Modern approaches to the synthesis and biological screening of 1,2,4-triazole-3-thiol derivatives (literature review)

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A – research concept and design; B – collection and/or assembly of data; C – data analysis and interpretation; D – writing the article; E – critical revision of the article; F – final approval of the article

Aim. To systematize and critically analyze current scientific publications on the synthesis and biological screening of 1,2,4-triazole-3-thiol derivatives and to summarize the relationship between their structure and pharmacological activity. Special attention was paid to the prospects of using these compounds as scaffolds for the development of new biologically active substances and potential active pharmaceutical ingredients.

Materials and methods. The review included publications by domestic and foreign authors devoted to methods for the synthesis, chemical modification, and biological evaluation of 1,2,4-triazole-3-thiol derivatives. Literature retrieval was carried out in the Scopus, Web of Science, PubMed, and Google Scholar databases using Ukrainian- and English-language keywords related to 1,2,4-triazoles, triazole-3-thiols, synthesis, and biological activity. The selected sources were analyzed by systematization, comparative assessment, and generalization of data on synthetic approaches, thiol-group transformations, directions of structural modification, and the results of pharmacological screening.

Results. The analysis showed that 1,2,4-triazole-3-thiol derivatives represent an important class of heterocyclic compounds with broad possibilities for purposeful structural modification and a wide spectrum of biological effects. Their synthesis is most often based on cyclization reactions involving thiosemicarbazides, hydrazides, isothiocyanates, and related intermediates, whereas the efficiency of the process depends on solvent, temperature, catalyst, and the nature of substituents. The summarized literature indicates that these compounds may exhibit antimicrobial, antifungal, antiviral, antioxidant, anti-inflammatory, anticonvulsant, and antitumor activity, while the thiol group plays a decisive role in further S-functionalization and in shaping physicochemical and pharmacological properties.

Conclusions. 1,2,4-Triazole-3-thiol derivatives are a promising platform for medicinal chemistry because their reactivity allows targeted modification and the reported biological screening results confirm the expediency of further search for new low-toxicity and pharmacologically promising compounds in this series.

Keywords: 1,2,4-triazole-3-thiol, triazole derivatives, synthesis, biological screening, pharmacological activity, structure – activity relationship.

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Сучасні підходи до синтезу та біологічного скринінгу похідних 1,2,4-тріазол-3-тіолу (огляд літератури)

В. В. Кальченко, Р. О. Щербина

Мета роботи – систематизувати та критично проаналізувати сучасні наукові публікації, присвячені синтезу та біологічному скринінгу похідних 1,2,4-тріазол-3-тіолу, а також узагальнити відомості про взаємозв'язок між їхньою будовою та фармакологічною активністю. Окрему увагу приділено оцінюванню перспектив використання цих сполук як молекулярних платформ для створення нових біологічно активних речовин і потенційних активних фармацевтичних інгредієнтів.

Матеріали і методи. До огляду включено публікації вітчизняних і зарубіжних авторів, присвячені методам синтезу, хімічній модифікації та біологічному оцінюванню похідних 1,2,4-тріазол-3-тіолу. Пошук літератури здійснювали в базах даних Scopus, Web of Science, PubMed і Google Scholar. Використовували україномовні та англомовні ключові слова, пов'язані з 1,2,4-тріазолами, тріазол-3-тіолами, синтезом і біологічною активністю. Відібрані джерела проаналізовано методами систематизації, порівняльного оцінювання й узагальнення даних щодо синтетичних підходів, перетворень за участю тіольної групи, напрямів структурної модифікації та результатів фармакологічного скринінгу.

Результати. Аналіз даних фахової літератури засвідчив, що похідні 1,2,4-тріазол-3-тіолу є важливим класом гетероциклічних сполук із можливостями цілеспрямованої структурної модифікації та широким спектром біологічної дії. Їхній синтез найчастіше ґрунтується на реакціях циклізації за участю тіосемікарбазидів, гідразидів, ізотіоціанатів і споріднених проміжних сполук. Ефективність процесу залежить від природи розчинника, температури, каталізатора й характеру замісників.

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Keywords: 1,2,4-triazole-3-thiol, triazole derivatives, synthesis, biological screening, pharmacological activity, structure – activity relationship.

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Висновки. Узагальнені дані свідчать, що такі сполуки можуть мати антимікробну, протигрибкову, противірусну, антиоксидантну, протизапальну, протисудомну та протипухлинну активність, а тіольна група відіграє визначальну роль для наступної *S*-функціоналізації, формування фізико-хімічних і фармакологічних властивостей. Похідні 1,2,4-тріазол-3-тіолу є перспективною платформою для медичної та фармацевтичної хімії, оскільки їхня реакційна здатність забезпечує можливість цілеспрямованої модифікації, а результати біологічного скринінгу підтверджують доцільність подальшого пошуку нових малотоксичних і фармакологічно перспективних сполук цього ряду.

Ключові слова: 1,2,4-тріазол-3-тіол, похідні тріазолу, синтез, біологічний скринінг, фармакологічна активність, структура – активність.

Актуальні питання фармацевтичної і медичної науки та практики. 2026. Т. 19, № 2(51). С. 184-194

According to current scientific research, the rapid development of medical and pharmaceutical science has significantly contributed to the improvement of both the quality and duration of human life. A major role in this process has been played by advances in organic and medicinal chemistry, which have enabled the identification of active components in drugs, as well as the design and implementation of synthetic compounds with predictable biological properties. Further progress in medicinal chemistry has focused on the targeted modification of already known biologically active molecules to enhance their efficacy and safety.

Despite considerable scientific achievements, the search for new highly effective and low-toxicity biologically active compounds remains relevant. This is due to the fact that a significant number of drugs currently used for the prevention and treatment of various diseases exhibit insufficient therapeutic effectiveness or are associated with undesirable side effects.

Consequently, heterocyclic compounds, particularly 1,2,4-triazole derivatives, have attracted special attention from researchers, as they demonstrate a broad spectrum of biological activity and substantial potential for further chemical modification.

Aim

To systematize and critically analyze current scientific publications on the synthesis and biological screening of 1,2,4-triazole-3-thiol derivatives and to summarize the relationship between their structure and pharmacological activity. Special attention was paid to the prospects of using these compounds as scaffolds for the development of new biologically active substances and potential active pharmaceutical ingredients.

