# THIONYL CHLORIDE CATALYZED SYNTHESIS AND ANTIMICROBIAL ACTIVITIES OF SOME 2-BENZYLIDENE-1-TOSYLHYDRAZINES

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**Keywords:** 2-benzylidene-1-tosylhydrazines; IR and NMR spectra; antimicrobial activities.

More than 85 % yields of ten substituted 2-benzylidene-1-tosylhydrazines have been prepared by thionyl chloride assisted condensation of 1-tosylhydrazine and substituted benzaldehydes in room temperature. They are characterized by their physical constants, analytical, and spectroscopic data. The antimicrobial activities of these hydrazines were evaluated by Bauer-Kirby disc diffusion method.

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## INTRODUCTION

Generally, sulphur substituted compounds have a significant role in developing pharmaceutical chemistry filed.[1] Numerous medicinally important products are made up of heterocyclic sulphur compounds using challenging synthetic reproductions. Hydrazones and hydrazides are currently a significant class of therapeutically active compounds.[2, 3] The suitable intermediates are produced by the heterocyclic hydrazone compounds like thiazolidin-4-one[4] or 1, 3-benzothiazin-4-one.[5] Hydrazones can act as polydentate ligands, depending on the nature of the attached group of hydrazone substituent. In organic synthesis, sulphur containing hydrazones shows interesting pharmaceutical derivatives and essential intermediates.[6] Pharmacophoric hydrazone derivatives are newly designed based on highly bio-activity, appear vital activity and biologically important position. The interesting and valuable field for variety of heterocyclic compounds prepared from sulphur hydrazides, because they have medication active like antibacterial,[7] exhibit a great interest due to their importance in synthesis a which have antifungal,[8] anti-inflammatory[9] herbicidal,[10] inhibitory activity,[11] analgesic activity,[12] anticholinergic and antihistaminic,[13] activity of regulating growth in plant[14] etc. Within the above view, no information available in literature in the past for synthesis and infectious activities of 2-benzylidene-1-tosylhydrazines. Therefore, the authors have taken efforts for the synthesis of some substituted 2-benzylidene-1-tosylhydrazines and studied the antibacterial and antifungal activities by Bauer-Kirby[15] disc diffusion method.

## EXPERIMENTAL

### Materials and Methods

All chemicals procured from the chemical company of Aldrich Bangalore. To detect the melting points of all prepared tosylhydrazines are found in Suntex melting point apparatus with capillary tubes. The ultraviolet spectra of the tosylhydrazines synthesized have been noted using double beam-ELICO BL222 Bio-Spectrophotometer. Fourier transform infrared spectra (KBr, 4000-400 $cm^{-1}$) have been documented on AVATAR-300 FT-IR spectrophotometer. The BRUKER-500MHz NMR spectrometers were used for noted proton and $^{13}C$ spectra in the $CDCl_3$ solvent using tetramethylsilane as internal standard. Microanalysis of all compounds was performed in Thermofinnigan CHN analyzer.

### Synthesis of 2-benzylidene-1-tosylhydrazines

The appropriate mixture of 1-tosylhydrazine (100 mmol) and *ortho*, *meta* and *para* substituted benzaldehydes (100 mmol), 15 mL of diethyl ether and (100 mmol) of thionyl chloride were added. The reaction content was vigorously agitated at normal temperature for 30 minutes[16] (Scheme 1). After complete renovation of the tosylhydrazines as monitored by thin layer chromatogram, the mixture may allow to 20 minutes for an undisturbed condition. The method of filtration is used to the removal of unreacted reagents. The crude product was cleaned with deionized water and recrystallized from absolute ethanol, dried well and kept in a desiccator. The synthesized 2-benzylidene-1-tosylhydrazines have been regarded as by their physical constants, elemental analysis, and spectroscopic data and are presented in Table 1. The ultraviolet, infrared and nuclear magnetic resonance spectroscopic data of synthesized 2-benzylidene-1-tosylhydrazines are shown in Table 2.

