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# Synthesis and Biological Activity of Some Novel 4-(5-Mercapto-1,3,4-thiadiazol-2-yl)-2-phenyl-5-[2-phenylvinyl]-2,4-dihydro-3*H*-1,2,4-triazol-3-one

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**Abstract**: A novel and efficient route have been designed for the synthesis of 4-(5-mercapto-1,3,4-thiadiazol-2-yl)-2-phenyl-5-[2-phenylvinyl]-2,4-dihydro-3*H*-1,2,4-triazol-3-one. All the synthesized compound were characterized by elemental analysis, IR, $^{1}$H NMR, $^{13}$C NMR and mass spectra. All the synthesized products were evaluated for their antibacterial activity against *B. Subtilis* and *E.Coli* and antifungal activity against *A. niger* and *C.Albican* respectively. The results indicate that the present compounds may serve as better fungicides when compared to bactericides. The synthesized compounds have turned to be wonder by possessing antimicrobial properties.

**Keywords:** Sydnone, 1,3,4-Thiadiazole, Triazole, Antimicrobial activity.

## Introduction

The therapeutic effects of 1,2,4-triazole and 1,2,4-triazol-3-one containing compounds have been well studied for a number of pathological conditions including inflammation, cancer, pain, tuberculosis or hypertension[1-9]. In addition, it was reported that 1,3,4-thiadiazoles exhibit various biological activities possibly due to the presence of the C=N-C-S moiety[10]. Moreover, synthesis of triazoles fused to another heterocyclic ring has attracted wide spread attention due to their diverse applications as antibacterial, antidepressant, antiviral, antitumorial and anti-inflammatory agents, pesticides, herbicides dyes, lubricant and analytical reagents[11]. Among these, the commonly known systems are generally triazoles fused to pyridines, pyridazines, pyrimidines, pyrazines and triazines. Although there are not many triazoles fused to thiadiazines or thiadiazoles, a number of them are incorporated into

a wide variety of therapeutically important compounds possessing a broad spectrum of biological activities[12-15]. In this connection, some biheterocyclic compounds containing two 1,2,4-triazol-3-one rings or both 1,2,4-triazol-3-one and 1,3,4-thiadiazole rings have been synthesized in our laboratory as antimicrobial compounds[16].

Sydnones are a novel class of meso-ionic compounds with unique chemical and physical properties. A vast array of sydnone derivatives have been found to show varied biological properties[17], antioxidant activity[18] and liquid crystalline properties[19]. Furthermore, sydnones have been used as precursors in 1,3-dipolar additions,[20] material chemistry[21] and in battery applications[22]. In continuation of our effort to develop benign synthetic methods for sydnone and oxadiazolines[23] we report here a new series of 4-(5-mercapto-1,3,4-thiadiazol-2-yl)-2-phenyl-5-[(*E*)-2-phenylvinyl]-2,4-dihydro-3*H*-1,2,4-triazol-3-one containing 1,3,4-thiadiazole rings. It was interesting to study the influencing biological behaviors with various substituted oxadiazoles. Therefore, we felt it of interest to study the chemical reactivity of these heterocyclic 1,3,4-thiadiazole moieties.

## Experimental

Melting points were determined in one end open capillary tubes on a Buchi 530 melting point apparatus and are uncorrected. Infrared (IR) spectra were recorded for the compounds on Perkin Elmer Spectrum RXI Spectrophotometer in KBr. $^{13}$C nuclear magnetic resonance ($^{13}$C NMR) and $^{1}$H nuclear magnetic resonance ($^{1}$H NMR) spectra were recorded for the compounds on Advance bruker (300 MHz) instrument. Chemical shifts are reported in parts per million (ppm) using tetramethylsilane (TMS) as an internal standard. All the new compounds have given CHN analysis within ±0.4% of the theoretical values. The purity of the compounds was confirmed by thin layer chromatography using silica gel glass plates and a solvent system of benzene:ethanol (8:2). The spots were developed in iodine chamber and visualized under ultra violet lamp.

