The Pharmaceutical and Chemical Journal, 2016, 3(2):300-303

Available online www.tpcj.org

Research Article

ISSN: 2349-7092
CODEN(USA): PCJHBA

Microwave Assisted Synthesis and Antimicrobial Screening of 3-(4-Methoxy)-1-Phenylprop-2-en-1-One

Asmau Nasiru Hamza, George Kizito Igomu

Department of Pharmaceutical and Medicinal Chemistry, Ahmadu Bello University, Zaria, Nigeria.

Abstract In an effort to develop novel antimicrobial agents, 3-(4-methoxy)-1-phenylprop-2-en-1-one was synthesized from acetophenone and methoxybenzaldehyde using the conventional Claisen-Schmidt condensation and microwave assisted methods. The conventional Claisen-Schmidt condensation afforded a yield of 35.29% in three hours. Whereas, the microwave assisted method gave 73.94% yield of 3-(4-methoxy)-1-phenylprop-2-en-1-one with two minutes. The synthesized 3-(4-methoxy)-1-phenylprop-2-en-1-one was characterized by means of Fourier transform Infrared (FTIR) spectroscopy, Shinoda's test and melting point analysis. The antibacterial activity of 3-(4-methoxy)-1-phenylprop-2-en-1-one was tested using the cup plate method, and was found to have no activity against the organisms tested at the doses used.

Keywords 3-(4-methoxy)-1-phenylprop-2-en-1-one, antimicrobial activity, synthesis, characterization, Claisen-Schmidt condensation, microwave

Introduction

Sub-Sahara African countries have the highest risk of contracting infectious diseases, with an estimation of 81% cases and 91% deaths in 2010. Children below five years of age are most severely affected [1]. Antibiotics are powerful agents for fighting illness and disease caused by bacteria and other microbes. Since the discovery of penicillin as a powerful antibacterial agent, antibiotics have become critical in the fight against infectious diseases caused by bacteria. However, widespread antibiotic use has promoted the emergence of antibiotic-resistant pathogens, including multidrug resistant strains [2]. At present, the appearance of more and more pathogenetic bacterial species resistant to conventional antibiotics has resulted in either high expenses or failure in the treatment of infectious diseases. An alarming increase in resistance of bacteria that cause community acquired infections has also been documented, especially in *Staphylococci* and *Pneumococci*, which are main causes of disease and mortality [3]. With the emergence of new microbial strains resistant to many conventional available antibiotics there is growing interest in the discovery of new antibacterial agents. Toxicity in allergies and potential side effects such as digestion issues, gastro intestinal discomfort, nausea, vomiting and diarrhea resulting from antibiotic use demands the synthesis and production of safe antibiotic for use. About 10-20% of hospital inpatients experience adverse drug reaction [4]. The problem of antibiotic resistance coupled with that of adverse drug reaction has led to the search of newer, effective and safer agents.

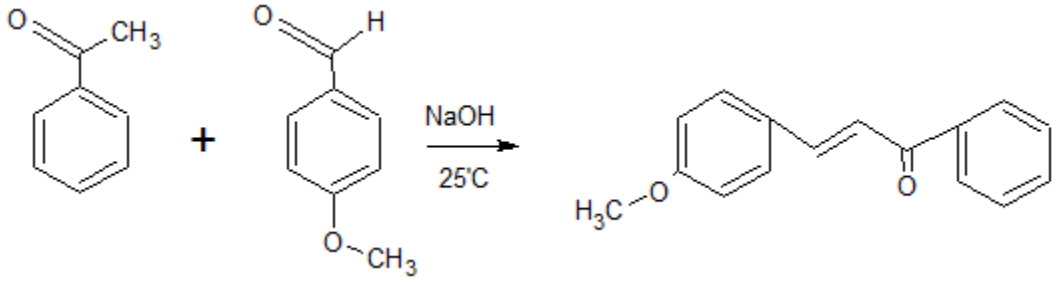
Chalcones (1, 3-diaryl-2-propen-1-ones) belong to the flavonoid family. They consist of open-chain flavonoids in which the two aromatic rings are joined by a three-carbon α, β -unsaturated carbonyl system. Chalcones are essential intermediate compounds in flavonoid biosynthesis, and they are easily found in arboreal or smaller plants. They can be obtained by several chemical methods. Claisen–Schimidt's condensation (aldolic condensation) is the most used method for the synthesis of chalcones. Many studies have shown that some chalcones are compounds of great chemical and pharmacological interest because they exhibit many biological activities such as antimicrobial, antitumor, antimalarial, cytotoxic, antidepressant, anti-inflammatory, anti HIV, anticancer, anti protozoa etc [5]. The antimicrobial activity of chalcones with electron releasing groups such as methoxy and hydroxyl showed better antibacterial activity than the others not having such groups. Compounds having pharmacophores such as chloro,

