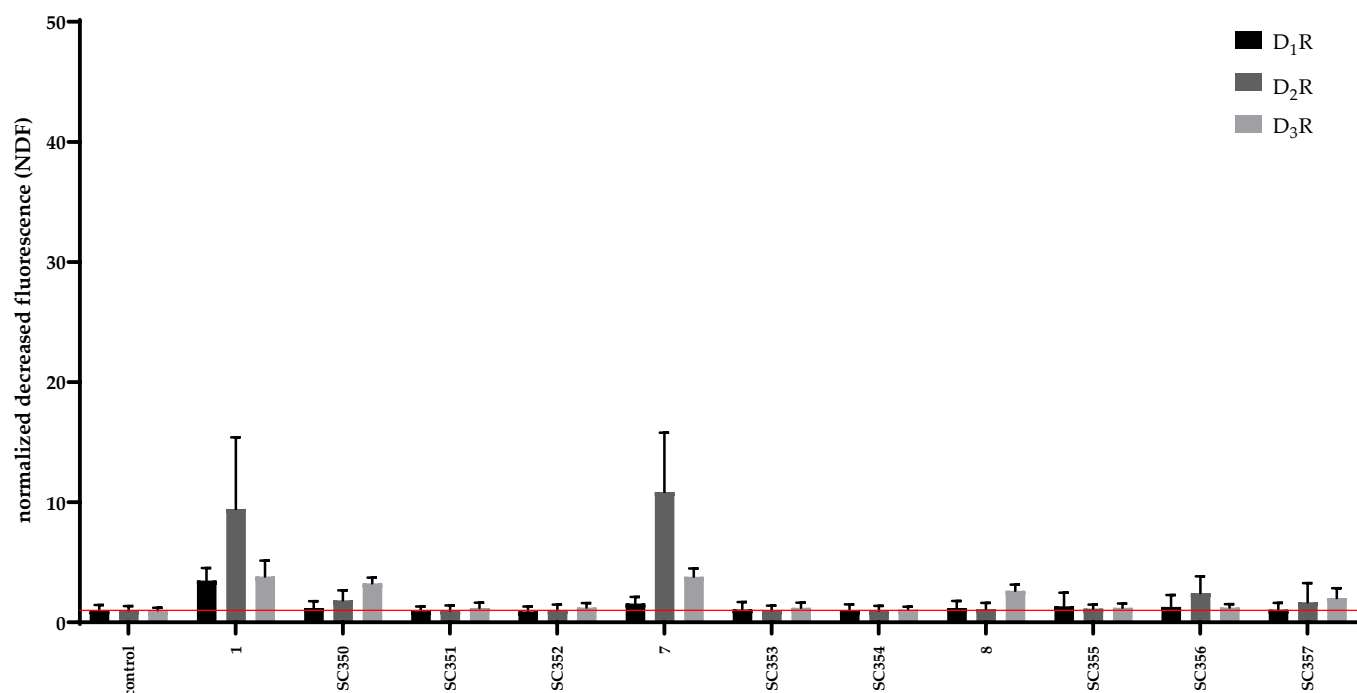
**Figure S7.** Comparison of biological activity of selected compounds at DR subtypes D<sub>1</sub>R (black), D<sub>2</sub>R (dark grey) and D<sub>3</sub>R (light grey). Compound binding is shown as NDF in comparison to the control. Activities were measured in biological duplicates (two technical replicates each). Error bars show standard deviations (SD). The red line indicates a NDF of 1, thus, an inactive ligand at 10  $\mu$ M screening concentration. NDF, normalized decreased fluorescence.

