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# Spectral and Biological investigation of 5-Phenyl-1,3,4-oxadiazole-2-thiol

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**Abstract**
In the current study, a compound 5-phenyl-1,3,4 -oxadiazole-2-thiol was synthesized by converting variously benzoic acids successively into the corresponding esters, hydrazides. The structure of the synthesized compound was confirmed based on 1H-NMR, IR, UV-Vis and mass spectral data. The synthesized compounds were screened for antimicrobial activity against *Escherichia coli, Bacillus subtilis* and *Staphylococcus aureus* and fungus *Candida albican, Aspergillusniger* and *Candida krusei*.

## 1. Introduction

Over the last few decades, the rapid emergence of drug resistance in the treatment of infectious diseases emphasizes worldwide need for novel antimicrobial agents so current scenario greatly demands newer, safer and effective antimicrobial agents that will the overcome this problem. A number of researchers have reported antimicrobial activities in 1,3,4-oxadiazoles.

In this direction, various scientists have been engaged to synthesize new compounds related to various chemical groups. Literature survey revealed that 1,3,4-oxadiazole derivatives possessed broad spectrum of biological activities *viz* anthelmintic [1], anticancer [2], antiprotozol [3], anticonvulsant [4-5], anti-inflammatory [6], analgesic [7], antifungal [8], antibacterial [9] and many more.

The vibrational analysis of the title compound has been studied[10-11].Thecomplete vibrational analysis of the polyatomicmolecules is possible only when both the IR andRaman spectral data are available[12].The 1H-NMR analysis[13] and UV-Vis analysis[14] of the title compound also has been studied.

## 2. Methods and Materials

First ethyl benzoate (2) was prepared by refluxing benzoic acid (1) with ethyl alcohol in the presence of concentratedsulfuric acid for 4 hours. After maximum completion ofreaction, conc. solution of base was added to the reactionmixture for neutralization of excess organic acid andsulfuric acid to their respective salts. By using solventextraction method we get ethyl benzoate in organic layerand both the salts were washed by aqueous layer. Nextstep is the synthesis of benzohydrazide (3) by allowing ethyl benzoate to react with 80% hydrazine hydrate inmethanol at room temperature along with vigorousstirring for 3 hrs. The solid separated out was filtered andwashed with *n*-hexane. Further the compound 5-phenyl-1,3,4-Oxadiazol-2-thiol (4) was synthesized by refluxing compound 3, with carbon disulphide and potassium hydroxide in ethanol for 6 hours. On completion of reaction, ice cold distilled water was addedto the reaction mixture and it was then acidified to set the pH around 2-3 to put out the synthesized product in theform of precipitates which were filtered and washed with distilled water. The product was finally recrystallized from methanol [15,16] as shown in Fig.1.

All the reagents and solvents were generally received from commercial supplier. Reactions were done in dried glassware. Melting points were taken in open capillaries by thermionic melting point apparatus, (Campbell Electronic Mumbai, India) and are uncorrected. The purity of the newly synthesized compounds was checked by thin layer chromatography (TLC) on silica gel-G coated plates by using different solvent systems. Infrared (IR) spectra were determined on Bruker IFS-66 FTIR (Bruker Bioscience, USA) using KBr pallets and wave number (ν) was reported in $cm^{-1}$. The $^1$H-NMR spectra were taken on Jeol GSX -300 FT NMR (Jeol, Tokyo, Japan) in $CDCl_3$ or DMSO-$d_6$, and chemical shifts (δ) are given in ppm. Tetramethylsilane (TMS) was used as internal reference standard. Mass spectra were recorded on Spec Finnigan Mat 8230 MS. The carbon, hydrogen and nitrogen analysis were performed on Carlo Erba-1108 (Carlo Erba, Milan, Italy), and the results were found within± 0.4% of the theoretical values. The electronic spectra (UV-Vis) were recorded on a Perkin-ElmerLambda 15 UV-Vis spectrophotometer, using $10^{-3}$mol·$dm^{-3}$ solutions in DMF.