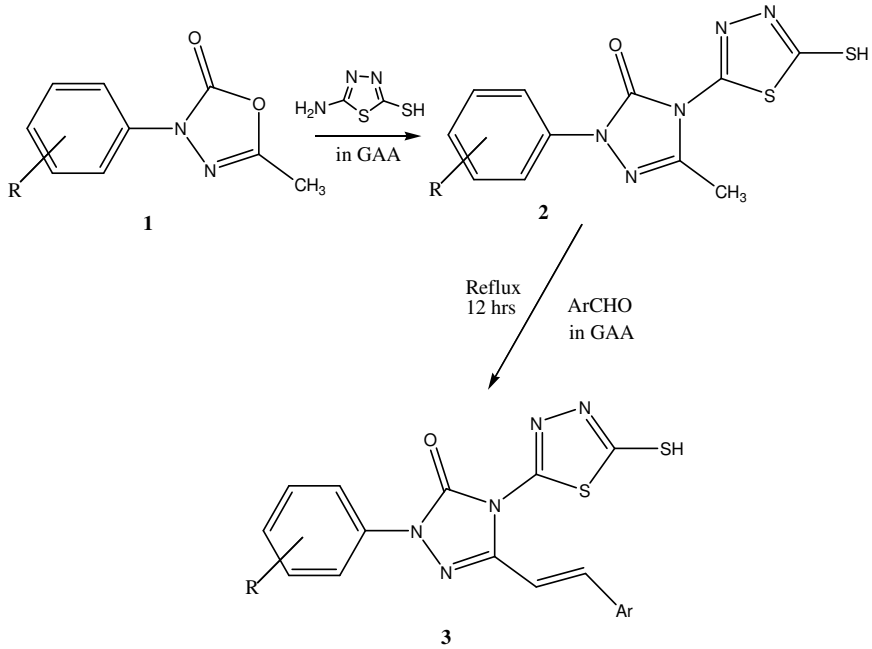
All the chemicals purchased were of analytical reagent grade, and were used without further purification stated is confirmed by measuring M.P. Synthesis of 3-aryl sydnones, oxadiazolines and triazoles derivatives by slight modification in our reported literature methods[23].

### *General procedure for compounds **2a-2h** (Scheme 1)*

To the 5-methyl-3-phenyl-1,3,4-oxadiazol-2(3*H*)-one (0.01 M) (**1**), 5-amino-1,3,4-thiadiazole-2-thiol (0.01 M) in glacial acetic acid (GAA) was added and refluxed for 4 h. Obtained reaction mixture was poured into crushed ice and left overnight. The solid which separated out was filtered, washed thoroughly with cold distilled water, dried and recrystallised from hot ethanol. The other derivatives are also synthesized by same method. The yield, melting point and other physical properties of synthesized compound are recorded in Table 1.

### *General procedure for compounds **3a-3h** (Scheme 1)*

The title compounds were synthesized by following the procedure: Solution of **2** (0.01 M) and opportune benzaldehyde (0.01 M) were reacted with glacial acetic acid (10 mL) and refluxed for 12 h. The solid **4** which separated out was filtered with suction and recrystallised from dimethylformamide to give pure compound. The physical data of the compound **3** are given in Table 2. The IR spectra, $^{13}$C NMR spectra and $^{1}$H NMR spectra of the title compounds are as follows:




**1** **2** **3**

**Scheme 1**

**Table 1**

| S. No. | **2a** | **2b** | **2c** | **2d** | **2e** | **2f** | **2g** | **2h** |
|---|---|---|---|---|---|---|---|---|
| R | H | COOH | $COOC_2H_5$ | $COOCH_3$ | $COCH_3$ | *p*-Cl | *m*-Cl | *p*-$OCH_3$ |
| Mol weight | 291.35 | 335.36 | 363.41 | 349.38 | 333.38 | 325.79 | 325.79 | 321.37 |

