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*Research Article*

# A Combined Synthetic and DFT Study on the Catalyst-Free and Solvent-Assisted Synthesis of 1,3,4-Oxadiazole-2-thiol Derivatives

**Mohammad Soleiman-Beigi,[1] Reza Aryan,[2] Maryam Yousofizadeh,[1] and Shima Khosravi[1]**

[1] *Department of Chemistry, Ilam University, P.O. Box 69315-516, Ilam, Iran*
[2] *Department of Chemistry, Faculty of Science, University of Zabol, Zabol, Iran*

Correspondence should be addressed to Mohammad Soleiman-Beigi; soleimanbeigi@gmail.com

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A novel practical and efficient catalyst-free method for the synthesis of 5-substituted 1,3,4-oxadiazole-2-thiols has been developed, which is assisted by reaction solvent (DMF). The solvent effects on product selectivity were studied based on Onsager's reaction field theory of electrostatic solvation. The ab initio theoretical studies on the effect of solvents on the process also supported the suitability of DMF as the reaction medium for the preparation of 1,3,4-oxadiazole-2-thiol derivatives.

## 1. Introduction

1,3,4-Oxadiazole-2-thiol(thione) derivatives are an important class of five-membered heterocyclic compounds that have attracted much attention due to their applications as key intermediates in organic synthesis [1–3], biological activity studies [4–6], and theoretical chemistry [7–9]. 1,3,4-Oxadiazole-2-thiol derivatives display various types of biological activities [10, 11], including antibacterial, antimycotic, anti-inflammatory, hypotensive, fungicidal, and anticonvulsant activities [12]. Recently, they were also found as trans-cinnamate 4-hydroxylase ($C_4H$) [13] and glycogen synthesis kinase-3$\beta$ (GSK-3$\beta$) inhibitors [14]. In addition, their derivatives play an important role in the field of coordination chemistry because of their potential multifunctional donor sites, via either exocyclic sulfur or endocyclic nitrogen atoms [15, 16].

Although many studies have been reported concerning the biological activities and structural investigations of 1,3,4-oxadiazole-2-thiol derivatives, we have found only few procedures describing the synthesis, and no reports concerning the effect of solvent on the synthesis and tautomerization of these compounds in the literature. By far, the most common strategy for the synthesis of 1,3,4-oxadiazole-2-thiols involves the interaction of acid hydrazides with carbon disulfide in the presence of alcoholic potassium hydroxide [17–20]. In the past few years, catalyst-free reactions have been noticed as important routes for the development of organic synthesis methodologies due to their environmentally friendly importance and economic advantages [21, 22]. Furthermore, in order to obtain pure 1,3,4-oxadiazole-2-thiols in the presence of a catalyst such as KOH, the reaction mixture should be neutralized because the parent compound of 1,3,4-oxadiazole-2-thiol is acidic ($pK_a$ = 3.85) [23]. This makes the procedure rather difficult and reduces the yield of the product.

In view of the importance of ab initio calculations to study the solvent effects in the synthesis and tautomerization of organic compounds [24, 25] and the above-mentioned issues, we have been prompted to investigate the synthesis of 1,3,4-oxadiazole-2-thiols in solution conditions and to explore the effect of solvent both experimentally and theoretically.

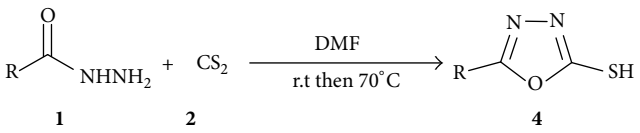
## 2. Results and Discussion

To optimize the reaction conditions with regard to the solvent, the reaction of benzhydrazide (1.0 mmol) with carbon disulfide (3.0 mmol) was primarily studied as the model reaction in a variety of accessible solvents at 70°C (Table 1). As

Table 1: Ring closure of substrates as a function of solvent.

| Entry | Solvent | Time (h) | Yields (%)* |
|---|---|---|---|
| (1) | $C_2H_5OH$ | 21 | 10 |
| (2) | $CHCl_3$ | 21 | — |
| (3) | $CH_3CN$ | 21 | 72 |
| (4) | $PhCH_3$ | 23 | trace |
| (5) | DMF | 3 | 92 |
| (6) | $H_2O$ | 18 | 8 |
| (7) | DMF/$H_2O$ (10/1) | 7.2 | 64 |
| (8) | DMF/$H_2O$ (4/1) | 8.5 | 48 |

*Isolated yield of pure product.




