COMPOUNDS BEARING \((E)\)-BUT-2-ENE LINKER AND EVALUATION OF THEIR REACTIVATION ACTIVITY AGAINST CHLORPYRIFOS-INHIBITED ACETYLCHOLINESTERASE

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The reactivators of acetylcholinesterase (AChE, EC 3.1.1.7) are very important components in the treatment of intoxications caused by organophosphate inhibitors such as nerve agents and pesticides \(^{[1]}\). These inhibitors covalently bind to active site of mentioned enzyme and irreversibly inhibit its activity. The reactivator breaks the inhibitor-enzyme covalent bond and restores its activity. Unfortunately, there is no reactivator applicable for every type of inhibitor; it means that every structural change in the molecule of inhibitor needs a specific structure of the reactivator \(^{[2]}\). Therefore, development of more potent compounds able to reactivate broader spectrum of inhibitors is a major challenge actual from the point of view of war operations, accidents or terroristic attacks.

Six potential AChE reactivators were synthesized using modification of currently known synthetic pathways. Their potency to reactivate AChE inhibited by insecticide chlorpyrifos was tested \textit{in vitro}. According to the results, \((E)\)-1-(2-hydroxyiminomethylpyridinium)-4-(4-hydroxyiminomethylpyridinium)-but-2-ene dibromide seems to be the most potent AChE reactivator. The reactivation potency of these compounds depends on structural factors such as constitution of the linking chain between both pyridinium rings, position of the oxime moiety at the pyridinium ring and presence of quaternary nitrogens \(^{[3]}\).

\[ \text{N} \quad \text{HON=HC} \quad \text{N} \quad \text{CH=NOH} \]


The work was supported by the grant of Grant Agency of Charles University No. 302/2005/B-CH/FaF and by the grant of the Ministry of Defence of Czech Republic No. ONVLAJEP 20031.