dichloro and fluoro groups exhibit more antifungal activity than the others. Chalcone derivatives with these substituents show greater antimicrobial activity [6,7]. In this work, 3-(4-methoxy)-1-phenylprop-2-en-1-one was synthesized using conventional (Claisen-Schmidt condensation) and solvent free methods [8]. The antimicrobial activity of synthesized 3-(4-methoxy)-1-phenylprop-2-en-1-one was evaluated against gram positive and gram negative bacteria using the cup plate method.

Materials and Methods

Synthesis and characterization of . 3-(4-methoxy)-1-phenylprop-2-en-1-one

All starting materials and solvents for the experiments were of analytical grade, and were used without further purification. 3-(4-methoxy)-1-phenylprop-2-en-1-one was synthesized by the reaction between methoxybenzaldehye and acetophenone in the presence of NaOH according to the following equation:



Procedure for the synthesis of 3-(4-methoxy)-1-phenylprop-2-en-1-one via Claisen-Schmidt condensation

A mixture of 0.12ml of acetophenone (0.01mol) and 0.12ml methoxybenzaldehyde (0.01mol) was prepared in 40ml ethanol in a round bottom flask placed on an ice bath. To this mixture, 10ml of 60% NaOH solution was added drop wise with continuous stirring for 30mins, the mixing was then continued for three hours at room temperature using a magnetic stirrer, after which the mixture was then kept in a refrigerator overnight until mixture became thick. The mixture was then diluted with 40ml ice-cold distilled water, filtered and washed well with the ice-cold water, dried in air and then recrystallized from ethanol.

Procedure for the synthesis of 3-(4-methoxy)-1-phenylprop-2-en-1-one using the microwave assisted method

1.22ml each of acetophenone (0.01mol) and methoxybenzaldehyde (0.01mol) was dissolved in minimum amount of ethanol in a conical flask and NaOH (60%) was added to it. The conical flask was covered with foil paper and then the flask was placed in domestic microwave oven. The reaction mixture was irradiated under 160-320 watt for 60-120 sec. The reaction mixture was cooled and the obtained solid was recrystallized from ethanol.

For each method, thin layer chromatography (TLC) with silica gel was used to monitor the progress of the reaction under the mixture of n-Hexane and ethyl acetate in 4:1 ratio as the best solvent system.

Characterization of 3-(4-methoxy)-1-phenylprop-2-en-1-one

Melting point of the synthesized 3-(4-methoxy)-1-phenylprop-2-en-1-one was determined using Gallenklamp melting point apparatus as described in the manufacturer's manual, and was uncorrected. For the chemical test (shinoda test) to determine the presence of flavonoid. 1ml of 10% ethanolic solution of the product was mixed with 0.5ml of 10% HCl and 3-4 pieces of magnesium metal. A reddish colour was formed indicating the presence of flavonoids**.** A Fourier Transform Infrared (FTIR) spectrum of 3-(4-methoxy)-1-phenylprop-2-en-1-one was recorded using Shimadzu spectrometer

Antimicrobial screening of 3-(4-methoxy)-1-phenylprop-2-en-1-one

20ml of sterile nutrient agar was poured into sterile petri-dish and allowed to solidify. The surface was flooded with 1ml of the inoculums and the excess decanted. The surface was allowed to dry. A sterile cork borer was then used to bore six holes of about 2.5cm equal size on the surface. 0.1ml of the methanolic solution of the product, at different concentration of 100mg/ml, 50mg/ml, 25mg/ml, 12.5mg/ml and 6.25mg/ml were dropped into each hole and 1mg/ml of gentamicin was dropped into one of the hole as standard. The plate was kept for 2hours at room temperature to allow for diffusion and incubated at 37^{o}C overnight. The zone of inhibition were measured with a ruler from different angles of the plate and recorded to the nearest millimeter.

