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Research Article

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Synthesis and Antimicrobial Studies of 3-(3-Hydroxy-4-Methoxyphenyl)-1-Phenylprop-2-en-1-One

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Abstract This paper reports on the synthesis of 3-(3-hydroxy-4-methoxyphenyl)-1-phenylprop-2-en-1-one by Claisen-Schmidt condensation of acetophenone with an aromatic aldehyde (vanillin) in the presence of aqueous solution of 60% sodium hydroxide at room temperature. The percentage yield of 3-(3-hydroxy-4-methoxyphenyl)-1-phenylprop-2-en-1-one was found to be 32.3% after recrystallization from ethanol. The synthesized 3-(3-hydroxy-4-methoxyphenyl)-1-phenylprop-2-en-1-one was characterized using Fourier Transform Infrared (FTIR) spectroscopy, Shinoda's test, and melting point measurement. The synthesized compound was tested for its antibacterial activities by cup plate method against the bacterial strains of Staphylococcus Aureus, Pseudomonas Aeruginosa, Bacillus subtilis, and Escherichia coli. Gentamicin was used as the control for the antimicrobial screening. The synthesized of 3-(3-hydroxy-4-methoxyphenyl)-1-phenylprop-2-en-1-one was did not show antimicrobial activity at the doses used.

Keywords 3-(3-hydroxy-4-methoxyphenyl)-1-phenylprop-2-en-1-one, characterization, synthesis, antimicrobial activity

Introduction

Infectious diseases are caused by pathogenic microorganisms (bacteria, viruses, parasites or fungi). According to the published data in 2008, infectious diseases were responsible for the death of more than 8.7 million people worldwide in 2008. Infectious diseases have a negative societal and economic impact. Antimicrobial resistance is the ability of microbes to an antimicrobial drug that was originally effective for treatment of infections caused by it. Resistant microorganisms are able to withstand attack by antimicrobial drugs, such as antibacterial drugs (e.g., antibiotics), antifungals, antivirals, and antimalarial, so that standard treatments become ineffective and infections persist. Multi-resistant strains of microorganisms are continuously appearing, triggering the need for a permanent search and development of new drugs [1-3].

The use of conventional antimicrobial drugs can have many unintended side-effects. The repeated use of many drugs can lead to an accumulation of a drug or harmful by-products from the metabolism of a drug, in human organs. This accumulation of toxic chemicals can lead to organ damage, and even organ failure and/or death. Broad-spectrum antibiotics in the family of fluoroquinolones can cause neurotoxicity by directly damaging neuronal receptors. Gentamicin can cause loss of hearing and phototoxicity [2-4].

Chalcones posses a wide variety of pharmacological activities, they may carry many different substituents such as methyl, isopentyl, methoxy and hydroxyl, which may be present on either rings of the chalcone molecule [5-8]. Many higher plants have been found to contain dihydrochalcones. Some chalcones have antitubercular, antioxidant, antibacterial, antifungal, anticancer activity and inhibit the production of nitric oxide and interleukin-1. Thus, licochalcone A, a chalcone obtained from licorice has better antibacterial activity than the cationic antimicrobial peptides in the presence of NaCl or protease. Licochalcone A also showed potent antibacterial and antifungal activity against *E. coli* K-12 IFO 3301, *Pseudomonas aeruginosa* IFO 3923, *B. subtilis* IFO 3007, *S. aureus* 209P IFO 12732 and some other strains. Chalcones also show very good activity against resistant microbial strains. Functionalized chalcones showed potent antibacterial activity against drug-sensitive strains of *S. aureus [3]*. Hence, there is a continuous interest in the research community to synthesize and test new analogs of chalcones. The main

aim of the present work is to synthesize a substituted chalcone, namely 3-(3-hydroxy-4-methoxyphenyl)-1-phenylprop-2-en-1-one, and evaluate its antimicrobial activity against some Gram positive and Gram negative bacteria.

