STUDY OF THE CYANIDATION REACTIONS OF ALIPHATIC AMINES

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Abstract. *The article presents data on the synthesis of α-aminonitriles on the basis of ethylenediamine and a number of other secondary and primary aromatic amines. Acetone cyanohydrin, sodium, potassium and ammonium salts of cyanic acid were used as the cyaniding agent.*

Keywords: *methylamine, ethylamine, dimethylamine, diethylamine, morpholine, piperidine, acetone cyanohydrin, sodium cyanide, potassium cyanide, ammonium cyanide, product yield, IR spectra.*

ИССЛЕДОВАНИЕ РЕАКЦИЙ ЦИАНИРОВАНИЯ АЛИФАТИЧЕСКИХ АМИНОВ

Аннотация. *В статье приведены данные по синтезу α-аминонитрилов на основы алифатическими аминами. В роли цианирующего агента использованы ацетонциангидрин, натриевое, калиевое и аммониевое соли цианистой кислоты.*

Ключевые слова: *метиламин, этиламин, диметиламин, диэтиламин, морфолин, пиперидин, ацетонциангидрин, натрий цианид, калий цианид, аммоний цианид, выход продукта, ИК-спектры.*

Entering. Today, in the world, it is very important to develop methods of targeted synthesis of new organic molecules with high biological activity, containing various functional groups, and to use them in practice. Aminonitriles and their modification products occupy an important place among such molecules. In this direction, it is important to create highly effective drugs that substitute for import and export, and further improve their biological properties. The use of chemical plant protection agents and plant-growing chemical compounds increases the resistance of plants to various diseases, ensures early ripening of crops, and creates the basis for increasing

productivity and obtaining high-quality products. We can include α-aminonitriles, nitrile derivatives of α-amino acids, which are very necessary for the life of living organisms, among plant-growing substances. Also, the α-aminonitrile fragment is found in various alkaloids, and the α-amidoacetonitrile group is an important fragment of new hypoglycemic drugs and promising pharmacological and agrochemical agents.

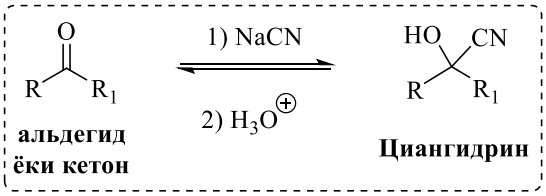
Literature review

Research in the field of chemistry and biology of aminonitriles began in the middle of the 19th century. In a number of countries of the world, researches with combinations of this class are being conducted intensively. In particular, foreign scientists - A. Strecker, T. Opatz, J.P. Hurvois, P. Galletti, D. Giacomini, A.M. Nauth, X. Feng, T. Kawasaki, N. Takamatsu, S.I. Murahashi, V.V. Zhdankin, H. Shen, C. Yan, M. Rueping, E.N. Jacobsen, C. Kunick, F. Fleming studied the synthesis, modification and application of aminonitriles. The development of this direction in our country was supported by H.M. Shakhidoyatov, N.D. Abdullayev, M.G. Levkovich, B. Tashkhodjayev, B.J. Elmuradov, V.A. Saprikina, T.F. With their research, Ibragimov and others have contributed to the synthesis, reactivity, chemical transformation of aminonitriles, their structure and biological activity.

In the scientific literature [1,2] researches have been carried out with aminonitriles, but in this direction, the development of multicomponent one-pot synthesis (One-pot synthesis) methods of homologous series of aliphatic, aromatic and heterocyclic mono- and bis-aminonitriles, their various substitutions and coupling reactions, as well as information on syntheses of biologically active compounds among them is rare.

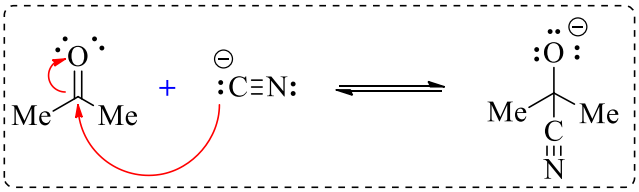
Research Methodology

When hydrogen cyanide (HC≡N) is added to aldehydes and ketones, it forms hydroxyalkanenitriles, commonly called cyanohydrins:



The reaction mechanism can be roughly described as follows: the reaction consists of two stages, the first stage - a nucleophilic attack of the cyanide anion formed in an acidic environment of sodium cyanide on the carbonyl group, and a new alkoxide anion with a C-C bond is formed :

