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# SYNTHESIS AND CHARACTERIZATION OF SOME NOVEL CHALCONE DERIVATIVES

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**ABSTRACT**

Chalcones are the important constituent of many natural sources and have a wide variety of biological activities. Following Claisen-Schmidt condensation reaction, a number of chalcones were prepared by the reaction between derivatives of acetophenones with variously substituted benzaldehydes in Sodium hydroxide solution and Ethanol medium at 25-30°C.The synthesized chalcones were confirmed by Infrared, $H^1$NMR and Mass studies. The above chalcones were checked for their antibacterial and antifungal activities.

**Keywords:**Chalcone,Claisen-Schmidt condensation, Benzaldehyde, Acetophenone, Antibacterial activity, Antifungal activity.



## INTRODUCTION

Due to the rapid development of resistance towards antibiotics, the need for the development of new antibacterial agents has been a very important step for research. The leading challenge for human life are diverse diseases and the fast development of microbial resistance towards existing drugs. Researchers nowadays are directed towards the design of new drugs with better pharmacokinetic profile and lesser toxicity.

Chalcones and its derivatives form an important group of natural products. Chalcones act as a well known key intermediate for various heterocyclic compounds. Chalcone derivatives have exhibited various biological activities such as antimicrobial[1,2],antitumour[3,4] anti-inflammatory[5], antibacterial[6,7], antimalarial[8], antioxidant[9,10],antitoxicity[10] and anticancer[6,11].Chalcones were also synthesized by Microwave assistance[12] and proved to give better yield. In present studies, we synthesized and characterized five novel chalcone derivatives(5a-e) derived from variously substituted acetophenones with differently substituted benzaldehydes.

## EXPERIMENTAL

**Synthesis of *N*-(3-acetyl phenyl)-2-chloroacetamide (3)**

To a stirred solution of 3-amino acetophenone in glacial acetic acid at 25-30°C, chloroacetylchloride in acetic acid was added. After completion of the reaction, 0.5 M Sodium acetate solution was charged and stirred for 30 minutes. The obtained product was filtered and dried at 55-60°C for 10 hours in a hot air oven. The crude product was further purified using ethanol.

**Synthesis of 2-(4-acetamidophenoxy)-*N*-(3-acetyl-phenyl)acetamide (4)**

To a stirred solution of Potassium carbonate in *N,N*-dimethylformamide ,a solution of *N*-(3-Acetyl-phenyl)-2-chloro-acetamide (**3)** in *N,N*-dimethylformamide was charged slowly at 25-30°C and maintained for 30 min after that N-(Hydroxyphenyl)acetamide (**4**) was added and heated for 3 hours at reflux temperature.


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The reaction progress was monitored by TLC, once the reaction was complete, it was then poured into chilled water. The obtained product was filtered, washed with water, dried in a hot air oven and weighed. The crude product was further purified using rectified spirit.

**General Procedure for the Synthesis of Substituted chalcones (5 a-d)**
An equimolar quantity of 2-(4-Acetamidophenoxy)-*N*-(3-Acetyl-phenyl)acetamide and substituted benzaldehyde were taken in ethanol. 20% NaOH solution was added and the reaction mass was continued for 24 hours. After the reaction was complete, it was then quenched into water and acidified with 10 % Hydrochloric acid and the obtained product was filtered, dried in a hot air oven and weighed. The crude product was further purified using ethanol.

**General Procedure for the Synthesis of Substituted chalcones (5 e)**
Equimolar quantity of 2-(4-Acetamidophenoxy)-*N*-(3-Acetyl-phenyl)acetamide and Furfuraldehyde were taken in ethanol. 20% NaOH solution was added and the reaction mass was maintained for 24 hours. After the reaction was complete, it is then quenched into chilled water and acidified with 10 % Hydrochloric acid to obtain the product. The crude product was further purified using ethanol.

**N-(3-acteylphenyl)-2-chloroacetamide (3)**
Yellowish brown solid, $^1$H NMR (300MHz DMSO): δ 2.61 (s, 3H), 4.21 (s, 2H ), 7.44 (t, 1H,*J*= 7.8Hz ),7.74 (d, 1H, *J*=7.8Hz ), 7.90 (d, 1H, *J*=7.8Hz),8.05 (s, 1H,), 8.48 (s, 1H, NH).

**2-(4-acetamidophenoxy)-N-(3-acetylphenyl)acetamide (4)**
Yellowish brown solid, $^1$H NMR (300MHz DMSO): δ 2.11(s, 3H), 2.60 (s, 3H), 4.60 (s, 2H), 6.93 (d, 2H, *J*=8.1HZ), 7.41 (t, 1H, *J*=7.8Hz), 7.52 (d, 2H, *J*=8.1Hz), 7.68 (d, 1H, *J*=7.8Hz), 7.96 (d, 1H, *J*= 7.8Hz), 8.21 (s, 1H), 9.36 (s, 1H), 9.43 (s, 1H).

