Supplementary Information

Understanding the Structural Requirements of Hybrid (*S*)-6-((2-(4-Phenylpiperazin-1-yl)ethyl)(propyl)amino)-5,6,7,8-tetrahydronaphthalen-1-ol and its Analogs as D2/D3 Receptor Ligands: A 3D QSAR Investigation

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Table 1. Additional 3D QSAR Model Statistics for Dopamine Receptor Ligands

	I[a]	II [b]	III [c]	IV [d]	V [e]	VI [f]	VII [g]	VIII [h]
Test Set	8,9,13, 16,927, 40,41	8,9,13, 16,9,27, 40,41	8,9,13, 16,927, 40,41	8,9,13, 16,9,27, 40,41	8,9,13, 16,9,27, 40,41	8,9,13, 16,9,27, 40,41	8,9,13, 16,9,27, 40,41	8,9,13, 16,9,27, 40,41
r^2_{cv}	0.644	0.714	0.665	0.71	0.249	0.498	0.339	0.528
r^2_{conv}	0.864	0.929	0.889	0.898	0.937	0.911	0.935	0.925
SEE	0.3	0.221	0.275	0.26	0.189	0.209	0.196	0.194
Comp	3	4	4	3	5	6	6	6
F value	63.47	94.826	58.28	87.76	80.91	57.09	62.58	55.64
$Pr^2=0$	0.00	0. 00	0. 00	0.00	0.00	0.00	0.00	0.00
Steric	0.640	0.667	0.067	0.083	0.658	0.385	0.059	0.028
Elecst	0.360	0.333	0.165	0.103	0.342	0.615	0.143	0.176
Hydro.	0.00	0.00	0.226	0.215	0.00	0.00	0.186	0.204
Donor	0.00	0.00	0.197	0.241	0.00	0.00	0.328	0.300
Accp.	0.00	0.00	0.345	0.357	0.00	0.00	0.285	0.292
r^2_{pred}	0.807	0.902	0.818	0.881	0.199	0.614	0.371	0.608

[a]CoMFA Model based on atom-based alignment and Gasteiger-Hückel charges for D2 receptor binding affinity.

[b]CoMFA Model based on flexible alignment and Gasteiger-Hückel charges for D2 receptor binding affinity.

[c]CoMSIA Model based on flexible alignment and MOPAC charges for D2 receptor binding affinity.

[d]CoMSIA Model based on atom-based alignment and Gasteiger-Hückel charges for D2 receptor binding affinity.

[e]CoMFA Model based on atom-based alignment and Gasteiger-Hückel charges for D3 receptor binding affinity.

[f]CoMFA Model based on flexible alignment and MOPAC charges for D3 receptor binding affinity.

[g]CoMSIA Model based on atom-based alignment and Gasteiger-Hückel charges for D3 receptor binding affinity.

[h]CoMSIA Model based on flexible alignment and MOPAC charges for D3 receptor binding affinity.

Table 2. Additional 3D-QSAR selectivity (D2/D3) Model Statistics for Dopamine Receptor Ligands

	I[a]	II [b]	III [c]	IV [d]
Test Set	6,8,13,18,22,24,31,41	6,8,13,18,22, 24,31,41	6,8,13,18,22, 24,31,41	6,8,13,18,22, 24,31,41
r^2_{cv}	0.596	0.601	0.791	0.768
r^2_{conv}	0.980	0.973	0.977	0.898
SEE	0.099	0.116	0.104	0.206
Comp	5	5	5	2
F value	259.44	186.32	209.43	122.88
$Pr^2=0$	0.00	0.00	0.00	0.00
Steric	0.642	0.660	0.064	0.051
Elecst	0.358	0.340	0.146	0.146
Hydro.	0.00	0.00	0.180	0.143
Donor	0.00	0.00	0.272	0.299
Accp.	0.00	0.00	0.333	0.361
r^2_{pred}	0.809	0.740	0.753	0.628

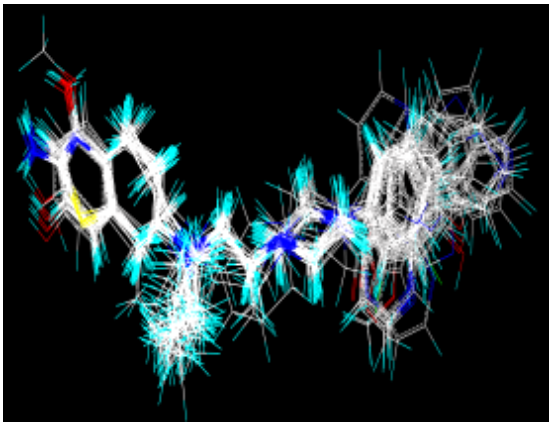
[a] CoMFA Model based on atom-based alignment and Gasteiger-Huckel charges for dopamine D3 selectivity.

[b] CoMFA Model based on flexible alignment and Gasteiger-Huckel charges for dopamine D3 selectivity.

[c] CoMSIA Model based on atom-based alignment and Gasteiger-Huckel charges for dopamine D3 selectivity.

[d] CoMSIA Model based on flexible alignment and MOPAC charges for dopamine D3 selectivity.

a)



b)

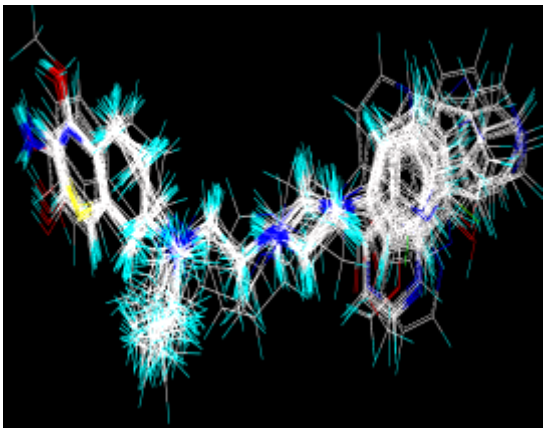


Figure 1. a) Flexible alignment for D2/D3 (selectivity) analysis and b) atom-based alignment for D2/D3 binding (selectivity) analysis with compound **42** as a template.