Results and Discussion

The completion of the reaction was determined by the disappearance of reactant spots in the thin layer chromatogram and appearance of a single product spot, and the different R_f value between the reactants (acetophenone 0.59, and methoxybenzaldehyde 0.41) and the product (0.53) shows that a new compound was

formed. The conventional method and the microwave method gave the same R_f value in 0.53 which means that the two different methods gave the same product. As presented in Table 4.1, the microwave assisted method gave a higher yield (73.94%) of 3-(4-methoxy)-1-phenylprop-2-en-1-one than the conventional method (35.29%). Reaction under microwaves is an effort toward "green chemistry" with low-boiling solvents at high temperature in closed vessels. The probable mechanisms involved in microwaves heating are depolarization, Ohmic heating and interfacial polarization. With capabilities for rapid heating and cooling, concurrent heating and cooling and differential heating, facilitated novel chemical reactions and processes. This maybe the probable reason for its high yield as this method gives high yields, relatively short reaction times, low cost, simple experimental procedures, and finally, it is in agreement with the green chemistry protocols.

The very narrow range (50-53°C) of the uncorrected melting points of the synthesized 3-(4-methoxy)-1-phenylprop-2-en-1-one indicates the purity of the compound. The appearance of reddish coloration in shinoda's test indicates the presence of flavonoid which clarifies the fact that the product 3-(4-methoxy)-1-phenylprop-2-en-1-one belongs to the flavonoid family.

Table 1: Yield and some physical properties of 3-(4-methoxy)-1-phenylprop-2-en-1-one

	Conventional method	**Microwave method**
Yield, (%)	35.29	73.94
R_f value	0.53	0.53
Melting Point,^oC	50-53	50-53
Appearance	Yellow powder	Yellow powder

Further structural analysis of 3-(4-methoxy)-1-phenylprop-2-en-1-one was performed using Fourier Transformed Infrared Spectroscopy (FTIR). The FTIR spectrum displayed in Figure 1 confirms the presence of the methoxy functional group in 3-(4-methoxy)-1-phenylprop-2-en-1-one as evidenced by the appearance of prominent bands 1597 cm^{-1} (C = C stretching), 1302 cm^{-1} and 1014 cm^{-1} (C —O — C stretching) coupled, and 3447 cm^{-1} (overtone of C = O stretching)

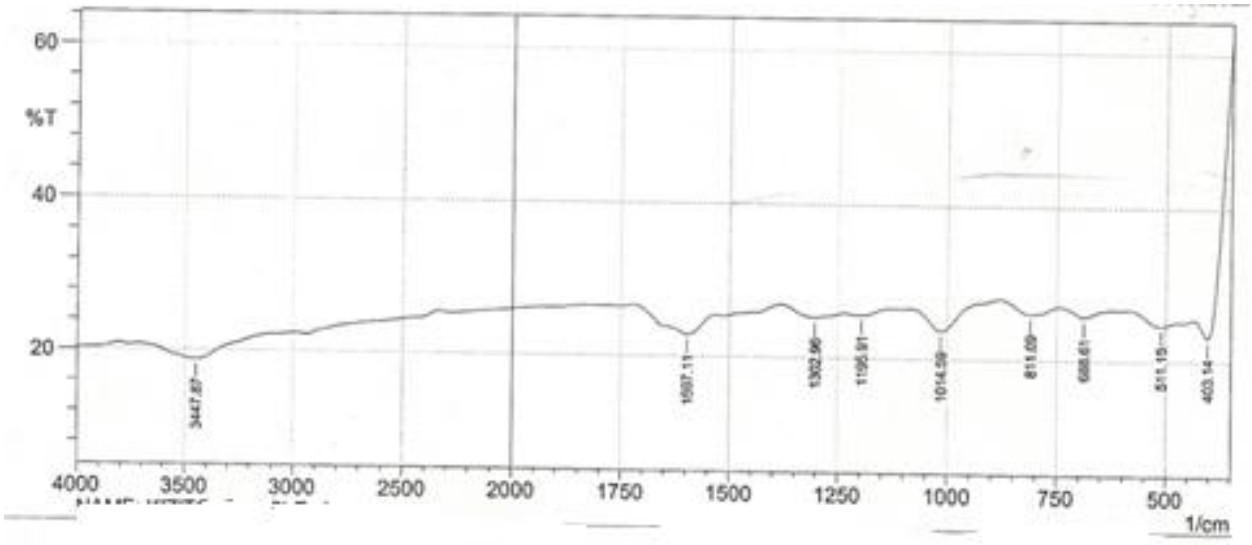


Figure 1: FTIR spectrum of 3-(4-methoxy)-1-phenylprop-2-en-1-one

The synthesized 3-(4-methoxy)-1-phenylprop-2-en-1-one was tested for its *in vitro* antibacterial activity against two Gram-positive bacteria (*Staphylococcus aureus* and *Basilus subtilis*) and two Gram-negative bacteria (*Escherichia coli* and *Pseudomonas aeruginosa*) at various concentrations of 100mg/ml, 50mg/ml 25mg/ml, 12.5mg/ml and 6.25mg/ml using the cup plate method by measuring the zone of inhibition in mm and gentamicin (1mg/ml) was used as the reference antibacterial agents. The results obtained are summarized in Table 2.

