SYNTHESIS OF PHOSPHORUS TACRINE ANALOGUES AS A NEW POTENTIAL ANTI-ALZHEIMER'S DISEASE AGENTS

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Alzheimer's disease (AD) is neurodegenerative disorder that is the most common form of dementia [1]. In 2015, there were about 29.8 million people with AD and it is estimated that the number will triple in the middle of this century [2].

Tacrine was one of the first drugs used in AD treatment. Despite the potent reversible ability to inhibit of acetylcholinesterase (AChE) and butyrylcholinesterase (BChE), hepatotoxicity was the main reason for the withdrawal tacrine from use. Nevertheless, due to the favorable pharmacokinetic and pharmacotherapeutic profile, it has a high potential for application, therefore it is widely used in medical chemistry for the design of compounds as potential anti-AD drugs [3].

A series of novel phosphorus tacrine derivatives was obtained in three steps, including synthesis of 9-chlorotacrine, connection of 9-chlorotacrine with hexamethylenediamine, 1,8-diaminooctane and 1,12-diaminododecane linkers and reaction of obtained tacrine diamine analogues with corresponding acid ester to give nine tacrine organophosphorus compounds. All of the obtained final structures were characterized by ^{1}H NMR, ^{13}C NMR, ^{31}P NMR and MS.

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