Synthesis, Characterization and Antimicrobial Screening of Novel Ortho Hydroxy Chalcones

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**KEYWORDS**

Chalcones, Claisen-Schmidt condensation, Characterization, Antimicrobial activities.

**ABSTRACT**

New series of chalcones (1a-j) were synthesized by Claisen-Schmidt condensation of 2-hydroxy, 5-methyl aceto phenone with several aromatic aldehydes in presence of aqueous solution of sodium hydroxide. The synthesized chalcones compounds were characterized by Physical and spectral methods such as melting point, IR, \textsuperscript{1}H-NMR and Mass analysis. All the synthesized compounds have been screened and evaluated for antibacterial activity against \textit{Staphylococcus aureus} gr +ve, \textit{Escherichia coli} gr –ve, \textit{Bacillus subtilis} gr +ve, \textit{Salmonella typhi} gr –ve, and antifungal activity against \textit{Aspergillus oryzone}, \textit{Aspergillus niger}. DMSO was used as solvent control for their antimicrobial activity using disc diffusion method. Synthesis and biological evaluation of chalcones have been a topic of special interest to organic and medicinal chemists. The new structural classes of compounds may prove as lead molecules and good candidates for the future investigations.

**Introduction**

The chalcones (1, 3-diaryl-2-propenones) and their derivatives are important intermediates in organic synthesis (Straub, 1995; Sandler and Karo, 1972; Bergman Bergman \textit{et al.}, 1959). They serve as starting material for the synthesis of variety of heterocyclic compounds which are of physiological importance. Due to the presence of enone functionality in chalcone moiety confers biological activity upon it, like anti-inflammatory anti-bacterial (Chikhalia \textit{et al.}, 2008), anti-cancer (Kotra \textit{et al.}, 2010), cytotoxic activity (Go \textit{et al.}, 2005), anti-hyperglycemic (Satyanarayana \textit{et al.}, 2004), (Ballesteros \textit{et al.}, 1995), antifungal, (Go \textit{et al.}, 2005), antioxidant (Mukerjee Mukerjee \textit{et al.}, 2001), antimalarial (Liu \textit{et al.}, 2003), antituberculosis (Sivakumar \textit{et al.}, 2007), analgesic (Sivakumar \textit{et al.}, 2003), anti-HIV
Herein, we report the synthesis of some novel chalcone analogues using a conventional base catalyzed, Claisen Schmidt condensation reaction and their possible antibacterial activity.

**Materials and Methods**

**Claisen-Schmidt Condensation**

The most convenient method is the Claisen Schmidt condensation of equimolar quantities of aryl methyl ketone with aryl aldehyde in the presence of alcoholic alkali(Taylor et al., 1967).

The synthesis of chalcone compounds incorporating with hetero cycles became great importance in medicinal chemistry(Padhy et al., 2003; Nakum and Shah, 2002). The hetero atoms in their structure such as (S, N, O) explain variety applications in the biological engineering and in other field of their specific structures(Nagham, 2013).

**Experimental**

Melting points of the compounds were determined in open capillary tubes and are uncorrected, IR Spectra were recorded on Shimadzu FT-IR Spectrometer using potassium bromide pellets, 1H NMR was determined on a Bruker Avance II 400 Spectrometer against TMS as internal standard. Mass spectra were recorded on waters Micromass Q-T of Micro spectrometry.

**Method for the Synthesis of Novel Chalcones**

A mixture of substituted acetophenone (1 mmol), substituted aldehyde (1 mmol) and KOH (2 mmol, in minium H2O) were taken in ethanol and stirred at 50-60°C temperature for one hour. The completion of reaction was monitored by TLC. The products were isolated by acidification of the cool diluted acid solution and obtained solid product was filtered and washed with water and recrystallize by ethanol to get pure product.

**Results and Discussion**

The synthesis of the newly chalcones were accomplished according to the Claisen-Schmidt condensation of ortho hydroxy ketones with several aromatic aldehyde under microwave irradiation, as indicated to Scheme1. The corresponding reactions proceeded smoothly and in good to excellent yields (70-95 %). The newly synthesized chalcones were characterized by their chemical, physical and spectral analysis data and are further subjected to antimicrobial studies which exhibit moderate to good activity.

**Spectral Analysis of the Compounds**

The newly compounds were done by spectral analysis (IR, 1H NMR, MASS) and the results are shown below :

![Chemical Structure](image)

3e- (E)-1-(2-hydroxy-3-iodo-5-methyl phenyl)-3-(3-hydroxy-4-nitrophenyl)prop-2-en-1-one

**Compound 3e:** FTIR (KBr, cm⁻¹): 1617(C=O), 1581(C=C), 1439(C-C Aromatic str), 1313(N-O sym.stretch).
**HNMR:**

\[ ^1\text{HNMR}-2.33(s, 3H, CH}_3, 7.21(d, 1H, H_1), 7.58(s, 1H, H_3), 7.77(d, 1H, H_4), 7.62(s, 1H, OH), 7.81(d, 1H, H_6), 7.97(d, 1H, H_2), 8.12(d, 1H, H_β, J=15Hz), 8.21(s, 1H, H_5), 13.40(s, 1H, OH ortho)\]

**M.S. (m/z):** (M) = 424(M-1).

![Compound 3g](image)

**Compound 3g:**- FTIR (KBr, cm\(^{-1}\)): 1631(C=O), 1565(C=C), 1435(C-C Aromatic str), 660(C-Br).

\[ ^1\text{HNMR}-2.30(s, 3H, CH}_3, 7.37(dd, 1H, H_2), 7.45(d, 1H, H_α, J=15Hz), 7.65(dd, 1H, H_3), 7.88(d, 1H, H_4), 8.09(d, 1H, H_6), 8.17(d, 1H, H_5), 8.23(d, 1H, H_β, J=15Hz), 13.38(s, 1H, OH).\]

**M.S. (m/z):** (M) = 397(M-1), 399(M+1).

### Antimicrobial Activity

Antimicrobial screening was done using disc diffusion method (Afaf et al., 2000) at a concentration of 100µg/ml.

