Bacteriological studies of new substituted hydroxy-1, 3-propanediones and 4-methyl-5-chloroacetophenones

Pradip V. Tekade

Department of Chemistry, Jankidevi Bajaj College of Science, Jamnalal Bajaj Marg, Civil lines, Wardha-442001-M.S. India

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ABSTRACT: The titled compounds were screened for antibacterial activity against gram + & gram – bacteria such as Escherichia coli, Bacillus subtilis, Staphylococcus aureus, and Pseudomonas aeruginosa, Proteus vulgaris and Enterobacter aerogenes by using Muller Hinton Hiveg Agar No.2 MV-1084 (Hi-Media). All the screened compounds were found inactive against Bacillus subtilis, Enterobacter aerogenes and Escherichia coli. The produced compounds have shown average to good antibacterial activity.

Keywords: hydroxy-1,3-propanediones; antibacterial activity; chloroacetophenones

Introduction

1, 3-Propanedione is used as a starting material for the synthesis of flavanones and their derivatives viz. flavones, isoxazolines, isoxazoles, pyrazolines and pyrazoles. These compounds showed diverse biological activities [1-6]; such as antimicrobial [7], antibacterial [8], insecticidal, antifungal, pharmaceuticals, antipyretic, antitubercular, antiflammatory and insect repellent properties. Chlorodiketones [9] are found to posses’ antihelmenthic and antifungal activities. The synthesis of 1-(2′-hydroxy-4′-methyl-5′-chlorophenyl)-3-(2′-chlorophenyl)-1,3-propanedione has been reported [3] by Baker-Venkatarma transformation of 2-(2′-chlorobenzooyloxy)-4-methyl-5-chloroacetophenone.

The literature survey reveals that, much work has been done over many years for the study of antimicrobial activities of heterocyclic compounds on gram + and gram -
microorganisms and also antifungal activities on fungi. The synthesized new substituted β-diketone (3a-c) as well as substituted 2-hydroxy acetophenone (1) and 2-benzoyloxy acetophenones (2a-c) were not yet been studied for antimicrobial activities. Thus, it was thought of interest to study the antibacterial activities of these compounds against pathogenic organisms with the help of paper disc method and disc diffusion method.

Screenings of following compounds were carried out against the bacteria such as *Escherichia coli*, *Bacillus subtilis*, *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Proteus vulgaris* and *Enterobacter aerogenes* by using Muller Hinton Hi-Veg Agar MV-1084 (Hi-Media). The following Compounds were tested.

2-hydroxy-4'-methyl-5-chloroacetophenone (1)

1-(2'-hydroxy-4'-methyl-5'-chlorophenyl)-3-(4'-chlorophenyl)-1,3-propanedione (3a)

1-(2'-hydroxy-4'-methyl-5'-chlorophenyl)-3-(2'-chlorophenyl)-1,3-propanedione (3b)

1-(2'-hydroxy-4'-methyl-5'-chlorophenyl)-3-(4'-methoxyphenyl)-1,3-propanedione (3c)

2-(2'-chlorobenzoyloxy)-4-methyl-5-chloroacetophenone (2a)

2-(4'-chlorobenzoyloxy)-4-methyl-5-chloroacetophenone (2b)

2-(4'-methoxybenzoyloxy)-4-methyl-5-chloroacetophenone (2c)

The newly substituted hydroxy-1,3-propanediones and 4-methyl-5-chloroacetophenone were synthesized by microwave irradiation [10] as well as by conventional methods [3] as described elsewhere. The structures of some compounds were confirmed on the basis of chemical properties, analytical data and spectral analysis (viz. IR, UV, PMR, 13C, Mass fragmentation). Newly substituted 1-(2'-hydroxy aryl)-3-(aryl)-1,3-propanediones (3a-c) have been synthesized by base catalyzed Baker-Venkatraman transformation of 2-benzoyloxyacetophenone (2a-c). The chemicals used for the synthesis were of analytical reagent grade.

**Material and Methods**

**Preparation of wet disc for antibacterial activity**

Discs (6.25 mm) in a diameter from whatman filter paper were punched and batches of 100 in screw-capped bottles were dispersed and sterilized by dry heat at 140 °C for 60 minutes. DMSO solvent is used for the preparation of the solution so that 1 mL contains 100 times the amount of the compound required in the disc. 1 mL solution of
the compound was added to each bottle of 100 discs and as a whole of this volume is absorbed. It was assumed that each disc contains approximately 0.01 mL. Discs were sorted in wet conditions.

**Cultural medium**

The medium used throughout the experiment was Muller Hinton Hiveg MV-1084 (Indian Make) agar No. 2 and having following composition.

The media was prepared by suspending 36 g ingredients in 1 L distilled water. It was boiled to dissolve the medium completely and was sterilized by autoclave at 1.02 atm pressure at 121 °C temperature. It was cooled to about 50 °C and poured into sterile petri plates and allowed to solidify.