1 2 4

Scheme 1

shown in Table 1, the best result was obtained in DMF (entry 5).

It seems that the polarity of aprotic organic solvents has a great effect on the yield of 1,3,4-oxadiazole-2-thiol. The yield of the product increases with increasing dipole moment of the organic aprotic solvent (Table 1).

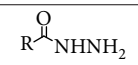
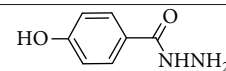
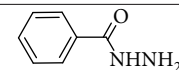
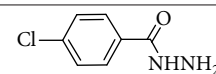
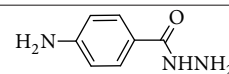
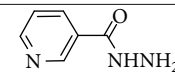
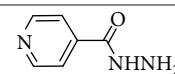
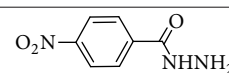
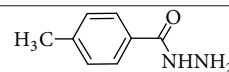
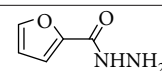
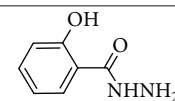
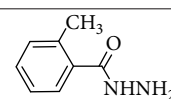
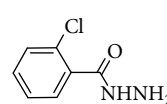
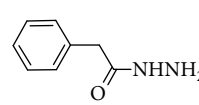
Various aliphatic, aromatic, and heteroaromatic hydrazides were tested in DMF at 70°C (Scheme 1). Aromatic and heteroaromatic hydrazides gave target products in good to excellent yields (Table 2), whereas the procedure did not work with aliphatic hydrazide as well as aromatics and heteroaromatic hydrazides to yield target products (Table 2, entry 13).

In fact, from these reactions, we have isolated 1,3,4-oxadiazole-2-thiols **4** with no evidence for the formation of any byproducts such as 1,3,5-thiadiazole **5** or 1,5-dibenzoylthiocarbazide **6** derivatives (Scheme 2).

The results from these experiments encouraged us to investigate the effect of solvent on this reaction theoretically with ab initio Lee-Young-Parr (B3LYP) level of theory using Gaussian 03w software program [26] on a Pentium IV computer. The structures of two possible tautomers of 1,3,4-oxadiazole-2-thiol(thione) are presented in Figure 1.

The geometry optimizations of the tautomers (I) and (II) were carried out at B3LYP/6-311++G(d,p) with taking into account the polarity of medium in gas phase ($\varepsilon = 1$) and in different solvents using self-consistent reaction field (SCRF) method by using SCIPCM solvent model (Table 3). The values of absolute energy ($E$) and solvent-solute interaction energy in Table 3 indicate more stability (more negative value) for both tautomers in more polar solvents (Table 3, $E$ and $E_{SSI}$ columns). The highest solution energy values (difference between gaseous and solvated states) for tautomer (I) and (II) are in DMF and $CH_3CN$, respectively ($E_S$ = 5.0459 kcal/mol for tautomer (I) in DMF and $E_S$ = 6.4991 kcal/mol for tautomer II in $CH_3CN$). Furthermore, when the $E_S$ values in different solvents are examined, the

Table 2: Synthesis of 5-substituted 1,3,4-oxadiazole-2-thiols **4** in DMF.

| Entry |  | Products | Time (h) | Yields (%)* |
|---|---|---|---|---|
| (1) |  | **4a** | 4.45 | 70 |
| (2) |  | **4b** | 3.20 | 96 |
| (3) |  | **4c** | 3.45 | 94 |
| (4) |  | **4d** | 3.30 | 87 |
| (5) |  | **4e** | 7.0 | 91 |
| (6) |  | **4f** | 6.0 | 81 |
| (7) |  | **4g** | 4.0 | 84 |
| (8) |  | **4h** | 6.0 | 85 |
| (9) |  | **4i** | 8.0 | 61 |
| (10) |  | **4j** | 9.0 | 80 |
| (11) |  | **4k** | 3.30 | 96 |
| (12) |  | **4l** | 4.50 | 98 |
| (13) |  | **4m** | 12.0 | trace |

*Isolated yield of pure product.