*All the products gave satisfactory NMR, IR and MS data Isolated yield.*

**Table 2.** Elemental Analysis of the compounds.

| S. No. | R | Meting Point $^0$C | Yield, % | Molecular formula | Elemental analysis Found (Calc), % | | | |
|---|---|---|---|---|---|---|---|---|
| | | | | | C | H | N | S |
| **3a** | H | 197-98 | 89 | $C_{18}H_{13}N_5OS_2$ | 56.98 (56.97) | 3.46 (3.45) | 18.47 (18.46) | 16.92 (16.90) |
| **3b** | COOH | 200-01 | 87 | $C_{19}H_{13}N_5O_3S_2$ | 53.90 (53.89) | 3.10 (3.09) | 16.55 (16.54) | 15.16 (15.14) |
| **3c** | $COOC_2H_5$ | 211-12 | 72 | $C_{21}H_{17}N_5O_3S_2$ | 55.87 (55.86) | 3.80 (3.79) | 15.52 (15.51) | 14.21 (14.20) |
| **3d** | $COOCH_3$ | 232-33 | 68 | $C_{20}H_{15}N_5O_3S_2$ | 54.93 (54.91) | 3.47 (3.46) | 16.02 (16.01) | 14.67 (14.66) |
| **3e** | $COCH_3$ | 256-57 | 76 | $C_{20}H_{15}N_5O_2S_2$ | 56.98 (56.99) | 3.60 (3.59) | 16.63 (16.62) | 15.22 (15.21) |
| **3f** | *p*-Cl | 223-24 | 79 | $C_{18}H_{12}ClN_5OS_2$ | 52.24 (52.23) | 2.93 (2.92) | 16.93 (16.92) | 15.48 (15.49) |
| **3g** | *m*-Cl | 194-95 | 82 | $C_{18}H_{12}ClN_5OS_2$ | 52.24 (52.23) | 2.93 (2.92) | 16.93 (16.92) | 15.48 (15.49) |
| **3h** | *p*-$OCH_3$ | 211-12 | 80 | $C_{19}H_{15}N_5O_2S_2$ | 55.72 (55.73) | 3.70 (3.69) | 17.11 (17.10) | 15.65 (15.66) |

*4-(5-Mercapto-1,3,4-thiadiazol-2-yl)-5-methyl-2-phenyl-2,4-dihydro-3H-1,2,4-triazol-3-one (**3a**)*

**IR** (cm $^{-1}$): 1693 (C=O), 1650 (C=C) Alkene, 1530 (C=N), 1317 (CN), 688 (CS); **$^{13}$C NMR** (300 MHz, δ): 118.7, 121.6, 124.4, 126.4, 128.0, 128.7, 129.0, 135.2, 137.8, 139.0, 152.0, 155.0, 184.0; **$^{1}$H NMR** (300 MHz, δ): 5.16 (d, 1H, olefinic CH), 6.6-7.92 (a set of signals, 12 aromatic protons and olefinic CH).

*4-{4-(5-Mercapto-1,3,4-thiadiazol-2-yl)-5-oxo-3-[(E)-2-phenylvinyl]-4,5-dihydro-1H-1,2,4-triazol-1-yl}benzoic acid (**3b**)*

**IR** (cm $^{-1}$): 1700 (C=O), 1611 (C=C) Alkene, 1520 (C=N), 1313 (CN), 675 (CS); **$^{13}$C NMR** (300 MHz, δ): 118.6, 121.5, 125.9, 126.3, 128.1, 128.6, 130.5, 135.2, 139.1, 143.0, 152.2, 155.1, 169.4, 184.2; **$^{1}$H NMR** (300 MHz, δ): 3.73 (s, 3H, $CH_3$), 5.74 (d, 1H, olefinic CH), 6.83-8.00 (a set of signals, 12H, aromatic protons and olefinic CH).

