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# Synthesis of Chalcone And Their Derivatives as Antimicrobial Agents By Using Poly Ethylene Glycol PEG(400)

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## ABSTRACT

*As a part of organic studies in developing new antimicrobial, we report the synthesis of a new class of structurally level derivatives. In the present study, new chalcones- a-h have been synthesized by the reaction of acetyl p-toluidine with different aromatic aldehydes in the presence of aq solution NaOH, ethanol and PEG(400) used as a catalyst at room temperature. The structure of these compounds has been investigated by IR, NMR, and Mass spectrometry. The antimicrobial activity of the novel products was evaluated by filter paper disc diffusion method.*

**Keywords:** Chalcones, Acetyl-p-toluidine, Aromatic aldehydes, PEG (400); Antimicrobial activity.

## INTRODUCTION

Despite the rapid progress in science, the treatment of infectious disease still remains a serious problem of concern to the scientific community, mainly because of the wide range of factors leading to the emergence of these disease and increased number of pathogenic microorganism with resistance to multiple drugs, including the gram positive bacteria [1-5].

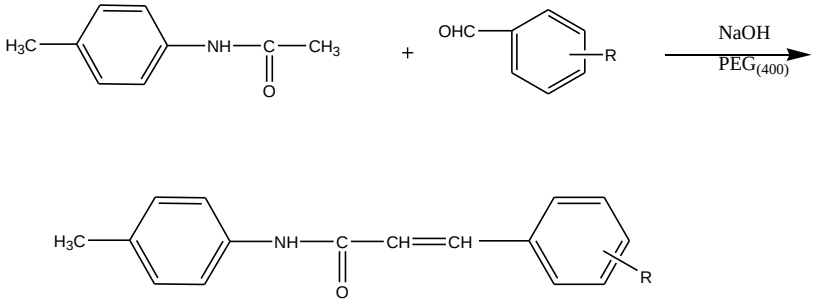
Chalcones structurally represent open –chain flavonoid in which the two aromatic rings are joined by a three-carbon □ □ □-unsaturated carbonyl system (1.3-diphenyl-2-propen-1 one). In the plants, they are considered to be precursors of flavonoids and isoflavonoids. Chalcones are known to possess different types of biological activity [6] such as antimicrobial [7], anti-inflammatory, antimimotic anti-invasive, anti-fungal, anti-malarial, anti-plasmodial, anti-tumor and anti-cancer properties [8-10] and modulation of p-glycoprotein-mediated multi-drug resistance [11-13]. Furthermore, chalcones are known as the Key intermediate in the synthesis of various biologically active heterocyclic compounds [14].

Chalcone and its derivatives are primarily synthesized in the laboratory using Claisen-Schmidt, reaction, in which acetophenone or its derivatives is reacted with benzaldehyde or its derivatives using strong base. Such as NaOH or KOH or these days PEG is used as a catalyst in polar solvent as shown in following reaction.

## MATERIALS AND METHODS

Acetyl-p-toluidine and all aromatic aldehyde were purchased from Sigma Aldrich. PEG (400) used was of Thomas baker. Ethanol and other chemicals of A.R. grade were used as received.

**Experimental:** Synthesis of chalcone is a single step method. A mixture of acetyl-p-toluidine (0.01 mol) and appropriate (R) (0.01 mol) was stirred in ethanol and then aqueous solution of NaOH (40%, 10 mL.) was added to it and in this solution 2mL PEG (400) was added as a catalyst with continuous stirring. The mixture was kept at room temp for two hours. The sodium salt of chalcone separated was decomposed by ice-cold HCl (30%) chalcone was filtered, washed with water (50 mL), dried and recrystalized from absolute ethanol.




where R = 2-Cl, 6-F, 2-OH, 5-Br, 4-F, 3-$OCH_3$, 4-OH, 2, 4-diOH, 4-Cl, 2-$NO_2$

**Scheme 1.** Synthesis of some new chalcones of acetyl-p-toluidine

The yield of the synthesized compounds was found to be significant in the presence of PEG (400) catalyst. Elemental analysis confirmed percentage of carbon, hydrogen and oxygen to be similar to the calculated values.

**Physical measurements and analytical data:** The melting point was determined in open capillaires on electro thermal apparatus and is uncorrected. The purity of all compounds were checked by thin layer Chromatography using protected silica 60F-254 Plate using hexane; ethylacetate, chloroform (6:2:2) as mobile phase. Microanalysis of carbon, hydrogen and oxygen of the compounds were carried on a Heraeus Carlo Erba 1108 elemental analyzer. IR spectra were recorded on Perkin-Elmer RX-1 infrared spectrometer in the range 4000-450$cm^{-1}$. $^{1}$H-NMR, $^{13}$C-NMR spectra of the compound were recorded on a Bruker Advance 300 MHz. The $ESI^{+}$ mass spectra were recorded on a JEOL-Accu TOF JMS-100LC mass spectrometer. The results presented in table 1.

