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Research Article

Copper (I) assisted catalyst synthesis of substituted allenes and their biological studies

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ABSTRACT

The present study addresses the synthesis of 1,2-dienes from terminal alkynes, during the rearrangement process in the presence of Cu (I) Catalyst. Terminal alkynes were prepared by using aldehyde or ketone in the presence of sodium actylide and allenes formed under mild conditions. The structures of synthesized compounds were confirmed by using TLC, FT-IR, ^{1}H-NMR and mass spectroscopic techniques. The synthesized 1,2-dienes were screened for their antibacterial activity against *Escherichia coli, Staphylococcus aureus.* The antibacterial analysis shows that compound **2f** scored good activity compared to the all other synthesized compounds. Besides, the compounds 1-(4-chlorobuta-2,3-dien-2-yl)benzene (**2b)** and (**2e)** also shows moderate antibacterial activity.

Keywords: Aquatic plants; antimicrobial; tannins; phenolic compounds; alkaloids

INTRODUCTION

1,3- dienes or allenes are very important synthons for organic reactions, synthesizing the natural products and as well as substrates for drug targets (Hopf., *et al., 1980 &* Hassan., *et al.,2007*). Allenes are distinctive class of compounds which elevates chemical reactivity due to their two contiguous carbon-carbon double bonds (Brandsma., *et al., 1981*). The allene derivatives exhibit mechanism-based enzyme inhibitors, cytotoxic, or antiviral agents (Schuster., *et al., 1984*). Hence, it needs requirement of further developments in efficient stereo selective synthesis of allene derivatives (Hoffman-Rodar., *et al., 2004*).

The continual study of Cu(I) catalytic system (Munirajasekhar., *et al., 2011*) provides a series of hallo allenes. The present study synthesized the allenes from propargyl alocohols. These propargyl alcohols in presence of Cu(I) catalytic system it forms acetylene-copper (I) Π-complex as an intermediate, which undergoes further rearrangement lead to the formation of chloro allenes in good yields. All the synthesized compounds were studied for their antibacterial activity against *Escherichia coli, Staphylococcus aureus* and compared to the ampicillin as a standard drug.

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MATERIALS AND METHODS

Reagents and Chemicals

Chemicals and analytical grade solvents were obtained from local companies in India. Aldehyde (or) Ketone – Avra chemicals limited, Chennai, Tetrahydrofuran (THF) – SD Fine chemicals limited, Chennai. Sodium metal- SD Fine chemicals limited, Chennai. Ammonium chloride- Rankem chemicals limited, Chennai. Hexane- SD Fine chemicals limited, Chennai. Ethylacetate- SD Fine chemicals limited, Chennai. Hydrochloric acid- Rankem chemicals limited, Chennai. Petroleum ether- SD Fine chemicals limited, Chennai. Ethanol- SD Fine chemicals limited, Chennai. These chemicals and solvents were used in the reactions without further purification.

Instrumentation and Chromatographic Condition

The melting points were determined in open capillary tube and are uncorrected. The progress and completion of the reaction was monitored by using thin layer chromatography (TLC). FT-IR spectra were recorded in the VIT University, Vellore. IR spectra were recorded in KBr Pellet on Avatar 330 FT-IR spectrometer ranges from 4000 to 400 cm-1. ^{1}H NMR and Mass spectra were recorded on IIT Madras. The ^{1}HNMR was spectra recorded on GEOL-JMS D–500 (MHz) NMR spectrometer (Trimethylsilane was internal reference and $CDCl_3$ as a solvent). GC-Mass spectra were recorded on Shimandzu (at 70 eV). The progress and purity of the compounds were monitored by using thin layer chromatography on (Hexane 60%: Ethyl acetate 40%) and visualized by UV-chamber and Iodine chamber.

General Procedure for the Synthesis of Propargyl alcohols 1(a-f)

Aldehyde or ketone (10 mmol) was taken in a round bottom flask fitted with a dropping funnel. After that 10 ml of dry THF was added drop by drop continuously while stirring. The stirring was continued for 2 hrs, then sodiumacetylide and and 5g of ammonia chloride was added in to the round bottom flask. Then the reaction mixture was continued for overnight stirring to ensure the all ammonia was evaporated. The completion of the reaction was monitored by using TLC. The crude product was extracted by using dry THF and it was further purified by the using column chromatography by hexane: ethyl acetate (60/40 %) solvent.