Materials and Methods

Synthesis and characterization of 3-(3-hydroxy-4-methoxyphenyl)-1-phenylprop-2-en-1-one

The synthesis of 3-(3-hydroxy-4-methoxyphenyl)-1-phenylprop-2-en-1-one was accomplished via the Claisen-Schmidt condensation of acetophenone and vanillin in the presence of aqueous alcoholic alkali solution (60 % NaOH) at room temperature. Progress of the reaction was monitored using thin layer chromatography (TLC) with n-hexane and ethyl acetate in a ratio of 7:1 as the developing solvent.Appearance of a single new spot and disappearance of the reactants spots indicate formation of the product. 1.2ml (0.01mol) of acetophenone and 1.52g (0.01mol) of the substituted benzaldehyde (vanillin) were mixed in 40ml ethanol/rectified spirit solvent in a round bottom flask placed on an ice bath. To this 10ml of 60%NaOH solution was added drop wise with continuous stirring for 30 minutes. The mixing was then continued for another 2-3 hours at room temperature using magnetic stirrer, after which the mixture was kept in a refrigerator overnight, until it became thick. The mixture was then diluted with 40ml ice-cold distilled water, filtered, washed, and then recrystallized from rectified ethanol [9].

The melting point of the synthesized 3-(3-hydroxy-4-methoxyphenyl)-1-phenylprop-2-en-1-one was determined using Gallenklamp melting point apparatus following the procedure described in the manufacturer's manual. The reported melting point was uncorrected. Fourier Transform Infrared (FTIR) spectrum was recorded on a Shimadzu FTIR 8201 PC spectrophotometer. Shinoda's test for detecting the presence of flavonoids was carried out as follows: 1 ml of 10% ethanolic solution of the studied sample was mixed with 0.5ml of 10% hydrochloric acid and magnesium metal,and the colour change observed.

Determination of antimicrobial activity using cup plate method

Standard strains of *Staphylococcal aureus, Pseudomonas aeruginosa, Bacillus subtilis, and Escherichia coli* were obtained from the department of pharmaceutics and pharmaceutical microbiology, Ahmadu Bello University, Zaria, Nigeria. Culture media was prepared according to manufacturer's specification. Inoculated agar plates were prepared. 6 holes of about 7mm in diameter were cut with sterile cork borer. The agar plugs was removed by a sterile ampoule file. The sample solution or gentamicin solution used as standard was placed in each of the hole. It was then left at room temperature for 2 hours, and then incubated at 37^0C for 24 hours. The size of the inhibition zone was then recorded. Gentamicin was used as the control.

Results and Discussion

The synthesized 3-(3-hydroxy-4-methoxyphenyl)-1-phenylprop-2-en-1-one appears to be a white yellowish powder. The result of the thin layer chromatography (TLC) on silica gel plate indicates the purity of the 3-(3-hydroxy-4-methoxyphenyl)-1-phenylprop-2-en-1-one with R_f value of 0.6. The melting point was found to be 45-48^{o}C. Further evidence for the formation of 3-(3-hydroxy-4-methoxyphenyl)-1-phenylprop-2-en-1-one was obtained by chemical test of flavonoid which gave orange coloration. The FTIR spectrum of 3-(3-hydroxy-4-methoxyphenyl)-1-phenylprop-2-en-1-one is shown in Figure 1. The spectrum is characterized by prominent bands at 3677.14 cm^{-1}(O-H stretching), 3440.16 cm^{-1} (overtone of C=O stretching), 1026.16 cm^{-1} (C-O stretching). 2933.83 cm^{-1}(C-H stretching), 1636.65 cm^{-1}(C=C stretching), and 1026.16 cm^{-1}(C-O stretching).

The antimicrobial activity of the compound was evaluated using cup plate method. The results of the antimicrobial screening of 3-(3-hydroxy-4-methoxyphenyl)-1-phenylprop-2-en-1-one and gentamicin are summarized in Table 1. The results shows that the synthesized compound has no antibacterial activity at the doses tested, compared to the gentamicin which was used as a reference antibacterial agent against the bacterial strains of *Staphylococcus aureus, Pseudomonas aeruginosa, Bacillus subtilis, and Escherichia coli.* The possible reason for the lack of antimicrobial activity might be that 3-(3-hydroxy-4-methoxyphenyl)-1-phenylprop-2-en-1-one possess free hydroxyl group in position 4 (B ring) appears to be a very important requirement, When the hydroxyl group is methylated or in other positions, the chalcone is not active [7]. Methoxy groups in B ring were inactive, regardless of their A ring structures. This means that methoxy groups seem to abolish the hydrophilic property of the phenol hydroxyl moiety which can affect penetration of antibiotics through bacterial cell walls [10].