**Screening results**  
**in vitro activity screened at 10  $\mu$ M**



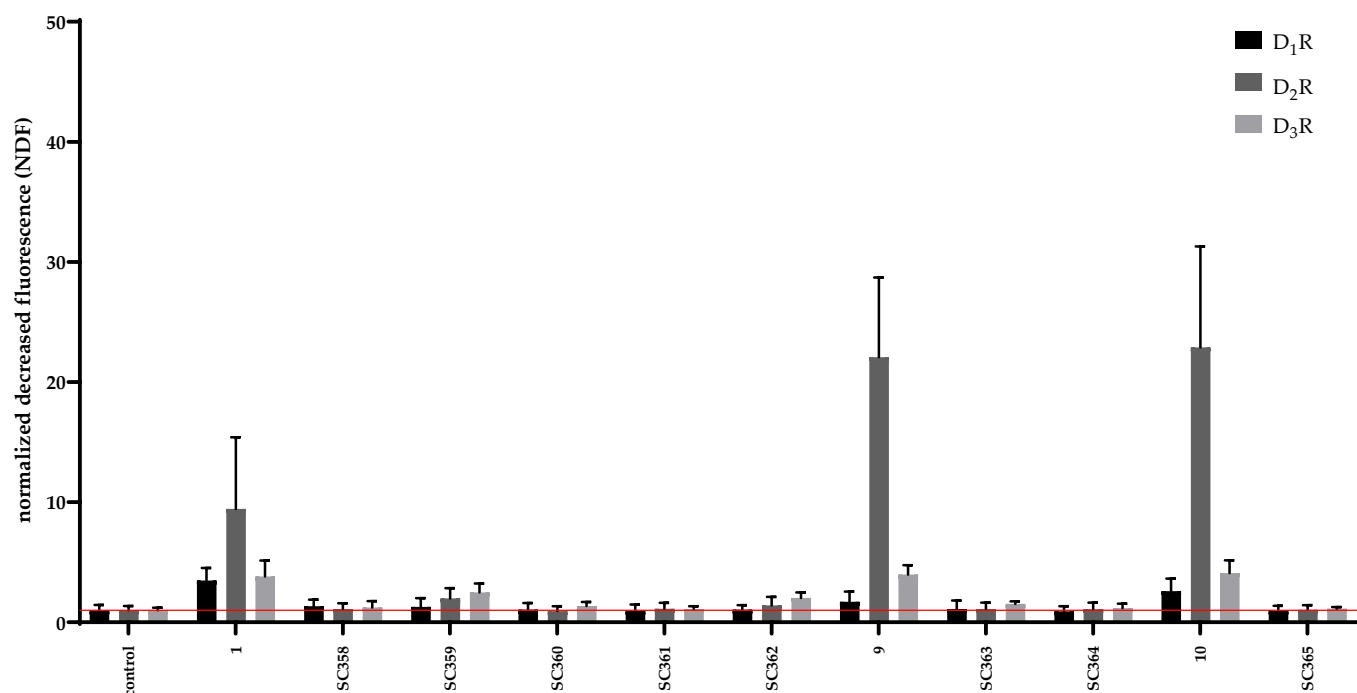
**Figure S8.** Comparison of biological activity of selected compounds at DR subtypes D<sub>1</sub>R (black), D<sub>2</sub>R (dark grey) and D<sub>3</sub>R (light grey). Compound binding is shown as NDF in comparison to the control. Activities were measured in biological duplicates (two technical replicates each). Error bars show standard deviations (SD). The red line indicates a NDF of 1, thus, an inactive ligand at 10  $\mu$ M screening concentration. NDF, normalized decreased fluorescence.

**Screening results**  
**in vitro activity screened at 10  $\mu$ M**



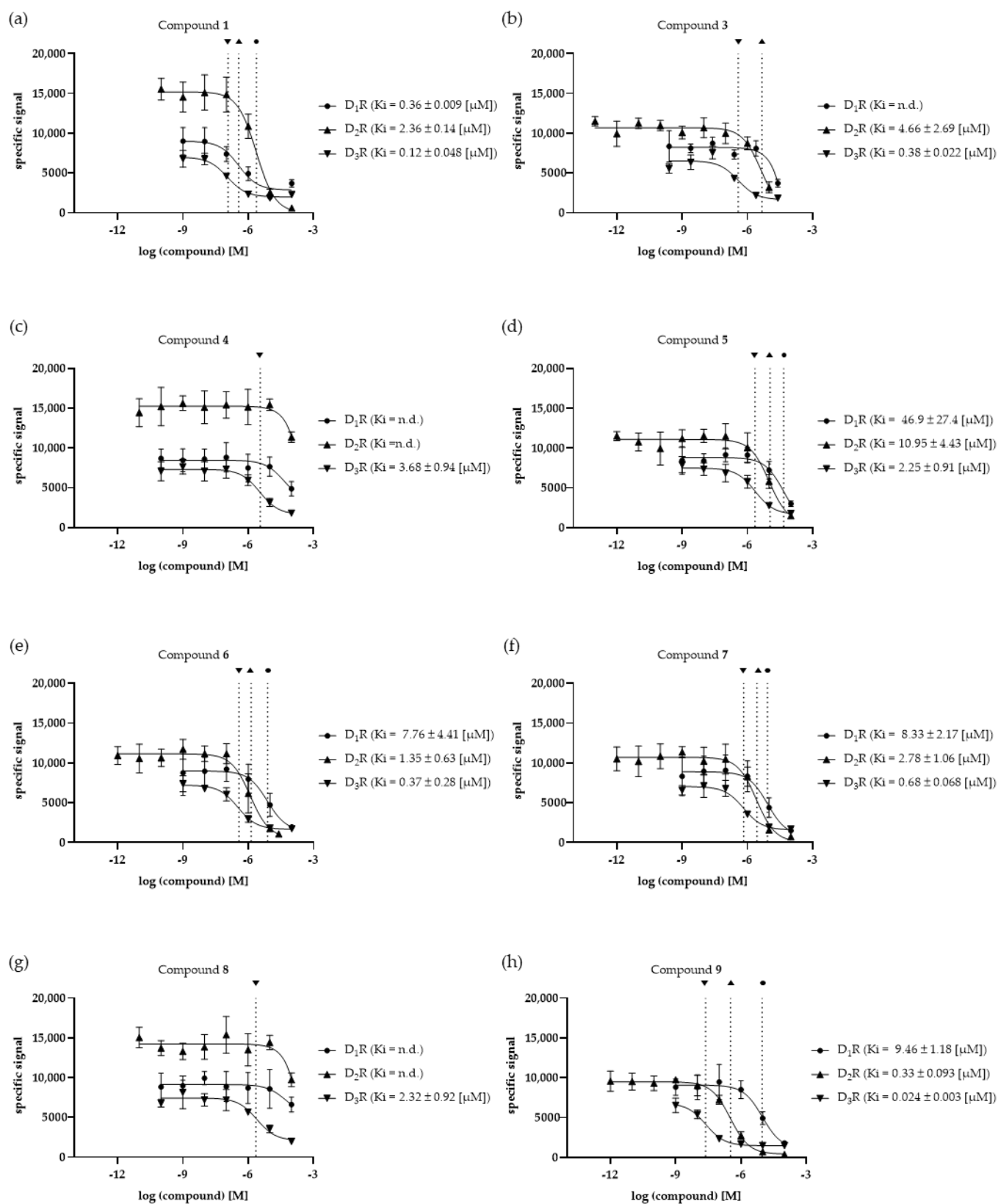
**Figure S9.** Comparison of biological activity of selected compounds at DR subtypes D<sub>1</sub>R (black), D<sub>2</sub>R (dark grey) and D<sub>3</sub>R (light grey). Compound binding is shown as NDF in comparison to the control. Activities were measured in biological duplicates (two technical replicates each). Error bars show standard deviations (SD). The red line indicates a NDF of 1, thus, an inactive ligand at 10  $\mu$ M screening concentration. NDF, normalized decreased fluorescence.

