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Synthesis of Chalcone and Estimating Its Antimicrobial Properties

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ABSTRACT

Chalcones are the condensation product of acetophenone in combination with aromatic aldehydes with strong base. They are having dominant role in modern co-ordination chemistry. A series of chalcone derivatives were synthesized by the process of claisen-Schmidt condensation of substituted 3-cinnamoyl-4-hydroxy-6-methyl-2-pyrones. The synthesized compounds were characterized by IR and NMR spectral analysis. The derivatives were also used for the estimation of antimicrobial properties. From the study it was found that the synthesized compounds are efficient for further research work in pharmaceutical and agricultural industries.

KEYWORDS: 3-acetyl-6-methyl-2H-pyran-2,4-(3H) dione, Dehydroacetic acid (DHA), Chalcone, 3-cinnamoyl-4-hydroxy-6- methyl-2-pyrones, IR, ^{1}HNMR, Antibacterial activity, Antifungal activity

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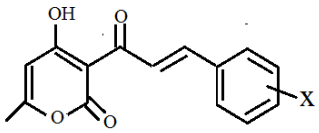
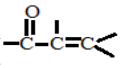
INTRODUCTION

The study of heterocyclic compounds is an evergreen field in organic chemistry. It always attracts the attention of scientists working not only in area of natural compounds but also in synthetic organic chemistry.

Chalcones represent an important class of natural as well as synthetic products and some of them are having wide range of pharmaceutical activity such as antibacterial[1], antitumour, anticancer, antitubercular, antiinflammatory, antioxidant, antimalarial, antileishmanial[2-4]etc. The presence of reactive α, β- unsaturated keto group in chalcones is found to be responsible for their biological activity[5].

Chalcones considered to be the precursor of many heterocarbon containing compounds are abundant in edible plant and in chemical forms which is widespread distribution in fruits, vegetables, spices, tea and soy based foodstuff, have been recently subjects of great interest for their interesting pharmacological activities. These activities are largely attributed due to α, β unsaturated ketone moiety[6]. Chalcones are the condensation product of dehydroacetic acid with aromatic substituted aldehydes in the presence of NaOH. Chalcone and its derivatives play important role in modern co-ordination chemistry these compounds possessing novel structural features, interesting spectral and magnetic properties have been the subject of intensive research due to their importance in medical, agricultural, analytical, biological and industrial fields[7].



The basic skeleton of chalcones is widely figured in natural products and is known to have multi-pronged activity. Chalcones have been isolated from natural sources and many more have been synthesized and studied.They have received much importance in recent years because of their diverse biological activity and synthetic utility like antimicrobial, anticancer etc[8-10].In recent years there has been a growing interest in compounds containing a carbonyl group directly linked to α, β-unsaturated system (chalcone) and their presumed role in the prevention of various degenerative diseases. Chalcones are important compounds because of their contributions to human health and their multiple biological effects, it is believed that the [] moiety imparts biological characteristics to this class of compound, some chalcone and their derivatives are reported to have insect repellent properties[11]. Chalcones are of a high interest due to their use as starting material in the synthesis of a starting material in the synthesis of a series of various heterocyclic compounds. Thus the synthesis of chalcones has generated vast interest to organic as well as for medicinal

chemists.Chalcones are α, β -unsaturated ketone containing the reactive ketoethylenic group [–C(=O)–CH= CH]. These are coloured compounds because of the presence of the chromophore [–C(=O)–CH= CH] which depends on the presence of other auxochromes. Different methods are available for the preparation of chalcones the most convenient method is the claisen-schimdt condensation of equimolar quantities of DHA ketone with aryl aldehyde in the presence alcoholic alkali[12-13].

