Čadež et al. Click-chemistry-derived oxime library reveals efficient reactivators of nerve agent-inhibited butyrylcholinesterase suitable for pseudocatalytic bioscavenging. Archives of Toxicology, 2025, Supplementary material
https://doi.org/10.1007/s00204-025-03985-6

Supplementary material

# Click-chemistry-derived oxime library reveals efficient reactivators of nerve agent-inhibited butyrylcholinesterase suitable for pseudocatalytic bioscavenging

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## Contents

# S1. Reactivation efficacy of cyclosarin inhibited BChE *in vitro*

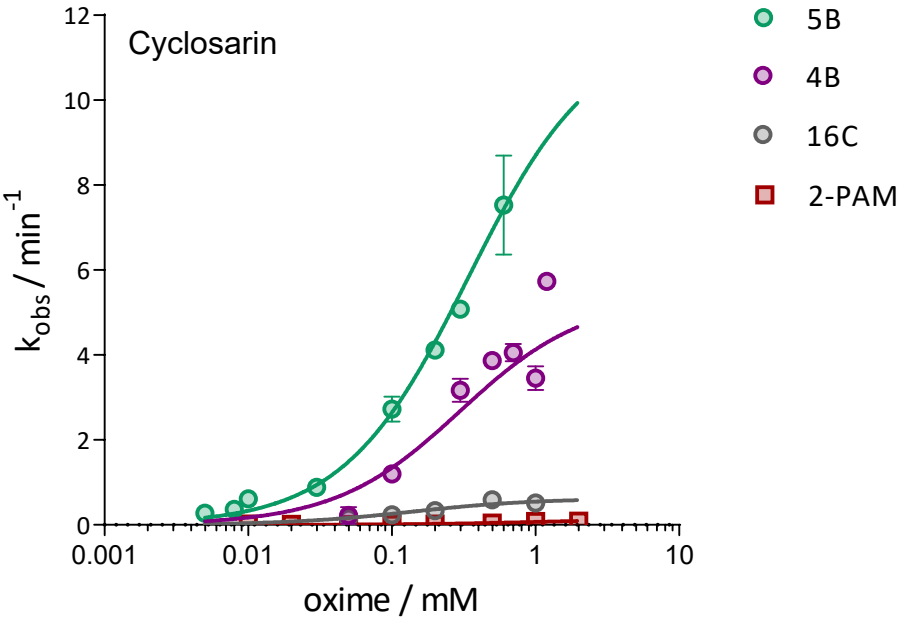


**Figure S1**. Reactivation kinetics of cyclosarin-inhibited BChE by the selected oximes. The results are expressed as mean ± SEM calculated from at least three experiments.

# S2. Biphasic response of cyclosarin inhibited BChE reactivated with oxime 16C

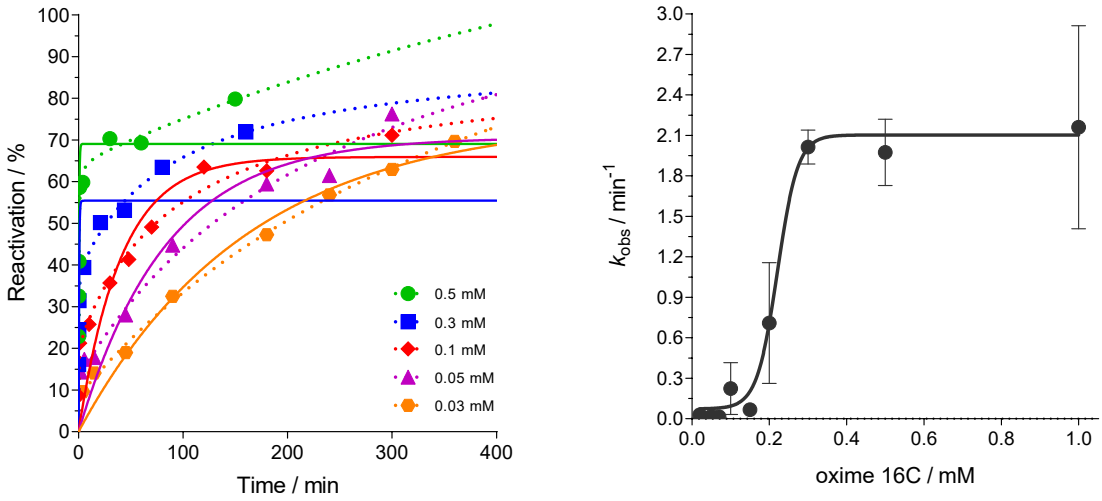


**Figure S2**. Deviation from the typical hyperbolic model in the reactivation of sarin-inhibited BChE with oxime 16C. The left graph shows changes in reactivation percentage over time, with dependence described by a theoretical single-phase curve (solid line) and a modified two-phase curve (dashed line) for each oxime concentration. The right graph illustrates the dependence of observed reactivation rates on oxime concentration. The mean of at least seven experiments ± SEM is presented.

