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Original Article

SPECTRAL STUDIES AND ANTIMICROBIAL SCREENING FOR SOME NOVEL CHALCONES ANALOGUES

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ABSTRACT

Objective: The present work aim to study the spectral and antimicrobial activity for synthesized chalcones

Methods: The synthesized Chalcones were characterized by Physical and spectral methods such as melting point, IR, ^{1}H-NMR and Mass analysis. The synthesized compounds have been screened for their antimicrobial activity.

Results: The biological data showed that compounds III, VII had strong activities against the Staphylococcus aureus, Bacillus subtilis, and Pseudomonas aeruginosa, but not activity against fungus.

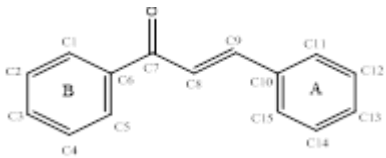
Conclusion: The main purpose to use an easy and useful method to synthesize biologically active chalcone.

Keywords: Chalcones, Synthesis, Spectral studies, Antimicrobial Activity

INTRODUCTION

Chalcones are α, β-unsaturated ketones including two aromatic rings (ring A and B) which have a diverse array of substituents. Rings are interconnected by a highly electrophilic three carbon α, β-unsaturated carbonyl system that assumes linear or nearly planar structure [1-3] they contain the keto ethylenic group (–CO–CH=CH-) [4]. Chalcones have a crystal structure. The dihedral angle between the two phenyl rings is 13.0(1) °, and the dihedral angle from the plane of C7/C8/C9 to the phenyl rings (C1 to C6 and C10 to C15) are 13.8(1) ° and 2.6(1) °, respectively, indicating that the central C7-C8-C9 fragment lies nearly in the phenyl ring plane of C10 to C15, but rather more displaced out of the other benzene ring of C1 to C6. The molecule forms a zigzag chain by C-H···π (arene) hydrogen bonds along the c axis.

There also exist intermolecular hydrogen bonding interactions involving C11 acting as H-bond donor, via H11, to O in the adjacent molecules at-x,1-y,1-z, resulting in a three-dimensional network [5]. By Claisen Schmidt condensation reactions can be readily prepared chalcones due to it is very easy and simple to conduct as well as inexpensive.



Chalcones are illustrious intermediates for synthesizing various heterocyclic compounds like pyrazolines, pyrimidines, isoxazolines, cyanopyridine, benzodiazepines benzothiazepines and flavones [6].

Chalcones have displayed a broad spectrum of pharmacological activities, such as anticancer [7-11], antiprotozoal (antileishmanial and antitrypanosomal) [12], anti-inflammatory [13-14], antibacterial [15, 16], anti filarial [17], antifungal [18, 19], antimicrobial [20], larvicidal [21], anticonvulsant [22], antioxidant [23-25] activities have been reported. They have also shown inhibition of the enzymes, especially mammalian alpha-amylase [26], cyclo-oxygenase (COX) [27] and monoamine oxidase (MAO) [28].

Experiment

The purity and completion of the reaction were monitored by TLC. Melting points of the compounds were determined in open capillary tubes and are uncorrected, IR Spectra were recorded on Shimadzu FT-IR, the sample was mixed with KBr and pellet technique was adopted to record the spectra in cm-^{1},^{1}H NMR spectra was determined on a Bruker Avance II 400 Spectrometer against TMS as internal standard DMSO-d6 as a solvent. Mass spectra were recorded on waters Micromass Q-T of Micro spectrometry.

General procedure for the preparation of chalcones

Equimolar quantities of substituted hydroxy acetophenone and aromatic aldehyde in a minimum quantity of alcohol were dissolved 40% KOH in water was added in portions, at room temperature. The reaction flask was loosely corked and kept at room temperature for about 20-21 hour.

The contents of the flask were poured over crushed ice and then acidified by 10% HCl. The solid mass separated was filtered, washed with cold water and dried, then recrystallized from a suitable solvent.

RESULTS AND DISCUSSION

Novel chalcones have been synthesized by Claisen Schmidt condensation reactions between substituted benzaldehydes with substituted hydroxyl acetophenones. The synthesized chalcones confirmed by IR spectral data showing sharp bands in the range between 1600–1660 cm^{-1} indicated the presence of C=O group. Chalcones (3a-i) were also confirmed by ^{1}HNMR spectral analysis. Inspection of the ^{1}HNMR

Spectra suggested that the chalcones were geometrically pure and configured trans ($JH_\alpha=H_\beta$=15Hz).

