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SYNTHESIS, CHARACTERIZATION AND ANTIBACTERIAL ACTIVITY OF FEW CHALCONES

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ABSTRACT

In an effort to develop anti-bacterial agents, a series of Chalcones were synthesized by condensing 4-chloro, 2-hydroxyacetophenone with aldehyde derivatives in dilute ethanolic sodium hydroxide solution at room temperature according to claisen-schmidt condensation. The synthesized compounds were characterized by means of their IR, ^{1}H-NMR spectral data and elemental analysis. All these compounds were tested for their anti-bacterial activity by agar well diffusion method.

KEY WORDS: *Chalcone, Synthesis, Antibacterial activity, IR, ^{1}NMR and Elemental analysis.*

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INTRODUCTION

Chalcone is a generic term given to compounds bearing the 1, 3-diphenyl-2-propen-1-one frame work and belong to the flavonoid family[1-3]. These are used to synthesize several derivatives like cyanopyridines, pyrozolines, isoxazoles and pyrimidines having different ring systems[4-7]. These derivatives show non-linear optical (NLO) properties with excellent blue light transmittance and good crystallizability[8].

Chalcones constitute an important group of natural products and some of them posses a wide range of biological activities such as anti-malarial, anti-viral, anti-HIV, anti-tubercular etc. Chalcones represent an important class of natural compounds with a variety of biological activities[9]. Recent studies on biological evaluation of chalcones revealed that most of the compounds are found to be anti-bacterial, anti-fungal[10], anti-cancer, anti-inflammatory,anti-hyperglycemic[11] and anti-malarial[12] agents.

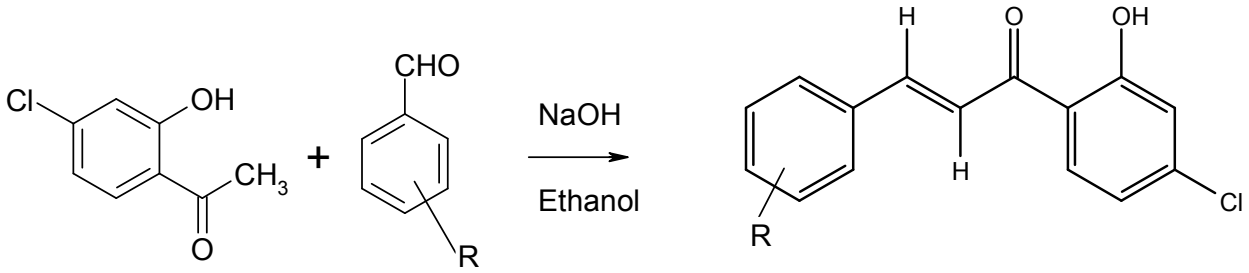
Chalcones are also well known intermediates in the synthesis of heterocyclic compounds[13-14]. Geiger and Conn during their chemical studies on the structure of Calvicin found that a structural feature which was responsible for anti-bacterial activity was α, β-unsaturated keto functional group[15].

Literature reveals that the present work deals with the reaction of 4-chloro, 2-hydroxyacetophenone with different aromatic aldehydes to form chalcones **(1-4)**, and the success of all the various synthesized compounds were assigned on the basis of their elemental analysis, IR, ^{1}H-NMR spectral studies and further screening the compounds for their antibacterial activity.

MATERIALS AND METHODS

All the products were synthesized and characterized by their spectral analysis. The chemicals 4-chloro, 2-hydroxyacetophenone, benzaldehyde, 4-chloro benzaldehyde, 2,4-dichlorobenzaldehyde, 4-chloro, 2-methoxybenzaldehyde, Sodiumhydroxide, hydrochloric acid and ethanol were purchased from E-Merk or Qualigens (AR quality) reagents, pure distilled solvents were used throughout the work. Ethanol (Bengal, B.P, 78^{0}C) was refluxed with calcium oxide for six hours and allowed to stand over night. Later, it was distilled and distillate was fractionated over sodium ethoxide. Melting points were determined in an open capillary tube and are uncorrected. IR spectra were recorded in KBr on a JASCO FT/IR-5300. ^{1}H-NMR were recorded on brucker spectrometer at 300 MHz in $CDCl_3$, (900W).

