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Enantioselective alkynylation of cyclopentanone: Synthesis, dimerization, and cross-coupling transformations of 1-ethynylcyclopentan-1-ol

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ABSTRACT

In the present investigation, the preparation of 1-ethynylcyclopentan-1-ol was carried out via the enantioselective alkynylation of cyclopentanone using a $Zn(OTf)_2$/TBAF·$3H_2O$ complex catalytic system. The process was carried out in acetonitrile (MeCN) medium for 120 minutes at –10 °C. The molar ratio of acetylene to cyclopentanone was adjusted to 2:1, while the combined loading of the catalytic system $Zn(OTf)_2$/TBAF·$3H_2O$ was maintained at 0.05 mol with respect to the starting materials. Furthermore, its subsequent oxidative homolytic dimerization and Sonogashira-type C–C cross-coupling reaction with benzyl chloride were explored. A comprehensive study was performed on various parameters affecting the formation process and the efficiency of acetylene alcohol derivatives, such as temperature regime, reaction time, catalytic composition and solvent polarity, stoichiometric ratios of reagents and substrates, as well as the identity and proportion of transient intermediates and side-products. Based on the acquired experimental data, the optimal conditions for the nucleophilic addition–coupling pathway were established, and the plausible reaction mechanisms were proposed. The obtained compounds were thoroughly characterized, and their equilibrium constants, molecular structures, purity levels, and chemical composition were verified using modern physicochemical analysis techniques.

1. Introduction

The chemistry of acetylene compounds serves as a universal foundation widely used in fine organic synthesis, and today the synthesis of a new generation of organic compounds based on acetylene and its homologues continues to develop [1–16]. Extensive investigations are currently being carried out across the world to establish novel approaches for the synthesis of hormones [17], vitamins [18], fungicidal agents [19], and enzyme inhibitors [20–22] derived from acetylenic frameworks.

The main emphasis of these studies is directed toward elucidating the underlying reaction pathways, evaluating the influence of diverse physicochemical parameters on product yields, employing innovative catalytic systems, developing scalable technological processes, and assessing the pharmacological [23], environmental [24], and biological [25–26] characteristics relevant to their targeted utilization.

The presence of a triple bond, a hydroxyl group, and a labile hydrogen atom in the molecule of acetylenic alcohols allows for the synthesis of new types of organic compounds through various reactions such as nucleophilic substitution [27], addition [28], oxidation [29], rearrangement [30], and cyclization [31] with different organic reagents. Among the compounds synthesized based on acetylenic alcohols are vinyl ethers [32] and esters [33], diols [34], indoles [35–36], α-hydroxyketones [37–38], diynols [39], diindiyols [40], and naphthopyrans [41]. Today, countries such as Italy, Russia, China, Japan, and Egypt are leading in the

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widespread application of these compounds in medicine, textiles, cosmetics, and agriculture [42–44].

In recent years, significant progress has been made in the formation of new C–C bonds through the alkynylation of carbonyl compounds using various catalytic systems. Notably, in 2018, researchers from the University of Warsaw developed a regioselective synthesis of homopropargylic alcohols based on isatin derivatives, employing copper triflate as a Lewis acid catalyst in aqueous media with allenylboronic acid as the nucleophilic reagent. The enantioselective synthesis achieved the highest regioselectivity when (S)-SEGPHOS was used as a chiral ligand [45]. Using (S)-Br_2-BINOL as a chiral ligand, the reaction of allenylboronic acids with highly stereoselective ketones led to the synthesis of tertiary homopropargylic alcohols [46]. Denmark and his research team performed the nucleophilic addition of propargylsilanes to aldehydes at –20 °C for 22 hours using a catalytic system composed of (R)-DM-BINAP/$AgBF_4$/TEA/KF in methanol as the solvent, achieving yields ranging from 11% to 77%. The resulting acetylenic alcohols contained alkyl, aryl, aromatic, heteroaromatic, and cyclic radicals within their structures [47]. In 2019, scientists from Kazi Nazrul University and the National Institute of Technology Durgapur in India developed an efficient aqueous electrosynthesis process, in which nucleophilic addition of organometallic propargyl reagents to electrophilic carbonyl compounds was carried out under aqueous electrochemical conditions using $ZnCl_2$. It was demonstrated that this aqueous solution containing zinc salts could be reused for up to five cycles without significant loss of reactivity, and high yields of acetylenic alcohols were still obtained [48]. Additionally, the ethynylation of aldehydes containing aryl, heteroatom, and naphthyl radicals was performed at room temperature in the presence of acetylene bromide, with CuCl and Mn powder in acetonitrile as the solvent and trifluoroacetic acid as the activating agent. The influence of various substituents on the product yield of aromatic aldehydes was studied [49-50].

