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Research Article

SYNTHESIS AND ANTIMICROBIAL STUDY OF SOME CHLORINE CONTAINING CHALCONES

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ABSTRACT

A series of nine chlorine containing chalcones were synthesized by condensing *p*- chloroacetophenone with different aromatic aldehydes in the presence of 40% sodium hydroxide and ethanol at 5-10^{0}C according to Claisen-Schmidt condensation. The structures of all the synthesized compounds have been characterized on the basis of analytical and spectral data. The antimicrobial activites of the synthesized compounds (3a-3i) were evaluated by Agar diffusion method by measuring zone of inhibition; Ciprofloxacin and Ketoconazole were used as standard drugs. All the synthesized chalcones have shown significant antimicrobial activity.

Key words: Synthesis, Chalcones, Antimicrobial activity.

INTRODUCTION

Chalcones are medicinally important class of compounds. Many chalcone derivatives of either natural or synthetic origin are known to possess various biological activities such as antibacterial[1,2], antifungal[3], antioxidant[4], anti-inflammatory[5] and antitumour[6] activities. They also serve as a back bone for the synthesis of various heterocyclic compounds. The presence of α, β unsaturated functional group is responsible for antimicrobial activity, which can be altered depending upon the type of substituent present on the aromatic rings[7]. Chalcones with chlorine substitution has been known to possess anti-microbial activity[8]. In this view, the present work is oriented towards synthesizing some chlorine containing chalcones according to 'Claisen-Schmidt condensation' by condensing *p*-chloroacetophenone with different aromatic aldehydes in the presence of 40% sodium hydroxide and ethanol at 5-10^{0}C. All the synthesized compounds have been characterized on the basis of their m.p, TLC, IR and ^{1}H NMR data. The antimicrobial activity of these compounds (3a-3i) was evaluated by Agar diffusion method.

MATERIALS AND METHOD

Experimental

Melting points were determined by open capillary and are uncorrected. The purity of the compounds was checked using precoated TLC plates (MERCK, 60F) using chloroform: methanol: water (1:4:5) solvent system. The plates were visualized under UV light (254nm). IR spectra were recorded using KBr on Shimadzu FTIR model 8400 spectrophotometer, ^{1}H NMR spectra in DMSO on a BRUKER FT-NMR instrument using TMS as internal standard.

General procedure for the synthesis of chlorine containing chalcones (3a-3i)

A mixture of *p*-chloroacetophenone 1 (0.01 mol) and different aromatic aldehydes 2(a-i) (0.01 mol) in ethanol (25ml) was cooled for 10-15^{o}C in ice bath. To the cooled solution 40% sodium hydroxide (5ml) was added drop wise with continuous stirring for 30 minutes using magnetic stirrer and then left overnight. The reaction mixture was poured into crushed ice and acidified carefully using dilute hydrochloric acid. The solid obtained was filtered, washed with ice-cold water, dried and recrystallised from ethanol to give compounds (3a-3i).

1-(4-Chlorophenyl)-3-phenyl-prop-2-en-1-one (3a):

IR (KBr cm^{-1}): 1660 (C=O), 1600 (C=C), 830 (Ar-Cl). ^{1}H-NMR (DMSO δ ppm): 8.05 (1H, d, =CH –Ar), 7.60 (1H, d, -CO -CH=), 7.14 – 7.80 (9H, m, Ar –H).

1-(4-Chlorophenyl)-3-(2-hydroxy phenyl)-prop-2-en-1-one (3b):

IR (KBr cm^{-1}): 1647 (C=O), 1581 (C=C), 835 (Ar-Cl) 3414 (OH). ^{1}H-NMR (DMSO δ ppm): 8.08 (1H, d, =CH –Ar), 7.50 (1H, d, -CO -CH=), 4.4 (1H, s, - OH), 6.4 – 7.7 (8H, m, Ar –H).

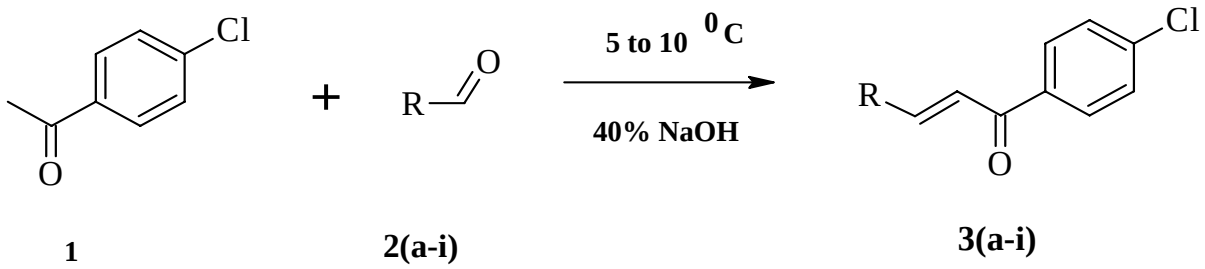
1-(4-Chlorophenyl)-3-(4-hydroxy phenyl)-prop-2-en-1-one (3c):

