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# ECOFRIENDLY MICROWAVE ASSISTED SYNTHESIS OF 7-(SUB-PHENYL)-6-(SUB-BENZOYL)-5-METHYL-2,4,7-TRIHYDRO-3,4,8-TRIAZAINDEN-1-ONES

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## ABSTRACT

Cyclocondensation has been carried out for the synthesis of novel ring junction N-substituted pyrimidine derivatives viz. 7-(Sub-phenyl)-6-(sub-benzoyl)-5-methyl-2,4,7-trihydro-3,4,8-triazainden-1-ones III(1-16) by using microwave assisted method in presence of $POCl_3$ + PPA mixture acts both as a catalyst and as a solvent which makes the process ecofriendly, economic and easy.

**Keywords :** cyclocondensation, pyrimidine derivatives, Microwaves, ecofriendly.

## INTRODUCTION

Pyrimidine does not exist in nature but its different derivatives are found as a part of more complex systems and are widely distributed. Pyrimidines are an integral part of genetic materials viz. DNA and RNA. Their analogues have been extensively studies over a century. In the family of heterocyclic compounds, pyrimidines and their ring fused derivatives are an important class of compounds in medicinal and pharmaceutical chemistry and have been reported to exhibit a broad spectrum of biological activities[1], possessing antiproliferative[2], antiviral[3], antitumor[4], antiinflammatory[5], analgesic[6], antibacterial[7], antifungal[8], antihistaminic[9], antiHIV[10], blood platelet disaggregation[11], calcium channel blockers[12], antihypertensive[13],also used for treatment of neurological , psychiatric disorder[14] and hyper uricemia[15] etc. as well as fused pyrimidines are used in a variety of agrochemicals, natural and veterinary products[16]. The use of microwave energy to accelerate the organic reactions is of increasing interest and offers several advantages over conventional heating techniques[17] like many fold reduction in reaction time, easy workup and so cleaner products.[18-20]

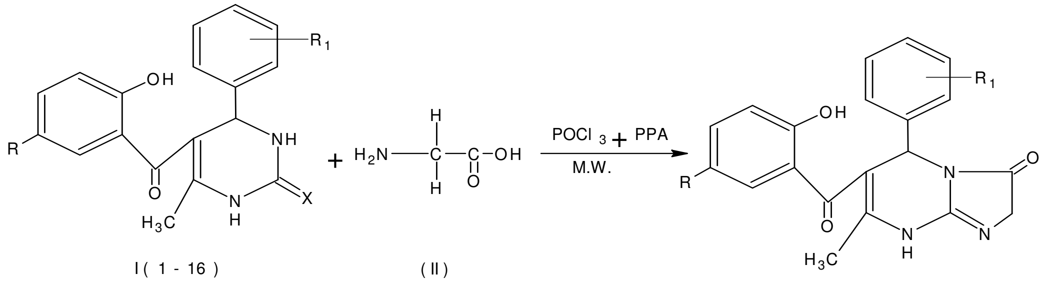
Microwave provide an alternative green approach to environmentally unaccepted procedures using toxic and expensive reagents leading to higher atom economy. A large number of condensation reactions had been carried out by microwave irradiation. In the last few years there has been a growing interest in the use of microwave heating in organic synthesis.

Keeping in view the advantages of microwave heating and pyrimidines as a integral part of genetic materials viz. DNA and RNA, in the present investigation we have carried out the synthesis of some ring junction N-substituted pyrimidine derivatives viz. 7-(Sub-phenyl)-6-(sub-benzoyl)-5-methyl-2,4,7-trihydro-3,4,8-triazainden-1-ones III(1-16) by cyclocondensation of various 6-Methyl-5-(sub-benzoyl)-4-(sub-phenyl)-3,4-dihydro-1-H-pyrimid-2-one/thiones**I(1-16)**with amino acid such as glycine in presence of PPA and $POCl_3$ mixture[21] under microwave irradiation so as to minimize the pollution.

## EXPERIMENTAL

The melting points reported are uncorrected and were taken in open capillaries. The IR spectra were recorded on instrument model- Spectrum one, serial no-68515 using KBr palates. The UV spectra were recorded on Systronic spectrophotometer-119. $^1$H-NMR spectra were recorded on Varian mercury spectrometer YH-300 MHz. The elemental analysis was carried out on Perkin-Elmer-2400 CHN analyzer. The purity of the products and progress of the reaction was monitored by TLC on silica gel plates and HPLC. The reactions were carried out in scientific microwave oven (RG31L1, 700W, 2450 MHz).

**General Procedure for the synthesis of 7-(Sub-phenyl)-6-(sub-benzoyl)-5-methyl-2,4,7-trihydro-3,4,8-triazainden-1-ones III(1-16)** – A mixture of 6-methyl-5-(sub-benzoy)-4-(sub-phenyl)-3,4-dihydro-1-H-pyrimid-2-one/thione (0.01Mole) and glycine (0.01mole) was suspended in reaction flask containing $POCl_3$ (0.05 mole) and catalytic amount of freshly prepared PPA. Then reaction mixture was exposed to microwaves at medium high power for 1-3 minutes till the HCl evolution subsides. After completion of reaction, reaction mixture was allowed to cool upto 25 $^0$C, diluted with water and neutralized by ammonia solution. Finally Crude product was filtered,dried and recrystallized from methanol.