The objective of this research is the synthesis of 1-ethynylcyclopentanol via the enantioselective alkynylation of cyclopentanone using a highly basic catalytic system, and the subsequent investigation of its chemical transformations. This includes performing a dimerization reaction within a CuCl/TMEDA/CCl_4 catalytic system and cross-coupling reactions within a $Pd(OAc)_2$/CuCl/Et_3N/MeCN/H_2O catalytic system. Furthermore, the work entails the characterization of the synthesized compounds to determine their structure, composition, and physico-chemical properties.

2. Materials and Methods

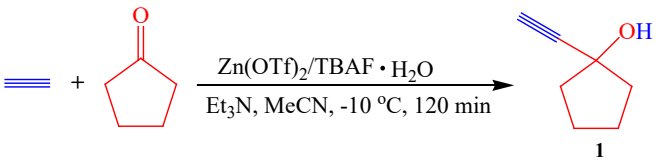
The ^1H and ^{13}C NMR spectra were obtained on a Bruker Avance spectrometer operating at 400 and 100.6 MHz, respectively, in the temperature range of 20–25 °C using solutions of $CDCl_3$, acetone-d_6, or C_6D_6, with residual solvent peaks taken as internal standards. The infrared spectra of the synthesized products were recorded on a Thermo Scientific Nicolet iS50 FT-IR spectrometer equipped with a Raman module (USA).

3. Results and Discussion

3.1. Synthesis of 1-ethynylcyclopentan-1-ol using the $Zn(OTF)_2$/TBAF·$3H_2O$ catalytic system.

The reaction was carried out in a double-walled reactor made of thermally and mechanically durable transparent glass with a capacity of 1000 ml. The reactor was sealed with a six-necked glass cap. A Dimroth reflux condenser, a stirrer, and a digital thermometer with a measurement range from -50 to +150°C were then installed on the reactor in a specific order. First, using a dropping funnel, 10.4 g (0.025 mol) of $Zn(OTf)_2$, 7.8 g (0.025 mol) of TBAF·$3H_2O$, and 39 ml (0.75 mol) of MeCN were sequentially added to the reactor and stirred together for 60 minutes to prepare a suspension. Then, acetylene was introduced into the resulting suspension, and a solution of Et_3N (7 ml) and cyclopentanone (0.05 mol) with a total volume of 12 ml was added dropwise over 30 minutes using the dropping funnel. To prevent polymerization of acetylene, the target product 1-ethynylcyclopentan-1-ol, intermediates, and by-products during the reaction, hydroquinone was added to the suspension before the starting materials were introduced into the system. The temperature in the reactor was controlled using liquid nitrogen. After all components - substrate, reagent, catalyst, and solvent - were completely added, the catalyst mixture was continuously stirred at -10°C for 30 minutes. The resulting mixture was then left to settle for 360 minutes. Afterward, it was extracted three times (3×25 ml) with diethyl ether. The organic layer obtained from the extraction was first purified from solvents and then fractionally distilled under vacuum. As a result, 1-ethynylcyclopentan-1-ol was separated as an individual fraction and synthesized with a 92% yield.

The general reaction scheme and mechanism were proposed based on research results and literature sources [50].



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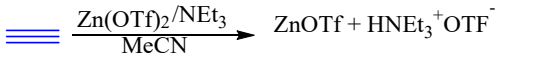
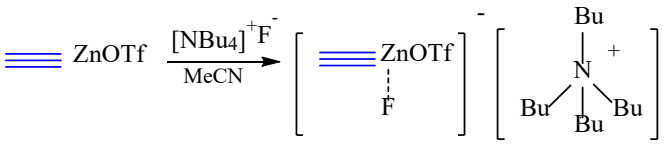
The mechanism of the nucleophilic addition reaction of acetylene to the *sp*²-hybridized carbon atom of the cyclopentanone molecule was investigated using zinc trifluoromethanesulfonate as a catalyst, tetra-*n*-butylammonium fluoride (TBAF) as a strong base, and the bipolar solvent acetonitrile, which forms a donor–

