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**Research Article**

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# Evaluation of the antimicrobial activities of novel 1,2 and 1,5-diols

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**ABSTRACT**

*The synthesis of novel 1,2-diols **1-5** and 1,5-diols **6&7** have been carried out as reported[8,9] from our laboratory. The compounds **1-5, 6&7** were screened for their antimicrobial activity. They have been tested for antibacterial activity against Gram –Positive bacteria Staphylococcus aureus and against Gram-Negative bacteria Escherichia coli, Klebsiella pneumoniae, Salmonella thypi and Vibrio cholera.The antifungal activity has been tested against Candida albicans and Aspergillus flavus.*

**Keywords:** Antimicrobial activity, antibacterial activity, antifungal activity, 1, 2–diols, 1, 5-diols.

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## INTRODUCTION

The hydroxyl structural moiety is found in numerous pharmaceutically active compounds and therefore represents an interesting template for medicinal chemistry [1]. In particular phenyl ethanol derivatives have good antifungal properties [2, 3]. 2-[2-(Hydroxymethyl) Phenyl] ethanol derivatives are reported [4] as potential antibacterial agents. Eckstein et al. [5] found that 2-nitropropan-1, 3-diol derivatives possessed antifungal activity. Croshaw, Groves, and Lessel [6] examined 2-bromo-2-nitropropan-1, 3-diol and showed it to be active against both bacteria and, to a lesser extent, fungi. The antimicrobial studies of 3-hetarylazoquinoline-2,4-diol compounds has been reported [7]. Hence herein we report the antimicrobial studies of the novel 1,2-diols, **1-5** and 1,5–diols **6&7** whose synthesis is reported [8,9] from our laboratory..

## EXPERIMENTAL SECTION

All m.ps are uncorrected. The homogeneity of the compounds was checked by Thin Layer Chromatography (TLC) over silica gel. $^{1}$H NMR spectra were recorded in $CDCl_3$ using TMS as an internal standard on a Bruker 300 spectrometer at 500 MHz.$^{13}$C NMR were recorded on a Bruker 300 spectrometer at 75 MHz and mass spectra on Jeol DX 303 spectrometer.

**General Procedure for the Synthesis of 1, 2-diols, (1-5)**

To a solution of aryl magnesium bromide in dry THF at 0°C under $N_2$ atmosphere [prepared from magnesium (Mg)(0.03mol) and aryl bromide (0.03mol)], the dione (0.01mol) in dry THF was added drop wise over a period of 15 – 20 minutes. After completion of addition, the mixture was stirred at 0° C under $N_2$ atmosphere for 2 h followed by stirring at room temperature under $N_2$ atmosphere for 3h. After the completion of reaction as evidenced by TLC, the reaction was quenched with a saturated solution of ammonium chloride ($NH_4Cl$) (50mL). The product was extracted with diethyl ether (2x50ml). The ether layer was washed with water followed by brine and dried over anhydrous sodium sulphate ($Na_2SO_4$) and evaporated. Purification of the crude product by column chromatography on silica gel (100 – 200 mesh) using hexane – ethyl acetate (9:1) as eluent gave the corresponding product.

**General Procedure for the Synthesis of 1, 5-diols, (6&7)**

To a solution of the 1,2-diol [(**3**or **4**) 0.0005 mol].in dry t-BuOH(10ml) was added a suspension of t-BuOK (0.0005 mol.) in dry t-BuOH (10ml).The mixture was refluxed under nitrogen atmosphere for 4h and quenched with a saturated solution of ammonium chloride (10 ml). The product formed was extracted with diethyl ether (3x 10 ml). The ether layer was washed with water, dried over anhydrous sodium sulphate and evaporated. Purification of the residue by column chromatography on silica gel, with ethyl acetate- hexane (1: 10 ml) as eluent afforded the corresponding 1, 5- diol

**Antimicrobial activity**

In this work, we report the *in vitro* study of antimicrobial activity of the novel 1,2-diols **(1-5),** and1,5-diols **6&7** against Gram –Positive bacteria *Staphylococcus aureus* and against Gram-Negative bacteria *Escherichia coli, Klebsiella pneumoniae, Salmonella thypi and Vibrio cholera.*The antifungal activity has been tested against the fungi *Candida albicans and Aspergillus flavus.*

**Antimicrobial assay**

Screening of antimicrobial activity was carried out in the following sequence

(i) Preparation of nutrient agar (ii) Preparation of Mc Ferland standards (iii) Inoculums preparation. (iv) *In vitro* Antimicrobial Sensitivity Determination by Agar well diffusion method.

