Available Online at

http://www.ijcpa.in

July - September 2016

DOI : http://dx.doi.org/10.21276/ijcpa

International Journal of CHEMICAL AND PHARMACEUTICAL ANALYSIS

eISSN: 2348-0726 ; pISSN : 2395-2466

Research Article | Volume-3 | Issue-4 | Article ID: 1053

# SYNTHESIS, CHARACTERIZATION AND ANTIMICROBIAL EVALUATION OF NOVEL 1,3,4-OXADIAZOLE DERIVATIVES

**Neha G. Solanki* and M. K. Thakor[1]**

[1]Municipal Arts and Urban Bank Science College, Mehsana (Guj.) India

***Corresponding Author:** Email: nehasl9434@gmail.com*

Received: 14 June 2016 / Revised: 12 September 2016 / Accepted: 20 September 2016 / Available online : 30 September 2016

**ABSTRACT**

*The title heterocyclic compounds (3a-h) namely 3-((4-(3,5-diphenyl-3,3a-dihydrothiazolo[4,5-c]isoxazol-6(5H)-yl)phenyl)sulfonyl)-5-methyl-1,3,4-oxadiazole-2(3H)-thione were prepared by treatment of hydroxyl amine with phenylidine derivative (2a-h) containing oxadiazolo-sulfonyl-thiazolidinones nucleus. All the compounds were studied for spectral studies and monitored for antimicrobial activity.*

***Keywords*** *– 1,3,4-Oxadiazole, Spectral studies, Thiazolidinones, Hydroxyl amine, Antimicrobial activities.*

## 1. INTRODUCTION

Oxadiazole derivatives exhibit an broad spectrum of biological activities as well as pharmaceutical applications *viz.* antibacterial, antifungal, anti-inflammatory, antitubercular, anti-HIV, anticancer and anticonvulsant activities etc[1-6]. Recently, thiazolidinones containing other heterocyclic systems were also reported to possess useful biological activities[7-10]. Compounds containing oxadiazole and thizolidinone nucleus were reported to number of biological activities like, such as antibacterial, antifungal and anti-inflammatory activity[11-13]. Hence, it was thought of interest to prepared novel oxadiazolo-sulfonyl-thiazolidinones moieties which may enhance the drug activity of compounds. In continuation of our previous work[14], the present article discuss about synthesizes and characterization of 3-((4-(3,5-diphenyl-3,3a-dihydrothiazolo[4,5-c]isoxazol-6(5H)-yl)phenyl)sulfonyl)-5-methyl-1,3,4-oxadiazole-2(3H)-thione (3a-h) derivatives. Also the antimicrobial evaluation of all synthesized compounds was carried out. The synthetic approach is shown in **Scheme-1**.

## 2. EXPERIMENTAL

3-(4-(5-methyl-2-thioxo-1,3,4-oxadiazole-3(2H)-ylsulfonyl)phenyl)-2-phenyl thiazolidin-4-one **(1)** was prepared according to method reported in literature [14]. All other chemicals used were of laboratory grade. The melting point was determined by open capillary tube method.

**2.1 Preparation of 3-(arylmethylene)-3-(4-(5-methyl-2-thioxo-1,3,4-oxadiazole-3(2H)-yl sulfonyl) phenyl)-2-phenyl thiazolidin-4-one (2a-h):**

A mixture of 3-(4-(5-methyl-2-thioxo-1,3,4-oxadiazole-3(2H)-ylsulfonyl)phenyl)-2-phenylthiazolidin-4-one **(1)**, (0.01mole) with different aromatic aldehydes in ethanol (30ml) was refluxed on a water bath for 5-6 hrs. The solid mass separated out was filtered, washed with water and dried to give the desired compounds in range between 67-82% yields. The yields, melting points and elemental data of these compounds are given in **Table-1**.

