# Synthesis and Antimicrobial Activity of 5-benzylidenebarbituric acids: A structure -reactivity Study.

**K. Radhakrishnan1\*, P. Mohandass1, S. Sankaralingam2, S. Chandra Mohan3**

1Department of Chemistry, Saraswathi Narayanan College, Perungudi, Madurai – 625022, Tamil Nadu, India.

2Department of Botany, Saraswathi Narayanan College, Perungudi, Madurai – 625022, Tamil Nadu, India

3Division of Phytochemistry, Shanmuga Centre for Medicinal Plants Research, Thanjavur- 613007, Tamil Nadu, India.

\*Corresponding author: Dr. K. Radhakrishnan**,**  email: prskradha61@gmail.com; Contact: +919443686474

**ABSTRACT**

A very simple and highly efficient synthesis was established for the reaction of barbituric acid and substituted benzaldehydes to provide novel substituted 5-benzylidenebarbituric acids. Synthezied substituted 5-benzylidenebarbituric acids were characterized by 1H and 13C NMR spectral analysis. The antibacterial activities and structure reactivity correlation of the compounds have been studied.

**Keywords:** Substituted 5-benzylidene barbituric acids; antibacterial, correlation studies.

**INTRODUCTION**

The barbituric acid derivatives are clinically useful. By substituting two protons in C-5 position during barbiturate synthesis, acidity of the whole molecule can be reduced and an unsaturated group can be added for the later incorporation of para hydrogen into the molecule [1]. Benzylidene barbituric acids as potential organic oxidizers [2] are applied for preparing pyrimidine derivatives [3]. The benzylidene barbituric acids are the important building blocks in synthesizing pyrazolo [3,4-d]pyrimidines and pyrido[2,3-d]pyrimidines [4,5]. They also have a broad range of biological activities Some barbituric acid derivatives have been widely used as sedative, hypnotic, anticonvulsant, antispasmodic, as well as local anesthetic agents [6]. Benzylidene barbituric acids are useful as potential organic oxidizers, for the preparation of oxadeazaflavines [7] and for the unsymmetrical synthesis of disulfides [8]. Some of them have been recently studied as nonlinear optical materials [9]. Several 5-benzylidenebarbituric acids were prepared in the absence of solvent by the influence of infrared irradiation. These molecules were obtained by means of a Knoevenagel condensation between barbituric acid and various benzaldehydes [10]. Recently we have reported the substituent effects on zone of inhibition against the growth of microorganisms in various substituted 2-benzylidene-1,3-indandiones [11]. In continuation of our research interest in the structure - reactivity study, we have synthesized substituted 5-benzylidenebarbituric acids and studied the antibacterial activity to find out the substituent effect on 5-benzylidenebarbituric acid.

**EXPERIMENTAL**

All chemical used were purchased from Sigma Aldrich. Purity of the compounds was checked by TLC on silica gel G plate. 1H and 13C spectra were obtained on a BRUKER AMX 400 MHz spectrometer. Chemical shift of 1H were measured with the peak of DMSO at δ 2.51 as the internal reference, while those of 13C were recorded with the central peak of DMSO at δ 39.90 as the internal reference.

**General procedure for the synthesis of 5-benzylidenebarbituric acids (1 to 7)**

5-benzylidenebarbituric acid and its substituted compounds (1 to 7) were prepared by the modified procedure of Branko Jursic(2001) [12].

To the calculated amount of the pure benzaldehyde (2 g, 0.015mol) and barbituric acid (1.55g, 0.015 mol) in warm ethyl alcohol was added a 10% solution of sodium hydroxide (catalytic amount) and the reaction mixture stirred for 2 hours. After completion of the reaction as indicated by TLC, the reaction mixture was left overnight (scheme I). Solid product was separated by filtration and washed several times with cold methanol.



Scheme I: Synthesis of 5-benzylidenebarbituric acids.

Spectral analysis of compounds (1 to 7)

Compound 1*:5-(4’-methoxybenzylidene)barbituric acid*

1H NMR: δ 3.877 (s,3H), 7.065 (d,2H), 8.252(s,1H), 8.369 (d,2H), 11.175 (s,1H), 11.302 (s,1H);13C NMR: δ 56.22,114.41,116.00,125.62,137.96,150.67,155.46,162.64,163.92,164.39.