**Table-I:** Chalcone Obtained by the condensation of Acetyl, p-toluidine with various substituted aldehydes

| S. No. | Substituted (R) | Molecular Formula | M.P. °C | % Yield | Carbon (%) | | Hydrogen (%) | | Nitro gen (%) | | Oxy gen (%) | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | Found | Calcd. | Found | Calcd. | Found | Calcd. | Fo und | Calcd. |
| 1. | Benzaldehyde | $C_{16}H_{15}NO$ | 200 | 81 | 81.01 | 80.98 | 6.32 | 6.37 | 5.90 | 5.90 | 6.75 | 6.74 |
| 2. | 2-Methoxy Benz | $C_{17}H_{17}NO_2$ | 245 | 82 | 76.40 | 76.38 | 6.36 | 6.41 | 5.24 | 5.24 | 11.98 | 11.97 |
| 3. | 4-methoxy Benz. | $C_{17}H_{17}NO_2$ | 248 | 74 | 76.40 | 76.38 | 6.36 | 6.41 | 5.24 | 5.24 | 11.98 | 11.97 |
| 4. | 3-bromo Benz | $C_{16}H_{14}BrNO$ | 270 | 87 | 60.75 | 60.78 | 4.43 | 4.46 | 4.43 | 4.43 | 5.06 | 5.06 |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 5. | 3-methoxy,4-hydro. Benz. | $C_{17}H_{17}NO_3$ | 358 | 89 | 72.08 | 72.07 | 6.00 | 6.05 | 4.94 | 4.94 | 16.96 | 16.94 |
| 6. | 4-chloro Benz | $C_{16}H_{14}ClNO$ | 242 | 88 | 70.84 | 70.72 | 5.16 | 5.19 | 5.16 | 5.15 | 5.90 | 5.89 |
| 7. | Furfural | $C_5H_{14}NO_3$ | 218 | 80 | 70.31 | 70.30 | 5.46 | 5.51 | 5.40 | 5.47 | 18.75 | 18.73 |
| 8. | 2-Chloro6-Fluro Benz. | $C_{16}H_{13}ClFNO$ | 255 | 89 | 66.43 | 66.33 | 4.49 | 4.52 | 4.84 | 4.83 | 5.53 | 5.52 |

## RESULTS AND DISCUSSION

**That data obtained of the synthesized compounds**

**1(P-toluidine--yl)-3-phenyl)prop-2ene-1-one (a)** : Crystalline, white, yield: 84%, mp 200ºC;Anal. Calc. for $C_{16}H_{15}NO$; C 80.98, H 6.37, N 5.90, O; 6.74(%), found; C 81.01, H 6.32; N 5.90, O 6.75(%), IR ($cm^{-1}$): 3423 (C=0 strong vib), 1657 (c=c), 1402(C-O-C), $^1$H-NMR (400 MHz, $CdCl_3$). δ(in ppm)=7.85 (d,2H Ar-H), 7.38-7.35 (d, 2H, Ar-H), 7.25 (d, 1H.RCH=C) 7.15-7.06(m, 2H, ss-H), $^{13}$C-NMR (100 MHz, $CdCl_3$) □ (in ppm); 168.89, 135.65, 134.01, 129.91, 129.91, 129.53, 120.41, MS m/z 237 ($M^+$)

**1(p-toluidine-yl)-3-(2-methoxy phenyl) prop. 2ene-1-one (b)**: shiny White solid; yield 79% mp; 314ºC; Anal.Calc. for $C_{17}H_{17}NO_2$, C 75.87, H 5.97 N 5.53, O 12.63(%); Found C 75.88, H 5.92, N 5.53, O 12.6 (%) IR ($cm^{-1}$); 1690(C=O), 1560 (C=C), 1265 (C-O-C); $^1$H-NMR (400 MHz, $CdCl_3$) δ (in ppm) 7.88 (d, 2H, Ar-H), 7.40-7.35 (d, 2H, Ar-H) 7.29 (S, 1H, CH), 7.19-7.12 (m, 2H, Ar-H), $^{13}$C-NMR(100 MHz, $cdCl_3$) δ (in ppm) 170.80, 137.60, 132.01, 130.90, 129.70, 120.60 MS m/z 253 ($M^+$).

