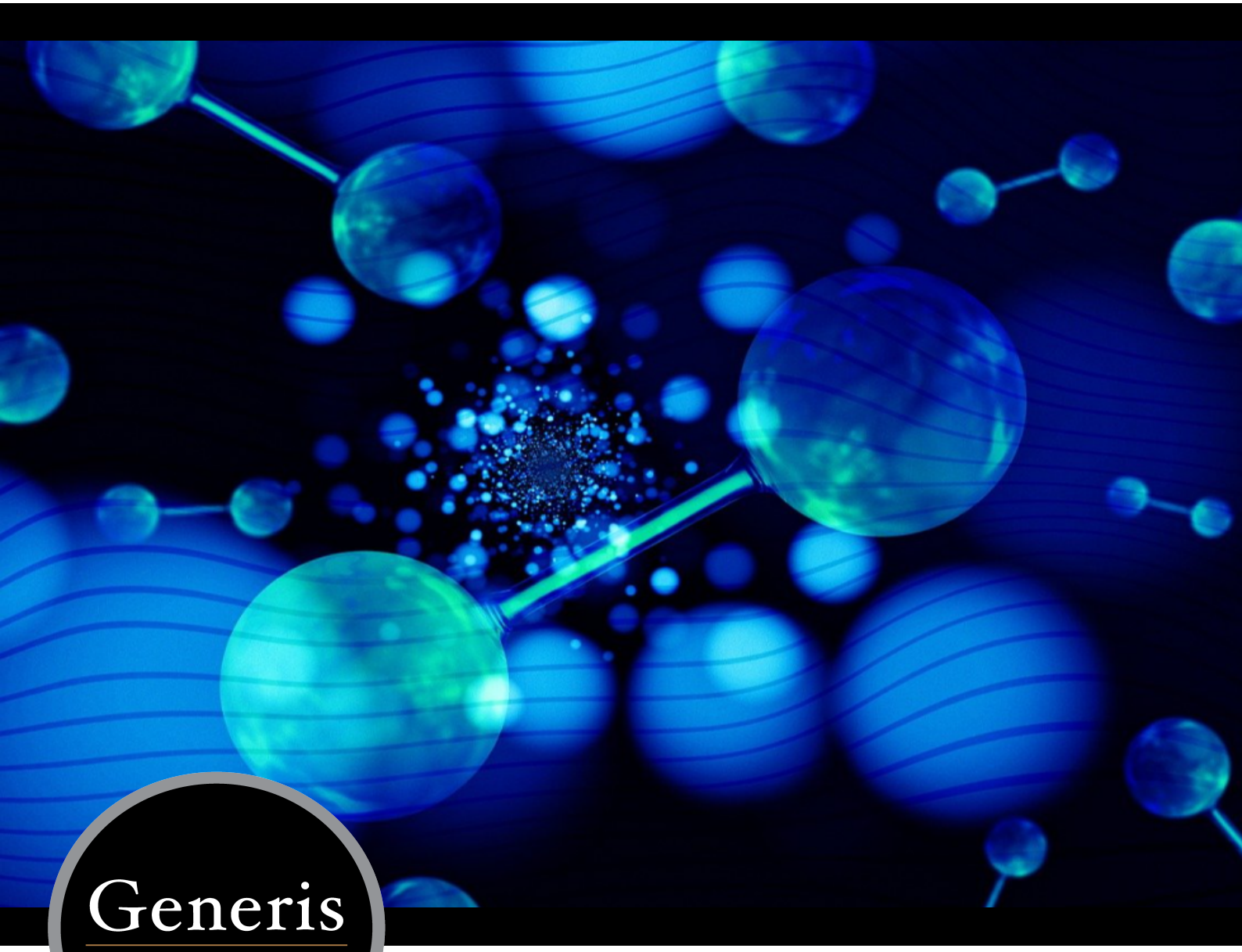
Saitkulov Foziljon Ergashevich



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Title: ***SYNTHESIS OF SOME QUINAZOLIN-4-ONE SERIES HETEROCYCLIC COMPOUNDS AND THEIR BIOLOGICAL ACTIVITIES***

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TABLE OF CONTENTS

1. SYNTHESIS AND BIOLOGICAL ACTIVITY OF HYDROCHLORID QUINAZOLIN-4-ONE

Abstract: By the interaction of anthranilic acid with formamide, an almost quantitative yield of quinazoline-4-oh was obtained. Optimal reaction conditions were established: temperature 130-140 °C, duration 2 hours. Quinazoline-4-oh hydrochloride was obtained from quinazoline-4-oh by passing hydrogen chloride with 96% yield. These compounds at a dose of 100-150 mg/kg exhibit 92% anthelmintic activity against fascioles common in cattle, sheep and goats.

