# MICROWAVE ASSISTED SOLVENT FREE SYNTHESIS OF FEW THIAZOLE DERIVATIVES AS POTENT ANTIFUNGAL AGENT

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**ABSTRACT:-** In this research work one pot synthesis of 1,3-substituted thiazolidin-4-ones,(IVa-IVh) have been carried out from carbonyl compound, amine and thiocarboxylic acid in molar proportion under microwave irradiation for 1-2 minutes, in solvent free condition. In vitro assay of newly synthesized compound were carried out to test antifungal activity by disc diffusion method against Fusarium oxysporum and Rhizoctonia solani.

**Keywords:-** 1,3-thiazolidin-4-ones, microwave irradiation, antifungal Activity

## INTRODUCTION

Thiazoles are a familiar group of heterocyclic compounds possessing wide variety of biological activities, and their usefulness as medicines are well established. Thiazole nucleus is also an integral part of all the available penicillin's, which have revolutionized the therapy of bacterial diseases [1]. Thiazoles have attracted continuing interest because of their varied biological activities [2], which have found applications in the treatment of allergies [3], hypertension [4], inflammation [5], schizophrenia[6], microbial infections [7,8], HIV infections [9], hypnotics [10] and for the treatment of pain [11]. They have been also used as fibrinogen receptor antagonists with antithrombotic activity [12] and as new inhibitors of bacterial DNA gyrase B [13]. Recently reported studies on the microwave irradiation for the synthesis of heterocyclic compound revealed that it is safe, rapid, economic and convenient, eco-friendly method for chemical synthesis. Pollution free synthesis, lesser reaction time, easy workup and minimum use of solvent are the major advantages of this technique A serious constrain of this method is selection of

appropriate solvent, which can be avoided by synthesis under solid phase solvent free condition. These facts have promoted us to synthesize some new thiazolidiones using microwave irradiation under solvent free condition.

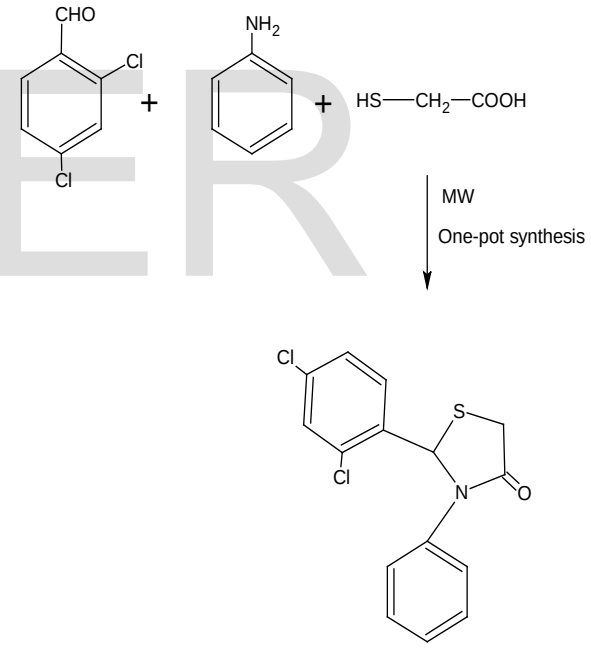
**EXPERIMENTAL –**

All the synthesized compounds have been characterized on the basis of chemical properties, elemental and spectral analysis. The melting points were measured in a open glass capillary and are uncorrected**.**IR spectra in KBr were recorded on instrument Perkin Elmer - Spectrum RX-IFTIR. $^{1}$H-NMR spectra were recorded on FT NMR Spectrometer model Advance-II (Bruker) Its $^{1}$H frequency is 400 MHz, while for $^{13}$C the frequency is 100 MHz. ($CDCl_3$ and DMSO-$d_6$) using TMS as an internal standard. All reactions were monitored by TLC using silica gel 60-f-254plates. All reactions were carried out in scientific microwave oven (Scientific microwave system model RG31lL1,700w, 2450MHz).satisfactory C,H,N analysis were carried out for most of the compounds on Thermo Scientific (FLASH 2000) CHN Elemental Analyzer at RSIC, Punjab university, Chandigarh.

**Table I: Physical data of synthesized 1,3-thiazolidin-4-ones**

| Compound | R | R' | M.P.($^0$C) | MOLECULAR FORMULA | YEILD(%) |
|---|---|---|---|---|---|
| 4a | -$C_6H_5$ | -$C_6H_5$ | 155 | $C_{15}H_{13}NOS$ | 85 |
| 4b | -$C_6H_5$ | -$C_6H_4Cl$ | 163 | $C_{15}H_{12}ClNOS$ | 80 |
| 4c | -$C_6H_5$ | -$C_6H_4Br$ | 145 | $C_{15}H_{12}BrNOS$ | 84 |
| 4d | -$C_6H_5$ | -$C_6H_3Cl_2$ | 169 | $C_{15}H_{11}Cl_2NOS$ | 82 |
| 4e | -$C_6H_5$ | -$C_4H_3O$ | 131 | $C_{13}H_{11}NO_2S$ | 83 |
| 4f | -$C_6H_5$ | -$C_2H_5$ | 123 | $C_{11}H_{13}NOS$ | 78 |
| 4g | -$C_6H_5$ | -$C_6H_4OH$ | 137 | $C_{15}H_{13}NO_2S$ | 76 |
| 4h | -$C_6H_5$ | -$C_6H_4OCH_3$ | 136 | $C_{16}H_{15}NO_2S$ | 84 |