Elemental analysis was carried out on a FLASH EA 1112 series Chn Report Thermo Finnigan. Chalcones were synthesized by Claisen-Schmidt condensation[16] using ethanol as reaction solvent. The chemicals and solvents used were of laboratory grade and were purfied. Completion of the reaction was monitered by thin layer chromotography (TLC) on pre-coated sheets of silica gel-G (Merk, Germany) usng iodine vapour for detection. Column chromotography was performed on silica gel (Merck, 60-120 mesh). The synthetic pathway is presented in **Scheme 1** and physicochemical data and spectroscopic data for the synthesized compouns are given in **Table1, Table 2** and **Table3.**

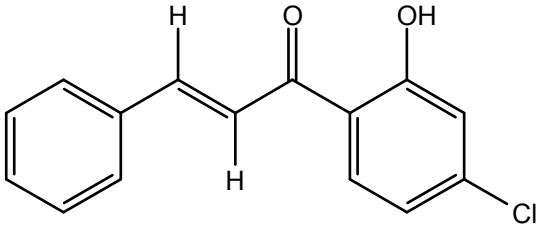


1. R=H
2. R=4 -chloro
3. R=2, 4 -dichloro
4. R=2 -methoxy, 4-chloro

Scheme1: Synthetic diagram of 4-chloro, 2-hydroxy substitued Chalcones

(1) Synthesis of 4'-cloro, 2'-hydroxy chalcone

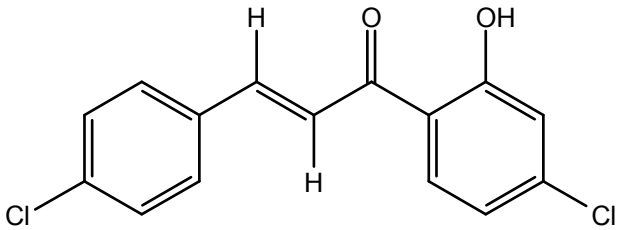
An equimolar mixture of 2.0gm (0.0125 moles) 4-chloro, 2-hydroxyacetophenone and 1.3gm (0.0125 moles) benzaldehyde are dissolved in ethanol in 150 ml conical flask. The mixture was stirred with a magnetic stirrer and NaOH 50% (16 ml) was added drop wise into it. The mixture was stirred at room temperature until it was solidified. After the completion of the reaction (monitored by TLC), the crude mixture was poured into ice water and then acidified the product with 10%HCl solution in cold condition. The bright yellow coloured compound was collected on a Buckner funnel under suction pump. The solid is washed with water thoroughly and dried and recrystallized from absolute ethanol to give 4'-chloro, 2'-hydroxy chalcone **(1)** as light yellow solid.



4'-cloro, 2'-hydroxy chalcone (1)

(2) Synthesis of 4,4'-dichloro, 2'-hydroxy chalcone

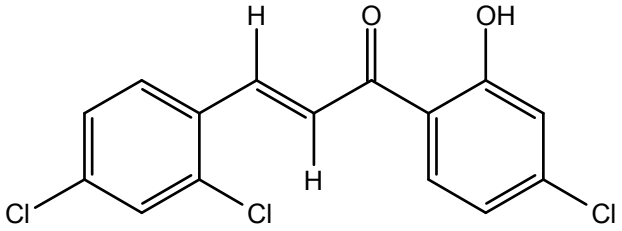
Reaction of 4-chloro, 2-hydroxyacetophenone (2.0 gms) with 4-chloro benzaldehyde (1.6 gms) give 4,4'-dichloro, 2'-hydroxy chalcone **(2)** by the above procedure.



4,4'-dichloro, 2'-hydroxy chalcone (2)

(3) Synthesis of 2, 4, 4'-trichloro, 2'-hydroxy chalcone

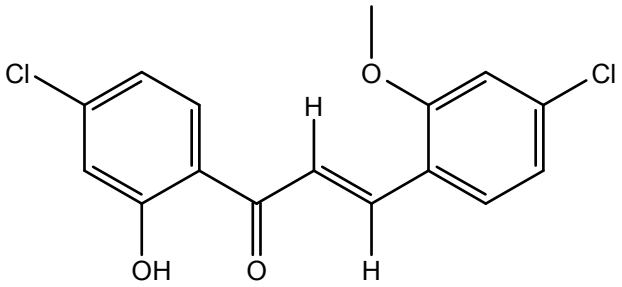
2, 4, 4'-trichloro, 2'-hydroxy chalcone**(3)** was obtained by the above procedure. The starting material used were 4-chloro, 2-hydroxyacetophenone (2.2 gms) and 2, 4 -dichloro benzaldehyde (2.0 gms) in ethanol.



