Supplementary Material

Structure-Activity Relationships Based on 3D-QSAR CoMFA/CoMSIA and Design of Aryloxypropanol-amine Agonists with Selectivity for the Human β3-Adrenergic Receptor and Anti-Obesity and Anti-Diabetic Profiles

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Table S1. q^2 and N values for all field combinations of CoMFA and CoMSIA.[a]

Model	q^2	N
CoMFA-S	0.442	3
CoMFA-E	0.331	12
CoMFA-SE	0.537	6
CoMSIA-S	0.293	2
CoMSIA-E	0.135	2
CoMSIA-H	-0.071	5
CoMSIA-D	-0.024	2
CoMSIA-A	-0.014	2
CoMSIA-SE	0.566	7
CoMSIA-SEH	0.669	20
CoMSIA-SEHD	0.654	20
CoMSIA-SEHA	0.674	6
CoMSIA-SED	0.66	16
CoMSIA-SEA	0.651	5
CoMSIA-SEDA	0.601	7
CoMSIA-SH	0.464	7
CoMSIA-SD	0.551	6
CoMSIA-SA	0.409	4
CoMSIA-SHD	0.561	9

Table S1. *Cont.*

CoMSIA-SHA	0.403	8
CoMSIA-SDA	0.622	15
CoMSIA-SHDA	0.613	20
CoMSIA-EH	0.536	20
CoMSIA-ED	0.349	2
CoMSIA-EA	0.48	3
CoMSIA-EHD	0.422	5
CoMSIA-EHA	0.598	6
CoMSIA-EDA	0.328	2
CoMSIA-EHDA	0.508	7
CoMSIA-HD	0.02	6
CoMSIA-HA	0.004	20
CoMSIA-HDA	0.107	20
CoMSIA-DA	-0.062	1
CoMSIA-ALL	0.669	6

[a] q^2 = the square of the LOO cross-validation (CV) coefficient; N = the optimum number of components.

Table S2. Randomizations of biological activity for the execution of the Y-random test.

Random-1	Random-2	Random-3	Random-4	Random-5	Random-6	Random-7	Random-8	Random-9	Random-10
6.4685	7.2076	6.4685	6.2924	6.8861	6.4685	6.3979	6.4815	5.6021	6.585
4.9208	6.2924	6.4815	6.7447	7	6.8861	5.6021	6.3565	7.2076	6.3979
6.3565	6.7959	5.0315	7.2076	5.8539	6.7959	6.5528	6.5528	6.7447	6.8861
6.6383	6.3565	6.2924	6.6383	6.6383	5.8539	5.8539	5.0315	6.5528	5.6021
7.2076	6.5528	6.5528	4.9208	6.5686	6.5686	4.9208	6.6383	6.5686	6.5528
6.5528	6.3979	6.5686	6.5528	6.585	6.5528	6.5686	6.5686	6.5528	6.7447
5.6021	6.7696	6.6383	5.8539	6.3279	6.1871	6.5528	6.8861	6.6383	6.3279
3.8861	7	6.585	6.3565	6.1871	7.2076	6.4685	6.699	5.0315	6.1871
6.3979	6.5686	6.5528	7	7.2076	6.7696	6.7447	6.3279	6.1871	6.7959
7	6.3279	3.8861	6.5528	6.4685	6.7447	7	6.6021	6.3565	6.699
6.7447	6.5686	6.5686	6.4815	6.6021	4.9208	5.699	6.2924	6.5528	6.5686
7	6.5528	5.699	6.4685	6.2924	7	7	6.7696	6.585	5.8539
5.0315	6.5528	5.6021	6.7696	7	6.699	6.7959	6.1871	6.4815	6.6383
6.4815	6.7447	6.7696	6.699	6.5528	6.6021	6.5686	7.2076	6.3279	6.2924
6.5528	5.699	4.9208	6.3279	6.7696	6.5686	6.6021	4.9208	7	6.5686
6.7959	4.9208	6.1871	6.585	6.7447	6.4815	7.2076	7	5.8539	6.7696
6.5686	3.8861	7	5.0315	4.9208	6.3565	6.2924	6.585	6.4685	6.5528
6.699	6.8861	7.2076	6.5686	6.3565	6.6383	6.585	6.4685	7	6.5528
6.3279	5.8539	6.3279	7	6.699	5.0315	6.3565	6.5528	6.699	7
5.8539	6.4815	6.7959	6.3979	6.3979	6.3279	6.4815	6.7447	6.7696	6.6021
6.2924	6.699	6.3565	6.7959	6.5528	6.5528	6.1871	6.7959	6.3979	5.699
6.7696	6.6021	6.8861	5.699	5.699	6.5528	6.7696	7	6.5686	7.2076
5.699	7	7	6.5686	6.5528	6.2924	6.5528	6.5686	6.7959	7
6.5686	6.6383	6.699	5.6021	6.4815	6.3979	6.3279	5.8539	5.699	6.4685
6.1871	5.6021	6.6021	6.6021	6.5686	6.585	6.699	5.699	3.8861	6.3565
6.5528	6.1871	5.8539	6.8861	5.0315	3.8861	3.8861	6.5528	6.8861	6.4815
6.8861	6.585	6.5528	3.8861	6.7959	5.699	6.8861	6.3979	4.9208	3.8861
6.6021	6.4685	6.7447	6.5528	5.6021	7	6.6383	5.6021	6.6021	5.0315
6.585	5.0315	6.3979	6.1871	3.8861	5.6021	5.0315	3.8861	6.2924	4.9208