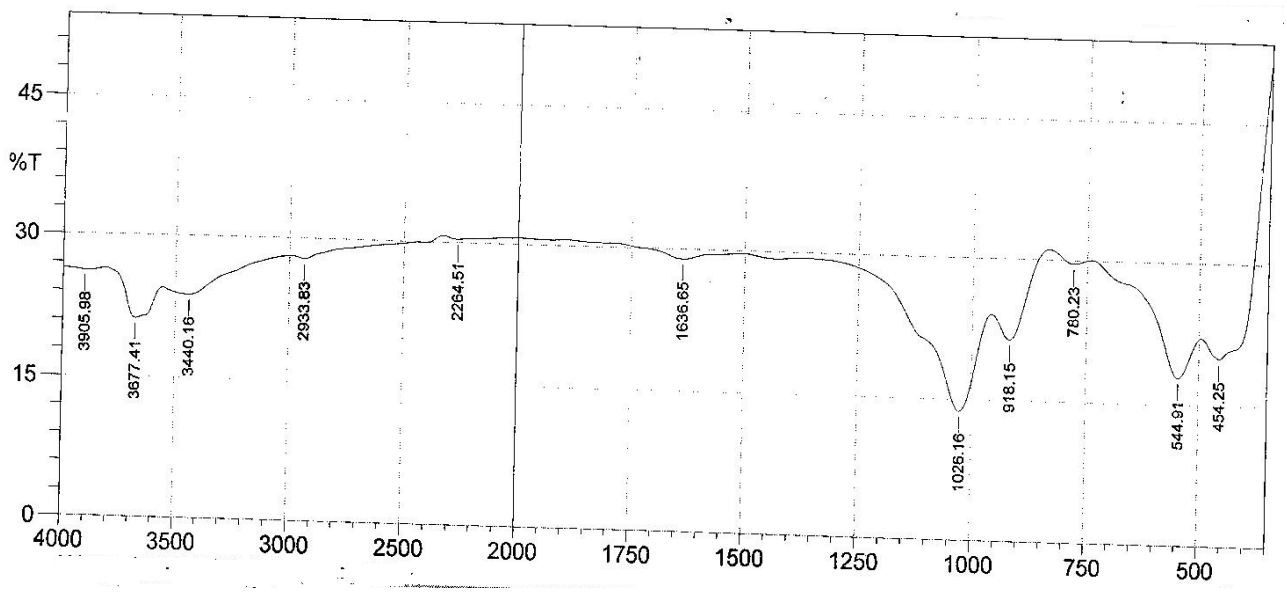

Figure 1: FTIR spectrum of 3-(3-hydroxy-4-methoxyphenyl)-1-phenylprop-2-en-1-one

Table 1: Results of the antimicrobial screening of 3-(3-hydroxy-4-methoxyphenyl)-1-phenylprop-2-en-1-one

Microorganism	100mg/Ml	50mg/Ml	25mg/Ml	6.25mg/Ml	Control, 1mg/Ml (Gentamicin)
E Coli	0	0	0	0	30mm
	0	0	0	0	25mm
S Aureus	0	0	0	0	30mm
	0	0	0	0	30mm
B Subtilis	0	0	0	0	20mm
	0	0	0	0	36mm
P Aeruginosa	0	0	0	0	28mm

Conclusion

(3- (3 -hydroxyl - 4 - methoxy) -1 – phenyl prop - 2 - en - 1 - one) was successfully synthesized with a percentage yield of 32.3%. The synthesized compound was tested for its antibacterial activities by cup plate method against the bacterial strains of *Staphylococcus Aureus*, *Pseudomonas Aeruginosa*, *Bacillus subtilis, and Escherichia coli.* Gentamicin was used as the control for the antimicrobial screening. The synthesized of 3-(3-hydroxy-4-methoxyphenyl)-1-phenylprop-2-en-1-one was did not show antimicrobial activity at the doses used.

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