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Synthesis and Characterization of Acetylene Alcohols Via Alkynylation of Heteroatomic Aldehydes with Phenylacetylene Under Various Reaction Parameters Completed with Spatial Chemical Structure, Literature Review, and Bibliometric Analysis

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ABSTRACT

This study explores the synthesis of novel acetylene alcohols via the alkynylation of heteroatomic aldehydes with phenylacetylene using a ProPhenol/Me_2Zn catalytic system. The research systematically investigates key reaction parameters, including reaction duration and temperature, to optimize product yield and selectivity. A detailed reaction mechanism was developed based on these findings. The reactivity of various heteroatomic aldehydes in the alkynylation reaction was analyzed, revealing a reactivity trend influenced by electronic and steric effects. This ranking provides valuable insights into the selectivity of acetylene alcohol formation. The synthesized acetylene alcohols were thoroughly characterized using ^{1}H-NMR and ^{13}C-NMR (structural elucidation). Additionally, a comprehensive literature review and bibliometric analysis were conducted to contextualize the study within existing research, highlighting trends, advancements, and future directions in the field of acetylene alcohols. These findings contribute to a better understanding of alkynylation chemistry and its applications in organic synthesis and material science.

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1. INTRODUCTION

Acetylene alcohols are one of the main sources in the synthesis of organic compounds [1]. These compounds play a crucial role in the development of pharmaceuticals, agrochemicals, and fine chemicals due to their versatile reactivity and functionalization potential. Their synthesis has gained significant attention in recent years as researchers aim to develop more efficient and selective methods.

One of the main methods of synthesis of acetylene alcohols is the asymmetric addition of aldehydes to metal alkynes [2]. Propargyl alcohols were synthesized in high yield by Chinese scientists based on the reaction of carbonyl compounds with acetylene in the presence of $ZnCl_2$ and Et_3N [3]. The enantioselective addition of terminal acetylene and aldehydes to $Zn(OTf)_2$ and N-methylephedrine in a solvent containing H_2O at 84-1000 ppm allowed us to achieve high efficiency and synthesize acetylene alcohols with a yield of 99% [4]. Acetylene alcohols were synthesized with a yield of 96% as a result of the alkynylation of an aromatic aldehyde with phenylacetylene in the presence of a new catalyst in a mixture with alkynyl zinc after dissolving a chiral sulfonamide ligand and titanium(S)-BINOL in tetrahydrofuran [5]. Secondary acetylene alcohols were obtained by reacting monosubstituted acetylene compounds with aldehydes in the presence of ruhetyl and tetrahydrofuran. The reaction was carried out at a temperature of 0°C, and acetylene alcohols were synthesized with a yield of 81-98% [6].

Despite these advancements, several challenges remain in the synthesis of acetylene alcohols. These include the need for highly selective catalysts, optimization of reaction conditions, and scalability for industrial applications. Additionally, many conventional synthesis methods rely on expensive or toxic reagents, making sustainable alternatives highly desirable.

The reactions of the synthesis of acetylene alcohols were studied by reacting acetylene and its homologs with magnesium bromide compounds in a tetrahydrofuran solution of aldehydes, and a product was obtained in high yield (70%) [7]. The processes of alkynylation of aromatic, aliphatic, alicyclic, and heteroaromatic aldehydes and aldehydes with aliphatic, aromatic, functional alkynes were carried out by Schmidt and his scientific group based on the Favorsky reaction, that is, under mild conditions, in a 30% aqueous solution of Bu_4NON at a temperature of 5-20°C within 2 hours. As a result, propargyl alcohols were synthesized with a selective yield of 72–93% [8]. The reaction of propargyl alcohol with aromatic halides resulted in a series of alkynols. These alkynols were then treated with organometallic nucleophiles followed by sulfur dioxide to produce oxathiolene oxides [9]. The asymmetric addition of phenylacetylene to aldehydes without the use of $Ti(OiPr)_4$ and $Zn(OTf)_2$ catalysts was carried out based on sulfamidoaminoalcohol, an ephedrine derivative, and the synthesis of propargyl alcohols was achieved with high efficiency (99%) [10].

Given these challenges, this study aims to explore improved methodologies for the synthesis of acetylene alcohols by optimizing reaction parameters and catalyst selection. This research seeks to enhance yield, enantioselectivity, and sustainability in acetylene alcohol synthesis while addressing limitations in traditional methods. By refining reaction conditions and exploring novel catalytic systems, this study contributes to the ongoing development of efficient and environmentally friendly synthesis strategies for these valuable compounds.

In the works of Yin Ngai Sum, Dingyi Yu, and Yugen Zhang, propargyl alcohols were synthesized under mild conditions in the presence of CaC_2 without a metal catalyst and achieved high efficiency [11]. Catalytic reactions of the enantioselective alkynylation of aromatic aldehydes to terminal alkynes, including phenylacetylene, isopropylsilyl, and

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acetylene, were carried out using complex catalytic systems with high catalytic activity based on the ligand BINOL and $Ti(OiPr)_4$. In this case, complex catalytic systems were formed with high catalytic activity of the pre-prepared Et_2Zn BINOL-$Ti(OiPr)_4$. The process was carried out at room temperature, and accordingly, chiral aromatic acetylene alcohols were synthesized with yields of 92-98% [12]. For the first time, using acetaldehyde, cyclohexanecarbaldehyde and benzaldehydes, the following methods for the synthesis of acetylene alcohol from enantioselective alkynylation reactions with phenylacetylene in the presence of the complex catalytic system $ZnEt_2/Ti(OiPr)_4$ have been developed: 4-phenylbutyn-3-ol-2 (84.4%), 1-phenylhexenin-4-1-ol-3 (72.0%), 1,3-diphenylpropin-2-ol-1 (88.8%), 1-cyclohexyl-3-phenylpropin-2-ol-1 (77.5%) [13].