The antimicrobial activity of the newly chalcones was evaluated by Disc diffusion Method [29].

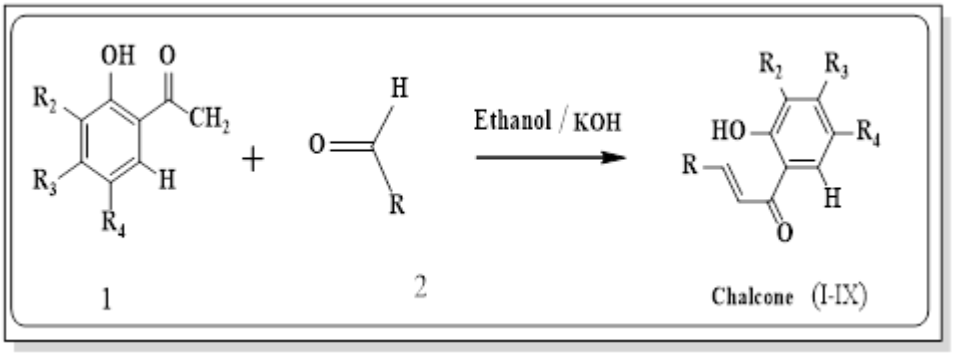
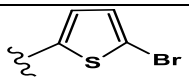
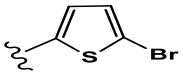
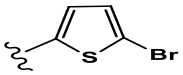
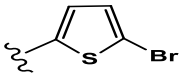
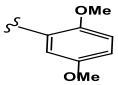
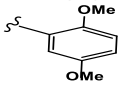
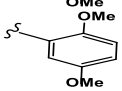
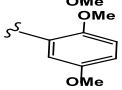
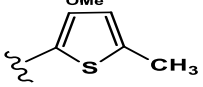


Table 1: Synthesis chalcones

Entry	Code No	Substituents			
		R_2	R_3	R_4	R
1	I	I	H	Br	
2	II	Cl	H	I	
3	III	I	OH	I	
4	IV	Cl	H	Cl	
5	V	I	H	Br	
6	VI	Cl	H	I	
7	VII	I	OH	I	
8	VIII	Cl	H	Cl	
9	IX	Cl	H	I	

Spectral analysis of the synthesized chalcones

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

I. *(E)*-1-(5-bromo-2-hydroxy-3-iodophenyl)-3-(5-Bromothiophen-2-yl)-2-methylbut-2-en-1-one

FTIR (KBr, cm^{-1}):-1629 (C=O), 1558(C=C), 1412(C-C Aromatic str), 673(C-Br).

^{1}HNMR:-7.28(d,1H$_1$), 7.59(d,1H$_2$), 7.72(d,1H,Hα, J=15Hz), 7.98(d, 1H, Hβ,J=15Hz), 8.12(s,H$_3$,Ar-H), 8.49(s,1H$_4$, Ar-H), 13.72(s,1H,OH).

M. S. (m/z):-514(M$^+$), 515(M+1), 512(M-2).

II. *(E)*-3-(5-bromothiophen-2-yl)-1-(3-chloro-2-hydroxy-5-iodophenyl) prop-2-en-1-one

FTIR (KBr, cm^{-1}):-3429(OH), 1627 (C=O), 1542(C=C), 1419(C-C Aromatic str), 798(C-Cl), 621(C-Br).

^{1}HNMR:-7.29(d,1H$_1$),7.59(d,1H$_2$),7.67(d,1H,Hα, J=15Hz), 7.96(d, 1H, Hβ,J=15Hz), 8.00(s,H$_3$,Ar-H), 8.47(s,1H$_4$, Ar-H), 13.29(s,1H,OH).

M. S. (m/z):-470(M+1), 468(M-1).

III. *(E)*-3-(5-bromothiophen-2-yl)-1-(2,4-dihydroxy-3,5-diiodophenyl) prop-2-en-1-one

FTIR (KBr, cm^{-1}):-3408(OH), 1614 (C=O), 1565(C=C), 1404(C-C Aromatic str), 629(C-Br).

