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RESEARCH ARTICLE

Synthesis, Characterization and Antimicrobial Activity of Novel Chalcones Analogues

BUSHRA AHMED KATEB[1,2], ABDULKAREEM ALI HUSSIEN[1,2], P. A. KULKARNI[1], M. A. BASEER[1]

[1]P. G. Research Center, Department of Chemistry, Yeshwant Mahavidyalaya, Nanded-431602 (MS), India

[2]Hodiedah University, Education College, Yemen

nice1422@gmail.com

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Abstract: A new series of chalcones (**3a-j**) have been prepared by Claisen-Schmidt condensation between substituted acetophenone and substituted aldehyde. All these 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 for their antimicrobial activity.

Keywords: Chalcones, Spectral analysis, Anti microbial Activity

Introduction

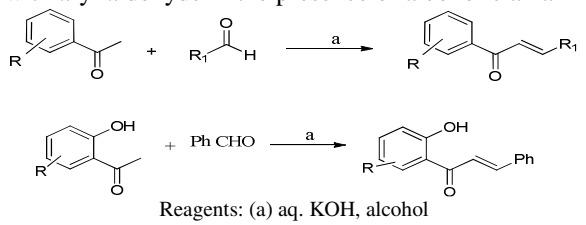
Chalcones are a major class of natural products belonging to the flavonoid family. They are considered as the precursors of flavonoids and isoflavonoids. They are also the precursors of a number of biologically important heterocycles such as benzothiazepines, pyrazolines and flavones[1].

Chalcones (trans-1, 3-diaryl-2propen-1-ones) are *α, β*-unsaturated ketones consisting of two aromatic rings 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 electron ketoethylenic group (–CO– CH=CH-). Chalcones possess conjugated double bonds and a completely delocalized π- system on both benzene rings. Chalcones have been used as intermediate for the preparation of compounds having therapeutic value[5-7]. Chalcones and their derivatives, whether synthetic or naturally occurring are an interesting and significant group of molecules as they possess a wide range of pharmacological activities such as anti-inflammatory, antimicrobial, antifungal, antibacterial, antioxidant, cytotoxic antitumor, anticancer, antimitotic, antileishmanial, anti-malarial, antitubercular, antiviral and so on[8-21].

Claisen-Schmidt condensation

Synthetic method of preparing chalcones

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[22].



Reagents: (a) aq. KOH, alcohol

Scheme 1

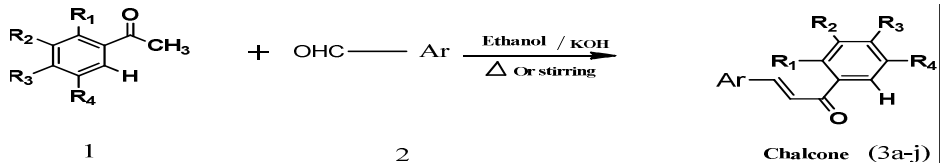
The synthesis of chalcone compounds incorporating with hetero cycles became great importance in medicinal chemistry[23-24]. The hetero atoms in ther structure such as (S, N, O) explain variety applications in the biological engineering and in other field of their specific structures[25].

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 substituted acetophenone (1 mmol), substituted aldehyde (1 mmol) and KOH (2 mmol, in minium H_2O) 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.

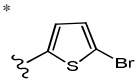


Scheme 1. Synthesis of chalcones

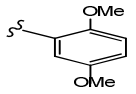
Table 1. Substituted Acetophenones

Comp. No	Product	R_1	R_2	R_3	R_4	Ar*
1	**3a**	H	I	OH	I	Ar_1
2	**3b**	OH	I	H	I	Ar_1
3	**3c**	OH	I	H	Cl	Ar_1
4	**3d**	OH	I	H	CH_3	Ar_1
5	**3e**	H	I	OH	I	Ar_2
6	**3f**	OH	I	H	I	Ar_2
7	**3g**	OH	I	H	Cl	Ar_2
8	**3h**	OH	I	H	CH_3	Ar_2
9	**3i**	H	I	OH	I	Ar_3
10	**3j**	OH	Br	H	Cl	Ar_4

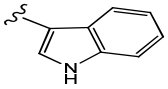
Where *



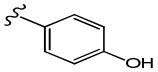
Ar_1



Ar_2



Ar_3



Ar_4

Results and Discussion

A variety of novel chalcones were synthesized via Claisen-Schmidt condensation of substituted acetophenones and aromatic benzaldehyde (Table 1). The reaction proceeded at room temperature. Work up procedure is simple and yield of the product is excellent.