**2.2 Preparation of 3-((4-(3,5-diphenyl-3,3a-dihydrothiazolo[4,5-c]isoxazol-6(5H)-yl) phenyl) sulfonyl)-5-methyl-1,3,4-oxadiazole-2(3H)-thione (3a-h):**

The reaction mixture of 3-(arylmethylene)-3-(4-(5-methyl-2-thioxo-1,3,4-oxadiazole-3(2H)-ylsulfonyl)phenyl)-2-phenylthiazolidin-4-one **(2a-h)** (0.01 mol) in ethanol (50 mL) containing hydroxyl amine (0.01 mol) was reflux on a steam-bath for 4-5 hours. Ethanol was removed by distillation under reduced pressure. The product was filtered, washed with water and recrystallized from ethanol to get the desired compound **3-((4-(3,5-diphenyl-3,3a-dihydrothiazolo[4,5-c]isoxazol-6(5H)-yl)phenyl)sulfonyl)-5-methyl-1,3,4-oxadiazole-2(3H)-thione (3a-h)**, which were obtained in range between 62-73% yield. The yields, melting points and elemental data of these compounds are given in **Table-2**.

## 3. BIOLOGICAL SCREENING

### 3.1 Antibacterial activities

The antibacterial activities of all the compounds were studied against gram-positive bacteria and gram-negative bacteria at a concentration of 50µg/ml by agar cup plate method. A methanol system was used as control in this method. Similar conditions using tetracycline as a control was used standard for comparison. The area of inhibition of zone measured in cm. Compounds **3d** was found more toxic for microbes. Other compounds found to be less or moderate active than tetracycline **Table-3**.

### 3.2 Antifungal Activities

The fungicidal activity of all the compounds was studied at 1000 ppm concentration in vitro. Plant pathogenic organisms used were *Candida albicans, Aspergillus niger and Aspergillus clavatus, and Fusarium oxyporium*. The antifungal activities of all the compounds **(3a-h)** were measured on each of these plant pathogenic strains on a potato dextrose agar (PDA) medium. Such a PDA medium contained potato 200g, dextrose 20g, agar 20g and water 1c. Five days old cultures were employed. The compounds to be tested were suspended (1000ppm) in a PDA medium and autoclaved at $120^{o}$ C for 15 min. at 15 atm. pressure. These media were poured into sterile Petri plates and the organisms were inoculated after cooling the Petri plates. The percentage inhibition for fungi was calculated after five days using the formula given below:

**Percentage of inhibition = 100(X-Y) / X**

Where, X = Area of colony in control plate

Y = Area of colony in test plate

The fungicidal activity displayed by various compounds **(3a-h)** is shown in **Table-4**.

