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# SYNTHESIS, CHARACTERIZATION AND ANTIMICROBIAL ACTIVITY OF SOME NEW BARBITONE DERIVATIVES

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## ABSTRACT

Some new 1-(p-Methoxyphenyl)-3-[4'-(p-methylbenzyloxy)-3' methoxyphenyl]-prop-2-en-1-one (1a-l) and 5-[1'-Aryl-3'-{4"-(p-methybenzyloxy)-3"-methoxyphenyl}-prop-2'-en-1'-ylidene]-pyrimidine-2, 4, 6- (1H, 3H, 5H)-triones (2a-l) were prepared. All the prepared compounds were characterized by their spectral (I.R., N.M.R., Mass) data and screened for their antimicrobial activities.

**KEYWORDS:** Chalcone, Barbitone, Antimicrobial activities.

## INTRODUCTION

The emerging role of barbitones in pharmaceutical chemistry as well as in biochemistry stimulated tremendous interest in the synthesis[1-3] of barbitones of therapeutic interest. Most important is the effect of barbiturates on the central nervous system. Barbituric acid derivatives constitute an important class of compounds possessing diverse type of biological properties including hypnotic, sedative, anticonvulsant, cardiovascular etc. Different methods are used for the preparation of barbitones in literature.[4-5] Some barbituric acid derivatives used as sedative and hypnotic is carbubarb[6], which is used as veterinary anesthetic. Some isoxazolo pyrimidines have been studied because of their potential as pesticidal[7-8] activity. Some barbiturates showing cardiovascular[9-11] and analgesic and anti-inflammatory activities[12] have been reported.

This inspired us to synthesize 1-(p-Methoxyphenyl)-3-[4'-(p-methylbenzyloxy)-3' methoxyphenyl]-prop-2-en-1-one (1a-l) and 5-[1'-Aryl-3'-{4"-(p-methybenzyloxy)-3"-methoxyphenyl}-prop-2'-en-1'-ylidene]- pyrimidine-2, 4, 6- (1H,3H,5H)-triones (2a-l).

The structure of synthesized compounds were assigned based on Elemental analysis, I.R. $^{1}$H-NMR and Mass spectral data. The antimicrobial activity was assayed by using the cup-plate agar diffusion method[13] by measuring the zone of inhibition in mm. All the compounds were screened *in vitro* for their antimicrobial activities[14] against varieties of bacterial strains such Staphylococcus aureus, *Bacillus subtillis*, *Escherichia coli*, Proteus vulgaris and fungi *Aspergillus niger* at 40 μg concentration. Standard drugs like Ampicillin, Amoxicillin, Norfloxacin, Benzyl penicillin and Griseofulvin were used for comparison purpose (Table-1).

## RESULTS AND DISCUSSION

The synthesis of 1-(p-Methoxyphenyl)-3-[4'-(p-methylbenzyloxy)-3' methoxyphenyl]-prop-2-en-1-one (1a-l) and 5-[1'-Aryl-3'-{4"-(p-methybenzyloxy)-3"-methoxyphenyl}-prop-2'-en-1'-ylidene]- pyrimidine-2, 4, 6- (1H,3H,5H)-triones (2a-l) was carried out in two steps, first by the condensation of 4-[(2-chlorobenzyl)oxy]-3-methoxy benzaldehyde (1) with different aromatic acetophenone by Claisen-shmidt condensation in presence base catalyst to give chalcone derivatives (1a-l), which in next step were refluxed with barbituric acid in presence of glacial acetic acid to yield barbitone derivatives ( 2a-l). (scheme-1). The formulas of the selected compounds were confirmed by the elemental analysis and their structures were determined by IR,$^{1}$ H-NMR, and mass spectral data.

### Antibacterial Activity

It has been observed from the microbiological data that all compounds **(1a-l)** and **(2a-l)** were found to be mild to moderately active against Gram positive and Gram negative bacterial strains. The screening data indicated that among chalcone and barbitone derivatives, tested compounds **1c, 1h** and **2i, 2j** possesses very good against *S.aureus.* However, the compounds **1j, 1h** and 2d, 2j displayed comparable activity against *B.subtilis.* The compounds **1e, 1i,** and **2d, 2l** showed greater degree of antibacterial activity against ***E.coli.*** However, the compounds **1e, 1i,** and **2f, 2g** showed mildly active against ***P.vulgaris***. All the compounds were found to possess moderate to good activity against Gram positive and Gram negative strains.