**Synthesis of 2-(substituted phenyl)-3-phenylthiazolidin-4-one(**IVa-IVh**)** - A neat rection technology for one pot synthesis of the starting material 2-(substituted phenyl)-3-phenylthiazolidin)-4-one by condensation of aromatic aldehyde(0.01M), aniline(0.01M), and thioglycolic acid(0.01M). Reaction carried out under scientific microwave oven for 1-1.5 min. The reaction mixture was cooled at room temperature and poured in ice-cold water. The product thus separated out was filtered and crystallized from ethanol to get fine crystals of 2-(substituted phenyl)-3-phenylthiazolidin-4-one . (IVa-IVh)






## RESULT AND DISCUSSION -

Literature survey revealed that thiazolidiones belong to an important group

of heterocyclic compounds with diverse biological activity and synthesized by using multistep protocol. The present work describe solvent less one pot synthetic methodology towards the construction of series of thiazolidione derivative under microwave irradiation. This is a three Component reaction involving amino compound ,aldehyde and thioglycolic acid under M.W. irradiation .PMR spectra shows doublet at 3.23 and 3.30 due to germinal coupling of cyclic CH grp , a singlet for CH at 2.7 and aromatic protons with 7.0 to 7.5δ. singlet at 10.1 and a singlet at 3.7 also confirms the possibility of keto enol tautomerism in the molecule .IR frequency also agrees with the fact by showing frequencies at 1649 C=O(keto form), 3296(C-OH stretch (enol form) and other frequencies . $^{13}$CNMR spectra also showing two signals in aliphatic region 43.27(CH) and 28.34($CH_2$) WHERE AS 168.4 (C=O) ,slight lower values due to nitrogen and aromatic rings and 166.6 C-OH (enol form) furthermore confirms the keto enol tautomerism in the compounds,remaining signals are in the aromatic region 119 -138δ

The reaction has been suggested to proceed via imine formation followed by attack of sulphur nucleophile on the imine carbon. The reaction involves intramolecular cyclisation with the elimination of water to give thiazolidione derivative. Microwave irradiation facilitate the easy removal of water within few minute.

**1) 2-(2,4-dichlorophenyl)-3-phenylthiazolidin-4-one(IVd)-**

brown crystalline solid, M. P..169$^0$C,IR in $cm^{-1}$ - 3296 [C-OH stretch (enol form)], 3089,3146 (C-H aromatic stretch), 2944,2876 (C-Stretch aliphatic), 1804-1949 (Combination band), 1649 C=N, 1649 C=O(keto form), 1598,1551,1482 (C=C), 1333 (C-N), 903(1,2,4trisubstituted oop),692(monosubstitued oop)

$^1$HNMR400 MHz (CDCl3): -Chemical Shift (δ)-2.7 ( s,1H, CH) , 3.30(dd,1H,CH) ,3.23(d,1H,CH) ,3.7(s,1H, =CH) ,7.0 - 7.5(m,8H, Ar-H) , 10.1[s,1H, C-OH(enol)]

$^{13}$CNMR-100 MHz.($CDCl_3$andDMSO$d_6$) - Chemical Shift(δ)-43.27, 28.34, 168.4, 138.9, 128.3, 119.27, 123.43, 128.54, 138.6, 119.07, 128.55, 123.24, 128.55, 119.07

Observed %C= 55.54, %N=4.12, %S=9.85, %Cl =21.84, %H=3.41, %O=4.81

Calculated %C= 55.57, %N=4.32, %S=9.89, %Cl =21.87, %H=3.42, %O=4.93

**ANTIFUNGAL ACTIVITY**-: All the synthesized compounds were screened for their antifungal activity viz. *fusarium oxysporum, Rhizoctonia solani* by using disc diffusion method for their antifungal activity.The punch discs of 6.25 mm diameter of Whatman filter paper no. 1 were prepared and dispensed in the batches of 100 each in screw capped bottles. These were sterilized by dry heat at $140^0$C for 60 minutes. The solutions of 1000 ppm and 100 ppm concentrations of test compounds were prepared in dimethyl formamide (DMF) solvent separately. The discs were soaked, assuming that each disc will contain approximately 0.01 ml of test solution

**Table 2 - In vitro antifungal screening of above tested compounds**

| Sr.No. | Tested Compounds | Fungus (zone of inhibition in mm) | | | |
|---|---|---|---|---|---|
| | | *Fusarium oxysporum* | | *Rhizoctonia solani* | |
| | | 100 ppm | 1000 ppm | 100ppm | 1000ppm |
| 1 | IVa | 8 | 12 | 10 | 13 |
| 2 | IVb | 20 | 22 | 22 | 23 |
| 3 | **IVc** | 18 | 19 | 20 | 21 |
| 4 | IVd | - | 3 | 6 | 10 |
| 5 | IVe | **21** | **28** | **20** | **28** |
| 6 | IVf | 18 | 18 | 19 | 21 |
| 7 | IVg | **19** | **27** | **22** | **29** |
| 8 | IVh | 11 | 15 | 12 | 18 |

The observations show that activity of compound IVe and IVg are maximum against both the fungi . Almost all the compounds were active against all the test pathogens. The compound IVe and IVg is the most dominant among all the test compounds. Their inhibitory impact on the bacterial growth is remarkable.

**CONCLUSION**-: This was an attempt to synthesize biologically potential heterocyclic moiety in solvent free reaction condition that leads to considerable saving in the reaction time and energetically

profitable. The solvent free condition contributes to saving in cost, time and diminishes the waste disposal problem and environmental pollution this work may bring research fraternity towards sustainable development.

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