# S3. Reactivation efficacy of cyclosarin inhibited AChE *in vitro*

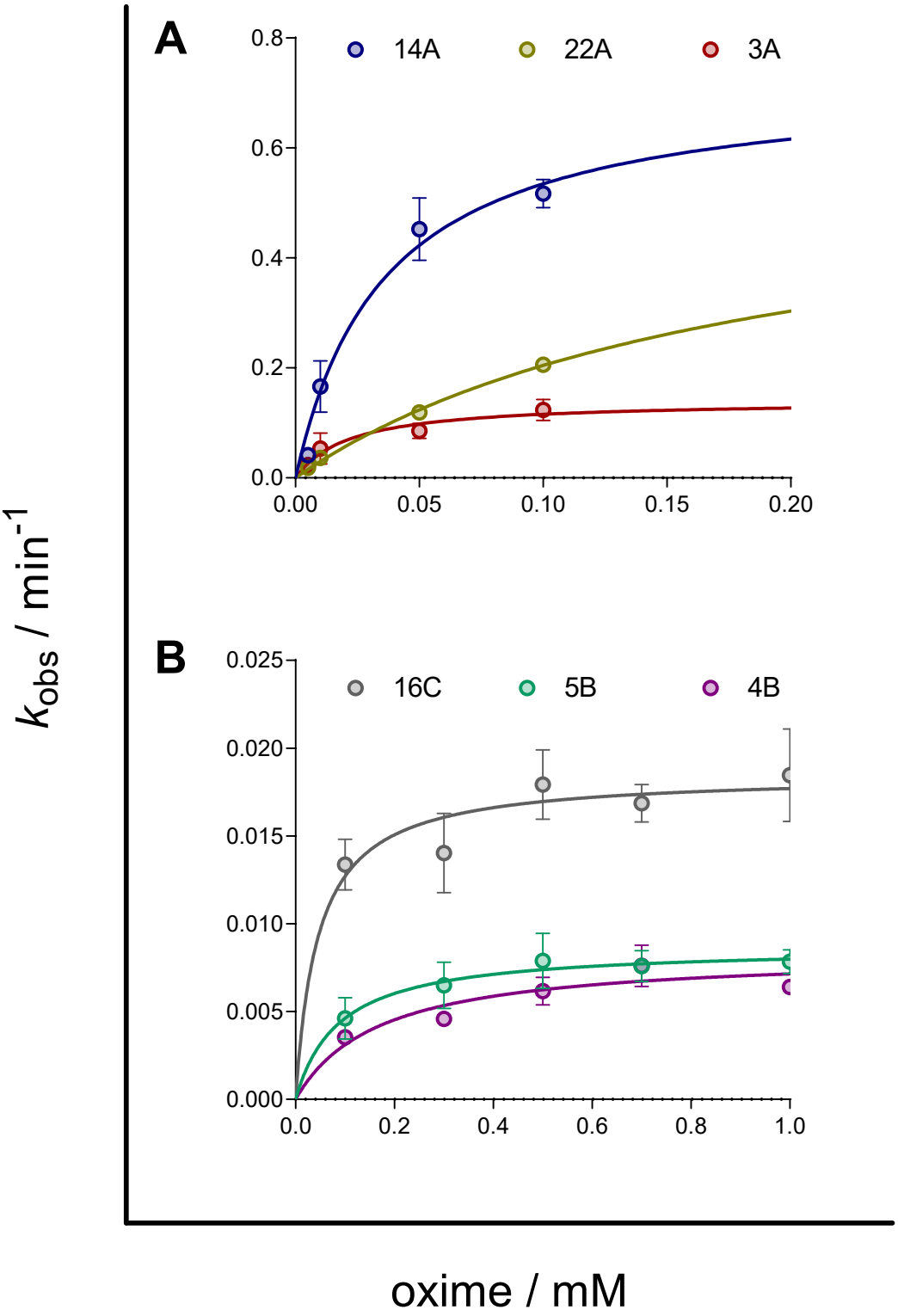


**Figure S3**. Reactivation kinetics ($k_{obs}$) of cyclosarin-inhibited AChE determined with (A) bis-pyridinium (14A, 22A or 3A) and (B) mono-pyridinium (16C, 5B or 4B) oximes.