Diacetylene alcohol 3-methyl-1,5-diphenylpentadiyne-2,4-ol-3, which has high activity in vaccination against smallpox, was synthesized in the presence of the Jocich reaction of phenylethynylmagnesium bromide with ethyl acetate [14]. Secondary acetylene alcohols were obtained by the interaction of monosubstituted acetylene compounds with aldehydes in the presence of ethylzinc and tetrahydrofuran [15]. Aromatic and heteroatom aldehydes were treated with acetylene in the KOH-H_2O-DMSO catalytic system, and secondary propargyl alcohols were synthesized in 46-67% yields. This process was carried out at atmospheric pressure in 3 layers in the temperature range of 5-7°C [16]. As a result of exposure of R–CC–MgX compounds to carbonyl compounds (aldehydes, ketones) in a solution of tetrahydrofuran and diethyl ether, the corresponding acetylene alcohols were synthesized in yields of 57–85% using the Grignard reaction [17]. By reacting aromatic, aliphatic, and vinyl aldehydes with phenylacetylene or 1-hexine at room temperature, propargyl alcohols such as 1-(3-chlorophenyl)-3-phenylpropin-2-ol-l, 1-(2,4-chlorophenyl)-3-phenylpropin-2-ol-1 have been synthesized in yields up to 98% [18]. Acetylene alcohols are synthesized by the reaction of methyl propyl ketone, dimethyl ketone, methyl isopropyl ketone, and pinocholines with phenylacetylene using an organomagnesium compound. The effect of diethyl ether and tetrahydrofuran solvents on the reaction yield was studied, and a high yield was obtained when the process was carried out in a tetrahydrofuran solution [19].

2. LITERATURE REVIEW

Acetylene alcohols, also known as propargyl alcohols, are important intermediates in organic synthesis and play a crucial role in the pharmaceutical, agrochemical, and materials science industries. Their unique triple bond and hydroxyl functional group offer a versatile platform for further transformations, making them valuable in developing biologically active compounds and advanced materials. The synthesis of acetylene alcohols typically involves the alkynylation of aldehydes or ketones, a fundamental reaction in modern organic chemistry. This section provides an overview of the existing literature on the synthesis, reaction mechanisms, catalytic systems, and potential applications of acetylene alcohols.

2.1. Synthesis of Acetylene Alcohols

The most widely adopted approach for synthesizing acetylene alcohols is the nucleophilic addition of terminal alkynes to carbonyl compounds. Several catalytic systems have been developed to facilitate this reaction with high efficiency and selectivity.

2.1.1. Alkynylation using organometallic reagents

One of the earliest and most well-established methods for synthesizing acetylene alcohols is the use of organometallic reagents such as Grignard reagents (RMgX), organozinc

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compounds (RZnX), and lithium alkynylides (RC≡CLi) [20]. The Grignard reaction involves the addition of alkynylmagnesium halides to aldehydes or ketones, yielding acetylene alcohols in high yields under mild conditions. However, challenges such as side reactions, regioselectivity issues, and moisture sensitivity limit the applicability of Grignard reagents in large-scale synthesis [21].

The use of organozinc reagents offers an alternative, as they exhibit better functional group tolerance and higher selectivity. For example, the $ZnEt_2$-mediated alkynylation of aldehydes in the presence of ligands such as BINOL or ProPhenol has been reported to yield acetylene alcohols with enantioselectivity exceeding 90% [22].

2.1.2. Catalytic systems for alkynylation

The development of catalytic systems for the direct alkynylation of carbonyl compounds has received significant attention due to concerns over atom efficiency, sustainability, and waste minimization. Several catalysts have been employed, including transition metal catalysts, Lewis acids, and organocatalysts.

(i) Transition Metal Catalysts: Zinc, copper, and titanium-based catalysts are widely used in alkynylation reactions. The $Ti(OiPr)_4/ZnEt_2$ system, for example, has been shown to facilitate the addition of alkynes to aldehydes under mild conditions, producing high yields of acetylene alcohols with minimal side reactions [23].

(ii) Lewis Acid Catalysts: The use of $Zn(OTf)_2$ and $BF_3 \bullet Et_2O$ enhances reaction rates by activating the carbonyl group, making it more susceptible to nucleophilic attack. Recent studies have also explored lanthanide-based catalysts, which offer improved regio- and stereoselectivity [24].

(iii) Organocatalysis: The emergence of organocatalysts, such as chiral amines and sulfonamides, has led to the development of metal-free methods for acetylene alcohol synthesis. These systems are particularly attractive for green chemistry applications, as they reduce toxic metal waste [25].

2.1.3. Solvent and Temperature Effects

The choice of solvent and reaction temperature significantly impacts the efficiency of acetylene alcohol synthesis. Studies have shown that polar aprotic solvents such as tetrahydrofuran (THF), dimethyl sulfoxide (DMSO), and acetonitrile (MeCN) enhance reaction rates and product yields. THF, in particular, has been identified as an optimal solvent, as it stabilizes reaction intermediates and facilitates efficient catalyst activity [26].

Reaction temperature also plays a key role in optimizing product yield. While lower temperatures (-5 to 0°C) improve selectivity by suppressing side reactions, higher temperatures (>10°C) often result in undesirable by-products such as vinyl ethers and diols [27].

2.2. Reaction Mechanisms in Acetylene Alcohol Synthesis

The alkynylation of aldehydes and ketones follows a bifunctional activation mechanism, where both the carbonyl group (electrophile) and the alkyne (nucleophile) are simultaneously activated.

(i) In metal-catalyzed reactions, the Lewis acid component of the catalyst enhances electrophilic activation, while the alkynyl nucleophile is deprotonated by a Brønsted base to improve nucleophilicity.