**1(p-toluidine-yl)-3-(4-methoxy phenyl) prop-2-ene-1-one (c)** : Shiny white Solid; yield; 74.90%; mp. 248ºC Anal Calc. for $C_{17}H_{17}NO_2$:, C, 76.38; H; 6.41; N; 5.24; O;11.97 Found; C; 76.40; H; 6.36; N; 5.24; O;11.98(%), IR ($cm^{-1}$): 1692 (C=O), 1562 (C=C), 1272 (C-O-C); $^1$H-NMR (400MHz $CdCl_3$) □ (in ppm)= 7.89 (S, 1H, CH) 7.42-7.37 (d 2H, Ar-H), 7.30 (S, 1H, CH), 7.20-7.13 (m, 2H, Ar-H), $^{13}$C-NMR (100 MHz CdCl3), δ (in ppm) 172.70, 138.70, 135.02, 132.10, 130.80, 123.20 MS m/z 267 ($M^+$).

**1(p-toluidine-yl)-3-(3bromo phenyl) prop-2-ene-1-one (d)**: Light Yellow; yield; 87.30%; mp. 274ºC Anal Calc. for $C_{16}H_{14}BrNO$:, C, 60.78; H; 4.46; Br; 25.27, N; 4.43; O; 5.06 Found; C; 60.95; H; 4.44; Br. 25.07, N; 4.44; O; 5.07(%), IR ($cm^{-1}$): 1695 (C=O), 1565 (C=C), 1275 (C-O-C); $^1$H-NMR (400MHz $CdCl_3$) □ (in ppm)=7.90 (S, 1H, CH) 7.45-7.38 (d 2H, Ar-H), 7.32 (S, 1H, CH), 7.22-7.15 (m, 2H, Ar-H), $^{13}$C-NMR (100 MHz CdCl3), δ (in ppm)=190.90, 145.60, 140.02, 135.20, 132.40, 125.10 MS m/z 316 ($M^+$).

**1(p-toluidine-yl)-3-(3methoxy-4-hydroxy) prop-2-ene-1-one (e)**: Shiny Yellow Solid; yield; 88.34%; mp. 358ºC Anal Calc. for $C_{17}H_{17}NO_3$:, C, 72.07; H; 6.05; N; 4.94; O; 16.94 Found; C; 72.08; H; 6.00; N; 4.94; O; 16.96(%), IR ($cm^{-1}$): 1700 (C=O), 1575 (C=C), 1280 (C-O-C); $^1$H-NMR (400MHz $CdCl_3$) □ (in ppm)=7.92 (S, 1H, CH) 7.50-7.42 (d 2H, Ar-H), 7.35 (S, 1H, CH), 7.32-7.19 (m, 2H, Ar-H), $^{13}$C-NMR (100 MHz CdCl3), δ (in ppm) 175.80, 140.80, 137.10, 133.20, 132.10, 125.10 MS m/z 283 ($M^+$).

**1(p-toluidine-yl)-3-(4-chloro phenyl) prop-2-ene-1-one (f)** : Shiny Yellow Solid; yield; 88%; mp. 242ºC Anal Calc. for $C_{16}H_{14}ClNO$:, C, 70.72; H; 5.19; Cl; 13.05, N; 5.15; O; 5.89 Found; C; 70.84; H; 5.16; Cl. 13.09, N; 5.16; O; 5.90(%), IR ($cm^{-1}$): 1695 (C=O), 1565 (C=C), 1275 (C-O-C); $^1$H-NMR (400MHz $CdCl_3$), δ (in ppm)=7.85 (S, 1H, CH) 7.45-7.40 (d 2H, Ar-H), 7.32 (S, 1H, CH), 7.29-7.16 (m, 2H, Ar-H), 13 CNMR (100 MHz CdCl3)□ □ (in ppm)=173.80, 139.80 136.02, 134.20, 132.70, 124.10 MS m/z 271 ($M^+$).

**1(p-toluidine-yl)-3-(3-furfural) prop-2-ene-1-one (g)** : Shiny Yellow Solid; yield; 80%; mp. 218ºC Anal Calc. for $C_{15}H_{14}NO_3$:, C, 70.30; H; 5.51; N; 5.47; O; 18.73(%) Found; C; 70.31; H; 5.46; N; 5.46; O; 18.73(%), IR ($cm^{-1}$): 1598 (C=O), 1470 (C=C), 1170 (C-O-C); $^1$H-NMR (400MHz $CdCl_3$), δ (in

ppm)=7.65 (S, 1H, CH) 6.85-6.80 (d 2H, Ar-H), 6.40 (S, 1H, CH), 6.35-6.30 (m, 2H, Ar-H), 13 CNMR (100 MHz CdCl3)□ □ (in ppm)=170.80, 137.60, 132.01, 130.90, 129.70, 120.60 MS m/z 253 ($M^+$).

