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Synthesis of an Organophosphorus Analog of Acetylcholine

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Poster Presentation 1

SYNTHESIS OF AN ORGANOPHOSPHORUS ANALOG OF ACETYLCHOLINE

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Acetylcholinesterase (AChE) is an important enzyme in our nervous system. In normal nerve function, AChE catalyzes the hydrolysis of acetylcholine (ACh) into its respective components, choline and acetate. Recent interest has been focused on AChE because of its potential role in the pathology of neurodegenerative diseases such as Alzheimer's disease. Studies have revealed that the active site of AChE contains an esteratic and several hydrophobic/anionic subsites. AChE is inhibited by organophosphorus (OP) compounds like sarin and soman. As a result, OP compounds have been used to study the structure of AChE and the mechanism by which it catalyzes the hydrolysis of ACh. No conclusion has been made as to the stereoselectivity of the phosphorylation of AChE because recent studies have yielded conflicting results. As a result, the synthesis of a conformationally constrained organophosphorus analog of ACh may provide definitive information about the stereoselectivity of the mechanism of AChE phosphorylation. Furthermore, it may increase understanding in the process of aging of the enzyme after phosphorylation. We present our efforts in the synthesis of that OP inhibitor.