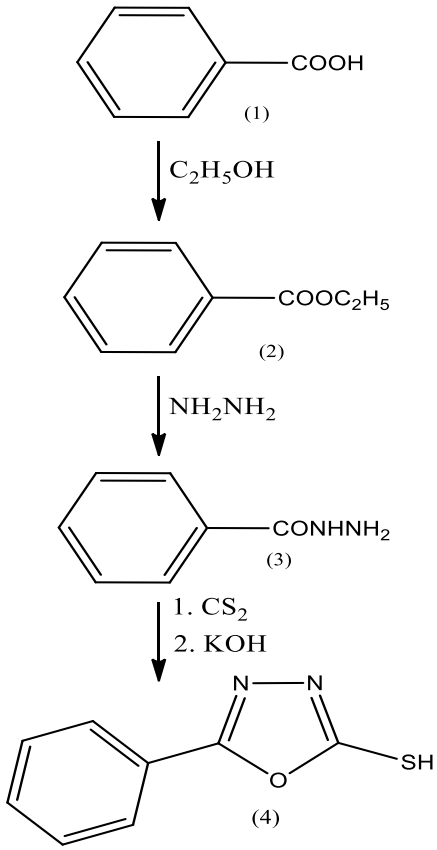


**Fig.2** 5-Phenyl-1,3,4-oxadiazole-2-thiol

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## 3. Antimicrobial activity

The antimicrobial activity was assayed *in vitro* by the twofold broth dilution[17]against bacteria *Escherichia coli, Bacillus subtilis* and *Staphylococcus aureus* and fungus *Candida albican,Aspergillusniger*and *Candida krusei*. The minimal inhibitory concentrations (MIC, µg/ml) were defined as the lowest concentrations of compound that completely inhibited the growth of each strain. All compounds, dissolved in dimethylsulfoxide, were added to culture media .Mueller Hinton Broth for bacteria and Sabouraud Liquid Medium for fungi to obtain final concentrations ranging from 125 µg/ml to 1.592 µg/ml. The amount of dimethylsulfoxide never exceeded 1% v/v. Inocula consisted of 5.0 $x10^4$ bacteria/ml and 1.0 $x10^3$ fungi/ml. The MICs were read after incubation at 37 °C for 24 h (bacteria) and at 30°C for 48 h (fungi). Media and media with 1% v/v dimethylsulfoxide were employed as growth controls. Chloroamphenicol and fluconazole were used as reference antibacterial and antifungal drugs, respectively.

To detect the type of antimicrobial activity, subcultures were performed by transferring 100 µl of each mixture remaining clear in 1 ml of fresh medium. The minimal bactericidal concentrations (MBC, µg/ml) and the minimal fungicidal concentrations (MFC, µg/ml) were read after incubation at 37 °C for 24 h and at 30 °C for 48 h, respectively.

## 4. Result and Discussion

### 4.1 Spectral analysis

Heteroaromatic structure shows the presence of C-H stretching, in-plane bending vibrations in the regions 3200-3000 $cm^{-1}$ and 900-1200 $cm^{-1}$ respectively. In this region the bands are not affected appreciably by the nature of the substituent. The FTIR bands at 3111, 2935, 2742 and 2548$cm^{-1}$ and FT-Raman bands at 3068, 2634 and 2563 $cm^{-1}$ in 5-phenyl-1,3,4-oxadiazole-2-thiol is assigned to C-H stretching modes. The bands at 1271, 1265, 1173 $cm^{-1}$ have been assigned to C-H in-plane bending vibrational modes.

The IR and Raman bands identified at 2438 and 2398 $cm^{-1}$are assigned to S-H stretching mode.

The C=N stretching frequencies in the Raman spectrum of crystalline 5-phenyl-1,3,4-oxadiazole-2-thiol occur in the range 1600-1450 $cm^{-1}$. In the present investigation, the Raman bands observed at 1467 $cm^{-1}$ have been assigned to C=N stretching vibrations. The very strong IR peak and the strong Raman peak observed at 1471$cm^{-1}$is assigned to C-N stretching mode.

The carbon-carbon stretching vibrations of the title compound have been observed at 1400 to 1320 $cm^{-1}$. The medium Raman bands identified at 912 and 825 $cm^{-1}$ have been assigned to C-C in-plane bending.

Carbon-sulphur stretching vibrations of the title compound have been observed at 704 cm-1. The medium Raman bands identified at 680 cm-1 have been assigned to C-S in-plane bending. These assignments are in good agreement with the literature.(table1).

In the $^1$H-NMR spectra, the singlet signal at δ13.77 ppm is assigned to SH based on the position of this peak in the spectrum of the parent 5-phenyl-1,3,4-oxadiazole-2-thiol molecule. The assignment of the peak at δ7.62-7.49 ppm of five proton of phenyl ring in the title compound. (table2).

