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**Research Article**

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# Microwave Assisted One Pot Synthesis of 2,3- Diaryl-1,3-Thiazolidine-4-Ones

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**ABSTRACT**

*Recently, we have carried out operationally simple, efficient, one pot synthesis of 2,3- diaryl-1,3-thiazolidine-4-ones by condensation of substituted aromatic amines and aldehydes in presence of thioglycolic acid with solid catalyst anhydrous zinc chloride in dioxane by microwave irradiation for 10 min. The yields of the products were excellent. The structure of the synthesized compounds has been established on the basis of IR, NMR, $C^{13}$ NMR spectroscopic techniques. The antimicrobial activities of the synthesized compounds were tested in vitro against the sensitive organisms Staphylococcus aureus (Gram positive bacteria) and Escherichia coli (Gram negative bacteria) by using the disc diffusion method.*

**Keywords:** Thiazolidinones; *S. aureus*; *E. coli*; Microwave

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## INTRODUCTION

The 4-thiazolidinones can be synthesized by conventional as well as non-conventional route leading to their formation by the reaction between an amine, a carbonyl compound and thio-glycolic acid. The presence of 1,3-thiazolidin-4-ones is seen in number of chemicals used as drugs. The reactions begin by formation of an imine which in its turn undergoes attack by generated sulfur nucleophile, followed by intramolecular cyclization with elimination of water. It is revealed that C-2 and N-3 substituted thiazolidinones possess diverse degrees of inhibition against bacteria and fungi. It is also observed that substitution with electron-withdrawing group/s on aromatic ring presented varied degrees of inhibition against Gram-positive and Gram-negative bacteria. There is much scope in this promising substituted thiazolidine-4-one moieties and hence have received considerable attention during last few years as they are gifted with variety of activities and have wide range of therapeutics properties. Thiazolidine-4-one and its derivatives are very important in medicinal chemistry because of their varied biological activities and pharmacological properties i.e. Antifungal [1], Antioxidant [2] Anti-inflammatory [3], Anti YFV (yellow fever virus) activity [4], Antibacterial [5,6], Antitubercular [7,8], Antimicrobial [9-11]. With extensive literature search, it was presumed that the thiazolidine-4-Ones substituted with aryl groups which themselves contain electron withdrawing substituents, at C-2 and N-3 positions might enhance the antimicrobial activity. Hence, we have synthesized a few thiazolidine-4-one derivatives from various amines and aldehydes by employing microwave irradiation, a greener synthetic root.

## EXPERIMENTAL SECTION

All chemicals were of synthetic grade (S.D. Fine Chem. Ltd. Mumbai, India). Melting points were determined by electro-thermal apparatus and are uncorrected. Products were recrystallized from absolute ethanol as a solvent. The purity of compound was checked by the TLC on silica gel G plates. These derivatives were purified by column chromatography on silica gel (60-120 mesh). The compounds were characterized by using IR, $^1$H NMR and mass spectral analysis. IR spectra were recorded on Perkin-Elmer spectrum in the form of KBr Pellet. $^1$H NMR was recorded in $CDCl_3$ on Perkin-Elmer R-32 spectrum using TMS as internal standard.

**Experimental Procedure**

**General procedure for synthesis of 2,3-(substituted )diaryl-1,3-thiazolidine-4-ones:**

To the mixture of an amines (0.01 mol), an aldehydes (0.01 mol), and thioglycolic acid (0.01 mol) dissolved in 1,4 dioxane (20 ml), a pinch of anhydrous zinc chloride was added and was irradiated in microwave oven for 10 minutes. The progress of the reaction was monitored by TLC. Depending upon the need, heating in the microwave was carried on for some more time (1-2 min.). The reaction mixture was cooled and poured in ice, filtered, washed with water and dried.

**Spectral data of representative compounds:**

**2-(2-Nitrophenyl)-3-(4- Chlorophenyl)-1,3-thiazolidin-4-one ( 1a ): IR** (KBr) : 2921 (C-H), 1675 (>C=O), 1495 (-$NO_2$), $cm^{-1}$; **1H NMR**($CDCl_3$): δ, 4.0 (s, 2H), 6.1 (s, 1H), 7.2-7.4 (m, 8H );**$^{13}$C NMR**($CDCl_3$) : δ, 171.23, 149.71, 141.65, 138.57, 132.89, 129.27, 128.99, 128.42, 126.44, 124.47, 64.76, 33.43.