MECHANISM OF CHALCONE FORMATION

The mechanism of chalcone synthesis is presented as follow,

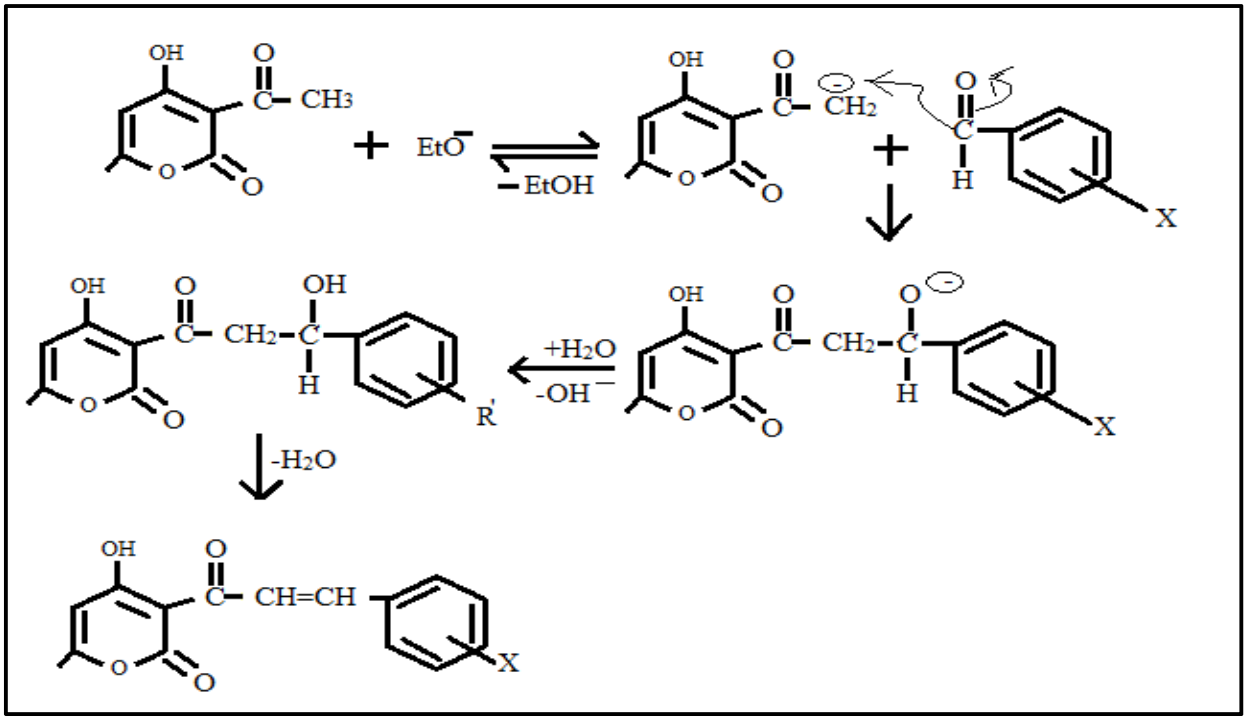


Fig.1 Mechanism OfChalcone Synthesis

METHODOLOGY

The present study was carried onchalcone were synthesized by employing claisen-schimdt condensation. The method has been implementing for the synthesis of chalconesis presented as follow.

Synthesis of chalcone

Equimolar quantities of dehydroacetic acid (DHA) and aromatic aldehyde in minimum quantity of ethanol were dissolved and 8-10 drop of piperidine was added as catalyst and reaction mixture was refluxed for a reaction time 12-18 hr. After reaction time check the TLC of reaction mixture, dried and recrystallized from suitable solvent, the M.P. and yield are shown in (**Table 1**). The purity of synthesized chalcones was checked by TLC on microscopic solid with silica gel-G

layers. The spots were exposed in iodine chamber, the structure of the chalcones were assigned on the basis of elemental analysis (**Table 2**) and spectral data (IR and ^{1}HNMR) as shown in **Table 3** and **Table 4** characteristic tests for chalcone.

Analytical Characterizations

IR spectra of compounds were scanned on FT-IR spectrometer. ^{1}HNMR spectra were recorded in $CDCL_3$ on AVANCE-500 MH_Z instrument using TMS as an internal standard, (chemical shift are given in, δ ppm).Elemental analysis is carried out with a perkin-Elmer model 2400 series II apparatus, the results of elemental analysis (C, H, N) were within ± 0.4% of the calculated values. The observed peaks and the respective values were presented in the respective tables.

IR Spectra

IR spectra of chalcones showed characteristic band at near region 3100-3430 cm^{-1} due to -OH stretching vibration. 1646-1658 cm^{-1} due to -C=O stretching vibration. Lowering of normal -C=O to the lower wave number is attributed to the presence of α, β unsaturated double bond and phenolic hydroxyl group at ortho position. All the chalcone showed absorption in the region 1598-1620cm^{-1} due to (-CH=CH) ethylenic double bond. 1714-1729 cm^{-1} for lactone carbonyl group.