Table 3: Calculated energies and dipole moments at the B3LYP level with 6-311++G**.

| Parameter | Tautomer | $\varepsilon = 1$ | $\varepsilon = 36.7$ | $\varepsilon = 36.04$ | $\varepsilon = 24.3$ | $\varepsilon = 8.93$ | $\varepsilon = 2.38$ |
|---|---|---|---|---|---|---|---|
| $E^{a}$ | I | −891.5045327 | −891.5125739 | −891.5125732 | −891.5123820 | −891.5114328 | −891.5082445 |
| $E^{a}$ | II | −891.5219806 | −891.532338 | −891.532345 | −891.532098 | −891.530870 | −891.526763 |
| $E_{SSI}{}^{b}$ | I | — | −891.5125695 | −891.5125688 | −891.5123776 | −891.5114296 | −891.5081894 |
| $E_{SSI}{}^{b}$ | II | — | −891.5323358 | −891.5323396 | −891.5320928 | −891.5308670 | −891.5267218 |
| $E_{HB}{}^{c}$ | I | — | 5.0432 | 5.0427 | 4.9228 | 4.3279 | 2.2946 |
| $E_{HB}{}^{c}$ | II | — | 6.4980 | 6.5004 | 6.3455 | 5.5764 | 2.9752 |
| $E_{S}{}^{d}$ | I | — | 5.0459 | 5.0455 | 4.9255 | 4.3299 | 2.3292 |
| $E_{S}{}^{d}$ | II | — | 6.4991 | 6.5039 | 6.3485 | 5.5779 | 3.0013 |
| $\Delta E_{HB}{}^{e}$ | — | — | 1.4548 | 1.4577 | 1.4227 | 1.2485 | 0.6806 |
| $\Delta E_{S}{}^{f}$ | — | — | 1.4532 | 1.4584 | 1.4230 | 1.2480 | 0.6721 |
| $\mu^{h}$ | I | 0.9773 | 1.3208 | 1.3207 | 1.3117 | 1.2664 | 1.1266 |
| $\mu^{h}$ | II | 1.7771 | 2.3823 | 2.3838 | 2.3699 | 2.3012 | 2.0700 |

[a]Energy (hartrees). [b]Solvent-solute interaction energy (hartrees). [c]Hydrogen bond strength (kcal/mol). [d]Solution energy (kcal/mol). [e]Difference between the hydrogen bond strength of I and II ($E_{HB}$(II) − $E_{HB}$(I)) in kcal/mol. [f]Difference between the solvation energies of I and II ($E_S$(II) − $E_S$(I)) in kcal/mol. [h]Dipole moment (debye).

Table 4: The geometrical parameters of the tautomer I calculated at the B3LYP level with 6-311++G** basis set[a].

| | $\varepsilon = 1$ | $\varepsilon = 36.7$ | $\varepsilon = 36.04$ | $\varepsilon = 24.3$ | $\varepsilon = 8.93$ | $\varepsilon = 2.38$ |
|---|---|---|---|---|---|---|
| Bond lengths | | | | | | |
| C1=N4 | 1.2941 | 1.2955 | 1.2955 | 1.2954 | 1.2953 | 1.2947 |
| C2=N5 | 1.2925 | 1.2951 | 1.2951 | 1.2950 | 1.2946 | 1.2936 |
| C2–O3 | 1.3570 | 1.3554 | 1.3554 | 1.3555 | 1.3558 | 1.3563 |
| C1–O3 | 1.3769 | 1.3738 | 1.3738 | 1.3739 | 1.3743 | 1.3759 |
| C2–S17 | 1.7520 | 1.7497 | 1.7497 | 1.7497 | 1.7502 | 1.7510 |
| S17–H18 | 1.3485 | 1.3476 | 1.3476 | 1.3476 | 1.3477 | 1.3480 |
| C1–C6 | 1.4568 | 1.4570 | 1.4570 | 1.4570 | 1.4569 | 1.4569 |
| C6–C7 | 1.4029 | 1.4033 | 1.4033 | 1.4033 | 1.4033 | 1.4031 |
| C7–C9 | 1.3891 | 1.3898 | 1.3898 | 1.3898 | 1.3896 | 1.3894 |
| C9–C13 | 1.3961 | 1.3967 | 1.3967 | 1.3967 | 1.3967 | 1.3964 |
| C13–C11 | 1.3937 | 1.3945 | 1.3945 | 1.3944 | 1.3943 | 1.3940 |
| C11–C8 | 1.3918 | 1.3921 | 1.3921 | 1.3921 | 1.3921 | 1.3919 |
| C8–C6 | 1.4010 | 1.4018 | 1.4018 | 1.4018 | 1.4017 | 1.4014 |
| Bond angles | | | | | | |
| N5C2S17 | 129.73 | 130.27 | 130.27 | 130.26 | 130.25 | 129.94 |
| H18S17C2 | 92.70 | 93.49 | 93.49 | 93.47 | 93.40 | 93.04 |
| N4C1C6 | 129.13 | 129.45 | 129.45 | 129.44 | 129.40 | 129.28 |
| C1O3C2 | 102.24 | 102.75 | 102.75 | 102.74 | 102.68 | 102.47 |
| N5N4C1 | 107.18 | 107.11 | 107.11 | 107.12 | 107.13 | 107.16 |

