Supporting information

Exploring the multifunctionality of thioflavin- and deferiprone-based molecules as acetylcholinesterase inhibitors for potential application in Alzheimer's disease

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Complete References

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Table S1. Crystal and Refinement Data for **BXc**, **BTc, Hppp** and **Cppp**

cryst data	**BXc**	**BTc**
formula	$C_{16}H_{14}N_2O_3$	$C_{16}H_{14}N_2O_2S$
fw	282.29	298.35
crystal system	monoclinic	monoclinic
space group	$P2_1/c$	$P2_1/c$
color of crystal	colorless	pale yellow
a (Å)	9.2499(4)	9.7184(4)
b (Å)	17.8481(7)	13.6885(6)
c (Å)	9.1282(4)	10.8658(5)
α (deg)	90	90
β (deg)	115.0460(10)	106.839(3)
γ (deg)	90	90
V [Å^3]	1365.30(10)	1383.50(10)
Temp (K)	100.0(2)	90.0(1)
Z	4	4
D_{calcd} [g/cm^3]	1.373	1.432
μ (Mo Kα) [cm^{-1}]	0.97	2.40
F_{000}	592	624
θ_{min}-θ_{max} (deg)	2.28 – 30.18	2.19 – 30.10
hkl range	-13/10,-24/25,-12/11	-13/13,-19/19,-15/13
reflections collected	23774	21989
independent reflections (R_{int})	4018 (0.029)	4066 (0.038)
observed reflection [I>2s(I)]	3200	3256
agreement indexes [I>2s(I)]	R(F) = 0.038 $R_w(F^2)$ = 0.090	R(F) = 0.037 $R_w(F^2)$ = 0.085
agreement indexes (all data)	R(F) = 0.052 $R_w(F^2)$ = 0.098	R(F) = 0.054 $R_w(F^2)$ = 0.095
GOF (all data)	1.02	1.05

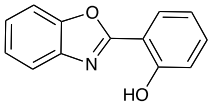
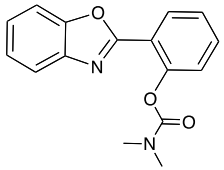
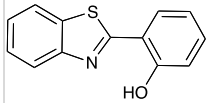
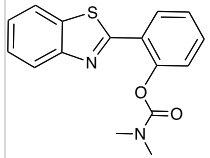
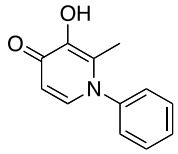
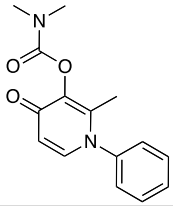
cryst data	**Hppp**	**Cppp**
formula	$C_{12}H_{11}NO_2$ MeOH	$C_{15}H_{16}N_2O_3$
fw	233.26	272.30
crystal system	triclinic	triclinic
space group	P_{-1}	P_{-1}
color of crystal	colorless	colorless
a (Å)	7.597(1)	7.9251(4)
b (Å)	9.601(2)	8.3409(4)
c (Å)	9.999(2)	11.1686(6)
α (deg)	100.928(4)	97.746(3)
β (deg)	111.838(3)	110.719(3)
γ (deg)	107.261(3)	95.600(3)
V [Å^3]	608.4(2)	1114.6(2)
Temp (K)	90(1)	100(2)
Z	2	2
D_{calcd} [g/cm^3]	1.273	1.338
μ (Mo Kα) [cm^{-1}]	0.91	0.94
F_{000}	248	288
θ_{min}-θ_{max} (deg)	2.33-28.78	2.75-28.26
hkl range	-10/10, -12/13, -13/13	-10/10, -11/10, -14/14
reflections collected	13793	12110
independent reflections (R_{int})	3135 (0.039)	3322 (0.027)
observed reflection [I>2s(I)]	2250	2665
agreement indexes [I>2s(I)]	R(F) = 0.050 $R_w(F^2)$ = 0.131	R(F) = 0.042 $R_w(F^2)$ = 0.108
agreement indexes (all data)	R(F) = 0.075 $R_w(F^2)$ = 0.147	R(F) = 0.055 $R_w(F^2)$ = 0.118
GOF (all data)	1.04	1.02

Table S2. Selected bond lengths (Å) and angles (º) in **BXc**, **BTc**, **Cppp** and **Hppp**