### Antifungal Activity

The antifungal data revealed that compounds were least toxic to the fungal strain. However mild activity was shown by the compounds against ***A.niger*.** The antibacterial activity was compared with standard drug viz. and antifungal activity was compared with standard drug viz. Griseofulvin. The screening data indicated that among chalcone and barbitone derivatives, tested compounds **1l, 1e,** and **2a, 2e** showed maximum activity against *A.niger.*

All other compounds exhibit mild to moderate antifungal activity against *A.niger*.

**Experimental Section**

Melting points were taken in open capillary tubes are uncorrected. IR spectra ($cm^{-1}$) were recorded on Shimadzu-435-IR Spectrophotometer and $^1$H-NMR spectra on Bruker spectrometer(300MHz) using TMS as an internal standard, chemical shift in δ ppm.

***General procedure for the preparation of 1-Aryl-3-[4'-(p-methylbenzyloxy)-3'-methoxyphenyl]-propenones***

Take a mixture of 4-[(p-methylbenzyl)oxy]-3-methoxy benzaldehyde (1) (0.01M) and 4-methoxy acetophenone (0.01) in methanol, add a NaOH (0.002M) to the reaction mixture . The reaction mixture was magnetically stirred for 12 hrs and then left overnight. After it was pour over ice and neutralized with dil.HCl and ethanol is added for crystallization.

***1-Aryl-3-[4'-(p-methylbenzyloxy)-3'-methoxyphenyl]-propenones***

Yield 76%, m.p. 112$^0$C; IR(KBr) : ν 2968,2841,1456 (Alkane,-$CH_3$), 1255 (-$OCH_3$), 1255 (Ar-O-C), 1663 (C=O), 1591 str. (C=C), 3064,1511,1133,806 (Aromatic), $cm^{-1}$; $^1$H-NMR ($CDCl_3$) : δ 3.84, (s,6H,-$OCH_3$), 7.00 & 7.20 (d,2H,-CH=CH-), 5.08(s,2H,-O-$CH_2$-), 6.96-8.05(m,11H, Ar-H), Mass m/z 388 .M.F.:$C_{25}H_{24}O_4$.

***General procedure for the preparation of 5-[1'-Aryl-3'-{4"-(p-methybenzyloxy)-3"-methoxyphenyl}-prop-2'-en-1'-ylidene]- pyrimidine-2, 4, 6- (1H,3H,5H)-triones (2a-l)***

A solution of 1-(p-Methoxyphenyl)-3-[4'-(p-methylbenzyloxy)-3'-methoxyphenyl]-prop-2-en-1-one (4.98g, 0.01M) and barbituric acid (1.28g, 0.01M) in methanol (40ml) was refluxed in presence of gla. acetic acid (catalytic amount) for 12 hrs. The reaction mixture was poured in crushed ice, filtered washed and dried, crystallized from methanol, Yield 76%, m.p.122$^0$C. $C_{29}H_{26}N_2O_6$; Required: C, 69.73; H, 5.21; N, 5.61 %; Found: C, 69.69; H, 5.11; N, 5.11 %. Similarly, other barbitones were prepared. The physical data are recorded in Table No. 1.

***5-[1'-Aryl-3'-{4"-(p-methybenzyloxy)-3"-methoxyphenyl}-prop-2'-en-1'-ylidene]-pyrimidine-2, 4, 6- (1H,3H,5H)-triones***

Yield 76%, m.p. 122 $^0$C; IR(KBr) : ν 2957,1456 (Alkane,-$CH_3$), 1253 (-$OCH_3$), 1267 (Ar-O-C), 1548 (C=C), 3084,1498,1145 (Aromatic), 3305 (-NH-), $cm^{-1}$; $^1$H-NMR ($CDCl_3$) : δ 3.87 (s,3H,- $OCH_3$), 10.0,11.2 (s,2H,-NH), 5.16 (s, 2H, -O-$CH_2$-), 6.87-8.04 (m,13H, Ar-H),2.31,2.38(s,6H,-$CH_3$) .Mass m/z 499 . M.F.:$C_{29}H_{26}N_2O_6$.