**Table 1.** Physical constants, yield and analytical data of substituted 2-benzylidene-1-tosylhydrazines

| No. | X | MF | MW | Yield, % | Mp., ºC | Microanalysis(%) | | |
|---|---|---|---|---|---|---|---|---|
| | | | | | | C | H | N |
| 1 | H | $C_{14}H_{14}N_2O_2S$ | 274 | 89 | 98-99 | 61.22(61.29) | 5.12(5.14) | 10.18(10.21) |
| 2 | 3-Br | $C_{14}H_{13}N_2O_2SBr$ | 353 | 92 | 135-136 | 47.63(47.60) | 3.71(3.68) | 7.937.85) |
| 3 | 2-Cl | $C_{14}H_{13}N_2O_2SCl$ | 308 | 94 | 124-125 | 54.48(54.46) | 4.18(4.24) | 9.02(9.07) |
| 4 | 4-Cl | $C_{14}H_{13}N_2O_2SCl$ | 308 | 92 | 118-119 | 54.44(54.46) | 4.17(4.24) | 9.04(9.07) |
| 5 | 4-F | $C_{14}H_{13}N_2O_2SF$ | 292 | 95 | 124-125 | 57.58(57.52) | 4.42(4.48) | 9.52)(9.58) |
| 6 | 3-OH | $C_{14}H_{14}N_2O_3S$ | 290 | 88 | 129-130 | 57.96(57.92) | 4.82(4.86) | 9.63(9.65) |
| 7 | 4-OH | $C_{14}H_{14}N_2O_3S$ | 290 | 87 | 127-128 | 57.94(57.92) | 4.81(4.86) | 9.61(9.65) |
| 8 | 4-$CH_3$ | $C_{15}H_{16}N_2O_2S$ | 288 | 90 | 127-128 | 62.50(62.48) | 5.57(5.59) | 9.68(9.71) |
| 9 | 2-$NO_2$ | $C_{14}H_{13}N_3O_4S$ | 319 | 91 | 122-123 | 52.69(52.66) | 4.06(4.10) | 13.12(13.16) |
| 10 | 3-$NO_2$ | $C_{14}H_{13}N_3O_4S$ | 319 | 93 | 110-111 | 52.68(52.66) | 4.08(4.10) | 13.14(13.16) |

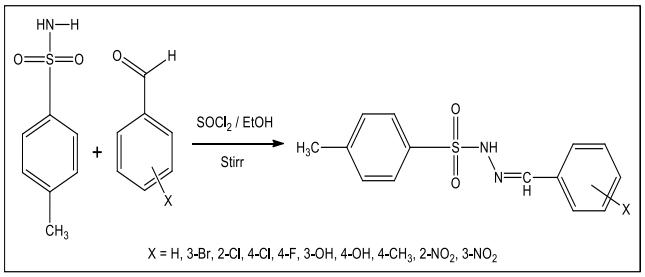
Values in the parenthesis are calculated

**Table 2.** The ultraviolet absorption maxima ($\lambda_{max,}$ nm), infrared absorption (ν, $cm^{-1}$) and NMR chemical shifts (δ, ppm) spectral values of substituted 2-benzylidene-1-tosylhydrazines compounds.

| No. | X | UV, $\lambda_{max}$, nm | IR, ν, $cm^{-1}$ | | | | $^1$H NMR, δ, ppm | | | $^{13}$C NMR, δ, ppm | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | C=N | $SO_2$ (sym) | $SO_2$(asym) | N-H | N-H | C-H | $CH_3$ | C=N | $CH_3$ |
| 1 | H | 279.0 | 1591.27 | 1168.86 | 1307.74 | 3219.19 | 9.961 | 8.1170 | 2.4288 | 127.96 | 21.57 |
| 2 | 3-Br | 299.0 | 1521.84 | 1166.93 | 1344.38 | 3194.12 | 9.892 | 8.2742 | 2.3847 | 127.94 | 21.58 |
| 3 | 2-Cl | 293.0 | 1568.13 | 1136.07 | 1305.81 | 3080.32 | 9.886 | 8.0462 | 2.3534 | 128.32 | 21.36 |
| 4 | 4-Cl | 295.0 | 1510.26 | 1161.15 | 1325.10 | 3207.62 | 9.766 | 8.2680 | 2.3743 | 127.79 | 21.51 |
| 5 | 4-F | 304.5 | 1597.06 | 1168.86 | 1330.88 | 3186.40 | 9.989 | 8.0324 | 2.4148 | 127.96 | 21.62 |
| 6 | 3-OH | 279.0 | 1516.05 | 1159.22 | 1367.74 | 3221.12 | 9.792 | 8.7468 | 2.3400 | 127.79 | 21.45 |
| 7 | 4-OH | 279.0 | 1560.41 | 1170.79 | 1357.89 | 3197.98 | 9.668 | 8.6554 | 2.5003 | 127.77 | 21.49 |
| 8 | 4-$CH_3$ | 270.5 | 1597.06 | 1168.86 | 1330.88 | 3188.33 | 9.221 | 8.2994 | 2.3677 | 127.39 | 21.68 |
| 9 | 2-$NO_2$ | 290.0 | 1506.41 | 1165.00 | 1361.74 | 3211.48 | 9.811 | 8.7884 | 2.4480 | 127.78 | 21.49 |
| 10 | 3-$NO_2$ | 279.0 | 1514.12 | 1159.22 | 1357.89 | 3211.48 | 9.644 | 8.9266 | 2.3815 | 127.79 | 21.51 |