**(E)-2-(4-acetamidophenoxy)-N-(3-(3-(4-dimethylamino)phenyl)acryloyl)phenyl)acetamide (5a)**
Yellowish brown solid, IR (KBr) (cm$^{-1}$) 3625(amide NH), 2672 (CH),1067(C=C), 1697 (CO), 1519 (amide CO), 2360 (C-N). $^1$H NMR : δ 2.03 (s, 3H), 3.04 (s, 6H), 4.62 (s, 2H), 6.69 (d, 1H, *J*=7.8Hz), 6.93 (d, 2H, *J*=8.4Hz), 7.38-7.43 (m, 2H), 7.49 (d, 2H, *J*=8.4Hz), 7.57 (d, 1H, *J*= 7.8Hz), 7.64-7.76(m, 3H), 7.94 -8.03 (m, 2H), 8.25 (d, 1H, *J*= 7.8Hz), 9.69 (s, 1H), 10.08(s, 1H). Mass of $C_{27}H_{27}N_3O_4$= 457.20.

**(E)-2-(4-acetamidophenoxy)-N-(3-(3-(p-tolyl)acryloyl)phenyl)acetamide(5b)**
White solid, IR (KBr) (cm$^{-1}$) 3502(amide NH), 2823 (CH),1168(C=C), 1658 (CO), 1608(amide CO), 2360(C-N). $^1$H NMR : δ 2.05 (s, 3H), 2.41 (s, 3H), 4.70 (, 2H), 6.98 (d, 2H, *J*=6.9Hz), 7.29 (d, 2H, *J*=7.2Hz), 7.53 (d, 2H, *J*=7.5Hz), 7.74-7.82 (m, 4H), 7.89 (d, 1H, *J*=6.6Hz), 8.03 (d, 1H, *J*=8.1Hz), 8.26 (d, 2H, *J*=7.8Hz), 9.82 (s, 1H), 10.27 (s, 1H). Mass of $C_{26}H_{24}N_2O_4$= 428.17.

**(E)-2-(4-acetamidophenoxy)-N-(3-(3-(o-tolyl)acryloyl)phenyl)acetamide(5c)**
Yellowish brown solid, IR (KBr) (cm$^{-1}$) 3494(amide NH), 2669 (CH), 1689 (CO), 1608 (amide CO), 2360 (C-N). $^1$H NMR : δ 2.05 (s, 3H), 2.56 (s, 3H), 4.71 (s, 2H), 6.98 (d, 2H, *J*=8.1Hz), 7.33 (t, 2H, *J*=9.0Hz), 7.54-7.56 (m, 2H), 7.72 (d, 2H, J= 15.3 Hz), 7.93-7.90 (m,2H), 7.96-8.06 (m,2H), 8.29-8.38 (m, 2H), 9.83 (s, 1H), 10.31 (s, 1H). Mass of $C_{26}H_{24}N_2O_4$= 428.17.

**2-(4-acetamidophenoxy)-N-(3-cinnamoylphenyl)acetamide(5d)**Brown solid, IR (KBr) (cm$^{-1}$) 3490(amide NH), 2669 (CH), 1662 (CO), 1608(amide CO), 2360(C-N). $^1$H NMR : δ 2.07 (s, 3H), 4.60 (s, 2H), 6.92 (d, 2H, *J*= 8.4Hz), 7.41-7.45 (m, 2H), 7.50-7.53 (m, 3H), 7.59-7.66 (m, 3H), 7.73-7.76 (m, 3H), 7.98 (d, 1H, *J*=8.7Hz), 8.03 (s, 1H), 9.46 (s, 1H), 9.68 (s, 1H). Mass of $C_{25}H_{22}N_2O_4$= 414.16.

**(E)-2-(4-acetamidophenoxy)-N-(3-(3-(furan-2-yl)acryloyl)phenyl)acetamide (5e)**
Yellowish brown solid, IR (KBr) (cm$^{-1}$) 3491(amide NH), 2850 (CH), 1658 (CO), 1608 (amide CO), 2360 (C-N).$^1$H NMR : $^1$H NMR (300MHz DMSO): δ 2.05 (s, 3H), 4.65 (s, 2H), 6.60 ( s, 1H), 6.93 (d, 2H, *J*=9Hz), 7.42-7.60 (m, 6H), 7.74 (s, 1H), 8.00-8.12 (m, 2H), 8.35 (s, 1H), 9.72 (s, 1H), 10.17 (s, 1H).

