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RESEARCH ARTICLE

Synthesis, Characterization and Antibacterial Activity of Some Chalcones

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ABSTRACT

A series of chalcones (1a-1f) have been synthesized by condensation of a variety of aromatic ketones and aromatic aldehyde derivatives. These synthesized compounds have been characterized by IR, ^{1}H NMR. The antibacterial activity of the synthesized compounds was evaluated against bacteria such as *Escherichia coli, Proteus mirabilis* and *Staphylococcus aureus* by cup or agar well assay method.

KEYWORDS

Aromatic Aldehyde Derivatives, Aromatic Ketones, Chalcones, Spectral Studies, Antibacterial Activity, Ethanol

INTRODUCTION

The chemistry of chalcones has generated intensive scientific studies throughout the world. Especially interest has been focused on the synthesis and biodynamic activities of chalcones. These compounds are also known as benzalacetophenone or benzylidene acetophenone. In chalcones, two aromatic rings are linked by an aliphatic three carbon chain. Chalcone bears a very good synthon so that variety of novel heterocycles with good pharmaceutical profile can be designed.

Different methods are available for the preparation of chalcones[1-3]. The most convenient method is the Claisen-Schimdt condensation of equimolar quantities of arylmethylketone with aryl aldehyde in the presence of alcoholic alkali[4].

Chalcones are used to synthesize several derivatives like cyanopyridines, pyrazolines isoxazoles and pyrimidines having different heterocyclic ring systems[5,6].

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Chalcones are open chain flavonoids, valuable intermediates in the synthesis of many active pharmaceutical drugs like biosynthesis of flavonoids. Chalcones represent an essential group of natural as well as synthetic products and some of them possess wide range of pharmacological activity such as antibacterial[7], antitumour[8], anticancer[9], antitubercular[10], anti-inflammatory[11], antioxidant[12], antimalarial[13], antileishmanial etc. Chalcones and their derivatives are of high interest materials due to their antioxidant properties[14]. Chalcone form an important group of natural compounds which are easy to synthesize. Chalcones are aromatic ketones and key biosynthetic intermediates for combinatorial assembly of different heterocyclic scaffolds[15]. Chalcones display a wide range of pharmacological properties, including cytotoxity towards cancer cell lines[16]. Chalcone molecules have variety of pharmacological activities, attracted medicinal chemists therefore several strategies have been developed to synthesize[17]. Chalcone is a strong hydroxyl antioxidant, their ability to act as free radical acceptors; the metal complexing properties of these molecules may make some contribution to their total activity.

The presence of reactive α, β- unsaturated keto group in chalcones is found to be responsible for their biological activity. Introduction of metal ion in to chalcone compounds can bring about significant changes in biological effects[18,19].

In the present work chalcones have been prepared according to Claisen-Schmidt condensation by condensing ketone with aromatic aldehydes. These compounds were screened for their antibacterial activity.

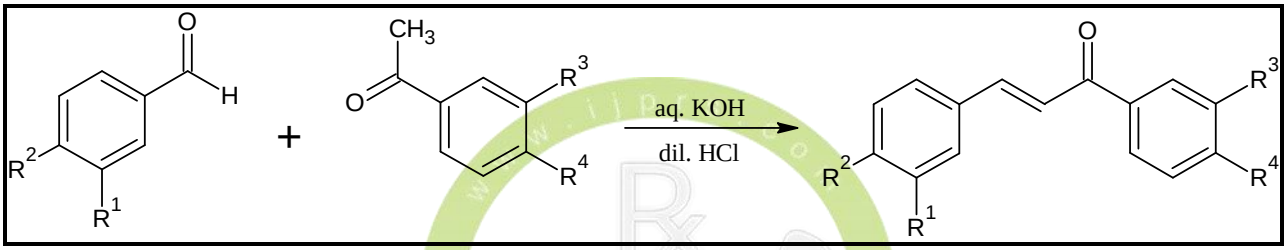
General Procedure

Solution Phase Conventional Method

A mixture of aromatic ketone and aldehyde was stirred in ethanol (30 ml). Then an aqueous solution of KOH (40%, 15 ml) was slowly added to it. The reaction mixture was kept overnight at room temperature and then it was poured in to crushed ice and acidified with dil. HCl.

The solid separated was filtered and recrystallized from ethanol. The chalcones (1a-1f) were obtained by the reaction of aromatic aldehyde with aromatic ketone derivatives in a 1:1 molar ratio in ethanol.

The characterization data of the synthesized compounds have been tabulated in Table 1. The reaction scheme is represented in Figure-1.