**Table 3.** Antibacterial activities of substituted 2-benzylidene-1-tosylhydrazines compounds

| Entry | X | (Zone of inhibition(mm) values) | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | (Gram +ve bacteria) | | | | (Gram -ve bacteria) | | | | | |
| | | S. Aureus | S. Pyogenes | M. Luteus | B. Substilis | K. Pneumoniae | V. Parahaem-dyticus | K. Oxytoca | P. Mirabilis | E. Coli | P. Aeruginosa |
| 1 | H | 6 | 6 | 6 | 6 | 7 | 6 | 6 | 7 | 6 | 6 |
| 2 | 3-Br | 6 | 6 | 6 | 7 | 7 | 6 | 6 | 7 | 7 | 7 |
| 3 | 2-Cl | --- | 7 | --- | 7 | 8 | 6 | 8 | 6 | 7 | 6 |
| 4 | 4-Cl | 6 | 6 | 6 | 6 | 6 | 6 | --- | 6 | 8 | 6 |
| 5 | 4-F | 6 | --- | --- | --- | 6 | 6 | 6 | 7 | 6 | 6 |
| 6 | 3-OH | 6 | 7 | 6 | 6 | 8 | 6 | 7 | 6 | 8 | 6 |
| 7 | 4-OH | 6 | 6 | 6 | --- | 8 | 6 | 6 | --- | 7 | --- |
| 8 | 4-CH3 | 6 | 6 | 6 | 6 | 7 | --- | --- | 6 | 7 | --- |
| 9 | 2-NO2 | 7 | 6 | --- | 7 | 10 | 6 | 6 | 6 | 6 | 6 |
| 10 | 3-NO2 | 7 | --- | 6 | 6 | --- | 6 | 6 | 6 | 6 | 6 |
| Standard | Ciprofloxacin | 9 | 9 | 8 | 7 | 10 | 9 | 9 | 10 | 8 | 11 |
| Control | DMSO | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |




**Scheme 1.** Synthesis of substituted 2-benzylidene-1-tosylhydrazines thionyl chloride assisted condensation of 1-tosylhydrazine and substituted benzaldehydes

## RESULTS AND DISCUSSION

These multi-prolonged activities present in different 2-benzylidene-1-tosylhydrazines have been examined against respective microbes-bacteria such as *Staphylococcus aureus, Staphylococcus pyogenes, Micrococcus luteus, Bacillus subtilis, Klebsiella pneumonia, Vibro cholera, Klebsillaoxytoca, Proteus Mirabilis, Pseudomonas aeruginosa* and *Escherichia coli bacterial* species. And fungal strains such as *Mucor species, Aspergillus niger*, and *Trichoderma viride* fungal strains.

### Antibacterial sensitivity assay

Antibacterial sensitivity assay has been accomplished using Kirby-Bauer[15-17] disc diffusion technique. In each Petri plate, about 0.5 $cm^3$ the sterile glass spreader are used to spread the sample of test bacteria to over the medium uniformly at solidified Mueller-Hinton agar. The sterile forceps are used to impregnated by Whatman No.1 filter paper (5 mm diameter), the compound containing the solution to place the medium. To avoid the water droplets collection on plates upside down over the medium, to incubated at 37 °C for 24 hours. The inhibition zone values of diameter are visually surveyed after 24 hours at the plates. Same procedure is used to measure for triplicate values.

The synthesized 2-benzylidene-1-tosylhydrazines compounds are screened for the antibacterial study is shown in Figure S1 (Plates 1-20) (See supplementary material 1). Following four gram-positive bacterial strains *S. Aureus,*[17] *S. Pyogenes,*[18] *M. Luteus,*[19] *B. Substilis*[20, 21] *and* six gram-negative strains *K. Pneumoniae,*[22] *V. Parahaemdyticus,*[23] *K. Oxytoca,*[24] *P. Mirabili,*[25] *E. Coli,*[26] *P. Aeruginosa*[27] are used for antibacterial study of all the synthesized 2-benzylidene-1-tosylhydrazines. The technique of disc diffusion was followed at a concentration of 250 µg $mL^{-1}$ with Ciprofloxacin taken as the standard. The inhibition zone values are used to compare in Table 3 is the corresponding chart of clustered column is shown in **Figure 1.**