[a]Bond lengths and bond angles are in Å and degrees, respectively.

orders of tautomers stability according to $E_S$ values are as follows (see Table 3, the values of $E_S$):

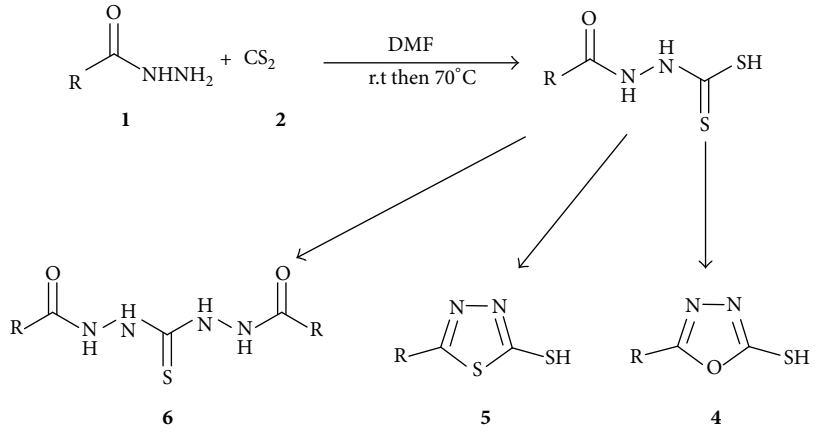
$$\begin{aligned} &\text{for tautomer (I),} \\ &\quad \text{DMF} > \text{CH}_3\text{CN} > \text{C}_2\text{H}_5\text{OH} > \text{CH}_2\text{Cl}_2 > \text{Toluene}, \\ &\text{for tautomer (II),} \\ &\quad \text{CH}_3\text{CN} > \text{DMF} > \text{C}_2\text{H}_5\text{OH} > \text{CH}_2\text{Cl}_2 > \text{Toluene}. \end{aligned} \quad (1)$$

Therefore, the highest calculated $E_{HB}$ and $\Delta E_{HB}$ (difference between $E_{HB}$ of both tautomers) values were obtained in DMF and acetonitrile with highest dipole moments. These findings emphasize the role of more polar solvents such as DMF and acetonitrile in the formation of 1,3,4-oxadiazole-2-thiol(thione). Most importantly, it can be seen that tautomer (I) has the lowest solution energy (more stability) in DMF in comparison to tautomer (II), which prefers acetonitrile (Table 3).

Table 5: The geometrical parameters of the tautomer I calculated at the B3LYP level with 6-311++G** basis set[a].

