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SYNTHESIS AND PROPERTIES OF SOME 5-(2-BROMO-4-FLUOROPHENYL)-4R-1,2,4-TRIAZOL-3-THIOL DERIVATIVES

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Introduction. In recent years, the chemistry of nitrogen-containing heterocyclic compounds has attracted more and more attention from the scientific community. This is primarily due to the fact that over the past decades, medicines that include the 1,2,4-triazole nucleus in their structure have been widely used in medicine. This nucleus is characterized by a wide range of biological activity and relative low toxicity. The study demonstrates that the combination of 1,2,4-triazole with a digalogenated phenyl fragment is predicted to lead to new properties that require detailed study. Thus, this area of research remains relevant.

Materials and methods. The starting material was 5-(2-bromo-4-fluorophenyl)-4R-1,2,4-triazol-3-thiol. This compound was subjected to reactions with alkyl, cycloalkyl, aryl, and heterohalogen derivatives (using such reagents as iodomethane, bromoethane, 1-bromopropane, 1-bromobutane, 1-bromopentane, 1-bromohexane, 1-bromoheptane, 1-bromocane, 1-bromonane, 1-bromodecane, chlorocyclohexane, benzyl bromide, 2-bromothiophene, 2-chloropyrimidine). The reaction was carried out in methyl alcohol by adding an equimolecular amount of potassium hydroxide and boiling the reaction mixture to pH=7 for 2-16 hours (depending on the alkylating agent). After cooling, the reaction solution was filtered and the solvent was evaporated in vacuo. The obtained crystalline compounds were crystallized from a water-methanol mixture. The structure of the synthesized substances was confirmed by a set of modern physicochemical methods using the equipment available at the ZSMPhU.

To identify potentially biologically active substances, we applied in silico screening methods (Swiss Target Prediction), such as molecular docking (AutoDock), predicting biological activity and toxicity (Toxicity Estimation Software Tool (TEST)). After analyzing the data obtained, we found that the synthesized compounds were highly likely to exhibit antimicrobial, antifungal, anti-inflammatory analgesic, antihypoxic, and antioxidant activities. These results became the basis for further development of the strategy for studying the biological properties of the synthesized series of compounds using in vitro and in vivo methods.

The results of the study include the synthesis of 14 new substances, optimization of their structure and determination of their structure, except for intermediates. The press screening studies showed that the synthesized substances are likely to exhibit antimicrobial, antifungal, anti-inflammatory, analgesic, antihypoxic, and antioxidant activity.

The conclusions note that in the course of the study, a number of 5-(2-bromo-4-fluorophenyl)-4R-1,2,4-triazol-3-thiol derivatives, including alkyl, cycloalkyl, aryl, and heteryl thiol derivatives, were successfully synthesized and the probable manifestation of biological action was investigated. The obtained results provide grounds for further studies of the biological activity of these compounds.