Multicomponent condensations as an easy and accessible method for creating bioactive compounds

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Many substances used in medicinal chemistry, agrochemicals, and dyes have a nitrogen-containing heterocyclic framework. For example, essramycin **1** is the first triazolopyrimidine antibiotic with strong antibacterial activity. Just 6.25 µg/ml of the triazolopyrimidine-6-carboxylic acid derivative **2** is enough for 92% inhibition of the growth of Mycobacterium *tuberculosis* H37Rv. The 6-hydrazidetriazolopyrimidine derivative **3** has demonstrated potent activity against Gram-positive and Gram-negative bacterial strains, and the thiosemicarbazide derivative **4** has potent activity against Gram-positive strains [1].

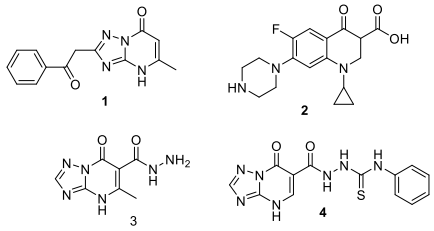

Figure 1. Biologically active pyrimidine derivatives

We have previously synthesized a series of 3-amino-1,2,4-triazolopyrimidine derivatives [2]. In order to diversify the structure of these derivatives and study their biological activity, we carried out a number of modifications, including methylation, acetylation, reduction, and aromatization reactions.

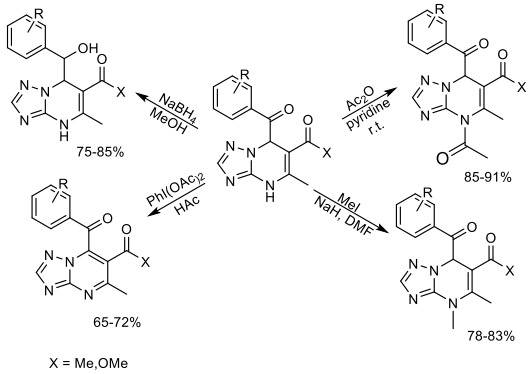

Figure 2. Scheme of the modification of 3-amino-1,2,4-triazole derivatives

It turned out that methylation with methyl iodide in the presence of KOH in acetonitrile does not lead to the formation of a product, unlike the reaction with NaH in dimethylformamide in an inert medium. Acetylation occurs both for compounds containing an acetylacetone fragment and for compounds with an acetoacetic ester residue. Aromatization occurs only at high temperatures - boiling in acetic acid - while the reduction of the aryl fragment is possible at 0°C in methanol. The structures of the obtained compounds were confirmed by ^{1}H and ^{13}C NMR, as well as COSY, HMBC, NOESY spectroscopy, and mass spectrometry.

[1] J. A. Mokariya, D. P. Rajani, M. P.Patel. *Arch. Pharm.* **2023**; 356:e2200545.

[2] Natal'ya V. Chechina, Nadezhda N. Kolos, Irina V. Omelchenko, Vladimir I. Musatov. *Chemistry of Heterocyclic Compounds* **2018**, 54(*1*), 58-62.