(ii) Enantioselective reactions often rely on chiral ligands, such as BINOL derivatives, to control stereochemical outcomes and improve asymmetric induction [28].

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Computational studies suggest that the rate-determining step in these reactions is the formation of the C–C bond between the carbonyl carbon and the alkynyl nucleophile. The stability of reaction intermediates and transition states heavily depends on solvent polarity and catalyst structure [29].

2.3. Applications of Acetylene Alcohols

Acetylene alcohols are valuable intermediates in various industrial applications.

(i) Pharmaceutical Applications. Many acetylene alcohol derivatives exhibit antiviral, anti-inflammatory, and anticancer properties. For example, propargyl alcohol derivatives have been investigated for their potential to inhibit SARS-CoV-2 proteases, making them promising candidates for antiviral drug development [30].

(ii) Organic Synthesis and Materials Science. Acetylene alcohols are widely used as building blocks in polymer synthesis, electronic materials, and bioactive molecules. Their triple-bond functionality enables further functionalization, leading to the synthesis of heterocyclic compounds, enediynes, and natural product analogs [31].

(iii) Catalysis and Green Chemistry. Recent research has focused on using acetylene alcohols as catalysts or ligands in asymmetric synthesis. Their ability to coordinate metal centers makes them valuable in enantioselective catalytic processes, promoting sustainable synthetic methodologies [32].

The synthesis and applications of acetylene alcohols have been extensively studied, with significant advancements in catalytic methodologies, reaction optimization, and industrial applications. Transition metal-catalyzed alkynylation, particularly using zinc and titanium-based catalysts, remains the most effective route for high-yield synthesis. Emerging trends in organocatalysis and green chemistry offer promising pathways for sustainable production. Future research is expected to explore new catalyst designs, reaction engineering approaches, and broader applications in pharmaceuticals and materials science.

3. METHODS

The reaction was carried out in a 2,000 mL four-neck flask made of heat-resistant transparent glass, equipped with a reflux condenser, a dropping funnel, a thermometer, and a stirrer. The flask was initially charged with 120 mL of tetrahydrofuran (THF), followed by the careful addition of 95 g (1.0 mol) of dimethylzinc and 127.7 g (1.25 mol) of phenylacetylene under an argon atmosphere. The mixture was stirred continuously for 60 minutes.

A solution of 159.7 g of PropPhenol ligand in 120 mL of THF and 185 g (1.0 mol) of 3-bromo-4-pyridinecarbaldehyde was then added dropwise over 60 minutes. The reaction mixture was cooled hermetically to -5 to 0°C and stirred for 22 hours. After completion, the mixture was quenched with a saturated aqueous solution of NH_4Cl (50 mL) and stirred for an additional period.

The organic fraction was extracted using diethyl ether (3 × 100 mL), followed by washing with water (3 × 50 mL). The organic layer was dried over anhydrous Na_2SO_4, and the solvents were removed under normal conditions. The crude product was purified using silica gel 60-column chromatography, employing a 20:1 CH_2Cl_2:Et_2O eluent system. As a result, 1-(3-bromopyridinyl-4)-3-phenylpropin-2-ol-1 was obtained with an 80% yield. The reaction system also contained 11% by-products and 9% unreacted 3-bromo-4-pyridinecarbaldehyde.

Using this method, the following acetylene alcohols were synthesized with their respective yields:

(i) 1-(thiophenyl-2)-3-phenylpropin-2-ol-1 (64%)

(ii) 1-(3-methylthiophenyl-2)-3-phenylpropin-2-ol-1 (67%)

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(iii) 1-(furanyl-2)-3-phenylpropin-2-ol-1 (87%)
(iv) 1-(pyridinyl-3)-3-phenylpropin-2-ol-1 (75%)
(v) 1-(quinolinyl-2)-3-phenylpropin-2-ol-1 (72%)
(vi) 1-(3-bromopyridinyl-4)-3-phenylpropin-2-ol-1 (80%).

4. RESULTS AND DISCUSSION

Figure 1 presents a bibliometric analysis of research publications related to acetylene alcohols, displaying a total of 1,831 documents retrieved using the search query "acetylene AND alcohols" in the TITLE-ABS-KEY field. The analysis covers a publication period from 1916 to 2025 and highlights the evolution of research interest in this topic over time. Data was obtained from Scopus database, in which detailed information regarding this bibliometric analysis is explained elsewhere [33-35].

