

1-ETINILSIKLOGEKSANOLNING AYRIM KETONLAR BILAN TETRABUTILAMMONIY GIDROKSID YORDAMIDA ENANTIOSELEKTIV ALKINILLANISH ASOSIDA ATSETILEN DIOLLAR SINTEZI

Sarvinov TIRKASHEVA¹ (sarvinovizisogovna@mail.ru), Odiljon ZIYADULLAEV¹ (bulak2000@yandex.ru),
 Abduvahob IKRAMOV² (ikromov2003@list.ru), Forxod BURIEV¹ (farhodbu.pochta@gmail.com)

¹Chirchik State Pedagogical University, Chirchik, Uzbekistan

²Tashkent Chemical-Technological Institute, Tashkent, Uzbekistan

The purpose of the research is to develop a method of synthesizing new acetylene diols, to determine their structure, physico-chemical properties and to create optimal conditions by studying the effect of various environments on product yield. For the first time, nucleophilic coupling reactions of 1-ethynylcyclohexanol with some ketones - cyclohexanone, acetophenone, para-chloroacetophenone, adamantanone, methylhexylketone and ethyl-n-butyl ketones were studied using the $Bu_4NOH/DMSO/H_2O$ catalytic system. New acetylene diols - 1-(2-(1-hydroxy-3-cyclohexyl)ethynyl)cyclohexanol (1), 1-(3-hydroxy-3-phenylbut-1-ynyl)cyclohexanol (2), 1-(3-(4-chlorophenyl)-3-hydroxybut-1-ynyl)cyclohexanol (3), 1-(2-(1-hydroxyadamantanil)ethynyl)cyclohexanol (4), 1-(3-hydroxy-3-methyldec-1-ynyl)cyclohexanol (5) and 1-(3-ethyl-3-hydroxyhept-1-ynyl)cyclohexanol (6) were synthesized in the process. The effects of the catalyst for the synthesis of acetylene diols, the nature of the solvent, the mole ratio of the starting materials, the temperature, and the duration of the reaction were systematically analyzed. The composition, structure and purity of the synthesized acetylene diols were determined by modern physical and chemical research methods.

Keywords: 1-ethynylcyclohexanol, aliphatic, cyclic and aromatic ketones, catalytic system, acetylene diols, product yield, solvents

СИНТЕЗ АЦЕТИЛЕН ДИОЛОВ НА ОСНОВЕ ЭНАНТИОСЕЛЕКТИВНОГО АЛКИНИЛИРОВАНИЯ С ИСПОЛЬЗОВАНИЕМ ТЕТРАБУТИЛАММОНИЯ ГИДРОКСИДА С НЕКОТОРЫМИ КЕТОНАМИ 1-ЭТИНИЛЦИКЛОГЕКСАНОЛА

Сарвинов ТИРКАШЕВА¹ (sarvinovizisogovna@mail.ru), Одилжон ЗИЯДУЛЛАЕВ¹ (bulak2000@yandex.ru),
 Абдувахоб ИКРАМОВ² (ikromov2003@list.ru), Форход БУРИЕВ¹ (farhodbu.pochta@gmail.com)

¹Чирчикский государственный педагогический университет, Чирчик, Узбекистан

²Ташкентский химико-технологический институт, Ташкент, Узбекистан

Цель исследования разработка метода синтеза новых ацетиленовых диолов, определение их структуры и физико-химических свойств и создание оптимальных условий изучением воздействия различных сред на выход продукта. Впервые были изучены реакции нуклеофильного соединения 1-этинилциклогексанола с некоторыми кетонами, такими как циклогексанон, ацетофенон, пара-хлорацетофенон, адамантанон, метилгексилкетон и этил-н-бутилкетон с использованием каталитической системы $Bu_4NOH/DMSO/H_2O$. В этом процессе были синтезированы новые ацетилендиолы, такие как 1-(2-(1-гидроксициклогексил)этинил)циклогексанол (1), 1-(3-гидрокси-3-фенилбут-1-инил)циклогексанол (2), 1-(3-(4-хлорфенил)-3-гидроксибут-1-инил)циклогексанол (3), 1-(2-(1-гидроксиадамантанил)этинил)циклогексанол (4), 1-(3-гидрокси-3-метилдек-1-инил)циклогексанол (5) и 1-(3-этил-3-гидроксигепт-1-инил)циклогексанол (6). Для синтеза ацетилендиолов систематически анализировали влияние катализатора, природы растворителя, молярных соотношений исходных материалов, температуры и продолжительности реакции. С помощью современных физико-химических методов исследования были определены состав, строение и чистота синтезированных ацетилендиолов.

Ключевые слова: 1-этинилциклогексанол, алифатические, циклические и ароматические кетоны, каталитическая система, ацетилен диолы, продуктовая выход, растворители

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Sarvinov TIRKASHEVA¹ (sarvinovizisogovna@mail.ru), Odiljon ZIYADULLAYEV¹ (bulak2000@yandex.ru),
 Abduvahob IKRAMOV² (ikromov2003@list.ru), Forxod BO'RIYEV¹ (farhodbu.pochta@gmail.com)