IR (KBr cm^{-1}): 1653 (C=O), 1579 (C=C), 829 (Ar-Cl) 3456 (OH). ^{1}H-NMR (DMSO δ ppm): 8.06 (1H, d, =CH –Ar), 7.59 (1H, d, -CO -CH=), 4.6 (1H, s, - OH), 6.7 – 7.8 (8H, m, Ar –H).

1-(4-Chlorophenyl)-3-(2-chloro phenyl)-prop-2-en-1-one (3d):

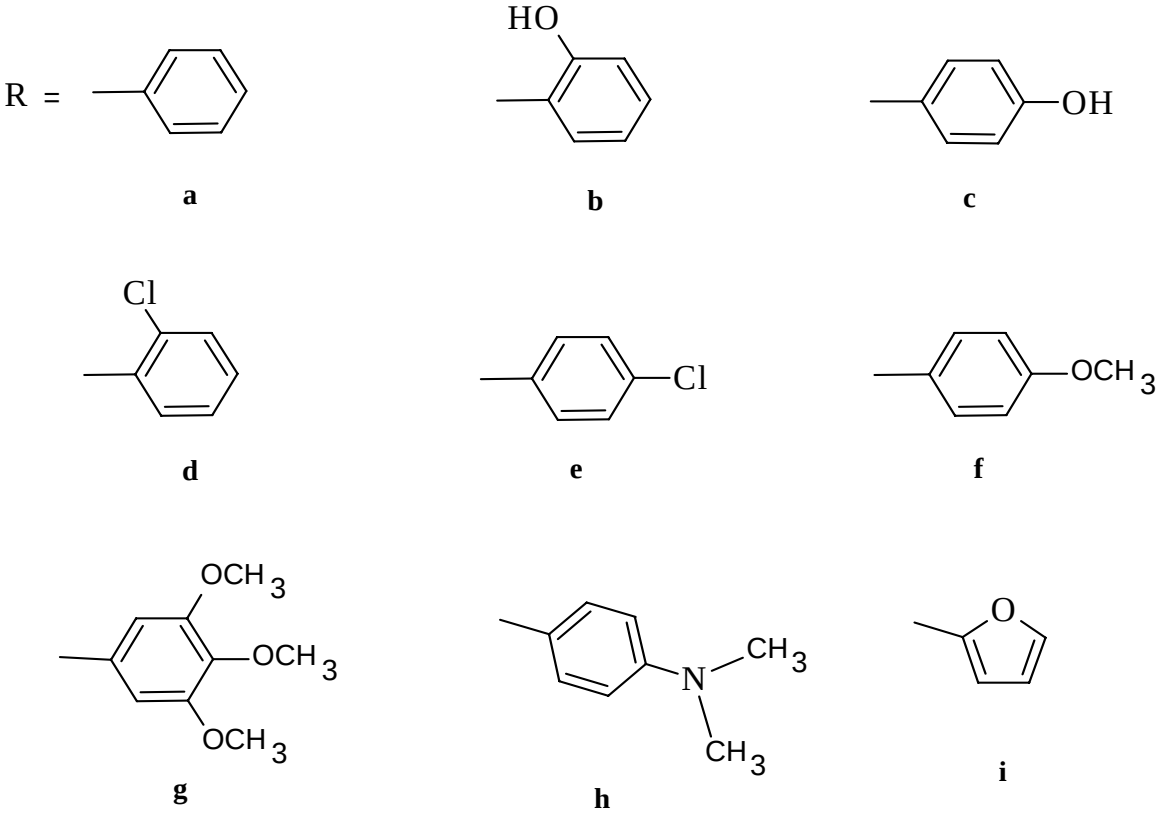
IR (KBr cm^{-1}): 1654 (C=O), 1597 (C=C), 827 (Ar-Cl). ^{1}H-NMR (DMSO δ ppm): 8.14 (1H, d, =CH –Ar), 7.38 (1H, d, -CO -CH=), 7.10 – 7.80 (8H, m, Ar –H).