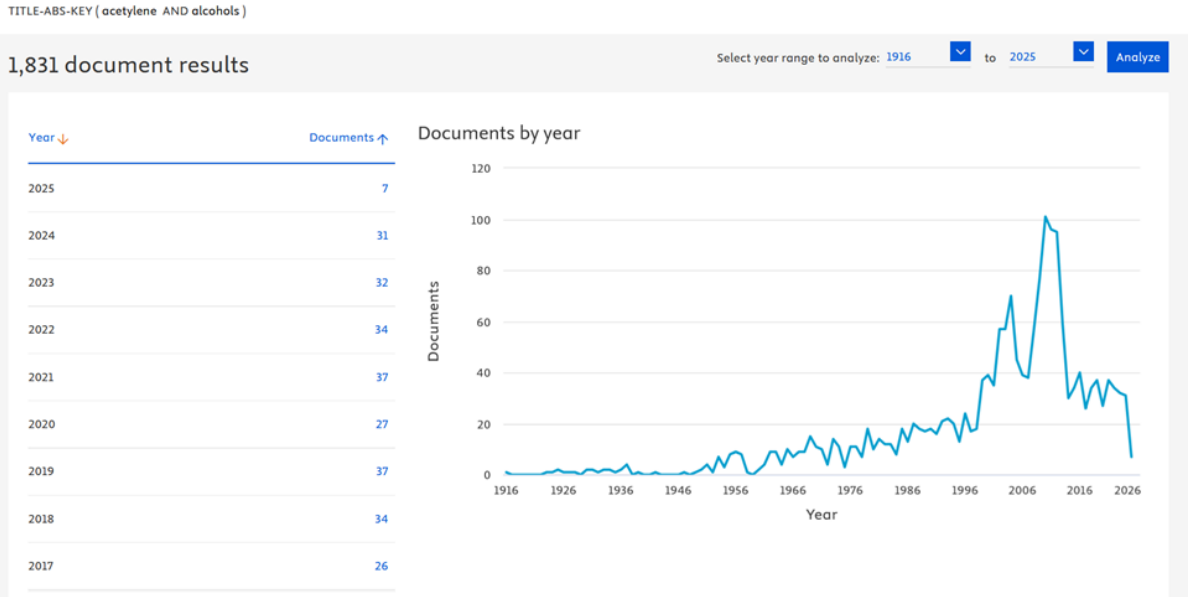

Figure 1. Bibliometric analysis of research publications on keyword acetylene alcohols (1916–2025).

Figure 1 shows the distribution of published documents per year. From 1916 to the 1980s, the number of publications remained relatively low, indicating limited research interest during this period. However, a gradual increase can be observed, suggesting a steady progression in scientific studies on acetylene alcohols. Beginning in the early 2000s, research activity experienced a sharp rise, reaching its peak around 2010–2015, with more than 100 publications per year at its highest point. This peak may have been driven by advancements in synthetic methodologies, catalysis, and industrial applications.

Following the peak, a decline in publications is observed from 2016 onward, with the number of studies decreasing but still maintaining a relatively high level compared to the earlier decades. This decline could be attributed to several factors, including a possible saturation of fundamental research, shifts in scientific focus toward other related fields, or reduced funding for research in this area. Despite this decline, the consistent number of annual publications between 2017 and 2023 (ranging from 26 to 37 documents per year) indicates ongoing scientific interest in acetylene alcohol chemistry.

The table on the left provides a closer look at research activity in recent years (2017–2025). The number of publications per year remains fairly stable from 2017 to 2023, with a slight drop in 2024 (31 documents) and only 7 documents recorded for 2025. The lower count for

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2025 is likely due to incomplete data, as many papers submitted in this year may still be under review or awaiting publication.

This bibliometric analysis illustrates the historical development and recent trends in research on acetylene alcohols. The sharp increase in publications from the early 2000s to 2015 suggests a period of major scientific discoveries and technological advancements in the field. The subsequent decline after 2020 may indicate that foundational research has been well-established, with current studies focusing on refinements, novel applications, or interdisciplinary integrations. Future research in this field may be directed toward green chemistry approaches, novel catalytic systems, and pharmaceutical applications, which could sustain interest and lead to further innovations.

The data represents the number of documents published per year, while the table on the left shows the annual publication count from 2017 to 2025. The data reflects the overall trend of research activity in this field over time. Data was taken from Scopus database on February 2025.

Acetylene alcohols were synthesized by reacting the ProPhenol ligand with dimethylzinc (Me_2Zn) in tetrahydrofuran (THF). This reaction led to the formation of a bisrux complex, which functions as a bifunctional catalyst, activating both reagents simultaneously. The reaction scheme is presented in **Figure 2**, illustrating the alkynylation of heteroatomic aldehydes with phenylacetylene catalyzed by the ProPhenol/Me_2Zn/THF system, based on literature reports [36-37].

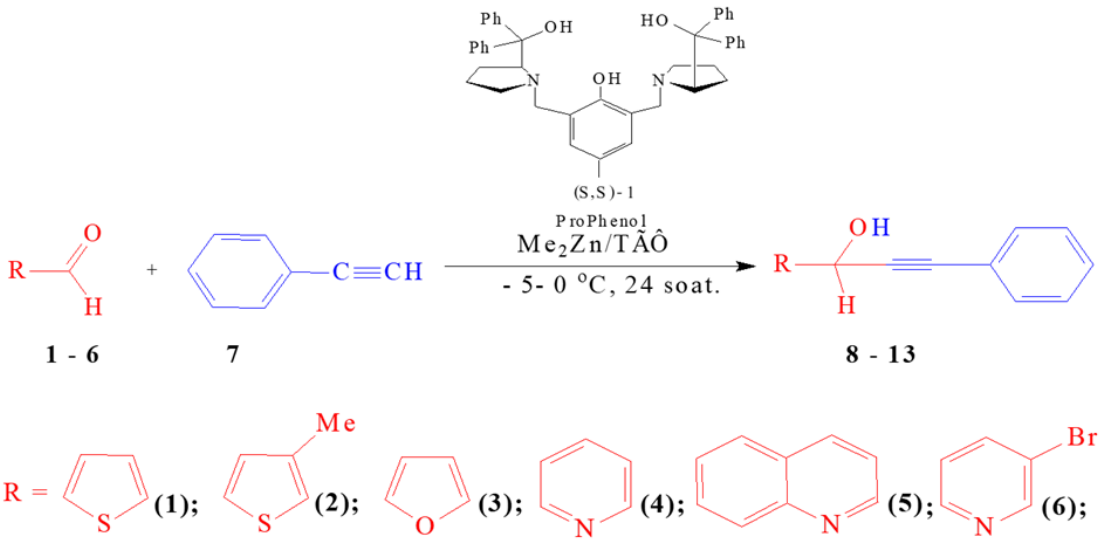

Figure 1. Reaction scheme for the alkynylation of heteroatomic aldehydes (1-6) with phenylacetylene (7) in the presence of the ProPhenol/Me_2Zn/THF catalytic system, leading to the formation of acetylene alcohols (8-13). The catalytic process occurs at -5 to 0°C over 24 hours.

