Original Research

Evaluation Of Antimicrobial Activity Of Novel Series Of Ortho Hydroxy Chalcones

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Submitted on: 27.12.16; Revised on: 24.01.17; Accepted on: 12.02.17

Abstract

Numbers of Novel Chalcones were synthesized by reacting several substituted aryl aldehydes and ortho hydroxyl acetophenone, prepared by Claisen-Schmidt condensation reaction in NaOH solution in ethanol. The synthesized Chalcones compounds were characterized by Physical and spectral methods IR, ^{1}H-NMR and Mass analysis. All the synthesized compounds have been screened and evaluated for antibacterial activity against *Staphylococcus aureus* gr +ve, *Escherichia coli* gr –ve *Bacillus subtilis* gr +ve, *Salmonella typhi* gr –ve , and antifungal activity against *Aspergillus oryzoe*, *Aspergillus niger*, using disc diffusion method. Most of the compounds showed significant antibacterial and antifungal activities. In this article efforts have been made to throw some light on the synthesis and biological activities of chalcones.

Keywords: Ortho hdroxy Chalcones, Synthesis, Antimcrobial Activity.

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Indian Research Journal of Pharmacy and Science; 11(2016) 868-874
Journal Home Page: https://www.irjps.in

INTRODUCION

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. Novel chalcones were synthesized because it is known to exhibit various biological activities. Chalcones basic structure includes two aromatic ring bound by an α, β-unsaturated carbonyl group, a unique template associated with very diverse application[1]. Chalcones (trans-1, 3-diaryl-2propen-1-ones) are α, β-unsaturated ketones consisting of two aromatic rings (ring A and B) having diverse array of substituents. Rings are interconnected by a highly electrophonic three carbon α, β-unsaturated carbonyl system that assumes linear or nearly planar structure [2-4]. They contain the ketoethylenic group (–CO– CH=CH-). Chalcones possess conjugated double bonds and a completely delocalized π-electron system on both benzene rings. Chalcones have been used as intermediate for the preparations of compounds having therapeutic value [5-7]. Due to the presence of enone functionality in chalcone moiety confers biological activity upon it, like anti-inflammatory [8], antifungal [9], antioxidant [10], antimalarial [11], antituberculosis [12],analgesic [13], anti HIV [14]and antitumor [15] activities. Different methods are available for the preparation of chalcones[16-18].The most convenient method is the Claisen-Schimdt condensation of equimolar quantities of arylmethylketone with aryl aldehyde in the presence of alcoholic alkali[19].

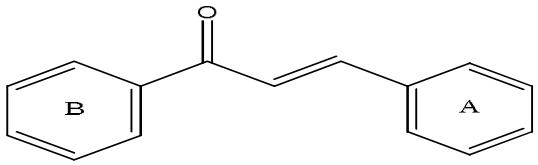
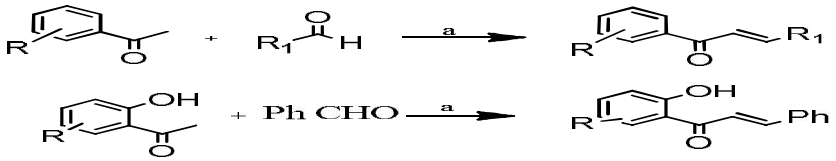


Figure-1: Chalcone

MATERIALS AND METHODS:

Claisen-Schmidt condensation

The most convenient method is the Claisen Schimdt condensation of equimolar quantities of aryl ketone with aryl aldehyde in the presence of alcoholic alkali[19].



Reagents: (a) aq. KOH, alcohol

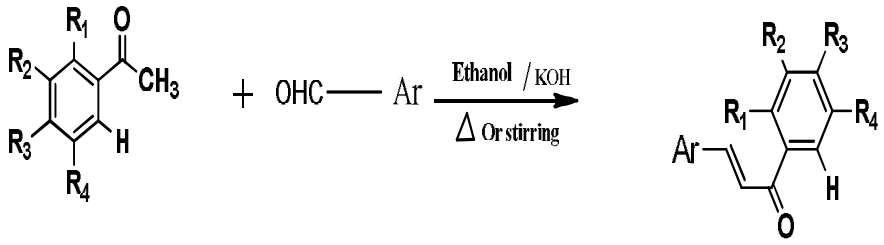
Experimental

Melting points of the compounds were determined in open capillary tubes and are uncorrected, IR Spectra were recorded on Shimadzu FT-IR Spectrometer using potassium bromide pellets, ^{1}H NMR was determined on a Bruker Avance II 400 Spectrometer against TMS as internal standard. Mass spectra were recorded on waters Micromass Q-T of Micro spectrometry.