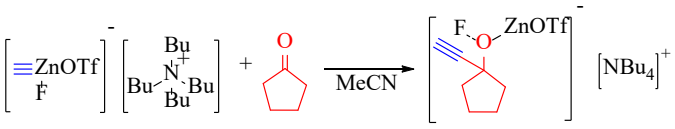
acceptor complex. In this process, the $Zn(OTf)_2$ catalyst exerts an orientational effect on the triple bond of the acetylene molecule in the acetonitrile solution, forming a π-complex. The proton bound to the *sp*-hybridized carbon of acetylene interacts with the nitrogen atom of the triethylamine molecule via a donor–acceptor bond, leading to deprotonation of the acetylene. As a result, the cationic part of the zinc triflate salt in the system associates with the acetylene anion to form a stable nucleophilic reagent - zinc ethynyl triflate. Through electrostatic interactions, the complex compound $HNEt_3^+ \cdot OTf^-$ is also formed [51].



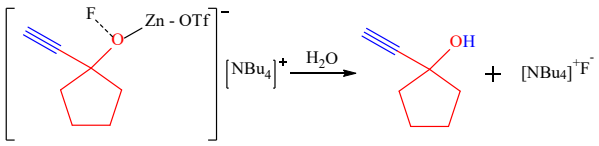
The resulting nucleophilic reagent further reacts with tetra-n-butylammonium fluoride (TBAF), which ensures a strongly basic environment, lowers the activation energy of the reaction, increases the reaction rate, and serves as a source of highly electronegative fluoride ions. This leads to the formation of an ethynyl zinc triflate-fluoride–tetra-*n*-butylammonium complex salt.



The fluoride ion shifts the triflate anion toward itself, leading to the cleavage of the ionic bond between the zinc atom and the *sp*-hybridized carbon, resulting in the formation of a free carbocation in the system. Due to the high electronegativity of oxygen, the carbonyl group becomes strongly polarized, and the carbon atom acquires a partial positive charge. As a result of the nucleophilic attack by the carbocation, the π-bond of the carbonyl group is broken, and the sp^2-hybridized carbon transitions to an sp^3 hybridized state.



In the subsequent step of the reaction, the product undergoes hydrolysis under the influence of water, yielding 1-ethynylcyclopentan-1-ol and regenerating the initial catalytic system.



In this process, the complex compound $HNEt_3^+ \cdot OTf^-$ in the system reacts with the triflate anion released from the alcohol, forming Et_3N, $Zn(OTf)_2$, and water. A comprehensive evaluation of parameters including temperature, reaction time, solvent characteristics, and the ratio of initial reagents was performed to determine their effect on the formation of 1-ethynylcyclopentan-1-ol in the presence of complex catalytic systems. In this process, a mathematical model was developed to qualitatively and quantitatively evaluate the influence of factors such as temperature, time, and the ratio of starting materials on the reaction progress and product yield. Additionally, the optimal conditions for synthesizing the product in quantitative yields were investigated using the Box–Wilson method as reported in the literature [52].

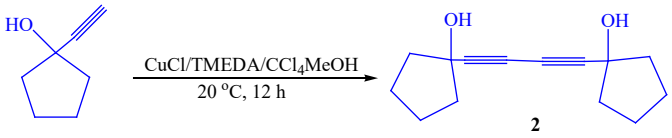
As the object of this study, the alkynylation reaction of cyclopentanone with acetylene was carried out using a strongly basic catalytic system $Zn(OTf)_2/TBAF \cdot 3H_2O$, where acetonitrile (MeCN) was used as the solvent, resulting in a high product yield. It is well known that aprotic solvents are preferred in nucleophilic addition reactions because they do not contain acidic hydrogen atoms. Instead, they possess atoms with lone pairs of electrons, which allows them to strongly solvate the cationic part of the reagent and partially satisfy its electron affinity. This facilitates the heterolysis of polar reagents and enhances the nucleophilicity of the resulting carbanion. Consequently, the reaction rate increases. In the synthesis of 1-ethynylcyclopentan-1-ol, acetonitrile provides a favorable homogeneous medium and plays a key role in dissolving certain solid-state reagents and catalysts involved in the reaction. Additionally, the low viscosity and high solubility properties of MeCN create favorable conditions for the spatial interaction between the reactants and substrate. Moreover, the ability of MeCN to act as a catalyst during the hydrolysis of $Zn(OTf)_2$ positively influences the yield of 1-ethynylcyclopentan-1-ol. According to the experimental findings, the nucleophilic alkynylation of cyclopentanone with acetylene was optimized under the following conditions: the process was carried out in acetonitrile (MeCN) medium for 120 minutes at –10 °C. The molar ratio of acetylene to cyclopentanone was adjusted to 2:1, while the combined loading of the catalytic system $Zn(OTf)_2/TBAF \cdot 3H_2O$ was maintained at 0.05 mol with respect to the starting materials. Under these optimized conditions, the formation of 1-ethynylcyclopentan-1-ol reached a maximum yield of 92%. The molecular structure of the obtained product was verified using ^1H and ^{13}C NMR spectroscopy: ^1H NMR ($CDCl_3$, δ, ppm): 2.41 (s, 1H, C≡CH), 1.97 (s, 1H, OH), 1.89–1.65 (m, 8H, $4CH_2$). ^{13}C NMR (δ, ppm): 87.63, 73.92, 70.74, 43.22, 23.53. To further evaluate the reactivity of 1-ethynylcyclopentan-1-ol, its oxidative dimerization and cross-coupling with benzyl chloride were examined.