As shown in **Figure 3** (Step I), the ProPhenol ligand reacts with dimethylzinc (Me_2Zn) in tetrahydrofuran (THF), resulting in the deprotonation of its hydroxyl groups. This leads to the formation of a stable bisrux complex, which serves as the active catalyst. In the next stage, the bisrux complex interacts with phenylacetylene (**Figure 3**, Step II), facilitating a hydrogen exchange. This interaction forms a reactive intermediate, essential for the subsequent alkynylation reaction.

The catalytic intermediate, as depicted in **Figure 3** (Step III), functions as a bifunctional catalyst. The Lewis acid activates the electrophile, while the Brønsted base facilitates

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nucleophile deprotonation. Under alkaline conditions, the Brønsted base facilitates nucleophile deprotonation, promoting the conversion of the aldehyde into its enol form (**Figure 3**, Step IV). The Lewis acid coordinates with the aldehyde carbonyl group, enhancing its electrophilicity (**Figure 3**, Step IV). Due to the intrinsic acidity of phenylacetylene, a nucleophilic attack occurs at the activated carbonyl carbon.

During the final stage, as shown in **Figure 3** (Step V), zinc alkoxide is released via metal exchange, regenerating the active catalyst and allowing the reaction cycle to continue. Upon zinc alkoxide dissociation, proton transfer takes place, leading to the formation of acetylene alcohols with high yields (**Figure 3**, Step V).

The effects of key reaction parameters—including reagent quantities, temperature, reaction time, catalyst type, and solvent choice—on the yield of acetylene alcohols were systematically studied using the ProPhenol/Me_2Zn/THF catalytic system. This approach was found to be the most efficient under optimized conditions.

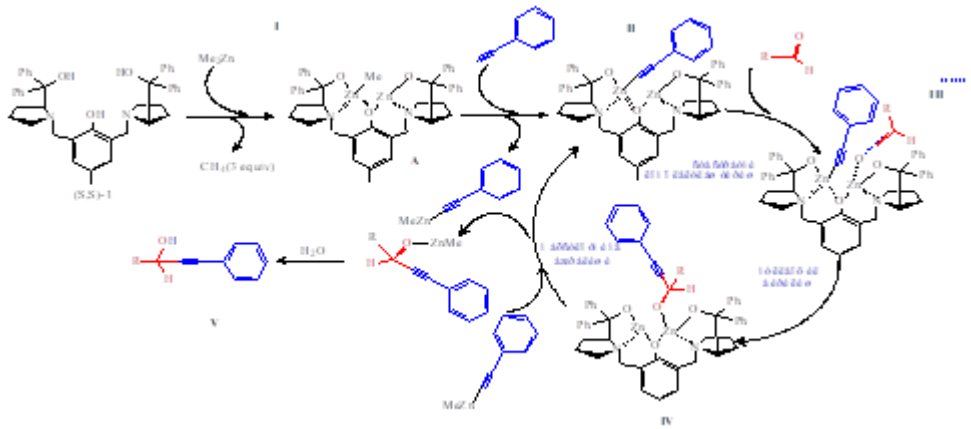

Figure 3. Proposed reaction mechanism for the alkynylation of heteroatomic aldehydes using the ProPhenol/Me_2Zn/THF catalytic system. The process proceeds via a bifunctional catalytic cycle: (I) formation of the bisrux complex, (II) interaction with phenylacetylene, (III) Lewis acid activation of the aldehyde, (IV) nucleophilic attack and enol formation, and (V) catalyst regeneration and product formation.

The effect of varying the molar ratios of aldehydes and alkynes on the yield of acetylene alcohols was investigated (**Table 1**). When the amount of alkyne exceeds that of the aldehyde, the reaction efficiency improves due to a higher availability of the alkyne reagent, leading to increased product formation. As shown in **Table 1**, the highest yields were observed when phenylacetylene was in excess (1:1.25 ratio), suggesting that an optimal alkyne concentration enhances reaction efficiency. Conversely, when aldehydes were in excess (1.25:1), product yield decreased due to side reactions, including the formation of diols from aldehyde-alcohol interactions. This suggests that excess aldehyde promotes undesired side reactions that compete with the main reaction. At a 1:1 molar ratio, competing side reactions, such as acetylenediol formation and vinylation, reduced the overall yield due to the generation of vinyl ethers as by-products. The formation of these by-products is likely due to secondary reactions between the intermediate acetylene alcohols and aldehydes, leading to unwanted etherification.

The effect of temperature and solvent selection on the yield of acetylene alcohols was systematically investigated to determine optimal reaction conditions. Reactions were conducted at temperatures ranging from -15°C to 10°C in acetonitrile (MeCN), dimethyl sulfoxide (DMSO), and tetrahydrofuran (THF) (**Table 2**).

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At -15°C, the product yield was low due to reduced catalyst solubility and decreased reaction kinetics, limiting substrate activation. Raising the reaction temperature to 10°C resulted in a lower product yield, likely due to increased side reactions and reduced selectivity. In contrast, at -5 to 0°C, the yield of acetylene alcohols increased, likely due to an optimal balance between reaction kinetics and selectivity, minimizing side reactions.

The effect of solvent polarity and coordination ability on acetylene alcohol yield was also investigated to determine their role in reaction efficiency. As shown in **Table 2**, the highest product yields were obtained when tetrahydrofuran (THF) was used as a solvent, indicating its superior role in stabilizing the catalytic system. THF, due to the presence of a lone pair on the oxygen atom, effectively stabilizes the catalytic species and enhances reactivity, leading to increased product yield.