Analysis of the inhibition zone (mm) values reveals that the all the substituted 2-benzylidene-1-tosylhydrazines compounds were shown satisfactory antibacterial action *S. Aureus* bacterial strain except 2-chloro substituent. The inhibition zone (mm) values reveal that the all the substituted 2-benzylidene-1-tosylhydrazines compounds were shown satisfactory and good antibacterial action against *S. Pyogenes* bacterial strain except for 4-fluoro and 3-nitro substituents. The inhibition zone (mm) values reveals that the benzohydrazide compounds have shown satisfactory and moderate antibacterial activity against *M. Luteus* bacterial strain. The inhibition zone (mm) values reveal that the substituted 2-benzylidene-1-tosylhydrazines compounds have shown satisfactory antibacterial activity against *M. Luteus* bacterial strain except for 2-chloro, 4-fluoro, and 2-nitro substituents.

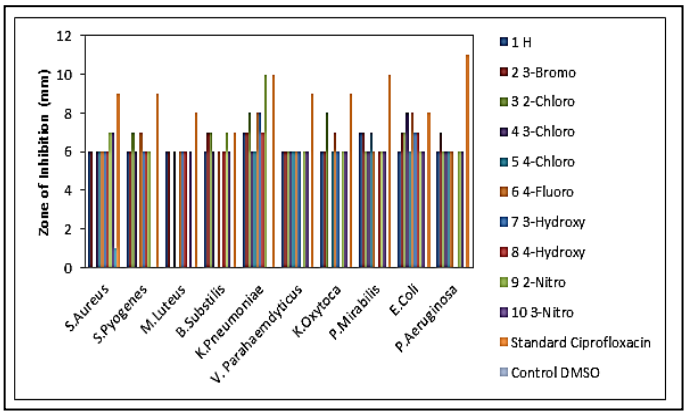



**Figure 1.** Antibacterial activities chart of clustered column substituted 2-benzylidene-1-tosylhydrazines

Analysis of the inhibition zone (mm) values reveal that the some substituted 2-benzylidene-1-tosylhydrazines compounds shown good antibacterial activity and remaining substituted 2-benzylidene-1-tosylhydrazines compounds have a satisfactory antibacterial action against *B. Substilis* bacterial strain except for 4-fluoro and 4-hydroxy substituents.

The 2-nitro substituted 2-benzylidene-1-tosylhydrazines compound shown good antibacterial activity and remaining substituted 2-benzylidene-1-tosylhydrazines compounds have a good antibacterial action against *K. Pneumoniae* bacterial strain except for 3-nitro substituent.

The inhibition zone (mm) values reveal that the 2-benzylidene-1-tosylhydrazines compounds have been shown moderate antibacterial action against *V. Parahaemdyticus* bacterial strain except for 4-methyl substituent. The inhibition zone (mm) values reveal that the 2-benzylidene-1-tosylhydrazines compounds have shown satisfactory antibacterial action against *K. Oxytoca* bacterial strain except for 4-chloro and 4-methyl substituents. The inhibition zone (mm) values reveal that the 2-benzylidene-1-tosylhydrazines compounds have been shown satisfactory and moderate antibacterial action against *P. Mirabilis* bacterial strain except for 4-hydroxy substituent. The 4-chloro and 3-hydroxy substitute 2-benzylidene-1-tosylhydrazines compounds have been shown good antibacterial activity, and remaining substituents have moderate antibacterial activity against *E. Coli* bacterial strain. The inhibition zone (mm) values reveal that the 2-benzylidene-1-tosylhydrazines compounds have shown

satisfactory antibacterial action against *P. Aeruginosa* bacterial strain except for 4-hydroxy and 4-methyl substituents.

**Antifungal sensitivity assay**

Antifungal sensitivity assay has been performed using Kirby-Bauer[15] disc diffusion technique. PDA medium is prepared and then sterilized as stated earlier. The fungal species containing (1 mL) Petri-plate then poured PDA medium in ear bearing heating condition. The anti-fungal action of the synthesized substituted 2-benzylidene-1-tosylhydrazines benzohydrazide compounds had been studied against three fungal species *A. Niger*,[28] *M. Specie*,[29] and *T.Viride*.[30-32]

The species are spreading over the plates uniformly using clockwise and anti-clockwise rotations. The about 15 mg sample is used to prepare the test solution of substituted 2-benzylidene-1-tosylhydrazines in DMSO solvent (1 mL). The impregnation is followed by the disc in the test solution. The medium has been permitted to solidify and kept for 24 hours.

