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# Synthesis of Chalcone Derivatives and Their Antimicrobial Properties

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## ABSTRACT

*Chalcones are the condensation product of acetophenone in combination with aromatic aldehydes in the presence of strong base. Chalcones are having prominent role in modern coordination chemistry. A series of chalcone derivatives were prepared by Claisen-Schmidt condensation of substituted 3-cinnamoyl-4-hydroxy-6-methyl-2-pyrones. The chalcone synthesized by base catalyzed condensation of 3-acetyl -6-methyl-2H-pyran-2,4-(3H)dione (DHA) with different aromatic aldehyde. The synthesized compounds were characterized by IR and HNMR spectra's. The derivatives were also used for the estimation of biological properties. From the study it was found that the synthesized compounds are efficient for further research work.*

**Keywords:** 3-Acetyl-6-methyl-2H-pyran-2,4-(3H)dione, DHA, Chalcone, 3-Cinnamoyl-4-hydroxy-6-methyl-2-pyrones, Antibacterial activity, Antifungal activity

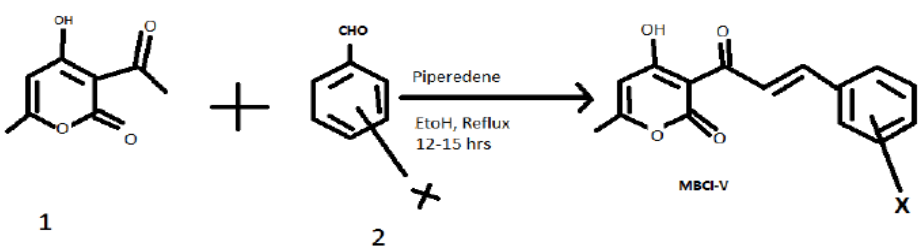
## INTRODUCTION

Chalcones are the important ligand molecules used for the synthesis of complexes with desired properties. The existence of the α,β-unsaturated ketone moiety in chalcones is a common part found in a large number of biological active compounds [1], Therefore, chalcone derivatives from nature or synthetic origin exhibit diverse pharmacological activities, such as antimicrobial [2], antitumor [3], anticancer [4], radical scavenger [5] and inhibitor of topoisomerase I [6].

3-Acetyl -6-methyl-2H-pyran-2,4-(3H) dione (DHA) appears to organic and inorganic chemistry in field of co-ordination chemistry. In organic synthesis DHA chalcones are probably the most widely used intermediate for various heterocyclic ring systems [7]. Chalcones have shown promising therapeutic efficiency for the management of several diseases due to vast array of structural modifications. In fact not many structurally diverse compounds exhibit association with such a wide range of pharmacological activity [8] among cytotoxicity [9], antitumor, anti-inflammatory, antiplasmodial, antioxidant and antibacterial with antifungal are widely cited. They also possess antiviral, antimalarial, antihyperglycemic activities [10].

The presence of reactive α, β-unsaturated keto function in chalcone is found to be responsible for their antimicrobial activity, which may be altered depending on the type and position of substituent on the aromatic ring [11]. The synthesis and reactivity of chalcones has been a topic of research interest for well over a century. The present work deals with the synthesis of chalcones of dihydroacetic acid with different aromatic aldehydes and keto groups [12]. The synthesized compounds were multi various roles of transition metal complexes in biochemistry has been directly the development of new chemistry with metal ligand system [13].

The chalcone possesses biological activity up to a distinct level so; such complexes are used in the management of microbial load in the pharmaceutical, medical as well as agriculture industry [14]. So keeping this interest in mind the present study was designed to synthesize the chalcone derivatives and estimating its analytical biological properties.




**Scheme 1: Synthesis substituted 3-cinnamoyl-4- hydroxyl-6 methyl-2-pyrones**

## MATERIALS AND METHODS

### Synthesis of substituted 3-Cinnamoyl-4-Hydroxy-6- Methyl-2-Pyrones (MBCI-V)

A solution dehydroacetic acid (10 mmol) and the aromatic aldehyde (10 mmol) were taken and 8-10 drop of piperedine as a catalyst was dissolved in 30 ml of ethanol solvent, the reaction mixture was refluxed for a reaction time 12-15 h. After reaction time compounds were checked by Thin Layer Chromatography (TLC). Then the mixture were filtered, dried and recrystallized with suitable solvent i.e., chloroform [15]. Melting points were determined in open capillary and are uncorrected. IR spectra were recorded on Perkin Elmer R-X-IFT-IR spectrometer using potassium bromide pellet, $^1$HNMR's were determined on a Bruker Advance 11400 NMR spectrometer against Tetramethylsilane (TMS) as internal standard. Purity of compounds was checked by TLC.