# S4. Molecular modeling

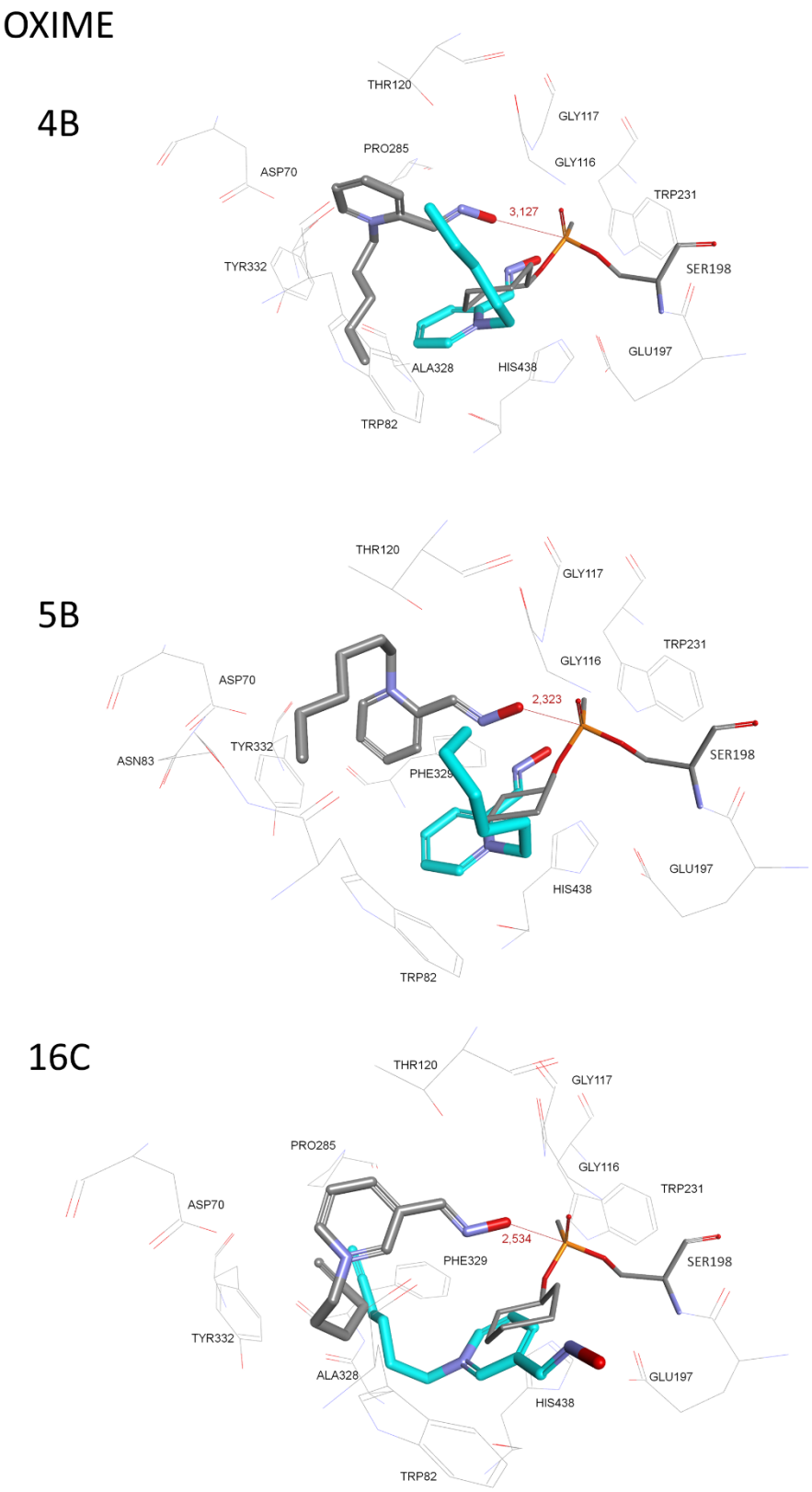


**Figure S4.** Superposition of binding poses of oximes in the active site of native BChE (blue) and in the near-attack conformation in BChE-cyclosarin conjugate (grey; given in **Figure 5**). The red line indicates the distance of the oxime group from the phosphorus atom of cyclosarin conjugate.

