Synthesis of quinazolin-4-one and its application in some areas of bioengineering

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Abstract. Until this research, many studies have been conducted with benzimidazoles and quinazolones, but there is almost no comparative information in the literature about the synthesis of 2- placed quinazolone and quinazolintion and their selective methylation under different conditions, as well as their biological activity. Therefore, among these compounds, 2-substituted It is desirable to systematically study the synthesis of quinazolin-4-one and -thiones, to determine the factors affecting the course of reactions, to carry out some chemical changes of the obtained 2-substituted quinazolin-4-one and -thiones and their derivatives, and to identify new biologically active compounds.

1 Introduction

The government of Uzbekistan attaches great importance to the future prosperity of the field of agriculture, medicine and veterinary medicine. Especially great attention is paid to the activities carried out in livestock and chemical processing of land areas.

In order to increase the integration of chemical and Biological Sciences in our country, to increase the quality efficiency in education, several measures have been implemented.

Attention is paid by the staff of the Institute of scientific investigation to the need to widely develop scientific research on the creation of compounds in the cultivation of agricultural products against the loss of wild grass, against fungi and bacteria, antihelements and pest control agents, that is, effective fresh rapidly decomposing and not collecting pesticides in the environment, further improving their chemical and biological properties.

Scientific innovations in chemistry and biology of benzimidazoles and quinazolones began more than 100 years ago. In many countries of the world, even now, research on the basis of this class of compounds is being carried out intensively. In particular, foreign Scientists-N. Siddiqui, V.S. Padalkar, R. Hussain, A. Teimouri, T. Narender, W.K. Tchaikovsky, J.P. Michael, K. Nepali, S.B. Mhaske, M.T. Richers, W.R. Bowman has been involved in the study of the synthesis, reactions, and applications of benzimidazoles and quinazolones in practice. S. on the development of these directions in our republic.Yu.

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syunusov, H.N. Aripov, T.S.Tulyaganov, H.M. Shahidoyatov, N.D. Abdullaev, N.K. Rozhkova, N.A. Aliev, K.Giyasov, S.A. Hasanov, Ch.Sh. Kadyrov, B.J. Elmuradov, A.T. Ayupova, I.B. Payziev, N.S. Mukhamedov, B. Diabodzhaev, D.I. Egamov, A.Sh. with his research, Abdurazakov and others have contributed to the synthesis of quinazolones, benzimidazole and benzoxazolinones and their derivatives, the implementation of chemical transformations and the determination of their biological activity.

Preparations based on heterocyclic compounds – benzimidazols and quinazolones (benzopyrimidinones) in agricultural, medical and veterinary practice in the world are herbicides, fungicides (carbendazim, benomil), bactericides, antihelminth (albendazole) and hypotensive (bendazole) agents, as well as drugs against viruses, microbes, colds and cancer (imatinib, erlotinib) drug adjective-hand. Also, as a result of research on the biological activity of compounds (thioamides), in which the sulfur atom was secreted, medicinal compounds were found against tuberculosis, bacteria, wounds and tumors; in addition, compounds that manifestation herbicide and insecticide activities for rural juiciness were diluted.

Therefore, it is very relevant to carry out scientific and practical research to carry out the purposeful synthesis and chimaeval transformations of the thioamides of the benzimidazols and quinazolones series, in which the pharmacophore in question disassembled the fragment of heterocyclic compounds, their physicochemical and biological properties, the creation of new drugs based on selected active ingredients.

2 Methods and results

It is of great interest that chemical processes in open and closed chain compounds containing an amide functional group of organic chemistry have a doublet nature, because in these compounds chemical bonds are formed by affecting the oxygen or nitrogen atom in the substance.

There are other representatives of organic chemistry with ambident properties, in which imino, amide and enol tautomerism are in equilibrium. When such organic compounds undergo chemical reactions, the chemical reaction takes place in the oxygen or nitrogen atom.

Quinazolin-4-ones, like other organic compounds, form ambident and polydent anions, and these processes are carried out in the presence of NaOH or KOH, the resulting negative charge is equally distributed on all oxygen and nitrogen atoms. This anion is called a polydentate anion. It has been studied whether chemical processes in quinazolin-4-ones take place in O4 or N3 or N1 atoms. This decision is of great theoretical and practical interest in finding reaction centers in heterocyclic compounds [1-3].

As a result of the analysis of substituted quinazolin-4-ones and their other representatives in the second case, we got such a conclusion. Solvent, temperature and duration of time affect the implementation of chemical processes.