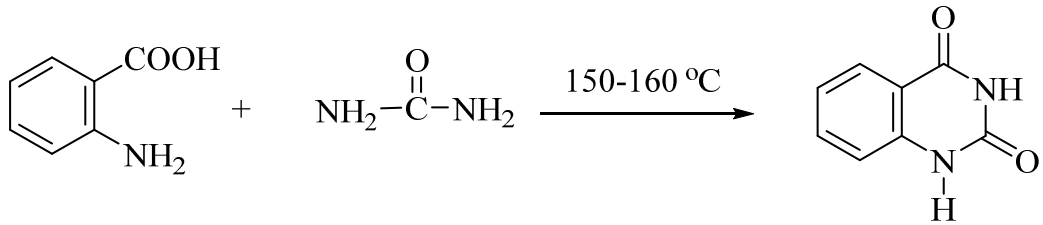
Key words: Formamide, quinazoline-4-one, quinazoline-4-oh hydrochloride fascioliasis, stability of the drug, medamine, albendazole, cattle, sheep and goats, activity against fascioliasis.

Introduction

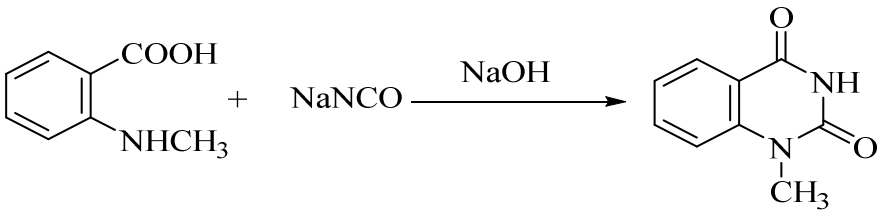
The government attaches more importance to the further increase of folk medicine. A significant place in these activities has been removed from the chemicalization of agriculture and animal husbandry. The Government drew attention to the need for extensive development of scientific research on the creation of herbicides, fungicides, anthelmintic drugs and drugs for pest control of agricultural crops, the organization and search for industrial production of new pesticides. A number of biologically active drugs are known from derivatives of quinazoline-4-one and its sulfur analog quinazoline-4-thion [1]. Recently, scientists from various countries have led to the creation of a large group of highly effective anthelmintic drugs, among the derivatives of quinazoline-4-one [2]. Infection with various kinds of helminths is a widespread disease among both humans and animals. The main requirements for new anthelmintic drugs should be considered a high therapeutic index, a wide spectrum of action, ease of administration, in particular, single-dose treatment and stability of the drug in dosage forms [3-4].

Results

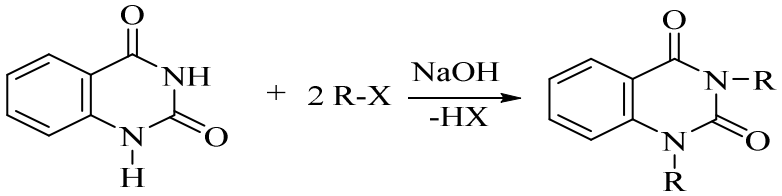
It is known from the literature that quinazoline-2,4-dione is synthesized by heating a mixture of anthranilic acid with mochevina at 150-160°C [5].



The cyclization reaction of N-methylanthranilic acid with sodium cyanate under alkaline conditions resulted in the synthesis of 1-Methylqinazoline-2,4-dione [6].

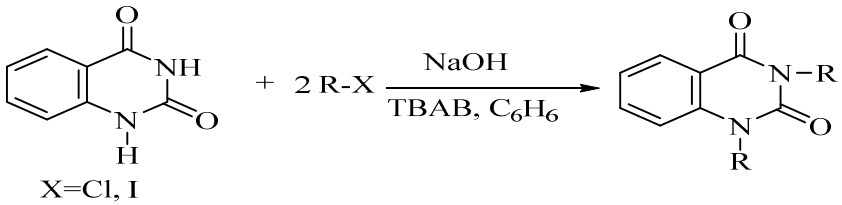


From the reaction of quinazoline-2,4-dione with alkylgalogenides under alkaline conditions, 1,3-dialkylchinazoline-2,4-diones were obtained with high prosent (A-method) [7].