## RESULTS AND DISCUSSION

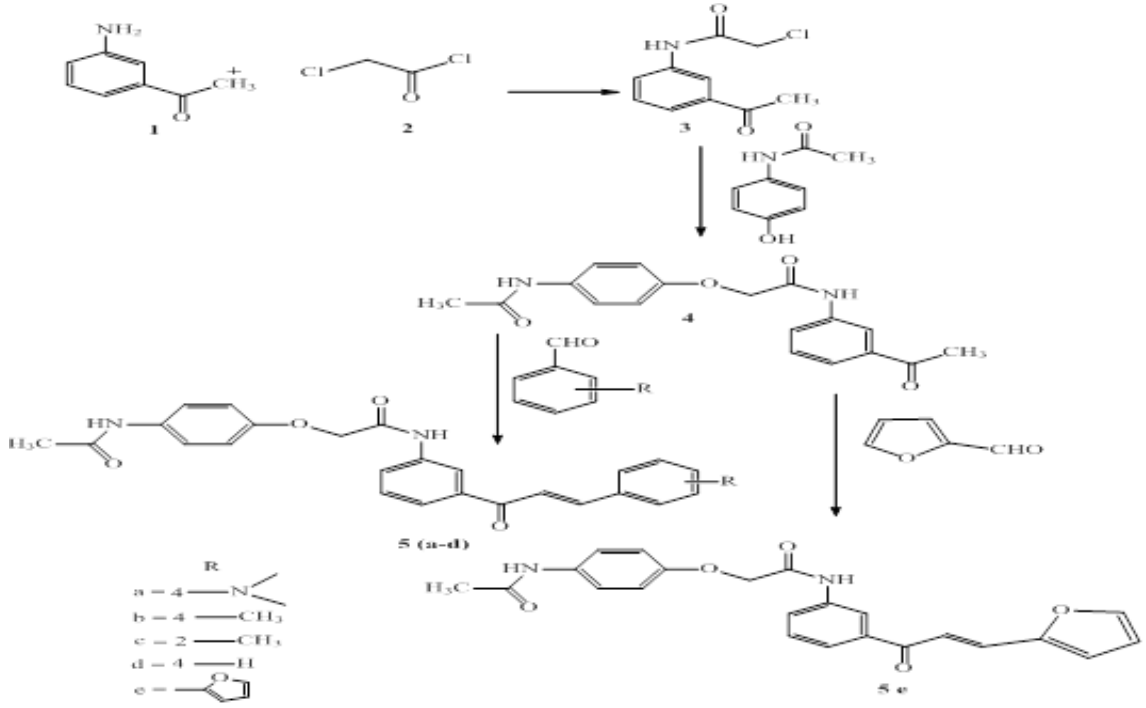
The structure of Chalcone derivatives was confirmed by IR,H $^1$NMR and Mass spectra. The various reactions are explained in Scheme-1.The chemical report of the chalcone derivatives is given in Table-1. H$^1$ NMR Spectrum of compound 5b is given in Fig.-1.

Table-1: Physical Constants of the Chalcone Derivatives

| Comp. Code | R | Molecular Formula | M. Wt | Yield % | MP ($^0$C) |
|---|---|---|---|---|---|
| 5a | 4-$(CH_3)_3N$ | $C_{27}H_{27}N_3O_4$ | 457.52 | 45 | 90 |
| 5b | 4-$CH_3$ | $C_{26}H_{24}N_2O_4$ | 428.48 | 65 | 110 |
| 5c | 2-$CH_3$ | $C_{26}H_{24}N_2O_4$ | 428.48 | 60 | 118 |
| 5d | 4-H | $C_{25}H_{22}N_2O_4$ | 414.45 | 50 | 142 |
| 5e | $C_5H_5O_2$ | $C_{23}H_{20}N_2O_5$ | 404.42 | 60 | 125 |

### Antibacterial Activity

The synthesized chalcones were subjected to antibacterial studies. The compound 5e exhibited very good activity whereas the compounds 5a, 5b, 5c & 5d exhibited good to reasonable activity against *E. coli, S. aureus, K. pneumonia* and *B. subtilis* at both the concentrations i.e. 100µg/ml and 200 µg/ml. Antibacterial activity of all the compounds was carried out by disc diffusion technique. Anti-microbial activity was also tested *in vitro* against *E. coli, S. aureus, K. pneumonia ,B. subtilis* and referred with Streptomycin (10µg) -standard drug. The inhibition Zones for the chalcones against organisms were calculated.




Scheme-1

### Disc-diffusion Assay

The effect of various compounds on selected bacterial strains was assayed by Disc diffusion method. The concentrations of the test compounds were 100 µg, 200 µg and standard drug Streptomycin 10 µg/disc. The Details of the organisms and their anti-microbial activity expressed in millimeters is given in Table-2.

### Antifungal Activity

The synthesized chalcones were screened for Antifungal activity using Fluconazole 15µg & Clotrimazole 15µg as Standard. The diameters of zone of inhibition observed were measured (Table-3).