Table 2 confirms that solvent efficiency follows the trend: acetonitrile < dimethyl sulfoxide < tetrahydrofuran, with THF demonstrating the highest reaction selectivity and yield. The optimized reaction conditions included a molar ratio of aldehyde:phenylacetylene:catalyst (1:1.25:0.25), a reaction temperature of -5 to 0°C, and a reaction duration of 24 hours. Under these conditions, the highest yields were achieved, with THF as the preferred solvent (8-64%, 9-67%, 10-87%, 11-75%, 12-72%, 13-80%).

Table 1. Effect of aldehyde-to-phenylacetylene molar ratio on the yield of acetylene alcohols. Reactions were conducted at -5 to 0°C for 24 hours using the ProPhenol/Me_2Zn catalytic system with a fixed molar ratio of 0.25:1. Higher yields were observed when phenylacetylene was in slight excess (1:1.25), while excess aldehyde (1.25:1) led to decreased yield due to side reactions.

Acetylene alcohol	Product yield, % aldehyde: phenylacetylene		
	1:1	1:1,25	1,25:1
8	55	64	60
9	60	67	63
10	80	87	84
11	68	75	71
12	64	72	68
13	71	80	76

Table 2. Effect of temperature and solvent choice on the yield of acetylene alcohols (8-13). Reactions were conducted at three temperatures (-15°C, -5 to 0°C, and 10°C) using MeCN, DMSO, and THF as solvents. The highest yields were observed at -5 to 0°C, with THF as the most effective solvent, while MeCN resulted in the lowest product yields.

Temperature, °C	Solvent	Product yield, %					
		8	9	10	11	12	13
-15	MeCN	44	46	70	56	51	58
-5-0		51	52	76	62	60	65
10		47	49	73	59	55	61
-15	DMSO	50	55	76	60	62	70
-5-0		60	62	84	70	68	76
10		55	58	80	65	64	72
-15	THF	55	58	78	65	62	70
-5-0		64	67	87	75	72	80
10		60	63	83	70	67	75

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The composition, purity, and structure of the synthesized acetylene alcohols were analyzed using 1H, 13C NMR spectra (Bruker Avance 400 and 100 MHz, at a temperature of 20-25°C, in the presence of CDCl3 and C6D6 solvents). Detailed information regarding NMR is explained elsewhere [38].

The results from NMR are the following:

(i) *1-(thiophenyl-2)-3-phenylpropin-2-ol-1* ***(8)*** *– R_f= 0.36; (64%), ^{1}H NMR: δ 8.12 (m, 2H, 2CH$_{Th}$), 7.57 (m, 5H, 5CH$_{Ph}$), 7.24 (m, 1H, CH$_{Th}$), 5,89 (d, 1H), 2.34 (d, 1H, OH); ^{13}C NMR: δ 149.3, 129.6, 128.1, 127.0, 126.3, 121.5, 88.9, 84.7, 64.9.*

(ii) *1-(3-methylthiophenyl-2)-3-phenylpropin-2-ol-1* ***(9)*** *– R_f= 0.38; (67%), ^{1}H NMR: δ 7.69 (m, 2H, 2CHPh), 7.35 (m, 5H, 3CHPh, 2CHTh), 5.62 (d, 1H), 2.23 (d, 1H, OH), 1.96 (s, 3H, CH3); ^{13}C NMR: δ 142.7, 131.3, 128.3, 127.2, 125.9, 122.1, 89.6, 85.8, 63.2.*

(iii) *1-(2-furanyl)-3-phenylpropyne-2-ol-1* ***(10)*** *– R_f= 0.43; (87%), ^{1}H NMR: δ 7.46 (m, 3H, 3CHPh), 7.25 (m, 3H, 2CHPh, CHF), 6.42 (m, 1H, CHF), 6.29 (m, 1H, CHF), 5.26 (d, 1H), 1.97 (d, 1H, OH); ^{13}C NMR: δ 154.2, 144.3, 129.6, 127.8, 121.7, 112.2, 107.5, 89.6, 84.4, 66.9.*

(iv) *1-(pyridinyl-3)-3-phenylpropin-2-ol-1* ***(11)*** *– R_f= 0.35; (75%), ^{1}H NMR: δ 8.44 (m, 2H, 2CH$_{Pir}$), 7.59 (m, 2H, 2CH$_{Pir}$), 7.41 (m, 2H, 2CH$_{Ph}$), 7.33 (m, 3H, 3CH$_{Ph}$), 5.74 (d, 1H), 2.86 (d, 1H, OH); ^{13}C NMR: δ 152.6, 146.7, 134.2, 132.1, 129.8, 127.3, 121.5, 86.9, 83.7, 60.4.*

(v) *1-(quinolinyl-2)-3-phenylpropin-2-ol-1* ***(12)*** *– R_f= 0.49; (72%), ^{1}H NMR: δ 8.27 (d, 1H, CHNaphth), 8.16 (m, 3H, 3CHNaphth), 7.68 (m, 2H, 2CHNaphth), 7.37 (m, 2H, 2CHPh), 7.18 (m, 3H, 3CHPh), 5.44 (d, 1H), 2.69 (d, 1H, OH); ^{13}C NMR: δ 159.4, 148.7, 136.5, 129.4, 127.9, 126.3, 121.6, 89.8, 84.6, 65.3.*

(vi) *1-(3-bromopyridinyl-4)-3-phenylpropin-2-ol-1* ***(13)*** *– R_f= 0.33; (80%), ^{1}H NMR: δ 8.52 (m, 2H, CH$_{Pir}$), 7.76 (s, 1H, CH$_{Pir}$), 7.46 (m, 2H, 2CH$_{Ph}$), 7.14 (m, 3H, 3CH$_{Ph}$), 5.23 (d, 1H), 2.18 (d, 1H, OH); ^{13}C NMR: δ 152.6, 147.5, 127.8, 126.2, 121.8, 120.4, 88.3, 85.6, 57.4.*

The quantum chemical properties of acetylene alcohols, including total molecular energy, energy of formation, thermal energy, electronic energy, nuclear energy, and dipole moments, were calculated using the semi-empirical PM3 method in the HyperChem Activation 7.0 program (with the STAT package) (**Table 3**). These energy values provide insights into the stability, reactivity, and electronic structure of acetylene alcohols, aiding in understanding their chemical behavior.