¹Chirchiq davlat pedagogika universiteti, Chirchiq, O'zbekiston

²Toshkent kimyo-texnologiya instituti, Toshkent, O'zbekiston

Tadqiqotning maqsadi yangi atsetilen diollar sintez qilish usulini ishlab chiqish, ularning tuzilishi, fizik-kimyoviy xossalarni aniqlash va mahsulot unumiga turli muhitlarining ta'sirini o'rganish orqali optimal sharoit yaratishdan iborat. Ilk marotaba 1-etinil-siklogeksanolning ayrim ketonlar - siklogeksanon, atsetofenon, para-xloroatsetofenon, adamantanon, metilgeksilketon va etil-n-butilketonlar bilan $Bu_4NOH/DMSO/H_2O$ katalitik sistemasi yordamida nukleofil birikish reaksiyalari o'rganildi. Jarayonda yangi atsetilen diollari-1-(2-(1-gidroksisiklogeksil)etinil)siklogeksanol (1), 1-(3-gidroksi-3- fenilbut-1-inil)siklogeksanol (2), 1-(3-(4-xlorofenil)-3-gidroksibut-1-inil)siklogeksanol (3), 1-(2-(1-gidroksiadamantanil)etinil)siklogeksanol (4), 1-(3-gidroksi-3-metildek-1-inil)siklogeksanol (5) va 1-(3-etil-3-gidroksigep-1-inil)siklogeksanol (6) sintez qilingan. Atsetilen diollari sintezi uchun katalizator, erituvchi tabiati, boshlang'ich moddalar mol nisbatlari, harorat, reaksiya davomiyligi ta'siri tizimli tahlil qilingan. Sintez qilingan atsetilen diollarining tarkibi, tuzilishi va tozaligi zamonaviy fizik-kimyoviy tadqiqot usullari orqali aniqlangan.

Kalit so'zlar: 1-etinilsiklogeksanol, alifatik, siklik va aromatik ketonlar, katalitik sistema, atsetilen diollari, mahsulot unumi, erituvchilar

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Introduction

Nowadays, in many scientific schools of the world, the preparation of drugs against cancer is one of the most urgent issues. Particularly, for the first time at the beginning of the XX th century, the scientists of the national cancer institute in the United States of America found that compounds containing three bonds, acetylene diols and their derivatives

are present in the organism of plants, fungi, micro-organisms and marine invertebrates, but in very small quantities [1, 2]. Professor Valery M. Dembitsky and his scientific school discovered the anti-cancer properties of more than 300 acetylene diols and lipids found in plants, it aroused great interest among world scientists [3]. J.G. Ferreira and his colleagues, when the process was carried out from

terminal acetylene in the presence of the *n*-butyllithium catalyst, the solvent THF was formed at a temperature of $-78\text{ }^{\circ}\text{C}$, and then, as a result of its reaction with a ketone in the presence of ammonium chloride, acetylene diols were synthesized with a yield of 62-92%. Moreover, racemates of acetylene diols (up to 99% yield) were obtained from acetylenic dioxydiacetylenide, which was synthesized enzymatically in the presence of lipase B and in the potassium carbonate with solvent methanol for 2 hours at room temperature and the synthesized acetylene diols have been shown to have anticancer properties through test analyses [4]. By J.L. Princival and J.G. Ferreira for the synthesis of acetylene diols under optimal conditions, the reaction of acetylene bislithium salt with paraformaldehyde as a Lewis acid using 0,5 mmol CeCl_3 catalyst for 4 hours at $-40\text{ }^{\circ}\text{C}$ gave the highest yield (90%) [5]. Spanish scientist Abdeslam Abou and his team synthesized a 1:1 mixture of diastereomers of acetylene diols with 36-95% yield as a result of alkynylation of vicinal dihalogen derivatives of alkynes with ketones or aldehydes using lithium naphthalenide. The process was carried out in THF solution, at a temperature of $-78\text{ }^{\circ}\text{C}$ for 3 hours. Synthesis of acetylene diols with a yield of 39-59% was achieved when using a catalytic system consisting of DTBB (1,4-di-*tert*-butylbenzene) and using lithium metal instead of lithium naphthalenide for this reaction [6].

Synthesis of some acetylene alcohols, which are widely used as intermediates in organic synthesis, was carried out based on the reaction of nucleophilic addition that is forming C-C bonds of alkynes to aldehydes and ketones with the help of various catalytic systems [7-11]. Acetylenic alcohols and diols were also obtained based on metal-catalytic coupling of alkynes in stoichiometric proportions in the presence of organometals (lithium-organic compounds, Grignard reagents), and then coupling to carbonyl group as a result of catalytic activation of alkyne derivatives [12-14]. High productivity in alkynylation reactions of aldehyde with alkynes in the presence of organic zinc catalysts was demonstrated. A number of metal complex catalysts (Ag [15], Rh [16], In [17], Cr [18], Ti [19], Cu [20], Ru [21] and Pd [22]) have also been successfully used for the synthesis of acetylene alcohols. However, such methods have recognized disadvantages, including problems such as the toxicity and high cost of some catalysts of this category in the process of synthesizing pharmacological drugs, as well as the extraction of metal residues. Furthermore, for the ethynylation of aldehydes and ketones, the interphase transfer method was used in the fluorobenzene organic phase and in the $\text{Bu}_4\text{NBr}/\text{NaOH}/\text{H}_2\text{O}$ catalytic system, but in the reaction of aromatic aldehydes and ketones with phenylacetylene, the products gave low yields (30-35%) [23]. In the process of alkynylation of arylaromatic ketones with

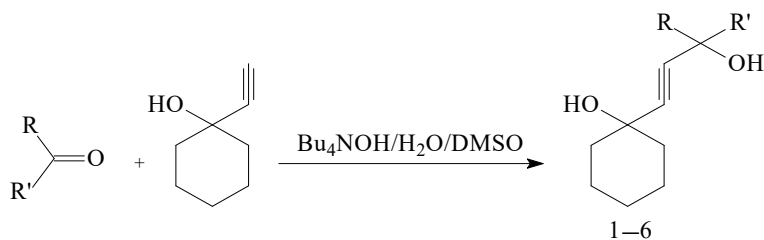
arylacetylenes, ammonium organic salts such as Bu_4NF , Bu_4NCl , Bu_4NBr , Bu_4NJ , Me_4NBr and HTAB were analyzed. For this alkynylation process, the solvent THF, 10 mmol KOH, 0,1 mmol Bu_4NCl was used for 3 days at room temperature, giving the best results [24].