Compound 2:*5-(4’-hydroxybenzylidene)barbituric acid*

1H NMR: δ 6.878 (d,2H), 8.213 (s,1H), 8.320 (d,2H), 10.851 (s,1H), 11.117(s,1H), 11.249 (s,1H);

13C NMR: δ 114.61, 115.97, 124.24, 138.77, 150.70, 156.05,162.75,163.48,164.59.

Compound 3:*5-(4’-methylbenzylidene)barbituric acid*

1H NMR: δ 2.385 (s,3H), 7.304 (d,2H), 8.094 (d,2H), 8.255 (s,1H), 11.218 (s,1H), 11.365 (s,1H);

13C NMR: δ 118.30, 129.33, 130.31, 134043, 143.96, 150.68, 155.46, 162.26, 164.08.

Compound 4:*5-benzylidenebarbituric acid*

1H NMR: δ 7.485 (m,3H), 8.073 (d,2H), 8.285 (s,1H), 11.238 (s,1H), 11.397 (s,1H);

13C NMR: δ 119.55, 128.52, 132.69, 133.11, 133.54, 150.69, 155.20, 162.03, 163.87.

Compound 5: *5-(4’-chlorobenzylidene)barbituric acid*

1H NMR: δ 7.518 (d,2H), 8.069 (d,2H), 8.243 (s,1H), 11.275 (s,1H), 11.425 (s,1H);

13C NMR: δ 120.09, 128.55, 132.01, 135.15, 137.21, 150.65, 153.52, 162.04, 163.67.

Compound 6: *5-(4’-bromobenzylidene)barbituric acid*

1H NMR: δ 7.670 (d,2H), 7.979 (d,2H), 8.223 (s,1H), 11.272 (s,1H), 11.421 (s,1H);

13C NMR: δ 120.24, 126.29, 131.51, 132.40, 135.15, 150.65, 153.56, 162.04, 163.67.

Compound 7: *5-(4’-nitrobenzylidene)barbituric acid*

1H NMR: δ 8.017 (d,2H), 8.245 (d,2H), 8.324 (s,1H), 11.329 (s,1H), 1.504 (s,1H);

13C NMR: δ 123.15, 123.37, 132.69, 140.48, 148.49, 150.68, 151.63, 161.62, 163.13.

Antibacterial Activity:

Agar well-diffusion method was followed to determine the  
antimicrobial activity. Nutrient agar (NA) and Potato Dextrose Agar (PDA) plates were  
swabbed (sterile cotton swabs) with 8 hours old -broth culture of respective bacteria. Wells (6mm) were made in each of these plates using sterile cork borer. Briefly, agar plates were  
inoculated with bacterial strain under aseptic conditions and wells (diameter = 6 mm) were  
filled with 50 µl of the test samples and incubated at 37°C for 24 hours. After the incubation  
period, the diameter of the growth of inhibition zones were measured.   
 Threeinhibition zone diameter measurements were taken for each well and averaged, for each replicatesthe readings were taken in three different fixed directions and the average values were recorded. The average inhibition zone diameter for the various bacteria are shown in Table 1.

**RESULTS AND DISCUSSION**

In this study, gram-positive bacteria (*Staphylococcus aureus*) and five gram-negative bacteria (*Escherichia coli, Klebsiella oxytoca, Proteus mirabilis, Pseudomonas aeruginosa and Shigella sonnei )* were used. The result of the present study showed a broad range of antibacterial activity, shown in Figure 1. The order of antibacterial activity of compounds (1 to 7) for all the microorganism were in the following sequence.

-OCH3<-OH < -CH3< -H < -Cl < -Br< -NO2

**Table 1**. Antibacterial activity (zone of inhibition(mm) values) of substituted

5-benzylidenebarbituric acid

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **S.No.** | **Name of the microorganism** | **Inhibition zone diameter** | | | | | | |  |
| **Standard (Amphotericin-B)** | **-OCH3** | **-OH** | **-CH3** | **-H** | **-Cl** | **-Br** | **-NO2** |
| 1 | *Escherichia coli* | 21 | 9 | 10 | 12 | 14 | 16 | 17 | 20 |
| 2 | *Klebsiella oxytoca* | 16 | 8 | 12 | 14 | 16 | 20 | 21 | 28 |
| 3 | *Proteus mirabilis* | 18 | 7 | 9 | 10 | 11 | 16 | 19 | 22 |
| 4 | *Pseudomonas aeruginosa* | 21 | 11 | 13 | 15 | 16 | 20 | 23 | 28 |
| 5 | *Shigella Sonnei* | 16 | 8 | 10 | 11 | 12 | 14 | 18 | 21 |
| 6 | *Staphylococcus aureus* | 18 | 7 | 12 | 13 | 14 | 16 | 23 | 28 |