**Screening results**  
**in vitro activity screened at 10  $\mu$ M**



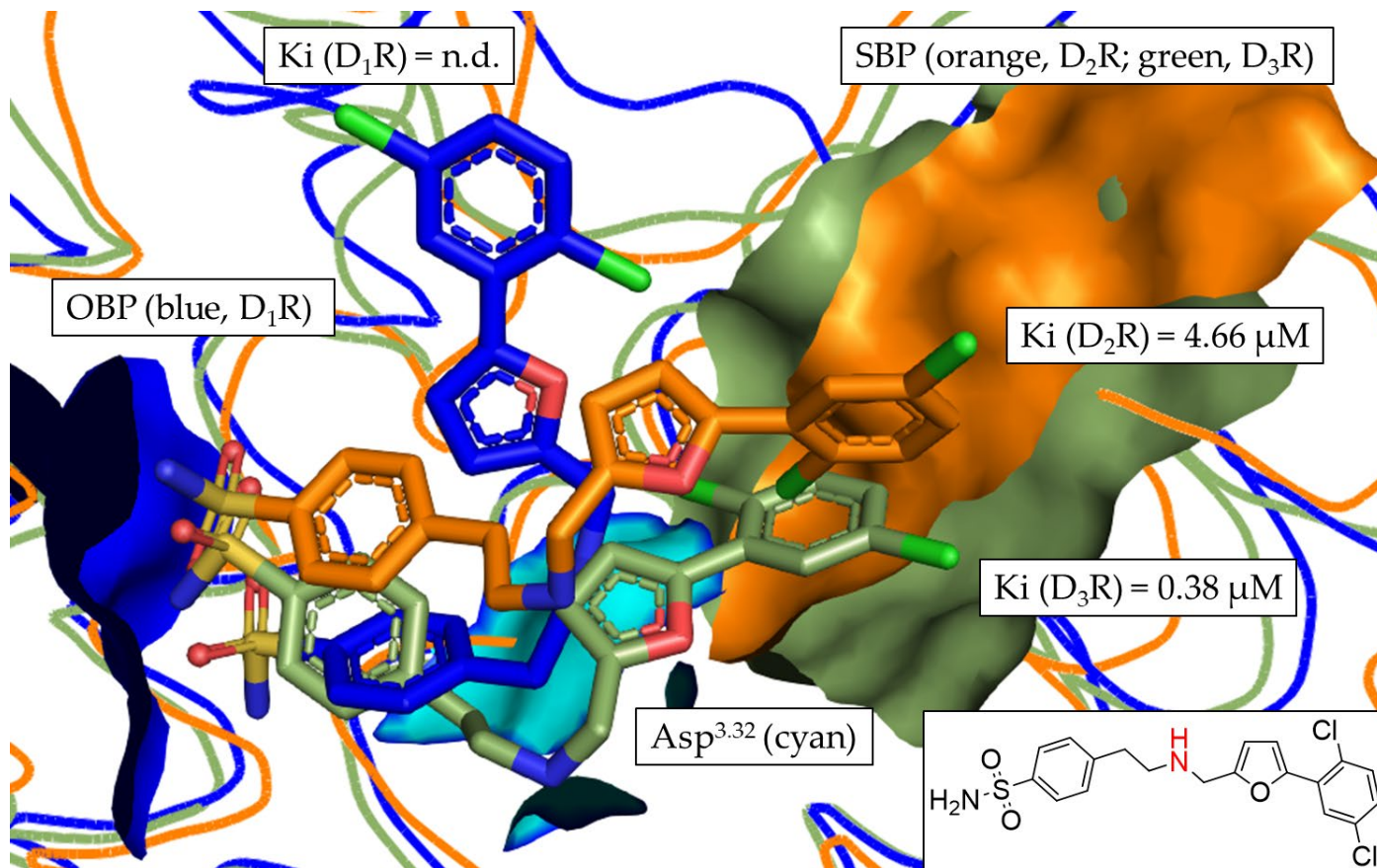
**Figure S10.** Comparison of biological activity of selected compounds at DR subtypes D<sub>1</sub>R (black), D<sub>2</sub>R (dark grey) and D<sub>3</sub>R (light grey). Compound binding is shown as NDF in comparison to the control. Activities were measured in biological duplicates (two technical replicates each). Error bars show standard deviations (SD). The red line indicates a NDF of 1, thus, an inactive ligand at 10  $\mu$ M screening concentration. NDF, normalized decreased fluorescence.