I ( 1 - 16 )

( II )

III ( 1 - 16 )

Where,
R = CH $_3$, Cl
R$_1$ = H, 2 - OH, 4 - OH, 4 - NO $_2$
X = O, S

Scheme-1

Table-1: Characterization data of 7-(Sub-phenyl)-6-(sub-benzoyl)-5-methyl- 2,4,7-trihydro -3,4,8-triazainden-1-ones III(1-16)

| Compd.<br>III(1-16) | R | R$_1$ | X | M.W. time (min.) | Yield (%) | M.P. ($^0$C) |
|---|---|---|---|---|---|---|
| 1 | -$CH_3$ | H | O | 1.5 | 85 | 220$^0$C |
| 2 | -$CH_3$ | 2-OH | O | 1.0 | 87 | 217$^0$C |
| 3 | -$CH_3$ | 4-OH | O | 1.5 | 86 | 237$^0$C |
| 4 | -$CH_3$ | 4-$NO_2$ | O | 1.5 | 82 | 245$^0$C |
| 5 | -$CH_3$ | H | S | 1.0 | 83 | 207$^0$C |
| 6 | -$CH_3$ | 2-OH | S | 1.5 | 86 | 213$^0$C |
| 7 | -$CH_3$ | 4-OH | S | 1.5 | 85 | 231$^0$C |
| 8 | -$CH_3$ | 4- $NO_2$ | S | 2.0 | 86 | 222$^0$C |
| 9 | Cl | H | O | 1.5 | 86 | 213$^0$C |
| 10 | Cl | 2-OH | O | 1.0 | 87 | 232$^0$C |
| 11 | Cl | 4-OH | O | 1.0 | 81 | 217$^0$C |
| 12 | Cl | 4-$NO_2$ | O | 2.0 | 82 | 238$^0$C |
| 13 | Cl | H | S | 1.5 | 81 | 225$^0$C |
| 14 | Cl | 2-OH | S | 1.5 | 84 | 237$^0$C |
| 15 | Cl | 4-OH | S | 2.0 | 86 | 239$^0$C |
| 16 | Cl | 4-$NO_2$ | S | 2.5 | 88 | 258$^0$C |

## RESULTS AND DISCUSSION

Cyclocondensation, in presence of $POCl_3$ and PPA is a versatile method for the preparation of ring junction N-substituted pyrimidine derivatives.[22-24] Cyclo-condensation does not proceed in $POCl_3$ or PPA alone and similar is true in the one pot synthesis of title compounds III(1-16)**.** Maximum yields of III(1-16) can be achieved by using a mixed reagent.

The mixed reagent already been used for the preparation of several nitrogen bridgehead system but its scope has not been studied in detail. The present investigation gives the importance of mixed reagent in the preparation of ring junction N-substituted pyrimidine derivatives. The yields are maximum in one step process (80 – 90%) and cleaner products are obtained. Furthermore its use in presence of microwave irradiation makes the process eco-friendly, economic and makes a new path in green chemical transformation. The structures of prepared novel compounds were confirmed by using IR,NMR and UVspectroscopic data and elemental analysis.

The IR spectrum of compound 7-(2-hydroxyphenyl)-6-(2'-hydroxy-5'-methyl benzoyl)-5-methyl-2,4,7-trihydro-3,4,8-triazainden-1-one III(2) showed prominent peaks at 3351 cm$^{-1}$ (-OH stret.) 2945 cm$^{-1}$ (-C-H stret.), 1654 cm$^{-1}$ (C=O stret.),1416 cm$^{-1}$ (C=Cstret.), 1114 cm$^{-1}$ (-C-O stret), 1028 cm$^{-1}$ (-C-N stret.), 665 cm$^{-1}$(C=C-N stret). $^1$H- NMR spectrum of III(2) showed a characteristic singlet for –N-H at $\delta$ 0.6, singlet for $CH_3$- at $\delta$ 2.37, singlet for Ar-$CH_3$ at $\delta$ 2.27, singlet for O=C-$CH_2$ at $\delta$3.96 , singlet for –CH proton at $\delta$ 2.35, multiplet for seven aromatic protons at $\delta$ 6.76 – 7.46, singlet for aromatic –OH at $\delta$ 15.45 and singlet for aldehydic –OH at $\delta$ 15.75.The UV spectrum of III (2) showed $\lambda_{max}$ corresponding to n $\pi^*$ transition.

The IR spectrum of compound 7-phenyl-6-(2'-hydroxy-5'-chlorobenzoyl)-5-methyl-2,4,7-trihydro-3,4,8-triazainden-1-one III (9) showed prominent peaks at 3431 cm$^{-1}$ (-OH stret.), 3020 cm$^{-1}$ (-C-H stret.), 1653 cm$^{-1}$ (C=O stret.), 1506 cm$^{-1}$ (C=C stret.), 1404 cm$^{-1}$ (-C-O stret.), 1022 cm$^{-1}$ (-C-N stret), 757 cm$^{-1}$ (C-Cl). $^1$H NMR spectrum of III (9) showed a characteristic singlet at $\delta$ 0.89 for-NH, singlet for $CH_3$- at $\delta$ 2.41, singlet for O=C-$CH_2$ at $\delta$ 3.74, singlet for –CH proton at $\delta$ 1.26, multiplet for aromatic protons at $\delta$ 7.27-7.61, singlet for aromatic –OH at $\delta$ 6.16. The UV spectrum of III(9) showed $\lambda$max corresponding $n \rightarrow \pi^*$ transition .Elemental analysis satisfied the proposed structure.

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