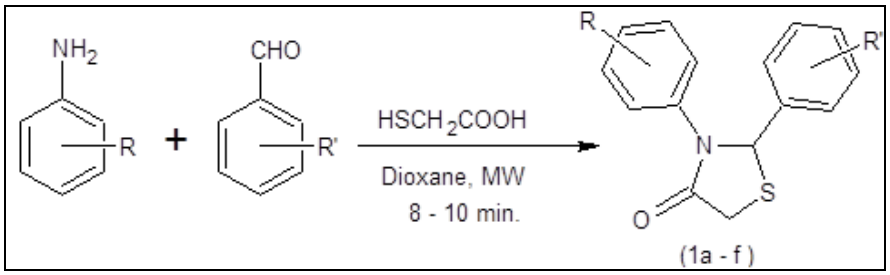
**2-(4-Bromophenyl)-3-(4- Chlorophenyl)-1,3-thiazolidin-4-one (1b): IR** (KBr) : 2969 (C-H ), 1635 (>C=O), $cm^{-1}$ ; **$^1$H NMR** (CDCl3): δ 3.9 (s, 2H), 6.2 (s, 1H), 7.0-7.4 (m, 8H) ; **$^{13}$C NMR** ($CDCl_3$) : δ, 171.09, 139.73, 137.11, 133.00, 129.09, 128.87, 127.21, 119.00, 56.04, 47.37.

**2-(2-Chlorophenyl)-3-(4- Chlorophenyl)-1,3-thiazolidin-4-one (1c): IR** (KBr) : 2969 (C-H), 1635 (>C=O), $cm^{-1}$ .**$^1$H NMR** ($CDCl_3$): δ 3.9 (s, 2H), 6.2 (s, 1H), 7.0-7.4 (m, 8H). **NMR** (CDCl3) : δ 171.09, 139.73, 137.11, 133.00, 129.09, 128.87, 127.21, 119.00, 56.04, 47.37.

**2-(2-Nitrophenyl)-3-(4- Bromophenyl)-1,3-thiazolidin-4-one(1d): IR** (KBr) : 2921 (C-H), 1675 (>C=O), 1495 ($NO_2$), $cm^{-1}$.**1H NMR** ($CDCl_3$) : δ, 4.0 (s, 2H), 6.1 (s, 1H), 7.2-7.4 (m, 8H) .**$^{13}$C NMR** ($CDCl_3$) : δ 171.23, 149.71, 141.65, 138.57, 132.89, 129.27, 128.99, 128.42, 126.44, 124.47, 64.76, 33.43.

**2-(4-Nitrophenyl)-3-(4- Bromophenyl)-1,3-thiazolidin-4-one (1e):IR** (KBr) : 2921 (C-H ), 1675 (>C=O), 1495 (-$NO_2$), $cm^{-1}$. **1H NMR** ($CDCl_3$) : δ,4.0 (s, 2H), 6.1 (s, 1H), 7.2-7.4 (m, 8H) .**$^{13}$C NMR** ($CDCl_3$) : δ 171.23, 149.71, 141.65, 138.57, 132.89, 129.27, 128.99, 128.42, 126.44, 124.47, 64.76, 33.43.

**2-(4-Bromophenyl)-3-(4- Bromophenyl)-1,3-thiazolidin-4-one (1f): IR** (KBr) : 2969 (C-H), 1635 (>C=O), $cm^{-1}$ .**1H NMR** ($CDCl_3$): δ,3.9 (s, 2H), 6.2 (s, 1H), 7.0-7.4 (m, 8H). **NMR** ($CDCl_3$): δ, 171.09, 139.73, 137.11, 133.00, 129.09, 128.87, 127.21, 119.00, 56.04, 47.37.




**a] R = 4-Cl, R$^/$ = 2-$NO_2$ b] R = 4-Cl, R$^/$ = 4-Br c] R = 4-Cl, R$^/$ = 2-Cl**

**d] R = 4-Br, R$^/$ =2-$NO_2$ e] R = 4-Br, R$^/$ = 4-$NO_2$ f] R = 4-Br, R$^/$ = 4-Br**

## RESULTS AND DISCUSSIONS

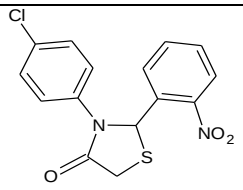
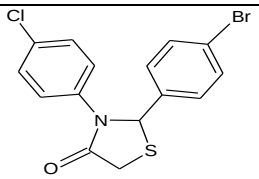
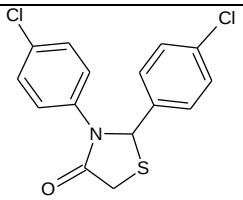
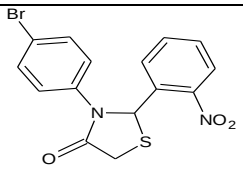
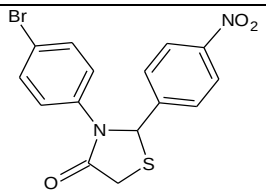
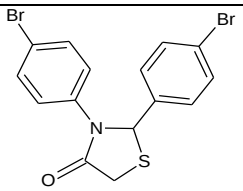
Cyclocondensation seems to be critical step for obtaining high yields of 4-thiazolidinones. So, microwave technique and various dehydrating agents may be used for improving yields. Direct and rapid heating by microwave irradiation makes it an ideal tool in organic synthesis as microwave heating has been shown to dramatically reduce reaction times, increase product yields, rapid optimization of conditions and enhance product purities by reducing unwanted side-reactions compared with conventional heating methods. Hence we have employed this protocol for one pot synthesis of targeted compounds.