General method for the synthesis of chalcones

A mixture of Ortho hdroxy acetophenone (1 mmol), substituted aryl aldehyde (1 mmol) and KOH (2 mmol, in minium H_2O) were taken in ethanol and stirred for one hour in cool condition. The completion of reaction was monitored by TLC. The products were isolated by acidification of the cool diluted acid solution and obtained solid product was filtered and washed with water and recrystallize by ethanol to get pure product.

Scheme-1



1 2 Chalcone (3a-j)

R_1 = OH, R_2 = I, R_3 = H, R_4 = Br

RESULT AND DISCUSSION:

The newly chalcones were carried out according to the Claisen-Schmidt condensation of ortho hydroxyl ketones with several aromatic aldehyde as indicated to Scheme1. The corresponding reactions proceeded smoothly and in good to excellent yields (65-90 %). The newly synthesized chalcones were characterized by their chemical, physical and spectral analysis data and are further subjected to antimicrobial studies which exhibit moderate to good activity.

Table1. Physical data of synthesized Chalcones

Comp.no	Product	Mol. Formula	Yield %	M.P.(°C)
1	4a	$C_{15}H_9IO_2ClBr$	90	178
2	4b	$C_{15}H_{10}O_3IBr$	80	158
3	4c	$C_{15}H_9O_2IBr_2$	70	198
4	4d	$C_{15}H_9O_4INBr$	75	210
5	4e	$C_{15}H_9O_5INBr$	75	185
6	4f	$C_{14}H_{10}BrISO_2$	80	122
7	4g	$C_{13}H_9O_2INBr$	80	120
8	4h	$C_{17}H_{11}O_2IBrN$	70	130
9	4i	$C_{15}H_9IO_2ClBr$	70	112
10	4j	$C_{15}H_9O_2IBr_2$	65	128

Scheme-1. Synthesis of Chalcones

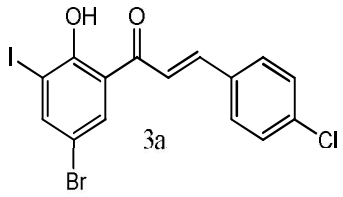


Figure-2 *E*)-1-(5-bromo-2-hydroxy-3-iodophenyl)-3-(4-chlorophenyl)prop-2-en-1-one

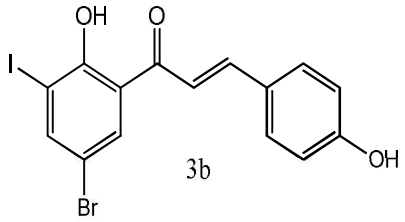


Figure-3 (*E*)-1-(5-bromo-2-hydroxy-3-iodophenyl)-3-(4-hydroxyphenyl)prop-2-en-1-one

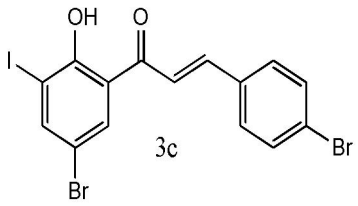


Figure-4 (*E*)-3-(4-bromophenyl)-1-(5-bromo-2-hydroxy-3-iodophenyl)prop-2-en-1-one

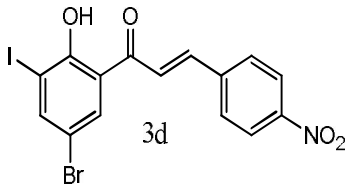


Figure-5 (*E*)-1-(5-bromo-2-hydroxy-3-iodophenyl)-3-(4-nitrophenyl)prop-2-en-1-one