Materials and methods

The materials for this review included scientific publications by domestic and international authors dedicated to the synthesis and study of the biological activity of 1,2,4-triazole derivatives, in particular 1,2,4-triazole-3-thiols. The analysis was based on articles from peer-reviewed scientific journals, monographs, and review papers published in open scientometric databases. During the study, methods of systematic analysis, generalization, and comparative evaluation of the literature data were applied.

Special attention was given to modern approaches for the synthesis of 1,2,4-triazole derivatives, features of their chemical modification, and results of biological screening, allowing assessment of the relationship between compound structure and pharmacological activity.

Results

Analysis of current scientific sources has shown that 1,2,4-triazole-3-thiol derivatives constitute an important class of heterocyclic compounds with broad possibilities for structural modification and significant biological potential. The generalization of literature data made it possible to identify the main synthetic approaches, features of their chemical behavior, and key directions for research into their pharmacological properties.

It has been established that the synthesis of these compounds is most often based on cyclization reactions involving thiosemicarbazides, hydrazides, and related reagents. The efficiency of the synthesis largely depends on the reaction conditions, including the nature of the solvent, temperature, and catalysts. It was found that no universal synthetic method exists, and optimal conditions require individual selection depending on the structure of the starting components.

It has been shown that the reactivity of 1,2,4-triazole-3-thiol derivatives is primarily determined by the presence of the thiol group, which readily participates in nucleophilic substitution reactions. In most cases, modification occurs at the sulfur atom, leading to the formation of *S*-substituted products, whereas involvement of the Nitrogen atoms is less pronounced and depends on the reaction conditions. This opens opportunities for the controlled synthesis of compounds with predetermined properties.

Analysis of *in silico* studies confirmed their significant role in modern medicinal chemistry. Molecular modeling methods allow preliminary evaluation of compound interactions with biological targets, prediction of pharmacokinetic properties, and selection of the most promising structures. The agreement between computational predictions and experimental data demonstrates the effectiveness of this approach as a preliminary screening step.

It has also been shown that 1,2,4-triazole-3-thiol derivatives exhibit a broad spectrum of biological activities, including antifungal, antimicrobial, antioxidant, and anticonvulsant effects. In some cases, their efficacy is comparable to that of known drugs, confirming the promise of further research in this area.

Synthesis of 1,2,4-triazole-3-thiol derivatives. Derivatives of 1,2,4-triazole are currently considered one of the most promising classes of heterocyclic compounds in medicinal and pharmaceutical chemistry [1,2,3,4,5]. One of the structural features of substituted 1,2,4-triazoles is their ability to undergo tautomeric transformations, which enables interaction with various biological targets, including enzymes and receptor proteins [6]. The presence of Nitrogen atoms in the

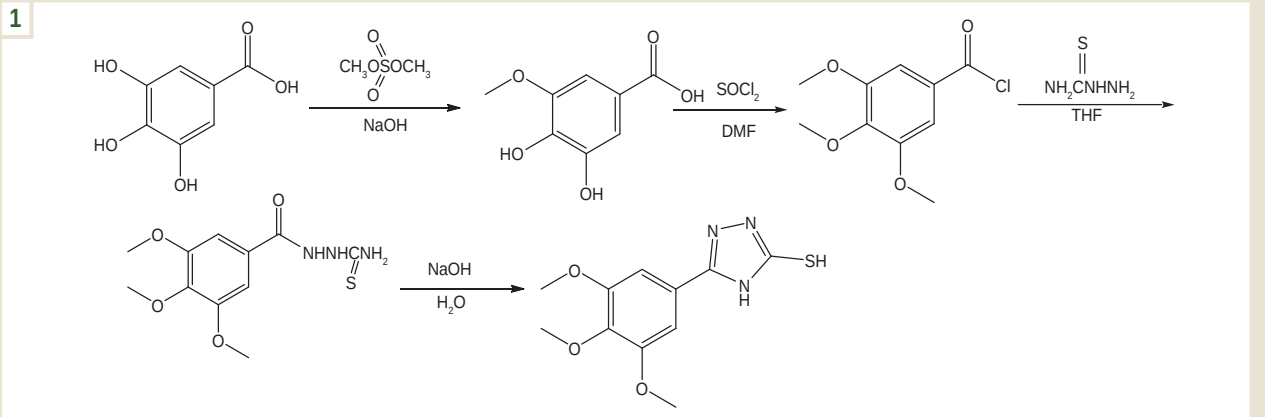

Fig. 1. Scheme of the synthesis of 5-(3,4,5-trimethoxyphenyl)-4*H*-1,2,4-triazole-3-thiol.

heterocyclic system contributes to the formation of hydrogen and coordination bonds, which positively affects the pharmacological potential of these compounds [7,8]. Some representatives of this class also exhibit cardioprotective and neuroprotective activities, making them attractive candidates for the development of new drugs.

A significant advantage of 1,2,4-triazole derivatives is the wide range of possibilities for targeted chemical modification [9]. Variation in the nature of substituents in the 1,2,4-triazole ring positions and their subsequent functionalization allows regulation of lipophilicity, bioavailability, and toxicological characteristics of the compounds [10,11]. This, in turn, opens opportunities for optimizing pharmacological activity and reducing the risk of side effects. These properties have led to the development of numerous synthetic approaches for obtaining such compounds, which have been proposed over recent decades and continue to be actively improved [1,12,13,14,15,16,17].

The scientific literature describes numerous methods for the synthesis of 1,2,4-triazole-3-thiol derivatives based on the use of various starting substrates, including thiosemicarbazides, carboxylic acid hydrazides, isothiocyanates, esters, and amides of thiocarboxylic acids [18,19]. Cyclocondensation, intramolecular heterocyclization, nucleophilic substitution, and functionalization of the thiol group can proceed under different conditions-acidic, neutral, or basic media-using conventional heating, microwave irradiation, or catalysts. At the same time, even minor variations in synthesis parameters can significantly influence the course of the reaction process, its rate, the selectivity of target heterocycle formation, and the yield of the final product [20].

At the same time, the accumulated data on the synthesis of 1,2,4-triazole-3-thiol derivatives are predominantly descriptive in nature and are often focused on the preparation of individual compounds without a thorough comparative analysis of alternative methods [21,22]. In a significant number of studies, there is a lack of systematic evaluation of the advantages and disadvantages of the proposed synthetic approaches, their scalability, reproducibility, and compliance with modern environmental requirements. This complicates the practical application of the available results in further research, especially in the development of a series of new derivatives with predicted physicochemical and biological properties.

