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Reaction of 1,3-oxazine with 2,4-dihydrazinyl-6-methylpyrimidines

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Abstract

Current research in the field of chemistry of biologically active azines occupies a leading position in the heterocyclic chemistry. Pyrimidine derivatives are the most-studied group among diazines. A group of unsaturated oxo-derivatives of the 6*H*-1,3-oxazin-6-one is the least studied one among them.

Many 1,3-oxazin-6-ones are used as starting compounds for the preparation of variety of acyclic and heterocyclic systems the synthesis of which by other methods is multistage or impossible. Therefore, the search for new biologically active compounds among the products of 2,5-substituted 4-hydroxy-6*H*-1,3-oxazin-6-ones with *N*-nucleophiles reaction is an actual task.

Investigation of previously obtained 1,3-oxazines revealed that they have anti-inflammatory, sedative, anti-microbial activity. However, the biological activity of the products of their interaction with the binucleophilic nitrogen-containing reagents was not examined.

The aim of this work is the synthesis of new previously undescribed biologically active 1,2,4-triazoles, demonstration of their structure by means of state of the art physicochemical analysis methods and the screening of biological activity of 1,2,4-triazoles using PASS computer program.

Derivatives of 1,2,4-triazoles (**I**) were obtained by reaction of 2,5-substituted 4-hydroxy-6*H*-1,3-oxazin-6-ones with 2,4-digidrazinil-6-methylpirimidine in an anhydrous polar organic methanol solvent without heating under stirring for 45-50 hours. The resulting precipitate was filtered and washed with a small amount of ethyl acetate. The product yield amounted to 76-82%. The individuality of the all obtained compounds was confirmed by TLC in the system of methanol: ethyl acetate – 4:1. The structure of the compounds was proved by modern physicochemical analysis methods: ^{1}H NMR, IR- and UV-spectroscopy and mass-spectrometry.

Before starting the study of biological activity *in vivo*, prediction of probable biological activities of the prepared compounds **I** was carried out by a computer program PASS (Prediction of Activity Spectra for Substances). This approach saves time and effort when searching for analog drugs. The results of the screening of biological activity using the PASS program have shown anti-inflammatory activity with a probability of (Ra > 0.6), antifungal, antimicrobial with probability (Ra > 0.35, 0.37, respectively), analgesic activity with a probability of (Ra > 0.8), antiviral activity with a probability of (Ra > 0.9). A further stage of the work is experimental confirmation of these types of activity.

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