Supplementary Information

Synthesis and evaluation of 2,3,4,9-tetrahydro-1*H*-carbazole derivatives as selective acetylcholinesterase inhibitors: Potential anti-Alzheimer's agents

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Compound No.	InChI	Biological Activity (IC_{50})[a]	
		IC_{50} (µM) AChE	IC_{50} (µM) BChE
Donepezil	1/C22H27N/c1-2-6-19(7-3-1)17-23-12-10-18(11-13-23)14-20-15-21-8-4-5-9-22(21)16-20/h1-9,18,20H,10-17H2	0.0427 ± 0.078	1.216 ± 0.045
1	1/C12H13N/c1-3-7-11-9(5-1)10-6-2-4-8-12(10)13-11/h1,3,5,7,13H,2,4,6,8H2	2.02 ± 0.479	8.97 ± 0.450
2	1/C12H12N2O2/c15-14(16)8-5-6-12-10(7-8)9-3-1-2-4-11(9)13-12/h5-7,13H,1-4H2	2.68 ± 0.652	7.31 ± 0.890
3	1/C12H14N2/c13-8-5-6-12-10(7-8)9-3-1-2-4-11(9)14-12/h5-7,14H,1-4,13H2	0.0388 ± 0.852	0.482 ± 0.180
4	1/C13H14N2O2/c1-14-12-5-3-2-4-10(12)11-8-9(15(16)17)6-7-13(11)14/h6-8H,2-5H2,1H3	0.0324 ± 0.432	2.553 ± 0.770
5	1/C14H16N2O2/c1-2-15-13-6-4-3-5-11(13)12-9-10(16(17)18)7-8-14(12)15/h7-9H,2-6H2,1H3	1.94 ± 0.400	6.04 ± 0.610
6	1/C15H18N2O2/c1-2-9-16-14-6-4-3-5-12(14)13-10-11(17(18)19)7-8-15(13)16/h7-8,10H,2-6,9H2,1H3	4.19 ± 0.630	14.38 ± 0.150
7	1/C16H20N2O2/c1-2-3-10-17-15-7-5-4-6-13(15)14-11-12(18(19)20)8-9-16(14)17/h8-9,11H,2-7,10H2,1H3	4.50 ± 0.560	11.21 ± 0.780
8	1/C17H22N2O2/c1-2-3-6-11-18-16-8-5-4-7-14(16)15-12-13(19(20)21)9-10-17(15)18/h9-10,12H,2-8,11H2,1H3	5.24 ± 0.873	13.29 ± 0.520

9	1/C18H24N2O2/c1-2-3-4-7-12-19-17-9-6-5-8-15(17)16-13-14(20(21)22)10-11-18(16)19/h10-11,13H,2-9,12H2,1H3	4.88 ± 0.578	12.05 ± 0.320
10	1/C19H26N2O2/c1-2-3-4-5-8-13-20-18-10-7-6-9-16(18)17-14-15(21(22)23)11-12-19(17)20/h11-12,14H,2-10,13H2,1H3	12.43 ± 0.698	9.16 ± 0.310
11	1/C19H18N2O4S/c1-13-6-9-15(10-7-13)26(24,25)20-18-5-3-2-4-16(18)17-12-14(21(22)23)8-11-19(17)20/h6-12H,2-5H2,1H3	6.90 ± 0.810	7.63 ± 0.880
12	1/C13H14N2O4S/c1-20(18,19)14-12-5-3-2-4-10(12)11-8-9(15(16)17)6-7-13(11)14/h6-8H,2-5H2,1H3	8.41 ± 0.566	9.03 ± 0.650
13	1/C18H16N2O4S/c21-20(22)13-10-11-18-16(12-13)15-8-4-5-9-17(15)19(18)25(23,24)14-6-2-1-3-7-14/h1-3,6-7,10-12H,4-5,8-9H2	13.64 ± 0.829	11.98 ± 0.300
14	1/C19H18N2O2/c22-21(23)15-10-11-19-17(12-15)16-8-4-5-9-18(16)20(19)13-14-6-2-1-3-7-14/h1-3,6-7,10-12H,4-5,8-9,13H2	2.78 ± 0.326	10.0 ± 0.800
15	1/C14H18N2/c1-2-15-10-7-8-14-12(9-10)11-5-3-4-6-13(11)16-14/h7-9,15-16H,2-6H2,1H3	1.64 ± 0.528	1.82 ± 0.326
16	1/C15H20N2/c1-2-9-16-11-7-8-15-13(10-11)12-5-3-4-6-14(12)17-15/h7-8,10,16-17H,2-6,9H2,1H3	2.21 ± 0.823	1.79 ± 0.681
17	1/C16H22N2/c1-2-3-10-17-12-8-9-16-14(11-12)13-6-4-5-7-15(13)18-16/h8-9,11,17-18H,2-7,10H2,1H3	0.203 ± 0.208	4.13 ± 0.268
18	1/C17H24N2/c1-2-3-6-11-18-13-9-10-17-15(12-13)14-7-4-5-8-16(14)19-17/h9-10,12,18-19H,2-	2.27 ± 0.400	7.82 ± 0.427

	8,11H2,1H3		
19	1/C19H20N2O2S/c1-13-6-9-15(10-7-13)24(22,23)21-14-8-11-19-17(12-14)16-4-2-3-5-18(16)20-19/h6-12,20-21H,2-5H2,1H3	3.63 ± 0.946	4.68 ± 0.589
20	1/C13H16N2O2S/c1-18(16,17)15-9-6-7-13-11(8-9)10-4-2-3-5-12(10)14-13/h6-8,14-15H,2-5H2,1H3	5.75 ± 0.750	6.14 ± 0.457
21	1/C18H18N2O/c1-2-6-14(7-3-1)21-20-13-10-11-18-16(12-13)15-8-4-5-9-17(15)19-18/h1-3,6-7,10-12,19-20H,4-5,8-9H2	11.28 ± 0.622	13.24 ± 0.482
22	1/C19H20N2/c1-2-6-14(7-3-1)13-20-15-10-11-19-17(12-15)16-8-4-5-9-18(16)21-19/h1-3,6-7,10-12,20-21H,4-5,8-9,13H2	5.40 ± 0.382	9.45 ± 0.726

[a] Mice acetylcholinesterase was obtained from brain and butyrylcholinesterase from serum. The AChE activity was measured by the method of Ellman spectrophotometric method with slight modification.[1, 2]This was measured on basis of the formation of yellow color due to the reaction of thiocholine with dithiobisnitrobenzoate ions. The rate of formation of thiocholine from Acetylthiocholine Iodide in the presence of cholinesterase was measured using a spectrophotometer. 0.5 mL of clear supernatant liquid of the brain homogenate was pipetted out into 25 mL volumetric flask and dilution was made with a freshly prepared 5,5'-Dithiobis-(2-nitrobenzoic acid) (DTNB) solution (10 mg DTNB in 100 mL of Sorenson phosphate buffer, pH 8.0). From the volumetric flask, two 4 mL portions were pipetted out into test tubes. Into one of the test tube, 2 drops of donepezil solution was added. 1 mL of substrate solution (75 mg of Acetylthiocholine iodide per 50 mL of distilled water or 75 mg of Butyrylthiocholine iodide per 50 mL of distilled water) was pipetted out into both of the test tubes. The test tube containing donepezil was taken as blank and the absorbance of the test sample was read spectrophotometrically (DU 640B spectrophotometer, Beckman Coulter Inc., CA, USA) at 420 nm and IC_{50} values have been calculated. All experiments have been performed in triplicate.

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