The generalization and critical analysis of existing synthetic methods make it possible not only to systematize fragmented literature data but also to establish general patterns in the formation of the 1,2,4-triazole-3-thiol fragment, to determine the relationship between the structure of starting reagents and the efficiency of heterocyclization, and to outline the most promising directions for chemical modification. Particular importance is attached to the study of modern approaches aimed at reducing the number of synthetic steps, using less toxic reagents and solvents, decreasing energy consumption, and improving the economic efficiency of processes [23,24]. Therefore, a comprehensive generalization of information on the synthesis methods of 1,2,4-triazole-3-thiol derivatives is an important scientific task that forms the theoretical basis for the further development of the chemistry of these heterocyclic systems.

Such generalization contributes to the formation of a comprehensive understanding of the capabilities and limitations of existing synthetic approaches, facilitates the rational selection of optimal methods for obtaining target compounds, and serves as a foundation for the development of new, more efficient and technologically advanced synthetic routes for promising biologically active substances.

A group of researchers has proposed and implemented a stepwise approach to the synthesis of 17 new 1,2,4-triazole derivatives containing a thioether fragment of 1,3,4-thiadiazole. The target compounds were obtained through sequential organic transformations using appropriate heterocyclic precursors followed by functionalization with a thioether group *(Fig. 1)*. The structures of the synthesized compounds were confirmed using modern physicochemical analytical methods [25,26].

As a result of the conducted studies, an efficient approach to the synthesis of starting compounds and *S*-alkyl derivatives of 4-(4-chlorophenyl)-5-(pyrrol-2-yl)-1,2,4-triazole-3-thiol was developed. The synthetic strategy was based on the

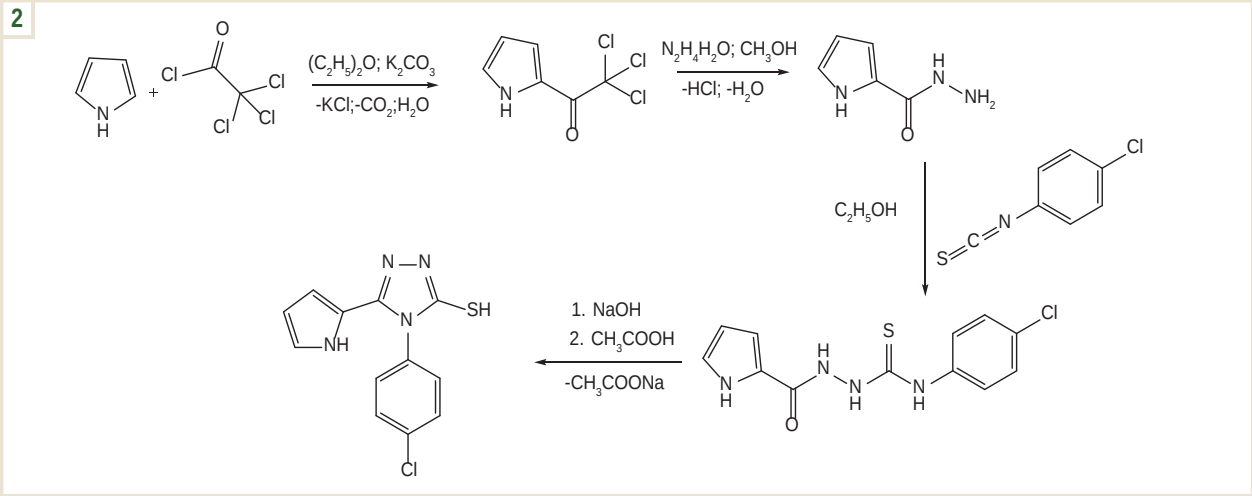

Fig. 2. Scheme of the synthesis of 4-(4-chlorophenyl)-5-(1*H*-pyrrol-2-yl)-4*H*-1,2,4-triazole-3-thiol.

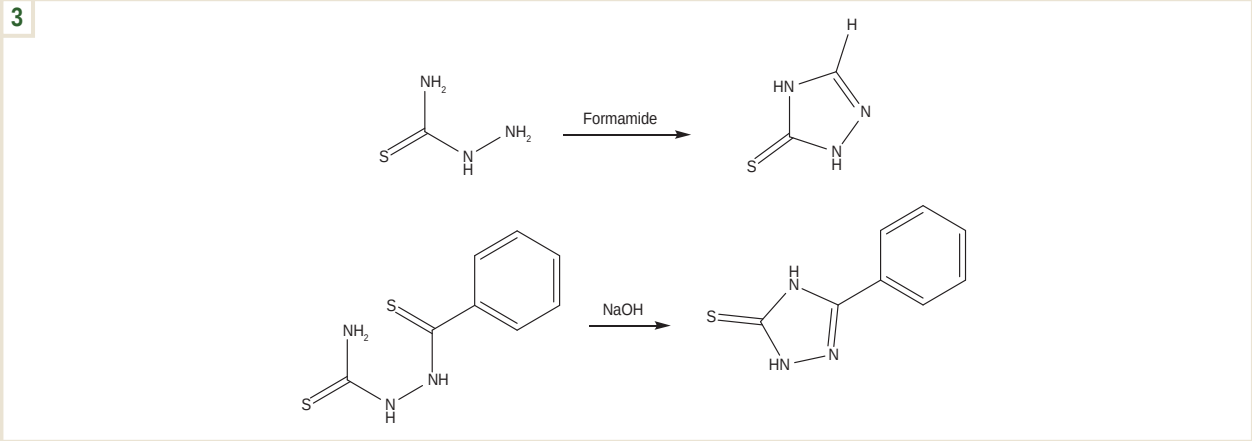

Fig. 3. Scheme of the synthesis of 5-phenyl-2,4-dihydro-3*H*-1,2,4-triazole-3-thione.

sequential implementation of targeted chemical transformations aimed at constructing the corresponding heterocyclic systems *(Fig. 2)* [27].

To obtain a series of substituted 1,2,4-triazole derivatives, classical approaches involving the cyclization of semicarbazides were applied. In particular, 1,2,4-triazole-3-thione was synthesized by the reaction of thiosemicarbazide with formamide, whereas 5-phenyl-1,2,4-triazole-3-thione was obtained from benzoylthiosemicarbazide in an alkaline medium of sodium hydroxide *(Fig. 3)* [28].