2, 4, 4'-trichloro, 2'-hydroxy chalcone (3)

(4) Synthesis of 4,4'-dichloro, 2-methoxy 2'-hydroxy chalcone

A mixture of 4-chloro, 2-hydroxyaetophenone (2.2 gms) and 4-chloro,2-methoxy benzaldehyde (2.2 gms) reacted in ethanol. The 4,4'-dichloro, 2-methoxy 2'-hydroxy chalcone **(4)** was obtained by the above described procedure.



4,4'-dichloro, 2-methoxy 2'-hydroxy chalcone (4)

RESULTS AND DISCUSSIONS

The Claisen-Schmidt condensation is an important C-C bond formation for the synthesis of 1, 3-diaryl-2-propen-1-ones (Chalcones). It is generally carried out by the use of strong bases such as NaOH or KOH in polar solvents (MeOH or DMF). Synthesis of chalcone is a single step method. The synthesized chalcone derivatives were undergone physicochemical characterization and the obtained results are given in **Table1**. The yields of the synthesized compounds were found to be significant. The structure of the synthesized compounds was confirmed by IR, ^{1}H-NMR and Elemental analysis. Elemental analysis showed that the percentage of carbon, hydrogen, chlorine and oxygen was found experimentally is equivalent to the calculated values in all compounds. All he compounds give the characteristic IR peak that proved that the presence of particular functional group and the obtained results are given in **Table2.** ^{1}H-NMR helps to find the different types of protons present in the structure and the obtained results are given in **Table3.**

4'-chloro 2'-hydroxy chalcone have the molecular formula $C_{15}H_{11}ClO_2$. The IR band at 1688cm^{-1} suggests the presence of (C=O) group. A band at 1595cm^{-1} indicate that the presence of (C=C) (Olefinic) group. A band at 1570 cm^{-1} & 1464 cm^{-1} indicates the presence of (C=C) (aromatic) group. A band at 2340cm^{-1}suggests the presence of (C-H) group. A band at 760.6 cm^{-1} indicates that the presence of (C-Cl) group. A band at 3110.5 cm^{-1} indicates the

presence of (-OH) group. Melting point of the compound is 123^0C which is uncorrected.

The molecular formula of **4,4'-dichloro, 2'-hydroxy chalcone** is $C_{15}H_{10}Cl_2O_2$. The IR band at 1657cm^{-1} suggests the presence of (C=O) group. A band at 1588cm^{-1} indicates that the presence of (C=C) (Olefinic) group. A band at 1566 cm^{-1} & 1383 cm^{-1} indicate the presence of (C=C) (aromatic) group. A band at 2364cm^{-1}suggests the presence of (C-H) group. A band at 755.5 cm^{-1} indicates that the presence of (C-Cl) group. A band at 3190.6 cm^{-1} indicates the presence of (-OH) group. Melting point of the compound is 138^0C which is uncorrected.

2, 4, 4'-trichloro, 2'-hydroxy chalcone have the molecular formula $C_{16}H_9Cl_3O_2$. The IR band at 1656cm^{-1} suggests the presence of (C=O) group. A band at 1575.5cm^{-1} indicates that the presence of (C=C) (Olefinic) group. A band at 1513 cm^{-1} & 1436 cm^{-1} indicate the presence of (C=C) (aromatic) group. A band at 2389.4cm^{-1}suggests the presence of (C-H) group. A band at 866.7 cm^{-1} indicates that the presence of (C-Cl) group. A band at 3086.5 cm^{-1} indicates the presence of (-OH) group. Melting point of the compound is 127^0C which is uncorrected.

The molecular formula of **4,4'-dichloro, 2-methoxy 2'-hydroxy chalcone** is $C_{16}H_{12}Cl_2O_3$. The IR band at 1654.5cm^{-1} suggests the presence of (C=O) group. A band at 1590cm^{-1} indicates that the presence of (C=C) (Olefinic) group. A band at 1580 cm^{-1} & 1435 cm^{-1} indicate the presence of (C=C) (aromatic) group. A band at 2350.5cm^{-1}suggests the presence of (C-H) group. A band at 868.6 cm^{-1} indicates that the presence of (C-Cl) group. A band at 3097.5 cm^{-1} indicates the presence of (-OH) group. Melting point of the compound is 134^0C which is uncorrected.