**Figure 1**: Antibacterial activity of substituted 5-benzylidenebarbituric acids

If atom or group attracts electrons less strongly than hydrogen, it is said to have +I effect (electron repelling or electron releasing) viz., -OCH3, -OH, -CH3 groups showing lesser zone inhibition values compared to unsubstituted phenyl ring (-H).

In order to express the effect of substituents quantitatively it was considered worthwhile to correlate the logarithm of inhibition zone diameter (IZD) of (1 to 7) at the same concentration with the Hammett substituent constants for all the microorganisms. The results of statistical SSP analysis are given in Table 2. The corresponding Hammett plot for *Klebsiella oxytoca* is shown in Figure2.

The positive value of the reaction constant (ρ) equation 1 indicates that electron withdrawing substituents increase the antibacterial activity and electron releasing substituents retard it.

log (IZD) = (0.36± 0.02) σp+ / σp + (1.20± 0.01) (1)

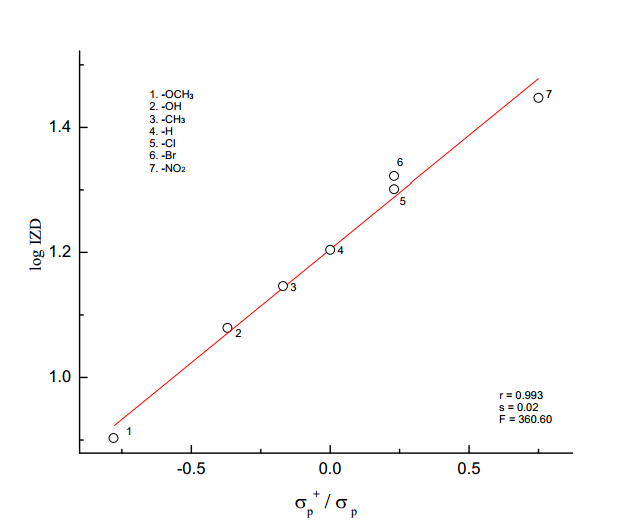
(r = 0.993, n=7, F = 360.60)

**Table 2**: Results of statistical treatment of log IZD (mm)with σp,σpo,σp+,σp+/ σp,σp+/ σp-,σp+/ σp/ σp-substituent constants using single parameter equation

[ Excluding -OH ]