Pyrimidine-2-thiol, together with the triazole fragment, is widely used in organic synthesis. In particular, it can be employed as a lactam-protecting group to prevent side reactions involving cyclic amides, and it can also serve as an intermediate in the synthesis of pharmaceutical compounds. Within the framework of these studies, new hybrid compounds of the (1,2,4-triazol-3(2*H*)-yl)methylthiopyrimidine type were synthesized *via* heterocyclization of intermediate carbothioamides *(Fig. 4)* [29].

The researchers determined the optimal conditions for the direct interaction of thiosemicarbazides with carboxylic acids in the presence of a polyphosphate ester (PPE), which made it possible to synthesize 1,2,4-triazole-3-thiol derivatives. The methodology involves carrying out the process in two consecutive stages: in the first stage, the thiosemicarbazide is acylated by the carboxylic acid in a chloroform medium in the presence of PPE at 90 °C using hydrothermal reaction equipment; in the second stage, the obtained acylated product undergoes cyclocondensation by treatment with an aqueous alkaline solution *(Fig. 5)* [19].

The application of the proposed synthetic approach allowed the preparation of 15 1,2,4-triazole-3-thiol derivatives, among which five compounds were synthesized for the first time. The structural identification of the obtained products was carried out using NMR spectroscopy and mass spectrometry. It was found that replacing chloroform with ethyl acetate as the reaction medium leads to a fundamentally different course of the process *(Fig. 6)*. The obtained results indirectly confirm the influence of the solubility of the acylation products in the reaction mixture on the efficiency of the synthesis. At the same time, the use of ethyl acetate was accompanied by the formation of a homogeneous reaction mass that was difficult to separate, highlighting the necessity of selecting the solvent individually depending on the structure of the target compounds.

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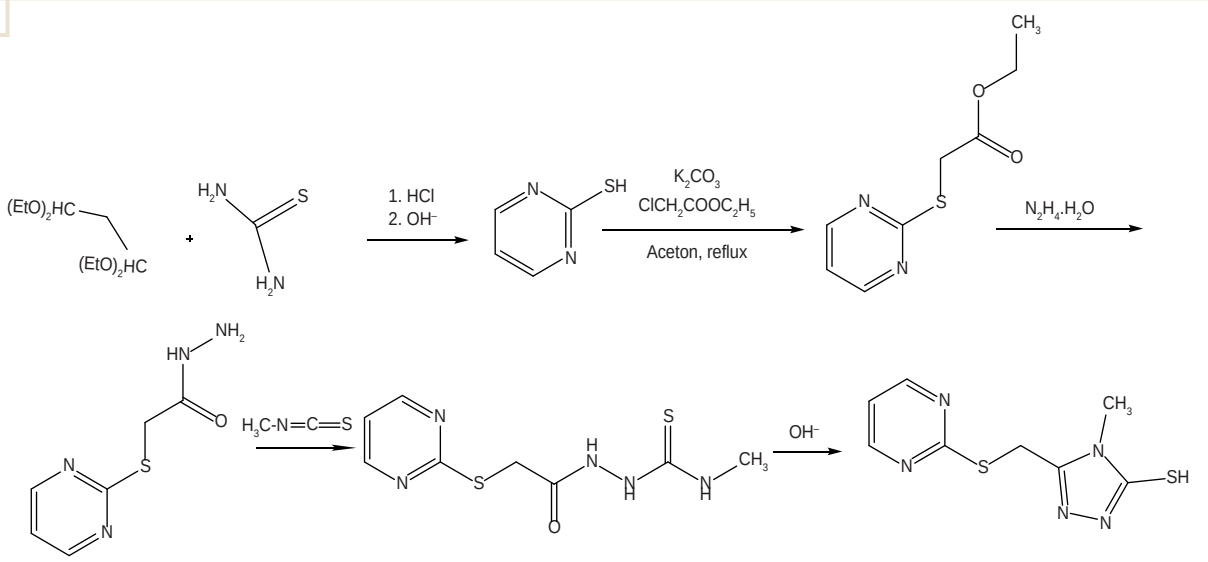

Fig. 4. Scheme of the synthesis of hybrids of 1,2,4-triazol-3(2*H*)-yl)methyl)thiopyrimidine.

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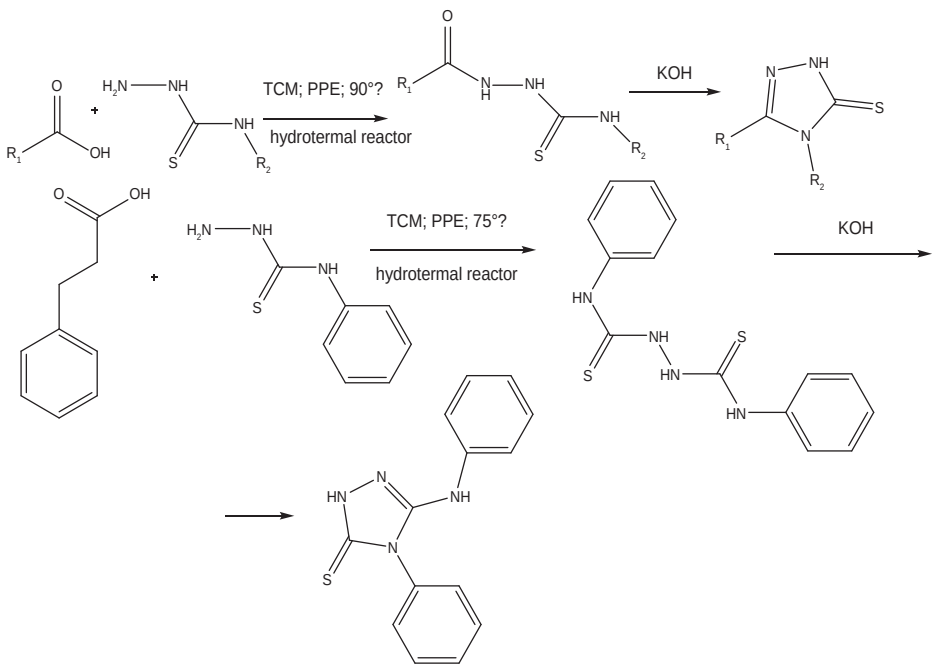

Fig. 5. Scheme of the synthesis of new 4-phenyl-5-(phenylamino)-2,4-dihydro-3*H*-1,2,4-triazole-3-thione.