Spectral Data

1(a): 3-methylpent-1-yn-3-ol: Yield 0.567g, 75%, mp 67 :C; IR (KBR): 3451 (OH str), 2974 (aliphatic C-H str), 2136 (C≡C str); ^{1}H NMR ($CDCl_3$): 1.14 (t, 3H, CH_3), 1.54 (s, 3H, CH_3), 1.87 (m, 2H, CH_2), 2.12 (s, 1H, OH), 2.54 (s, 1H, C≡CH). MASS: 99 (M+1).

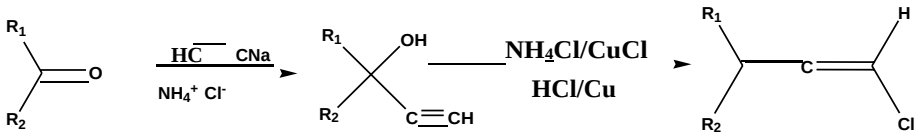
1(b): 1-ethynylcyclohexanol: Yield 0.585g, 76%, mp 40 :C; IR (KBR): 3419 (OH str), 2935 (aliphatic C-H str), 2104 (C≡C str); ^{1}H NMR ($CDCl_3$): 1.24-1.91 (m, 10H, cyclohexane aliphatic-H), 2.45 (s, 1H, OH), 2.66 (s, 1H, C≡CH); MASS: 125 (M+1).

1(c): 2-phenylbut-3-yn-2-ol: Yield 0.627g, 81%, mp 49-51:C; IR (KBR): 3388 (OH str), 3084 (Aromatic C-H str), 2930 (aliphatic C-H str), 2119 (C≡C str); ^{1}H NMR ($CDCl_3$): 1.80 (s, 3H, CH_3), 2.46 (s, 1H, OH), 2.69 (s, 1H, C≡CH), 7.27-7.70 (m, 5H, Ar-H); MASS: 170 (M+Na).

1(d): 1,1-diphenylprop-2-yn-1-ol: Yield 0.782g, 87%, mp 103:C; IR (KBR): 3525 (OH str), 3056 (Aromatic C-H str), 2911 (aliphatic C-H str), 2132 (C≡C str); ^{1}H NMR ($CDCl_3$): 1.59 (s, 1H, OH), 2.93 (s, 1H, C≡CH), 7.27-7.64 (m, 10H, Ar-H); MASS: 209 (M+1).

1(e): 1-(naphthalene-1-yl)prop-2-yn-1-ol: Yield 0.812g, 90%, mp 127:C; IR (KBR): 3392 (OH str), 2972 (aliphatic C-H str), 3094 (Aromatic C-H str), 2168 (C≡C str); ^{1}H NMR ($CDCl_3$): 2.12 (s, 1H, OH), 2.81 (s, 1H, C≡CH), 5..32 (m, 1H, Ar-CH), 7.13-7.52 (m, 7H, Ar-H); MASS: 183 (M+1).

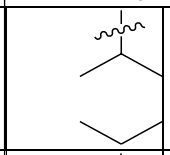
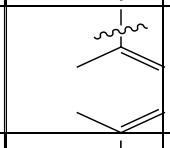
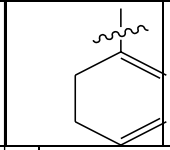
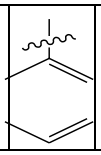
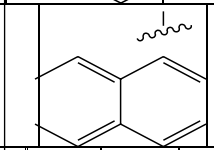
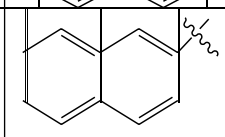
1(f): 1-(naphthalene-2-yl)prop-2-yn-1-ol: Yield 0.734g,



1(a-f) **2(a-f)**

Scheme: 1

Table 1: Physical data of the synthesized Hallo - Substituted Allenes

Compound	R_1	R_2	Molecular Formula	Yield
2a	C_2H_5	CH_3	C_6H_9Cl	84
2b		H	$C_8H_{11}Cl$	81
2c		CH_3	$C_{10}H_9Cl$	75
2d			$C_{15}H_{11}Cl$	65
2e		H	$C_{13}H_9Cl$	67
2f		H	$C_{13}H_9Cl$	69

87%, mp 163:C; IR (KBR): 3412 (OH str), 2894 (aliphatic C-H str), 3120 (Aromatic C-H str), 2177 (C≡C str); ^{1}H NMR ($CDCl_3$): 2.24 (s, 1H, OH), 2.52 (s, 1H, C≡CH), 5..56 (m, 1H, Ar-CH), 7.28-7.74 (m, 7H, Ar-H); MASS: 183 (M+1).