| | $\varepsilon = 1$ | $\varepsilon = 36.7$ | $\varepsilon = 36.04$ | $\varepsilon = 24.3$ | $\varepsilon = 8.93$ | $\varepsilon = 2.38$ |
|---|---|---|---|---|---|---|
| Bond lengths | | | | | | |
| C2=N16 | 1.2924 | 1.2932 | 1.2929 | 1.2929 | 1.2930 | 1.2926 |
| C2–N17 | 1.3559 | 1.3460 | 1.3459 | 1.3461 | 1.3472 | 1.3515 |
| C2–O15 | 1.3823 | 1.3745 | 1.3747 | 1.3750 | 1.3762 | 1.3781 |
| C3–O15 | 1.3709 | 1.3725 | 1.3725 | 1.3727 | 1.3721 | 1.3724 |
| C2–S1 | 1.6404 | 1.6552 | 1.6549 | 1.6545 | 1.6527 | 1.6471 |
| N17–H18 | 1.0073 | 1.0102 | 1.0100 | 1.0100 | 1.0096 | 1.0085 |
| C3–C4 | 1.4565 | 1.4560 | 1.4560 | 1,4561 | 1.4562 | 1.4561 |
| C4–C6 | 1.4028 | 1.4037 | 1.4036 | 1.4036 | 1.4035 | 1.4032 |
| C6–C9 | 1.3886 | 1.3895 | 1.3891 | 1.3891 | 1.3888 | 1.3888 |
| C9–C11 | 1.3965 | 1.3971 | 1.3971 | 1.3971 | 1.3970 | 1.3968 |
| C11–C7 | 1.3935 | 1.3945 | 1.3943 | 1.3943 | 1.3942 | 1.3938 |
| C7–C5 | 1.3918 | 1.3923 | 1.3923 | 1.3923 | 1.3922 | 1.3919 |
| C4–C5 | 1.4008 | 1.4017 | 1.4014 | 1.4014 | 1.4013 | 1.4010 |
| Bond angles | | | | | | |
| H18N17C2 | 125.51 | 126.38 | 126.32 | 126.30 | 126.20 | 125.92 |
| N16C3C4 | 127.98 | 128.35 | 128.14 | 128.13 | 128.10 | 128.14 |
| C4C3O15 | 119.31 | 119.38 | 119.57 | 119.57 | 119.53 | 119.38 |
| N17N16C3 | 103.50 | 103.77 | 103.78 | 103.77 | 103.71 | 103.65 |
| N17C2O15 | 102.98 | 103.78 | 103.80 | 103.77 | 103.66 | 103.37 |
| N17C2S1 | 131.15 | 131.43 | 131.19 | 131.19 | 131.24 | 131.16 |

[a]Bond lengths and bond angles are in Å and degrees, respectively.




Scheme 2

Moreover, calculations reveal that the highest dipole moment for tautomers (I) and (II) would be in DMF and acetonitrile, respectively. Herein, these data again support that the formation of (I) (thiol tautomer) is favored over the other tautomer in DMF as reaction solvent.

To ensure that hydrogen bonding with solvents of high polarity has a significant contribution in facilitating the formation of and stabilizing the thiol tautomer, we considered purposefully the changes in bond lengths and angles of two tautomers (Tables 4 and 5).

The values of C1=N4 and C2=N5 bond lengths (consider Figure 1 and Tables 4 and 5) experience maximum increment, while the C2–S17, C1–O3, C2–O3, and S17–H18 bond lengths experience maximum decline in DMF as solvent in comparison with gas phase values for tautomer (I). It is believed that these changes are the consequences of hydrogen bond formation between tautomer (I) and dimethylformamide as solvent. Similar phenomenon is observed for tautomer (II) in acetonitrile proving the idea of solvent assistance for the tautomer selectivity. According to these findings, the tautomer (I) is preferred mostly to be formed in DMF as solvent.

The structure of the compounds obtained has been confirmed by their NMR, IR, and physical properties. The IR spectrum of the product 4 exhibited characteristic weak bands at 3270–3050 $cm^{-1}$(NH), 2780–2720 $cm^{-1}$(SH), and

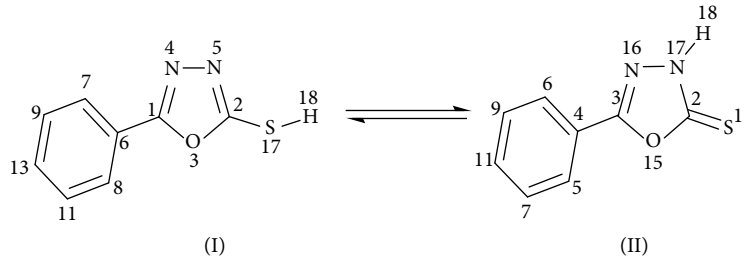



Figure 1: Equilibrium between 1,3,4-oxadiazole-2-thiol and 2-thione tautomers.

1630–1600 $cm^{-1}$ (C=N). $^1$H-NMR (DMSO-$d_6$) spectrum of the products 4 showed only one proton as singlet at 14.0–15.5 ppm. This information suggested that the product **4**, which was synthesized via the present method, existed mostly in the thiol form in solution, whereas the thiol-thione tautomerism was observed in their solid crystalline forms where the effect of solvent on tautomerism is cancelled. This fact is supported by DFT calculations in gaseous and solution phases. The energy difference between two tautomers is about 10.9 kcal/mol, which is accessible at room temperature (see Table 3, columns for E, $\varepsilon = 1.0$) and proves the observation of NH and SH bands in IR spectrum. This tautomerism is of course too fast to be observed in NMR.