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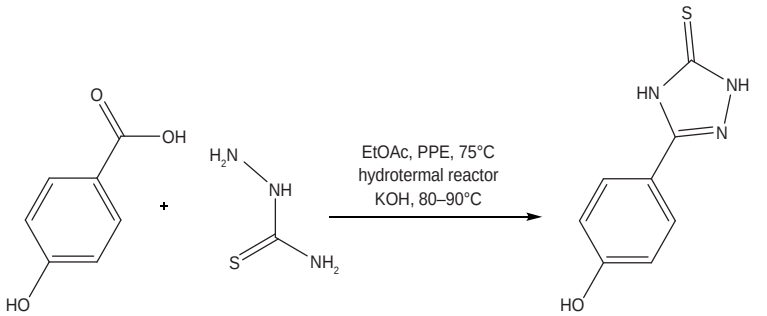

Fig. 6. Scheme of the synthesis of 5-(4-hydroxyphenyl)-2,4-dihydro-3*H*-1,2,4-triazole-3-thione *via* solvent replacement (chloroform with ethyl acetate).

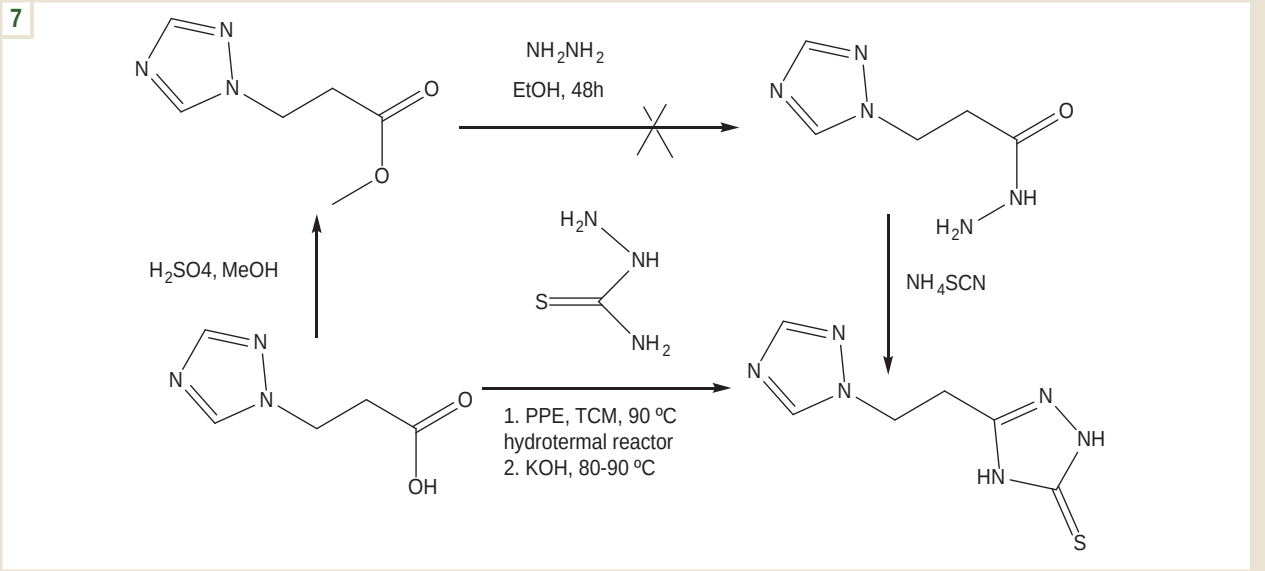

Fig. 7. Scheme of the convergent synthesis of 5-(2-(1*H*-1,2,4-triazol-1-yl)ethyl)-2,4-dihydro-3*H*-1,2,4-triazole-3-thione.

The practical value of the proposed approach to the synthesis of 1,2,4-triazole-3-thiol derivatives is particularly evident in cases where obtaining the corresponding hydrazides, required for classical synthetic methods based on isothiocyanates, is difficult or requires the use of specific and non-standard conditions.

A demonstrative example of such situation is the synthetic scheme shown in *Fig. 7*. It was found that the reaction of a methyl ester with hydrazine in ethanol or isopropanol did not lead to the formation of the target hydrazide, even after a prolonged reaction time (48 h). At the same time, a structurally related compound – 3-(1*H*-benzotriazol-1-yl) propanehydrazide – was successfully formed under analogous conditions, indicating a significant influence of the structure of the starting compound on the course of the reaction illustrated in the scheme in *Fig. 7*.

Chemical modification of 1,2,4-triazole-3-thiol derivatives. The need to generalize data on the reactivity of 1,2,4-triazole-3-thiol derivatives involving the thiol group is driven by the growing interest in this class of heterocyclic compounds as promising objects in medicinal, pharmaceutical, and bioorganic chemistry. The chemically active thiol group (-SH) within the molecule determines their ability to undergo various chemical transformations, including alkylation, acylation, oxidation, as well as the formation of thioethers, disulfides, and coordination compounds. This provides broad opportunities for the targeted synthesis of new functionalized derivatives.

At the same time, the literature contains a substantial amount of information regarding the influence of the electronic nature of substituents, thiol-thione tautomerism, reaction conditions, and reagent choice on the chemoselectivity and course of transformations involving the thiol group; however, these data are fragmented and unsystematized. The lack of a comprehensive summary complicates the prediction of the reactivity of 1,2,4-triazole-3-thiol derivatives, the rational design of synthetic routes, and the reproducibility of experimental results.

Systematizing the available information on thiol-group reactions is an important prerequisite for establishing general patterns of chemical behavior for this class of compounds, understanding the relationship between their structure and reactivity, and optimizing conditions for the synthesis of biologically active substances with predetermined properties. Implementing such an approach will contribute not only to deepening theoretical knowledge of 1,2,4-triazole-3-thiol chemistry but also to forming a scientifically grounded basis for the development of new pharmaceuticals and functional materials.