SCHEME:



1 **2(a-i)** **3(a-i)**

where, R=



a **b** **c**

d **e** **f**

g **h** **i**

1-(4-Chlorophenyl)-3-(4-chlorophenyl)-prop-2-en-1-one (3e):

IR (KBr cm^{-1}): 1656 (C=O), 1595 (C=C), 825 (Ar-Cl). ^{1}H-NMR (DMSO δ ppm): 8.04 (1H, d, =CH –Ar), 7.54 (1H, d, -CO -CH=), 7.20 – 7.80 (8H, m, Ar –H).

1-(4-Chlorophenyl)-3-(4-methoxy phenyl)-prop-2-en-1-one (3f):

IR (KBr cm^{-1}): 1656 (C=O), 1591 (C=C), 821 (Ar-Cl) 1168 (C-O-CH_3). ^{1}H-NMR (DMSO δ ppm): 8.14 (1H, d, =CH –Ar), 7.62 (1H, d, -CO -CH=), 3.83 (3H, s, O – CH3), 7.02 – 7.83 (8H, m, Ar –H).

1-(4-Chlorophenyl)-3-(3, 4, 5-trimethoxy phenyl)-prop-2-en-1-one (3g):

IR (KBr cm^{-1}): 1664 (C=O), 1587 (C=C), 817 (Ar-Cl) 1126 (C-O-CH_3). ^{1}H-NMR (DMSO δ ppm): 8.17 (1H, d, =CH –Ar), 7.65 (1H, d, -CO -CH=), 3.85 (9H, s, O –CH3), 7.2 – 7.9 (6H, m, Ar –H).

1-(4-Chlorophenyl)-3-(4-dimethylamino phenyl)-prop-2-en-1-one (3h):

IR (KBr cm^{-1}): 1649 (C=O), 1583 (C=C), 812 (Ar-Cl). ^{1}H-NMR (DMSO δ ppm): 8.11 (1H, d, =CH – Ar), 7.60 (1H, d, -CO -CH =), 3.15 (6H, s, N –CH_3), 6.7 – 7.7(8H, m, Ar –H).

1-(4-Chlorophenyl)-3-(furan-2-yl)-prop-2-en-1-one (3i):

IR (KBr cm^{-1}): 1654 (C=O), 1600 (C=C), 812 (Ar-Cl). ^{1}H-NMR (DMSO δ ppm): 8.07 (1H, d, =CH –Ar), 7.60 (1H, d, -CO -CH =), 6.60 – 7.90 (8H, m, Ar –H).

Antibacterial activity[1, 2, 8]

The antibacterial activity of all the synthesized compounds (3a-3i) were examined against different Gram-positive (*Bacillus subtilis* and *Staphylococcus aureus)* and Gram-negative (*Escherichia coli* and *Salmonella typhii*) organisms by measuring zone of inhibition. The antibacterial activity was performed by Agar diffusion method at the concentration level of 250µg/ml. Ciprofloxacin was used as standard drug at a concentration of 250µg/ml. Nutrient agar was used as culture media and DMSO was used as solvent control. The results of the antibacterial activity are shown in Table 2.

Antifungal activity[3, 8]

The antifungal activity of all the synthesized compounds (3a-3i) were examined against *Aspergillus niger* and *Candida albicans* by measuring zone of inhibition. The antifungal activity was performed by Agar diffusion method at the concentration level of 250µg/ml. Ketoconazole was used as standard drug at a concentration of 250µg/ml. Sabouraud dextrose agar was used as culture media and DMF was used as solvent control. The results of the antifungal activity are shown in Table 2.

Table 1: Physical Constants data of synthesized compounds

Compound	R	Mol. Formula	Yield (%)	M.P. (°C)	R_f Value
3a	C_6H_5	$C_{15}H_{11}OCl$	56	82	0.32
3_b	2-OH.C_6H_4	$C_{15}H_{11}O_2Cl$	60	180	0.73
3c	4-OH.C_6H_4	$C_{15}H_{11}O_2Cl$	51	81	0.61
3d	2-Cl.C_6H_4	$C_{15}H_{10}OCl_2$	48	122	0.44
3e	4-Cl.C_6H_4	$C_{15}H_{10}OCl_2$	55	138	0.67
3f	4-CH_3O.C_6H_4	$C_{16}H_{13}O_2Cl$	63	102	0.5
3g	3,4,5-$(CH_3O)_3$.C_6H_2	$C_{18}H_{19}O_4Cl$	58	80	0.58
3h	4-$(CH_3)_2N$.C_6H_4	$C_{17}H_{16}ONCl$	54	118	0.48
3i	C_4H_3O	$C_{13}H_9O_2Cl$	50	87	0.53