**1(p-toluidine-yl)-3-(2-chloro -6 fluro phenyl) prop-2-ene-1-one (h)** : Shiny Yellow Solid; yield; 86.50%; mp. 255ºC Anal Calc. for $C_{16}H_{13}ClFNO$:, C, 66.33; H; 4.52; Cl; 12.24, F; 6.56, N; 4.83; O; 5.52(%) Found; C; 66.43; H; 4.49; Cl. 12.28, F; 6.57; N; 4.84, O; 5.53(%), IR ($cm^{-1}$): 1720 (C=O), 1590 (C=C), 1295 (C-O-C); $^1$H-NMR (400MHz $CdCl_3$) □ (in ppm)=7.98 (S, 1H, CH) 7.55-7.45 (d 2H, Ar-H), 7.37 (S, 1H, CH), 7.35-7.25 (m, 2H, Ar-H), 13 CNMR (100 MHz CdCl3), δ (in ppm)=177.90, 142.70, 138.20, 134.10, 133.20, 127.20 MS m/z 289 ($M^+$).

## APPLICATIONS

**Antimicrobial activity:** The study of microorganisms is called microbiology. Most microorganisms are free living and perform useful activities that benefit animal and plant life. Without micro-organisms, dead organic matter would not be broken down and converted into the carbon, nitrogen and sulphur compounds which animals and plants require for their existence [15].

**Disc diffusion method:** Antimicrobial activity of all synthesized compound were determined by disc diffusion method. Disc diffusion techniques are used by most laboratories to test for antimicrobial sensitivity. Preparation of nutrient broth, subculture base layer medium, agar medium and peptone water was done as per the standard procedure. Disc measuring 5.00 mm diameter were punched from Whatman No. 1 filter paper. Stock solutions of synthesized compounds diluted in dimethyl sulphoxide (1% DMSO) to give final concentration 500µg $L^{-1}$., 1000µg $L^{-1}$. A reference standard for both gram positive and gram negative bacteria was made by dissolving accurately weighed quantity of chloramphenicol (500 and 100 µg $mL^{-1}$) respectively. The incubation was carried out at 37ºC for 24h. All the experiments were carried out in triplicate.

**Antibacterial activity:** All human phathogenio bacteria viz. klebsiella ($gm^{-ve}$), Escherichia Coli, Staphylococcus aureus ($gm^{+ve}$) [16], were purchased from Ajay Diagnostic, and Research Centre Jay Hospital, Agra India.

**Antifungal Activity:** The synthesized compounds were screened for their in vitro antifungal activity against Aspergillus niger; Aspergillus fumigatus, Candida albicans by measuring the zone of inhibition in mm [17-18]. The fungal activity was performed by filter paper disc plate method.

Antibacterial and Antifungal data of compounds
(Zone of inhibition measured in mm MIC = 10□ □ g $disc^{-1}$)

| | Antibaterial | | | Anti-fungal | | |
|---|---|---|---|---|---|---|
| **Compounds** | **Klebsiella.p** | **Escherichia coli** | **S. auresus** | **A. niger** | **A. fumigatus** | **C. albicans** |
| **a** | 10 | 09 | 08 | 08 | 08 | 09 |
| **b** | 08 | 09 | 07 | 12 | 07 | 06 |
| **c** | 12 | 10 | 09 | 10 | 07 | 06 |
| **d** | 10 | 08 | 07 | 10 | 06 | 05 |
| **e** | 10 | 07 | 08 | 08 | 05 | 03 |
| **f** | 08 | 08 | 06 | 06 | 07 | 06 |
| **g** | 07 | 06 | 06 | | 07 | 07 |
| **h** | 07 | 06 | 08 | | 07 | 06 |

This is an environmentally benign procedure and reduces the total reaction time and gives excellent yield of chalcones.

## CONCLUSIONS

The present work demonstrated the synthesis of chalcone in excellent yield in the presence of a reusable and environmentally benign reaction catalyst PEG(400), the structure of the synthesized compounds were confirmed from their respective, IR, 1H-NMR, $^{13}$C- NMR and mass studies. From the antimicrobial screening it was observed that all the compounds exhibited activity against all the organisms employed, the compound shows good antibacterial and anti fungal activity.

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