^{1}HNMR Spectra

^{1}HNMR spectra of compound were studied in $CDCl_3$ showed characteristics doublet signal near δ7.9-8.4 due to olefinic α, β proton respectively. However these doublets are coalesced with aromatic proton. Phenolic proton -OH appeared as singlet near δ13.6-16.14 was observed and aromatic proton is multiplet around δ6.4-8.0. For compound containing aromatic methyl group the singlet near at δ2.2-2.4 was observed. The characteristic singlet due to C^5H proton at δ6.0 cm^{-1} for lactone unit. The ethylenic proton shift at downfield in aromatic region is the characteristic of $-\overset{O}{\overset{\|}{C}}-CH=CH-$system. These findings are in agreements with those observed by different workers.

Synthesis of chalcone derivatives of 3-cinnamoyl-4-hydroxy-6-methyl-2-pyrones

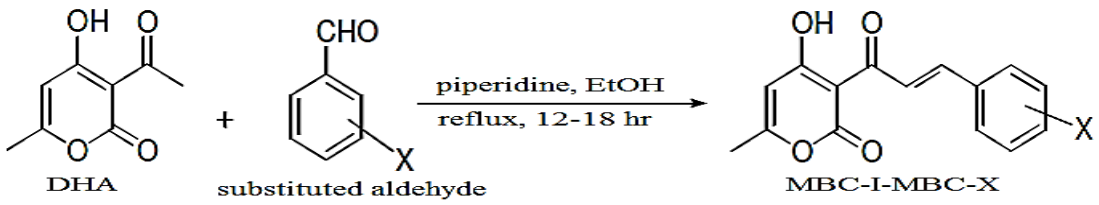


Fig. 2 Synthesis OfChalcones Derivatives Of 3-Cinnamoyl-4-Hydroxy-6-Methyl-2-Pyrones

BIOLOGICAL ACTIVITY

Preparation of media plates for maintenance of bacteria and fungus

Nutrient agar (28gm/1000ml) was dissolved in 1lit conical flasks and sterilized in autoclave at 121^0 C (15 lbs/ sq. inches) for 20 minutes. Potato dextrose agar (39 gm/lit) was dissolved in 1 lit conical flasks and sterilized in autoclave at 121^0 C (15 lbs/ sq. inches) for 20 minutes. After cooling medium was poured in sterilized petri plate about 25 ml. The media plates were inoculated aseptically with inoculums. The bacterial culture of *S. aureus*, *E. coli*, *Salmonella typhi*were inoculated on nutrient agar medium. The bacterial culture plates were incubated for 24 hr in Biological oxygen demand (BOD) incubator at 28^0 C temperature growth of organism. The fungus culture plates were inoculated on potato dextrose agar medium. The fungal culture of *Fusariumoxysporum*, *Candida albilans* and *Aspergillusflavas*plates were incubated at 35-37^0 C temperature in BOD incubator growth of organism.

Antimicrobial activity of compounds by agar well diffusion method

Prepared media plate which was not inoculated with pathogen was taken and the wells were bored into agar using a sterile 6 mm diameter cork borer, six bore was made in each plate. The culture of the test organism was spread on petri plate with sterilized spreader chalcone derivatives of desired concentration.The test compound (1 mg/mL) was dissolved in dimethyl sulphoxide and loaded on a sterile filter paper disc of 6 mm diameter. The petriplates containing nutrient agar medium were spread with 100µL of actively growing both culture of the test bacteria using sterile cotton swab and allowed to dry for 10 min. For fungal species, 100 µL of active culture was spreaded on PDA. Then the impregnated discs were placed on the surface of inoculated agar medium. With respect to control. DMSO is used as a control for testing antimicrobial activity. The positive control was taken as penicillin. The plates were allowed to incubate at room temperature for about 2 hr and then plate were transferred to incubator at 28° C for bacterial culture and 35-37°C for fungal culture. After 3-4 days zone of inhibitions were examined and recorded. The experiments were performed in replication and average diameters of the zones of inhibition were calculated.

RESULT AND DISCUSSION

The substituted chalcones of DHA were synthesized by claisen-Schmidt condensation reaction carried out between DHA and substituted benzaldehyde in ethanol having few drop of piperidine reflux in for 12-18 hr, to gives higher yield (70 -80%) of the respective chalcones (MBC-I-MBC-V). The structures of the synthesized compounds were confirmed by IR, ^{1}HNMR and elemental analysis (Analytical properties).

The entire compound gave the characteristic IR peaks for α, β unsaturated carbonyl group in the range 1646-1658 cm^{-1} corresponding to C=O stretching and C=C stretching in the range 1698-1620cm^{-1}.^{1}HNMR Spectra of the all synthesized compound showed characteristics olefinic portions of reactive, α, β unsaturated keto function occurs as doublet around range δ 7.9 -8.4 ppm for (MBC-I-MBC-V) respectively. All the synthesized compounds were also characterized for their antimicrobial activities.