3.2. Synthesis of 1,1'-(buta-1,3-diyne-1,4-diyl)bis (cyclopentan-1-ol) using the CuCl/TMEDA/CCl_4 catalytic system.

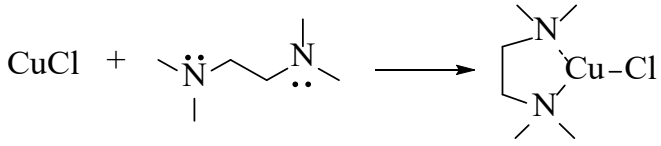
The dimerization was carried out in the

$CuCl/TMEDA/CCl_4$ catalytic system. For this purpose, a thermally stable five-neck flask was charged with an equimolar mixture of 1-ethynylcyclopentan-1-ol and TMEDA, which was stirred for 60 minutes to form a homogeneous emulsion. A suspension of CuCl (120 ml in methanol) was then introduced, and the reaction mixture was agitated for an additional 60 minutes. At 20 °C, 2 mol of tetrachloromethane (CCl_4) was added, and the mixture was stirred for 11 hours, followed by standing at ambient conditions for 24 hours. After completion, the solvent (MeOH) was removed under normal conditions. The residual mixture was dissolved in 300 ml of water and subjected to extraction with dichloromethane (3×200 ml). The combined organic phases were dried over anhydrous Na_2SO_4, and the solvent was removed under reduced pressure. The crude residue was purified by silica gel column chromatography (SiO_2 60) using stepwise elution with CH_2Cl_2:MeOH (100:1, 30:1), affording the target compound 1,1'-(buta-1,3-diyne-1,4-diyl)bis(cyclopentan-1-ol) as the isolated product, 185 g of 1,1'-(buta-1,3-diyne-1,4-diyl)bis(cyclopentan-1-ol) (85%) was synthesized.

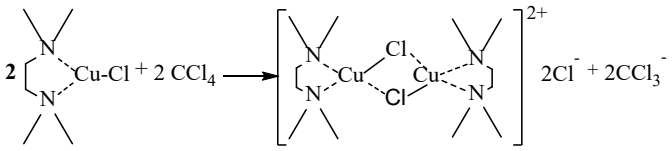
According to the literature sources, the general scheme and mechanism of the dimerization reaction were proposed as follows [53].



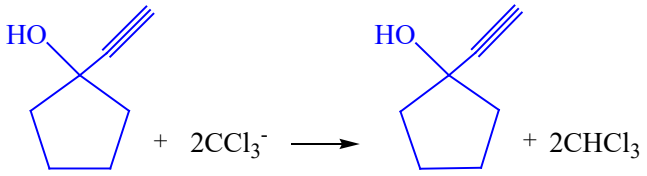
In the initial stage of the process, the catalyst CuCl reacts with the ligand TMEDA to form a copper(I) complex salt.



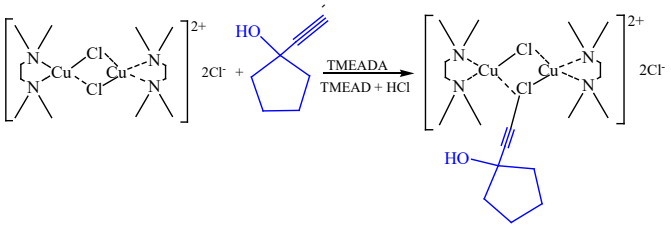
The resulting copper(I) complex salt is oxidized by the CCl_4 added to the system, converting it into a copper(II) complex, while generating a trichloromethanide anion. In this process, CCl_4 simultaneously acts as both the solvent and the oxidizing agent.