(0.01 mole) (0.01 mole)

Figure 1: Reaction scheme

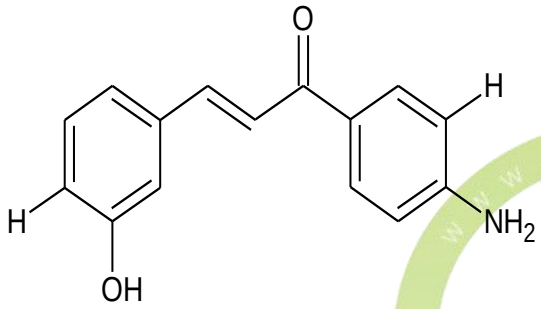
Table 1: Characterization data of the synthesized compounds (1a-1f)

Compound	R^1	R^2	R^3	R^4	Melting point (^oC)	Molecular Formula
1a	-OH	H	H	$-NH_2$	205-208	$C_{15}H_{13}NO_2$
1b	H	-OH	H	$-C_6H_5$	105-108	$C_{21}H_{16}O_2$
1c	H	-OH	H	-OH	165-168	$C_{15}H_{12}O_3$
1d	H	$-N(CH_3)_2$	H	$-NH_2$	179-182	$C_{17}H_{18}N_2O$
1e	-OH	$-OCH_3$	H	$-NO_2$	155-158	$C_{16}H_{13}NO_5$
1f	-OH	H	$-OCH_3$	$-OCH_3$	109-112	$C_{17}H_{16}O_4$

EXPERIMENTAL

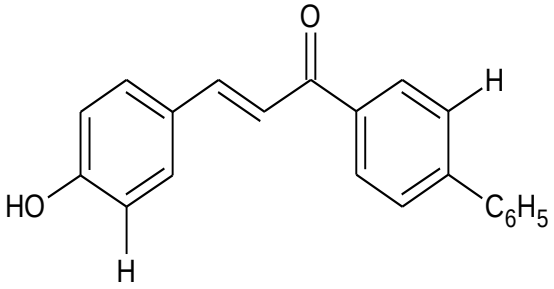
The melting points of all the synthesized compounds were recorded using VEEGO microprocessor based melting point apparatus. The IR spectra were recorded on Perkin Elmer Spectrometer in range 4000-400 cm^{-1} in KBr pellets. PMR spectra were recorded on Brucker Ac 400 F Spectrometer with TMS as internal standard using $CDCl_3$ and DMSO-d_6 as a solvent. The purity of compounds was checked on silica Gel-G Pellets by TLC. All chemicals and solvent used were of AR-grade.

Synthesis of (2E)-1-(4-aminophenyl)-3-(3-hydroxyphenyl) prop-2-en-1-one (1a)



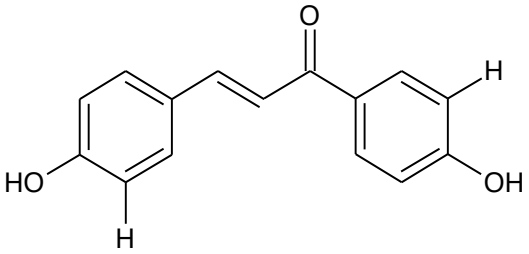
IR (KBr cm^{-1}): 1637-1480 (CH=CH), 1732 (C=O), 3055 (Ar CH), 3345,3365 (-NH_2), 3450 (OH); ^{1}HNMR ($CDCl_3$-d, δ, ppm): 4.6 (1H, s, C-3'-OH), 6.81 (1H, d, -CO-CH=), 7.10-7.24 (1H, d, =CH-Ar), 7.45-8.02 (8H, m, Ar-H).

Synthesis of (2E)-1-(biphenyl-4-yl)-3-(4-hydroxyphenyl) prop-2-en-1-one (1b)



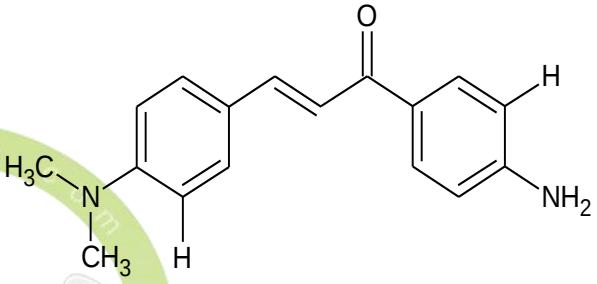
IR (KBr cm^{-1}): 1637-1484 (CH=CH), 1732 (C=O), 3058 (Ar CH), 3452 (OH); ^{1}HNMR ($CDCl_3$-d, δ, ppm): 4.9 (1H, s, C-4'-OH), 6.81 (1H, d, -CO-CH=), 7.05-7.32 (1H, d, =CH-Ar), 7.72-8.30 (14H, m, Ar-H).