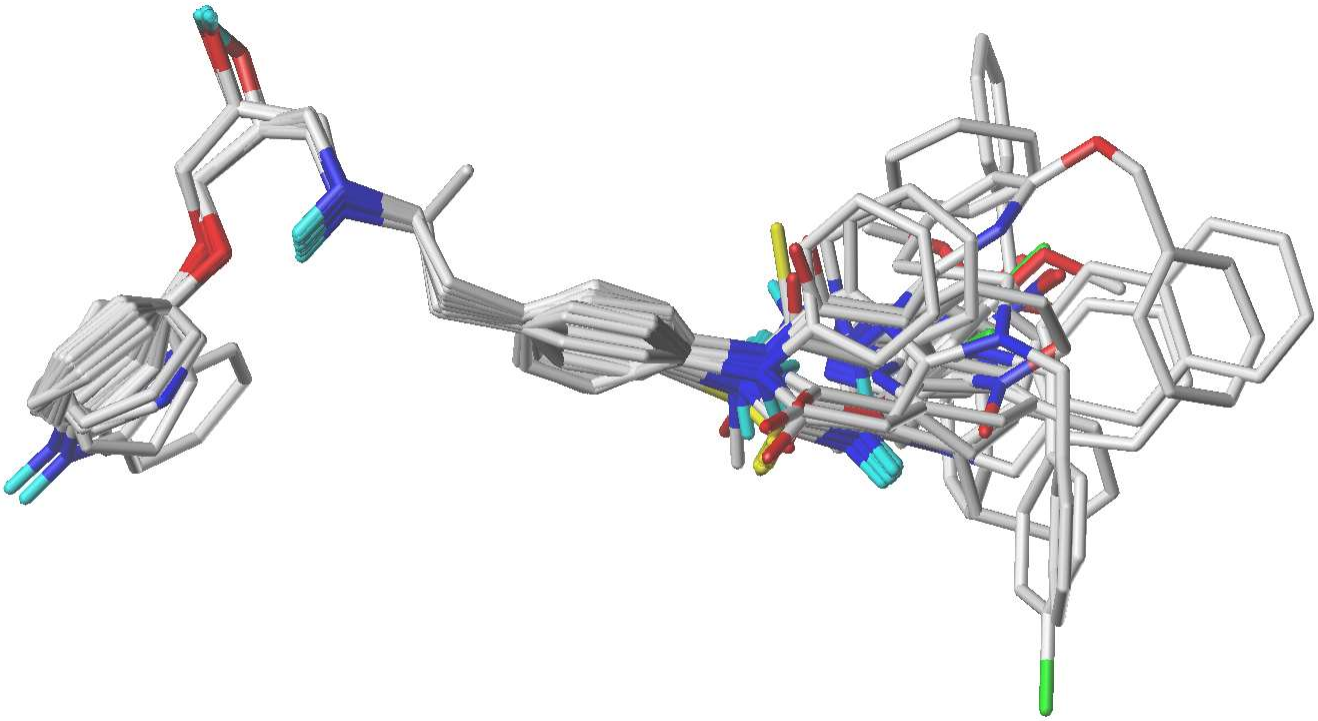

Figure S1. Distill-based alignment of optimized molecules by Powell method.

Table S3. Statistical parameters for CoMFA and CoMSIA based in the Powell minimization method.[a]

Parameter	CoMFA	CoMSIA
q^2	0.176	0.12
N	1	2
SEP	0.655	0.69
SEE	0.469	0.413
r^2	0.577	0.685
F	36.8	28.3
S	0.435	0.130
E	0.565	0.258
H	-	0.120
D	-	0.257
A	-	0.235

[a] q^2 = the square of the LOO cross-validation (CV) coefficient; N = the optimum number of components; SEP = standard error of prediction; SEE is the standard error of estimation of non CV analysis; r^2 is the square of the non CV coefficient; F is the F-test value; S, E, H, D and A are the steric, electrostatic, hydrophobic, hydrogen-bond donor, and hydrogen-bond acceptor contributions respectively.