### Spectroscopic data of synthesized chalcone (MBCI-MBCV)

*MBCI: 1-(4-hydroxy-6-methyl-2-oxa-2H-pyran-3-yl)-3-(3-nitrophenyl)-2-propenone*

IR ($cm^{-1}$, KBr): 3114 (OH), 3062 (CH aromatic), 2900 ($CH_3$), 1729 (Lactone C=O), 1648 (C=O), 1614 (CH=CH). $^1$HNMR ($CDCl_3$, δ/ppm): 2.30 (3H, s, $CH_3$), 6.0 (1H, s, $C^5$ DHA), 7.3 (1H, dd, -C=OCH), 8.2 (1H, dd, =CH-Ar), 6.5-8.4 (4H, m, Ar-H), 14.4 (1H, s, OH).

*MBCII: 1-(4-hydroxy-6-methyl-2-oxa-2H-pyran-3-yl)-3-(3,4,5-trimethoxyphenyl)-2-propenone*

IR ($cm^{-1}$, KBr): 3121 (OH), 2954 ($CH_3$), 1726 (Lactone C=O), 1651 (C=O), 1598 (CH=CH). $^1$HNMR ($CDCl_3$, δ/ppm), 2.4 (3H, s, $CH_3$), 3.93 (9H, s, 3x$OCH_3$), 6.0 (1H, s, $C^5$ DHA), 7.9 (1H, dd, -C=OCH), 8.2 (1H, dd, =CH-Ar) 6.6-7.2 (2H, m, Ar-H), 13.2 (1H, s, OH).

*MBCIII: 1-(4-hydroxy-6-methyl-2-oxa-2H-pyran-3-yl)-3-(3-methoxyphenyl)-2-propenone*

IR ($cm^{-1}$, KBr): 3117 (OH), 2969 ($CH_3$), 1722 (Lactone C=O), 1655 (C=O), 1597 (CH=CH), 1512 (CH=CH-Ar), 1487 (CH=CH). $^1$HNMR ($CDCl_3$, δ/ ppm): 2.1 (3H, s, $CH_3$); 3.9 (3H, s, $OCH_3$), 6.0 (1H, s, $C^5$ DHA), 7.9 (1H, dd, C=OCH), 8.2, (1H, dd, =CH-Ar), 6.2 -7.4 (4H, m, Ar-H), 14.6 (1H, s, OH).

*MBCIV: 1-(4-hydroxy-6-methyl-2-oxa-2H-pyran-3-yl)-3-(3,4-dimethoxyphenyl)-2-propenone*

IR ($cm^{-1}$, KBr): 3104 (OH), 2981 ($CH_3$), 1715 (Lactone C=O), 1658 (C=O), 1589 (CH=CH).
$^1$HNMR ($CDCl_3$, δ/ ppm): 2.4 (3H, s, $CH_3$), 3.9-4.0 (6H, s, 2xOCH3), 6.0 (1H, s, $C^5$ DHA), 7.9 (1H, dd, C=OCH), 8.3 (1H, dd, =CH-Ar), 6.8-7.3 (3H, m, Ar-H), 16.4 (1H, s, OH).

*MBCV: 1-(4-hydroxy-6-methyl-2-oxa-2H-pyran-3-yl)-3-(2-fluorophenyl)- 2-propenone*

IR ($cm^{-1}$, KBr): 3103 (OH), 2973 ($CH_3$), 1719 (Lactone C=O), 1646 (C=O), 1608 (CH=CH). $^1$HNMR ($CDCl_3$, δ/ppm): 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), 7.1-8.2 (4H, m, Ar-H), 15.8 (1H, s, OH).

## BIOLOGICAL ACTIVITY

### Antibacterial activity

The synthesized compounds were tested in *in vitro* for antimicrobial activity against bacterial isolates like *S. aureus*, *E. coli* and *Salmonella typhi* and fungi species like *Fusarium oxysporum*, *Candida albicans* and *Aspergillus flavus.* The concentrations of compounds were taken as 100 µg/ml each. The antimicrobial activity was tested by agar plate diffusion method. The concentrations used for screening were confirmed after estimating the Minimum Inhibitory Concentration (MICs) of each compound. The solvent used for assay was Dimethyl Sulfoxide (DMSO) which further diluted with water. Nutrient agar and Potato Dextrose Agar (PDA) was used as the growth medium for the bacterial and fungal species respectively. DMSO was used as a control. The results were compared with standard drug penicillin for antimicrobial activity by measuring the zone of inhibition in mm using 100 µg/ml. Antimicrobial activities was measured as a diameter of zone of inhibition (mm) [16].

