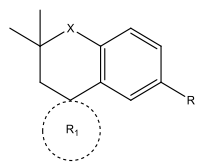
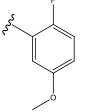
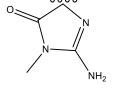
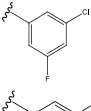
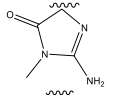
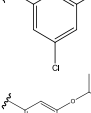
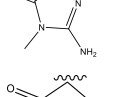
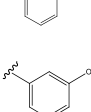
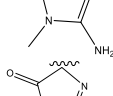
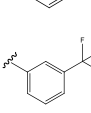
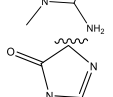
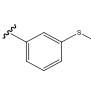
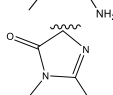
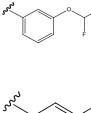
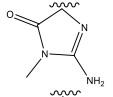
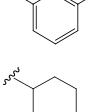
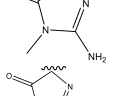
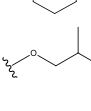
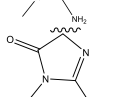
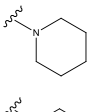
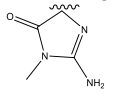
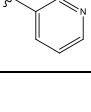
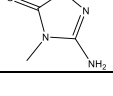





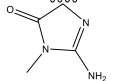

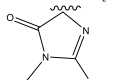

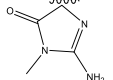

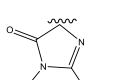
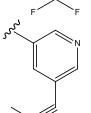
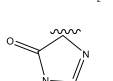

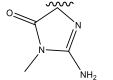

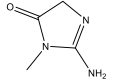

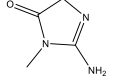

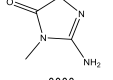

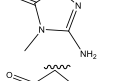

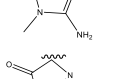

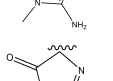

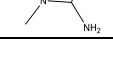



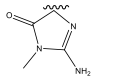

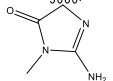

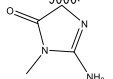

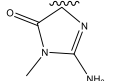

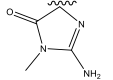

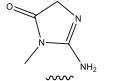

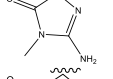

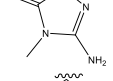

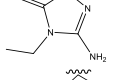

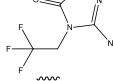

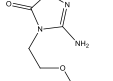

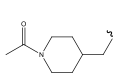

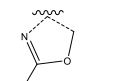
**Table 1** A Series of Spirocyclic BACE-1 Inhibitors and Their Structural Parameters and Inhibitory Activity.















Compd. No.	X	R	R <sub>1</sub>	MW	MATS6m	MATS8p	MATS6i	GATS2v	pIC <sub>50</sub>		ΔpIC <sub>50</sub>
									Obsd.a	Cald. From eq. 1	
1	O	Br		338.23	-0.02	-0.14	-0.15	0.64	4.43	4.74	0.31
2	O			335.44	-0.14	0.2	-0.11	0.78	6.34	6.18	-0.16
3	O			369.88	-0.11	0.25	-0.11	0.72	7.62	7.03	-0.59
4 <sup>b</sup>	O			360.45	-0.14	0.24	-0.11	0.74	7.03	6.91	-0.12
5	O			365.47	-0.14	0.16	-0.12	0.71	7.17	6.81	-0.36
6	O			365.47	-0.12	0.14	-0.13	0.71	5.77	6.54	0.77
7 <sup>b</sup>	O			365.47	-0.06	0.11	-0.09	0.71	5.14	6.32	1.18
8 <sup>b</sup>	O			404.32	-0.11	0.3	-0.11	0.67	7.55	7.93	0.38
9 <sup>b</sup>	O			383.46	-0.22	0.16	-0.07	0.69	7.22	7.9	0.68