The calculations revealed that compound 12 exhibited the lowest energy of formation (-3845.7 kcal/mol), indicating higher stability compared to the other acetylene alcohols. Compound 13 showed the highest dipole moment (3.165 D), suggesting greater molecular polarity, which could affect its solubility and reactivity. Additionally, the atomic charge of oxygen was found to be approximately -0.301 to -0.303 across most compounds, except for compound 13, where it was slightly positive (0.299), potentially influencing hydrogen bonding interactions.

Table 3. Quantum-chemical calculations of acetylene alcohols.

Acetylene alcohols	Total energy, kcal/mol	The energy of formation, kcal/mol	Thermal energy kcal/mol	Electronic energy, kcal/mol	Nuclear energy, ккал/моль	Dipole moment (D)	The atomic charge of oxygen
8	-50066.5	-2802.5	65.97	-279596.4	229529.9	1.726	-0.301
9	-53518.1	-3086.2	57.42	-320633.2	267115.1	1.835	-0.301
10	-52538.7	-2832.0	29.64	-287463.3	234925.4	1.777	-0.301
11	-52609.9	-3075.3	62.76	-308082.6	255432.7	2.922	-0.303
12	-64243.5	-3845.7	80.18	-422565.0	358321.5	1.871	-0.303
13	-60402.6	-3039.5	73.20	-348054.2	287651.7	3.165	0.299

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The purity of the synthesized acetylene alcohols was analyzed using chromatographic (TLC) and spectroscopic (^{1}H NMR, ^{13}C NMR) techniques, while their elemental composition was determined through elemental analysis (**Table 4** and **Table 5**). Elemental analysis was performed to confirm the molecular composition of acetylene alcohols and compare the experimentally obtained values with theoretically calculated values.

Table 4 and **Table 5** present the results of elemental analysis for acetylene alcohols, showing the calculated and experimentally determined percentages of carbon (C), hydrogen (H), oxygen (O), sulfur (S), nitrogen (N), and bromine (Br). The experimentally measured values closely matched the theoretical values, confirming the accuracy of the synthesis process. The highest degree of agreement was observed for compounds 8, 9, and 10, with differences between calculated and defined values remaining within ±0.05%. However, compound 13 showed the largest deviation, with the experimentally determined bromine content (27.73%) slightly lower than the theoretical value (27.87%), possibly due to trace impurities or measurement limitations.

Table 4. Elemental analysis results for acetylene alcohols.

Aa	Gross formula	Molecular weight, г/моль	Analysis results	Name of elements and their analysis, %					
				C	H	O	S	N	Br
8	$C_{13}H_{10}OS$	214	Calculated	72.89	4.67	7.47	14.95		
			Defined	72.87	4.70	7.47	14.96		
9	$C_{14}H_{12}OS$	228	Calculated	73.68	5.26	7.01	14.03		
			Defined	73.65	5.30	7.01	14.04		
10	$C_{13}H_{10}O_2$	198	Calculated	78.78	5.05	16.16			
			Defined	78.77	5.09	16.14			
11	$C_{14}H_{11}NO$	209	Calculated	80.38	5.26	7.65		6.69	
			Defined	80.36	5.30	7.65		6.69	
12	$C_{18}H_{13}NO$	259	Calculated	83.39	5.01	6.17		5.40	
			Defined	83.37	5.05	6.17		5.40	
13	$C_{14}H_{10}BrNO$	287	Calculated	58.53	3.48	5.57		4.87	27.87
			Defined	58.36	3.50	5.55		4.86	27.73

The biological activity of the synthesized acetylene alcohols was predicted using the PASS (Prediction of Activity Spectra for Substances) online program, which estimates potential pharmacological properties based on molecular structure (**Table 6**). The PASS program provides probability values for each pharmacological property: Pa (probability of activity) indicates the likelihood that a compound exhibits a given activity, while Pi (probability of inactivity) reflects the likelihood that the compound does not exhibit the activity.

The acetylene alcohols were analyzed for their potential therapeutic effects in treating skin diseases (eczema, psoriasis), cardiovascular conditions (ischemia, hypertension), and other biological activities such as fibrinolytic, antiviral, and analeptic properties. **Table 6** shows the predicted pharmacological properties, highlighting compounds with the highest Pa values, including fibrinolytic (0.713), ischemia treatment (0.902), and nicotinic antagonist (0.758) activities, suggesting strong pharmacological potential in these areas.

The Pa/Pi ratio (Ra/Pi) represents the activity-to-inactivity probability ratio, where higher values indicate stronger predicted activity. Notably, the highest Ra/Pi value (255.5) was observed for ischemia treatment, suggesting high potential efficacy for cardiovascular applications. Additionally, compounds with Pa values above 0.6 for eczema, psoriasis, and antiviral properties indicate their possible effectiveness in dermatological and antiviral treatments.

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Table 5. The spatial structure of the synthesized acetylene alcohol molecules, the charge distribution and electron density in the molecules. This was determined using the HyperChem Activation 7.0 program (with the STAT package).