From the result obtained, the synthesized 3-(4-methoxy)-1-phenylprop-2-en-1-one did not show antimicrobial activity against any of the tested organisms at the doses tested while the reference antibacterial agent in gentamicin showed significant activity against *S. aureus, B. subtilis, P. aeruginosa* but not against *E. coli* at 1mg/ml. Therefore the activity of the synthesized 3-(4-methoxy)-1-phenylprop-2-en-1-one when compared with the standard antibacterial agent (gentamicin) showed no activity.

Table 2: Inhibitory effects of 3-(4-methoxy)-1-phenylprop-2-en-1-one and a standard antibiotic on gram positive and gram negative test organisms.

	Zones of Inhibition (mm)					
Test organisms	**100 (mg/ml)**	**50 (mg/ml)**	**25 (mg/ml)**	**12.5 (mg/ml)**	**6.25 (mg/ml)**	**gentamicin (1mg/ml)**
B. subtilis	0.00	0.00	0.00	0.00	0.00	30.00
S. areus	0.00	0.00	0.00	0.00	0.00	40.00
E. coli	0.00	0.00	0.00	0.00	0.00	0.00
P. aeruginosa	0.00	0.00	0.00	0.00	0.00	34.00

Conclusion

3-(4-methoxy)-1-phenylprop-2-en-1-one was synthesized using the Claisen-Schmidt condensation reaction in the presence of sodium hydroxide at room temperature with a yield of 35.29% for conventional method and 73.94% for microwave assisted synthesis. The microwave synthesis proved to be highly efficient, fast and simple. The antimicrobial screening of 3-(4-methoxy)-1-phenylprop-2-en-1-one showed no activity at the tested doses.

References

1. Tiwari, B.; Pratapwar, A.S.; Tapas, A.R.; Butle, S.R.; Vatkar, B.S. (2010). Synthesis and antimicrobial activity of some chalcone derivatives. *Int. J. ChemTech Res. 2*, 499–503.
2. Nowak A. Martin, Jean-Baptiste Michel, Yuan Kui Shen, Aviva Presser Aiden, Adrian Veres, Matthew K. Gray, Joseph P. Pickett, Dale Hoiberg, Dan Clancy, Peter Norvig, The Google Books Team, Jon Orwant, Steven Pinker and Erez Lieberman Aiden (2010). Quantitative Analysis of Culture Using Millions of Digitized Books. Program for Evolutionary Dynamics, Harvard University, Cambridge, MA 02138, USA. Vol 331 no 6014pp.176-182.
3. Michel, C.I., Kraft, R., Restifo, L.L (2004). Defective neuronal development in the mushroom bodies of Drosophila Fragile X Mental Retardation 1 Mutants. J. Neurosci. 24(25): 5798—5809.
4. Goodman RH, Cambronne XA, Shen R, and Auer PL. (2012). RISCtrap: a robust approach for identifying microRNA targets. Proc. Natl. Acad. Sci. USA 109: 20473-20478.
5. Carlo, G.D., Mascolo. N., Izzo, A.A., and Capasso, F. (1999) Flavonoids: old and new aspects of a class of natural therapeutic drugs. *Life Sci.*, 65(4), pp. 337-353.
6. Li, R., Kenyon, GL., and Cohen, F. E. (1995). *In vitro* antimalarial activityof chalcones and their derivatives. *Journal of Medicinal Chemistry*, 38, 5031-7.
7. Clark, J. H., Ipharraguerre, I.R.,(2012). Chalcone Analogues Alone and in Combination with Antibiotics. Dairy sci., 84:E9-18.
8. Mukherji S. M., Singh S. P., Kapoor R. P.(2003). *Organic Chemistry*. International (P) Limited, Publishers, 2: 586-587.
9. Azad, M.; Munawar, M.A.; Siddiqui, H.L. (2007). Antimicrobial activity and synthesis of quinoline-base chalcones. *J. Appl. Sci*, *7*, 2485–2489.