## 6.2. Summary of $K_i$ values determined in vitro – overview of DR subtype selectivity

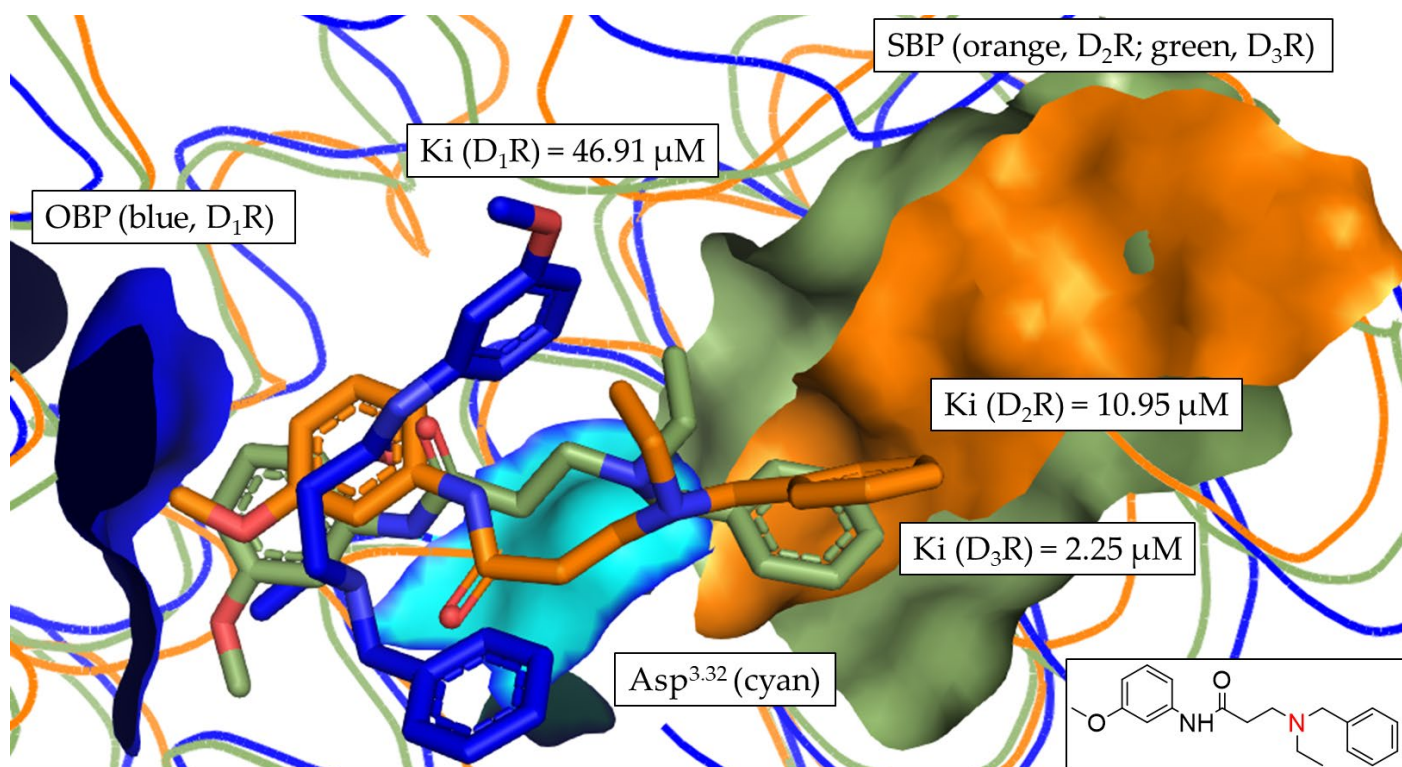


**Figure S11.** Comparison of the  $K_i$  values of compounds (a) 1, (b) 3, (c) 4, (d) 5, (e) 6, (f) 7, (g) 8 and (h) 9 determined at the investigated DR subtypes  $D_1R$ ,  $D_2R$  and  $D_3R$ . Vertical, dotted lines indicate the respective  $K_i$  values at the different DR subtypes.  $K_i$  values [ $\mu M$ ]  $\pm$  SD were determined with  $n = 6$ .