UV-Vis absorption spectra of 5-phenyl-1,3,4-oxadiazole- 2-thiol after the continuous prolonged irradiation (0, 5, 15, 30, 45 and 60 min) with UV-A light. Both the absorption maxima ($\lambda_{max}$= 203 nm and $\lambda_{max}$= 215 nm) decrease, and a slight bathochromic shift have been detected, at the end of any particular UV-irradiating period. The log values of the absorbance maxima plotted against irradiation time yielded a linear plot, suggesting the involved kinetics to be probably of pseudo-first order, depending on the 5-phenyl-1,3,4-oxadiazole- 2-thiol concentration only. (table3).

**Table:1** Vibrational assignments of fundamental frequencies ($cm^{-1}$) of 5-phenyl-1,3,4-oxadiazole-2-thiol.

| Species | Observed Frequencies ($cm^{-1}$) | | Calculate Frequencies ($cm^{-1}$) | Assignment |
|---|---|---|---|---|
| | FTIR | Raman | | |
| 4 | 3111(s) | - | 3115 | C-H stretching |
| 4 | - | 3068(s) | | C-H stretching |
| 4 | 2935(s) | - | - | C-H stretching |
| 4 | 2742(s) | 2634(w) | - | C-H stretching |
| 4 | 2548(s) | - | - | C-H stretching |
| 4 | 2438(s) | | 2450 | S-H stretching |
| 4 | - | 2398(w) | - | S-H stretching |
| 4 | 1597(s) | - | 1585 | C=N stretching |
| 4 | 1489(w) | - | - | C=N stretching |
| 4 | - | 1467(w) | - | C=N stretching |
| 4 | 1389(w) | - | - | C=C stretching |
| 4 | - | 1375(w) | - | C=C stretching |
| 4 | 1336(w) | | - | C=C stretching |
| 4 | 1271(s) | - | 1265 | C-H in plane bending |
| 4 | 1176(w) | - | - | C-H in plane bending |
| 4 | 1060(s) | - | 1078 | N=N stretching |
| 4 | 954(s) | - | - | N=N stretching |
| 4 | - | 912(m) | - | C-C in plane bending |
| 4 | - | 825(w) | - | C-C in plane bending |
| 4 | 704(s) | - | - | C-S-C in plane bending |
| 4 | - | 680(m) | - | C-S-C in plane bending |
| 4 | 623(s) | - | - | C-O-C in plane bending |
| 4 | 569(s) | - | - | C-C-H in plane bending |
| 4 | 491(s) | - | - | C-C-H in plane bending |

**Table 2**: 1H-NMR data of 5-phenyl-1,3,4-oxadiazole-2-thiol.

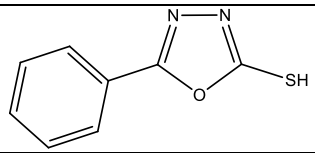
| Compound | δ/ ppm | Assignments |
|---|---|---|
|  | 7.62-7.49 | m, 5H of CH of phenyl |
| | 13.77 | s, 1H of SH of thiol |

**Table 3**: Electronic spectral data in 95% ethanol and DMF, λmax(nm) / εmax($10^3$ $mol^1.dm^3.cm$)

| Solvent | 5-phenyl-1,3,4-oxadiazole-2-thiol | | | |
|---|---|---|---|---|
| | I | II | III | IV |
| Ethanol | 202.5/0.82 | 222.5/0.34 | 306.5/0.47 | 250.00/0.42 |
| DMF | - | 225.6/0.61 | - | 315.2/0.52 |