In summary, we have developed a novel and efficient catalyst-free and solvent-assisted protocol for the synthesis of 5-substituted 1,3,4-oxadiazole-2-thiols with potential synthetic and pharmacological interest. Catalyst-free conditions, excellent yields, a simplified purification process, short reaction times, and safe handling of products are the main advantages of this method. The influence of solvents on the progress of the reaction has been studied experimentally and theoretically. DMF, as an accessible polar aprotic solvent, was found as most convenient medium to facilitate this process for the synthesis of 1,3,4-oxadiazole-2-thiols. Theoretical calculations using ab initio density functional theory (DFT) at B3LYP/6-311++G(d,p) level of theory confirmed that dimethylformamide (DMF) assisted the formation of only one of the expected tautomers (tautomer I) as the single observable product of the reaction.

## 3. Experimental

Chemicals were purchased from Merck and Aldrich chemical companies. Yields refer to isolated products. Melting points were determined by a Electrothermal 9100 apparatus. The IR spectra were obtained on a FT-IR Hartman-Bomen spectrophotometer as KBr disks. The $^1$H NMR (400 MHz) and $^{13}$C NMR (100 MHz) spectra were recorded on a Bruker Avance NMR spectrometer in DMSO-$d_6$ solutions. Elemental analyses were done on a Carlo-Erba EA1110CHNO-S analyzer. The progress of the reaction was followed by TLC using silica-gel SIL G/UV 254 plates. Products were characterized by comparing their physical and spectral data with those of the authentic samples [5, 17].

*3.1. General Procedure for Synthesis of 5-Substituted 1,3,4-Oxadiazole-2-thiol Derivatives* ***4a–m***. A mixture of acid hydrazide (1.0 mmol) and carbon disulfide (3.0 mmol) in DMF (2.0 mL) was stirred for 15 min at room temperature. The reaction mixture was then heated at 70°C for appropriated time (Table 2) until the ring closure completed. The reaction progress was checked by TLC monitoring (ethyl acetate: n-hexane (1 : 2)). After cooling to room temperature, the reaction mixture was poured dropwise into ice cold water (15 mL) to yield a solid (title compounds 4), which was collected by filtration, washed with water, and recrystallized from EtOH/water to give compounds **4a–m** in good to excellent yields.

*3.1.1.* 5*–(4-Hydroxyphenyl)-1,3,4-oxadiazole-2-thiol* ***4a***. mp 225–228°C; $^1$H NMR (DMSO-$d_6$): $\delta$ 6.93(d, 2H), 7.72(d, 2H), 10.40(s, 1H, OH), 14.53(br s, 1H, SH). $^{13}$C NMR (DMSO-$d_6$): $\delta$ 177.02, 162.41, 153.12, 128.12, 113.99, 108.93. IR (KBr disc): $\nu$ 3296, 3160, 2359, 1271 $cm^{-1}$. Anal. Calcd. For $C_8H_6N_2O_2S$: C, 49.47; H, 3.11; N, 14.42. Found: C, 49.38; H, 3.09; N,14.54.

*3.1.2. 5-Phenyl-1,3,4-oxadiazole-2-thiol* ***4b***. mp 218-219°C; $^1$H NMR (DMSO-$d_6$): $\delta$ 7.58(m, 3H), 7.85(m, 2H), 14.8(br s, 1H, SH). $^{13}$C NMR (DMSO-$d_6$): $\delta$ 123.00, 126.49, 129.88, 132.65, 160.65, 177.97. IR (KBr disc): $\nu$ 3143, 2352, 1289 $cm^{-1}$. Anal. Calcd. for $C_8H_6N_2OS$: C, 53.92; H, 3.39; N, 15.72. Found: C, 53.86; H, 3.42; N, 15.66.

*3.1.3. 5-(3-Pyridyl)-1,3,4-oxadiazole-2-thiol* ***4e***. mp 226-227°C. $^1$H NMR (DMSO-$d_6$): $\delta$ 7.59–7.62(m, 1H), 8.24(d, 1H), 8.78(d, 1H), 9.30(s, 1H), 14.83(br s, 1H, SH). $^{13}$C NMR (DMSO-$d_6$): $\delta$ 119.74, 124.72, 134.16, 147.19, 152.97, 159.21, 162.74, 178.05. IR (KBr disc): $\nu$ 3183, 2360, 1247 $cm^{-1}$. Anal. Calcd. for $C_7H_5N_3OS$: C, 46.92; H, 2.81; N, 23.45. Found: C, 46.80; H, 2.90; N, 23.40.