Table 2: Zone of inhibition (mm) data of synthesized compounds

Compound	Antibacterial activity				Antifungal activity	
	B. subtilis	S. aureus	E. coli	S. typhi	A. niger	C. albicans
3a	9	7	10	7	8	9
3b	10	12	11	10	6	7
3c	9	6	10	4	6	5
3d	9	4	8	8	10	12
3e	7	7	9	7	12	11
3f	8	7	6	6	7	9
3g	8	9	6	6	4	6
3h	7	6	9	8	10	9
3i	13	13	16	13	11	10
Control	-	-	-	-	-	-
Ciprofloxacin	16	15	19	15	-	-
Ketoconazole	-	-	-	-	18	16

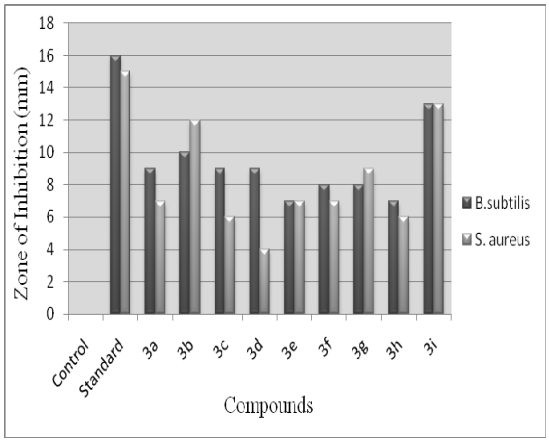


Fig. 1: Antibacterial activity (Gram-positive) of synthesized compounds

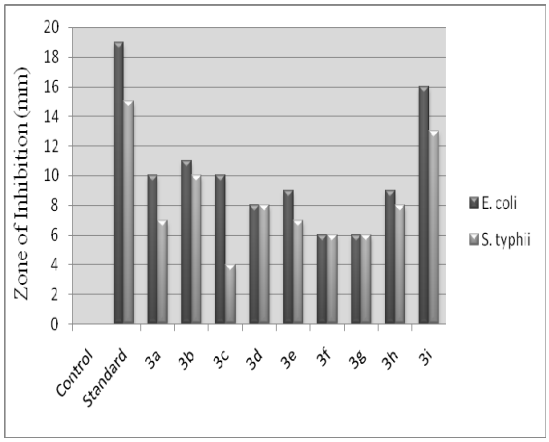


Fig. 2: Antibacterial activity (Gram-negative) of synthesized compounds

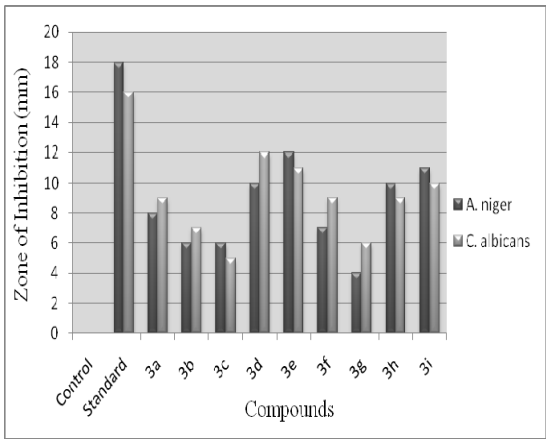


Fig. 3: Antifungal activity of synthesized compounds

RESULTS AND DISCUSSION

All the synthesized compounds (3a-3i) were purified by successive recrystallization using ethanol. The purity of the synthesized compounds was checked by performing TLC. The structures of the synthesized compounds were determined on the basis of their FTIR and ^{1}HNMR data.

The IR spectra of the synthesized compounds showed the presence of $\upsilon_{C=O}$ stretching bands at 1647-1664 cm^{-1} and $\upsilon_{C=C}$ stretching frequencies at 1579-1600 cm^{-1} corresponding to α, β-unsaturated carbonyl compounds. In ^{1}HNMR spectra of the synthesized compounds, the protons of α, β-unsaturated carbonyl compounds have given two doublets in the range of 7.5(δ, ppm) for H_α and 8.1 (δ, ppm) for H_β.

In accordance with the data obtained from antimicrobial activity, all the synthesized chlorine containing chalcones have shown mild to good activity against the tested microbes. Among these chlorine containing chalcones, compound bearing furan ring (3i) has shown good activity against all the tested bacteria and fungi.

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