In these processes, the deprotonation of the molecule under the influence of a base leads to the formation of an anion. In the second case, the anion formed as a result of deprotonation in quinazolin-4-ones containing a heteroatom is divided into an ambidient character., it has a negative charge on its atoms, or a polydent character, it is distributed among the fragments [4-6].

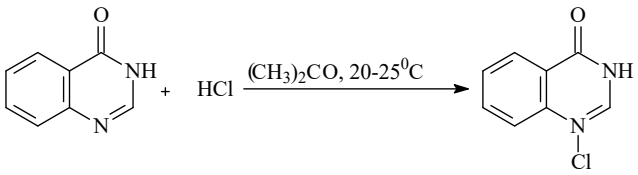
Alkylation of substances of this class, determination of its direction, determination of the resulting O4/N3 or O4/X2 or N1/X2 ratios have been properly studied at the Institut of Plant Substances Chemistry of UzFA. It is worth saying that these systems are complex, and it is somewhat difficult to determine the effect of this or that fragment.

There are many works on the synthesis of quinazoline-4-one and its derivatives. In most cases, synthesis is carried out from anthranilic acid and its derivatives. Known methods of

obtaining quinazoline-4-one it is not simple and affordable. The most widely used method is based on the use of hard-to-reach substances.

2.1 Use of quinazoline hydrochloride in bioengineering

Anthelminthic properties. By passing hydrogen chloride to the acetone solution of quinazoline-4-one, hydrochlorid quinazoline-4-one was obtained with almost quantitative yield.



Derivatives of quinazoline-4-oh have been studied for anthelmintic activity against gastric-intestinal fascioles of various concentrations in laboratory conditions. According to the test results, the derivative did not exhibit anthelmintic properties. On the other hand, it has been studied that quinazoline-4-oh hydrochloride has anthelmintic properties. Substances that fight certain anthelminths were obtained in the form of Medamine, Albendazole, a confirming (reference) agent in the fight against a wide range of spirals. Good results were achieved in cattle, sheep, goats when using quinazoline-4-one hydrochloride. At a dose of 100-150 mg/ kg, it exhibits 92% anthelmintic activity against fascioliasis.

In the future, it is possible to create drugs from among substances derived from quinazoline-4-oh and quinazoline-4-tion, which may exhibit high anthelmintic activity. Thus, the recommended quinazoline-4-oh hydrochloride can be used as an effective drug against fascioliasis helminthiasis.

Growth activity."Bukhoro-102" cotton seeds were used to evaluate the germination activity of the synthesized substances. Concentrations of 0.1%-0.001% of substances were used for laboratory experiments, and the growth regulator Novosil was selected as a standard.

Table-1 shows that 3-methyl quinazolin-4-one at concentrations of 0.01% showed a growth-promoting activity, root length by 42.7% compared to the comparative, stem height by 64.60 %, and when the drug is compared with the drug Novosil increased by 27.5% and 36.3%, respectively.

Table 1. Antiproliferative activity of derivatives of quinazolin-4-one methylation reaction against cotton "Bukhoro-102".

№	Sample	Concentration, %	Cotton plant	
			Root length %	Stem length %
1	Comparative	0	6	10
2	Novosil	0.0010	15.2	28.30
3	Quinazolin-4-on	0.0010	13.1	25.1
4	N3-methil quyinazolin-4-on	0.010	42.7	64.6
5	N3-methil quyinazolin-4-on	0.0010	36.1	59.5

This synthesized substance at a concentration of 0.001% It was found that the length of the root and stem of the cotton plant increased by 36.1% and 59.5% and by 20.9% and 31.2% compared to the standard. This table is represented graphically.