Level I



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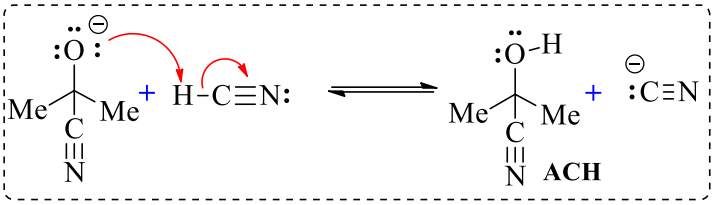
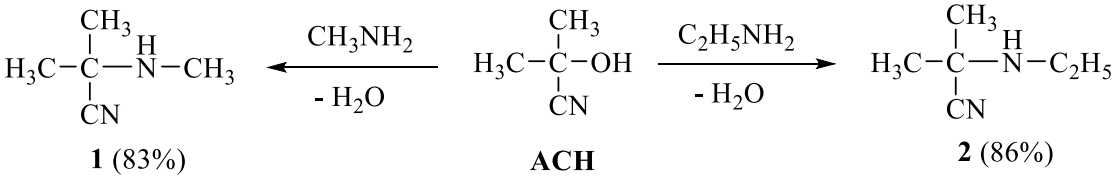


The second stage of the reaction is protonation, that is, the alkoxide anion is protonated under the influence of HCN, the cyanide anion is re-formed, and the process continues.

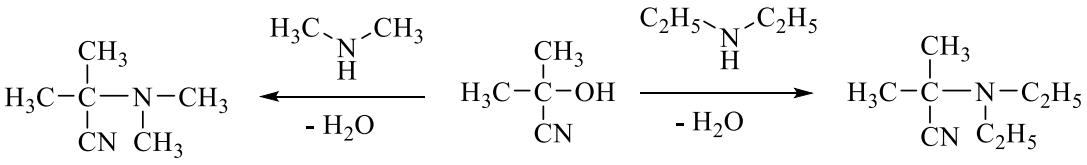
The reaction of acetoncyanohydrin (ACH) with methylamine and ethylamine was carried out by stirring the mixture of reagents: ACH:Amine - 1:1 ratio in hexane solvent for 2-2.5 hours at room temperature. It was found that the nitrilation reaction is exothermic and ends in a relatively short time, and 2-methyl-2-(methylamino)propanenitrile (1) and 2-(ethylamino)-2-methylpropanenitrile (2) were synthesized with high yields:



1 (83%) **ACH** **2** (86%)

Exothermic progress of the reaction is expressed by the basicity of the amines obtained for the reaction and the high acidity of acetocyanohydrin.

During the research, the reactions were carried out with secondary amines (dimethylamine and diethylamine) under the above conditions and the corresponding 2-(dimethylamino)-2-methylpropanenitrile (3) and 2-(diethylamino)-2-methylpropanenitrile (4) were obtained:

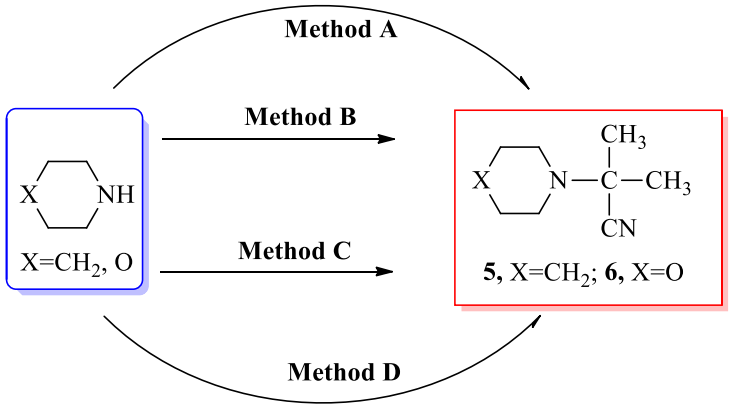


3 (88%) **ACH** **4** (94%)

It should be noted that the reactions proceeded very easily and the necessary products (3, 4) were synthesized with high yields. Table 2.1 lists the basicity and acidity constants of amines of different classes. Due to the electron-donating effect of alkyl groups, amines are stronger bases than ammonia. However, of all amines, secondary amines are the strongest bases. Tertiary amines have a lower basicity, which is due to the presence of spatial barriers for the transfer of a proton

to them and the solvation of the formed ammonium cation. In the gas phase without solvation effects, the basicity of amines decreases approximately in the following order: tertiary > secondary > primary > ammonia. However, this rule is violated in aqueous solutions: the presence of a third substituent creates a spatial (steric) barrier both for the addition of a proton and for the solvation of the formed cation by solvent molecules. Aromatic amines are weaker bases, which is due to the delocalization of the lone electron pair of the nitrogen atom along the aromatic nucleus.

Analysis and results (Analysis and results). Studies were continued in the presence of secondary heterocyclic amines. In particular, we were very interested in researching the reactions of acetoncyanohydrin with morpholine and piperidine, in terms of studying the biological activity of the obtained products.