(i) Preparation of nutrient agar

The nutrient agar was prepared by dissolving beef extract(1.5g), peptone(0.5g), yeast extract (1.5g), sodium chloride (0.5g) and agar (1.5g) 100ml of distilled water. The pH was adjusted to 7.2 followed by sterilization in an autoclave at $121^0$C / 15LB for 15 minutes. The sterile molten agar media was then cooled to $50^0$C. About 15 ml of the media was poured on a sterile petri-plate and allowed to cool to room temperature.

(ii) Preparation of 0.5 Mc Ferland standards

0.5ml of solution A (1.175g of barium chloride in 100 ml of distilled water) was added to 99.5 ml of solution B (1 ml of 0.36 N sulphuric acid in 100 ml of distilled water) and mixed well with magnetic stirrer, then distributed in test tubes with a screw cap of the same size as those containing the bacterial/ fungal culture.

(iii) Preparation of bacterial and fungal inoculums.

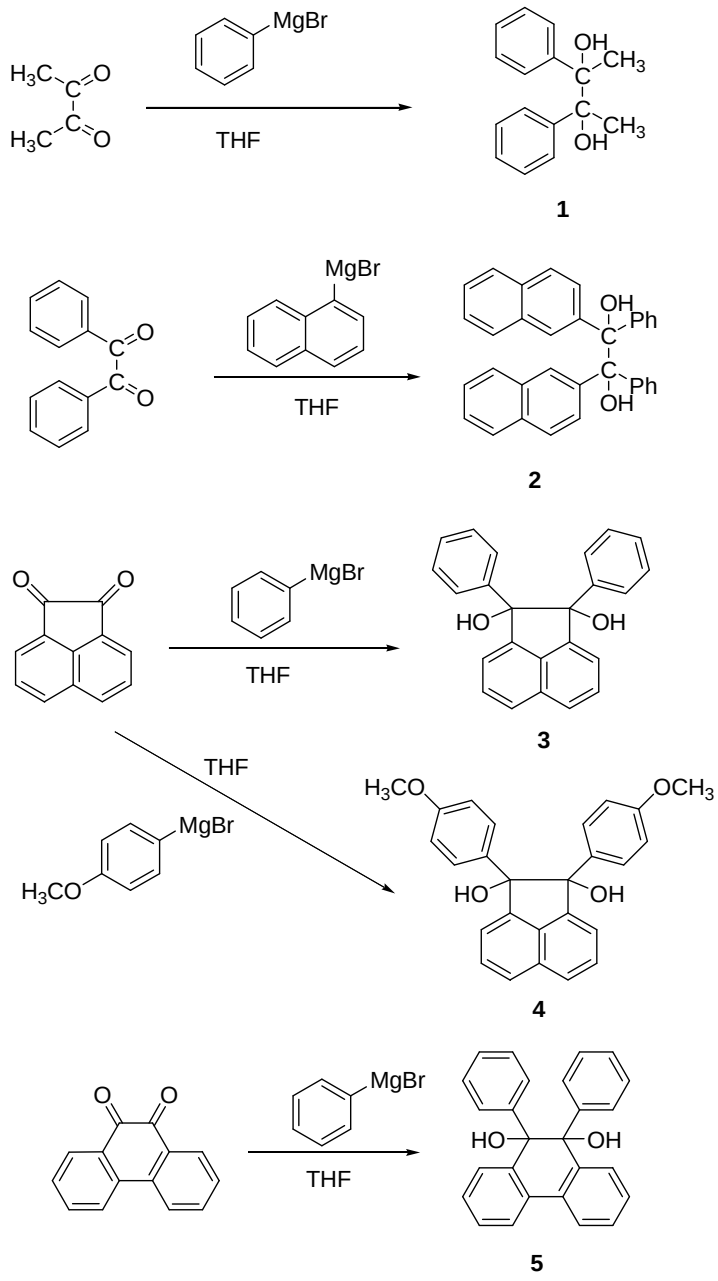
The cooled sterile broth medium was poured into sterile petri-plates having a uniform depth of 4mm; this is equivalent to approximately 25 ml in a 90mm plate. Once the medium had solidified then the culture was inoculated on the medium. The turbidity of the culture was adjusted with sterile broth so as to correspond to 0.5 Mc Ferland standards. Immediately after standardisation, a sterile cotton swab was immersed in the bacterial/ fungal suspension and then rotated and compressed against the wall of the test tube, so as to remove the excess fluid.

