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Studies toward the Total Synthesis of an Organophosphorus Analog of Acetylcholine

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Poster Presentation 5

STUDIES TOWARD THE TOTAL SYNTHESIS OF AN ORGANOPHOSPHORUS ANALOG OF ACETYLCHOLINE

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Acetylcholine is a vital neurotransmitter in the human nervous system. It functions in both the cardiac and smooth muscle synapses as well as the neuromuscular skeletal joints. The release of acetylcholine in the muscle cells stimulates the muscle to contraction. The acetylcholine must therefore be broken down quickly following its release to prevent continued contraction which would certainly result in death. Acetylcholine is broken down by the enzyme acetylcholinesterase, (AchE), via a hydrolysis mechanism. This mechanism is somewhat unclear in the involuntary muscles of the human body, and proposed mechanisms have been strongly debated. Organophosphorus (OP) compounds have been used throughout much of the study of the AchE mechanism as inhibitors of the enzyme. The total synthesis of a conformationally constrained OP analog of acetylcholine, combined with enzyme assays with such an analog, would demonstrate further the interaction between the OP inhibitors and AchE, as well as provide greater insight into the mechanism of the acetylcholine hydrolysis. We present a synthetic strategy for this compound and our progress on the synthesis of a model compound.