In this study the molecules were having importance in the pharmacophoric possession because of this pyrone and bromo, chloro,flouro groups may provide us the fruitful results in biological and medicinal purposes. And these complexes are having importance in the pharmaceutical and agricultural field for management of diseases and pest.

Table 1. Physical data of 3-cinnamoyl-4-hydroxy-6-methyl-2-pyrones (MBCI-MBCV)

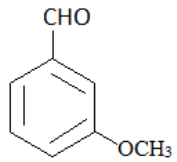
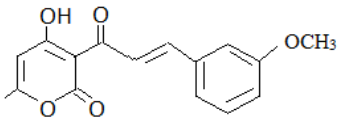
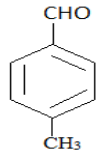
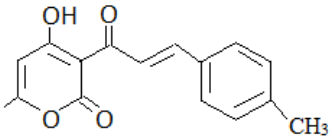
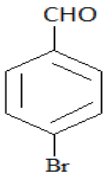
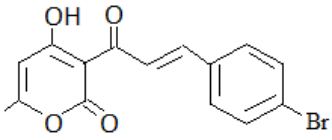
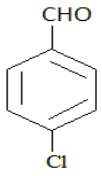
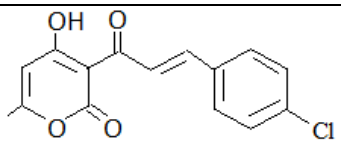
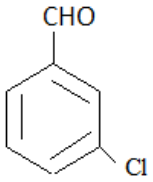
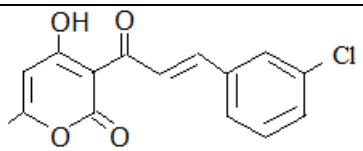
Sr. No.	Reactant	Product	Yield %	M.P. °C	Time in Hours
1.			85	174-176	20.30
2.			75	165-167	15.15
3.			70	176-178	12.30
4.			80	184-186	18.00
5.			80	148-150	18.30

Table 2. Analytical data of 3-cinnamoyl-4-hydroxy-6-methyl-2-pyrones (MBCI-MBCV)

Compound	% Calculated			% Found		
	C	H	N	C	H	N
MBC-I	67.13	4.89	-	67.08	4.47	-
MBC-II	71.11	5.18	-	71.31	5.02	-
MBC-III	53.73	3.28	-	53.35	3.12	-
MBC-IV	61.85	3.78	-	61.44	3.87	-
MBC-V	61.85	3.78	-	61.41	3.59	-

Table 3 IR spectral data of 3-cinnamoyl-4-hydroxy-6-methyl-2-pyrones (MBC-I-MBC-V)

Sr. No.	Compound	Position of absorption band (cm^{-1})
1.	MBC-I	3117 (OH), 2969, 2815 (CH str., CH_3), 1722 (C = O Lactone), 1655 (C = O), 1597 (CH = CH)
2.	MBC-II	3100 (OH), 2973 (CH str., CH_3), 1718 (C = O Lactone), 1655 (C = O), 1608 (CH = CH)
3.	MBC-III	3121 (OH), 2958, 2830 (CH str., CH_3), 1719 (C = O Lactone), 1644 (C = O), 1597 (CH = CH)
4.	MBC-IV	3429 (OH), 2870 (CH str., CH_3), 1717 (C = O Lactone), 1653 (C = O), 1612 (CH = CH)
5.	MBC-V	3418 (OH), 2972 (CH str., CH_3), 1716 (C = O Lactone), 1652 (C = O), 1620 (CH = CH)

Table 4 ^{1}HNMR spectral data of 3-cinnamoyl-4-hydroxy-6-methyl-2-pyrones (MBCI-MBCV)