Synthesis of (2E)-1, 3-bis (4-hydroxyphenyl) prop-2-en-1-one (1c)



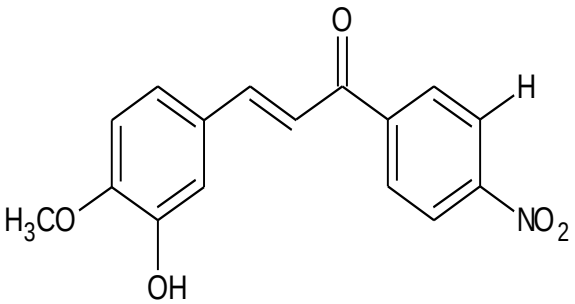
IR (KBr cm^{-1}): 1637-1492 (CH=CH), 1728 (C=O), 3023 (Ar CH), 3454 (OH); ^{1}HNMR ($CDCl_3$-d, δ, ppm): 4.9 (1H, s, C-4'-OH), 6.75 (1H, d, -CO-CH=), 7.34-7.58 (1H, d, =CH-Ar), 7.84-8.30 (8H, m, Ar-H),

Synthesis of (2E)-1-(4-aminophenyl)-3-[4-(dimethylamino) phenyl] prop-2-en-1-one (1d)



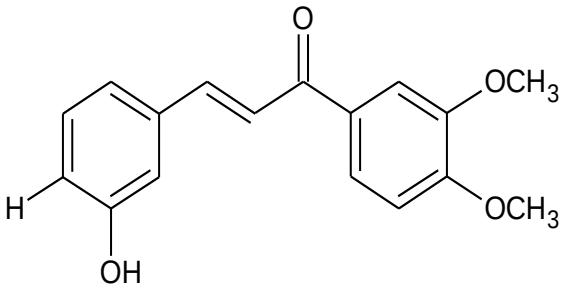
IR (KBr cm^{-1}): 1637-1492 (CH=CH), 1738 (C=O), 3046 (Ar CH), 3484, 3450 (-NH_2); ^{1}HNMR ($CDCl_3$-d, δ, ppm): 4.2 (6H,s,N(CH_3)$_2$), 6.72 (1H, d, -CO-CH=), 7.32-7.48 (1H, d, =CH-Ar), 7.82-8.10 (8H, m, Ar-H).

Synthesis of (2E)-3-(3-hydroxy-4-methoxyphenyl)-1-(4-nitrophenyl) prop-2-en-1-one (1e)



IR (KBr cm^{-1}): 3464 (OH), 3020 (Ar CH), 1725 (C=O), 1637-1464 (CH=CH), 1250-1345,1495-1525 (NO_2); ^{1}HNMR ($CDCl_3$-d, δ, ppm): 3.8 (1H, s, OCH_3), 4.7 (1H, s, -OH), 6.92 (1H, d, -CO-CH=), 7.74-7.81 (1H, d, =CH-Ar), 7.92-8.24 (7H, m, Ar-H).

Synthesis of (2E)-1-(3, 4-dimethoxyphenyl)-3-(3-hydroxyphenyl) prop-2-en-1-one (1f)



IR (KBr cm^{-1}): 1621-1490 (CH=CH), 1722 (C=O), 3022 (Ar CH), 3442 (OH); ^{1}HNMR ($CDCl_3$-d, δ, ppm): 3.6 (1H, s, OCH_3), 4.5 (1H, s, -OH), 6.72 (1H, d, -CO-CH=), 7.54-7.72 (1H, d, =CH-Ar), 7.94-7.10 (7H, m, Ar-H).

Antibacterial Activity

The antibacterial activity of synthesized chalcones was evaluated against following three bacterial strains:

(a) Escherichia coli

(b) Proteus mirabilis

(c) Staphylococcus aureus

Growth Medium Preparation for Bacteria

To culture all the bacteria nutrient agar medium was used. The composition of nutrient agar was:-

Peptone = 10 gm

Yeast extract = 10 gm

Beef extract = 6 gm

Agar = 30 gm

Distilled water = 2000 ml

The above mentioned quantities of Peptone, beef extract and agar were mixed with two litre of double distilled water. The pH of this medium was adjusted at 6.8 with the help of 0.1N hydrochloric acid and 0.1N sodium hydroxide. This medium was then transferred into conical flask, plugged and autoclaved at 121°C for 15 minutes.

Pathogenicity Test

Pathogenicity tests were carried out by cup or agar well assay method. These tests were carried out in 90 ml petriplates, which were throughly sterilized before their use. In each petriplate 30 ml of molten growth medium developed for bacteria was transferred and it was allowed to solidify at room temperature. 0.1 ml of bacterial culture was evenly spread over the whole surface of growth medium in petriplate. Thereafter a well of 10 mm diameter was dug in the growth medium with the help of pre-sterilized cork borer and it was filled with 500 ppm solution of test compound in DMF for antibacterial study. After that zone of inhibition caused by test compounds around the well was measured in mm. Same procedure was repeated for DMF and standard drug (Streptomycin) used. Results obtained in antibacterial studies are given in Table-2.

Table 2: Antibacterial Activity

Comp	Zone of inhibition (in mm)		
	E. coli	***Proteus mirabilis***	***Staphylococcus Aureus***
1a	22	17	19
1b	20	15	17
1c	19	12	13
1d	24	20	20
1e	18	14	12
1f	25	19	22
Streptomycin	27	23	25
DMF	-	-	-

(-) Indicates no activity against bacterial strains.

CONCLUSION

Structures of the synthesized chalcones were confirmed from their respective IR, ^{1}H-NMR spectral studies. From the antibacterial screening it was observed that all the synthesized compounds showed moderate to good activity.

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