All the newly synthesized chalcones were characterized by their chemical, physical and spectral analysis data (Table 2) and are further subjected to antimicrobial studies which exhibit moderate to good activity.

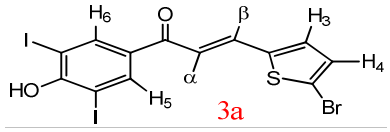
Table 2. Physical data of synthesized chalcones

Compd. No.	Product	Mol. Formula	Yield %	M.P., °C	Solubility
1	**3a**	$C_{13}H_7O_2I_2BrS$	90	176-178	DMF
2	**3b**	$C_{13}H_7O_2I_2BrS$	92	162	DMF
3	**3c**	$C_{13}H_7O_2ClIBrS$	80	178	DMF
4	**3d**	$C_{14}H_{10}O_2IbrS$	92	142	DMF
5	**3e**	$C_{17}H_{14}I_2O_4$	86	162-164	DMF
6	**3f**	$C_{17}H_{14}I_2O_4$	88	174-176	DMF
7	**3g**	$C_{17}H_{14}ClIO_4$	80	178	DMF
8	**3h**	$C_{18}H_{17}IO_4$	90	159	DMF
9	**3i**	$C_{17}H_{11}NI_2O_2$	88	150	DMF
10	**3j**	$C_{15}H_{10}BrClO_3$	85	108-110	DMF

Spectral analysis of the compounds

The structure of the compounds were done by spectral analysis (IR, ^{1}H NMR, Mass) and the results are shown below

*Compound **3a***



3a

(*E*)-3-(5-Bromothiophen-2-yl)-1-(4-hydroxy-3,5-diiodophenyl)prop-2-en-1-one

FTIR (KBr, cm^{-1}): 3224(OH), 1646(C=O), 1576(C=C), 1465(C-C Aromatic str), 683(C-Br). ^{1}H NMR: 7.24(d, 1H,H_3), 7.48(d,1H,H_4), 7.49(d, 1H, Hα, J=15Hz), 7.58(d, 1H, H β,J=15Hz) , 7.48(s1H,H_5), 7.53(s,1H ,H_6), 8.43(s, 1H, OH).
M.S. (*m/z*): (M)= 560(m), 561(m+1) ,558(m-2).

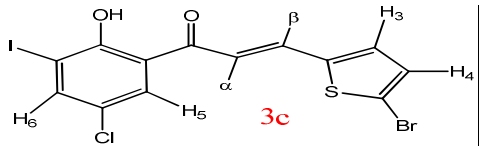
*Compound **3b***

3b

(*E*)-3-(5-Bromothiophen-2-yl)-1-(2-hydroxy-3,5-diiodophenyl)prop-2-en-1-one

FTIR (KBr, cm^{-1}): 3425(OH), 1623(C=O), 1546(C=C), 1419(C-C Aromatic str), 621(C-Br). ^{1}H NMR: 7.33(d, 1H,H_3), 7.48(d,1H,H_4), 7.73(d, 1H, Hα, J=15Hz), 7.97(d, 1H, H β, J=15Hz),8.27(s, 1H,H_5),8.55(s,1H ,H_6), 13.7(s, 1H, OH). M.S. (*m/z*): (M) = 558(m-2).

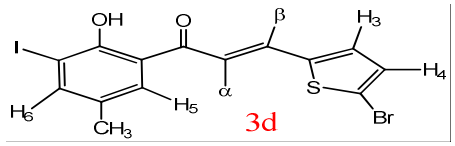
Compound ***3c***



(*E*)-3-(5-Bromothiophen-2-yl)-1-(5-hydroxy-3-iodophenyl)prop-2-en-1-one

FTIR (KBr, cm^{-1}): 3436(OH), 1635(C=O), 1526(C=C), 1419(C-C Aromatic str), 621(C-Br). 802(C-Cl), 675(C-Br). ^{1}H NMR: 7.12(d, 1H,H_3), 7.21(d,1H,H_4), 7.27(d, 1H, Hα, J=15Hz), 7.97(d, 1H, H β,J=15Hz), 8.23(s, 1H,H_5), 8.47(s,1H ,H_6), 13.46(s, 1H ,OH). M.S. (*m/z*): 468(m).