## 7. In silico insights into the DR binding pockets

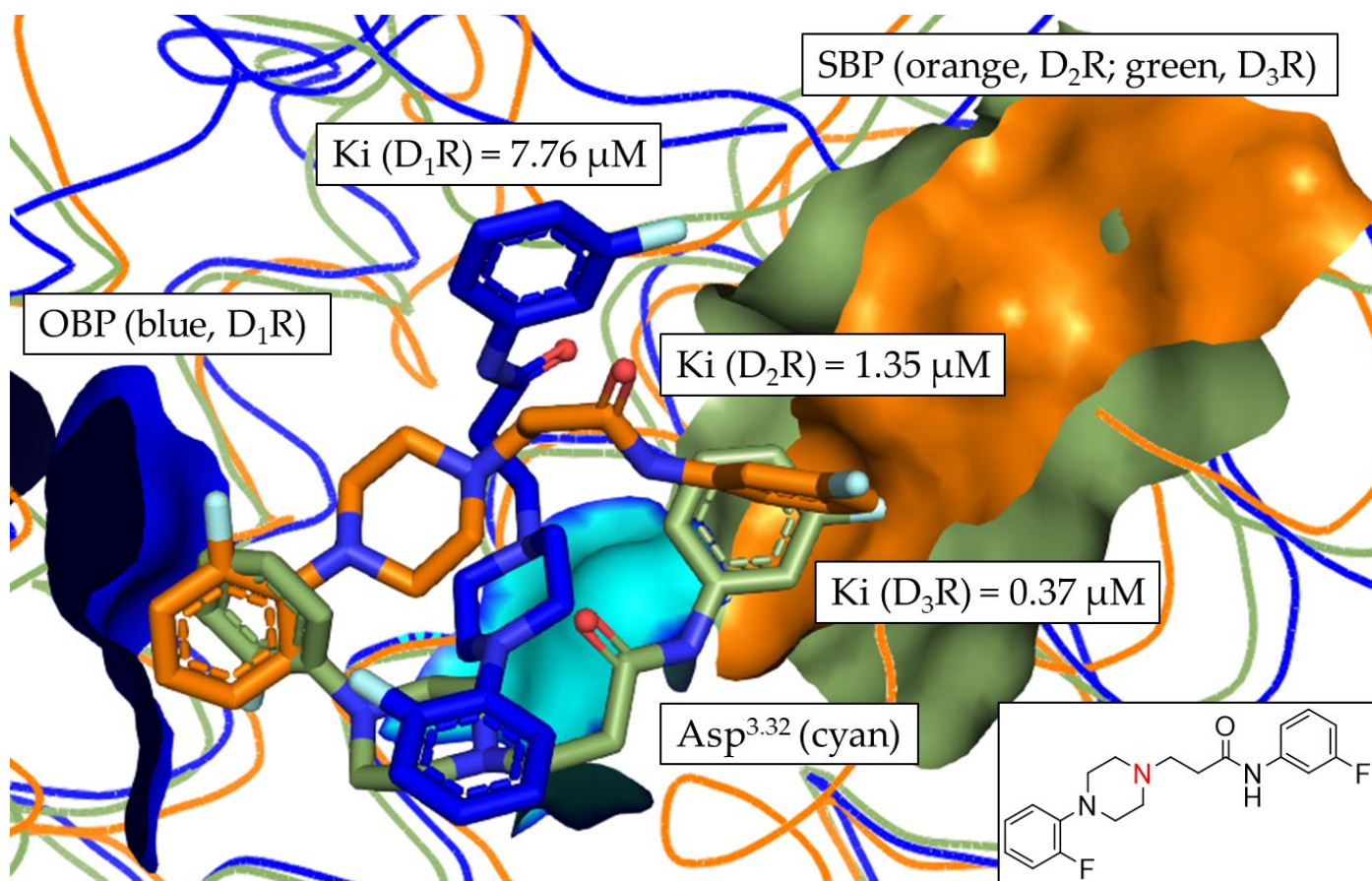


**Figure S12.** Alignment of the most frequent poses of compound **3** docked into D<sub>1</sub>R, D<sub>2</sub>R and D<sub>3</sub>R. The surface of the highly conserved OBP is shown in blue (based on D<sub>1</sub>R) consisting of Asp<sup>3.32</sup> (highlighted in cyan) and Ser<sup>5.42/5.43/5.46</sup>. The conserved SBP-surface is displayed in orange (D<sub>2</sub>R) and green (D<sub>3</sub>R) consisting of Val<sup>2.61</sup>, Leu<sup>2.64</sup>, Gly<sup>ECL1</sup>, Phe<sup>3.28</sup> and Cys<sup>ECL2</sup> (individual amino acid labels shown in Table 3), respectively. Ki values determined in vitro are shown for each DR subtype. 2D structure of compound **3** is shown. Amine functional group involved in formation of the salt-bridge is highlighted in red.