Table1
Physicochemical data of Chalcones

Comd	M.F.	Yield%	M.W	M.P^{0}C	Elemental Analysis							
					C		H		Cl		O	
					% found	% calcd	% found	% calcd	% found	% calcd	% found	% calcd
1	$C_{15}H_{11}ClO_2$	78	258.70	123	70.10	69.58	3.99	4.25	13.48	13.72	12.19	12.45
2	$C_{15}H_{10}Cl_2O_2$	84	293.20	138	59.90	61.39	3.12	3.41	23.92	24.2	10.63	10.92
3	$C_{16}H_9Cl_3O_2$	81	327.70	127	54.56	54.92	2.97	2.76	32.20	32.50	9.58	9.77
4	$C_{16}H_{12}Cl_2O_3$	76	359.20	134	58.82	58.60	3.38	3.66	19.91	19.76	13.15	13.36

Table2
IR spectral data of synthesized Chalcones

S.No	Compound	IR (cm^{-1}) υ (C=O), υ (C=C)(Ole),υ(C=C) (aro),υ (C-H)				υ (C-Cl)	υ (- OH)
1	4'- chloro, 2'-hydroxy chalcone	1668.3	1595.5	1570.9 1464	2340.5	760.6	3110.5
2	4, 4'- dichloro, 2'-hydroxy chalcone	1657	1588	1566 1383	2364	755.5	3190.6
3	2, 4, 4'-trichloro, 2'-hydroxy chalcone	1656.0	1575.57	1513 1436	2389.4	866.7	3086.5
4	4, 4'-dichloro, 2-methoxy, 2'- hydroxy chalcone	1654.5	1590.6	1580 1435	2350.5	868.6	3097.5

Table3
^{1}H-NMR spectral data of synthesized Chalcones

S.No	Compound	PMR(δ ppm)
1	4'- chloro, 2'-hydroxy chalcone	7.1-7.3 (m, 5H) 6.93 (S,3'H, J= 8.6Hz) 7.02 (d, 5'H ,J=8.1) 7.58 (d, 6'H, J=8.2Hz) 12.5(S,-OH); 7.90 (d, ethylenic).
2	4, 4'- dichloro, 2'-hydroxy chalcone	7.24(d,2H,6H, J= 8.5 Hz) 7.22 (d,4H, 5H, J= 8.4 Hz) 6.85(S, 3'H, J= 8.2Hz) 7.02 (d,5'H, J= 8.6 Hz) 7.5 (d, 6'H, J=8.3Hz) 7. 8 (S, ethylenic); 12.3 (S, -OH).
3	2, 4, 4'-trichloro, 2'-hydroxy chalcone	7.23(S, 3H, J= 8.45 Hz) 7.10 (d, 5H, J= 8.5Hz) 7.18(d, 6H, J=8.1); 6.93(S, 3'H, J=8.2Hz) 7.0(d,5'H,J=8.4Hz);7.58(d,6'H,J=8.3Hz) 13.0 (S,-OH); 8.17 (S, ethylenic)
4	4, 4'-dichloro, 2-methoxy, 2'- hydroxy chalcone	6.73(S,3H, J= 7.9 Hz) 6.78 (d,5H,J= 8.6 Hz) 7.13(d,6H,J= 8.55 Hz) 6.90 (S,3'H,J= 8.45 Hz);7.15(d, 5'H) 7.60 (d, 6'H, J=8.4Hz);3.75(S, -OCH_3) 13.6 (S, -OH); 8.25 (S, ethylenic).

Table4
Antibacterial data of synthesized Chalcones

S. No	Compounds	Mean zone of inhibition (in cm)	
		Agrobacterium tumifaciens	*Xanthomonas campestris*
1	4'- chloro, 2'-hydroxy chalcone	0.8	1.2
2	4, 4'- dichloro, 2'-hydroxy chalcone	1.0	0.8
3	2, 4, 4'-trichloro, 2'-hydroxy chalcone	0.3	1.0
4	4, 4'-dichloro, 2-methoxy, 2'- hydroxy chalcone	0.5	0.9

ANTIBACTERIAL ACTIVITY

All the newly synthesized substituted chalcone s were screened for antibacterial activity again st *Agrobacterium tumifaciens,*and *Xanthomonas campestris,* according to Agar well diffusion method. Nutrient agar medium was employed as culture and DMSO was used as solvent control for antibacterial activity. The results of screening are given in **Table 4.**

CONCLUSION

In conclusion we found that 4-chloro; 2-hydroxy substituted chalcones can be synthesized using the catalytic system NaOH/EtOH. The synthesized compounds were characterized by TLC, Melting point, IR spectroscopy, Elemental analysis and NMR spectroscopy. The results obtained from this study confirmed that the product has formed. Henceforth viewing these characteristic properties more compounds can be synthesized and subjected to pharmacological evaluation.

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