Research methods

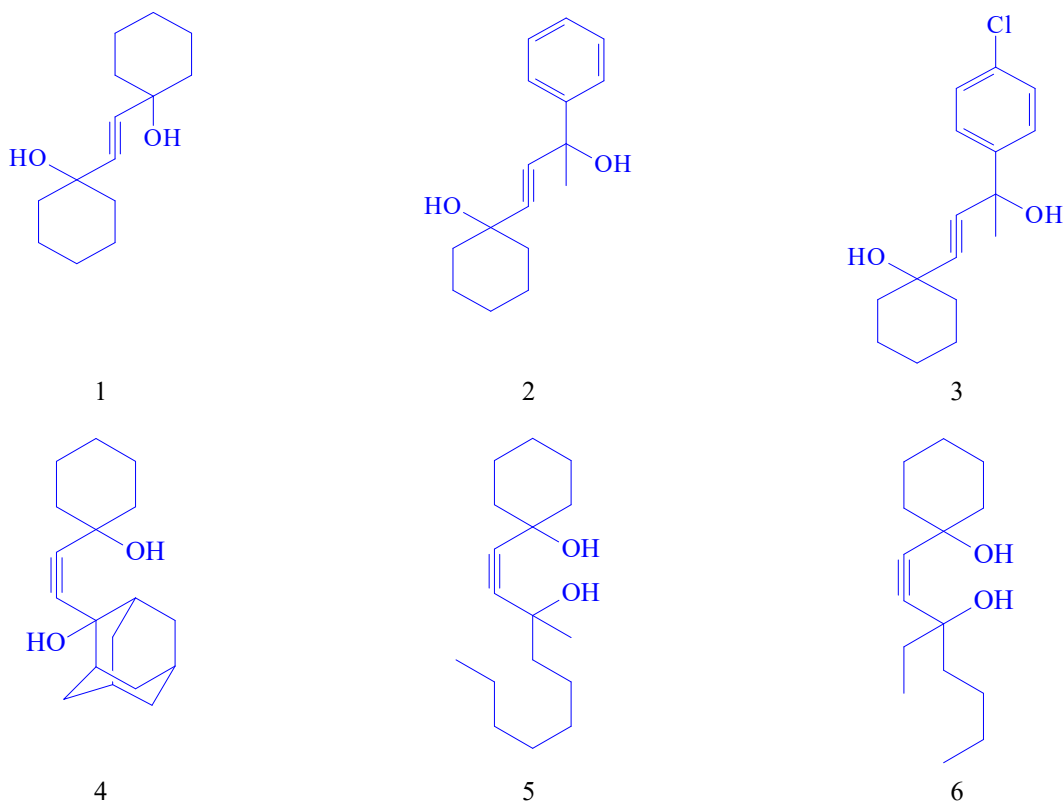
Synthesis of 1-(2-(1-hydroxycyclohexyl)ethynyl)cyclohexanol in the $\text{Bu}_4\text{NOH}/\text{DMSO}/\text{H}_2\text{O}$ catalytic system: The reaction was carried out in a specially prepared two-layer reactor with a volume of 5000 mL equipped with a mechanical stirrer (SPXFLOW Lightnin LB2, 20/150/2500 rpm branded), a dropping funnel (IsoLab TS29/32 branded, volume 200 mL), a reflux cooler (Dimrota TS29/32, 160 mm. branded) and a ground thermometer (Thermometer LLG-General $-10/+250\text{ }^{\circ}\text{C}$ branded). Firstly process was formed by mixing suspension with 259 g (1 mol) Bu_4NOH (40% aqueous solution) and 300 mL DMSO at $10\text{ }^{\circ}\text{C}$ for 60 minutes. 124 g (1 mol) of 1-ethynylcyclohexanol is added to the resulting catalytic system and hydroquinone is added to the system so that acetylene alcohol and acetylene diols do not polymerize the formed process. Then 1 mol (98 g) of cyclohexanol is added dropwise with stirring over 60 minutes, and then the process is quenched for 12 hours. The reaction mixture was diluted with cold water (1:1) and extracted with diethyl ether 3 times ($3\times 50\text{ mL}$) and washed with water ($3\times 100\text{ mL}$), dried with desiccant Na_2SO_4 for 2 h. The product is filtered and solvents are evaporated using a vacuum evaporator (made in Germany, Hei-VAP Core HL/G3), then the eluent (hexane/ethyl acetate) is passed through a silica gel 60 chromatography column, and the Rf values of the fractions are determined on the "Merck 60 F₂₅₄" thin-layer chromatography plate. Herein, 192 g of 1-(2-(1-hydroxycyclohexyl)ethynyl)cyclohexanol (86%), 12,4 g intermediate product, 6,8 g starting materials (3%) and 14,2 g extra products (6%) with yields were synthesized.