# S5. Molecular dynamics

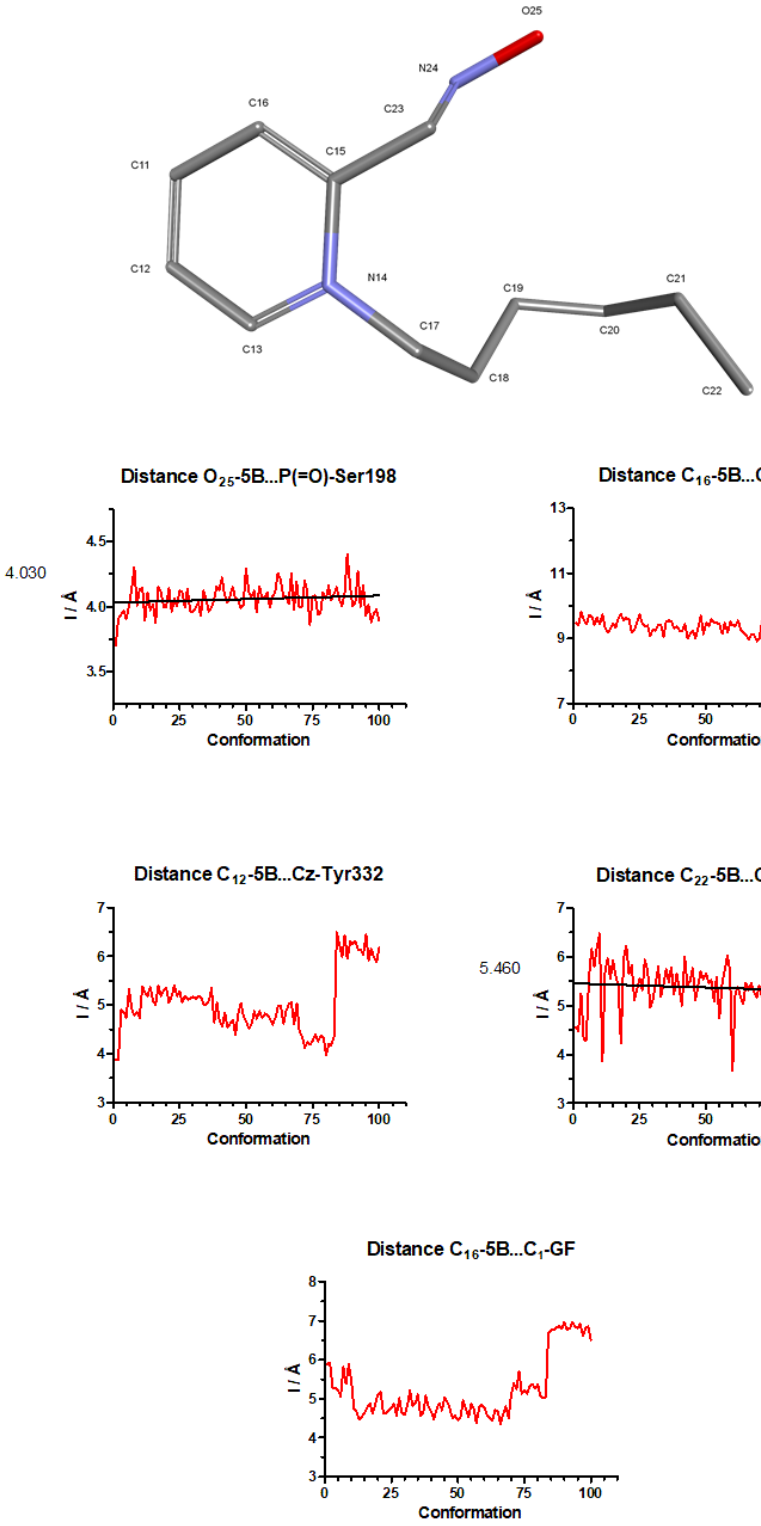


**Figure S5.** Molecular dynamics simulation (t=10 ns) of complex between an oxime 5B and cyclosarin-conjugate of BChE. Distances between atoms of 5B and selected atoms of BChE active site residues are shown. Distance average value (Å) is listed left of Y-axes.