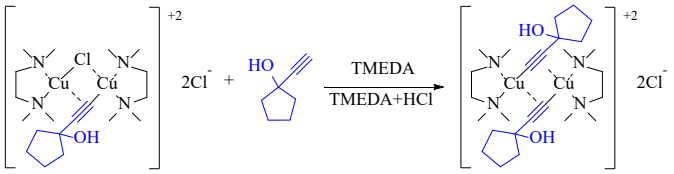
It is well known that the C≡C bond in the 1-ethynylcyclopentan-1-ol molecule is shorter than a regular σ bond and has higher bond energy, which increases the mobility of the hydrogen atom attached to the triple bond. As a result, the ≡C–H bond is more prone to cleavage. In the system, the trichloromethanide anion abstracts this labile hydrogen, leading to the formation of trichloromethane and the deprotonated 1-ethynylcyclopentan-1-ol anion [53].



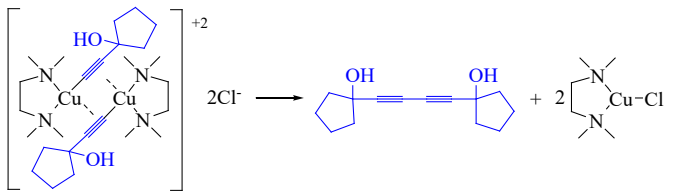
The resulting anionic base interacts with the copper(II) complex salt — the catalytic species present in the system — in the presence of TMEDA, leading to the formation of a copper(II) π-complex. The lone pairs of electrons on the two nitrogen atoms in TMEDA, which are not involved in bond formation, facilitate the reaction by forming donor–acceptor interactions with the hydrogen atom of 1-ethynylcyclopentan-1-ol and the chlorine atom in the copper(II) complex salt.



In a similar manner, the second copper atom in the complex salt also reacts with an equivalent amount of 1-ethynylcyclopentan-1-ol.



Oxidative elimination of the resulting intermediate leads to the formation of a copper(I) complex and a new C–C bond, resulting in the synthesis of 1,1'-(buta-1,3-diyne-1,4-diyl)bis(cyclopentan-1-ol).



The influence of catalyst type and loading, as well as the nature and concentration of reagents and substrates, together with temperature and reaction time, on the yield and selectivity of 1,1'-(buta-1,3-diyne-1,4-diyl)bis(cyclopentan-1-ol) was systematically investigated. At the preliminary stage, the role of solvent effects was examined, comparing the aprotic medium tetrahydrofuran (THF) with protic solvents such as methanol (MeOH) and ethanol (EtOH), and their impact

on product yield was summarized in Table 1. The effect of the catalyst nature on product yield was studied. When the reaction was carried out in CuCl, it demonstrated the highest selectivity. The 3d electron shell of copper enables it to form donor–acceptor bonds with ligands, which makes it highly suitable for homolytic addition reactions based on the redox process of copper transitioning from the monovalent cation to the divalent cation. It is well known that in copper(I) halides, the nuclear charge and electronegativity increase from iodine to fluorine; however, due to the very high activity of fluorine, copper(I) fluoride cannot exist in a stable state and quickly converts into copper(II) fluoride. Therefore, in this process, copper(I) chloride exhibited higher catalytic activity compared to other catalysts.

Table 1. Effect of the nature of catalysts and solvents on the yield of 1,1'-(buta-1,3-diyne-1,4-diyl)bis(cyclopentan-1-ol) (ligand TMEDA, temperature 20 °C, reaction duration 12 hours)

№	Solvents	Catalysts	Yield, %
1.	TGF	CuCl	47
	MeOH	CuCl	85
		CuBr	63
		CuI	56
	EtOH	CuCl	77
		CuBr	56
		CuI	49

In protic media, the pronounced dissociation of reagents facilitated more frequent ionic interactions. As demonstrated in the table, the synthesis of diynols proceeded with greater efficiency in methanol (MeOH), which possesses a higher dielectric constant and dipole moment relative to ethanol (EtOH).

When the process was carried out in the presence of CuCl, the formation of 1,1'-(buta-1,3-diyne-1,4-diyl)bis(cyclopentan-1-ol) proceeded with the highest selectivity, affording an 85% yield. It is established that within the halide series, the effective nuclear charge and electronegativity of Cu(I) increase from iodide to fluoride. Nevertheless, owing to the extreme reactivity of fluorine, Cu(I) fluoride is thermodynamically unstable and readily converts to Cu(II) fluoride. Consequently, Cu(I) chloride exhibited superior catalytic efficiency compared to the other copper halides under the given conditions.