Results and discussion

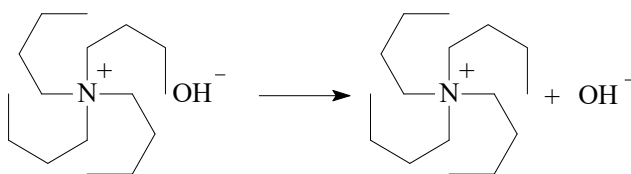
According to this method, the following acetylene diols-1-(2-(1-hydroxycyclohexyl)ethynyl)cyclohexanol (1), 1-(3-hydroxy-3-phenylbut-1-ynyl)cyclohexanol (2), 1-(3-(4-chlorophenyl)-3-hydroxybut-1-ynyl)cyclohexanol (3), 1-(2-(1-hydroxyadamantanyl)-ethynyl)cyclohexanol (4), 1-(3-hydroxy-3-methyldec-1-ynyl)cyclohexanol (5) and 1-(3-ethyl-3-hydroxyhept-1-ynyl)cyclohexanol (6) were synthesized as a result of the reactions of 1-ethynylcyclohexanol with some aliphatic, cyclic and aromatic ketones- cyclohexanone, acetophenone, para-chloroacetophenone, adamantanone, methylhexyl ketone and ethyl-*n*-butyl ketone in a basic environment using the $\text{Bu}_4\text{NOH}/\text{H}_2\text{O}/\text{DMSO}$ catalytic system based on tetra-*n*-butylammonium hydroxide and DMSO. The reaction scheme was proposed as followings [25].



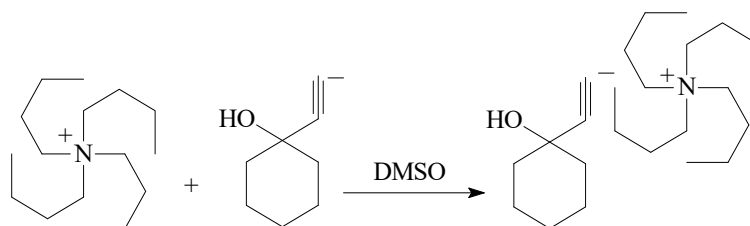
Here: RR' = -_cHex (1); R = -Me, R' = -Ph (2); R = -Me, R' = -Ph_pCl (3);



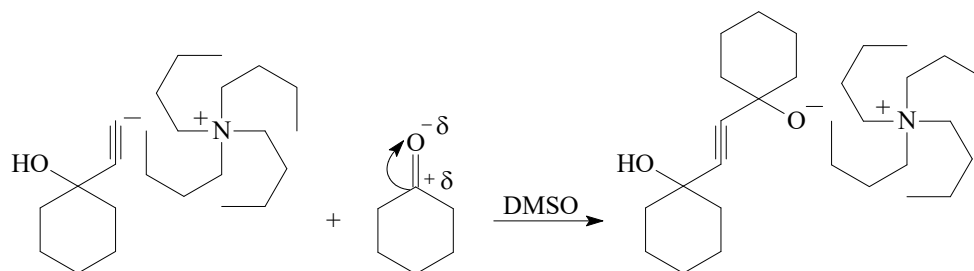
Reaction mechanism: (Synthesis 1 is given as an example): Initially, tetrabutylammonium hydroxide is separated into ions under the influence of DMSO, which is a nucleophilic solvent in the process.



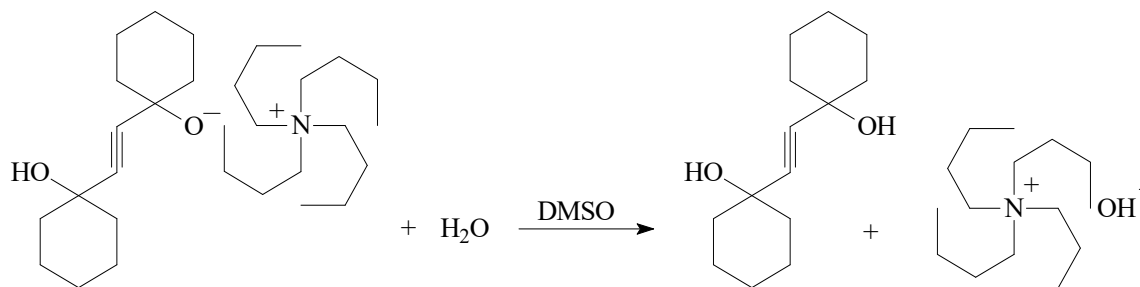
As a result, the hydroxide anion directly affects the *sp*-*s* bond and causes the deprotonation of the triple bond of 1-ethynylcyclohexanol. And the resulting nucleophilic ion forms an active intermediate



After cyclohexanone is added to the system, the carbonyl group undergoes a nucleophilic attack by the acetylide ion and forms an oxygen-centered anion of acetylene alcohol, which comes with the tetrabutylammonium cation as an intermediate.



The intermediate product formed by the tetrabutylammonium cation with the alkoxide anion forms 1-(2-(1-hydroxycyclohexyl)ethynyl)cyclohexanol as a result of the protonation of oxygen in an aqueous medium due to its low stability.



The conducted studies showed that in addition to the acetylene diol formed in this process, 1-ethynylcyclohexanone, cyclohexanone, alcoholates and complex salts of acetylene alcohol were also formed as an intermediate product, based on modern physical and chemical research methods.

The influence of temperature, duration of reaction, nature of solvent, catalyst and mole ratio of starting materials on yield of acetylene diols was systematically analyzed. It was initially carried out for the synthesis of acetylene diols in the presence of aprotic solvents - dimethylformamide (DMFA), dimethylsulfoxide (DMSO), acetone (ASE) and tetrahydrofuran (THF) and the effect on the product yield was studied. The obtained results are presented in figure 1.

