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Synthesis, Characterization and Antimicrobial Screening of Novel Ortho Hydroxy Chalcones

Abdulkareem Ali Hussien[1,2*], Bushra Ahmed Kateb[1,2], Shekh Saddam Husen[3] and P. A. Kulkarni[1]

[1]Department of Chemistry, Yeshwant Mahavidyalaya, Nanded-431602 (MS), India
[2]Hodiedah University, Education College, Yemen
[3]Swami Ramanand Teerth University, Nanded, India
**Corresponding author*

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A B S T R A C T

New series of chalcones(1a-j) were synthesized by Claisen-Schmidt condensation of 2-hydroxy, 5-methyl acetophenone with several aromatic aldehydes in presence of aqueous solution of sodium hydroxide.The synthesized chalcones compounds were characterized by Physical and spectral methods such as melting point, 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*. DMSO was used as solvent control for their antimicrobial activity using disc diffusion method. Synthesis and biological evaluation of chalcones have been a topic of special interest to organic and medicinal chemists. The new structural classes of compounds may prove as lead molecules and good candidates for the future investigations.

Introduction

The chalcones (1, 3-diaryl-2-propenones) and their derivatives are important intermediates in organic synthesis (Straub, 1995; Sandler and Karo, 1972; Bergman Bergman *et al.*, 1959). They serve as starting material for the synthesis of variety of heterocyclic compounds which are of physiological importance. Due to the presence of enone functionality in chalcone moiety confers biological activity upon it, like anti inflammatory anti-bacterial (Chikhalia *et al.*, 2008), anti- cancer (Kotra *et al.*, 2010), cytotoxic activity (Go *et al.*, 2005), anti-hyperglycemic (Satyanarayana *et al.*, 2004), (Ballesteros *et al.*, 1995), antifungal, (Go *et al.*, 2005), antioxidant (Mukerjee Mukerjee *et al.*, 2001), antimalarial (Liu *et al.*, 2003), antituberculosis (Sivakumar *et al.*, 2007), analgesic (Sivakumar *et al.*, 2003), anti HIV

(Tiwari *et al.*, 2000) and antitumor (Ducki *et al.*, 1998) activities.

Herein, we report the synthesis of some novel chalcone analogues using a conventional base catalyzed, Claisen Schmidt condensation reaction and their possible antibacterial activity.

Materials and Methods

Claisen-Schmidt Condensation

The most convenient method is the Claisen Schimdt condensation of equimolar quantities of aryl methyl ketone with aryl aldehyde in the presence of alcoholic alkali(Taylor *et al.*, 1967).

The synthesis of chalcone compounds incorporating with hetero cycles became great importance in medicinal chemistry(Padhy *et al.*, 2003; Nakum and Shah, 2002).The hetero atoms in ther structure such as (S, N, O) explain variety applications in the biological engineering and in other field of their specific structures(Nagham, 2013).

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.

Method for the Synthesis of Novel Chalcones

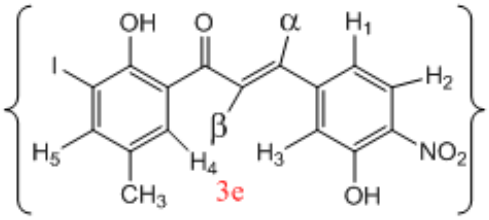
A mixture of substituted acetophenone (1 mmol), substituted aldehyde (1 mmol) and KOH (2 mmol, in minium H2O) were taken in ethanol and stirred at 50-60°C temperature for one hour. The completion of reaction was monitored by TLC. The products were isolated by acidification of the cool diluted acid solution and obtained solid product was filtered and washed with water and recrystallize by ethanol to get pure product.

Results and Discussion

The synthesis of the newly chalcones were accomplished according to the Claisen-Schmidt condensation of ortho hydroxy ketones with several aromatic aldehyde under microwave irradiation, as indicated to Scheme1. The corresponding reactions proceeded smoothly and in good to excellent yields (70-95 %). 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.

Spectral Analysis of the Compounds

The newly compounds were done by spectral analysis (IR,^{1}H NMR,MASS) and the results are shown below :

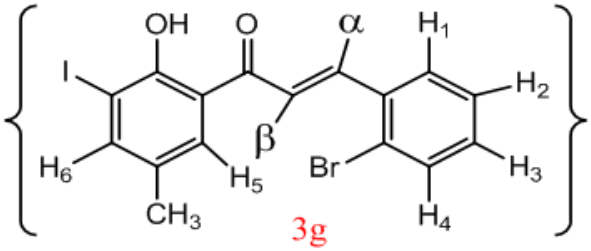


3e- (E)-1-(2-hydroxy-3-iodo-5-methyl phenyl)-3-(3-hydroxy-4-nitrophenyl)prop -2-en-1-one

Compound 3e:- FTIR (KBr, cm^{-1}): 1617(C=O),1581(C=C), 1439(C-C Aromatic str),1313(N-O sym.stretch).