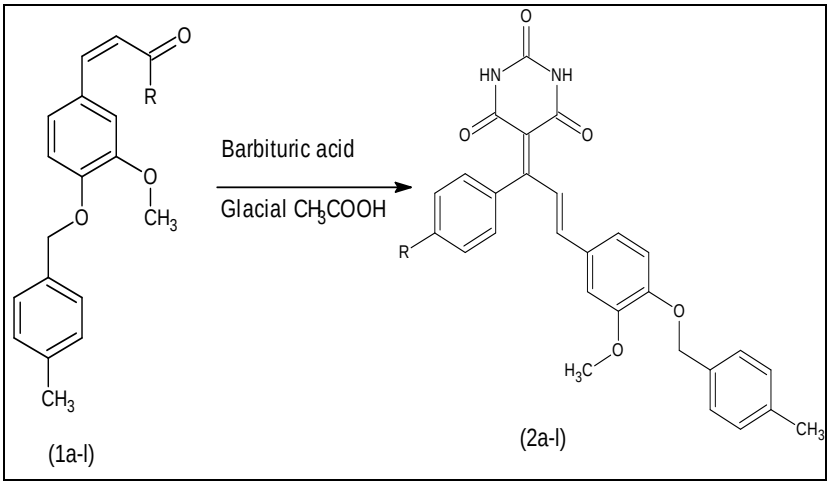
**Table-1.**

| Characterization data of the compounds (1a-l) and (2a-l) | | | | | | |
|---|---|---|---|---|---|---|
| **Compd No.** | **R** | **Molecular formula** | **Mole.Wt.** | **M.P. ($^0$C)** | **Nitrogen %** | |
| | | | | | **Calcd** | **Found** |
| 1a | -$C_6H_5$ | $C_{24}H_{22}O_3$ | 358 | 122 | - | - |
| 1b | -4-$NH_2$-$C_6H_4$ | $C_{24}H_{23}NO_3$ | 373 | 170 | 3.75 | 3.51 |
| 1c | -4-Br-$C_6H_4$ | $C_{24}H_{21}BrO_3$ | 437 | 112 | - | - |
| 1d | -4-Cl-$C_6H_4$ | $C_{24}H_{21}ClO_3$ | 392.5 | 108 | - | - |
| 1e | -2,4-($Cl_2$)-$C_6H_3$ | $C_{24}H_{20}Cl_2O_3$ | 427 | 140 | - | - |
| 1f | -2-OH- $C_6H_4$ | $C_{24}H_{22}O_4$ | 374 | 73 | - | - |
| 1g | -3-OH- $C_6H_4$ | $C_{24}H_{22}O_4$ | 374 | 78 | - | - |
| 1h | -4-OH- $C_6H_4$ | $C_{24}H_{22}O_4$ | 374 | 72 | - | - |
| 1i | -4-$OCH_3$-$C_6H_4$ | $C_{25}H_{24}O_4$ | 388 | 112 | - | - |
| 1j | -4-$CH_3$- $C_6H_4$ | $C_{25}H_{24}O_3$ | 372 | 134 | - | - |
| 1k | -3-$NO_2$- $C_6H_4$ | $C_{24}H_{21}NO_5$ | 403 | 92 | 3.47 | 3.32 |
| 1l | -4-$NO_2$- $C_6H_4$ | $C_{24}H_{21}NO_5$ | 403 | 148 | 3.47 | 3.29 |
| 2a | -$C_6H_5$ | $C_{28}H_{24}N_2O_5$ | 468.5 | 118 | 5.97 | 5.94 |
| 2b | -4-$NH_2$-$C_6H_4$ | $C_{28}H_{25}N_3O_5$ | 483.5 | 110 | 8.60 | 8.56 |
| 2c | -4-Br-$C_6H_4$ | $C_{28}H_{23}BrN_2O_5$ | 547.5 | 155 | 5.11 | 5.01 |
| 2d | -4-Cl-$C_6H_4$ | $C_{28}H_{23}ClN_2O_5$ | 502.9 | 138 | 5.56 | 5.51 |
| 2e | -2,4-($Cl_2$)- $_6H_3$ | $C_{28}H_{22}Cl_2N_2O_5$ | 537.3 | 132 | 5.21 | 5.11 |
| 2f | -2-OH- $C_6H_4$ | $C_{28}H_{24}N_2O_6$ | 484.5 | 136 | 5.77 | 5.72 |
| 2g | -3-OH- $C_6H_4$ | $C_{28}H_{24}N_2O_6$ | 484.5 | 172 | 5.77 | 5.73 |
| 2h | -4-OH- $C_6H_4$ | $C_{28}H_{24}N_2O_6$ | 484.5 | 140 | 5.77 | 5.74 |
| 2i | -4-$OCH_3$-$C_6H_4$ | $C_{29}H_{26}N_2O_6$ | 498.5 | 122 | 5.61 | 5.58 |
| 2j | -4-$CH_3$- $C_6H_4$ | $C_{29}H_{26}N_2O_5$ | 482.5 | 135 | 5.80 | 5.76 |
| 2k | -3-$NO_2$- $C_6H_4$ | $C_{28}H_{23}N_3O_7$ | 513.5 | 78 | 8.10 | 8.04 |
| 2l | -4-$NO_2$- $C_6H_4$ | $C_{28}H_{23}N_3O_7$ | 513.5 | 90 | 8.10 | 8.02 |