10	O			383.46	-0.11	0.16	-0.14	0.69	7.22	6.85	-0.37
11	O			387.87	-0.12	0.24	-0.1	0.7	7.41	7.48	0.07
12	O			387.87	-0.1	0.25	-0.12	0.7	7.44	7.3	-0.15
13 <sup>b</sup>	O			393.53	-0.09	0.09	-0.09	0.78	5.54	6.55	1.01
14	O			379.5	-0.12	0.12	-0.1	0.77	7.16	6.55	-0.61
15	O			403.44	-0.1	0.15	-0.12	0.74	7.13	6.94	-0.2
16 <sup>b</sup>	O			381.54	-0.12	0.21	-0.1	0.76	6.46	6.97	0.51
17	O			401.45	-0.11	0.16	-0.12	0.74	7.55	7.01	-0.55
18	O			353.43	-0.14	0.19	-0.1	0.76	7	6.61	-0.39
19	O			417.6	-0.12	0.1	-0.1	0.9	6.56	6.52	-0.03
20	O			331.46	-0.21	0.23	-0.17	0.79	6.37	6.25	-0.11
21 <sup>b</sup>	O			342.49	-0.13	0.18	-0.12	0.86	5.06	5.78	0.72
22 <sup>b</sup>	O			336.43	-0.15	0.23	-0.14	0.74	6.95	6.33	-0.61

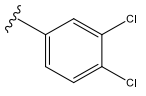
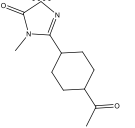
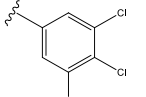
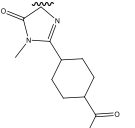
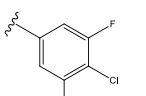
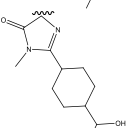
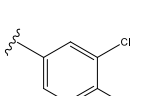
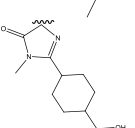
23	O			336.43	-0.13	0.16	-0.11	0.75	5.63	6.13	0.5
24 <sup>c</sup>	O			336.43	-0.13	0.2	-0.12	0.74	5.2	-	-
25	O			370.87	-0.12	0.29	-0.14	0.68	7.47	7.21	-0.26
26	O			404.43	-0.11	0.17	-0.14	0.7	7.2	7.16	-0.04
27 <sup>b</sup>	O			374.48	-0.13	0.24	-0.12	0.71	8	7.17	-0.83
28	O			354.42	-0.13	0.22	-0.14	0.72	6.89	6.55	-0.34
29	O			354.42	-0.15	0.22	-0.13	0.72	6.84	6.8	-0.03
30	O			337.42	-0.15	0.26	-0.17	0.69	6.82	6.55	-0.27
31	O			342.46	-0.01	0.31	-0.13	0.68	6.3	6.28	-0.02
32 <sup>b</sup>	O			382.46	-0.23	0.22	-0.01	0.76	6.64	8.19	1.56
33 <sup>b</sup>	S			403.94	-0.07	0.29	-0.07	0.66	7.64	7.97	0.33
34	CH2			385.9	-0.18	0.31	-0.08	0.72	7.62	8.06	0.44
35	S			376.52	-0.05	0.27	-0.07	0.69	7.33	7.18	-0.14

