SUPPORTING INFORMATION

Tandem 3D-QSARs approach as valuable tool to predict binding affinity data: design of new Gly/NMDA receptor antagonists as a key study

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• **Table 1. Training Set**

1,2,4-Triazolo[1,5-a]Quinazoline-2-Carboxylates
(TQX)

MOL	R	R ₇	R ₈	K _i (μM) [³ H]glycine
1	Et	H	H	16.7±1.2
2	Et	Cl	H	3.0±0.4
3	Et	H	Cl	88.2±15.0
4	Et	Cl	Cl	0.71±0.08
5	Et	CF ₃	H	1.8±0.3
6	Et	Br	H	2.6±0.2
7	H	Cl	H	0.17±0.02
8	H	H	Cl	3.5±0.8
9	H	Cl	Cl	0.074±0.003
10	H	CF ₃	H	0.57±0.08
11	H	Br	H	0.39±0.09
12	H	Cl	NO ₂	2.2±0.3
13	Et	Cl		23±5.7
14	Et	Cl		7.1±0.9
15	H	Cl		33.5±5.3
16	H	Cl		0.86±0.09
17	H	Cl		5.3±0.9
18	Et	Cl	NH ₂	4.8±0.5
19	Et	CF ₃		75±8
20	Et	CF ₃		71±4
21	Et	CF ₃		54±9
22	Et	CF ₃	NO ₂	62±12

23	Et	CF3	NH2	5.5±0.9
24	Et	NO2		84±7
25	Et	NO2	NHCOCH3	85±14
26	H	CF3		3.6±0.25
27	H	CF3		8.3±2.1
28	H	CF3		2.6±0.7
29	H	CF3		35±3
30	H	CF3		34±5
31	H	CF3	NO2	4.4±1.0
32	H	CF3	NH2	1.5±0.6
33	H	NO2		65±5.4
34	H	NO2	NH2	2.7±0.05

MOL	R	R ₇	R ₈	R ₉	K _i (μM) [³ H]glycine
35	Et	Cl	H	Cl	4.8±0.5
36	H	Cl	H	Cl	0.14±0.02

Pyrazolo[1,5-c]Quinazoline-2-Carboxylates (PQZ)

MOL	R ₁	R ₂	R ₈	R ₉	K _i (μM) [³ H]glycine
37	H	COOEt	H	H	33.3 ± 7
38	H	COOEt	Cl	H	26.5 ± 4.4
39	H	COOMe	Cl	Cl	1.3 ± 0.2
40	H	COOEt	Cl	NO ₂	10.6 ± 1.8
41	Br	COOEt	Cl	Cl	7.1 ± 0.7
42	COOEt	COOEt	H	H	2.95 ± 0.25
43	COOEt	COOEt	Cl	H	3.4 ± 0.4
44	COOEt	COOEt	Cl	Cl	50 ± 13
45	H	COOH	H	H	1.41 ± 0.3
46	H	COOH	Cl	H	0.48 ± 0.04
47	H	COOH	Cl	Cl	0.16 ± 0.04
48	H	COOH	Cl	NO ₂	1.1 ± 0.1
49	CH ₃	COOH	H	H	0.78 ± 0.17
50	Cl	COOH	Cl	H	0.18 ± 0.04
51	Cl	COOH	Cl	Cl	0.16 ± 0.01
52	Br	COOH	Cl	Cl	4.0±0.6
53	COOEt	COOH	H	H	1.15±0.2
54	COOEt	COOH	Cl	Cl	0.22 ± 0.04
55	COOH	COOH	H	H	0.54 ± 0.12
56	COOH	COOH	Cl	H	0.09 ± 0.01
57	COOH	COOH	Cl	Cl	0.059 ± 0.01

MOL	R ₂	R ₈	R ₉	K _i (μM) [³ H]glycine
58	COOH	H	H	2.0±0.4
59	COOMe	Cl	H	10.6±3.9
60	COOH	Cl	H	0.24±0.03
61	COOMe	Cl	Cl	4.0±1.0
62	COOH	Cl	Cl	0.19±0.02

Table 2. Test Set

1,2,4-Triazolo[1,5-a]Quinazoline-2-Carboxylates
(TQX)

MOL	R	R ₇	R ₈	K _i (μM) [³ H]glycine
63	Et	Cl		19±5.5
64	Et	Cl	NO ₂	10.24±2.1
65	H	H	H	1.1±0.02

Pyrazolo[1,5-c]Quinazoline-2-Carboxylates
(PQZ)

MOL	R ₁	R ₂	R ₈	R ₉	K _i (μM) [³ H]glycine
66	COOEt	COOH	Cl	H	0.86 ± 0.2
67	H	COOEt	Cl		57±9
68	H	COOH	Cl		8.2±3

Table 3. Additional Test Set

Pyrazolo[1,5-c]Quinazoline-2-Carboxylates
(PQZ)

MOL	R ₁	R ₂	R ₈	R ₉	K _i (μM) [³ H]glycine
72	COOEt	COOEt	CF ₃	H	3.2 ± 0.3
73	COOH	COOH	CF ₃	H	0.072 ± 0.01

1,2,4-Triazolo[1,5-a]Quinazoline-2-Carboxylates
(TQX)

MOL	R	R ₇	R ₈	K _i (μM) [³ H]glycine
78	Et	CN	H	22 ± 4
79	H	CN	H	2.2 ± 0.3