General procedure for the synthesis of chloro substituted allenes 2(a-f)

Powdered ammonium chloride (3 mmole) and copper powder (3 mmole) were taken into the round bottom flask and 0.5 ml of conc. hydrochloric acid was added. The reaction mixture was stirred vigorously stirred for 10 minutes. After that propargyl alcohol (10 mmoles) was added drop wise into the round bottom flask. Then the reaction mixture was continuous stirred for 2 to 2.5 hrs. The completion of the reaction was monitored by using TLC (Hexane 50 : Ethyl acetate 50). The crude product was filtered and then washed several times with petroleum ether and further purified by column chromatography. The final products were recrystalized from ethanol.

Spectral Data

2(a): 1-chloro-3-methylpenta-1,2-diene: Yield 0.624g, 80%, mp 47:C; IR (KBR): 2973 (alip hatic C-H str), 1959 (C=C=C str); ^{1}H NMR ($CDCl_3$): 1.01-107 (m, 3H, CH_3 - CH_2), 1.65 (s, 3H, CH_3), 2.12 (m, 2H, CH_2), 5.99 (s, 1H, C=C=CH); MASS: 117 (M+1).

2(b): (2-chlorovinylidene)cyclohexane: Yield 0.554g, 75%, mp 62:C; IR (KBR): 2973 (alip hatic C-H str), 1959 (C=C=C str); ^{1}H NMR ($CDCl_3$): 1.35-1.47 (m, 6H, Cyclohexane), 2.12-2.23 (m, 4H, Cyclohexane), 6.4 (s, 1H, C=C=CH); MASS: 143 (M+1).

2(c): 1-(4-chlorobuta-2,3-dien-2-yl)benzene: Yield 0.426g, 62%, mp 49:C; IR (KBR): 3058 (Aromatic C-H str), 2977 (alip hatic C-H str), 1950 (C=C=C str); ^{1}H NMR ($CDCl_3$): 1.81 (s, 3H, CH_3), 6.93 (s, 1H, C=C=CH).7.24-7.54 (m, 5H, Ar-H); MASS: 165 (M+1).

2(d): 3-chloro-1,1-diphenylpropa-1,2-diene: Yield 0.585g, 76%, mp 76:C; IR (KBR): 3064 (Aromatic C-H str), 2925 (alip hatic C-H str), 1948 (C=C=C str); ^{1}H NMR ($CDCl_3$): 6.12 (s, 1H, C=C=CH).7.05-7.45 (m, 10H, Ar-H); MASS: 227 (M+1).

2(e): 1-(3-chloropropa-1,2-dienyl)naphthalene: Yield 0.326g, 43%, mp 98:C; IR (KBR): 3023 (Aromatic C-H str), 2948 (alip hatic C-H str), 1953 (C=C=C str); ^{1}H NMR ($CDCl_3$): 6.23 (s, 1H, C=C=CH). 6.54 (m, 1H, Napthalenic proton), 7.32-7.61 (m, 5H, Ar-H); MASS: 201 (M+1).

2(f): 2-(3-chloropropa-1,2-dienyl)naphthalene: Yield 0.412g, 45%, mp 112:C; IR (KBR): 3047 (Aromatic C-H str), 2948 (alip hatic C-H str), 1909 (C=C=C str); ^{1}H NMR ($CDCl_3$): 6.52 (s, 1H, C=C=CH), 6.82 (m, 1H, Napthalenic Proton), 7.05-7.45 (m, 10H, Ar-H); MASS: 201 (M+1).

Antibacterial activity (Morita., *et al., 2003*) **:**

The antibacterial activity **(Figure. 1)** was determined using well-diffusion method by measuring the zone of inhibition in mm. All the synthesized compounds were evaluated antibacterial activity against *Escherichia coli* (gram negative), *Staphylococcus aureus* s (gram positive) bacterial strains. The compounds were tested at a concentration of 50 µg/mL. Ampicillin was used as a control. The results are given in **Table 2** and **Figure 2.**