Antifungal activity of all the synthesized compounds was screened using Fluconazole 15µg & Clotrimazole 15µg as a Standard drug. Anti-fungal activity was tested *in vitro* against *C.albicans and A.niger,* compounds 5a,5c and 5d showed good activity against both *C.albicans and A.niger* whereas the compounds 5a and 5e showed moderate activity against both the organisms.

Table-2: Antibacterial Activity

| Compound | Zone of Inhibition (mm) | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | *S. aereus* | | *B. subtilis* | | *E. coli* | | *K. pneumonia* | |
| | 100µg | 200 µg | 100µg | 200 µg | 100µg | 200 µg | 100µg | 200 µg |
| 5a | - | - | 10 | 14 | 9 | 15 | - | - |
| 5b | 9 | 13 | 8 | 12 | 10 | 14 | 7 | 9 |
| 5c | - | 12 | - | 11 | - | 9 | - | - |
| 5d | 9 | 14 | - | 14 | 11 | 13 | - | 12 |
| 5e | 10 | 15 | 10 | 13 | 9 | 14 | - | - |
| Streptomycin (10 µg) | 24 | 23 | 25 | 17 | | | | |

-Not active

Table-3: Antifungal Activity

| Compound | Zone of Inhibition (mm) | | | |
|---|---|---|---|---|
| | *C.albicans* | | *A.niger* | |
| | 100µg | 200 µg | 100µg | 200 µg |
| 5a | 13 | 15 | 9 | 13 |
| 5b | 9 | 14 | 10 | 12 |
| 5c | 12 | 16 | 11 | 13 |
| 5d | 14 | 18 | 8 | 12 |
| 5e | 11 | 14 | 12 | 14 |
| Fluconazole (15 µg) | - | | 27 | |
| Clotrimazole (15µg) | 22 | | - | |

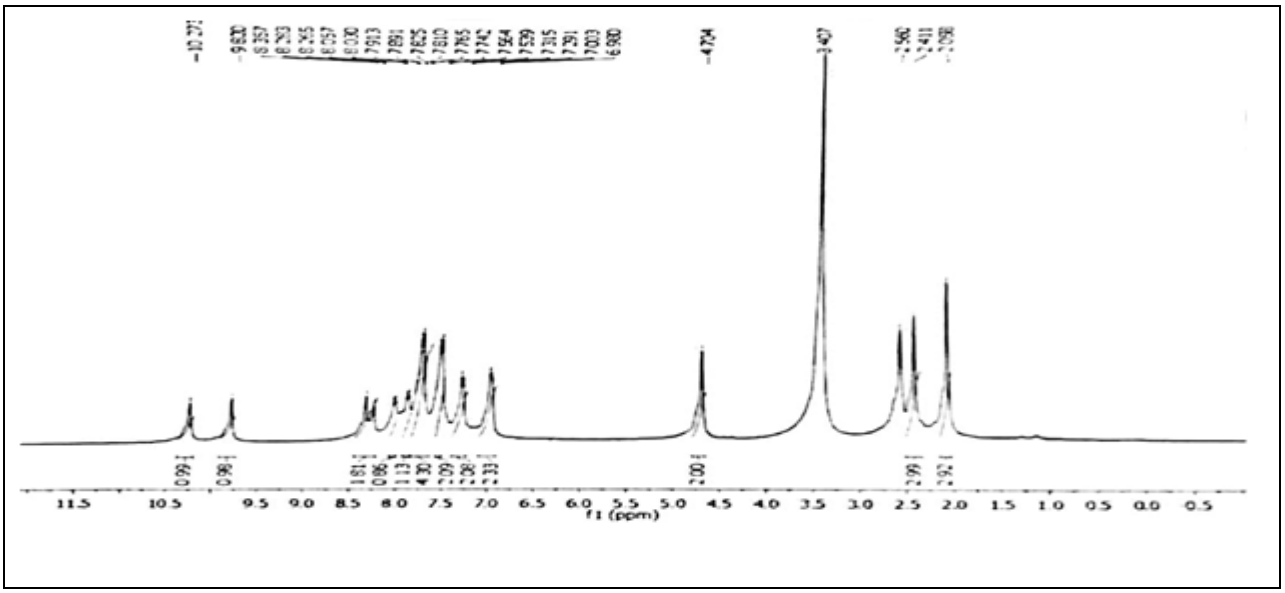



Fig.-1:H[1]NMR Spectrum of compound 5b

## CONCLUSION

The current study reveals the synthesis of some novel substituted chalcone derivatives. Chalconeswere confirmed by Infrared, H[1]NMR and Mass studies. Chalcones were evaluated for Antibacterial and Antifungal activities and were found to exhibit good to reasonable activity.

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