^{1}HNMR:- 2.33(s, 3H, CH_3),7.21(d,1H,H_1), 7.58(s, 1H, H_3), 7.77(d, 1H,H_4), 7.62(s,1H,OH), 7.81(d, 1H, Hα,J=15Hz), 7.97(d, 1H, H_2), 8.12 (d, 1H, H β,J=15Hz), 8.21(s, 1H, H_5), 13.40(s, 1H, OH ortho)

M.S. (m/z): (M)= 424(M-1).



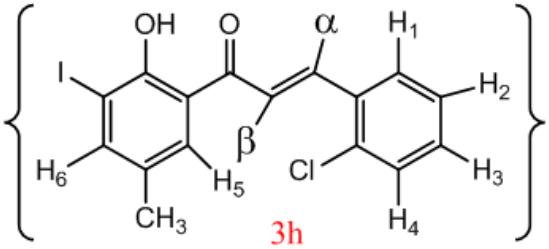
3g

3g- (E)-3-(2-bromophenyl)-1-(2-hydroxy-3-iodo-5-methylphenyl)prop-2-en-1-one

Compound 3g:- FTIR (KBr, cm^{-1}): 1631(C=O),1565(C=C), 1435(C-C Aromatic str),660(C-Br).

^{1}HNMR:- 2.30(s, 3H, CH_3),7.37(dd,1H,H_2), 7.46(d, 1H, Hα,J=15Hz),7.62 (d, 1H, H_1), 7.67(dd, 1H, H_3),, 7.87(d, 1H,H_4), 8.06(d, 1H, H_5), 8.14 (d, 1H, H β,J=15Hz), 8.17(d, 1H, H_6), 13.40(s, 1H, OH).

M.S. (m/z): (M)= 443(M+), 442(M-1), 444(M+1).



3h

3h- (E)-3-(2-chlorophenyl)-1-(2-hydroxy-3-iodo-5-methylphenyl)prop-2-en-1-one

Compound 3h:- FTIR (KBr, cm^{-1}): 1631(C=O),1564(C=C), 1435(C-C Aromatic str),729(C-Cl).

^{1}HNMR:- 2.31(s, 3H, CH_3),7.37(dd,1H,H_2), 7.45(d, 1H, Hα,J=15Hz),7.53(d, 1H, H_1), 7.65(dd, 1H, H_3),, 7.88(d, 1H,H_4), 8.09 (d, 1H, H β,J=15Hz), 8.19(d, 1H, H_5), 8.23(d, 1H, H_6), 13.38(s, 1H, OH).

M.S. (m/z): (M)= 397(M-1), 399 (M+1).

Antimicrobial Activity

Antimicrobial screening was done using disc diffusion method (Afaf *et al.*, 2000) at a concentration of 100µg/ml.

Procedure:- The test was performed according to the disk diffusion method 26 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 1210 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 500C for 1 hr to permit good diffusion and then transferred to an incubator at 370C. for 24hr for bacteria and 280C 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 3. The compounds show the moderate to good activity against bacteria and fungui.