^{1}HNMR:-7.28(d,1H$_1$), 7.56(d,1H$_2$), 7.67(d,1H,Hα, J=15Hz), 7.92(d, 1H, Hβ,J=15Hz), 8.23(s,H$_3$,Ar-H), 8.49(s,1H$_4$, Ar-H), 13.55(s,1H,OH).

M. S. (m/z):-576(M$^+$), 577(M+1), 578(M+2).

IV. *(E)*-3-(5-bromothiophen-2-yl)-1-(3,5-dichloro-2-hydroxyphenyl)prop-2-en-1-one

FTIR (KBr, cm^{-1}):-1636 (C=O), 1562(C=C), 1420(C-C Aromatic str), 794(C-Cl), 678(C-Br).

^{1}HNMR:-7.29(d,1H$_1$),7.59(d,1H$_2$),7.67(d,1H,Hα, J=15Hz), 7.96(d, 1H, Hβ,J=15Hz), 8.00(s,H$_3$,Ar-H), 8.47(s,1H$_4$, Ar-H), 13.29(s,1H,OH).

M. S. (m/z):-377(M-1).

V. *(E)*-3-(5-bromo-2-hydroxy-3-iodophenyl)-3-(2,5-Dimethoxyphenul)prop-2-en-1-one

FTIR (KBr, cm^{-1}):-3425(OH), 1635 (C=O), 1566(C=C), 1434(C-C Aromatic str), 640(C-Br).

^{1}HNMR:-3.82(s,3H,OMe), 3.86(s,3H,OMe), 7.01(s,1H$_3$), 7.06(d,1H$_1$), 7.67(d,1H$_2$), 8.02(d,1H,Hα, J=15Hz), 8.13(s,1H$_4$), 8.22(d, 1H, Hβ,J=15Hz), 8.54(s,H$_5$,), 13.85(s,1H,OH).

M. S. (m/z):-489(M$^+$), 490(M+1), 487(M-2).

VI. *(E)*-1-(3-chloro-2-hydroxy-5-iodophenyl)-3-(2,5-Dimethoxy phenul)prop-2-en-1-one

FTIR (KBr, cm^{-1}):-3436(OH), 1639(C=O), 1558(C=C), 1492(C-C Aromatic str), 702(C-Cl).

^{1}HNMR:-3.82(s,3H,OMe), 3.86(s,3H,OMe), 7.00(s,1H$_3$), 7.05(d,1H$_1$), 7.65(d,1H$_2$), 7.95(d,1H,Hα, J=15Hz), 7.99(s,1H$_4$), 8.23(d, 1H, Hβ,J=15Hz), 8.45(s,H$_5$,), 13.46(s,1H,OH).

M. S. (m/z):-444(M$^+$), 445(M+1), 443(M-1).

VII. *(E)*-1-(2,4-dihydroxy-3,5-diiodophenyl)-3-(2,5-Dimethoxy phenul)prop-2-en-1-one

FTIR (KBr, cm^{-1}):-3375(OH), 1625(C=O), 1541 (C=C), 1498(C-C Aromatic str),

^{1}HNMR:-3.82(s,3H,OMe), 3.86(s,3H,OMe), 6.99(s,1H$_3$), 7.05(d,1H$_1$), 7.65(d,1H$_2$), 7.93(d,1H,Hα, J=15Hz), 8.23(d, 1H, Hβ,J=15Hz), 8.45(s,H$_4$,), 8.67(s,1H$_5$), 14.75(s,1H,OH).

M. S. (m/z):-552(M$^+$), 551(M-1), 550(M-2).

VIII. *(E)*-1-(3,5-dichloro-2-hydroxyphenyl)-3-(2,5-dimethoxy-phenul) prop-2-en-1-one

FTIR (KBr, cm^{-1}):-1635(C=O), 1562(C=C), 1441(C-C Aromatic str), 707(C-Cl).

^{1}HNMR:-3.82(s,3H,OMe), 3.86(s,3H,OMe), 7.00(s,1H$_3$), 7.06(d,1H$_1$), 7.64(d,1H$_2$), 7.74(s,H$_4$,), 7.98(d,1H,Hα, J=15Hz), 8.21(d, 1H, Hβ,J=15Hz), 8.35(s,1H$_5$), 13.42(s,1H,OH).