**Table-2.**

| **Compd No.** | **Antibacterial activity (zone of inhibition in mm)** | | | | **Antifungal activity** |
|---|---|---|---|---|---|
| | **S.aureus** | **B.subtillis** | **E.coli** | **P.vulgaris** | **A.niger** |
| 1a | 10 | 17 | 17 | 15 | 16 |
| 1b | 18 | 14 | 15 | 18 | 15 |
| 1c | 20 | 15 | 15 | 16 | 14 |
| 1d | 16 | 17 | 18 | 13 | 13 |
| 1e | 14 | 10 | 19 | 18 | 20 |
| 1f | 15 | 12 | 13 | 17 | 15 |
| 1g | 18 | 16 | 16 | 15 | 17 |
| 1h | 19 | 18 | 15 | 16 | 18 |
| 1i | 12 | 16 | 19 | 19 | 18 |
| 1j | 13 | 19 | 16 | 15 | 16 |
| 1k | 18 | 15 | 15 | 14 | 17 |
| 1l | 12 | 17 | 17 | 11 | 19 |

| | | | | | |
|---|---|---|---|---|---|
| 2a | 13 | 14 | 17 | 11 | 19 |
| 2b | 13 | 14 | 17 | 13 | 15 |
| 2c | 19 | 16 | 19 | 14 | 13 |
| 2d | 19 | 28 | 20 | 15 | 11 |
| 2e | 16 | 13 | 17 | 18 | 23 |
| 2f | 17 | 13 | 15 | 19 | 11 |
| 2g | 15 | 17 | 14 | 19 | 16 |
| 2h | 14 | 17 | 13 | 16 | 14 |
| 2i | 21 | 21 | 17 | 14 | 14 |
| 2j | 21 | 21 | 17 | 14 | 14 |
| 2k | 18 | 21 | 19 | 11 | 12 |
| 2l | 19 | 20 | 21 | 10 | 18 |
| Ampicillin | 22 | 20 | 21 | 24 | 0 |
| Amoxicillin | 20 | 23 | 22 | 21 | 0 |
| Norfloxacin | 19 | 20 | 23 | 22 | 0 |
| Benzyl penicillin | 21 | 21 | 19 | 18 | 0 |
| Griseofulvin | 0 | 0 | 0 | 0 | 25 |




**Scheme-1.**

## CONCLUSION

The present study leads to a convenient synthetic method for the synthesis of new compounds. Which show significant antibacterial and antifungal activity. Further investigation with appropriate structural modification of the above compounds may result in therapeutically useful products.

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