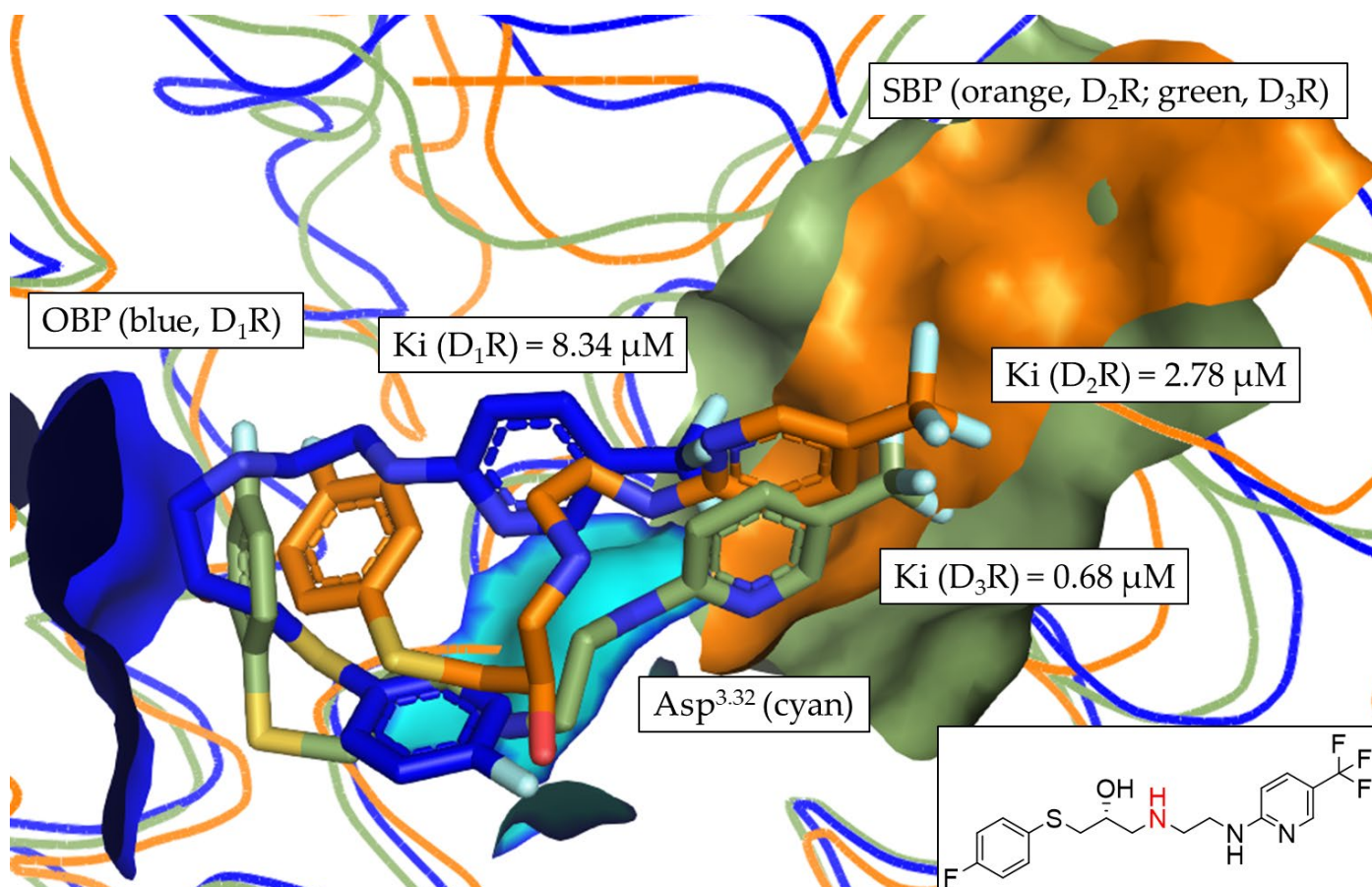


**Figure S13.** Alignment of the most frequent poses of compound **5** docked into D<sub>1</sub>R, D<sub>2</sub>R and D<sub>3</sub>R. The surface of the highly conserved OBP is shown in blue (based on D<sub>1</sub>R) consisting of Asp<sup>3.32</sup> (highlighted in cyan) and Ser<sup>5.42/5.43/5.46</sup>. The conserved SBP-surface is displayed in orange (D<sub>2</sub>R) and green (D<sub>3</sub>R) consisting of Val<sup>2.61</sup>, Leu<sup>2.64</sup>, Gly<sup>ECL1</sup>, Phe<sup>3.28</sup> and Cys<sup>ECL2</sup> (individual amino acid labels shown in Table 3), respectively. Ki values determined in vitro are shown for each DR subtype. 2D structure of compound **5** is shown. Amine functional group involved in formation of the salt-bridge is highlighted in red.