**Table 1. Composition of Muller Hinton Hi-Veg. agar**

<table>
<thead>
<tr>
<th>Ingredients</th>
<th>g L⁻¹</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hiveg acid Hydrolysate</td>
<td>17.50</td>
</tr>
<tr>
<td>Hiveg Infusion</td>
<td>2.00</td>
</tr>
<tr>
<td>Starch soluble</td>
<td>1.50</td>
</tr>
<tr>
<td>Agar</td>
<td>17.00</td>
</tr>
</tbody>
</table>

**Table 2. Method of preparation of media**

<table>
<thead>
<tr>
<th>Medium used</th>
<th>Muller Hinton Hiveg agar</th>
</tr>
</thead>
<tbody>
<tr>
<td>Size (plate)</td>
<td>8.5 cm in diameter</td>
</tr>
<tr>
<td>Depth of agar</td>
<td>14 mm</td>
</tr>
<tr>
<td>Distance between 2 discs</td>
<td>2 cm</td>
</tr>
<tr>
<td>Diameter of antibiotic disc</td>
<td>6.25 mm in diameter</td>
</tr>
</tbody>
</table>

**Test Procedure**

The culture material was inoculated in a nutrient broth and kept at 37 °C for 24 hours incubation. The culture plate Muller Hinton Hiveg agar was dried until its surface was free from visible moisture. The inoculating material was then flooded on the surface of Muller Hinton Hiveg agar uniformly taking all aseptic precautions. The plate was dried again for up to 30 minutes without further delay and the compound discs were applied at adequate spacing (2 cm or more apart) to the surface of the plate with sterile fine-pointed forceps and gently press to ensure full contact with the medium and moistening of the disc. Control was run using plane DMF solvent for aseptic conditions. The plates were incubated at 36 °C for 18-24 hours. After incubation degree of sensitivity to drugs is determined by measuring the visible clear areas of growth of free zones (zones of inhibition) produced by diffusion of antibiotics into the media from the discs.

Width of the zone of inhibition depends on: size of inoculums, nature of culture medium, presence of inhibitors, concentration of agar in the medium, thickness of the medium in the plate, condition and time of incubation, composition of antibiotic discs.
zones of inhibition are measured and reported. The results are cited in Table 3.

### Results and Discussion

**Table 3.** Showing zones of inhibition

<table>
<thead>
<tr>
<th>Comp. No.</th>
<th>E. coli (Gram-)</th>
<th>S. aureus (Gram+)</th>
<th>P. vulgaris (Gram-)</th>
<th>P. aeruginosa (Gram-)</th>
<th>B. subtilis (Gram+)</th>
<th>E. aerogenes (Gram-)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>-</td>
<td>++</td>
<td>+++</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>2a</td>
<td>-</td>
<td>++</td>
<td>+</td>
<td>++</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>2b</td>
<td>-</td>
<td>+++</td>
<td>+++</td>
<td>+</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>2c</td>
<td>-</td>
<td>+++</td>
<td>+</td>
<td>+++</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>3a</td>
<td>-</td>
<td>++</td>
<td>++</td>
<td>+++</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>3b</td>
<td>-</td>
<td>++++</td>
<td>+++</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>3c</td>
<td>-</td>
<td>++</td>
<td>+</td>
<td>-</td>
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</tr>
</tbody>
</table>

**+++++:** Very strongly active ≥ 20 mm, **+++:** Strongly active ≥ 15 mm, **++:** Active ≥ 8 mm, **+:** Moderately active ≥ 5 mm, **-:** Weakly active ≥ 3 mm, **-:** Inactive

From the results of screening against the bacteria *Escherichia coli*, *Bacillus subtilis*, *Staphylococcus aureus*, and *Pseudomonas aeruginosa*, *Proteus vulgaris* and *Enterobacter aerogenes*, the following conclusions were drawn from the Table 3.

All the screened compounds were found inactive against *Bacillus subtilis*, *Enterobacter aerogenes* and *Escherichia coli*. The compound 3b was found to have good activity against *Staphylococcus aureus*.

The compound 2-hydroxy-4'-methyl-5-chloroacetophenone (1) was inactive against *E. coli*, *P. aeruginosa*, *B. subtilis*, *E. aerogenes*, moderately active against *S. aureus* and active against *P. vulgaris*.

The compound 1-(2'–hydroxy-4'-methyl-5'-chlorophenyl)-3-(4'–chlorophenyl)-1,3-propanedione (3a) was inactive against *E. coli*, *B. subtilis*, *E. aerogenes*, moderately active against *S. aureus*, *P. vulgaris* and active against *P. aeruginosa*.

The compound 1-(2'–hydroxy-4'-methyl-5'-chlorophenyl)-3-(2'–chlorophenyl)-1,3-propanedione (3b) was inactive against *E. coli*, *B. subtilis*, *E. aerogenes*, *P. aeruginosa strongly* active against *S. aureus*, and active against *P. vulgaris*.

The compound 1-(2'–hydroxy-4'-methyl-5'-chlorophenyl)-3-(4'–methoxyphenyl)-1,3-propanedione(3c) was inactive against *E. coli*, *B. subtilis*, *E. aerogenes*, *P. aeruginosa moderately* active against *S. aureus*, and *P. vulgaris*.

The compound 2-(2'–chlorobenzoylxyloxy)-4-methyl-5-chloroacetophenone (2a) was inactive against *E. coli*, *B. subtilis*, *E. aerogenes*, moderately active against *P. aeruginosa S. aureus*, and weakly active against *P. vulgaris*.

The compound 2-(4’–chlorobenzoylxyloxy)-4-methyl-5-chloroacetophenone (2b) was
inactive against *E. coli*, *B. subtilis*, *E. aerogenes*, moderately active against, *P. aeruginosa* and active against *P. vulgaris, S. aureus*.

The compound 2-(4’-methoxybenzoyl oxy)-4-methyl-5-chloroacetophenone (2c) was inactive against *E. coli, B. subtilis, E. aerogenes*, moderately active against *P. vulgaris*, and active against *S. aureus and P. aeruginosa*.

### Conclusion

The biocidal evaluation of synthesized compounds shows average to good antibacterial activity. The synthesized compound shows more activity against gram – bacteria.

### Acknowledgments

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### References and Notes