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| S.No. | Bacteria | Scale | Ρ | R | S | F | Log(IZD)o | n |
| 1 | *Escherichia coli* | σP | 0.31±0.05 | 0.937 | 0.048 | 36.19 | 1.113±0.02 | 7 |
|  | σPo | 0.29±0.09 | 0.854 | 0.07 | 10.78 | 1.10±0.03 | 6 |
|  | σP+ | 0.21±0.02 | 0.969 | 0.034 | 76.36 | 1.159±0.01 | 7 |
|  | σP+/ σP | 0.25±0.02 | 0.977 | 0.03 | 104.92 | 1.135±0.01 | 7 |
|  | σP+/ σP- | 0.16±0.03 | 0.934 | 0.05 | 35.95 | 1.14±0.02 | 7 |
|  | σP+/ σP/ σP- | 0.18±0.03 | 0.929 | 0.05 | 31.38 | 1.12±0.02 | 7 |
| 2 | *Klebsiella oxytoca* | σP | 0.42±0.09 | 0.990 | 0.08 | 21.23 | 1.18±0.03 | 7 |
|  | σPo | 0.43±0.14 | 0.837 | 0.11 | 9.33 | 1.14±0.05  [ Excluding -OH ] | 6 |
|  | σP+ | 0.28±0.05 | 0.926 | 0.07 | 29.94 | 1.23±0.03 | 7 |
|  | σP+/ σP | 0.36±0.02 | 0.993 | 0.02 | 360.60 | 1.20±0.01 | 7 |
|  | σP+/ σP- | 0.22±0.04 | 0.901 | 0.08 | 21.81 | 1.22±0.03 | 7 |
|  | σP+/ σP/ σP- | 0.26±0.04 | 0.945 | 0.06 | 41.80 | 1.18±0.02 | 7 |
|  |  |  |  |  |  |  |  |  |
| 3 | *Proteus mirabilis* | σP | 0.44±0.08 | 0.922 | 0.08 | 28.2 | 1.07±0.03 | 7 |
|  | σPo | 0.45±0.13 | 0.868 | 0.1 | 12.26 | 1.03±0.05  [ Excluding -OH ] | 6 |
|  | σP+ | 0.28±0.06 | 0.911 | 0.08 | 25.5 | 1.13±0.03 | 7 |
|  | σP+/ σP | 0.36±0.05 | 0.959 | 0.06 | 57.12 | 1.1±0.02 | 7 |
|  | σP+/ σP- | 0.22±0.05 | 0.887 | 0.09 | 18.47 | 1.11±0.04 | 7 |
|  | σP+/ σP/ σP- | 0.26±0.05 | 0.915 | 0.08 | 25.73 | 1.08±0.03 | 7 |
| 4 | Pseudomonas aeruginosa | σP | 0.33±0.05 | 0.953 | 0.04 | 49.84 | 1.21±0.02 | 7 |
|  | σPo | 0.33±0.08 | 0.889 | 0.07 | 15.15 | 1.19±0.03  [ Excluding -OH ] | 6 |
|  | σP+ | 0.21±0.03 | 0.940 | 0.05 | 38.35 | 1.26±0.02 | 7 |
|  | σP+/ σP | 0.26±0.04 | 0.950 | 0.05 | 46.15 | 1.24±0.02 | 7 |
|  | σP+/ σP- | 0.17±0.03 | 0.940 | 0.05 | 37.76 | 1.25±0.02 | 7 |
|  | σP+/ σP/ σP- | 0.19±0.03 | 0.944 | 0.05 | 40.59 | 1.22±0.02 | 7 |
| 5 | Shigella sonnei | σP | 0.35±0.06 | 0.923 | 0.06 | 28.74 | 1.09±0.02 | 7 |
|  | σPo | 0.36±0.11 | 0.860 | 0.09 | 11.32 | 1.06±0.04  [ Excluding -OH ] | 6 |
|  | σP+ | 0.23±0.04 | 0.920 | 0.06 | 27.4 | 1.14±0.02 | 7 |
|  | σP+/ σP | 0.29±0.03 | 0.965 | 0.04 | 67.55 | 1.11±0.02 | 7 |
|  | σP+/ σP- | 0.18±0.04 | 0.908 | 0.07 | 23.36 | 1.12±0.03 | 7 |
|  | σP+/ σP/ σP- | 0.21±0.04 | 0.940 | 0.06 | 35.65 | 1.09±0.02 | 7 |
|  |  |  |  |  |  |  |  |  |
| 6 | Staphylococcus aureus | σP | 0.44±0.12 | 0.861 | 0.11 | 14.35 | 1.15±0.04 | 7 |
| σPo | 0.47±0.17 | 0.810 | 0.14 | 7.53 | 1.1±0.07 | 6 |
| σP+ | 0.29±0.07 | 0.873 | 0.1 | 16.09 | 1.21±0.04 | 7 |
| σP+/ σP | 0.39±0.05 | 0.962 | 0.06 | 62.09 | 1.18±0.02 | 7 |
| σP+/ σP- | 0.23±0.06 | 0.862 | 0.11 | 14.49 | 1.19±0.04 | 7 |
| σP+/ σP/ σP+ | 0.28±0.05 | 0.924 | 0.08 | 29.4 | 1.15±0.03 | 7 |

[ Excluding -OH ]



**Figure 2**. Hammett plot for Klebsiella oxytoca

DSP analysis has been performed for each of the resonance scale (σR, σR+, σR-). The best fit of DSP analysis for *Pseudomonas aeruginosa* is taken from satisfactory correlation coefficient (R) and least standard error (SE) of the regression equations (2) and (3) and the result obtained given in Table 3.

log (IZD) = (0.33 ± 0.08)σI + (0.37±0.08) σR + (1.22 ± 0.04) (2)

R = 0.963, SE = 0.05, n = 6, F = 19.09

log (IZD) = (0.35 ± 0.10) F + (0.34 ± 0.08) R + (1.21 ± 0.05) (3)

R = 0.941, SE = 0.06, F = 15.54

The sign of ρIand ρRare positive, reveals that the normal substituent effects operates on IZD, i.e. electron releasing substituents decrease the IZD and electron withdrawing substituents increase the IZD. The ρR values are rather smaller than ρI values and this reveals the importance of polar component.