*3.1.4. 5-(2-Chlorophenyl)-1,3,4-oxadiazole-2-thiol* ***4l***. mp 166–169°C. $^1$H NMR (DMSO-$d_6$): $\delta$ 7.55(t, 1H), 7.64(t, 1H), 7.70(d, 1H), 7.90(d, 1H), 14.8(br s, 1H, SH). $^{13}$C NMR (DMSO-$d_6$): $\delta$ 121.86, 128.32, 131.25, 131.67, 131.99, 133.78,

158.91, 177.85. IR (KBr disc): $\nu$ 3277, 2353, 1277 $cm^{-1}$. Anal. Calcd. for $C_8H_5ClN_2OS$: C, 45.18; H, 2.37; N,13.17. Found: C, 45.01; H, 2.51; N, 13.15.

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## References

[1] H. Foks, D. Pancechowska-Ksepko, M. Janowiec, Z. Zwolska, and E. Augustynowicz-Kopeć, "Synthesis and tuberculostatic activity of some (4-phenylpiperazin-1- ylmethyl)-1,3,4-oxadiazole and (4-phenylpiperazin-1-ylmethyl)-1,2,4-triazole derivatives," *Acta Poloniae Pharmaceutica*, vol. 61, no. 6, pp. 473–476, 2004.

[2] V. N. Atemov and O. P. Shaika, "Reactions involving the formation and recyclization of heterocycles," *Chemistry of Heterocyclic Compounds*, vol. 7, pp. 844–848, 1971.

[3] A. A. Zigaev and and G. G. Galust'yan, "Reaction of 5-aryl-1,3,4-oxadiazole-2(3H)-thiones with chloromethyl alkyl ethers," *Chemistry of Heterocyclic Compounds*, vol. 35, pp. 1104–1106, 1999.

[4] D. A. Charistos, G. V. Vagenas, L. C. Tzavellas, C. A. Tsoleridis, and N. A. Rodios, "Synthesis and a UV and IR spectral study of some 2-aryl-Δ2-1,3,4-oxadiazoline-5-thiones," *Journal of Heterocyclic Chemistry*, vol. 31, no. 6, pp. 1593–1598, 1994.

[5] S. Vijayaraghavan, R. R. Somani, P. Y. Shirodkar, and V. J. Kadam, "Microwave assissted synthesis and antimicrobial activity of some newer Mannich bases," *International Journal of PharmTech Research*, vol. 1, no. 3, pp. 811–815, 2009.

[6] D. H. Boschelli, D. T. Connor, D. A. Bornemeier et al., "1,3,4-Oxadiazole, 1,3,4-thiadiazole, and 1,2,4-triazole analogs of the fenamates: in vitro inhibition of cyclooxygenase and 5-lipoxygenase activities," *Journal of Medicinal Chemistry*, vol. 36, no. 13, pp. 1802–1810, 1993.

[7] S. S. Edram, G. A. Ozpinar, and M. T. Sacan, "Investigation on the aromaticity of 1,3,4-thiadiazole-2-thione and its oxygen analogs including their tautomeric forms," *Journal of Molecular Structure*, vol. 726, pp. 233–243, 2005.

[8] C. A. Tsoleridis, D. A. Charistos, and G. V. Vagenas, "UV and MO study on the deprotonation of some 2-aryl-Δ2-1,3,4-oxadiazoline-5-thiones," *Journal of Heterocyclic Chemistry*, vol. 34, no. 6, pp. 1715–1719, 1997.

[9] W. R. Sherman, "5-Nitro-2-furyl-substituted 1,3,4-oxadiazoles, 1,3,4-thiadiazoles, and 1,3,5-triazines[2]," *The Journal of Organic Chemistry*, vol. 26, pp. 88–95, 1961.

[10] V. Mickevicius, R. Vaickelioniene, and B. Sapijanskaite, "Synthesis of substituted 1,3,4-oxadiazole derivatives," *Chemistry of Heterocyclic Compounds*, vol. 54, pp. 215–218, 2009.