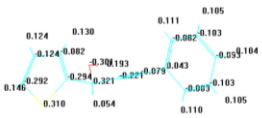
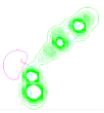
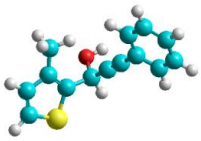
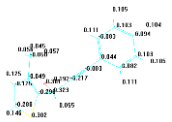
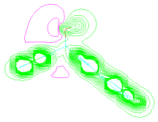
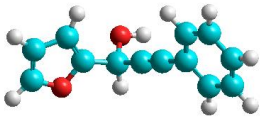
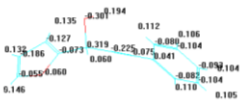
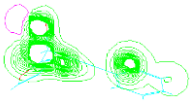
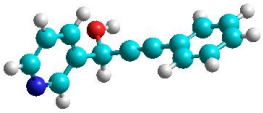
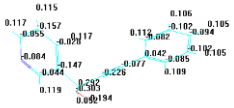
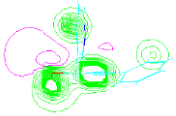
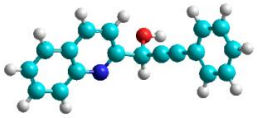
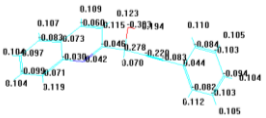
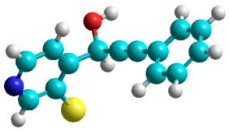
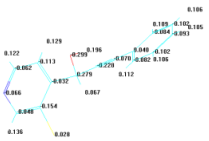
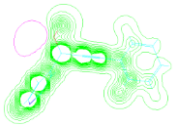
	3D structure of a molecule	Distribution of electron density in a molecule	The amount of charge of atoms in a molecule
8			
9			
10			
11			
12			
13			

Table 6. Pharmacological properties of acetylene alcohols.

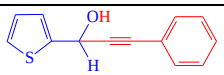
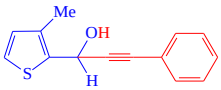
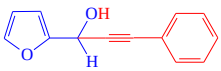
Compound	Probability	Pharmacological properties				
		For the treatment of eczema	For the treatment of psoriasis	For the treatment of skin diseases	For the treatment of neurosis	Antiviral
	Pa[1]	0.671	0.568	0.551	0.593	0.526
	Pi[2]	0.056	0.014	0.022	0.074	0.040
	Pa/Pi[3]	12	41	25	8	13
	Pa[1]	0.582	0.560	0.544	0.556	0.582
	Pi[2]	0.044	0.015	0.023	0.053	0.008
	Pa/Pi[3]	13	37	27	11	73
Compound	Probability	For the treatment of ischemia	For the treatment of hypertension	Fibrinolytic	Vasoprotector	For the treatment of eczema
	Pa[1]	0.902	0.735	0.713	0.582	0.629
	Pi[2]	0.004	0.005	0.018	0.023	0.073
	Pa/Pi[3]	255.5	147	40	2	7

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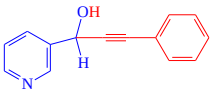
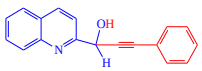
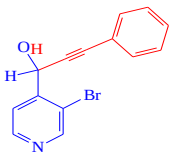
Table 6 (continue). Pharmacological properties of acetylene alcohols.

Compound	Probability	Pharmacological properties				
		For the treatment of eczema	**For the treatment of psoriasis**	**For the treatment of skin diseases**	**For the treatment of neurosis**	**Antiviral**
Compound	Probability	For the treatment of skin diseases	For the treatment of eczema	Fibrinolytic	Analeptic	Testosterone inhibitor
	Pa^1	0.693	0.697	0.654	0.615	0.678
	Pi^2	0.008	0.047	0.043	0.013	0.062
	Pa/Pi^3	87	15	15	47	11
Compound	Probability	For the treatment of eczema	Antiviral	Nicotinic antagonist	Corticosteroid inhibitor	Analeptic
	Pa^1	0.689	0.511	0.758	0.732	0.515
	Pi^2	0.049	0.046	0.019	0.007	0.013
	Pa/Pi^3	14	11	40	105	40
Compound	Probability	For the treatment of skin diseases	Kidney function stimulant	For the treatment of psoriasis	For the treatment of eczema	Oxygen absorber
	Pa^1	0.598	0.580	0.504	0.572	0.511
	Pi^2	0.016	0.050	0.023	0.099	0.047
	Pa/Pi^3	37.3	12	22	6	11

5. CONCLUSION

A series of novel acetylene alcohols were successfully synthesized via the alkynylation of heteroatomic aldehydes with phenylacetylene, employing the ProPhenol/Me_2Zn/THF catalytic system. The synthesized compounds were thoroughly characterized using spectroscopic (^{1}H NMR, ^{13}C NMR) and chromatographic (TLC) techniques, along with elemental analysis, confirming their purity and structural integrity. The effect of the ProPhenol/Me_2Zn/THF catalytic system on product yield was investigated, leading to the identification of optimized reaction conditions that enhance efficiency and selectivity. The reactivity of heteroatomic aldehydes in alkynylation reactions followed the order: thiophene-2-carbaldehyde < 3-methylthiophene-2-carbaldehyde < quinoline-2-carbaldehyde < pyridine-3-carbaldehyde < 3-bromo-4-pyridinecarbaldehyde < furan-2-carbaldehyde. This trend can be attributed to electronic effects and steric hindrance imposed by the substituents surrounding the carbonyl group. Furthermore, the biological activity of the synthesized acetylene alcohols was predicted using the PASS (online) program, revealing potential pharmacological applications, including antiviral, fibrinolytic, and dermatological activities. These findings suggest that the synthesized compounds could serve as promising candidates for further pharmacological evaluation and potential therapeutic applications.

6. AUTHORS' NOTE

The authors declare that there is no conflict of interest regarding the publication of this article. Authors confirmed that the paper was free of plagiarism.

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