Procedure

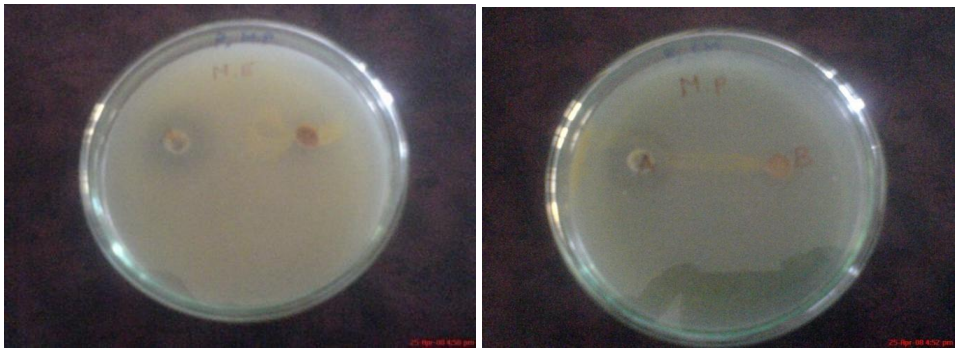
The synthesized final compounds were evaluated for their in vitro antibacterial activity against *E. coli* and *S. aureus* by the agar-well diffusion method. The test solutions (200 µL) were prepared in DMSO solvent. Muller Hinton agar was prepared and distributed to sterilized petri plates and allowed to solidify. The wells (7 mm thickness) were made using the borer and 200 µL of the test samples were added into the wells using micropipette. These plates were incubated at room temperature for 24 hrs to allow the maximum growth of organisms. The plates were incubated at 37°c for 24 hrs during which activity was evidenced by the presence of the zone of inhibition surrounding the well. The diameter of the zone of inhibition was shown in **Table 2**.

RESULTS AND DISCUSSION

The chloro substituted allenes **2 (a-f)** were synthesized by Cu (I) Cl. In this method reactions were carried out smoothly and gave good yields (Table1). The structures of the all novel compounds were characterized by FT-IR, ^{1}H NMR, and mass analysis. All the synthesized compounds shown in FT-IR spectra at 1950-1960 cm^{-1} absorption bands due to the strong allenic (C=C=C) absorption. All the compounds were shown absorption bands nearly 750 cm^{-1} due to the C-Cl stretching vibrations. ^{1}H NMR spectrum of all the compounds shown singlet of C=C=CH at δ 5.91 to δ 6.92 confirmed the

Table 2: Antibacterial activity of Chloro substituted Allenes

S. No	Compound	Diameter of zone of Inhibition (mm)	
		S. aureus	***E. coli***
1	**2a**	9	12
2	**2b**	12	15
3	**2c**	10	12
4	**2d**	9	16
5	**2e**	15	18
6	**2f**	16	19
7	Ampicillin	18	21



E. Coli *S. Aureus*

Figure 1: Antibacterial activity of compounds 2(a-f)

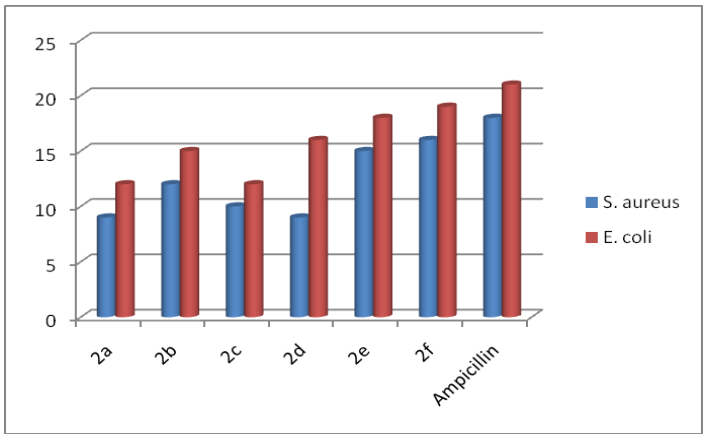


Figure 2: Graphical representation for the antibacterial Activity of compounds 2(a-f)

presence of allenic moiety and compounds 2a & 2c exhibit sharp singlet of CH_3 at δ 1.65 and δ 1.81 confirmed the presence methyl group in allenic compounds. Results of IR, ^{1}H NMR and mass analysis confirmed the formation of final allenic products. All the Synthesized compounds **2(a-f)** have been screened for antibacterial activity against *E. coli, S. aureus* comparing to the standard drug ampicillin and graphical representation was shown in the **Figure. 2.** It is evident from the graph that the compound **2c** showed poor antibacterial activity due to the presence of bulky methyl group adjacent to phenyl ring, but the compounds **2e & 2f** exhibited high antibacterial activity due to the bicyclic structure.

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