Table.1 Physical Data of Synthesized Chalcones

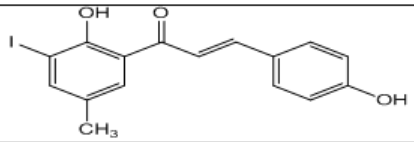
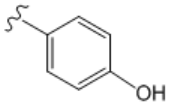
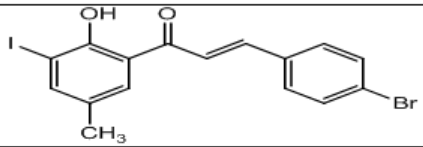
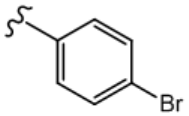
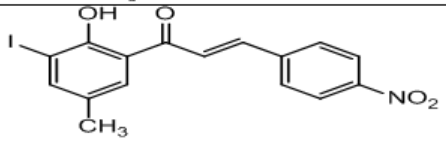
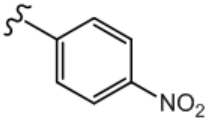
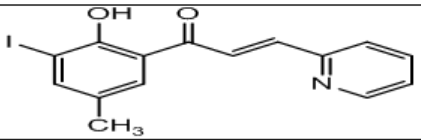
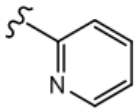
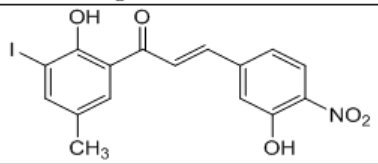
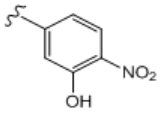
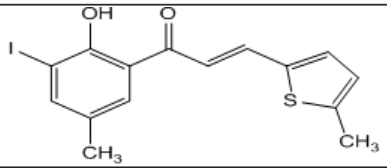
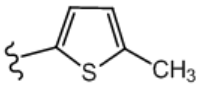
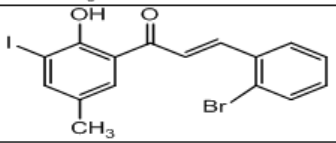
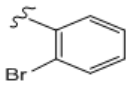
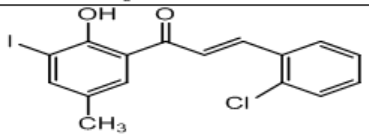
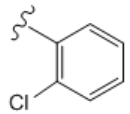
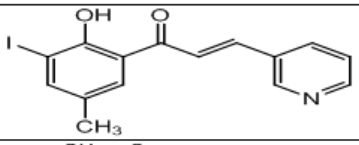
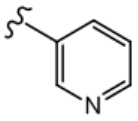
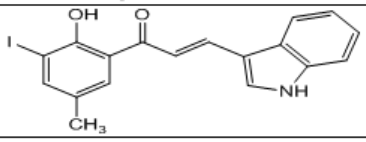
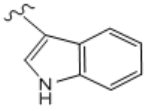
Comp.no	Product	Mol. Formula	Yield %	M.P.(°C)	Solubility
3a	3a	$C_{16}H_{13}O_3I$	85	104-106	DMF
3b	3b	$C_{16}H_{12}O_2IBr$	75	154-156	DMF
3c	3c	$C_{16}H_{13}O_4NI$	70	186-190	DMF
3d	3d	$C_{15}H_{12}O_2IN$	75	86-90	DMF
3e	3e	$C_{16}H_{12}O_5N$ I	80	194-196	DMF
3f	3f	$C_{15}H_{13}O_2IS$	85	106-108	DMF
3g	3g	$C_{16}H_{12}$ O_2BrI	90	130	DMF
3h	3h	$C_{16}H_{12}$ O_2ClI	80	118-120	DMF
3i	3i	$C_{15}H_{12}$ O_2NI	75	94-98	DMF
3j	3j	$C_{18}H_{14}$ O_2NI	95	110-112	DMF

Table.2 Antimicrobial Activity of Synthesized Compounds

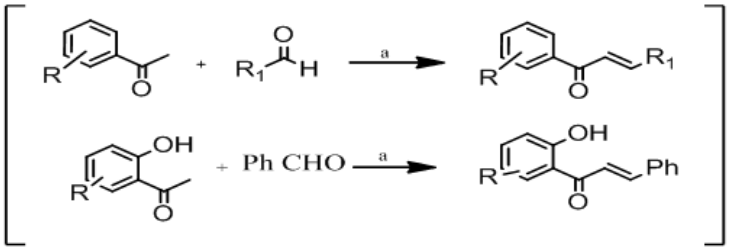
compounds	Gram positive bacterias		Gram negative bacterias		Fungus	
	Staph aureus	*Bacillus subtilis*	*Escherichia coli*	*S. typhi*	*Aspergillus oryzoe*	*Aspergillus niger*
3a	-	-	+	-	-	-
3b	+	-	-	-	-	-
3c	++	+	-	-	+	++
3d	+	-			-	++
3e	+	+	-	-	-	+
3f	-	-			-	+
3g	+	-	-	-	-	-
3h	+	-	-	-	-	-
3i	++	+	-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

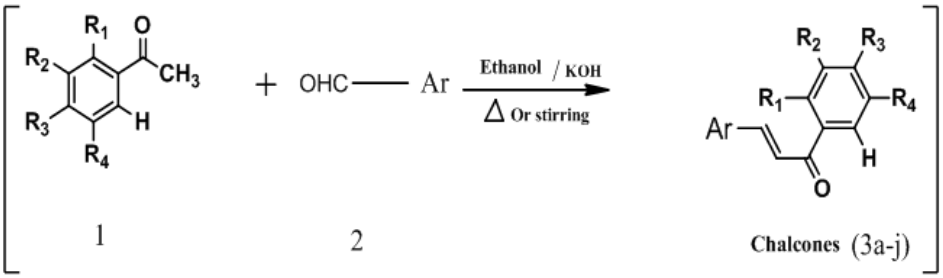
++ = Clear Zone of Inhibition
+ = Minimum Zone of Inhibition
- = No Effect
X = Not applicable
Standerd 1 Penciline +, Standerd 2 Streptomycin ++ (bacteria). Greseofulvin (fungus)

Scheme.1 Synthesis of Chalcones

Comp.no	Chalcones	Ar
3a		
3b		
3c		
3d		
3e		
3f		
3g		
3h		
3i		
3j		

Reagents.(a) aq. KOH, Alcohol





1 2

R_1 = OH, R_2 = I, R_3= H, R_4 = CH_3

In conclusion, here we have reported some novel chalcones using ortho hydroxyl 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 antibacterial activity revealed that of the compounds showed moderate to good activity against the pathogens used.

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