**Table 3**: DSP analysis of log IZD (mm) with dual parameter equations 2 and 3.

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| S.No | Bacteria | Scale | ρI | ρR | R | SE | F | Log(IZD)o | N | λ=ρR/ρI |
|
| 1 | *Escherichia coli* | σI ,σR | 0.24±0.08 | 0.35±0.08 | 0.954 | 0.05 | 15.2 | 1.14±0.03 | 6 | 1.46 |
|  | σI ,σR+ | 0.11±0.20 | 0.15±0.2 | 0.761 | 0.1 | 2.75 | 1.16±0.09 | 7 | 1.36 |
|  | σI ,σRo | 0.28±0.18 | 0.15±0.17 | 0.722 | 0.1 | 1.64 | 1.10±0.07 | 6 | 0.54 |
|  | σI ,σR- | 0.23±0.16 | 0.18±0.14 | 0.790 | 0.1 | 2.50 | 1.11±0.07 | 6 | 0.78 |
|  | F,R | 0.24±0.09 | 0.34±0.07 | 0.945 | 0.05 | 16.8 | 1.14±0.04 | 7 | 1.42 |
|  |  |  |  |  |  |  |  |  |  |
| 2 | *Klebsiella oxytoca* | σI ,σR | 0.33±0.11 | 0.55±0.12 | 0.956 | 0.07 | 15.83 | 1.21±0.05 | 6 | 1.66 |
|  | σI ,σR+ | 0.15±0.28 | 0.21±0.13 | 0.760 | 0.14 | 2.74 | 1.24±0.13 | 7 | 1.40 |
|  | σI ,σRo | 0.40±0.28 | 0.26±0.26 | 0.707 | 0.17 | 1.50 | 1.15±0.12 | 6 | 0.65 |
|  | σI ,σR- | 0.31±0.25 | 0.30±0.21 | 0.777 | 0.15 | 2.29 | 1.16±0.10 | 6 | 0.97 |
|  | F,R | 0.35±0.17 | 0.25±0.13 | 0.903 | 0.09 | 8.86 | 1.20±0.05 | 7 | 0.71 |
|  |  |  |  |  |  |  |  |  |  |
| 3 | *Proteus mirabilis* | σI ,σR | 0.45±0.13 | 0.44±0.14 | 0.940 | 0.08 | 11.40 | 1.06±0.06 | 6 | 0.98 |
|  | σI ,σR+ | 0.31±0.26 | 0.17±0.12 | 0.801 | 0.13 | 03.60 | 1.08±0.13 | 7 | 0.55 |
|  | σI ,σRo | 0.51±0.25 | 0.14±0.24 | 0.763 | 0.16 | 02.09 | 0.996±0.1 | 6 | 0.28 |
|  | σI ,σR- | 0.44±0.24 | 0.21±0.19 | 0.814 | 0.14 | 02.94 | 1.01±0.09 | 6 | 0.48 |
|  | F,R | 0.47±0.16 | 0.40±0.12 | 0.918 | 0.09 | 10.67 | 1.04±0.07 | 7 | 0.85 |
|  |  |  |  |  |  |  |  |  |  |
| 4 | *Pseudomonas aeruginosa* | σI ,σR | 0.33±0.08 | 0.37±0.08 | 0.963 | 0.05 | 19.09 | 1.22±0.04 | 6 | 1.12 |
|  | σI ,σR+ | 0.22±0.21 | 0.13±0.10 | 0.777 | 0.11 | 03.06 | 1.23±0.10 | 7 | 0.59 |
|  | σI ,σRo | 0.37±0.19 | 0.15±0.19 | 0.767 | 0.12 | 02.15 | 1.17±0.08 | 6 | 0.41 |
|  | σI ,σR- | 0.31±0.17 | 0.21±0.14 | 0.839 | 0.1 | 03.58 | 1.18±0.07 | 6 | 0.68 |
|  | F,R | 0.35±0.10 | 0.34±0.08 | 0.941 | 0.06 | 15.54 | 1.21±0.05 | 7 | 0.97 |
|  |  |  |  |  |  |  |  |  |  |
| 5 | *Shigella sonnei* | σI ,σR | 0.33±0.01 | 0.39±0.1 | 0.950 | 0.06 | 13.88 | 1.09±0.04 | 6 | 1.18 |
|  | σI ,σR+ | 0.21±0.22 | 0.15±0.1 | 0.782 | 0.11 | 03.15 | 1.11±0.10 | 7 | 0.71 |
|  | σI ,σRo | 0.38±0.22 | 0.14±0.2 | 0.731 | 0.13 | 01.72 | 1.04±0.09 | 6 | 0.37 |
|  | σI ,σR- | 0.31±0.18 | 0.22±0.15 | 0.825 | 0.11 | 03.20 | 1.06±0.08 | 6 | 0.71 |
|  | F,R | 0.35±0.13 | 0.33±0.1 | 0.920 | 0.07 | 10.98 | 1.08±0.06 | 7 | 0.94 |
|  |  |  |  |  |  |  |  |  |  |  |
| 6 | *Staphylococcus aureus* | σI ,σR | 0.38±0.15 | 0.61±0.16 | 0.940 | 0.09 | 11.34 | 1.18±0.07 | 6 | 1.61 |
|  | σI ,σR+ | 0.19±0.32 | 0.22±0.15 | 0.745 | 0.16 | 2.49 | 1.20±0.15 | 7 | 1.16 |
|  | σI ,σRo | 0..45±0.33 | 0.23±0.32 | 0.650 | 0.2 | 1.14 | 1.09±0.14 | 6 | 0.51 |
|  | σI ,σR- | 0.35±0.24 | 0.35±0.28 | 0.780 | 0.17 | 2.32 | 1.13±0.12 | 6 | 1.00 |
|  | F,R | 0.42±0.22 | 0.44±0.17 | 0.860 | 0.12 | 5.63 | 1.15±0.09 | 7 | 1.05 |