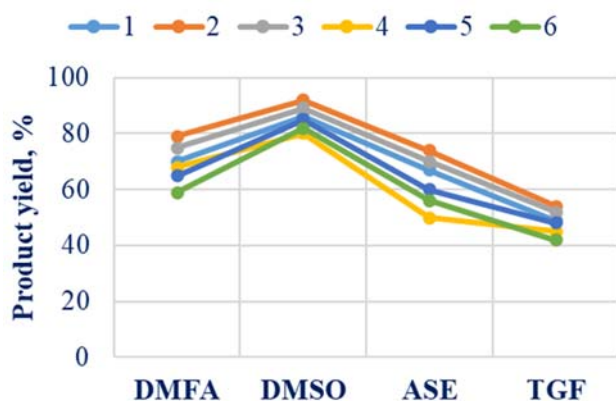


Figure 1. Effect of nature solvents on yield of acetylene diols (catalyst - Bu₄NOH).

Although the used aprotic solvents show favorable conditions for S_N2 reactions, it was determined according to the results of the analysis that the product yield is relatively high in DMSO. This process is explained as follows:

-DMFA and DMSO bipolar aprotic solvents facilitate the progress of nucleophilic exchange reactions. However, the manifestation of two different spatial configurations of DMFA leads to a decrease in the number of collisions with ions, and the lower solubility of acetylene derivatives compared to DMSO causes a decrease in the yield of acetylene diols.

-Due to the high dielectric constant ($\epsilon=40$) of DMSO compared to DMFA, THF and ASE (acetone), the high degree of dissociation of ion pairs, poor stabilization of anions and high stability of cations, DMSO alkynes in very good solubility, as well as partial catalytic properties in S_N2 reaction mechanisms, led to an increase in product yield, and acetylene diols were synthesized with 1-86%, 2- 92%, 3- 89%, 4-80%, 5-85%, 6-82% yield.

-The presence of keto and enol tautomerism of acetone, like most ketones, the low number of spatial collisions of ions in its solution, as well as the small amount of dipole moment, leads to a decrease in the product yield in the reaction.

-The low dielectric constant THF ($\epsilon=7.6$) causes a decrease in productivity due to the insufficient number of spatial collisions of alkyne ions with ketones.

In order to study the effect of temperature on the yield of acetylene diols and to determine alternative conditions, the process was carried out in the range from -5 °C to 20 °C (table 1).

Table 1

Effect of temperature on the yield of acetylene diols (catalyst- Bu₄NOH, solvent DMSO)

Temperature, °C	Product yield, %					
	1	2	3	4	5	6
-5	64	70	68	57	61	52
5	75	80	76	65	70	67
10	86	92	89	80	85	82
20	72	83	77	68	74	69

When the reaction was carried out in the Bu₄NOH/H₂O/DMSO catalytic system at 10 °C, it was observed that acetylene diols 1-86%, 2-92%, 3-89%, 4-80%, 5-85%, 6-82% were produced in high yield. From the observed reaction processes, it became clear that when the process was carried out in the range of -5÷5 °C, the unreacted initial products were detected by thin layer chromatography, which means that the dissociation of molecules into complete ions was not carried out, which caused the product yield not to be high.

When the process was increased to 20 °C, the formation of additional products of tetrabutylammonium hydroxide with initial reagents in the system, polymerization of acetylene diols, formation of tarry products, as well as formation of vinyl ethers of acetylene alcohols with diols led to a sharp decrease in product yield.

The effect in the duration of the reaction on the yield of acetylene diols was analyzed in the range of 60-180 minutes (presented in figure 2).

Where the starting reagent (1-ethynylcyclohexanol) and the substrate (ketone) remained incompletely reacted when carried out in the medium of tetrabutylammonium hydroxide and solvent DMSO for 60 minutes and 90 minutes at a temperature of 10 °C, it was determined by thin layer chromatography analysis, because of this, the production of an effective product was not achieved. The results of physico-chemical analysis showed that the process reached a more complete

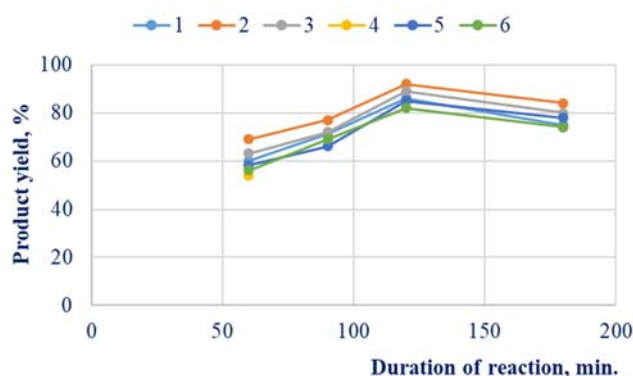


Figure 2. Effect of reaction duration on the yield of acetylene diols (catalyst Bu₄NOH, solvent DMSO, temperature 10 °C).

end during 120 minutes, which showed that the starting substances were completely dissolved in DMSO and showed a high degree of dissociation, being higher, the yield of acetylene diols was increased by 86% from (1) 71, 92% from (2) 77, 89% from (3) 73, 80% from (4) 64 and 85% from (5) 66 led to an increase from (6) 69 to 82%. When we increase the duration of the reaction to 180 minutes, the yield of acetylene diols increases from 1-86 to 75%, from 2-92 to 84%, from 3-89 to 79% as a result of the formation of complex alcohols, polyacetylene alcohols, vinyl ethers, resinous and polymer products. For example, vinylation with hydrogen in the hydroxy group of 1-ethynylcyclohexanol acetylene diol in the system results in the formation of divinyl oxydiols as by-products, resulting in a decrease in the yield of the main product.