(iv) *In vitro* Antimicrobial Sensitivity Determination by Agar well diffusion method.

In vitro antimicrobial sensitivity of the antibiotics and the test compounds synthesised were determined by well diffusion method as recommended by the National Committee for Clinical Laboratory Standards (NCCLS) [12]. The well diffusion test was performed using medium, as per the procedure described by Magaldi *et al* [13] .A sterilized 10 mm cork borer was used to make agar wells on the sterile nutrient agar plates. 24 hours sub cultured bacteria/ fungi were inoculated in the petri-plates, with a sterile cotton swab. Compounds were dissolved in DMSO solvent separately and poured in the wells with varying concentrations ranging from from 50µL, 100µL, 150µL and 200µL, using a micropipette. 100% DMSO was used as a control. The plates were incubated for 24 hours at $37^0$C. Antibiotic Streptomycin was used as a reference antibacterial agent and Amphotericin-B were used as a reference antifungal agent. The tests were carried out in triplicates.

## RESULTS AND DISCUSSION

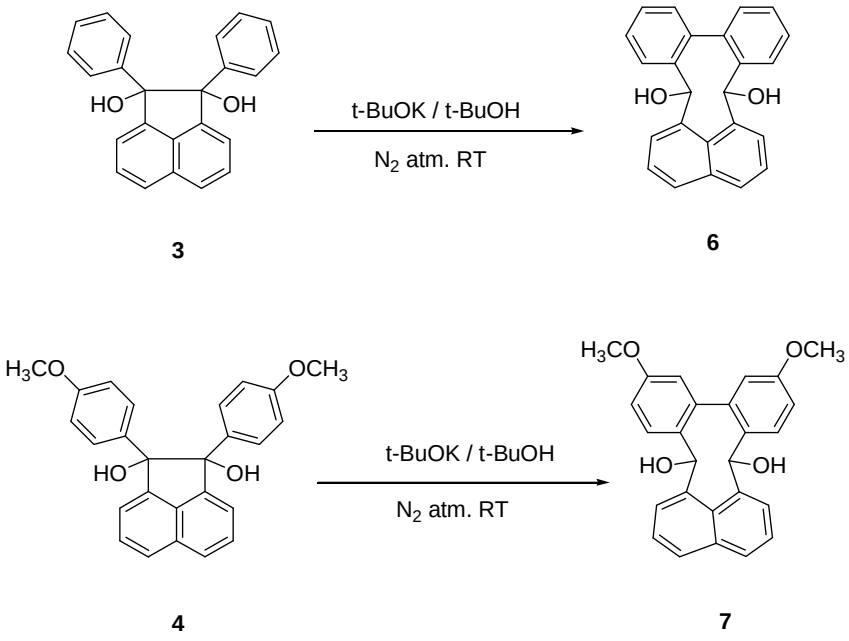
The synthesis of the different diols **1-5, 6 & 7** is outlined in **Scheme 1** and **Scheme 2.** Physical data of the diols are shown in **Table-1.** The TLC and melting points of all the diols **1-5, 6 & 7** are in agreement with the proposed structures reported [8,9] from our laboratory.




**Scheme - 1**

**Table I: Physical data of the diols, (1-7)**

| Entry | Product | Molecular Formula | Melting Point ($^0$C) | Yield(%) of Product |
|---|---|---|---|---|
| 1 | **1** | $C_{16}H_{18}O_2$ | 79 – 80 | 80 |
| 2 | **2** | $C_{34}H_{26}O_2$ | 123-125 | 79 |
| 3 | **3** | $C_{24}H_{18}O_2$ | 130-131 | 88 |
| 4 | **4** | $C_{26}H_{22}O_4$ | 159-160 | 70 |
| 5 | **5** | $C_{26}H_{20}O_2$ | 171-173 | 79 |
| 6 | **6** | $C_{24}H_{18}O_2$ | 119-120 | 88 |
| 7 | **7** | $C_{26}H_{22}O_4$ | 118-120 | 70 |




**Scheme- 2**

**Biological activities**

The results of *in vitro* study of antibacterial activity of the diols **(1-7)** against each of the five bacterial species (*Staphylococcus aureus, Escherichia coli, Klebsiella pneumoniae, Salmonella thypi and Vibrio cholera.*) are reported in the **Table- 2**