The dimerization reaction was conducted within a time range of 6–18 hours, reaching its highest yield at 12 hours. Prolongation of the reaction beyond this point resulted in a reduced yield of 1,1'-(buta-1,3-diyne-1-4-diyl)bis(cyclopentan-1-ol), which can be attributed to dehydration and subsequent polymerization of the dimeric intermediates, leading to the generation of polyacetylene by-products.

According to both experimental observations and theoretical considerations, the optimal parameters for the synthesis of 1,1'-(buta-1,3-diyne-1,4-diyl)bis(cyclopentan-1-ol) were established as performing the reaction in methanol with the CuCl/TMEDA/CCl_4 catalytic system at 20 °C for 12 hours, affording the highest yield (85%). The molecular structure of the isolated compound was validated by ^{1}H NMR and ^{13}C NMR spectroscopic techniques. ^{1}H NMR: δ 2.72 (s, 2H, 2OH), 2.07-1.62 (m, 8H, $4CH_2$), 1.44-1.37 (m, 8H, $4CH_2$). ^{13}C NMR: 84.63, 71.82, 68.13, 42.50, 23.24.

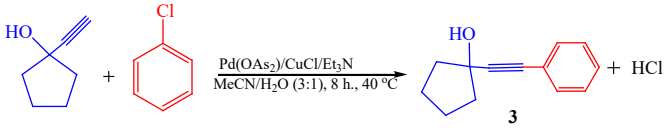
3.3. Synthesis of 1-(phenylethynyl)cyclopentan-1-ol in the $Pd(OAc)_2$/CuCl/Et_3N/MeCN/H_2O catalytic system

The Sonogashira cross-coupling was performed in a 500 mL five-neck round-bottom flask equipped with a dropping funnel, mechanical stirrer, thermometer, and reflux condenser. Initially, 16.5 g (0.15 mol) of 1-ethynylcyclopentan-1-ol together with 0.10 g (0.01 mol) of CuCl were introduced into the reactor. Subsequently, a suspension of 2.24 g (0.01 mol) of $Pd(OAc)_2$ prepared in a mixture of 15 mL MeCN and 5 mL H_2O (3:1 ratio) was added under stirring, and the temperature was controlled within 30–40 °C.

Afterwards, a suspension consisting of 11.25 g (0.10 mol) of benzyl chloride (C_6H_5Cl) and 20 g (0.2 mol, 15 mL) of triethylamine was added dropwise over 30 minutes. The reaction mixture was stirred at 40 °C for 7.5 h, and then left to stand for 30 min. Hydrolysis was carried out by treatment with 75 mL of cold water in three portions (3 × 25 mL) to remove the catalyst residues. The organic phase was subsequently extracted three times with 20 mL portions of dichloromethane (CH_2Cl_2).

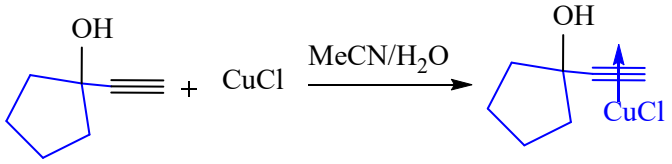
The combined extracts were dried over anhydrous $CaCl_2$ for 24 h, filtered, and the solvent was first evaporated under atmospheric pressure and then under reduced pressure. Purification of the crude product was performed by column chromatography on silica gel 60, using ethyl acetate/hexane (1:4) as the eluent. The Rf value was determined, and the target compound was isolated in pure form. As a result, 24.6 g of 1-(phenylethynyl)cyclopentan-1-ol was obtained, corresponding to a yield of 88%.

The general reaction scheme and mechanism were proposed based on research results and literature sources [54,55].

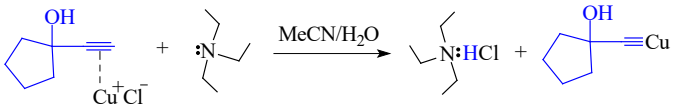


To carry out the Sonogashira coupling reaction, two catalytic cycles occur simultaneously under the influence of bimetallic catalysts CuCl and $Pd(OAc)_2$. In the first catalytic cycle, 1-ethynylcyclopentanol reacts with copper(I) chloride to form a π-complex. The process is

conducted in the presence of MeCN and water, which act as nucleophilic solvents.

