SYNTHESIS OF PYRIDO[1,2-*a*]PYRIMIDO[4,5-*d*]PYRIMIDINE DERIVATIVES AND EVALUATION OF THEIR INHIBITORY ACTIVITY AGAINST ACETYLCHOLINESTERASE

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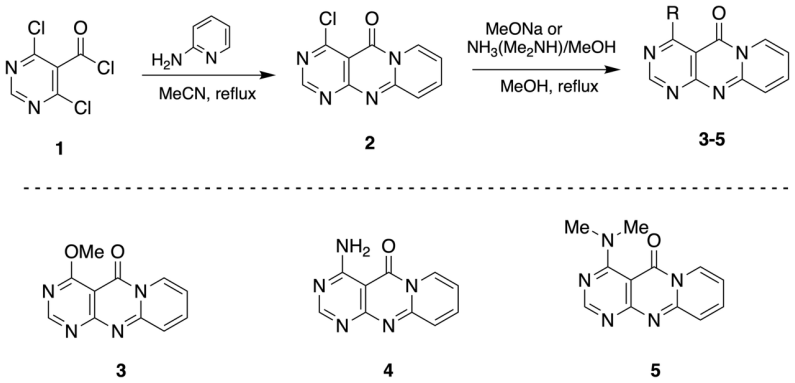
Pyrido[1,2-*a*]pyrimidine derivatives are an important class of bicyclic heterocycles with diverse biological activities. In addition, their use has been reported in the synthesis of tricyclic fused compounds, such as SARS-CoV-2-M Pro, SPOP, and chitinase inhibitors.

Considering the above, we report an efficient method for obtaining a heterofused system with a pyrido[1,2-*a*]pyrimidine moiety. 4,6-Dichloropyrimidine-5-carbonyl chloride **1** was used as the starting material. Reaction of **1** with 2-aminopyridine in boiling acetonitrile led to the formation of the pyrido[1,2-*a*]pyrimido[4,5-*d*]pyrimidin-5-one derivative **2** in high yield. Nucleophilic substitution with sodium methoxide, ammonia, or dimethylamine gave the target products **3**-**5**. The structures of the synthesized compounds were confirmed by elemental analysis, ^{1}H NMR, ^{13}C NMR, and MS spectral data.



Evaluation of the anticholinesterase activity of the synthesized pyrido[1,2-*a*]pyrimido[4,5-*d*]pyrimidin-5-one derivatives **3**-**5** showed that they have weak inhibitory activity against electric eel acetylcholinesterase. The dimethylamino-substituted derivative **5** had virtually no inhibitory effect on acetylcholinesterase at 50 μM, whereas compounds **3** and **4** showed higher inhibitory activity with IC_{50} values close to 40 μM. The obtained data can be used for further structural optimization of the pyrido[1,2-*a*]pyrimido[4,5-*d*]pyrimidine core and the development of more potent acetylcholinesterase inhibitors.