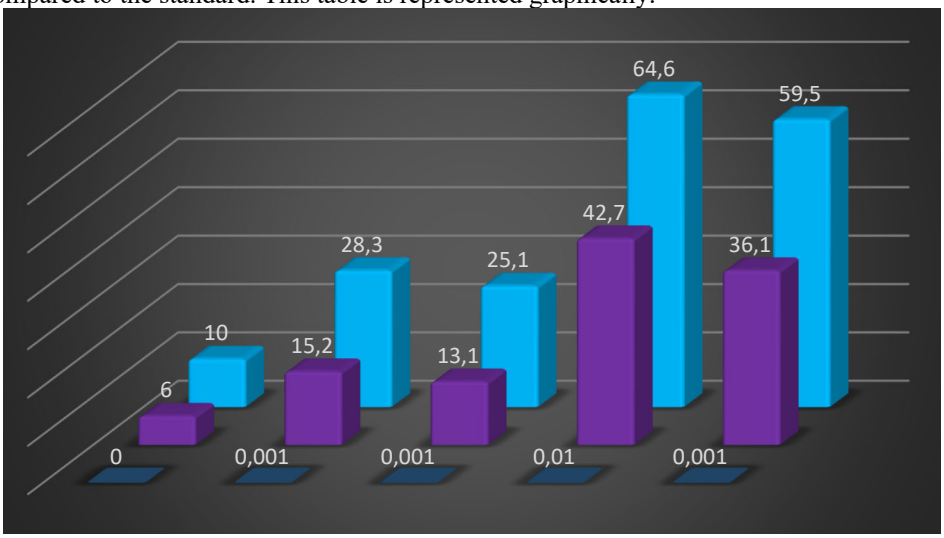


Fig. 1. Antiproliferative activity of derivatives of quinazolin-4-one methylation reaction against cotton "Bukhoro-102".

3 The exprimental part

Quinazoline-4-one. Method: A. 1.3701 g (0.01 mol) of o-aminobenzoic acid and 16.0585 ml (0.401 mol) of formic acid amide (p = 1.1301 g/ml) were placed in a three-necked beaker and a reflux condenser was installed. the mixture was heated at 130-135°C for 1.5 h. After 100% conversion, the reaction mixture was cooled to 25°C. Pieces of ice were placed in the pan and crushed, and the resulting substance was poured over it and left for 6-8 hours. The resulting crystals were filtered, dried, and recrystallized in water using activated charcoal. 12.7 g of quinazolin-4-one was synthesized.

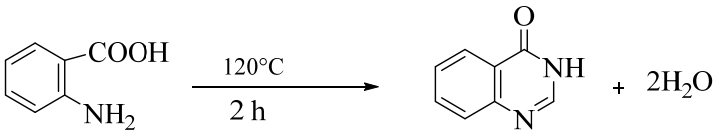
Method B. Similar to Method A, a mixture of 1.3701 g (0.01 mol) of o-aminobenzoic acid and 16.0585 ml (0.401 mol) of formic acid amide (p = 1.1301 g/ml) heating the Vood alloy at 130-135°C for 2 hours and received 13.92 g (96%) of quinazoline-4-one,

Methylation of quinazolin-4-one. 1.4501 g (0.01 mol) of quinazolin-4-one chlorocalcium was placed in a three-necked flask fitted with a tube, thermometer, and mechanical stirrer, 0.56 g (0.01 mol) of KOH in 50 mL of DMFA was added, and stirred for 5 min, then 1 .06 mL (r=1.33 g/ml) (0.01 mol) of methyl iodide was mixed with 5 mL of DMFA and placed in a flask. The mixture was heated in a water bath at 85-90°C for 4 hours. 100 ml of water was added, extracted with chloroform, dried over dry Na_2SO_4. Driven out. Recrystallized from alcohol. As a result, 2.8 g of 3-methylquinazolin-4-one is formed in 82% yield.

Preparation of quinazoline-4-one hydrochloride. To a mixture of 13.701 g (0.01 mol) of quinazoline-4-one and 50 ml of dry acetone, while stirring, hydrogen chloride gas, obtained from 11.703 g (0.01 mol) of sodium chloride 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 main goal of the work was to find optimal methods of synthesis of quinazoline-4-oh hydrochloride and to conduct laboratory tests to study anthelmintic activity.

Synthesis of quinazolin-4-one by the Nimentovsky method is carried out by dehydrogenation of two water molecules when o-amino benzoic acid is heated with a large amount of formic acid amide. This chemical reaction differs from other reactions in that it has a high quantitative yield and takes place at a relatively low temperature.



4 Conclusion

In the method, a mixture of o-amino benzoic acid and formic acid amid 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 (figure 2).

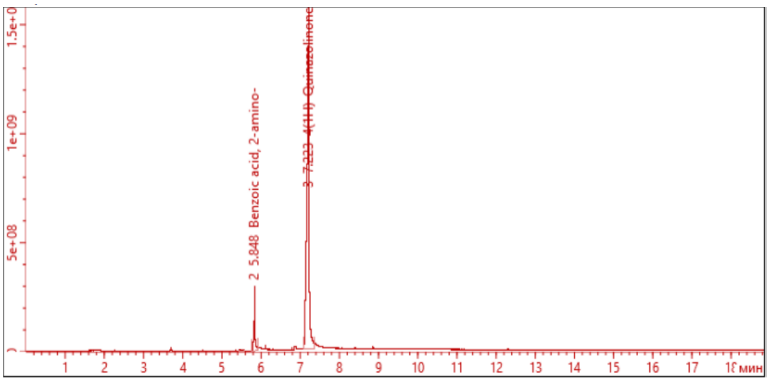


Fig. 2. Spectral analysis of synthesized quinazolin-4-one.