An original method for transformations involving the thiol group was proposed by the authors' team. Optimization of alkylation conditions through the selection of the alkylating agent, solvent, and base allowed for increased selectivity at the sulfur atom and higher yields of the target products. As a result, a series of new *S*-derivatives of 1,2,4-triazole were synthesized, and their structures were confirmed using modern physicochemical analytical methods (^{1}H and ^{13}C NMR, IR spectroscopy, mass spectrometry). It was demonstrated that the proposed approach is universal and can be applied to the modification of various substituted 1,2,4-triazol-3-thiols, expanding the possibilities for the targeted synthesis of potentially biologically active compounds *(Fig. 8)* [26].

Alkylation of thiols with haloalkanes is one of the most common and efficient methods for the synthesis of thioethers (sulfides) and is widely used in organic and medicinal synthesis. This process proceeds *via* a nucleophilic substitution mechanism, primarily of the S_N2 type, in which the thiol group (-SH), or more often its deprotonated form – the thiolate anion (RS^-) – acts as a nucleophile, attacking the electrophilic Carbon atom of the haloalkane *(Fig. 9)*.

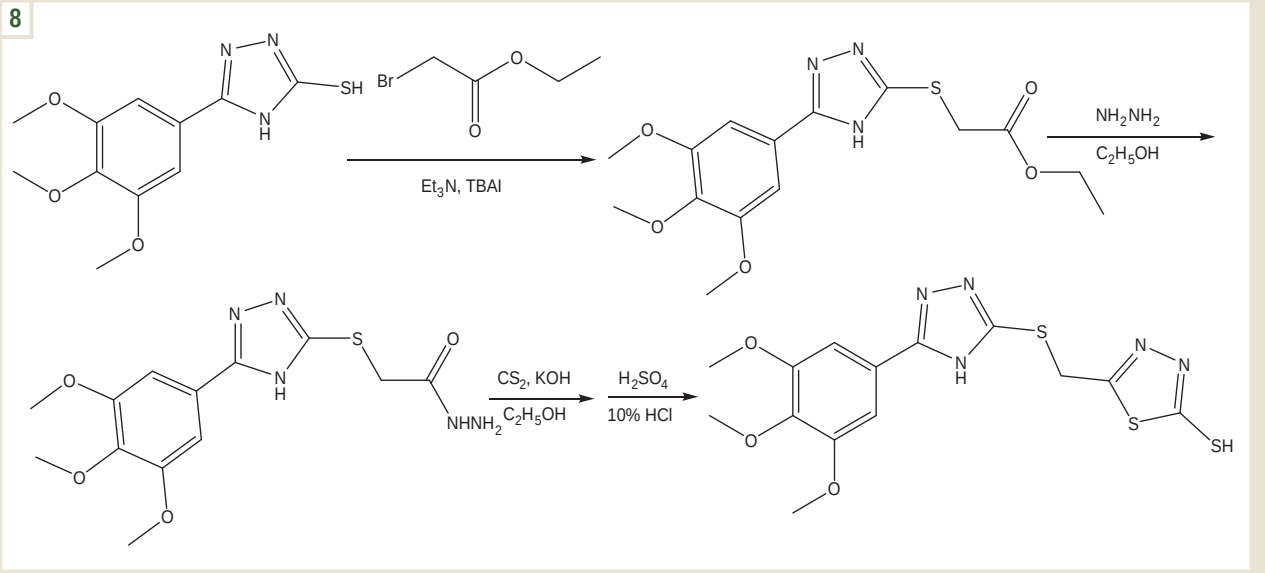

Fig. 8. Scheme of thiol-group transformations of new 5-(((5-(3,4,5-trimethoxyphenyl)-4*H*-1,2,4-triazol-3-yl)thio)methyl)-1,3,4-thiadiazole-2-thiol.

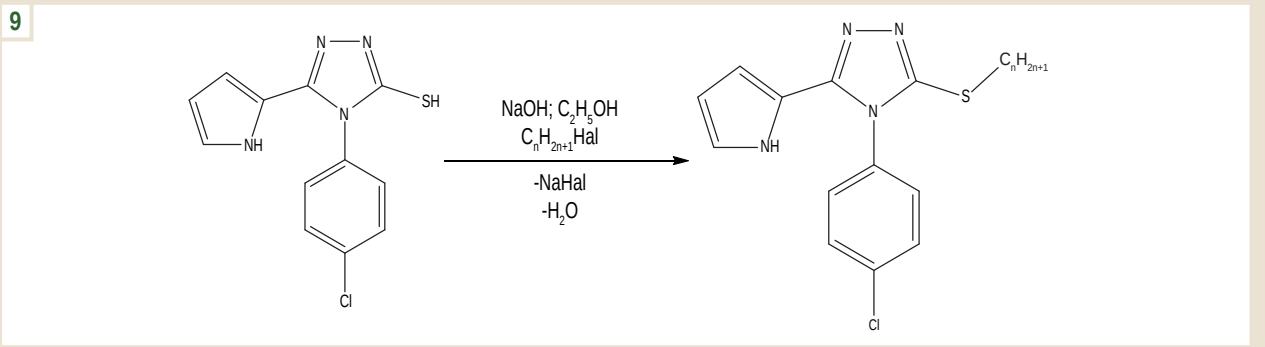

Fig. 9. Alkylation of 4-(4-chlorophenyl)-5-(1*H*-pyrrol-2-yl)-4*H*-1,2,4-triazole-3-thiol.

For reactions proceeding *via* the S_N2 mechanism, inversion of configuration at a chiral center is characteristic. In most cases, alkylation is carried out in the presence of bases (NaOH, K_2CO_3, NaH, organic amines), which ensure the formation of the reactive thiolate anion and help increase the reaction rate and selectivity. The high nucleophilicity of thiolate anions compared to alkoxides is a significant advantage, as it allows alkylation under milder conditions while achieving high yields of the target products [27].

The reaction of phenacyl bromide with 1,2,4-triazole-3-thiol exhibits a number of characteristic features due to the high electrophilicity of the α-haloketone and the ambident nucleophilic nature of the triazole thiol [28]. In the phenacyl bromide molecule, the bromine atom is located at the α-position relative to the carbonyl group, which leads to significant polarization of the C-Br bond and increases the electrophilicity of the methylene carbon atom, facilitating nucleophilic substitution reactions.

1,2,4-Triazole-3-thiol can exist in both thiol and thione tautomeric forms; however, under alkylation conditions, the primary reactive center is the sulfur atom of the thiol group, which exhibits considerably higher nucleophilicity compared to the Nitrogen atoms of the heterocyclic ring *(Fig. 10)*. In the presence of a base, a thiolate anion is formed, promoting an S_N2 mechanism with attack on the α-Carbon of phenacyl bromide and elimination of the bromide anion.