M. S. (m/z):-353(M$^+$), 351(M-2).

IX. *(E)*-1-(3-chloro-2-hydroxy-5-iodophenyl)-3-(5-methyl-thiophen -2-yl) prop-2-en-1-one

FTIR (KBr, cm^{-1}):-3380(OH), 1628 (C=O), 1554(C=C), 1429(C-C Aromatic str), 796(C-Cl).

^{1}HNMR:-2.45(s,3H,CH3), 7.46(d,1H,Hα, J=15Hz), 7.48(d,1H$_2$), 7.56(d,1H$_1$), 7.87(d, 1H, Hβ,J=15Hz), 8.20(s,H$_3$,Ar-H), 8.38(s,1H$_4$, Ar-H), 13.77(s,1H,OH).

M. S. (m/z):-403(M$^+$), 405(M-2).

Antimicrobial activity

The antimicrobial screening was done using disc diffusion method [29] at a concentration of 500µg/ml.

Procedure

The test was performed according to the disk diffusion method [29] 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 bacteria, fungi. Whatman filter paper disk of 5 mm diameter was sterilized by autoclaving for 15 min at 1210 c. The sterile disk was impregnated with different compounds (600 gm/disk). Agar plates were surface inoculated uniformly from the both culture of the tested microorganism.

Table 2: Physical data of synthesized chalcones

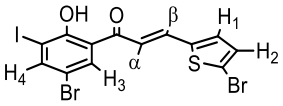
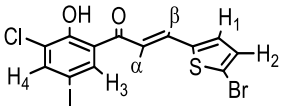
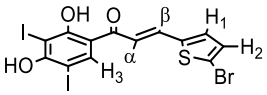
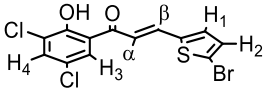
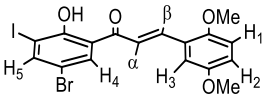
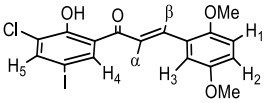
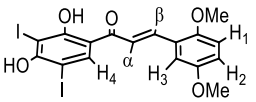
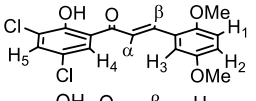
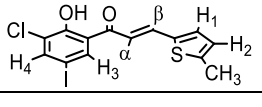
Entry	Molecular formula	M. P. °C	Yield (%)	Solubility	Product
I	$C_{13}H_7O_2IBr_2S$	174-176	80	DMF	
II	$C_{13}H_7O_2ICIBrS$	196	80	DMF	
III	$C_{13}H_7O_3I_2BrS$	158-160	75	DMF	
IV	$C_{13}H_7O_2Cl_2BrS$	150-152	70	DMF	
V	$C_{17}H_{14}O_4IBr$	176-178	85	DMF	
VI	$C_{17}H_{14}O_4ICl$	194	85	DMF	
VII	$C_{17}H_{14}O_5I_2$	180-182	70	DMF	
VIII	$C_{17}H_{14}O_4Cl_2$	150	70	DMF	
IX	$C_{14}H_{10}O_2ICIS$	108-112	90	DMF	

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,
I	+	+	-ve	-ve	-ve	-
II	+	+	-ve	-ve	-ve	-
III	++	++	+	++	-ve	-
IV	++	-	-ve	-ve	-ve	-
V	-	+	-ve	-ve	-ve	-
VI	+	-	-ve	-ve	-ve	-
VII	++	++	-ve	++	-ve	-
VIII	-	+	-ve	-ve	-ve	-
IX	++	-	-ve	+	-ve	-
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,-ve = Growth (Antibacteria and Antifungul Activities Observed), Standerd [1] Penciline+, Standerd [2] Streptomycin++Greseofulvin (fungus)

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 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 a 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.

CONCLUSION

In the present study, an easy and useful method to synthesize biologically active chalcone, using substituted acetophenone with substituted aldehyde with high yield. The newly synthesized chalcones were confirmed by spectral analysis like IR, ^{1}H-NMR and Mass 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.

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CONFLICT OF INTERESTS

Declare none

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