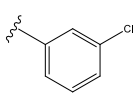
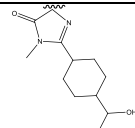
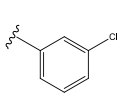
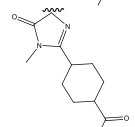
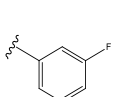
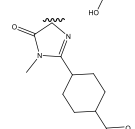
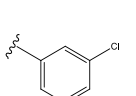
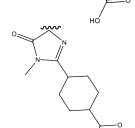
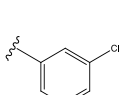
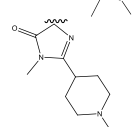
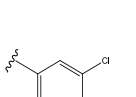
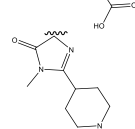
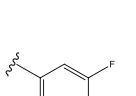
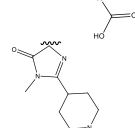
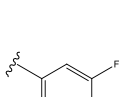
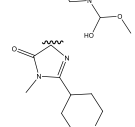
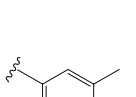
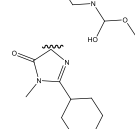
36	CH2			358.48	-0.22	0.3	-0.08	0.75	7.64	7.66	0.02
37	CH2			352.45	-0.2	0.29	-0.11	0.74	7.22	7.29	0.07
38	S			386.94	-0.06	0.38	-0.09	0.64	7.66	7.91	0.25
39 <sup>b</sup>	CH2			368.9	-0.18	0.39	-0.11	0.7	7.52	7.98	0.46
40	S			353.49	-0.06	0.31	-0.12	0.64	6.87	6.93	0.06
41	CH2			335.45	-0.24	0.36	-0.14	0.71	6.86	7.46	0.6
42	CO			335.4	-0.18	0.21	-0.19	0.74	6.15	6.14	-0.01
43	CF2			357.4	-0.09	0.26	-0.14	0.75	5.83	6.4	0.58
44	O			383.91	-0.09	0.06	-0.09	0.78	6.59	6.34	-0.25
45 <sup>c</sup>	O			437.88	-0.12	0.04	-0.08	0.78	6.22	-	-
46	O			413.94	-0.16	0.17	-0.12	0.76	6.91	7.43	0.52
47	O			481.04	-0.08	-0.07	0.05	0.84	7.66	7.91	0.26
48	CH2			341.87	-0.03	0.3	-0.12	0.76	6.1	6.01	-0.09

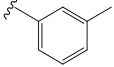
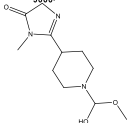
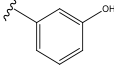
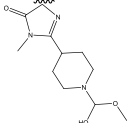
49	CH2			357.94	-0.13	0.23	-0.21	0.79	5.7	5.92	0.22
50	CH2			371.97	0.04	0.24	-0.14	0.83	5.24	5.44	0.2
51	CH2			382.93	0.03	0.01	-0.24	0.74	4.48	4.69	0.2
52	CH2			325.42	-0.05	0.16	-0.12	0.8	5.23	5.2	-0.03
53 <sup>b</sup>	CH2			325.42	-0.02	0.18	-0.13	0.81	5.72	5	-0.72
54	CH2			308.42	-0.05	0.29	-0.16	0.78	5.31	5.25	-0.06

<sup>a</sup>Taken from ref [5], <sup>b</sup>Test set, <sup>c</sup>Outlier

**Table 2** Some Proposed Compounds Belonging to the Series of Table 1 and their Predicted Activity

Compd. No.	X	R	R1	MW	MATS6m	MATS8p	MATS6i	GATS2v	pIC <sub>50</sub>
1	O			487.2	-0.05	0.02	0.19	0.76	9.34
2	O			522.65	-0.05	-0.06	0.17	0.73	9.63
3	O			522.65	-0.05	-0.06	0.17	0.73	9.63
4	O			487.2	-0.05	0.02	0.19	0.76	9.34

5	O			451.75	-0.03	-0.02	0.22	0.78	8.63
6	O			455.74	-0.02	0.2	0.28	0.61	10.57
7	O			439.29	0.05	0.32	0.12	0.67	9.02
8	O			463.76	-0.03	-0.01	0.23	0.79	8.88
9	O			455.74	-0.02	0.2	0.28	0.61	10.57
10	O			491.19	-0.04	0.22	0.25	0.59	11.22
11	O			486.75	-0.03	0.34	0.11	0.65	10.38
12	O			470.3	-0.01	0.21	0.04	0.7	8.82
13	O			456.32	0.18	0.28	0.33	0.62	9.9

14	O			444.31	0.18	0.32	0.32	0.63	9.81
15	O			448.3	0.11	0.22	0.26	0.67	9.4