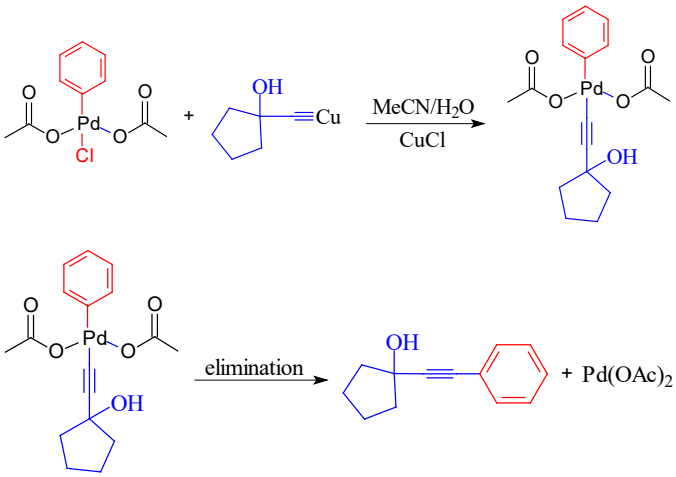


As a result of coordination via donor–acceptor interactions, the lone pair electrons on the nitrogen atom of triethylamine, which does not participate in bonding, bind to the hydrogen and chlorine atoms of the π-complex, leading to the formation of copper(I) acetylide salt.



In the second catalytic cycle, under the influence of the aryl group, $Pd(OAc)_2$ undergoes oxidation from the +2 to the +4 oxidation state, resulting in the coordination of both the aryl and chloride ligands to the palladium center.

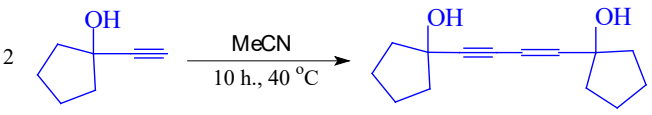
In the next step, under the influence of copper(I) acetylide, the oxidation state of palladium is reduced to Pd^0, followed by a reductive elimination that leads to the formation of the internal aromatic acetylene alcohol, 1-(phenylethynyl)cyclopentan-1-ol, thereby completing the catalytic cycle and allowing it to restart.



When the reaction was performed at 40 °C for 8 hours in the $CuCl/Pd(OAc)_2/Et_3N$ catalytic system, a high yield of 1-(phenylethynyl)cyclopentan-1-ol was obtained. The reaction course showed that at 20 °C, complete molecular dissociation into ionic species did not occur, leaving most of the starting reagents unreacted, as confirmed by thin-layer chromatography. At elevated temperatures of 60 °C, however, palladium(II) acetate interacted with the initial reagents to generate side products. Under these conditions, aromatic acetylenic alcohols underwent mutual coupling to give diynols, while polymerization processes yielded resinous by-products, markedly lowering the target product yield.

Extending the reaction time to 10 hours also resulted in diminished yields due to the formation of complex alcohols, polyacetylene derivatives, enynediols, and resinous impurities.

In particular, the transformation of 1-ethynylcyclopentan-1-ol led to the generation of an additional compound, 1,1'-(1-but-1-en-3-yne-1,4-diyl)bis(cyclopentan-1-ol), which further contributed to the reduction of the main product yield.



The influence of catalyst concentration on the synthesis of 1-(phenylethynyl)cyclopentan-1-ol was also investigated (Figure 1).

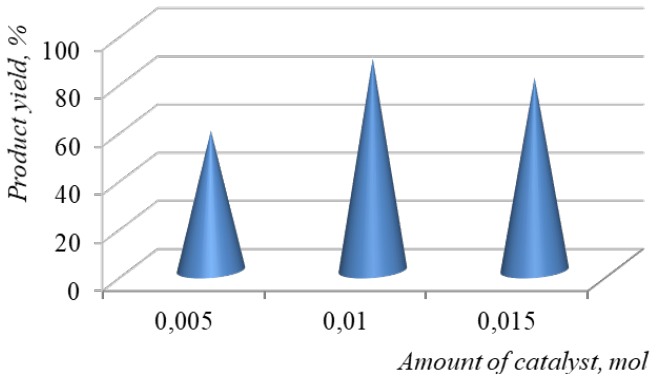


Fig. 1. Effect of catalyst amount on the yield of 1-(phenylethynyl)cyclopentan-1-ol (Temperature 40 °C, solvent MeCN, reaction duration 8 hours, 1-ethynylcyclopentan-1-ol: benzyl chloride in a molar ratio of 1.5:1)

It was determined that the use of 0,005 mol of catalyst resulted in a low yield, which was attributed to insufficient formation of active catalytic centers and a relatively high activation barrier.