As a result, the reaction predominantly yields the *S*-alkylated product – a phenacyl sulfide derivative of 1,2,4-triazole. The high regioselectivity at the Sulfur atom is due to a combination of the enhanced nucleophilicity of the *S* atom, favorable interaction of a "soft" nucleophile with a "soft" electrophilic center, and the thermodynamic stability of the resulting thioether bond. The use of polar aprotic solvents (DMF, DMSO, acetone) in combination with mild bases contributes to increased reaction rates and higher yields of the target products.

Under harsher conditions or if the nucleophilicity of the thiol group is reduced, competitive *N*-alkylation of the triazole ring is possible, although it is usually a minor pathway. The obtained phenacyl sulfide derivatives of 1,2,4-triazole are of interest as synthetic intermediates and as promising targets for further chemical modification and biological studies.

An original approach to the interaction of nucleoside phosphates with *S*-derivatives of 1,2,4-triazole was proposed

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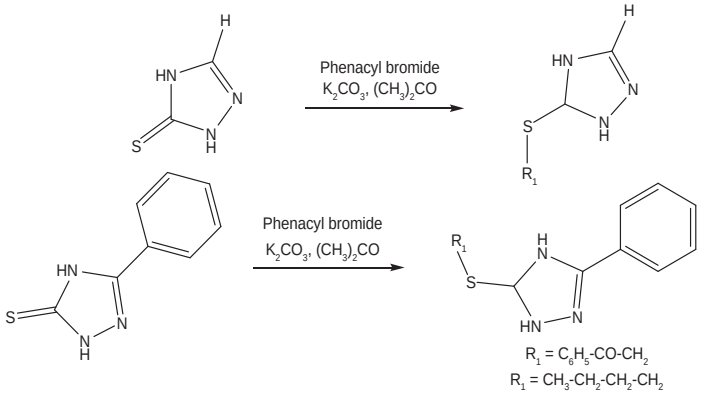

Fig. 10. Scheme of the synthesis of new *S*-derivatives of 1,2,4-triazole.

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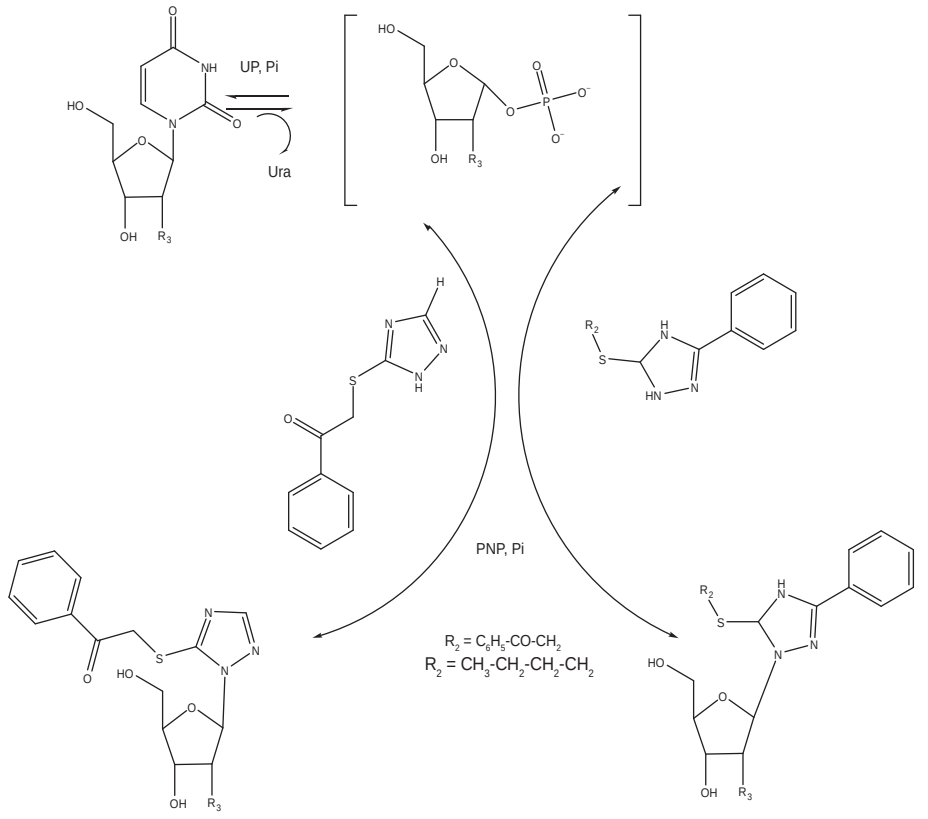

Fig. 11. Scheme of the interaction of a nucleoside phosphate with *S*-derivatives of 1,2,4-triazole.

by the authors' team [28]. Overall, this process can be considered as a nucleophilic substitution or phosphorylation at the Nitrogen atom of the heterocyclic ring, leading to the formation of new *N*-linked conjugates of the nucleoside-triazole type *(Fig. 11)*.

Such compounds are of considerable interest in medicinal chemistry, as they can mimic the structural motifs of natural nucleotides and potentially exhibit inhibitory activity against nucleotide-dependent enzymes.

Alkylation of (1,2,4-triazol-3(2*H*)-yl)methyl thiopyrimidines with haloalkanes is one of the key and widely used methods for the chemical modification of these heterocyclic systems, which is explained by the presence of multiple nucleophilic centers in their structure *(Fig. 12)*. The Sulfur atom of the thiopyrimidine fragment exerts a decisive influence on the course of the reaction; due to its high nucleophilicity and polarization capability, it predominantly undergoes alkylation, ensuring the selective formation of *S*-alkylated products.

In contrast, the Nitrogen atoms of the triazole ring exhibit significantly lower reactivity under standard conditions, so *N*-alkylation is usually a minor process and occurs only under harsher conditions or with the use of stronger alkylating agents [29].

