Development of a method for the synthesis of 5-methoxy pyrimidine derivatives

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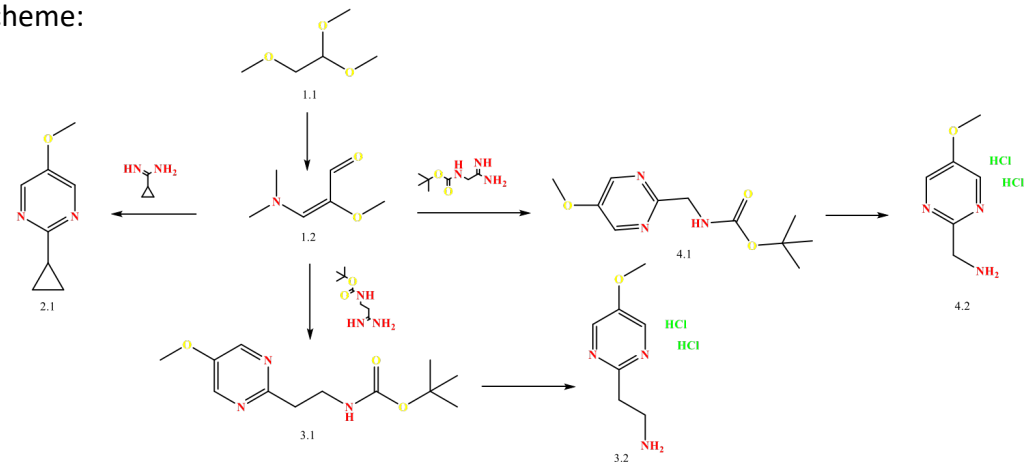
Introduction. Heterocyclic compounds containing a pyrimidine core represent an important group of natural and synthetic chemical compounds characterized by a wide range of biological activities and significant potential for medical applications as therapeutic agents in the treatment of various pathological conditions. According to scientific sources, compounds of this class exhibit pharmacological activity within the central nervous system (CNS), particularly anticonvulsant and antidepressant effects, which makes pyrimidine derivatives promising candidates for the development of drugs aimed at correcting CNS disorders [1]. In addition, an intensive search for new effective antitumor compounds is ongoing, among which trifluoromethyl-substituted pyrimidine derivatives are attracting particular attention [2]. The literature also reports on new promising directions for the use of pyrimidine structures in the development of antimalarial drugs [3]. In this regard, the development of new, simple and highly effective methods for the synthesis of pyrimidine derivatives remains a relevant scientific task.

Materials and methods. Organic synthesis methods, 1H NMR spectroscopy, LCMS.

Results and discussion. In the course of developing a new synthesis method, at the first stage, the starting material was 1,1,2-trimethoxyethane (1.1), which in turn reacts with phosphorus pentachloride in dimethylformamide at 0-60°C, 40 hours. Subsequently, a 30% solution of sodium methylate was used, 10-20°C, after isolation, the desired product (E)-3-(dimethylamino)-2-methoxyacrylaldehyde (1.2) was obtained. At the second stage of developing the method, a number of attempts were made to obtain 5methoxy derivatives of pyrimidine from the intermediate compound (1.2) and the optimal synthesis method with maximum yield was selected. It was found that aldehyde (1.2) reacts best with amidines in dry methanol in the presence of sodium methylate as a base. According to this method, 5-methoxy derivatives 2.1, 3.1 and 4.1 were synthesized, the purity of which was proven by NMR and LCMS, presented in scheme:



Conclusions. An effective synthesis method from 1,1,2-trimethoxyethane was developed, which enabled the direct synthesis of 5-methoxy-substituted pyrimidines, which in turn are analogues of biologically active substances and are synthetically active, making further transformations possible.

References

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