Method A: piperidine/morpholine:ACH- 1:1, heksane, boil (68^0C), 2 hours, efficiency (**5**, 88.3%; **6**, 83%).
Method B: piperidine/morpholine:NaCN:acetone - 1:1:1, heksane, boil (68^0C), 2 hours, AcOH (5%, 10 ml), 30 minutes, efficiency (**5**, 87%; **6**, 84.4%).
Method C: piperidine/morpholine:KCN:acetone - 1:1:1, heksane, boil (68^0C), 2 hours, AcOH (5%, 10 ml), 30 minutes, efficiency (**5**, 91.3%; **6**, 86%).
Method D: piperidine/morpholine:NH_4CN:acetone - 1:1:1, heksane, boil (68^0C), 2 hours, AcOH (5%, 10 ml), 30 minutes, efficiency (**5**, 80%; **6**, 75.4%).

Various methods of synthesis of α-aminonitriles have also been studied [3,4,5].

The obtained results showed that the yield of synthesized α-aminonitriles was not high when the reaction was carried out at room temperature, therefore, the reactions were heated and the desired α-aminonitriles (5, 6) were synthesized with high yields.

It is noteworthy that reaction products were obtained with good results when the reactions were carried out in the presence of a Dean-Stark probe. When heterocyclic secondary amine - morpholine was reacted with the same reagents, it was observed that the yield of the product was high. Therefore, when these reactions were carried out at the boiling temperature of the solvent (hexane) (68 oC), the yield of products was 80-91% in the case of piperidine, and 75.4-86% in the case of morpholine.

The approximate mechanism of the synthesis of aminonitriles in the presence of piperidine in the S method can be described as follows. The reaction can consist of 4 stages: in the first stage, the necessary cyanide acid can be formed from potassium cyanide and aqueous acetic acid to introduce a nitrile group into the molecule, in the second stage of the reaction, the cyanide anion can turn into an alkoxide anion as a result of a nucleophilic attack on acetone.

In the third step, as a result of protonation of this anion under the influence of acetic acid, a cyanating agent - acetonecyanohydrin (ASN) is formed, and in the fourth step, due to the nucleophilic exchange reaction between ASN and piperidine, as a result of dehydration, 2-methyl-2-(piperidin-1-yl)propanenitrile (5) is formed.

Experience part

IR-spectra of synthesized substances were recorded on Fourier spectrometer model 2000 (Perkin Elmer) on KVg tablets, mass spectra on MX-1303 equipment, PMR-spectra on JNM-4H-100 Varian Unity 400(+) equipment, internal standards CD3OD and GMDS chemical was carried out with the participation of compounds.

The progress of the reactions and the purity of the reaction product were checked by thin-layer chromatography on Silufol UV-254 special plates in various solvent systems, and information from scientific literature was used [6, 7].

Indicator chemical compounds and equipment: iodine vapor, UF-rays. The liquefaction temperature of the obtained substances was determined under a Bouets microscope.

Conclusion/Recommendations

During the study of the information presented in the scientific literature, it was found that carrying out cyanation reactions of amino compounds and obtaining the corresponding products has been attracting chemists for many years. The obtained results and the study of the biological activity of these compounds showed that it was possible to achieve the set goal by carrying out various syntheses of these compounds and studying their reactions under different conditions.

REFERENCES

1. Vargas Méndez L.Y., Kouznetsov V.V. First Girgensohnine Analogs Prepared Through InCl3-catalyzed Strecker Reaction and their Bioprospection. Curr. // Org. Synth. -2013; -№10. -P. 969–973.
2. Kushwaha R.N., Haq W., Katti S.B. Discovery of 17 Gliptins in 17-Years of Research for the Treatment of Type 2 Diabetes: A Synthetic Overview. // Chem Biol Interface. -2014; -№4. –P. 137–162.

3. Kodirov A.A., Boymurodov B., Eshtemirov E., Primov A. Aromatik aminlarning sianlash reaksiyalarini o‘rganish // O‘zMU xabarlari - 2022, - №3/2/1, - 370-372 betlar.
4. Кодиров А.А. Изучение реакции цианировония аминов // Universum: Химия и биология: - 2022. Часть 3. - № 12 (102), с. 27-30.
5. Chuliyev J.R., Yusupova F.Z., Kodirov A.A., Berdimurodov E.T., Turg‘unov K.K. Synthesis, X-Ray Characterization, IR Vibrational Frequencies, NMR Chemical Shiftsand DFT Propertiesof 2, 7-Dimethyl-2, 7-Dicyanide-3, 6-Diazaoctane // International Journal of Innovative Technology and Exploring Engineering (IJITEE) Volume-9 Issue-3, January -2020. -P. 396-404.
6. А. Кодиров ва бошқалар. ЎзМУ Хабарлари. 2021, 3/2. 304-307 бетлар.
7. Беккер Г., Бергер В., Домшке Г. Органикум // Практикум по органической химии. Пер с нем. Под. ред. Попова В.М., Пономарева СВ. - М.: Мир., 1979. Т.2. Стр. 353-380.