## RESULT AND DISCUSSION

The chalcones of DHA were synthesized by Claisen-Schmith condensation in good to excellent yield (Scheme 1) as shown in Table 1. The structures of all the compounds were established from IR and $^1$HNMR spectral analysis is mentioned above. The IR spectrum of compound MBCI-MBCV shows a broad band for OH group at (3000-3125 $cm^{-1}$) sharp and strong bands were observed at 1700-1750 $cm^{-1}$ for lactone carbonyl group. Another sharp band was observed at 1598-1650 $cm^{-1}$ due to the presence of carbonyl group and carbon-carbon bond of α,β-unsaturated chalcone system.

The $^1$HNMR spectra of MBCI-MBCV showed a characteristic singlet due to $C^5$-DHA proton δ 5.9-6.0 ppm for lactone unit. We observed that the olefinic protons of reactive α, β-unsaturated keto function occur as doublet around 7.9-8.4 respectively and broad singlet around at δ13.5-16.5 OH group of Lactone unit.

### Antimicrobial activity

The antimicrobial activity was tested against the bacterial species and fungal species and the effective zone of inhibition were observed at each concentration as mentioned in Table 2. The results were compared with standard penicillin and the control was taken as DMSO. There was no antimicrobial activity of DMSO on microbial growth. Both the organism's i.e., bacteria and fungi showed maximum zone of inhibition that were 18 mm and 20 mm, respectively.

**Table 1: Percentage yield and melting point of substituted 3-cinnamoyl-4-hydroxy-6- methyl-2-pyrones**

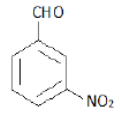
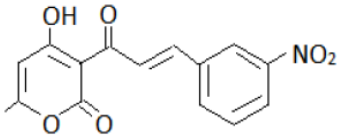
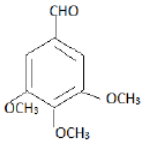
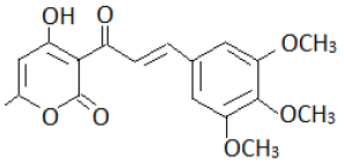
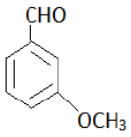
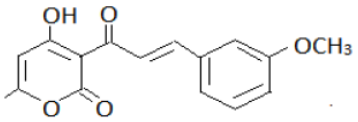
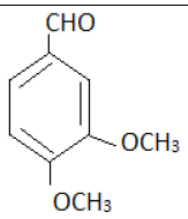
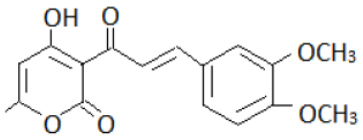
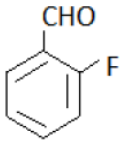
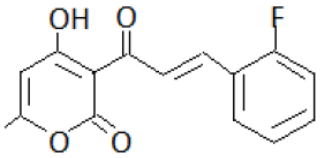
| Entry | X | Product | | Yield % | Melting point °C |
|---|---|---|---|---|---|
| 1 |  | MBCI |  | 70 | 190 |
| 2 |  | MBCII |  | 80 | 198 |
| 3 |  | MBCIII |  | 85 | 195 |
| 4 |  | MBCIV |  | 80 | 176 |
| 5 |  | MBCV |  | 84 | 160 |

**Table 2: Antimicrobial activity of chalcones**

| Compound | Bacteria (Zone of inhibition in mm) | | | Fungi (Zone of inhibition in mm) | | |
|---|---|---|---|---|---|---|
| | A | B | C | D | E | F |
| MBCI | 18 | 15 | 12 | 13 | 18 | 13 |
| MBCII | 16 | 18 | 15 | 18 | 15 | 19 |
| MBCIII | 17 | 17 | 18 | 14 | 16 | 20 |
| MBCIV | 12 | 13 | 17 | 19 | 12 | 15 |
| MBCV | 14 | 14 | 16 | 15 | 13 | 18 |
| Penicillin* | 10 | 11 | 12 | 12 | 11 | 12 |

*Standard, A-*S. aureus*; B-*E. coli*; C-*S. typhi*; D- *Fusarium oxysporum*; E-*Candida albicans;* F-*Aspergillus flavus*

## CONCLUSION

In conclusion, we have reported that the synthesized chalcones using DHA possessing a good to moderate biological properties. The newly synthesized chalcone compounds were characterized by using spectral data [15,16]. Further these compounds were tested for antimicrobial activity and it was found that they are having effective biological property. 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. These compounds are having further application in the pharmaceuticals and agriculture field for management of diseases and pest load.

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