**Table-2**

| S. No. | Organisms (Bacteria) | Zone of Inhibition (mm) | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | | **1 (Std.)** | **2 (Std.)** | **3 (Std.)** | **4 (Std.)** | **5 (Std.)** | **6 (Std.)** | **7 (Std.)** |
| 1 | *Escherichia coli* | 8 (21) | 8 (24) | 8 (23) | 11 (20) | - (24) | 9 (25) | 9 (23) |
| 2 | *Staphylococcus aureus* | 10 (22) | 9 (20) | 8 (20) | 9 (20) | 9 (18) | 10 (23) | - (20) |
| 3 | *Klebsiella pneumonia* | 8 (15) | 9 (15) | 8 (17) | 9 (18) | 9 (17) | 7 (13) | 7 (15) |
| 4 | *Salmonella thypi* | 8 (15) | 8 (15) | 9 (16) | 8 (18) | 9 (15) | 8 (18) | 10 (15) |
| 5 | *Vibrio cholera* | 9 (10) | 10 (10) | 7 (10) | 10 (10) | 9 (11) | 9 (10) | 7 (10) |

***(Std)*** *= Streptomycin. - = No zone of Inhibition*

The foregoing data shows that 1, **2, 3, 4, 6** and **7** are moderately active against *Escherichia coli.* The compounds **1-6** are moderately active against *Staphylococcus aureus.*, and compounds 1-7 are moderately active against, *Klebsiella pneumonia* and *Salmonella thypi*..The compounds 1-7 are highly active against *Vibrio cholera.*

The results of the antifungal activity of the tested novel compounds against the fungi *Candida albicans and Aspergillus flavus* are summerised in **Table -3** and **Table-4**.

**Table-3 - The antifungal activity of the novel diols against the fungi *Candida albicans***

| Entry | Compound (Diol) | Zone of Inhibition (mm) | | | |
|---|---|---|---|---|---|
| | | **Day 3** | **Day 4** | **Day 5** | **Day 6** |
| **1** | **1** | 5 | 7 | 8.5 | 9 |
| **2** | **2** | 5 | 7 | 8 | 9 |
| **3** | **3** | 5 | 7 | 8 | 10 |
| **4** | **4** | 6 | 7 | 8 | 9 |
| **5** | **5** | 6 | 7 | 8.5 | 9 |
| **6** | **6** | 7 | 8 | 8 | 8 |
| **7** | **7** | 6 | 8 | 8.5 | 9 |

**Table-4 - the antifungal activity of the novel diols against the fungi *Aspergillus flavus***

| Entry | Compound (Diol) | Zone of Inhibition (mm) | | | |
|---|---|---|---|---|---|
| | | Day 3 | Day 4 | Day 5 | Day 6 |
| **1** | **1** | 2 | 15 | 19 | 22 |
| **2** | **2** | - | 20 | 31 | 33 |
| **3** | **3** | - | 23 | 32 | 35 |
| **4** | **4** | - | 13 | 20 | 27 |
| **5** | **5** | 5 | 12 | 15 | 21 |
| **6** | **6** | - | 18 | 27 | 30 |
| **7** | **7** | - | 15 | 20 | 24 |

The fungus *Candida albicans* is the fourth most common human pathogen resistant to the drug Amphotericin- B. In this study the same drug was taken as standard control to compare the zone of inhibition with that of the synthesised organic compounds.

For antifungal study, the results were taken for consecutive four days from third day of incubation and given importance up to sixth day of incubation. From the data given in **Table – 3**, it is observed that all the seven organic compounds, played significant role on the pathogenic fungi

*Candida albicans***.** The growth control effect was very high than the standard, Amphotericin- B.

From the data given in **Table – 4**, it is observed that all the seven organic compounds, showed very good growth control against *Aspergillus flavus* from the fourth day of incubation.

From these antifungal activity results, the comparative account of inhibitory activity of the seven organic diols on *Candida albicans* and *Aspergillus flavus* revealed that the diol, **3**, showed very high inhibitory activity against *Candida albicans*. The diols **2, 3** & **6** showed very high inhibitory activity against *Aspergillus flavus*.

## CONCLUSION

In summary, we are reporting the antibacterial and antifungal studies of the novel 1,2-diols and 1.5-diols. The antibacterial studies reveal that the diols are having very high antibacterial activity against the bacteria *Vibrio cholera***.** The antifungal studies of the diols shows that the diols **2, 3** & **6** have high antifungal activity against the fungi *Candida albicans* and *Aspergillus flavus* compared to Amphotericin-B, which is resistant to these fungi.

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