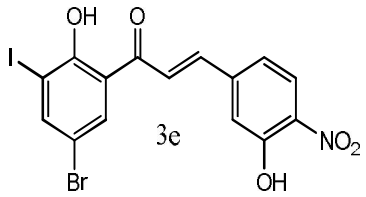


Figure-6 (*E*)-1-(5-bromo-2-hydroxy-3-iodophenyl)-3-(3-hydroxy-4-nitrophenyl)prop-2-en-1-one

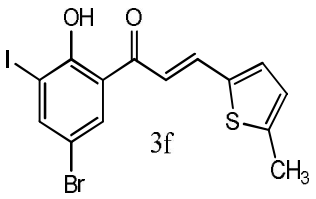


Figure-7 (*E*)-1-(5-bromo-2-hydroxy-3-iodophenyl)-3-(5-methylthiophen-2-yl)prop-2-en-1-one

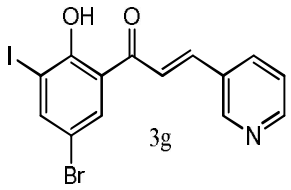


Figure-8 (*E*)-1-(5-bromo-2-hydroxy-3-iodophenyl)-3-(pyridin-3-yl) prop-2-en-1-one

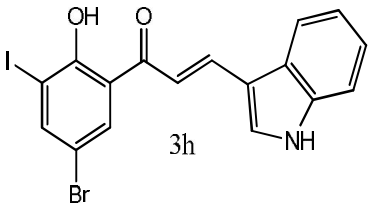


Figure-9 (*E*)-1-(5-bromo-2-hydroxy-3-iodophenyl)-3-(1*H*-indol-3-yl)prop-2-en-1-one

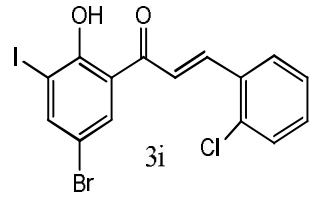


Figure-10 (*E*)-1-(5-bromo-2-hydroxy-3-iodophenyl)-3-(2-chlorophenyl)prop-2-en-1-one

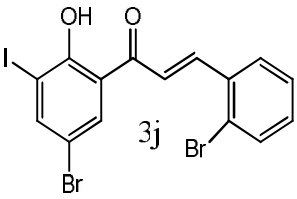
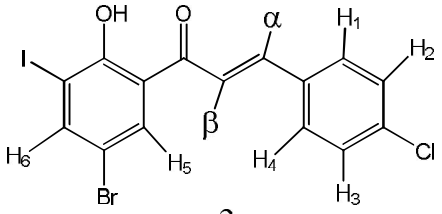


Figure-11 (*E*)-1-(5-bromo-2-hydroxy-3-iodophenyl)-3-(2-bromophenyl)prop-2-en-1-one

Spectral analysis of the compounds:

The structures of some the compounds were established from IR, ^{1}HNMR and mass analysis.



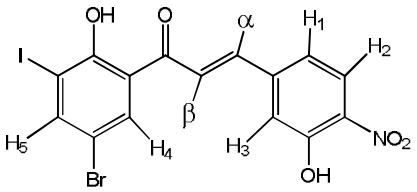
3a

Compound 3a :-

FTIR (KBr, cm^{-1}): 1634(C=O) ,1562(C=C) , 1428(C-C Aromatic str) ,815(C-Cl).

M.S. (m/z): 462(M-1), 464(M+1).

^{1}HNMR:- 6.95(d,1H ,H_1), 7.45(s, 1H, H_2), 7.63(d, 1H,H_4), 7.66(d,1H , H_3), 7.79(d, 1H, Hα,J=15Hz), 7.92(d, 1H, H_5), 8.12(s, 1H, H_6) 8.14(d, 1H, H β,J=15Hz), 12.35(s, 1H, OH ortho).



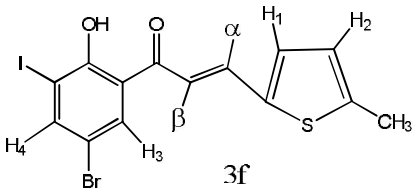
3d

Compound 3d :-

FTIR (KBr, cm^{-1}): 1614(C=O) ,1573(C=C) , 1429(C-C Aromatic str) ,1307(NO_2), 668(C-Br).