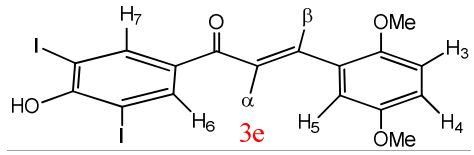
Compound ***3d***



(*E*)-3-(5-Bromothiophen-2-yl)-1-(2-hydroxy-3-iodo-5-methylphenyl)prop-2-en-1-one

FTIR (KBr, cm^{-1}): 3425(OH), 1639(C=O), 1569(C=C), 1415(C-C Aromatic str), 675(C-Br).802(C-Cl), 675(C-Br). ^{1}H NMR: 2.32(s,3H,CH3), 7.27(d, 1H,H_3), 7.52(d,1H,H_4), 7.65(d, 1H, Hα,J=15Hz), 7.95(d, 1H, H β,J=15Hz),7.85(s, 1H,H_5), 8.04(s,1H ,H_6), 13.46(s,1H, OH). M.S. (*m/z*): 450(m+1) ,448(m-1) ,447(m-2).

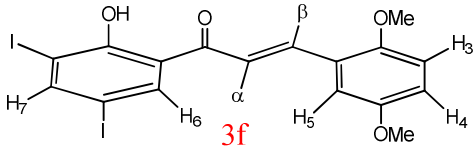
Compound ***3e***



(*E*)-3-(2,5-Dimethoxyphenyl)-1-(4-hydroxy-3,5-diiiodophenyl)prop-2-en-1-one

FTIR (KBr, cm^{-1}): 3382(OH), 1658(C=O), 1589(C=C), 1492(C-C Aromatic str). ^{1}HNMR: 3.81(s,3H,OMe), 3.85(s,3H,OMe), 7.00(S,1H_5)7.01(d,1H_3)7.57(d,1H_4), 7.78(d, 1H, Hα, J=15Hz), 8.00(d, 1H, H β,J=15Hz), 8.45-8.50(s,2H,H_6,H_7), 10.28(s, 1H, OH). M.S. (*m/z*): 536(m), 535(m-1) ,534(m-2).

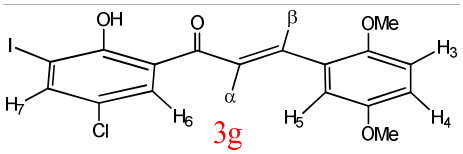
Compound ***3f***



(*E*)-3-(2,5-Dimethoxyphenyl)-1-(2-hydroxy-3,5-diiiodophenyl)prop-2-en-1-one

FTIR (KBr, cm^{-1}): 3433(OH), 1635(C=O), 1558(C=C), 1431(C-C Aromatic str). ^{1}HNMR**:** 3.82(s,3H,OMe), 3.86(s,3H,Ome), 7.02(S,1H_5)7.07(d,1H_3)7.46(d,1H_4),8.00(d, 1H, Hα, J=15Hz), 8.22(d, 1H, H β,J=15Hz), 8.23(s,1H,H_6), 8.57(s,1H_7), 13.84(s,1H, OH). M.S. (*m/z*): 535(m-1), 534(m-2).

*Compound **3g***

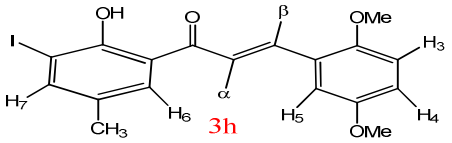


3g

(*E*)-1-(5-chloro-5hydroxy-3-iodophenyl)-3-(2,5-dimethoxyphenyl)prop-2-en-1-one

FTIR (KBr, cm^{-1}): 3425(OH), 1667(C=O), 1550(C=C), 1496(C-C Aromatic str). 785(C-Cl). ^{1}HNMR: 3.80(s,3H,Ome), 3.85(s,3H,Ome), 7.03(S,1H_5)7.22(d,1H_3)7.50(d,1H_4),8.04(d, 1H, Hα, J=15Hz), 8.12(d, 1H, H β,J=15Hz), 8.16(s,1H,H_6), 8.26(s,1H_7), 13.51(s,1H, OH). M.S. (*m/z*): 443(m-1) ,445(m+1).

