SYNTHESIS AND PROPERTIES OF 1,2,4-TRIAZOLE-3-THIOL DERIVATIVES WITH A THIADIAZOLE MOIETY

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Biological studies of synthetic analogs of heterocyclic compounds widespread in the animal and plant world have shown that most of them exhibit a wide range of biological actions. In this series, derivatives of 1,2,4-triazole, which are mainly of synthetic origin, are of particular interest. 1,2,4-triazole derivatives containing different heterocyclic fragments in the 5 position increase the possibility of new activity emergence.

According to the literature, esters containing a 1,2,4-triazole fragment in their structure often exhibit various types of biological activity. Some representatives of this class of compounds exhibit a hypotensive effect, have antitumor, fungicidal, antibacterial and other types of biological activities.

The goal of the robot was the targeted synthesis of esters 2-((4-phenyl-5-(((5-(phenylamino)-1,3,4-thiadiazol-2-yl)thio)methyl)-1,2,4-triazol-3-yl)thio)acetic acid and the establishment of their physicochemical and biological properties.

Materials and methods. Target esters were obtained in two ways. The first method was the alkylation of the starting 4-phenyl-5-(((5-(phenylamino)-1,3,4-thiadiazol-2-yl)thio)methyl)-1,2,4-triazole-3-thiol with methyl , ethyl, n-propyl, isopropyl, tert-butyl, n-pentyl, iso-pentyl ester of 2-chloroetanoic acid in propan-2-ol with an equivalent amount of sodium hydroxide.

The second method was based on the etherification of 2-((4-phenyl-5-(((5-(phenylamino)-1,3,4-thiadiazol-2-yl)thio)methyl)-1,2,4-triazol-3-yl)thio) acetic acid. For this, the alkylation of the starting 4-phenyl-5-(((5-(phenylamino)-1,3,4-thiadiazol-2-yl)thio)methyl)-1,2,4-triazole-3-thiol 2-chloroethanic acid in propan-2-ol in the presence of an equivalent amount of sodium hydroxide. The resulting acids were used in the reaction with aliphatic monohydric alcohols (methanol, ethanol, propan-1-ol, propan-2-ol, butan-1-ol, 1,1-dimethylethanol, pentan-1-ol, 3-methylbutane- 1-olom) in the presence of a catalytic amount of concentrated sulfuric acid. The reaction was carried out under microwave irradiation conditions.

The first way. To a solution of 0.01 mol of sodium hydroxide in 25 ml of propan-1-ol was added 0.01 mol of the corresponding thiol. To the resulting solution was added 0.01 mol of the corresponding 2-chloroethanoic acid ester. Heated for 1 hour. The solution was cooled and 50 ml of purified water was added. The resulting precipitate was filtered off, washed with purified water.

The second way. A mixture of 0.01 mol of the starting carboxylic acid, 25 ml of the corresponding alcohol, 0.5 ml of concentrated sulfuric acid. The prepared mixture is boiled for 12 hours, cooled, the solvent is evaporated, neutralized with aqueous sodium bicarbonate solution. The resulting precipitate is filtered off, washed on the filter with 50 ml of purified water. For analysis, purified by crystallization from a mixture of water and ethanol (1: 1).

For analysis, the synthesized compounds were purified by crystallization from methanol.

Synthesized compounds are white crystalline substances that are soluble in aliphatic monohydric alcohols, DMF and DMSO.

The structure of the synthesized substances was established using modern physicochemical methods of analysis: 1H NMR, IR, chromato-mass spectroscopy.

The next stage of work involved the establishment of the biological activity of the obtained substances. With the help of the «PASS On-line» Internet service, the possible biological activity of the obtained substances was predicted. The screening results are presented in table 1.

Prediction of possible antimicrobial activity

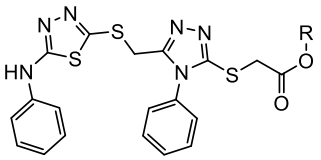

Table 1

№	R	Prediction, %	№	R	Prediction, %
1	CH_3	45	5	C_4H_9	32
2	C_2H_5	41	6	$C(CH_3)_3$	51
3	C_3H_7	35	7	C_5H_{11}	35
4	$CH(CH_3)_2$	39	8	$C_3H_5(CH_3)_3$	31

Results and discussion. Analysis of the obtained data revealed that an increase in the length of the carbon chain leads to a decrease in antimicrobial activity. In turn, the branching of the carbon chain of the alcohol residue of the ester group leads to an increase in this activity.

Conclusions. 8 new substances not previously described in the literature were synthesized. The structure of the obtained substances is confirmed by modern physicochemical methods of analysis, possible biological activity is predicted. The directions of the most perspective further researches in vivo are defined.