The optimal yield was reached with 0.01 mol of catalyst; however, further increase in catalyst loading reduced the selectivity of the reaction. This effect can be explained by the promotion of competing side reactions, in which 1-(phenylethynyl)cyclopentan-1-ol interacted with excess catalyst to form secondary alcohols and polymeric products, as confirmed by analytical data (Table 2 and 3).

Table 2. Some physical properties of the synthesized aromatic acetylene alcohols

No.	Brutto Formula	Molecular mass, g/mol	$T_{boil,}$ °C	n_d^{20}	$d_n^{20} g/sm^3$	Rf value
1	$C_7H_{10}O$	110	159	1,497	0,962	0,57
2	$C_{14}H_{18}O_2$	218	134	1,585	1,181	0,46
3	$C_{14}H_{16}O$	200	337	1,580	1,082	0,49

Table 3. Quantum-chemical calculations of the synthesized aromatic acetylene alcohols

No.	Heat of formation, kkal/mol	Van der Waals energy, kkal/mol	Coulomb energy, kkal/mol	Torsion energy, kkal/mol	Valence angle energy, kkal/mol	Bond energy, kkal/mol
1	14.2601	2,7381	0,9996	7,4586	0,3216	2,7422
2	28,5005	4,9105	2,2510	15,3717	0,6441	5,3232
3	9,5976	8,7581	1,0287	-1,8841	0,7511	0,9438

According to the results of the conducted research, the selected 1-ethynylcyclopentan-1-ol was synthesized through the Sonogashira coupling reaction with benzyl chloride using the $CuCl/Pd(OAc)_2/Et_3N$ catalytic system (in equimolar ratios of $CuCl:Pd(OAc)_2:Et_3N$) in an MeCN solution at 40 °C for 8 hours, yielding the highest amount of 1-(phenylethynyl)cyclopentan-1-ol (88%), which was chosen as the optimal condition for the process. The structure of 1-(phenylethynyl)cyclopentan-1-ol was confirmed by spectroscopic methods: ^{1}H-YaMR: δ 7.44-7.40 (m, 2H, Ph), 7.31-7.27 (m, 3H, Ph), 2.17 (s, 1H, OH), 2.09-2.02 (m, 4H), 1.91-1.84 (m, 2H), 1.81-1.75 (m, 2H). ^{13}C- YaMR: δ 131.98, 128.69, 128.59, 123.26, 93.26, 83.41, 75.22, 42.89, 23.89.

The composition of the synthesized compounds was confirmed by elemental analysis methods, their physical properties were determined using various modern physicochemical research techniques, and kinetic changes, spatial structures of the molecules, distribution of charges and electron density in the molecules, as well as quantum-chemical parameters were calculated using modern software.

4. Conclusion

A synthetic approach to obtain terminal acetylenic alcohol 1-ethynylcyclopentan-1-ol was elaborated through a nucleophilic alkynylation of acetophenone with acetylene in the presence of a complex catalytic system Zn(OTf)2/TBAF·3H2O. Alternative experimental conditions were optimized, a plausible reaction pathway was suggested, and the resulting compounds were structurally characterized.

The preparation of diacetylenic diol 1,1'-(buta-1,3-diyne-1,4-diyl)bis(cyclopentan-1-ol) was achieved via homocoupling of 1-ethynylcyclopentan-1-ol under oxidative conditions using the catalytic mixture CuCl/TMEDA/CCl4/MeOH. The influence of key parameters on reaction efficiency was systematically examined, while the purity of the target product was verified by chromatographic separation and spectroscopic analysis.

For the first time, the synthesis of internal acetylenic alcohol 1-(phenylethynyl)cyclopentan-1-ol was accomplished through a cross-coupling transformation of 1-ethynylcyclopentan-1-ol with benzyl chloride catalyzed by $Pd(OAc)_2/CuCl/Et_3N/MeCN/H_2O$. The mechanistic aspects of the process were elucidated, with the elementary steps and possible pathways being rationalized. The structural features, chemical composition, and purity of the final compound were confirmed by advanced physicochemical techniques, while its characteristic constants together with thermodynamic and quantum-chemical descriptors were determined.

Supplementary files

Supplementary file 1.

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