(\* when n=6, the -OH substituent was excluded.)

The Yukawa-Tsuno equation 4 and Table 4 for *Escherichia coli* proved the less contribution of resonance effect.

log IZD = (0.171±0.05) σpo + (0.211 ± 0.05) (σp+ - σpo) + (1.18 ± 0.02) (4)

(R = 0.981,SE = 0.03, n = 6, F = 38.16)

**Table 4:**Results of multiple regression analysis of log IZR (mm) with σp,( σp+- σp)  and σpo,

(σp+- σpo) constants using Yukava – Tsuno equation (4).

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| S.No. | Bacteria | Scale | Ρ | R | R | SE | F | n |
| 1 | *Escherichia coli* | σp,( σp+- σp) | 0.205±0.06 | 0.279±0.11 | 0.975 | 0.04 | 28.35 | 6 |
|  |  | σpo,( σp+- σpo) | 0.171±0.05 | 0.211±0.05 | 0.981 | 0.03 | 38.16 | 6 |
| 2 | *Klebsiella oxytoca* | σp,( σp+- σp) | 0.282±0.09 | 0.484±0.16 | 0.977 | 0.05 | 31.13 | 6 |
|  |  | σpo,( σp+- σpo) | 0.248±0.09 | 0.325±0.09 | 0.969 | 0.06 | 23.16 | 6 |
| 3 | *Proteusmirabilis* | σp,( σp+- σp) | 0.386±0.14 | 0.237±0.27 | 0.938 | 0.08 | 11.02 | 6 |
|  |  | σpo,( σp+- σpo) | 0.316±0.13 | 0.243±0.13 | 0.841 | 0.08 | 11.55 | 6 |
| 4 | *Pseudomonas aeruginosa* | σp,( σp+- σp) | 0.294±0.08 | 0.133±0.15 | 0.959 | 0.05 | 16.95 | 6 |
|  |  | σpo,( σp+- σpo) | 0.242±0.09 | 0.15±0.09 | 0.945 | 0.06 | 12.42 | 6 |
| 5 | *Shigella sonnei* | σp,( σp+- σp) | 0.294±0.1 | 0.239±0.19 | 0.954 | 0.06 | 15.04 | 6 |
|  |  | σpo,( σp+- σpo) | 0.239±0.09 | 0.215±0.1 | 0.948 | 0.06 | 12.24 | 6 |
| 6 | *Staphylococcus albus* | σp,( σp+- σp) | 0.326±0.14 | 0.504±0.26 | 0.953 | 0.08 | 15.01 | 6 |
|  |  | σpo,( σp+- σpo) | 0.272±0.14 | 0.637±0.26 | 0.942 | 0.09 | 11.74 | 6 |
|  |  |  |  |  |  |  |  |  |