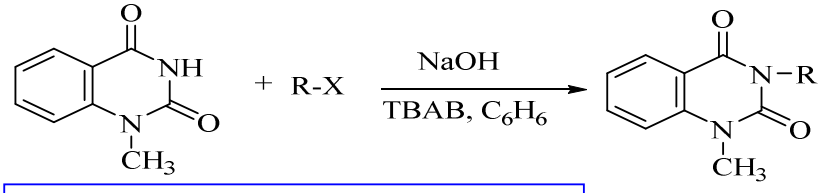


X=Cl, I
R=CH_3, R= н-C_3H_7, R= н-C_4H_9, R= $C_6H_5CH_2$

It should be noted that under the conditions of interphase catalysis [8], 80-95% oxidation of compounds (B) can be observed in these reactions.



Quinozoline-2,4-dione is an equivalent alkylating agent and is formed as a result of the reaction of 1,3-dialkylquinazolin - 2,4-dione to form 1- or 3-monoalkyl molecules[9].



R=н-C_3H_7, R=н-C_4H_9, R=$C_6H_5CH_2$
X=Cl, I

Synthesis of 1-methylquinazoline-2,4-dione alkyl iodides and benzyl chloride of Bilan tetrabutylammonium bromide (TBAB) ishtirok by interphase catalysis in sharoitide [10] as a result of alkylation of 1-methyl-3-alkyl(benzyl)quinazoline-2,4-diones not listed in the literature

There are many works on the synthesis of quinazoline-4-one and its derivatives [11-16]. In most cases, synthesis is carried out from anthranilic acid and its derivatives. Known methods of obtaining quinazoline-4-it is not simple and affordable. The most widely used method is based on the use of hard-to-reach substances.

Method and Methodology

Quinazoline-4-one. Method: A

13.7 g (0.1 mol) of anthranilic acid and 16 ml (0.4 mol) of formamide (p= 1.13 g/ sm^3) were placed in a two-neck flask equipped with a reverse refrigerator.

The reaction mixture was heated in a glycerin bath at 130-135 °C for 2 hours. After cooling to room temperature, the reaction mixture was poured into a glass containing crushed ice and left for 6-8 hours at room temperature. The fallen crystals were filtered, dried and recrystallized in water in the presence of activated carbon. Received 10.7 g (73.3%) of quinazoline-4-one**.**

T = 218ºC, R_f=0,63.

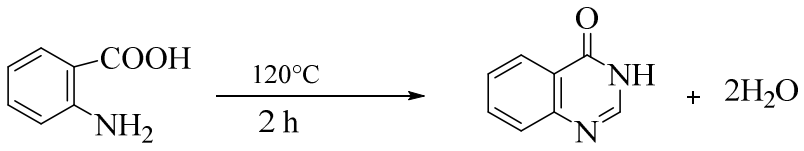
Method B. Similar to Method A, a mixture of 13.7 g (0.1mol) of anthranilic acid and 16 ml (0.4 mol) of formamide (p= 1.13 g/cm^3) heating the Vood alloy at 130-135 °C for 2 hours and received 13.92 g (96%) of quinazoline-4-one, T = 218 °C R_f = 0.63.

Preparation of quinazoline-4-one hydrochloride

To a mixture of 13.7 g (0.1 mol) of quinazoline-4-one and 50 ml of dry acetone, while stirring, hydrogen chloride gas, obtained from 11.7 g (0.1 mol) of sodium chloride and 9.8 g (0.1 mol) of sulfuric acid, was slowly passed through a gas outlet tube for an hour. After removal of the solvent, quinazoline-4-oh hydrochloride was isolated with almost quantitative yield, T=180-181°C.

The aim of the work was to obtain quinazoline-4-oh hydrochloride and laboratory tests for anthelmintic activity.

The synthesis of quinazoline-4-one by the Nimentovsky reaction proceeds when anthranilic acid is heated with an excess of formamide with the cleavage of two water molecules. The low yield in this reaction was tried to explain by its dehydration.



Depending on the reaction conditions, we increased the yield of quinazoline-4-one to 96% by two methods (A and B).

Method A. To obtain the substance quinazoline-4-one, 16 ml (0.4 mol) of formamide (p= 1.13 g/sm^3) was added to 13.7 g (0.1 mol) of anthranilic acid, and the reaction mixture was heated in a glycerin bath at 130-135 °C for 2 hours. Quinazoline-4-oh was obtained at 72% yields.