**Procedure:** The test was performed according to the disk diffusion method 26 adapted 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 bactria, fungi. Whatman filter paper disk of 5mm diameter were sterilized by autoclaving for 15 min at 1210 c. The sterile disk were impregnated with different compounds (600gm/disk). Agar plates were surface inoculated uniformly from the both culture of the tested microorganism. 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 72hrs for fungi.

The compounds were evaluated for antibacterial activity against *Staphylococcus aureus* gr +ve, *Escherichia coli* gr –ve *Bacillus subtilis* gr +ve, *Salmonela typhi* gr –ve, and antifungal activity against Aspergillus oryze, Aspergillus niger,. DMSO was used as solvent control. The results of antimicrobial data are summarized in table 3. The compounds show the moderate to good activity against bacteria and fungi.
Table. 1 Physical Data of Synthesized Chalcones

| Comp.no | Product | Mol. Formula  | Yield % | M.P.(°C) | Solubility |
|---------|---------|---------------|---------|----------|------------|
| 3a      | 3a      | C_{16}H_{13}O_{2}I | 85      | 104-106  | DMF        |
| 3b      | 3b      | C_{16}H_{13}O_{2}Br | 75      | 154-156  | DMF        |
| 3c      | 3c      | C_{16}H_{13}O_{2}IN | 70      | 186-190  | DMF        |
| 3d      | 3d      | C_{16}H_{13}O_{2}IN | 75      | 86-90    | DMF        |
| 3e      | 3e      | C_{16}H_{13}O_{2}IN | 80      | 194-196  | DMF        |
| 3f      | 3f      | C_{16}H_{13}O_{2}S | 85      | 106-108  | DMF        |
| 3g      | 3g      | C_{16}H_{13}O_{2}Br | 90      | 130      | DMF        |
| 3h      | 3h      | C_{16}H_{13}O_{2}Cl | 80      | 118-120  | DMF        |
| 3i      | 3i      | C_{16}H_{13}O_{2}N | 75      | 94-98    | DMF        |
| 3j      | 3j      | C_{16}H_{13}O_{2}N | 95      | 110-112  | DMF        |

Table. 2 Antimicrobial Activity of Synthesized Compounds

| compounds | Gram positive bacteria | Gram negative bacteria | Fungus |
|-----------|------------------------|------------------------|--------|
|           | *Staph aureus* | *Bacillus subtilis* | *Escherichia coli* | *S. typhi* | *Aspergillus oryzeo* | *Aspergillus niger* |
| 3a        | -                     | -                      | +        | -        | -                    | -                    |
| 3b        | +                     | -                      | -        | -        | -                    | -                    |
| 3c        | ++                    | +                      | -        | -        | +                    | ++                   |
| 3d        | +                     | -                      | -        | -        | ++                   |
| 3e        | +                     | +                      | -        | -        | -                    | +                    |
| 3f        | -                     | -                      | -        | -        | +                    |
| 3g        | +                     | -                      | -        | -        | -                    | -                    |
| 3h        | +                     | -                      | -        | -        | -                    | -                    |
| 3i        | ++                    | +                      | -        | -        | +                    | +                    |
| 3j        | +                     | +                      | +        | +        | +                    | +                    |
| DMSO      | -                     | -                      | -        | -        | -                    | -                    |
| Penciline 1 | ++                  | -                      | +        | -        | x                    | x                    |
| Streptomycin 2 | ++       | ++                     | ++       | ++       | x                    | x                    |
| Greseofulvin | x                   | x                      | x        | x        | x                    | -                    |

++ = Clear Zone of Inhibition
+ = Minimum Zone of Inhibition
- = No Effect
X = Not applicable
Standard 1 Penciline +, Standard 2 Streptomycin ++ (bacteria). Greseofulvin (fungus)
**Scheme 1** Synthesis of Chalcones

| Comp.no | Chalcones | Ar |
|---------|-----------|----|
| 3a      | ![Chemical Structure](image1) | ![Chemical Structure](image2) |
| 3b      | ![Chemical Structure](image3) | ![Chemical Structure](image4) |
| 3c      | ![Chemical Structure](image5) | ![Chemical Structure](image6) |
| 3d      | ![Chemical Structure](image7) | ![Chemical Structure](image8) |
| 3e      | ![Chemical Structure](image9) | ![Chemical Structure](image10) |
| 3f      | ![Chemical Structure](image11) | ![Chemical Structure](image12) |
| 3g      | ![Chemical Structure](image13) | ![Chemical Structure](image14) |
| 3h      | ![Chemical Structure](image15) | ![Chemical Structure](image16) |
| 3i      | ![Chemical Structure](image17) | ![Chemical Structure](image18) |
| 3j      | ![Chemical Structure](image19) | ![Chemical Structure](image20) |
In conclusion, here we have reported some novel chalcones using ortho hydroxyl acetophenone with several aromatic aldehydes with high yield. The newly synthesized chalcones were confirmed by spectral 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.

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