( \* The -OH substituent was excluded)

**CONCLUSION**

To summarize, substituted 5-benzylidenebarbituric acids have been synthesized and evaluated for their antibacterial activities. This reaction protocol offers a simple, easier work-up procedure and good yields. The compounds have been characterized by their spectral data. The antibacterial activities of all synthesized compounds have been studied. The inhibition zone diameter of these compounds has been correlated with Hammett substituent constants, F and R parameters. From the results of statistical analysis, the effects of substituent on the antibacterial activity of compounds have been studied.

**REFERENCES**

[1] Malihe F, Enayatollah S. Efficient synthesis of novel benzylidene barbituric and thiobarbituric acid derivatives containing ethyleneglycol spacers. J Iran Chem Soc., 2015, 12; 427–432.

[2] Deb ML, Bhuyan PJ . Uncatalysed Knoevenagel Condensation in Aqueous Medium at Room Temperature. Tetrahedron Lett., 2005, 46; 6453.

[3] Bigdeli MA, Sheikhhosseini E, Habibi A, Balalaie S. An experimental study of special leaving group behavior in the reaction of arylidenebarbituric acids with carbon nucleophiles . Heterocycles., 2011, 83; 107-116.

[4] Thokchom HS, Nongmeikapam AD, Laitonjam WS. Synthesis of fused pyrazolo-, isoxazolo-, pyrimido, and pyridopyrimidines. Can J Chem., 2005, 83; 1056-1062.

[5] Bo J, Long-Ji C, Tu Shu-Jiang, Wen-Rui Z, Yu Hai-Zhu Yu. Highly Diastereoselective Domino Synthesis of 6-Spirosubstituted Pyrido[2,3-d]pyrimidine Derivatives in Water . J Comb Chem., 2009, 11; 612-616.

### [6] Cheng X, Tanaka K and Yoneda F. [Simple New Method for the Synthesis of 5-Deaza-10-oxaflavin, a Potential Organic Oxidant](https://www.jstage.jst.go.jp/article/cpb1958/38/2/38_2_307/_article) Chem.Pharm.Bull., 1990, 38; 307-311.

[7] Figueroa-Villar JD, Rangel CE and Dos Santos LN. Synthesis of oxadeaza-flavines from barbituric acid and aromatic aldehydes. Synth, Commun. 1992, 22; 1159-1164.

[8] Tanka K, Cheng X and Yoneda F. Oxidation of thiol with 5-arylidene-1,3-dimethylbarbituric acids: Application to synthesis of unsymmetrical disulfide.Tetrahedron1988, 44; 3241.

[9] Ikeda A, Kawabe Y, Sakai T and Kawasaki K. Second-order hyperpolarizabilities of barbituric acid derivatives. Chem.Lett., 1989, 1803-1809.

[10] Alcerreca G, Sanabria R, Miranda R, Arroyo G, Tamariz J and Delgado F. Preparation of benzylidene barbituric acids promoted by infrared irradiation in absence of solvent. Synth. Commun., 2000,30; 1295–1301.

[11] Radhakrishnan K, Mohandass P, Sankaralingam S and Chandramohan S. Synthesis and Antimicrobial Activity of 2-Benzylidene-1,3 Indandiones: A Structure-Reactivity Study. Der Chemica Sinica., 2016, 7; 1-7.

[12] Branko S. Jursic., A simple method for knoevenagel condensation of α,β-conjugated and aromatic aldehydes with barbituric acid J.Heterocyclic Chem., 2001, 38; 655-657.