*Compound **3h***

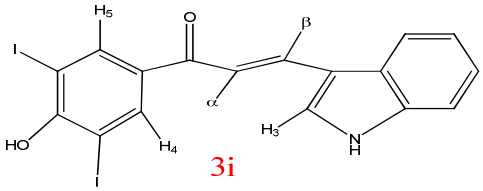


3h

(*E*)-3-(2,5-dimethoxyphenyl)-1-(2-hydroxy-3-iodo-5-methylphenyl)prop-2-en-1-one

FTIR (KBr, cm^{-1}): 3440(OH), 1631(C=O), 1562(C=C), 1430(C-C Aromatic str). ^{1}H NMR: 3.80(s,3H,Ome),3.85(s,3H,Ome), 7.03(S,1H_5)7.22(d,1H_3)7.50(d,1H_4),8.04(d, 1H, Hα, J=15Hz), 8.12(d, 1H, H β,J=15Hz), 8.16(s,1H,H_6), 8.26(s,1H_7), 13.51(s,1H, OH). M.S. (*m/z*): 423 (m-1).

*Compound **3i***

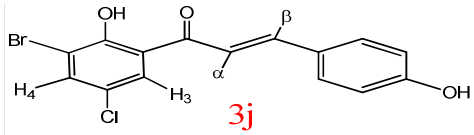


3i

(*E*)-1-(4- Hydroxy-3,5-diiodophenyl)-3-(1*H*-indol-3-yl)prop-2-en-1-one

FTIR (KBr, cm^{-1}): 1663(C=O), 1570(C=C), 1461(C-C Aromatic str). ^{1}H NMR: 7.18((d, 1H, Hα,J=15Hz), 7.26(d, 1H, H β,J=15Hz), 8.05(s,1H,H_3), 8.12(s,1H,H_4),8.14(S,1H,H_5), 8-8.45(m,4H,Ar-H) ,9. 95(s,1H, OH), 11.99(s,1H,NH) .M.S. (*m/z*): 423 (m-1).

*Compound **3j***



3j

(*E*)-1-(3-Bromo-5-chloro-2- hydroxyphenyl)-3-(4- hydroxyphenyl)prop-2-en-1-one

FTIR (KBr, cm^{-1}): 1641(C=O), 1563(C=C), 1422(C-C Aromatic str). ^1H NMR: 7.40((d, 1H, Hα,J=15Hz), 8.51(d, 1H, H β,J=15Hz), 7.44-7.77(m,4H,Ar-H), 9.95(s,1H, OH), 7.61(s,1H,H_3,Ar),7.72(s,1H,H_4), 11.99(s,1H,NH), 8.24(s,1H,OH). M.S. (*m/z*): 353 (M), 355(m+2), 351(m-2).

Antimicrobial activity

Antimicrobial screening was done using disc diffusion method[26] at a concentration of 500 µg/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 5 mm diameter were sterilized by autoclaving for 15 min at 121 ^oC. The sterile disk were impregnated with different compounds (600 g/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 ^oC for 1 h to permit good diffusion and then transferred to an incubator at 37 ^0C for 24 h for bacteria and 28 ^0C for 72 h for fungi.

The compounds were evaluated for antibacterial activity against *Staphylococcus aureus* gr +ve, *Escherichia coli* gr –ve *Bacillus subtilis* gr +ve, *Pseudomonas aeruginosa* 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. All compounds show the moderate to good activity against bacteria, but for all compounds did not stop the growth of *Aspergillus oryzoe* fungus and all compounds were not effective towards *Aspergillus niger* fungus.

Table 3. Antimicrobial activity of synthesized compounds

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

++ = Clear Zone of Inhibition + = Minimum Zone of Inhibition -ve = Growth (Antibacteria and Antifungul Activities Observed) - = No Effect X = Not applicable, Standerd 1 Penciline +, Standerd 2 Streptomycin++

Conclusion

We have reported some novel chalcones using substituted acetophenone with substituted aldehyde 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, the result was negative on fungus.

Acknowledgement

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