*Ethyl 4-{4-(5-mercapto-1,3,4-thiadiazol-2-yl)-5-oxo-3-[(E)-2-phenylvinyl]-4,5-dihydro-1H-1,2,4-triazol-1-yl}benzoate (**3c**)*

**IR** (cm $^{-1}$): 1691 (C=O), 1640 (C=C) Alkene, 1530 (C=N), 1275 (CN), 773 (CS); **$^{13}$C NMR** (300 MHz, δ): 3c.14.1, 60.9, 118.5, 121.7, 125.8, 126.5, 128.1, 128.5, 130.1, 135.3, 139.2, 142.1, 152.0, 155.2, 166.0, 184.1; **$^{1}$H NMR** (300 MHz, δ): 2.35 (s, 3H, $CH_3$), 5.84 (d, 1H, olefinic CH), 6.12-7.85 (a set of signals, 12H, aromatic protons and olefinic CH).

*Methyl 4-{4-(5-mercapto-1,3,4-thiadiazol-2-yl)-5-oxo-3-[(E)-2-phenylvinyl]-4,5-dihydro-1H-1,2,4-triazol-1-yl}benzoate (**3d**)*

**IR** (cm $^{-1}$): 1700 (C=O), 1668 (C=C) Alkene, 1591 (C=N), 1326 (CN), 752 (CS); **$^{13}$C NMR** (δ): 51.5, 118.7, 121.5, 125.5, 126.4, 128.0, 128.7, 130.3, 135.2, 139.0, 142.2, 152.1, 155.3, 166.0, 184.0; **$^{1}$H NMR** (300 MHz, δ): 5.52 (d, 1H, olefinic CH), 6.80-7.48 (a set of signals, 13H, aromatic protons and olefinic CH).

*2-(4-Acetylphenyl)-4-(5-mercapto-1,3,4-thiadiazol-2-yl)-5-[(E)-2-phenylvinyl]-2,4-dihydro-3H-1,2,4-triazol-3-one (**3e**)*

**IR** (cm$^{-1}$): 1700 (C=O), 1614 (C=C) Alkene, 1555 (C=N), 1326 (CN), 760 (CS); **$^{13}$C NMR**: (δ) 29.3, 118.6, 121.4, 126.3, 128.1, 128.6, 129.0, 132.4, 135.1, 139.1, 142.3, 152.0, 155.1, 184.2, 199.8; **$^{1}$H NMR** (300 MHz, δ): 5.12 (d, 1H, olefinic CH), 6.41-7.49 (a set of signals, 13H, aromatic protons and olefinic CH).

*2-(4-Chlorophenyl)-4-(5-mercapto-1,3,4-thiadiazol-2-yl)-5-[(E)-2-phenylvinyl]-2, 4-dihydro-3H-1,2,4-triazol-3-one (**3f**)*

**IR** (cm $^{-1}$): 1737 (C=O), 1610 (C=C) Alkene, 1532 (C=N), 1269 (CN), 733 (CS); **$^{13}$C NMR**: (δ) 118.7, 123.0, 126.4, 128.0, 128.7, 129.1, 129.9, 135.2, 135.9, 152.0, 155.0, 139.0, 184.0; **$^{1}$H NMR**: (300 MHz, δ) 5.60 (d, 1H, olefinic CH), 6.99 (d, 2H, olefinic CH), 6.78-8.01 (a set of signals, 14H, aromatic protons and olefinic CH).

*2-(3-Chlorophenyl)-4-(5-mercapto-1,3,4-thiadiazol-2-yl)-5-[(E)-2-phenylvinyl]-2, 4-dihydro-3H-1,2,4-triazol-3-one (**3g**)*

**IR** (cm $^{-1}$) 1700 (C=O), 1620 (C=C) Alkene, 1542 (C=N), 1274 (CN), 740 (CS); **$^{13}$CNMR** (δ): 118.8, 119.7, 122.0, 124.5, 126.2, 128.1, 128.6, 130.4, 134.5, 135.3, 139.0, 139.2, 152.1, 155.3, 184.2; **$^{1}$H NMR** (300 MHz, δ): 3.84 (s, 3H, CH3), 5.82 (d, 1H, olefinic CH), 6.72-7.94 (a set of signals, 13H, aromatic protons and olefinic CH).