M.S. (m/z): 490(M^+), 489(M-1).

^{1}HNMR:- 6.96(d,1H ,H_1), 7.61(s,1H , H_3)7.63(s, 1H, H_2), 7.71(d, 1H, Hα,J=15Hz), 8.02(d, 1H, H β,J=15Hz)8.16(s, 1H,H_4), 8.31(s, 1H, H_5), 8.59(s, 1H, OH), 12.26(s, 1H, OH ortho).



3f

Compound 3f :-

FTIR (KBr, cm^{-1}): 1628(C=O) ,1557(C=C) , 1425(C-C Aromatic str) , 671(C-Br).

M.S. (m/z): 448(M-1).

^{1}HNMR:- 2.45(s, 3H, CH_3), 7.46(d, 1H, Hα,J=15Hz), 7.48(d, 1H, H_2), 7.56(d,1H ,H_1), 7.87(d, 1H, H β,J=15Hz), 8.20 (s,1H , H_3) , 8.38(s, 1H,H_4), 13.77(s, 1H, OH ortho).

Antimicrobial activity:

Antimicrobial screening was done using disc diffusion method [20] at a concentration of 100µg/ml.

Procedure:- The test was performed according to the disk diffusion method [20] adopted with some modification for the prepared compound using Penciline and streptomycin as references. The prepared compounds were tested against one strain of Gram +ve bacteria, Gram –ve bactria, fungi. Whatman filter paper disk of 5mm diameter were sterilized by autoclaving for 15 min at 121^{0}C. The sterile disk were impregnated with different compounds (600gm/disk). Agar plates were surface inoculated uniformly from the both culture of the tested microorganism. The disk were placed on the medium suitably spaced apart on the plate were incubated at 50^{0}C for 1 hr to permit good diffusion and then transferred to an incubator at 37^{0}C. for 24hr for bacteria and 28^{0}C for 72hrs for fungi.

The compounds were evaluated for antibacterial activity against *Staphylococcus aureus* gr +ve, *Escherichia coli* gr –ve *Bacillus subtilis* gr +ve, *Salmonela typhi* gr –ve , and antifungal activity against Aspergillus oryzoe, Aspergillus niger,. DMSO was used as solvent control . The results of antimicrobial data are summarized in **table 2**. The compounds show the moderate to good activity against bacteria and fungui.

Table-2 Antimicrobial activity of synthesized Chalcones (3a-j).

compounds	Gram positive bacterias		Gram negative bacterias		Fungus	
	Staph aureus	**Bacillus subtilis**	**Escherichia coli**	**Pseudomonas aeruginosa**	**Aspergillus oryzoe**	Aspergillus niger,
3a	+	+	-	-	-	-
3b	+	+	+	+	++	+
3c	+	+	-	-	-	-
3d	+	+	-	-	-	-
3e	+	+	-	-	-	-
3f	+	+	-	-	-	-
3g	+	++	-	+	+	+
3h	+	++	+	-	+	-
3i	+	+	-	+	+	+
3j	+	+	-	-	+	-
Penciline 1	+	+	+	+	x	x
Streptomycin 2	++	++	++	++	x	x
Greseofulvin	x	x	x	x	-	-

++ = Clear Zone of Inhibition , + = Minimum Zone of Inhibition, - = No Effect, X = Not applicable

Standerd [1] Penciline +

Standerd [2] Streptomycin ++

CONCLUSION:

Successfully, in this work we have synthesized some novel chalcones using ortho hydroxy acetophenone with several aromatic aldehydes with high yield. The newly synthesized chalcones were confirmed by spectral analysis and further evaluated for their antimicrobial activity. The screening results revealed that the compounds 3a-j showed significant antimicrobial activity.

ACKNOWLEDGEMENT:

The authors are thankful to Head of department of Chemistry, Head of department of Microbilogy, Principal of Yeshwant College, Nanded for providing lab facilities for the research work.

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CONFLICT OF INTEREST REPORTED: NIL; SOURCE OF FUNDING: NONE REPORTED