The inhibition zone values of the plates have been examined and measured the diameters. The results had been recorded by the triplicate and repeating the same procedure. The antifungal action of substituted (2-benzylidene-1-tosylhydrazines compounds had been studied and are shown in Figure S2 for Plates (21-26) (See supplementary material 2), and the inhibition zone value of the effect is given in Table 4. The chart clustered column, shown in Figure 2.

Analysis of the inhibition zone (mm) values reveals that the substituted 2-benzylidene-1-tosylhydrazines compounds had shown satisfactory and moderate antifungal action against *A. niger* species. The inhibition zone (mm) values reveal that the substituted 2-benzylidene-1-tosylhydrazines compounds have shown satisfactory antifungal activity against *M. species* fungal species except for 4-hydroxy and 4-methyl substituents. The zone of inhibition (mm) values reveals that the substituted 2-benzylidene-1-tosylhydrazines compounds had shown satisfactory antifungal action against *T.viridie* fungal species.

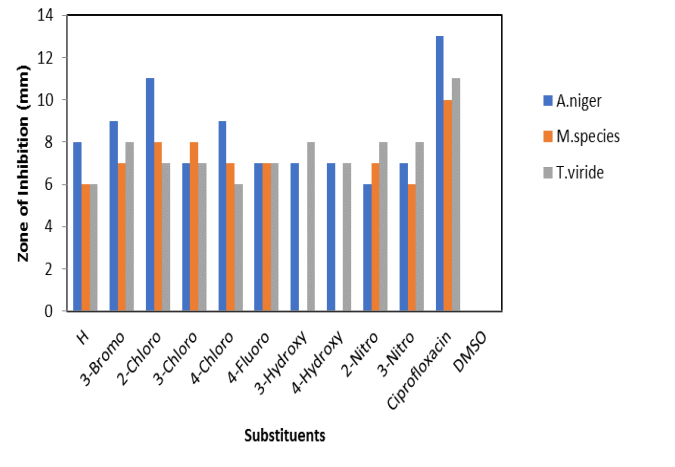



**Figure 2.** Antifungal activities chart of clustered column Substituted 2-benzylidene-1-tosylhydrazines compounds

**Table 4.** Antifungal action of substituted 2-benzylidene-1-tosylhydrazine compounds

| No. | X | Zone of inhibition(mm) | | |
|---|---|---|---|---|
| | | *A. Niger* | *M. Species* | *T. Viride* |
| **1** | H | 8 | 6 | 6 |
| **2** | 3-Br | 9 | 7 | 8 |
| **3** | 2-Cl | 11 | 8 | 7 |
| **4** | 4-Cl | 7 | 8 | 7 |
| **5** | 4-F | 9 | 7 | 6 |
| **6** | 3-OH | 7 | 7 | 7 |
| **7** | 4-OH | 7 | --- | 8 |
| **8** | 4-$CH_3$ | 7 | --- | 7 |
| **9** | 2-$NO_2$ | 6 | 7 | 8 |
| **10** | 3-$NO_2$ | 7 | 6 | 8 |
| Standard | Miconazole | 13 | 10 | 11 |
| Control | DMSO | --- | --- | --- |

## CONCLUSIONS

A sequence of ten numbers of substituted 2-benzylidene-1-tosylhydrazines compounds have been prepared by condensation of 1-tosylhydrazine and substituted benzaldehydes using thionyl chloride catalyst. These synthesized substituted 2-benzylidene-1-tosylhydrazines compounds have been characterized by their physical constants, microanalysis, and spectroscopic data. The parent 2-benzylidene-1-tosylhydrazines, 3-hydroxy substituted 2-benzylidene-1-tosylhydrazines, and 3-hydroxy 2-benzylidene-1-tosylhydrazines compounds have antibacterial activities against all ten bacterial strains. The 2-nitro- substituted benzylidene-1-tosylhydrazines shown better antibacterial activity against *K. Pneumoniae* strain. All the substituted 2-benzylidene-1-tosylhydrazines compounds have been good and satisfactory antibacterial activity against *E. Coli bac*terial strain. All the substituted 2-benzylidene-1-tosylhydrazines compounds have shown antifungal action against *T. Viridie* and *A. Niger* fungal species. All the substituted 2-benzylidene-1-tosylhydrazines compounds had shown antifungal action against *M. Specie* fungal species except 4-hydroxy and 4-methyl substituents.

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## CONFLICT OF INTEREST

Authors declare no conflict of interest.

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