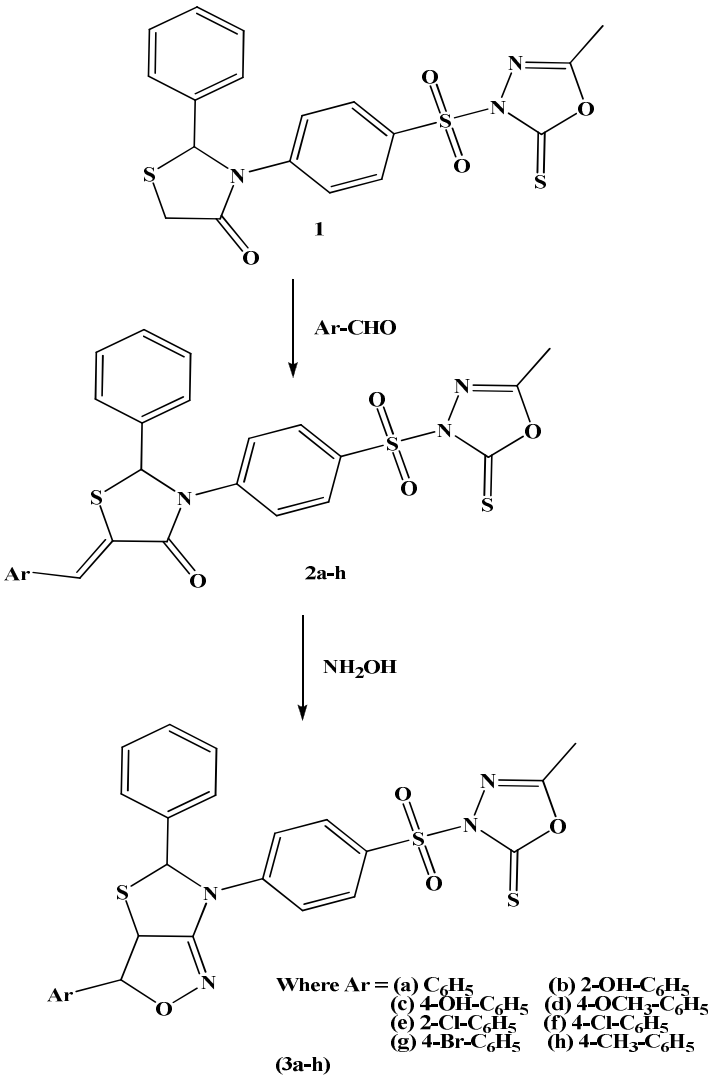
## 4. RESULTS AND DISCUSSION

3-(arylmethylene)-3-(4-(5-methyl-2-thioxo-1,3,4-oxadiazole-3(2H)-ylsulfonyl) phenyl)-2-phenylthiazolidin-4-one **(2a-h)** derivatives derived by condensation of 3-(4-(5-methyl-2-thioxo-1,3,4-oxadiazole-3(2H)-ylsulfonyl)phenyl)-2-phenylthiazolidin-4-one **(1)** with different substituted aromatic aldehydes. The structures assigned to intermediate were supported by the elemental analysis and IR spectra showing an absorption bands at 3415, 3418 (OH), 3035-3070 $cm^{-1}$ (C-H, of Ar), 2950,1370 $cm^{-1}$ (-$CH_3$), 2824 $cm^{-1}$ (-$OCH_3$), 1685-

1695 $cm^{-1}$ (C=O of thiazolidinone ring), 1635-1650 $cm^{-1}$(C=N), 1552-1568 $cm^{-1}$ (C=C), 1168 $cm^{-1}$ (C=S), 1078 $cm^{-1}$ (C-Cl), 1051 $cm^{-1}$ (C-Br), ~720 $cm^{-1}$ (C-S-C of thiazolidinone ring). **$^1$H NMR :** 7.30-8.25 (m,15H,Ar-H), 5.7 (s,1H,CH), 2.18 (s,3H,$CH_3$), 2b; 5.25 (s,1H,OH), 2c: 5.28 (s,1H,OH), 2d; 3.78 (s,1H,$OCH_3$). The C, H, N, S analysis data of all compounds from **Table-1** equivalent with their predicted structures.

3-((4-(3,5-diphenyl-3,3a-dihydrothiazolo[4,5-c]isoxazol-6(5H)-yl)phenyl)sulfonyl)-5-methyl-1,3,4-oxadiazole-2(3H)-thione **(3a-h)** was prepared by reaction of 3-(arylmethylene)-3-(4-(5-methyl-2-thioxo-1,3,4-oxadiazole-3(2H)-ylsulfonyl)phenyl)-2-phenylthiazolidin-4-one **(2a-h)** with hydroxyl amine. The structures of **(3a-h)** were confirmed by elemental analysis and IR spectra showing an absorption band at 3415, 3418 (OH), 3035-3070 $cm^{-1}$ (C-H, of Ar), 2950,1370 $cm^{-1}$ (-$CH_3$), 2824 $cm^{-1}$ (-$OCH_3$), 1635-1650 $cm^{-1}$(C=N), 1168 $cm^{-1}$ (C=S), 1078 $cm^{-1}$ (C-Cl), 1051 $cm^{-1}$ (C-Br), ~720 $cm^{-1}$ (C-S-C of thiazolidinone ring). The thiazodinone carbonyl missing in 3a-h derivatives support the structure of desired derivatives. $^1$H NMR : 7.21-8.10 (m,14H,Ar-H), 5.7 (s,1H,CH), 4.8-5.2 (s,2H,CH of isoxazole), 2.15 (s,3H,$CH_3$), 2b; 5.27 (s,1H,OH), 2c: 5.32 (s,1H,OH), 2d; 3.81 (s,1H,$OCH_3$). The C, H, N, S analysis data of all compounds from **Table-2** equivalent with their predicted structures.

The examination of elemental analytical data reveals that the elemental contents are consistence with the predicted structure shown in **Scheme-1**. The IR data along with NMR spectrum also direct for assignment of the predicted structure. The Compound **3d** shows good antibacterial and antifungal activity.