*4-(5-Mercapto-1,3,4-thiadiazol-2-yl)-2-(4-methoxyphenyl)-5-[(E)-2-phenylvinyl]-2,4-dihydro-3H-1,2,4-triazol-3-one (**3h**)*

**IR** (cm $^{-1}$): 1739 (C=O), 1642 (C=C) Alkene, 1542 (C=N), 1334 (CN), 759 (CS); **$^{13}$C NMR** (δ): 55.9, 114.5, 118.7, 122.6, 126.5, 128.1, 128.8, 130.0, 135.2, 139.1, 152.0, 155.0, 156.3, 184.0; **$^{1}$H NMR** (300 MHz, δ): 3.63 (s, 3H, CH3), 3.72 (s, 3H, CH3), 5.76 (d, 1H, olefinic CH), 6.60-7.86 (a set of signals, 12H, aromatic protons and olefinic CH).

*Biological activity*

All the newly synthesized compounds were screened for their antimicrobial activity by cup plate method at 100 µg/mL concentration in DMF against the Bacterial strains *viz.*, *E. coli* & *B. subtilis* and also against fungal strains *viz.*, *A niger* and *A. sereus*. Norfloxacin for bacteria and griseofulvin as the reference drugs respectively. Some these compounds were less active against the bacterial strains, but some of them showed selective fungal inhibitory activity. The antimicrobial data of synthesized compounds are given in Table 3.

**Table 3.** Anti-microbial activities of compounds.

| S. No. | Antibacterial | | Antifungal | |
|---|---|---|---|---|
| | *E.coli* | *B. subtilis* | *A. niger* | *C. Albicans* |
| 3a | 16 | 18 | 16 | 17 |
| 3b | 15 | 17 | 19 | 20 |
| 3c | 15 | 14 | 14 | 18 |
| 3d | 12 | 11 | 22 | 21 |
| 3e | 20 | 23 | 20 | 21 |
| 3f | 21 | 22 | 22 | 23 |
| 3g | 15 | 14 | 19 | 18 |
| 3h | 23 | 24 | 20 | 21 |
| Norf | 24 | 24 | -- | -- |
| Gris | -- | -- | 26 | 26 |
| DMF | 04 | 04 | 04 | 04 |

## Results and Discussion

The synthesized compounds were characterized by various spectral studies. Some of compounds (**3e, 3f** and **3h**) were found to be more susceptible towards the fungal strains as well as bacterial strains. (Figure 1 & 2)

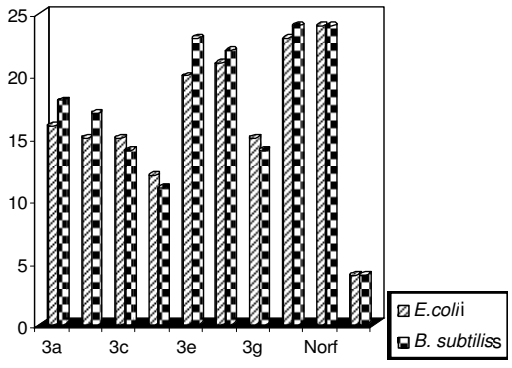



**Figure 1.** Antibacterial activity of synthesized compounds.

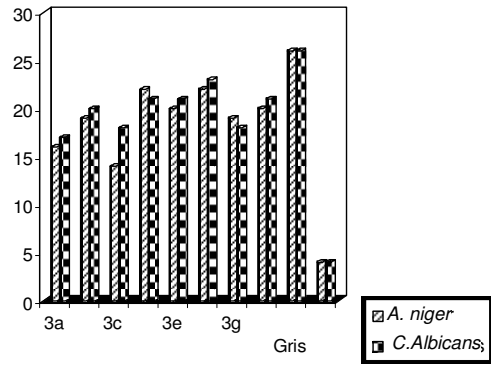



**Figure 2.** Antifungal activity of synthesized compounds.

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