Formation as a result of chemical processes and the purity of the substance were controlled by TLC, Silufol UV-254. (system benzene:chloroform 5:3). The melting temperature was determined on the "BOETIUS (Germany)" apparatus

The confirmatory mass spectrum of quinazolin-4-one was studied and confirmed by Chromatek Crystal using a Chromatek-Crystal 9000 mass spectrometric detector (figure 3).

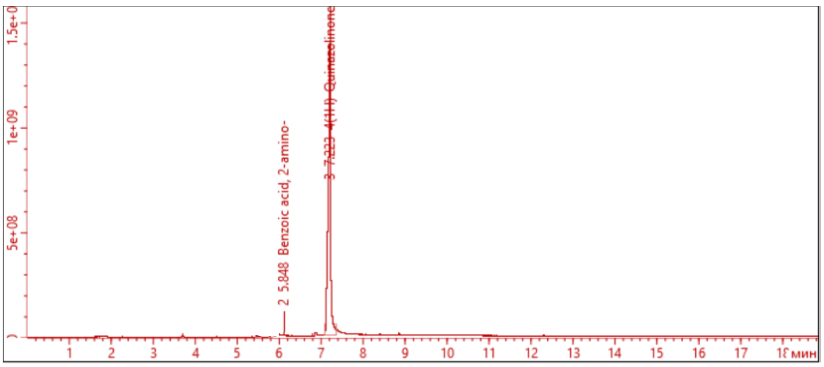
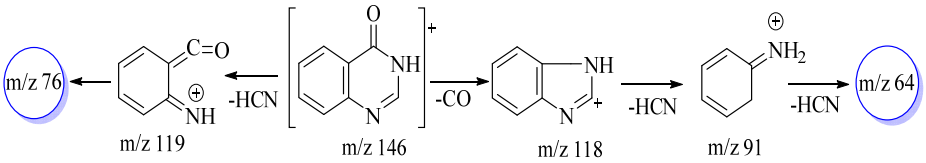


Fig. 3. Spectral analysis of synthesized quinazolin-4-one.

From the determination of the mass spectrum of quinazolin-4-one, it can be concluded that the dependence of the molecular mass on the charge is studied. In the mass spectrum of the quinazoline-4 molecule, CO and HCN are released from the decomposition of the molecule. Occurs with the release of two molecules of (M-CO)+ ion HCN.



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

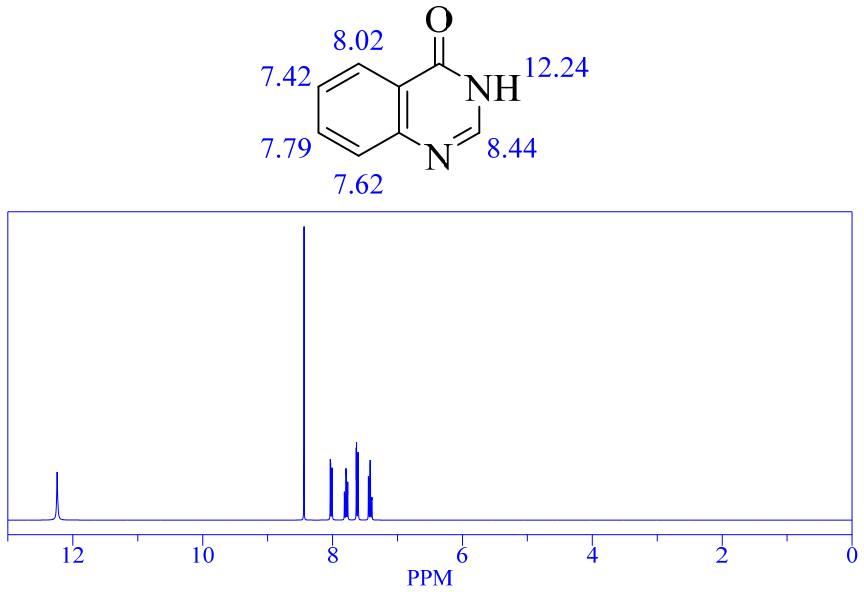


Fig. 4. The quinazoline-4-on molecule is fully consistent with valence angles 1HNMR spectra.

A one-step method for the synthesis of quinazolin-4-one was developed. In this case, it has been proven that it is convenient to react with o-aminobenzoic acid and formic acid amide in a ratio of 1:4.

The optimal temperature was established – 130-135 ° C, duration 2 h

It was shown that quinazoline-4-oh hydrochloride in doses of 100-150 mg/kg eliminates up to 100% of helminthiasis of gastrointestinal fascioles.

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