Supporting information

Conformational remodeling of femtomolar inhibitor-acetylcholinesterase complexes in the crystalline state

Yves Bourne*, Zoran Radic, Palmer Taylor, Pascale Marchot*

yves.bourne@afmb.univ-mrs.fr; pascale.marchot@univmed.fr

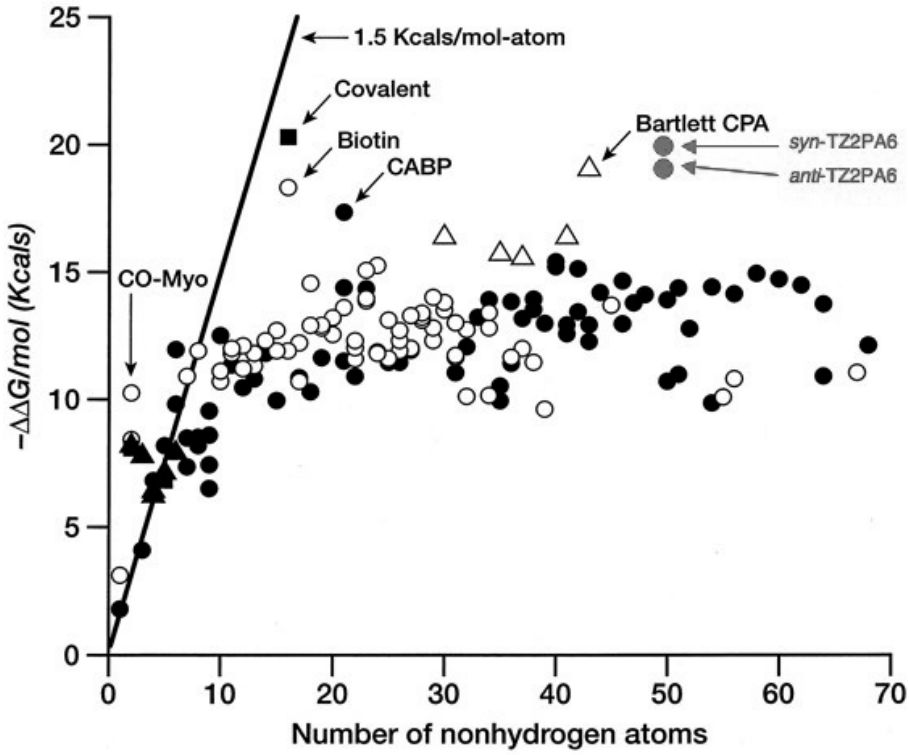

Figure S1. Free energy of binding of the TZ2PA6 *syn1* and *anti1* regioisomers to the Tyr337Ala mutant of mAChE, relative to that for various ligands and enzyme inhibitors and as a function of the number of nonhydrogen atoms in the ligand. The *syn1* and *anti1* regioisomers, of formulae $C_{42}H_{45}N_8$, contain 50 nonhydrogen atoms. The line has a slope of 1.5 kcal/mol and an intercept of 0. *Open triangles* stand for metal ions or metalloenzymes, *black triangles* for small anions, *open circles* for natural ligands, and *black circles* for enzyme inhibitors. The positions for some well-known ligands/inhibitors are displayed: carbon oxide (CO-Myo) for myoglobin; biotin for streptavidin; carboxyl arabinitol bisphosphate (CABP) for ribulose disphosphate carboxylase; peptide phosphonates (Bartlett CPA) for carboxypeptidase[38]. "Covalent" (*black square*) could denote 1,1,1-trifluoroacetophenone for AChE.[39] (Based on Fig. 1 in ref[26], with permission (Copyright 2004, National Academy of Sciences, USA).

References

(26) Kuntz, I.D.; Chen, K.; Sharp, K.A.; Kollman, P.A. *Proc. Natl. Acad. Sci. USA* **1999**, *96*, 9997-10002.

(38) Kaplan, A.P.; Bartlett, P.A. *Biochemistry* **1991**, *30*, 8165-70.

(39) Nair, H.K.; Lee, K.; Quinn, D.M. *J. Am. Chem. Soc.* **1993**, *115*, 9939-41.