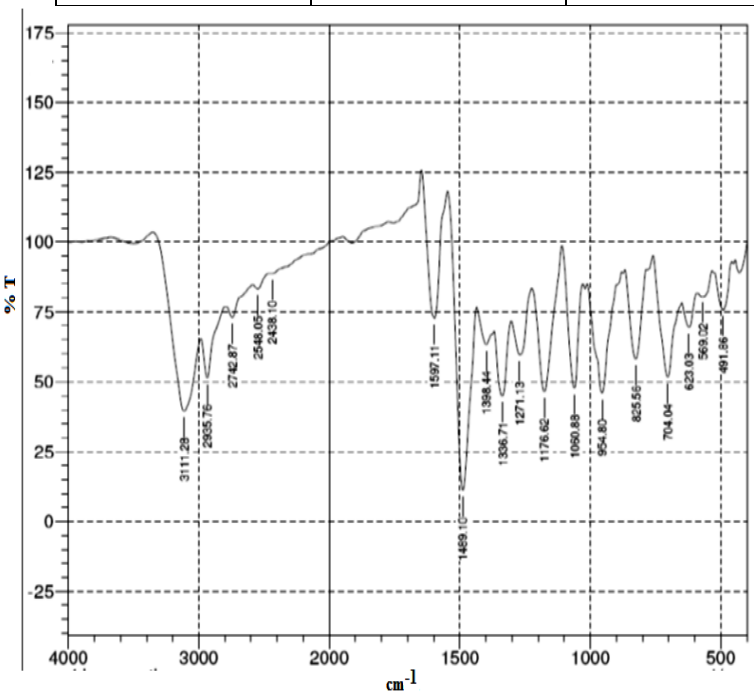



**Fig. 2** FTIR-Raman Spectroscopy of 5-phenyl-1,3,4-oxadiazole-2-thiol

**Table 4**: Minimal inhibitory concentration (MIC) µg/ml of 5-phenyl-1,3,4-oxadiazole-2-thiolagainst tested bacterial and fungal strains

| Compound No. | Minimal Inhibitory Concentration (MIC) µg/ml | | | | | |
|---|---|---|---|---|---|---|
| | E. coli | B. subtilis | S .aureus | C. albicans | A. niger | C. krusei |
| 4 | 1.592 | 3.125 | 6.25 | 1.592 | 3.125 | 1.592 |
| Chloroampheni col | 12.5 | 6.25 | 12.5 | - | - | - |
| Fluconazole | - | - | - | 12.5 | 12.5 | 6.25 |

**4.2 Antimicrobial activity (Minimal inhibitory concentration)**

Antibacterial activity of 5-phenyl-1,3,4-oxadiazole- 2-thiol (4) and standard drug, chloroamphenicol, was carried out at a concentration 250 µg/ml against *E. coli ATCC 25922*, *B. subtilis ATCC 1633* and *S. aureus ATCC 25923*. Results show the varying degree of antibacterial activity of all the compounds tested as given in table 4.

From the results obtained, it is clear that 5-phenyl-1,3,4-oxadiazole-2-thiol exhibited less activity against *E. coli ATCC 25922*, *B. subtilis ATCC 1633* than chloroamphenicol but *S. aureus ATCC 25923* displayed antibacterial property moderate to the reference drug.

The compound 5-phenyl-1,3,4-oxadiazole- 2-thiol (4) along with reference drug, fluconazole, were also tested for antifungal activity at a concentration of 250 µg/ml against *C. albicans ATCC 2091*, *A. niger ATCC 9029* and *C. krusei ATCC 6518*, and it is found that synthesized is showed very weak or moderate active as compared to standard drug.

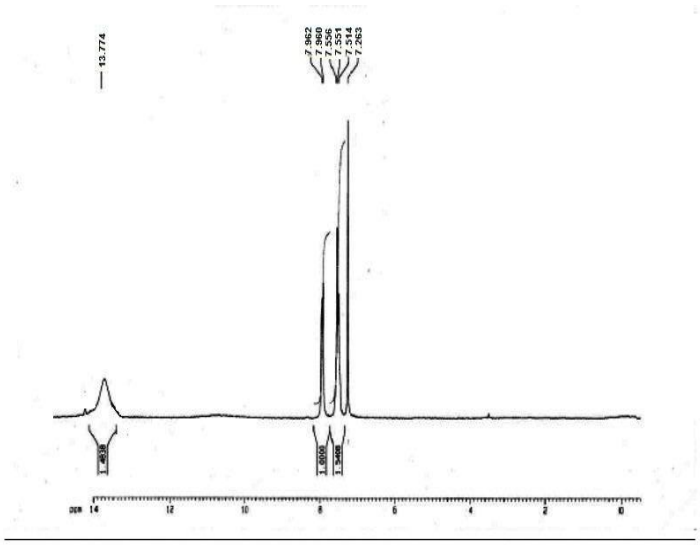



**Fig. 2** H-NMR Spectroscopy of 5-phenyl-1,3,4-oxadiazole-2-thiol

## 5. Conclusions

5-phenyl-1,3,4-oxadiazole- 2-thiol established using FTIR, UV-Vis and $^1$H-NMR spectroscopic method. Vibrational and electronic spectra confirmed the synthesized compound, 5-phenyl-1,3,4-oxadiazole- 2-thiol. The compound was tested for its *in vitro* antimicrobial activity and its activity against bacteria *Escherichia coli*, *Bacillus subtilis* and *Staphylococcus aureus* and fungus *Candida albican*, *Aspergillusniger*and *Candida krusei* compared to chloramphenicol and fluconazole, respectively.

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