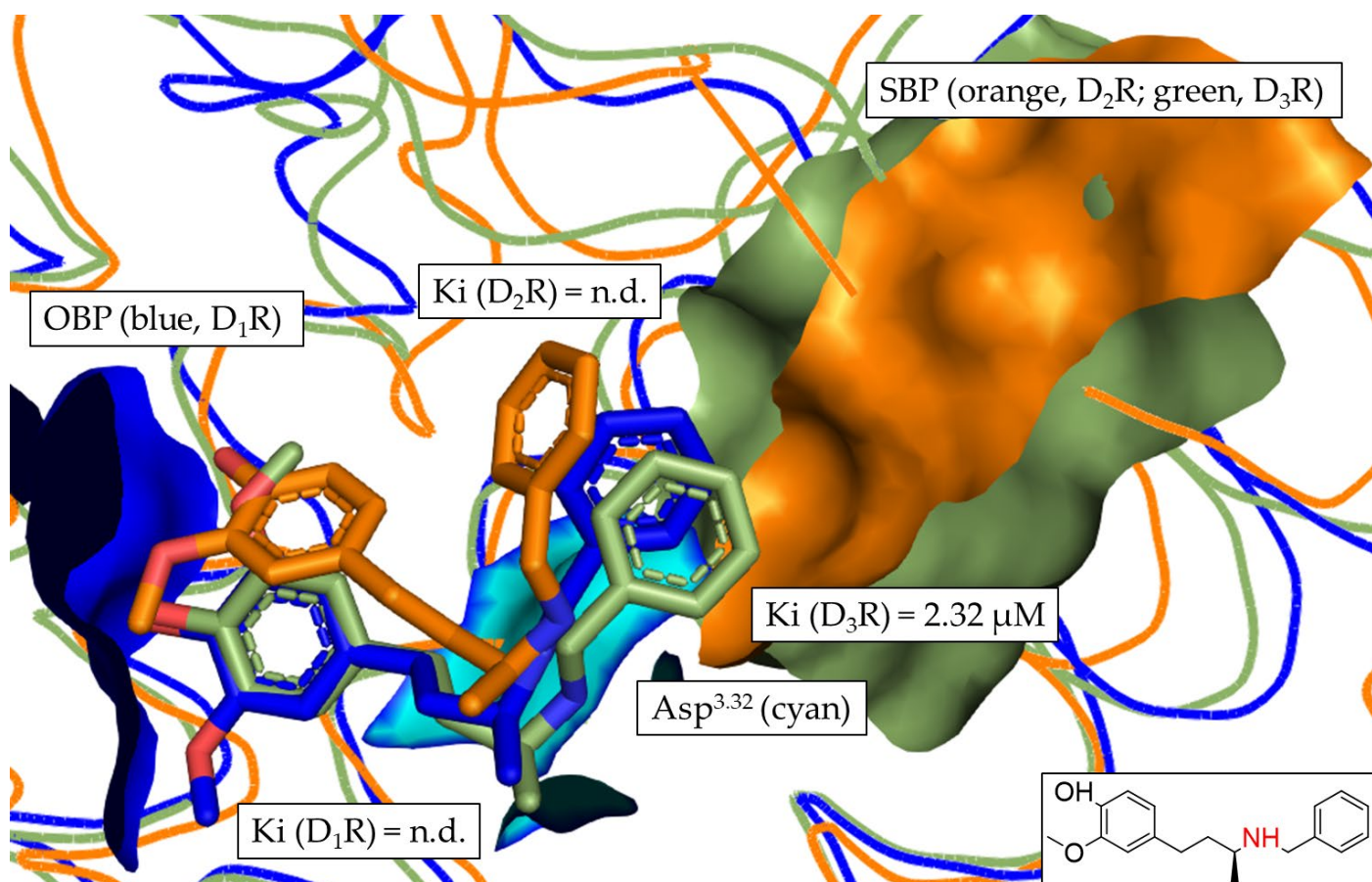




**Figure S14.** Alignment of the most frequent poses of compound 6 docked into D<sub>1</sub>R, D<sub>2</sub>R and D<sub>3</sub>R. The surface of the highly conserved OBP is shown in blue (based on D<sub>1</sub>R) consisting of Asp<sup>3.32</sup> (highlighted in cyan) and Ser<sup>5.42/5.43/5.46</sup>. The conserved SBP-surface is displayed in orange (D<sub>2</sub>R) and green (D<sub>3</sub>R) consisting of Val<sup>2.61</sup>, Leu<sup>2.64</sup>, Gly<sup>ECL1</sup>, Phe<sup>3.28</sup> and Cys<sup>ECL2</sup> (individual amino acid labels shown in Table 3), respectively. Ki values determined in vitro are shown for each DR subtype. 2D structure of compound 6 is shown. Amine functional group involved in formation of the salt-bridge is highlighted in red.