[11] G. Mekuskiene, P. Vainilavicius, A. Hetzheim, and R. Shematovich, "Synthesis of 5-(4,6-dimethyl-2-pyrimidinyl)-1,3,4-oxadiazole-2-thione and its alkylation, aminomethylation, and acylation," *Chemistry of Heterocyclic Compounds*, vol. 29, pp. 598–602, 1993.

[12] H. Chen, Z. Li, and Y. Han, "Synthesis and fungicidal activity against rhizoctonia solani of 2-Alkyl (Alkylthio)-5-pyrazolyl-1,3,4-oxadiazoles (Thiadiazoles)," *Journal of Agricultural and Food Chemistry*, vol. 48, pp. 5312–5315, 2000.

[13] N. Yamada, Y. Kataoka, T. Nagami, S. Hong, S. Kawai, and E. Kuwano, "5-Aryl-1,3,4-oxadiazole-2-thiols as a new series of trans-cinnamate 4-hydroxylase inhibitors," *Journal of Pesticide Science*, vol. 29, no. 3, pp. 205–208, 2004.

[14] M. Saitoh, J. Kunitomo, E. Kimura, and Y. Hayase, "Design, synthesis and structure-activity relationships of 1,3,4-oxadiazole derivatives as novel inhibitors of glycogen synthase kinase-3$\beta$," *Bioorganic & Medicinal Chemistry*, vol. 17, pp. 2017–2029, 2009.

[15] M. Singh, R. J. Butcher, and N. K. Singh, "Spectroscopic and structural studies of the 2D Mn(II) coordination polymer from a bridging Noxa, Npy bidentate ligand; tetra-n-butylammonium[5-(3-pyridyl)-1,3,4-oxadiazole-2-thiolate]," *Polyhedron*, vol. 28, no. 1, pp. 95–100, 2009.

[16] Y.-T. Wang and G.-M. Tang, "One new nickel coordination polymer with an unsymmetric 5-(4-pyridyl)-1,3,4-oxadiazole-2-thione: synthesis, structure and characterization," *Inorganic Chemistry Communications*, vol. 10, pp. 53–56, 2007.

[17] E. Hoggsrth, "2-Benzoyldithiocarbazinic acid and related compounds," *Journal of the Chemical Society*, pp. 4811–4817, 1952.

[18] M. A. Khali, S. M. El-Khawass, and M. G. Kassem, *ScientiaPharmaceutica*, vol. 48, p. 344, 1980.

[19] M. Belkadi and A. A. Othman, "A common route to the synthesis of 1,3,4-oxadiazole -2-thione and 1,2,4-triazole -3-thiols derivatives of trioses and pentoses as models for acyclic C-nucleosides," *Arkivoc*, vol. 2006, no. 11, pp. 183–195, 2006.

[20] J. Sandstrom and I. Wennerbeck, "Tautomeric cyclic thiones. Part II. Tautomerism, acidity and electronic spectra of thioamides of the oxadiazole, thiadiazole, and thiazole groups," *Acta Chemica Scandinavica*, vol. 20, pp. 57–71, 1966.

[21] B. Movassagh and M. Soleiman-Beigi, "Synthesis of sulfides under solvent- and catalyst-free conditions," *Monatshefte fur Chemie*, vol. 140, no. 4, pp. 409–411, 2009.

[22] S. T. Kadam and S. S. Kim, "Catalyst-free silylation of alcohols and phenols by promoting HMDS in $CH_3NO_2$ as solvent," *Green Chemistry*, vol. 12, no. 1, pp. 94–98, 2010.

[23] D. E. Horning and J. M. Muchowski, "Five-membered heterocyclic thiones. Part I. 1,3,4-Oxadiazole-2-thione," *Canadian Journal of Chemistry*, vol. 50, pp. 3079–3082, 1972.

[24] S. Pedersoli, C. F. Tormena, and R. Rittner, "Solvent effects in the conformational stability of $\alpha$-substituted acetamides through theoretical and experimental data," *Journal of Molecular Structure*, vol. 875, no. 1–3, pp. 235–243, 2008.

[25] A. Sen, A. Singh, and B. Ganguly, "Probing the influence of solvent effects on the conformational behavior of 1,4-diazacyclohexane systems," *Journal of Molecular Structure*, vol. 984, no. 1–3, pp. 294–299, 2010.

[26] M. J. Frisch, G. W. Trucks, H. B. Schlegel et al., *Gaussian 03, Revision C.01*, Gaussian, Wallingford, Conn, USA, 2004.