Conclusion

In the method, a mixture of anthranilic acid and formamide in a ratio of 1:4 was heated into Vood alloy at 130-135ºC for 2. The yield of quinazoline-4-one was 96%. Thus, heating plays an important role in the reaction output (Fig. 1).

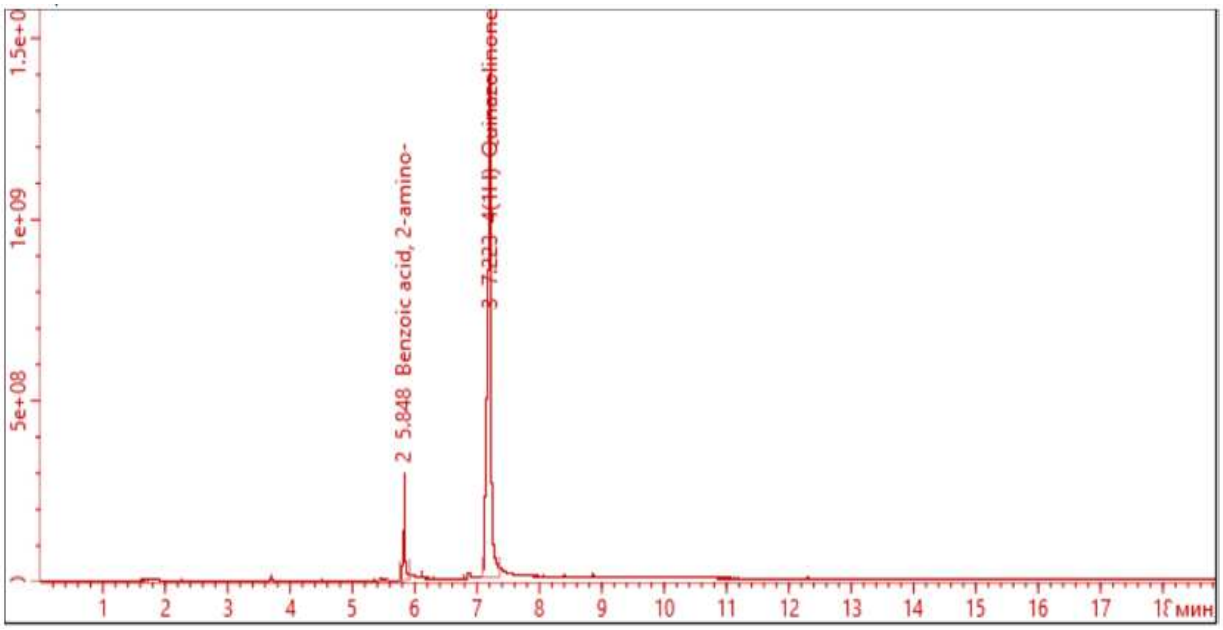


Fig.1

The purity of the product and the course of the reaction were controlled by TLC, Silufol UV-254. (system benzene:acetone 5:3). The melting point of quinazoline-4-oh was determined on the heating table "BOETIUS (Germany)".

The mass spectrum of quinazolin-4-one was removed by chromatek Crystal with the Chromatek-Crystal 5000 mass spectrometric detector, fully confirm the structure of quinazolin-4-one (Fig-2).