12

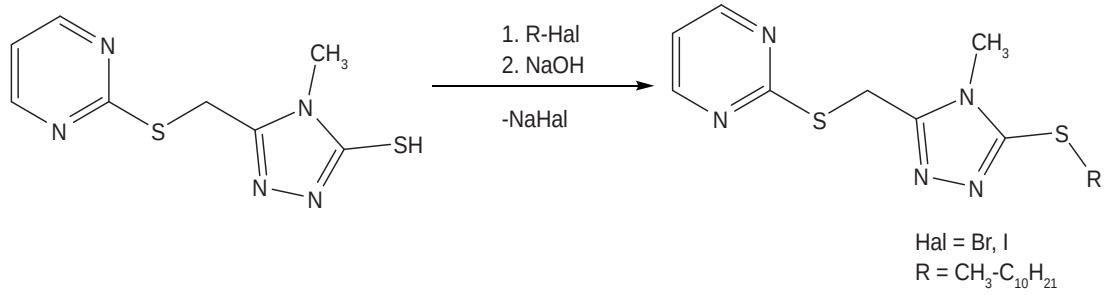

Fig. 12. Scheme of the synthesis of new *S*-derivatives of 1,2,4-triazole.

13

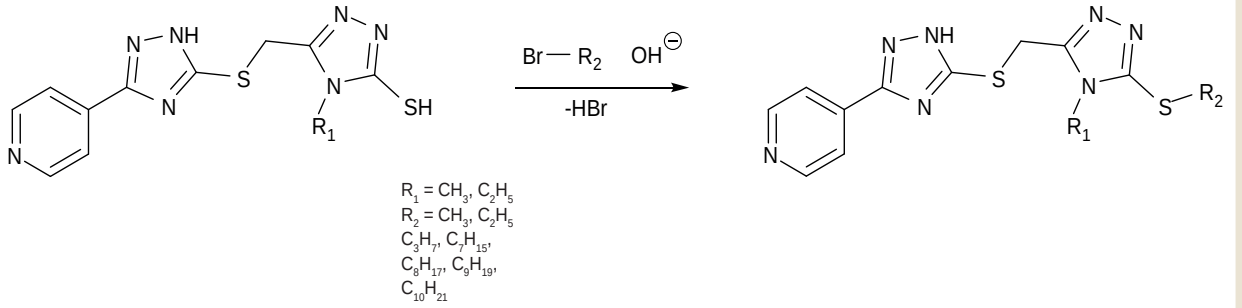

Fig. 13. Scheme of the synthesis of *S*-alkylated 4-alkyl-5-(((3-(pyridin-4-yl)-1*H*-1,2,4-triazol-5-yl)thio)methyl)-4*H*-1,2,4-triazole-3-thiols.

14

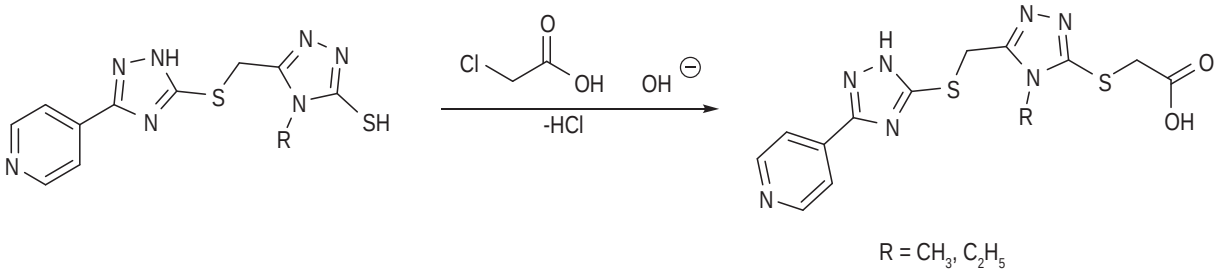

Fig. 14. Scheme of the synthesis of 2-((4-alkyl-5-(((3-(pyridin-4-yl)-1*H*-1,2,4-triazol-5-yl)thio)methyl)-4*H*-1,2,4-triazol-3-yl)thio)acetic acids.

1,2,4-Triazole derivatives containing a thiol group represent an important class of heterocyclic compounds, distinguished by high reactivity and a wide range of biological effects [30].

Of particular interest are the *S*-alkylated derivatives, as modification of the sulfur atom of the thiol group allows targeted control over the lipophilicity, chemical stability, and pharmacological properties of the compounds.

The corresponding *S*-alkylated products were obtained from 4-alkyl-5-(((3-(pyridin-4-yl)-1*H*-1,2,4-triazol-5-yl)thio) methyl)-4*H*-1,2,4-triazol-3-thiols, which contain a free thiol group at the third position of the 1,2,4-triazole ring *(Fig. 13)*. This functional group serves as the primary reactive center in subsequent *S*-alkylation processes.

Heterocyclic compounds containing 1,2,4-triazole and pyridine fragments occupy a key position in modern medicinal and pharmaceutical chemistry. The combination of two pharmacophoric rings – 1,2,4-triazole and pyridine – in a single molecule, along with thioether and carboxyl groups, creates favorable conditions for exhibiting diverse biological activities [31]. The carboxyl group of thioacetic acid enables ionic interactions with biomolecular targets and allows the formation of water-soluble salts, which is important for pharmaceutical applications *(Fig. 14)*.

Alkyl substituents at the 4th position of the 1,2,4-triazole ring modulate lipophilicity and membrane permeability, affecting both the level and spectrum of biological activity. The combination of these structural features makes these compounds promising as potential antimicrobial, antifungal, and anti-inflammatory agents and justifies the need for further pharmacological studies.

Conclusions

1. Analysis of recent literature sources has shown that 1,2,4-triazole-3-thiol derivatives represent a promising class of heterocyclic compounds with a broad spectrum of biological activities, including antimicrobial, antifungal, antiviral, antioxidant, and other effects, combined with relatively low toxicity.

2. It has been established that their pharmacological potential is largely determined by the possibility of targeted structural modification, particularly through the thiol group, which confers high reactivity and favors the formation of *S*-substituted products.

3. These compounds can be synthesized using various methods; however, no universal approach exists, and the efficiency of the processes depends on the reaction conditions and the nature of the starting components.

4. The generalization of data confirms the existence of a structure-activity relationship, providing a foundation for the rational design of new biologically active compounds. At the same time, the available studies are fragmentary and insufficiently systematized, which complicates their practical application.

5. The use of modern *in silico* methods has proven to be an effective tool for the preliminary selection of promising compounds.

Prospects for further research. The results indicate the expediency of further research on 1,2,4-triazole-3-thiol derivatives as a basis for the development of new pharmaceutical agents.

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