UDC:547.856

NEW METHODS OF SYNTHESIS OF QUINAZOLIN-4-THIONE

Saitkulov Foziljon Ergashevich, Elmuradov Burkhon Jurayevich
Tashkent state agrarian university, Uzbekistan
Institute of Chemistry of Plant Substances of the Academy Sciences of the Republic of Uzbekistan, Uzbekistan
fsaitkulov@bk.ru

Abstract: The article shows for the first time the methods of obtaining quinazolin-4-thione in high yields. Quinazolin-4-one thiolation reactions were carried out in two ways, P_2S_5 and Lawesson's reagent.

Key words: obtaining quinazolin-4-thione, Quinazolin-4-one, P_2S_5, Lawesson's reagent, stimulant, pesticide, veterinary, cancer, virus, cardiovascular disease drugs.

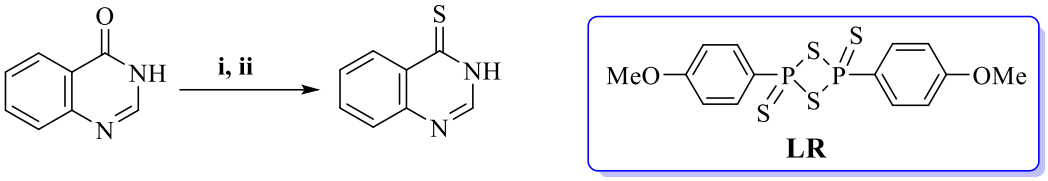
Introduction: It is very interesting to conduct fundamental research with heterocyclic compounds containing several active reaction centers in their molecule. The reason for this is that different isomeric products can be formed from one or another center of the reaction, as well as the synthesis of a product aimed at only one center of the reaction. For this reason, it is important to correctly choose factors affecting the type and yield of products (solvent, temperature, type and amount of reagents) in the implementation of such reactions. Because such compounds have versatile reactivity, important regularities can be found as a result of carrying out reactions under different conditions[1-10].

In particular, when compounds containing an amide group among organic substances are alkylated, the reaction takes place in different directions. Therefore, in such compounds, the reaction takes place by going to the oxygen atom or the nitrogen atom. Such systems can exist in different tautomeric forms: amide, imine and enol. Therefore, they undergo electrophilic exchange reactions differently, and isomeric products with different structures can be obtained.

From the data, it can be seen that it is relevant for the synthesis, modification of selected objects: pyrimidines and their condensed bicyclic products with thiophene, pyrrole, pyridine and benzene rings, and the search for biologically active substances among the obtained compounds. This is explained by the abundance of medicines for agriculture and medicine among them. Therefore, it is very important to develop methods for the synthesis of potential biologically active substances, and the search for "candidate" compounds with various biological activities (stimulant, pesticide, veterinary, cancer, virus, cardiovascular drugs) is an urgent task.

Analysis of results

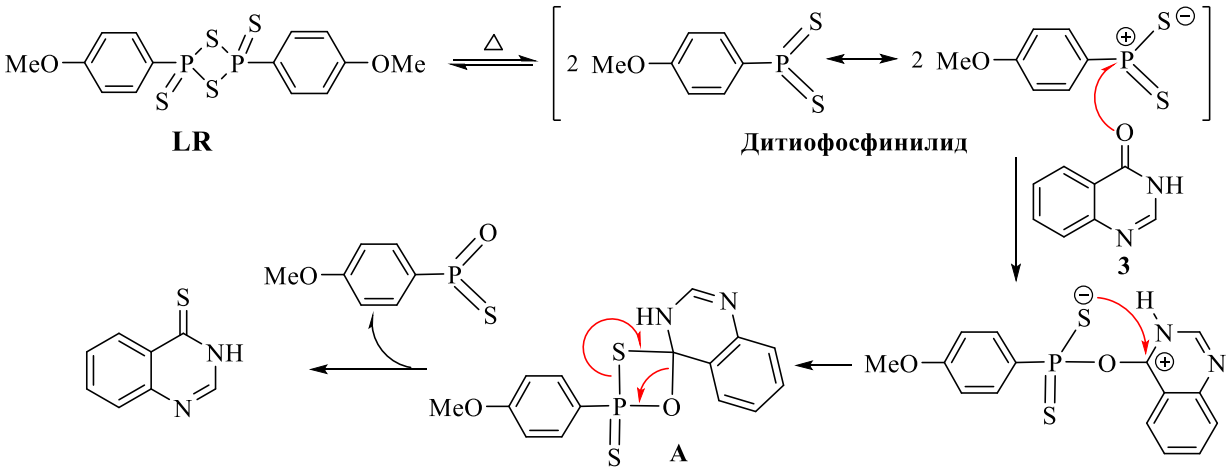
It is known that heterocyclic compounds containing a thione group are of great interest both theoretically and practically. The reason for this is the high synthetic potential of this group and the abundance of biologically active substances among compounds of this class. Quinazolin-4-one thiolation reactions were carried out in two ways: P_2S_5 and Lawesson's reagent:



i) **3**: **P_2S_5** - 1:1, *м*-ксилол (абс.), 139°C, 4 соат, 78%);
ii) **3**: **LR** - 1:0.5, толуол (абс.), 110°C, 1 соат (Ar) (97%)