Equimolar quantities of an amine, an aldehyde and thioglycolic acid were dissolved in dioxane. The mixture was heated in a microwave oven after adding a pinch of anhydrous zinc chloride to it to yield the product, as presented in scheme. Synthesised compounds were screened for antimicrobial activities against *E. coli* as Gram negative bacteria and *S. aureus* as Gram positive bacteria. The structures of synthesized compounds have been elucidated on the basis of spectral ($^1$H NMR, IR, Mass) and elemental analysis.

The yield of all synthesized compounds were found to be in the range of 70-89% and this was achieved, as expected, in very short time (10 min). The titled compounds were characterized by melting points and Rf values by using Ethyl acetate (20%) and n- hexane (80%) as a solvent system.

The synthesized derivatives (a-f) were established on the basis of elemental analysis and IR, NMR and Mass spectral analysis. The assigned structures were supported by spectral data. The singlet at 3.9 ppm due to $–CH_2$, at 6.2 ppm due to –CH and multiple in the range of 7.0-7.4 proved the formation of thiazolidine ring. The IR bands at 1675 $cm^{-1}$ for >C=O and at 2921 for C-H also appeared in usual region and supported the conclusion (Table 1).

**Table 1: Synthesis of 2,3-(substituted ) diaryl-1,3-thiazolidine-4-ones (1a-!f)**

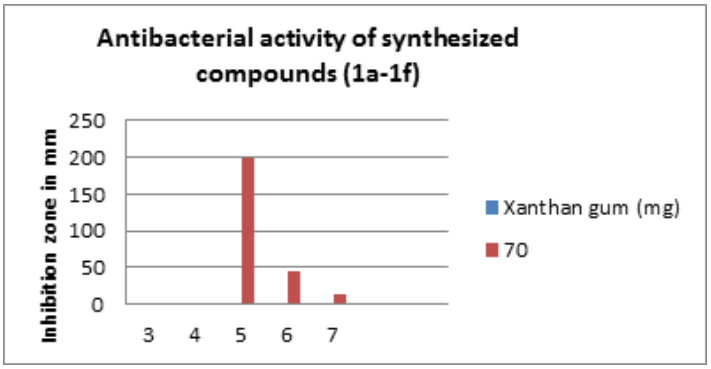
| Sr.No. | Entry | Compound | Yield (%) | M.P. °C |
|---|---|---|---|---|
| 1 | 1a |  | 72 | 126 |
| 2 | 1 b |  | 89 | 115 |
| 3 | 1c |  | 77 | 132 |
| 4 | 1d |  | 70 | 160 |
| 5 | 1e |  | 82 | 142 |
| 6 | 1f |  | 84 | 158 |

Mass spectra of thiazolidine- 4-one derivatives were useful and revealed molecular ion peaks corresponding to molecular formulae. Compounds containing -Cl showed (M+ and M+2) peaks in 3:1 and those with Br showed (M+ and M+2) peaks in1:1 ratio. As regards the biological activities, the synthesized compounds (1a-1f) were screened for their antimicrobial activities by using cup plate method. They were screened for Gram positive bacteria, *Staphylococcus aureus* and Gram negative bacteria viz. *Escherichia coli* by measuring the zone of inhibition at concentrations 100 mg/ml. The standard used for comparison was streptomycin. The compounds b, e, and f with electron withdrawing groups at position 4, in both the aryl substituents exhibited quiet good activity against *S. aureus* while compounds a and d showed moderate activity against *E. coli*. Compound c

exhibited equal activity against both the type of bacteria. Rest of the synthesized compounds from the list showed poor potency against both the kind of bacteria (Table 2).

**Table 2: Antibacterial activity of synthesized compounds (1a-1f)**

| Comp. (100 µg/ml) | Antibacterial activity(mm) | |
|---|---|---|
| | ***S.aureus*** | ***E.coli*** |
| 1a | 6 | 12 |
| 1b | 20 | 8 |
| 1c | 14 | 14 |
| 1d | 4 | 14 |
| 1e | 16 | 8 |
| 1f | 18 | 6 |
| Streptomycin | 23 | 22 |




## CONCLUSION

We have synthesized thiazolidine-4-one derivatives with substituted aryl moieties at 2 and 3 positions by resorting to the greener approach viz. microwave assisted irradiation which is one pot, simple and efficient protocol requiring a short time and giving high yields. All synthesized compounds were screened for antimicrobial activities. A few of them exhibited quite good activity as predicted in the beginning. The yields of products were excellent (70-89%). The reagents utilized in the proposed method were readily available. All the compounds were characterized by using analytical techniques.

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