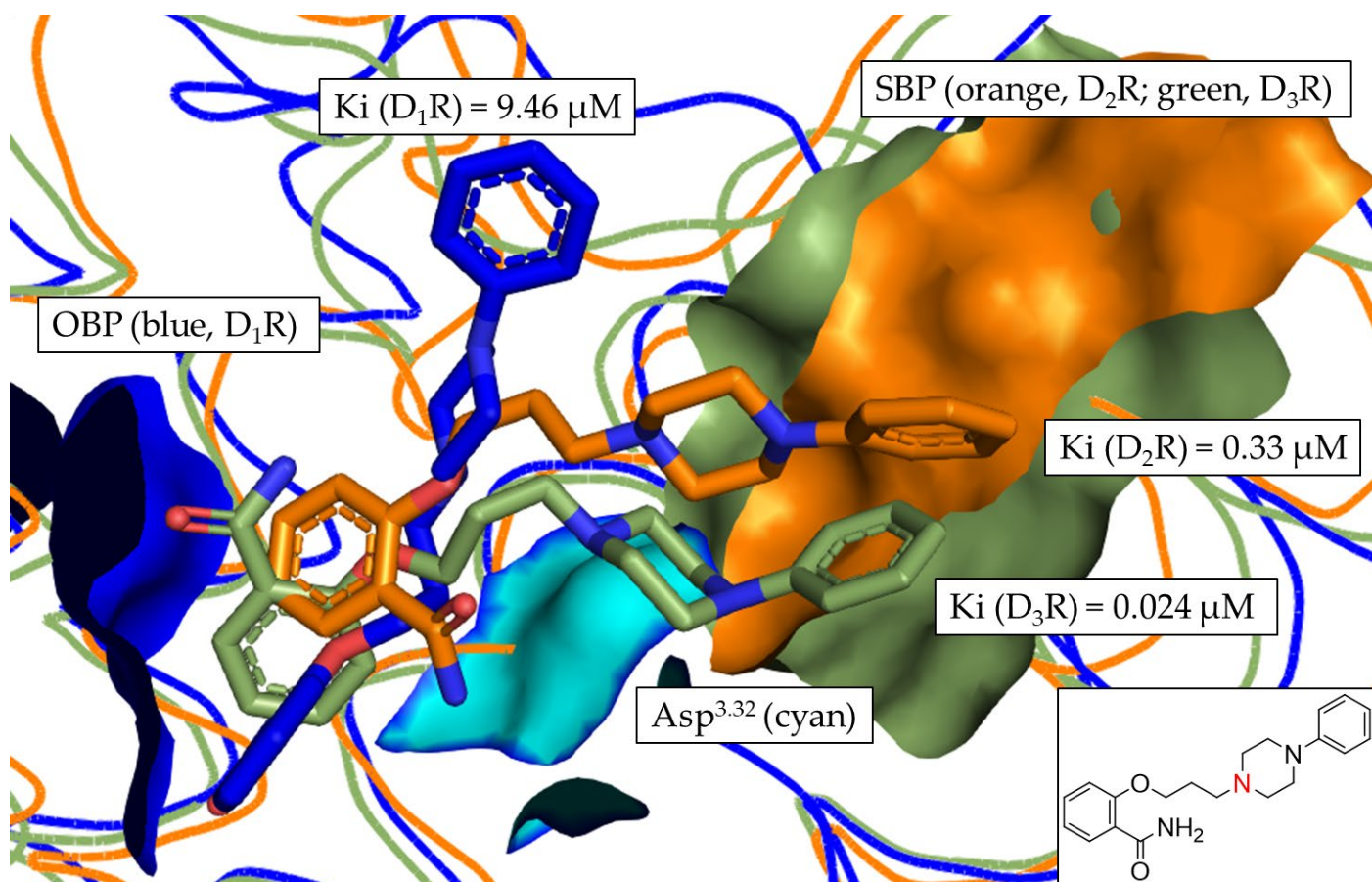


**Figure S15.** Alignment of the most frequent poses of compound **7** docked into D<sub>1</sub>R, D<sub>2</sub>R and D<sub>3</sub>R. The surface of the highly conserved OBP is shown in blue (based on D<sub>1</sub>R) consisting of Asp<sup>3.32</sup> (highlighted in cyan) and Ser<sup>5.42/5.43/5.46</sup>. The conserved SBP-surface is displayed in orange (D<sub>2</sub>R) and green (D<sub>3</sub>R) consisting of Val<sup>2.61</sup>, Leu<sup>2.64</sup>, Gly<sup>ECL1</sup>, Phe<sup>3.28</sup> and Cys<sup>ECL2</sup> (individual amino acid labels shown in Table 3), respectively. Ki values determined in vitro are shown for each DR subtype. 2D structure of compound **7** is shown. Amine functional group involved in formation of the salt-bridge is highlighted in red.



**Figure S16.** Alignment of the most frequent poses of compound 8 docked into D<sub>1</sub>R, D<sub>2</sub>R and D<sub>3</sub>R. The surface of the highly conserved OBP is shown in blue (based on D<sub>1</sub>R) consisting of Asp<sup>3.32</sup> (highlighted in cyan) and Ser<sup>5.42/5.43/5.46</sup>. The conserved SBP-surface is displayed in orange (D<sub>2</sub>R) and green (D<sub>3</sub>R) consisting of Val<sup>2.61</sup>, Leu<sup>2.64</sup>, Gly<sup>ECL1</sup>, Phe<sup>3.28</sup> and Cys<sup>ECL2</sup> (individual amino acid labels shown in Table 3), respectively. Ki values determined in vitro are shown for each DR subtype. 2D structure of compound 8 is shown. Amine functional group involved in formation of the salt-bridge is highlighted in red.





**Figure S17.** Alignment of the most frequent poses of compound **9** docked into  $D_1R$ ,  $D_2R$  and  $D_3R$ . The surface of the highly conserved OBP is shown in blue (based on  $D_1R$ ) consisting of Asp<sup>3.32</sup> (highlighted in cyan) and Ser<sup>5.42/5.43/5.46</sup>. The conserved SBP-surface is displayed in orange ( $D_2R$ ) and green ( $D_3R$ ) consisting of Val<sup>2.61</sup>, Leu<sup>2.64</sup>, Gly<sup>ECL1</sup>, Phe<sup>3.28</sup> and Cys<sup>ECL2</sup> (individual amino acid labels shown in Table 3), respectively. Ki values determined in vitro are shown for each DR subtype. 2D structure of compound **9** is shown. Amine functional group involved in formation of the salt-bridge is highlighted in red.