Sr. No.	Compound	Chemical shift (δ) in ppm ^{1}HNMR ($CDCl_3$, δ, ppm)
1.	MBC-I	2.2 (3H, s, CH_3), 3.9 (3H, s, OCH_3), 6.0 (1H, s, C^5 DHA), 7.8 (1H, dd, -C=OCH), 8.2 (1H, dd, =CH-Ar), 6.2-7.4 (4H, m, Ar-H), 14.8 (1H, s, OH)
2.	MBC-II	2.2 (3H, s, CH_3), 2.8 (3H, s, CH_3), 6.0 (1H, s, C^5 DHA), 7.8 (1H, dd, -C=OCH), 8.4 (1H, dd, = CH-Ar), 7.0-8.2 (4H, m, Ar-H), 15.2 (1H, s, OH)
3.	MBC-III	2.3 (3H, s, CH_3), 6.0 (1H, s, C^5 DHA), 7.8 (1H, dd, -C=OCH), 8.4 (1H, dd, =CH-Ar), 6.4-7.2 (4H, m, Ar-H), 14.0 (1H, s, OH)
4.	MBC-IV	2.3 (3H, s, CH_3), 6.0 (1H, s, C^5 DHA), 7.9 (1H, dd, -C=OCH), 8.4 (1H, dd, =CH-Ar), 6.6-8.3 (4H, m, Ar-H), 14.0 (1H, s, OH)
5.	MBC-V	2.3 (3H, s, CH_3), 6.0 (1H, s, C^5 DHA), 8.0 (1H, dd, -C=OCH), 8.4 (1H, dd, =CH-Ar), 6.6-8.2 (4H, m, Ar-H), 14.0 (1H, s, OH)

Table 5 Antimicrobial activities of chalcone derivatives

Compound	Bacteria (Zone of Inhibition in mm)			Fungi (Zone of Inhibition in mm)		
	A	B	C	D	E	F
MBC-I	14	19	21	16	18	17
MBC-II	15	17	19	13	16	14
MBC-III	18	15	18	15	17	12
MBC-IV	19	18	18	18	15	18
MBC-V	14	20	16	12	18	17
Chloramphenicol *	9	12	14	12	10	12
DMSO	-ve	-ve	-ve	-ve	-ve	-ve

***Standard**, **A**-*Staphylococcusaureus* , **B**-*Escherichia coli* , **C**- *Salmonella Typhi* , **D**-*Fusariumoxysporum*, **E**- *Candida albicans*, **F**-*Aspergillusflavus.*

REFERENCES

1. Fowler VG Jr, Sakoulas G, McIntyre LM, et al. Persistent bacteremia due to methicillin-resistant Staphylococcus aureus infection is associated with agr dysfunction and low-level in vitro resistance to thrombin-induced platelet microbicidal protein. J Infect Dis., 2004; 190 : 1140-1149.
2. Lewis JS and Jorgensen JH. Inducible clindamycin resistance in staphylococci: should clinicians and microbiologists be concerned? Clin Infect Dis., 2005; 40 : 280-5.
3. Garau J, Bouza E, Chastre J, et al., Management 4. of methicillin-resistant Staphylococcus aureus infections. ClinMicrobiol Infect., 2009; 15 : 125-36.
4. Mahady GB. Medicinal plants for the prevention and treatment 5. of bacterial infections. Curr Pharm Des., 2005; 11 : 2405-27.
5. Batovska D I, Todorova IT. Trends in utilization of the 6. pharmacological potential of chalcones. CurrClinPharmacol., 2010; 5 : 1-29.
6. Nowakowska Z. A review of anti-infective and anti-7. inflammatorychalcones. Eur J Med Chem., 2007; 42 : 125-37.
7. Sharma V, Singh G, Kaur H, et al., Synthesis 8. of β-ionone derived chalcones as potent antimicrobial agents. Bioorg Med ChemLett., 2012; 22 : 6343-6.
8. Mojzis J, Varinska L, Mojzisova G, et al.,Antiangiogenic effects of flavonoids and chalcones. Pharmacol Res., 2008; 57 : 259-65.
9. Kontogiorgis C, Mantzanidou M, Hadjipavlou-Litina D. Chalcones and their potential role in inflammation. Mini Rev Med Chem., 2008; 8 : 1224-42.
10. Brakstad OG, Aasbakk K, Maeland JA. Detection of Staphylococcus aureus by polymerase chain reaction amplification of the nuc gene. J ClinMicrobiol 1992; 30 : 1654-60.

11. Bignardi GE, Woodford N, Chapman A, et al.,. Detection of the mec-A gene and phenotypic detection of resistance in Staphylococcus aureus isolates with borderline or low-level methicillin resistance. J AntimicrobChemother 1996; 37 : 53-63.
12. Kondo Y, Ito T, Ma XX, et al. Combination of multiplex PCRs for staphylococcal cassette chromosome mec type assignment: rapid identification system for mec, ccr and major differences in junkyard regions. Antimicrob Agents Chemother., 2007; 51 : 264-74.