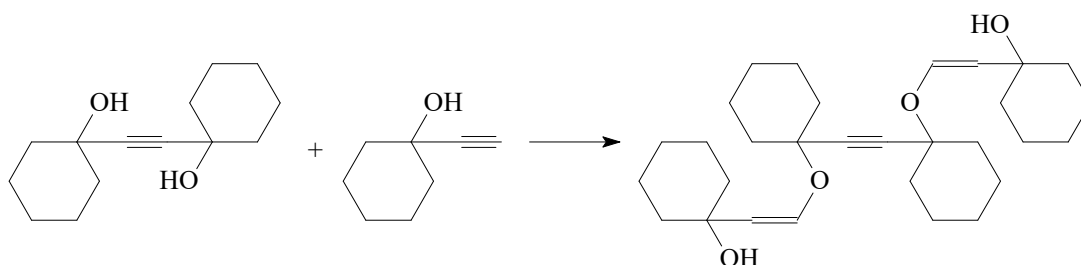


Table 2

The effect of the amount of starting materials on the yield of acetylene diols
 (reaction duration 120 min., temperature 10 °C)

Substrate : reagent amount of mol	Yield od acetylene diols, %					
	1	2	3	4	5	6
3:1	62	69	67	56	63	58
2:1	76	78	72	61	69	65
1:1	86	92	89	80	85	82
1:2	73	79	75	65	70	68

Table 3

Effect of catalyst- Bu₄NOH amount on the yield of acetylene diols (temperature 10 °C, solvent DMSO, reaction duration 120 min., acetylene alcohol: ketone 1:1 in the mole ratio)

Synthesized acetylene diols	The amount of the catalyst, relative to the amount of starting materials, mol			
	0,5	1,0	1,5	2,0
1	56	86	77	71
2	69	92	86	79
3	59	89	78	72
4	45	80	54	48
5	47	85	73	64
6	51	82	69	52

The effect of starting materials for the synthesis of acetylene diols, including substrate (ketone) and reagent (1-ethynylcyclohexanol) molar amounts was analyzed (Table 2).

As it can be seen from the table 2 above, when the amount of 1-ethynylcyclohexanol reacts with ketones in a mutually equivalent amount, it was found that acetylene diols were formed in high yield, intermediate and by-products were formed in low yield. When the amount of ketones is 3:1 and 2:1 in mol ratios compared to 1-ethynylcyclohexanol, the excess ketone undergoes an aldol condensation reaction with itself to form the corresponding diketone alcohol and acetylene diols to form acetylene ketaldiols.

If the amount of 1-ethynylcyclohexanol is taken in a larger amount than ketones, the reaction of 1-ethynylcyclohexanol with acetylene diol and the formation of acetylene mono- and divinylalcohols and polymer products, respectively, will cause a decrease in the yield of acetylene diols (Table 3).

Based on the results of the experiment, it can be seen from the data presented in the table 3 that the effect of different amounts of

the selected catalyst - Bu₄NOH on the productivity of the product was studied. When the amount of catalyst is 0,5 in relation to the amount of reagent and substrate in the system, the low yield of acetylene diols formation can be caused by the low formation of catalytically active centers and the high activation energy of the reaction. The amount of the catalyst was obtained in accordance with the equimolar ratio of the starting materials, and the highest yield was obtained, but increasing the amount of the catalyst to 1,5-2 mol caused a decrease in the yield. It should be noted that the increase in the amount is determined by the results of additional reactions in the system, i.e., synthesis of acetylene diols reacting with excess catalysts to form ammonium alcohols, as well as transformation into simple ethers or polymer products.

Spatial structure of synthesized acetylene diols (Figure 3), charge values of atoms (Figure 4), distribution of electron density (Figure 5), etc. were determined by calculating their reaction centers on the basis of HyperChem Activation 8,0 package STAT program.

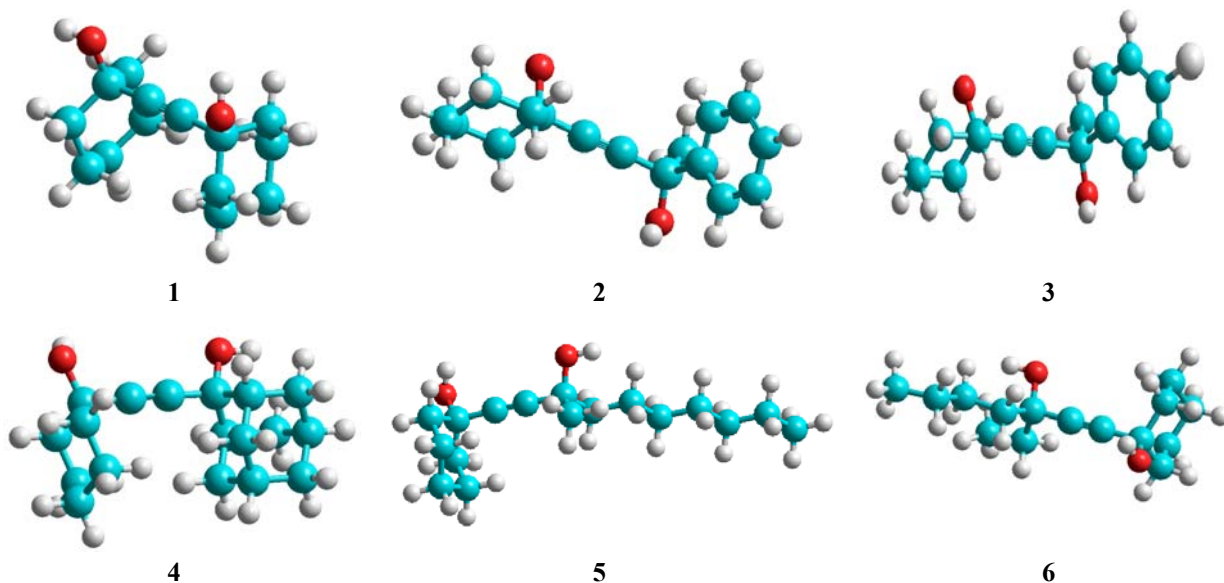


Figure3. 3D spatial structure of molecules.