Reactions with P_2S_5 are carried out by heating the reagents in an equimolar amount at the boiling temperature of m-xylene for 4 hours, and with LR at the boiling temperature of absolute toluene in an inert atmosphere (argon).

The approximate mechanism of the reaction carried out with Lavesson's reagent (LR) can be described as follows: usually, LR is in equilibrium with dithiophosphinilide, which has a high reaction activity when heated in an organic solvent. Its reaction with carbonyl compounds can lead to the formation of the intermediate spiro-thioxaphosphetane (A):



This cyclic compound (A) leads to the formation of stable P=O bond (4-methoxyphenyl)(thioxo)phosphine oxide and the desired thione as a result of thermal cycloreversion (reverse process to cycloaddition!). In the IR spectrum of the ion, there is an absorption frequency corresponding to the C=S bond at 1302 cm-1, in the 1H NMR spectrum, a singlet of the NH group at 13.86 m.u., a one-proton doublet signal of the N-2 proton at 8.59 m.u., 4 aromatics of the benzene ring signals of protons in the form of doublet and triplet appear at 7.62 (t), 7.74 (d), 7.90 (t) and

8.59 (d) m.u., and in the mass spectrum (M=162) m/z = 163 of the protonated molecular ion The detection of $[M^+H]^+$ confirms its structure.

Quinazolin-4-one and quinazolin-4-thione molecules contain C=O, C=S, C=N bonds and aromatic ring chromophores. Therefore, their UV spectrum has absorption frequencies specific to these groups. These molecules have absorption frequencies at 220, 311, 330 nm. The longest absorption line at 311 nm corresponds to the n→p* transition. It should be noted that the position of the main absorption lines increases during the transition to quinazolin-4-one and quinazolin-4-thione derivatives.

It should be noted that the thiolation reactions with LR occur at relatively low temperatures and in a short time, and the product is formed in quantitative yields, indicating that this method is efficient. As a result, a facile and highly efficient thiolation method of quinazolin-4-one (3) was developed.

Excremental part

Quinazolin-4-thione. Method A (in the presence of P_2S_5): A mixture of 1.46 g (0.01 mol) of quinazolin-4-one and 2.22 g (0.01 mol) of P_2S_5 in 50 ml of absolute m-xylene was refluxed for 4 hours, the mixture was cooled, and the reaction mixture was filtered. the residue was washed with m-xylene and treated with 7 mL (10%) NaOH. The resulting precipitate was filtered, washed with water, dried and recrystallized from hexane. As a result, 1.26 g (78%) of quinazolin-4-thione was obtained, melting point 288-289°C, Rf 0.3.

Method B (with Lavesson's reagent (LR)): A mixture of 1.46 g (0.01 mol) of quinazolin-4-one and 2.02 g (0.005 mol) of LR in 30 ml of absolute toluene was refluxed for 1 hour (inert gas, Ar). The mixture was cooled to room temperature, the precipitate was filtered and dried. As a result, 1.57 g (97%) of quinazolin-4-thione (28) was obtained, melting point 288-289°C (hexane). IR (n, cm−1): 1621 (C=N), 1566 (C=C), 1302 (C=S). 1H NMR (d, m.u., Hz): 13.86 (1H, wide.s., NH), 8.59 (1H, d, J = 8.0, H-5), 8.19 (1H, s, N-2) , 7.90 (1H, t, J = 7.5, N-7), 7.74 (1H, d, J = 8.0, N-8), 7.62 (1H, t, J = 7.1, N-6). LC-MS: m/z = 163 $[M^+H]^+$.

Conclusion

It should be said that methylation reactions in the corresponding -thione with respect to quinazolin-4-one mainly take place in the soft center - S4- sulfur atom. The main reason for this is that the electronegativity of the sulfur atom is smaller than that of the oxygen atom in quinazolin-4-ones, so the formation of the ambident ion is more difficult.