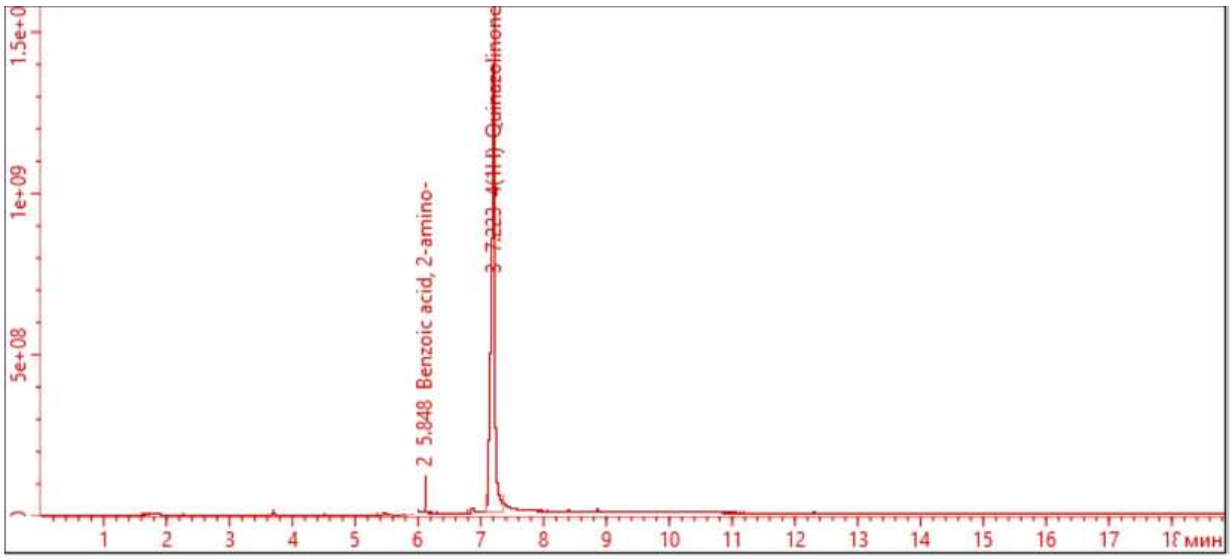
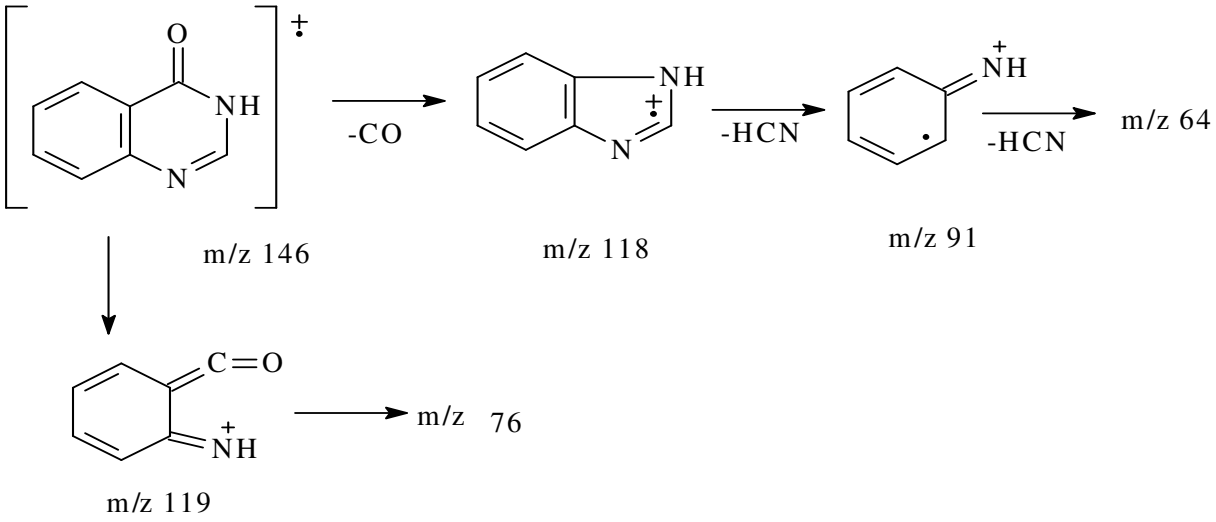
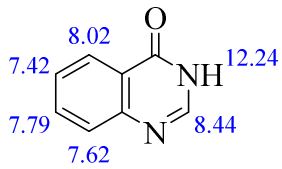