**Scheme-1**

**Table 1 :** Analytical Data and Elemental Analysis of Compounds (2a-h)

| Compd. | Fun. Group | Yield | M.P. $^0$C | Elemental Analysis | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | %C | | % H | | %N | | %S | |
| | | | | Found | Calc. | Found | Calc. | Found | Calc. | Found | Calc. |
| **2a** | $C_6H_5$ (521) | 75 | 218 | 57.56 | 57.5 | 3.67 | 3.6 | 8.06 | 8.0 | 18.14 | 18.1 |
| **2b** | 2-OH-$C_6H_5$ (537) | 78 | 210 | 55.85 | 55.8 | 3.56 | 3.5 | 7.82 | 7.8 | 17.89 | 17.8 |
| **2c** | 4-OH-$C_6H_5$ (537) | 82 | 212 | 55.85 | 55.8 | 3.56 | 3.5 | 7.82 | 7.8 | 17.89 | 17.8 |
| **2d** | 4-$OCH_3$-$C_6H_5$ (551) | 72 | 205 | 56.61 | 56.5 | 3.84 | 3.8 | 7.62 | 7.6 | 17.44 | 17.4 |
| **2e** | 2-Cl-$C_6H_5$ (556) | 70 | 221 | 54.00 | 53.9 | 3.26 | 3.2 | 7.56 | 7.5 | 17.30 | 17.2 |
| **2f** | 4-Cl-$C_6H_5$ (556) | 71 | 219 | 54.00 | 54.0 | 3.26 | 3.2 | 7.56 | 7.5 | 17.30 | 17.2 |
| **2g** | 4-Br-$C_6H_5$ (598) | 67 | 225 | 50.00 | 49.9 | 3.02 | 3.0 | 7.00 | 7.0 | 16.02 | 15.9 |
| **2h** | 4-$CH_3$-$C_6H_5$ (535) | 72 | 214 | 58.30 | 58.2 | 3.95 | 3.9 | 7.84 | 7.8 | 17.96 | 17.9 |

** Uncorrected*

**Table 2 :** Physical properties and Elemental Analysis of Compounds (3a-h)

| Compd. | Fun. Group | Yield | M.P. $^0$C | Elemental Analysis | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | %C | | % H | | %N | | %S | |
| | | | | Found | Calc. | Found | Calc. | Found | Calc. | Found | Calc. |
| **3a** | $C_6H_5$ (536) | 70 | 224 | 55.95 | 55.9 | 3.76 | 3.7 | 10.44 | 10.4 | 17.93 | 17.9 |
| **3b** | 2-OH-$C_6H_5$ (552) | 72 | 215 | 54.37 | 54.3 | 3.65 | 3.6 | 10.14 | 10.1 | 17.41 | 17.4 |
| **3c** | 4-OH-$C_6H_5$ (552) | 73 | 217 | 54.37 | 54.3 | 3.65 | 3.6 | 10.14 | 10.1 | 17.41 | 17.3 |
| **3d** | 4-$OCH_3$-$C_6H_5$ (566) | 69 | 212 | 55.11 | 55.1 | 3.91 | 3.8 | 9.89 | 9.8 | 16.98 | 16.9 |
| **3e** | 2-Cl-$C_6H_5$ (571) | 68 | 228 | 52.58 | 52.5 | 3.35 | 3.3 | 9.81 | 9.8 | 16.84 | 16.8 |
| **3f** | 4-Cl-$C_6H_5$ (571) | 66 | 224 | 52.58 | 52.5 | 3.35 | 3.3 | 9.81 | 9.8 | 16.84 | 16.8 |
| **3g** | 4-Br-$C_6H_5$ (615) | 63 | 231 | 48.78 | 48.7 | 3.11 | 3.1 | 9.10 | 9.0 | 15.63 | 15.6 |
| **3h** | 4-$CH_3$-$C_6H_5$ (550) | 69 | 219 | 56.71 | 56.7 | 4.03 | 4.0 | 10.17 | 10.1 | 17.47 | 17.4 |

** Uncorrected*

**Table 3 :** Antibacterial Activity of Compounds (3a-h)

| Compounds | Gram +Ve | | Gram –Ve | |
|---|---|---|---|---|
| | *Bacillus subtilis* | *Staphylococcus aureus* | *Escherichia Coli* | *Salmonella typhi* |
| **3a** | 54 | 58 | 63 | 55 |
| **3b** | 62 | 61 | 67 | 64 |
| **3c** | 57 | 59 | 61 | 57 |
| **3d** | 73 | 75 | 79 | 81 |
| **3e** | 52 | 54 | 54 | 56 |
| **3f** | 54 | 58 | 55 | 56 |
| **3g** | 57 | 52 | 53 | 58 |
| **3h** | 59 | 55 | 59 | 60 |
| **Tetracycline** | 67 | 61 | 78 | 80 |