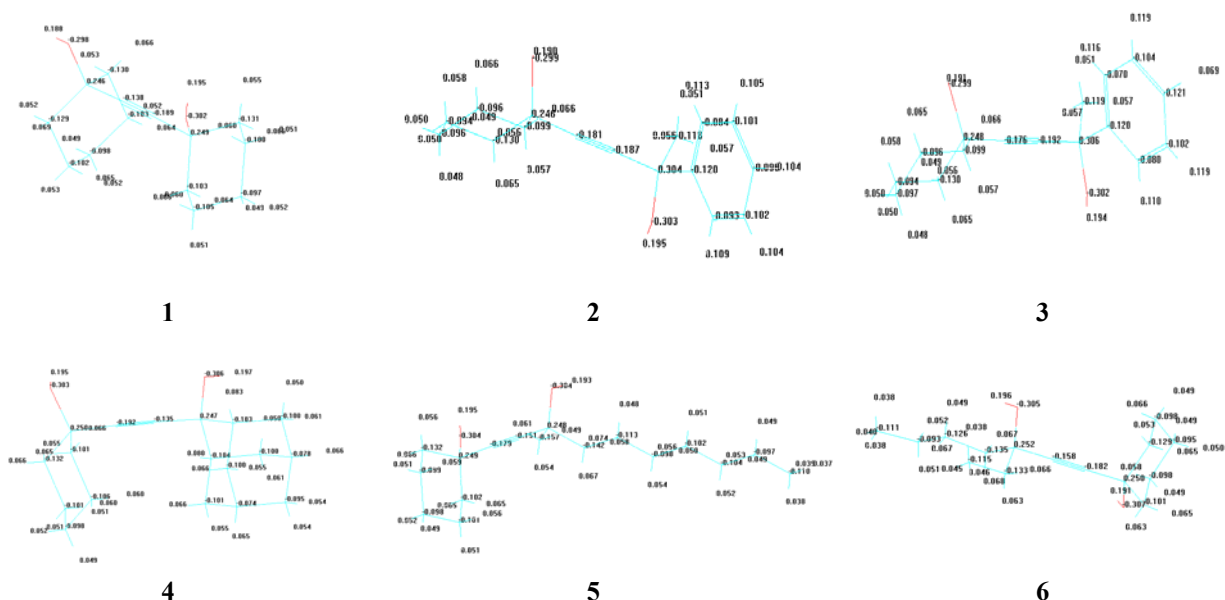


Figure4. Charge values of the atoms in the molecules.

Table 4

Results of elemental analysis of synthesized acetylene diols

Acetylene diols	Brutto formula	Molecular mass, g/mol	Analysis results	Element name and analysis, %			
				C	H	O	Cl
1	C ₁₄ H ₂₂ O ₂	222	Calculated	75,68	9,91	14,41	-
			Determined	75,63	9,97	14,39	-
2	C ₁₆ H ₂₀ O ₂	244	Calculated	78,69	8,20	13,11	-
			Determined	78,65	8,25	13,10	-
3	C ₁₆ H ₁₉ ClO ₂	278,5	Calculated	68,94	6,82	11,49	12,75
			Determined	68,93	6,87	11,48	12,72
4	C ₁₈ H ₂₆ O ₂	274	Calculated	78,83	9,49	11,68	-
			Determined	78,79	9,55	11,66	-
5	C ₁₇ H ₃₀ O ₂	266	Calculated	76,69	11,28	12,03	-
			Determined	76,64	11,35	12,01	-
6	C ₁₅ H ₂₆ O ₂	238	Calculated	75,63	10,92	13,45	-
			Determined	75,58	10,99	13,42	-