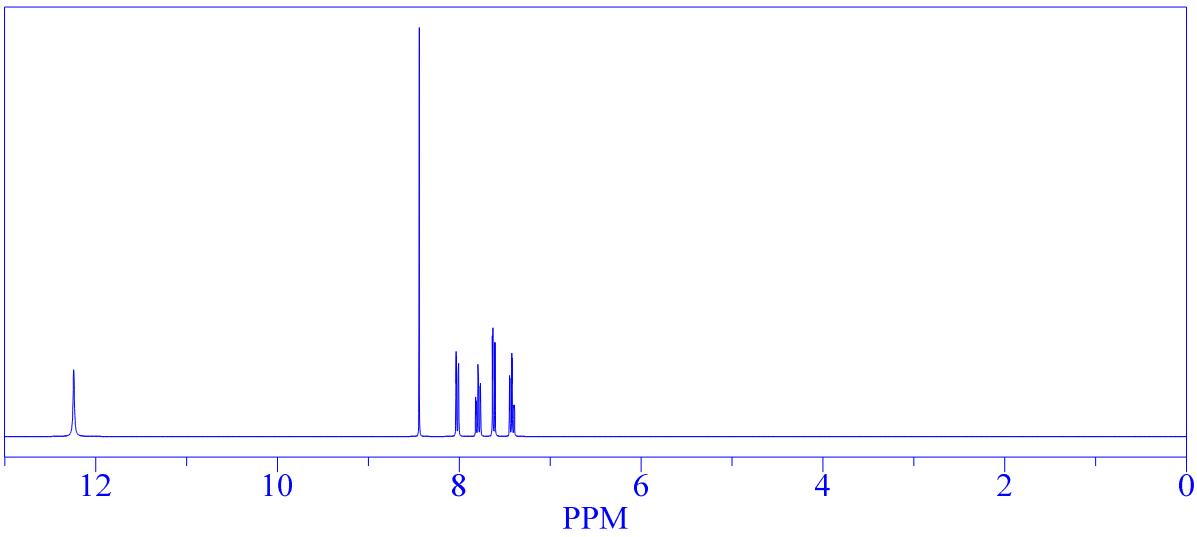
Fig.2

The mass spectrum of quinazoline-4-one is characterized by the presence of an intense peak of the molecular ion. The decay of the molecular ion quinazoline-4-it proceeds with the elimination of CO and HCN. Further fragmentation of the (M-CO)+ ion occurs with the releaseof two HCN molecules.



The structure of the quinazoline-4-on molecule is fully consistent with valence angles 1HNMR spectra.





Protocol of the C-13 NMR Prediction: (Lib=S)

Node Shift Base + Inc. Comment (ppm rel. to TMS)

C 161,0 165,0 1-amide

4,7 1 -1:C*C*C*C*C*C*1

? 1 unknown substituent(s) from N-amide

-8,7 general corrections

CH 145,7 162,8 1-imine

? 1 unknown substituent(s)

0,0 1 -C*R from N-imine

-17,1 general corrections

C 148,2 128,5 1-benzene

20,5 1 -N=C

-1,2 1 -C(=O)-N

0,4 general corrections

C 120,8 128,5 1-benzene

-6,5 1 -N=C

5,0 1 -C(=O)-N

-6,2 general corrections

CH 126,7 128,5 1-benzene

-6,5 1 -N=C

0,1 1 -C(=O)-N

4,6 general corrections

CH 126,6 128,5 1-benzene

1,3 1 -N=C

-1,2 1 -C(=O)-N

-2,0 general corrections

SYNTHESIS OF SOME QUINAZOLIN-4-ONE SERIES HETEROCYCLIC COMPOUNDS AND THEIR BIOLOGICAL ACTIVITIES

It is very interesting to conduct fundamental research with heterocyclic compounds containing several active reaction centers in the molecule. This is because different isomeric products can be formed from one or another reaction center, and product synthesis is focused on only one reaction center. Therefore, it is important to correctly choose the factors affecting the product type and productivity (solvent, temperature, type and amount of reactants) when carrying out such reactions. In particular, in the alkylation of compounds with an amide group among organic substances, the reaction proceeds in different directions. Therefore, in such compounds, the reaction proceeds along the path of transition to the oxygen atom or to the nitrogen atom. Such systems can exist in various tautomeric forms: amide, imine, and enol. Therefore, they enter into electrophilic exchange reactions differently and can give isomeric products of different structures. In the monograph, the methylation reactions of quinazolin-4-one and -thiones and their homologues in various solvents were studied, the synthesized new substances were proven and analyzed using modern physical research methods.

Saitkulov Foziljon Ergashevich

Saitkulov Foziljon Ergashevich was born in the Republic of Uzbekistan. In 1997, he entered the full-time department of Chemistry of Samarkand State University. In 2001, he graduated with honors. In 2001-2004, he worked as a chemistry teacher. In 2004-2006 he was a master's student at the Faculty of Chemistry of Samarkand State University. In 2006-2018 he worked as an assistant at the Faculty of Chemistry of Samarkand State University. He has published more than 120 articles and scientific dissertations in the Republic of Uzbekistan and foreign countries. In 2019, he worked as a chemistry teacher at the Samarkand City Institute for Training and Advanced Training of Personnel. Since 2020, he has been a senior lecturer and an associate professor at the Department of Biochemistry and Physiology of the Tashkent State Agrarian University. In 2024, he received a PhD in Chemical Sciences from the Academic Council of the Academy of Sciences of the Republic of Uzbekistan.

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