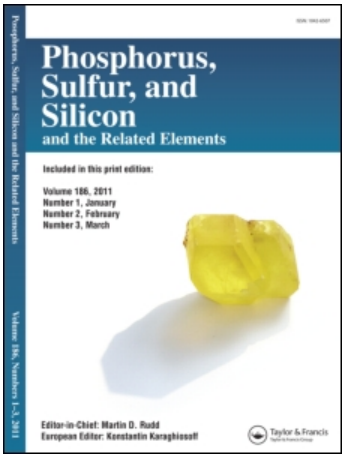

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O-[7-(1-Methylquinolinium)]-1,3,2-Dioxaphosphorinane 2-Oxide Iodide: A Reversible Anti-acetylcholinesterase and Irreversible Anti-butyrylcholinesterase Organophosphorus Ester

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O-[7-(1-Methylquinolinium)]-1,3,2-Dioxaphosphorinane 2-Oxide Iodide: A Reversible Anti-acetylcholinesterase and Irreversible Anti-butyrylcholinesterase Organophosphorus Ester

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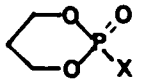
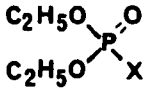
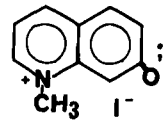
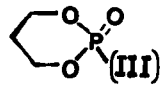
P.O.BOX 19 , NESS-ZIONA , ISRAEL.

Although cyclic organophosphates(OP) esters (I) and their open-chain analogs (II) demonstrate similar reactivity of a P atom towards nucleophilic

I ,  ; II,  ; III,  ; IV , 

displacement in aqueous solutions, the open-chain analogs (II) are thousand times more active as inhibitors of acetylcholinesterase(AChE). In order to explain the poor anti-ChE activity of I, a covalent molecular combination,IV, of the cyclic phosphate and an extremely effective leaving group (III) was prepared and evaluated .The new compound , IV , was found to inhibit progressively horse-serum butyrylcholinesterase(BuChE)at $t_{1/2}$=15 min.(2.9μM , pH 7.0, 25^0),whereas no progressive inhibition could be demonstrated for eel AChE incubated for several hrs under the same experimental conditions.Eel AChE was inhibited reversibly by IV with affinity constant,K_I=1.3x10^{-6} M. These findings may suggest the following: a. In order to compensate for overcrowding of the AChE active-site by large substituents it is essential to maintain flexibility of the four ligands attached to the P atom.It is further infered that cyclization does not permit such flexibility. b. BuChE differ considerably from AChE in the ability of the enzyme to provide simultaneous four-site interaction with tetrahedral OP inhibitors.