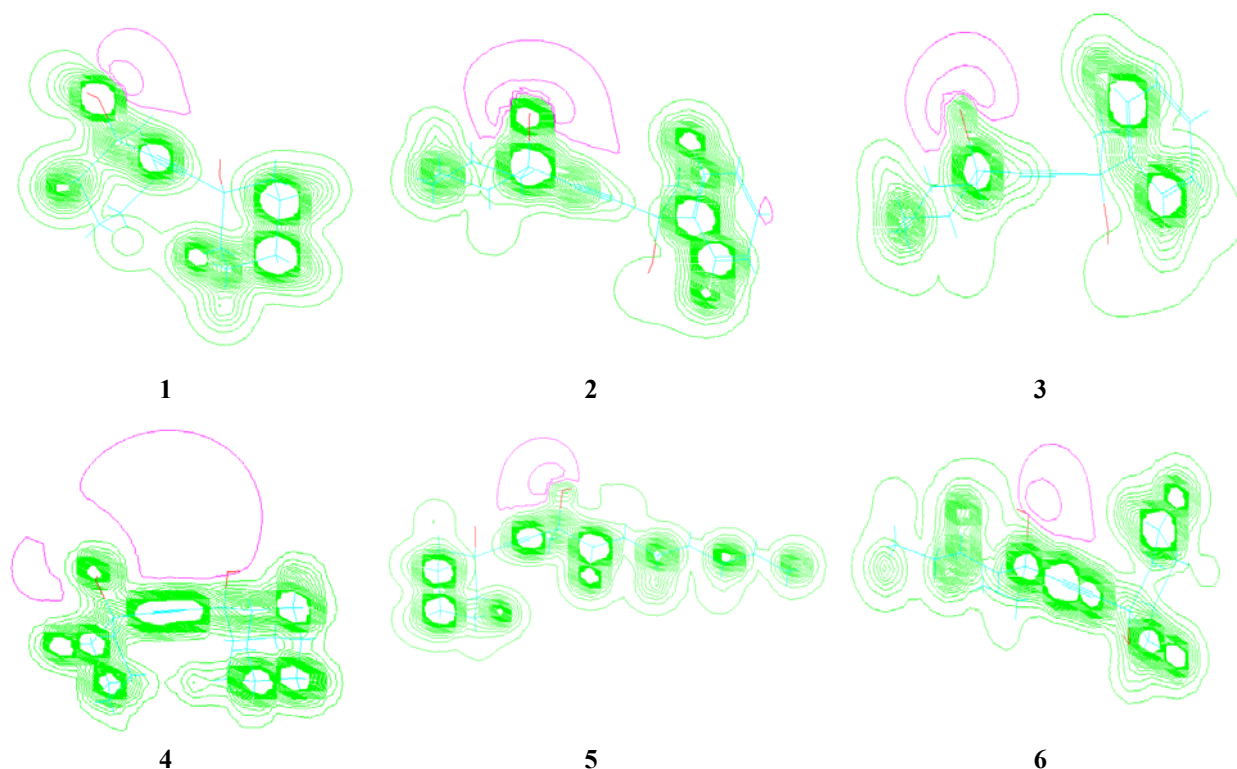


Figure 5. Distribution of electron densities in molecules.

Physic-chemical research methods

Some physical parameters, composition and structure of synthesized acetylene diols were studied by elemental analysis (Table 4) and ^1H , ^{13}C NMR (Bruker UltraShield TM 400 MHz branded).

1- ^1H – NMR (400 MHz, CDCl_3): d 2.67-2.61 (d, OH), 1.93-1.69 (t, 8H), 1.59-1.47 (m, 8H), 1.24-0.82 (m, 4H). ^{13}C – NMR (101 MHz, CDCl_3): d 87.5 ($\text{C}\equiv\text{C}$), 76.9, 68.1, 40.4, 39.8, 24.81, 23.1. Rf=0,85.

2- ^1H – NMR (400 MHz, CDCl_3): d 7.56-7.52 (m, 2H), 7.34-7.19 (m, 3H), 2.54-2.48 (d, OH), 1.92-1.86 (t, 4H), 1.81 (s, 3H), 1.52-1.46 (m, 4H), 1.21-0.96 (m, 2H). ^{13}C – NMR (101 MHz, CDCl_3): d 147.8, 129.2, 127.2, 86.3 ($\text{C}\equiv\text{C}$), 76.9, 76.4, 39.7, 34.1, 26.5, 19.7. Rf=0,67.

3- ^1H – NMR (400 MHz, CDCl_3): d 7.59-7.56 (d, 2H), 7.38-7.24 (m, 2H), 2.39-2.24 (d, OH), 1.89-1.84 (m, 4H), 1.82 (s, 3H), 1.53-1.46 (m, 4H), 1.46-1.41 (m, 2H). ^{13}C – NMR (101 MHz, CDCl_3): d 146.7, 131.5, 128.6, 125.2, 86.7 ($\text{C}\equiv\text{C}$), 68.5, 42.7, 32.4, 29.5, 18.5. Rf=0,57.

4- ^1H – NMR (400 MHz, CDCl_3): d 2.69-2.62 (d, OH), 1.97-1.85 (t, 4H), 1.62-1.54 (m, 6H), 1.47-1.40 (m, 8H), 1.24-0.94 (m, 4H). ^{13}C – NMR (101 MHz, CDCl_3): d 89.7 ($\text{C}\equiv\text{C}$), 76.4,

68.2, 42.3, 39.5, 36.8, 29.7, 28.2, 26.5, 19.3. Rf=0,63.

5- ^1H – NMR (400 MHz, CDCl_3): d 2.67-2.61 (d, OH), 1.93-1.69 (t, 8H), 1.59-1.47 (m, 8H), 1.24-0.82 (m, 4H). ^{13}C – NMR (101 MHz, CDCl_3): d 87.5 ($\text{C}\equiv\text{C}$), 76.9, 68.1, 40.4, 39.8, 24.81, 23.1. Rf=0,47.

6- ^1H – NMR (400 MHz, CDCl_3): d 2.69-2.62 (d, OH), 1.97-1.85 (t, 4H), 1.62-1.54 (m, 6H), 1.47-1.40 (m, 8H), 1.24-0.94 (m, 4H). ^{13}C – NMR (101 MHz, CDCl_3): d 89.7 ($\text{C}\equiv\text{C}$), 76.4, 68.2, 42.3, 39.5, 36.8, 29.7, 28.2, 26.5, 19.3. Rf=0,33.

Conclusion

For the first time, acetylene diols were synthesized based on the enantioselective nucleophilic coupling reaction of ketones in different nature with 1-ethynylcyclohexanol using a highly basic catalytic system - $\text{Bu}_4\text{NOH}/\text{DMSO}/\text{H}_2\text{O}$.

The effect of a number of factors on the product yield and the course of the reaction was systematically studied and based on the obtained results, the most alternative conditions of the processes were found. According to it, for the nucleophilic coupling reaction of selected ketones with 1-ethynylcyclohexanol, the temperature is 20 oC, the 1-ethynylcyclohexanol:ketone:catalyst is in a

1:1:1 mole ratio, the solvent is DMSO, and the reaction duration is 120 minutes, the synthesis of acetylene diols with the highest efficiency.

When analyzing the solvents selected for the synthesis of acetylene diols - DMFA, DMSO, ace-

tone and THF, the highest yield was obtained in DMSO.

The structure, composition, properties and purity of the synthesized acetylene diols were studied using modern physico-chemical research methods.

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