Bibliography

1. Saitkulov, F. E., Tashniyazov, A. A., Mamadrahimov, A. A., & Shakhidoyatov, K. M. (2014). 2, 3-Dimethylquinazolin-4 (3H)-one. *Acta Crystallographica Section E: Structure Reports Online*, *70*(7), o788-o788.
2. Sapaev, B., Saitkulov, F. E., Tashniyazov, A. A., & Normurodov, O. U. (2021). Study of methylation reactions of 2-phenylquinazoline-4-tion with "soft" and "hard" methylation agents and determination of its biological activity. In *E3S Web of Conferences* (Vol. 258, p. 04023). EDP Sciences.
3. Sapaev, B., Sapaev, I. B., Saitkulov, F. E., Tashniyazov, A. A., & Nazaraliev, D. (2022, June). Synthesis of 2-methylquinazoline-4-thione with the purpose of alkylation of 3-propyl 2-methylquinazoline-4-thione with alkylating agents. In *AIP Conference Proceedings* (Vol. 2432, No. 1). AIP Publishing.
4. Baymuratova, G., Nasimov, K., & Saitkulov, F. (2023). Synthesis of 6-benzylaminopurine and the study of biological active properties of cotton C-6424 plants. In *E3S Web of Conferences* (Vol. 389, p. 03032). EDP Sciences.
5. Khatamov, K., Saitqulov, F., Ashurov, J., & Shakhidoyatov, K. (2012). 3, 5, 6-Trimethylthieno [2, 3-d] pyrimidin-4 (3H)-one. *Acta Crystallographica Section E: Structure Reports Online*, *68*(9), o2740-o2740.
6. Foziljon Saitkulov, Bairamdurdi Sapaev, Khasan Nasimov, Dilorom Kurbanova and Nargiza Tursunova. Structure, aromatic properties and preparation of the quinazolin-4-one molecule. E3S Web of Conf., 389 (2023) 03075
7. Bairamdurdi Sapaev, Foziljon Saitkulov, Muattar Mamedova, Shahlo Saydaliyeva and Dilafruz Makhmudova. Chromato-mass-spectrometry of the analysis of the sum of the common mushrooms 01006 Published online: 04 September 2023
8. Саиткулов, Ф. Э., Элмурадов, Б. Ж., & Гиясов, К. (2023). Алкилирования хиназолин-4-она «мягким» и «жестким» алкилирующими АГЕНТАМИ. *Universum: химия и биология*, (1-2 (103)), 53-56.
9. Saitkulov, F., Qilichyeva, N., Abdullayev, B., Anvarov, A., & Ergasheva, M. (2022). Titrimetric analysis of calcium cation in" megaton" variety of cabbage. *International Bulletin of Applied Science and Technology*, *2*(10), 134-135.
10. Saitkulov, F., Farhodov, O., Olisheva, M., Saparboyeva, S., & Azimova, U. (2022). Chemical feeding method of lemon plant using leaf stomata. *Академические исследования в современной науке*, *1*(17), 274-277.
11. Boymuratova, G. O., Saitkulov, F. E., Nasimov, K. M., & Tugalov, M. (2022). To Examine the Processes of Biochemical Action Of 6-Benzylaminopurine with Cobalt-II Nitrate Dihydrate on the "Morus Alba" Variety of Moraceae Plant. *Eurasian Journal of Physics, Chemistry and Mathematics*, *3*, 39-42.

12. Murodillayevich, K. M., Shoyimovich, K. G., & Ergashevich, S. F. (2022). Chromoto-Mass Methods for Detecting Simple Esters in Chromatography-Mass Spectrometry Method. *international journal of biological engineering and agriculture*, *1*(6), 53-56.

13. Саиткулов, Ф. Э. (2022). Гиясов Кучкар, Элмурадов Бурхон Жураевич Метилирование 2-метилхиназолин-4-она «мягкими» и «жесткими» метилирующими агентами. *Universum: химия и биология*, (11-2), 101.

14. Saitkulov, F., Begimqulov, I., O‘ralova, N., Gulimmatova, R., & Rahmonqulova, D. (2022). Biochemical effects of the coordination compound of cobalt-II nitrate quinazolin-4-one with 3-indolyl acetic acid in the “amber” plants grades PHASEOLUS AUREUS. *Академические исследования в современной науке*, *1*(17), 263-267.

15. Saitkulov, F., Elmuradov, B., O’lmasova, K., & Alijonova, A. (2023). preparation of a mixed coordination compound cobalt-ii nitrate hexahydrate with quinazoline-4-one and 3-indolylacetic acid on “amber” plants of the phaseolus aureus variety. *Science and innovation in the education system*, *2*(1), 81-87.

16. Bairamdurdi Sapaev, Foziljon Saitkulov, Muattar Mamedova, Shahlo Saydaliyeva and Dilafruz Makhmudova. Chromato-mass-spectrometry of the analysis of the sum of the common mushrooms. BIO Web Conf., 65 (2023) 01006