BXc		**BTc**	
Atoms	**Distance**	**Atoms**	**Distance**
C1-C2	1.3982(14)	C1-C2	1.3957(19)
C2-C3	1.4033(14)	C2-C3	1.4022(19)
C3-C4	1.3793(17)	C3-C4	1.384(2)
C4-C5	1.3862(16)	C4-C5	1.387(2)
C5-C6	1.3866(14)	C5-C6	1.382(2)
C6-C1	1.3772(15)	C6-C1	1.3864(19)
C1-O1	1.3965(11)	C1-O1	1.3915(16)
Atoms	**Angle**	**Atoms**	**Angle**
C1-C2-C12-O13	176.3(12)	C1-C2-C12-S13	6.13(19)
C1-C2-C12-N11	-3(3)	C1-C2-C12-N11	-174.10(13)
C3-C2-C12-O13	-3(3)	C3-C2-C12-S13	-175.31(10)
C3-C2-C12-N11	178(2)	C3-C2-C12-N11	4.47(19)

Hppp		**Cppp**	
Atoms	**Distance**	**Atoms**	**Distance**
C3-O2	1.353(2)	C3-O2	1.404(1)
C4-O1	1.261(2)	C4-O1	1.252(2)
C2-N1	1.381(2)	C2-N1	1.389(2)
C2-C3	1.368(2)	C2-C3	1.363(2)
C3-C4	1.436(2)	C3-C4	1.447(2)
C4-C5	1.413(2)	C4-C5	1.447(2)
C5-C6	1.357(2)	C5-C6	1.354(2)
C6-N1	1.360(2)	C6-N1	1.373(2)
Atoms	**Angle**	**Atoms**	**Angle**
C8-C7-N1-C6	-70.15(19)	C8-C7-N1-C6	104.07(14)
C12-C7-N1-C6	107.45(16)	C12-C7-N1-C6	-75.52(15)
C12-C7-N1-C2	-71.92(19)	C12-C7-N1-C2	101.48(14)
C8-C7-N1-C2	110.48(16)	C8-C7-N1-C2	-78.93(15)

Table S3. Physicochemical properties and log BB calculated values. All the parameters are defined in the manuscript.

						
ID	**HBX**	**BXc**	**HBT**	**BTc**	**Hppp**	**Cppp**
MW	211.22	282.29	227.28	298.36	201.22	272.30
clogP	2.74	2.90	3.42	3.56	0.97	0.39
TPSA	46.26	55.57	33.12	42.43	40.54	49.85
LogD	3.01	3.06	3.82	3.86	2.35	2.38
HBA	2	2	2	2	3	3
HBD	1	0	1	0	1	0
rotatable bonds	1	3	1	3	1	3
ring count	3	3	3	3	2	2
Lipinski's rules	true	true	true	true	true	true
Lead likeness	true	true	true	true	true	true
Log BB	-0.13	-0.24	0.17	0.052	-0.31	-0.54

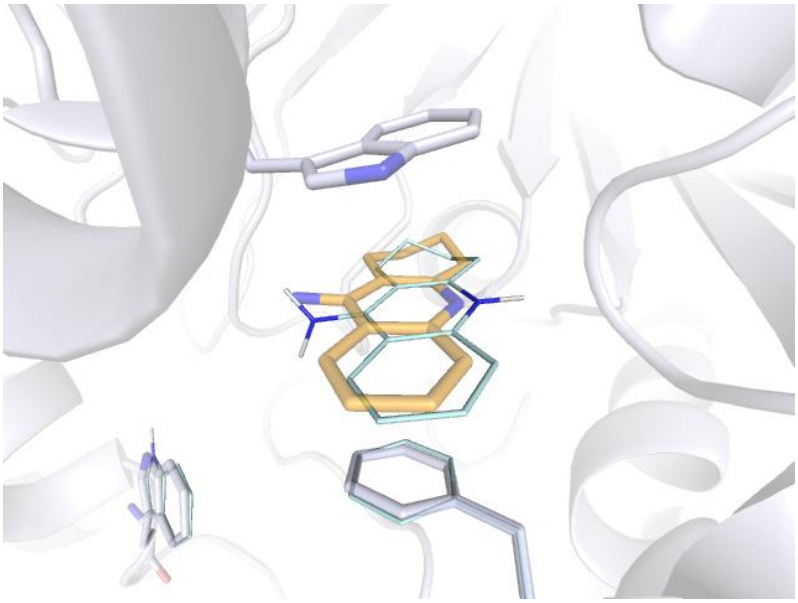


Fig. S1. Predicted binding mode of tacrine and X-ray crystallographic structure of *Torpedo Californica* AChE complex (PDB entry 1ACJ). Docked (in lines) and X-ray (in sticks) structures of the ligand are shown. Notably Phe330 and Trp279, allowed flexible during molecular docking, are coincident with X-ray position.