**Table 4 :** Antifungal Activity of Compounds (3a-h)

| Zone of Inhibition at 1000 ppm (%) | | | | |
|---|---|---|---|---|
| **Compounds** | ***Candida albicans*** | ***Aspergillus Niger*** | ***Aspergillus clavatus*** | ***Fusarium oxyporium*** |
| **3a** | 65 | 63 | 75 | 60 |
| **3b** | 64 | 67 | 65 | 62 |
| **3c** | 68 | 67 | 72 | 65 |
| **3d** | 76 | 78 | 72 | 75 |
| **3e** | 67 | 65 | 57 | 58 |
| **3f** | 68 | 67 | 60 | 60 |
| **3g** | 67 | 63 | 69 | 62 |
| **3h** | 65 | 63 | 75 | 60 |

## 5. CONCLUSION

The study of newly synthesized compounds were show moderate antibacterial and antifungal activities. 4-Thiazolidinone derivatives, was synthesized and characterized by different analytical techniques for their structure elucidation. Antibacterial and antifungal activities of these compounds indicated that compounds were found to be showing moderate activity against some bacteria compared to standard antibiotic drug.

## REFERENCES


**1.** K. A. Kumar, P. Jayaroopa, G. V. Kumar, *Int. J. ChemTech. Res.,***2012**, 4, 1782.

**2.** H. Khalilullah, M. J. Ahsan, Md. Hedaitullah, S. Khan, B Ahmad, Mini Rev. Med. Chem., **2012**, 12, 789.

**3.** P. Dholaria, K. Parikh, D. Joshi, *Int. J. Chemtech App.,* **2015**, 4, 1.

**4.** T. Chandra, N. Garg, S. Lata, K. K. Saxena, A. Kumar, Euro. J. Med. Chem., **2010**, 45, 1772.

**5.** P. J. Shah, *Oct. J. Env. Res.,* **2013**, 1, 205.

**6.** B. N. Sudha, C. Sridhar, V. G. Sastry, Y. S. R. Reddy, O. Sreevidya, S. Lavanya,

**7.** V.A. Jyothi, V. Nagesh, S. Sen, R. Chakraborty, *Ind. J. Chem.-B,* **2014**, 52B, 422.

**8.** D. Havrylyuk, B. Zimenkovsky, O. Vasylenko, C. W. Day, D. F. Smee, P. Grellier,

**9.** R. Lesyk, *Euro. J. Med. Chem.,* **2013**, 66, 228.

**10.** G. N. Masoud, A. M. Youssef, M. M. Abdel Khalek, A. E. Abdel Wahab,

**11.** M. Labouta, A. A. B. Hazzaa, *Euro. J. Med. Chem.,* **2013**, 22, 707.

**12.** K. S. Sharath Kumar, A. Hanumappa, M. Vetrivel, M. Hegde, Y. R. Girish, T. R.

**13.** Byregowda, S. Rao, S. C. Raghavan, K. S. Rangappa, *Bioorg. Med. Chem.,* **2015**, 25, 3616.

**14.** V. B. Arunlal, K. Vandana, C. R. Biju, Int. J. Curr. Pharm. Res., **2015**, 7, 1.

**15.** S. G. Kucukguzel, E. E. Oruc, S. Rollas, F. Sahin, A. Ozbek, *Euro. J. Med. Chem.,* **2002**, 37, 197.

**16.** Mohd. Amir, M. S. Y. Khan, M. S. Zaman, *Ind. J. Chem.,* **2004**, 43B, 2189.

**17.** S. Muralikrishna, P. Raveendrareddy, L. K. Ravindranath, S. Harikrishna, P. J. Rao, *Int. J. Chemtech. Res.,* **2014**, 6, 183.

**18.** S.D. Prajapati, M.K. Thakor, *J. Curr. Chem. Pharm. Sc.: **2013***, 3(3), 176-180