

ISSN 0974-4169 (Print)
0974-4150 (Online)

www.ajrconline.org



RESEARCH ARTICLE

Effect of substituent on the ^{13}C - NMR chemical shifts of substituted 5-benzylidenearbituric acids

P. Mohandass¹, K. Radhakrishnan^{*1}, S. Manimekalai², V. Suriyanarayanan³, S. Radhakrishnan⁴

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

²Department of Chemistry, E.M.G. Yadava Women's College, Madurai, Tamil Nadu, India

³Electro-organic Chemistry Division, CSIR-CECRI, Karaikudi-630003, Tamil Nadu, India

⁴Central Instrumentation Facilities, CSIR-CECRI, Karaikudi-630003, Tamil Nadu, India

*Corresponding Author E-mail: prskradha61@gmail.com

ABSTRACT:

Substituted 5-benzylidenearbituric acids have been prepared and characterized by ^1H and ^{13}C NMR spectral analysis. Investigation of substituents effect and mode of transmission of electronic effects have been carried out by ^{13}C NMR chemical shifts measurement and correlated it with LFER parameters in substituted 5-benzylidenearbituric acids.

KEYWORDS: ^1H and ^{13}C NMR, substituted 5-benzylidenearbituric acids, substituent effects.

INTRODUCTION:

Correlation of the chemical shift with substituent constant has been widely used to investigate the nature of the effect of the substituent on the physical properties of compounds. Electron density around the nucleus of interest (H,C) is mostly affected by the electron-donating and electron-withdrawing ability of the substituent. Therefore, a correlation between the observed chemical shift and any parameter representing such ability seems to be well-founded, and there are numerous reports on the subject¹.

The single substituent parameter (SSP) approach which is represented by equation (1) has been used to correlate the chemical shift of *m*- and *p*- substituted compound to unsubstituted compound using the Hammett σ_m and σ_p values. Values of ^{13}C were reported for the system of *m*- and *p*-substituted cinnamic acids².

The dual substituent parameter (DSP) approach, on the other hand, divides the effect of substituent effect into inductive (σ_I) and resonance (σ_R) parameters as represented in Eq. (2).

$$\delta = \rho\sigma + \delta^0 \dots \dots \dots (1)$$

$$\delta = \rho_I\sigma_I + \rho_R\sigma_R + \delta^0 \dots \dots \dots (2)$$

Yukawa and Tsuno proposed Eq. (3) for dealing with enhanced resonance effects

$$\delta = \rho\sigma + r(\sigma^+ - \sigma^-) + \delta^0 \dots \dots \dots (3)$$

The DSP analysis of sterically congested systems has been improved by TSP by using Charton's steric parameter (ν) using Eq. (4).

$$\delta = \rho_I\sigma_I + \rho_R\sigma_R + \rho_\nu\nu + \delta^0 \dots \dots \dots (4)$$

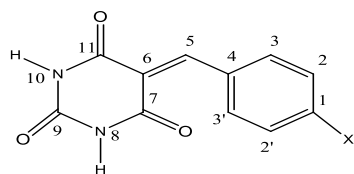
The magnitude, as well as the sign of ρ , should have a profound meaning on the mechanism of the transmission of the substituent effect. For example, correlations of the chemical shift of carbonyl carbon with the Hammett σ for the system of benzanilides, $\text{X-C}_6\text{H}_4\text{-CO-NH-C}_6\text{H}_4\text{-Y}$ show normal correlation when Y is varied, but the reverse correlation is observed when X is varied. π polarizations have been attributed for such observation.^{3,4} The magnitude of ρ_x (-2.838 ppm,

$r=0.940$) is larger than that of ρ_y (0.853 ppm, $r=0.975$) in DMSO- d_6 . The carbonyl carbon is directly bonded to the phenyl ring of $X-C_6H_4$, but it is separated by the nitrogen atom from C_6H_4-Y and therefore, the ρ_x should be larger than ρ_y . The estimation of sign and magnitude of the substituent chemical shift, however, seems to be complicated by many factors which affect the chemical shift.

Recently we reported the effect of substituents on the antimicrobial activities of substituted 2-benzylidene 1,3-indandiones⁵ and substituted 5-benzylidenebarbituric acids⁶. These above reports prompted us to undertake a detailed ^{13}C NMR spectral and correlation study of substituted 5-benzylidenebarbituric acids.

MATERIALS AND METHODS:

All chemicals used were purchased from Sigma Aldrich. The purity of the compounds was checked by TLC on silica gel G plate. Substituted 5-benzylidenebarbituric acids (Figure-1) were prepared by reaction of the corresponding substituted benzaldehyde with barbituric acid as reported earlier⁷.



(X = -OCH₃, -OH, -CH₃, -H, -Cl, -Br, -NO₂)

Figure - 1

Table 2: ^{13}C NMR chemical shifts of substituted 5-benzylidenebarbituric acid

| S. No. | Substituent X | C ₁ | C _{2,2'} | C _{3,3'} | C ₄ | C ₅ | C ₆ | C ₇ | C ₉ | C ₁₁ |
|--------|-------------------|----------------|-------------------|-------------------|----------------|----------------|----------------|----------------|----------------|-----------------|
| 1. | -OCH ₃ | 162.64 | 114.41 | 137.96 | 125.62 | 155.46 | 116 | 163.92 | 150.67 | 164.39 |
| 2. | -OH | 163.48 | 115.97 | 138.77 | 124.24 | 156.05 | 114.61 | 162.75 | 150.7 | 164.59 |
| 3. | -CH ₃ | 143.96 | 129.33 | 134.43 | 130.31 | 155.46 | 118.3 | 162.26 | 150.68 | 164.08 |
| 4. | -H | 133.11 | 128.52 | 133.54 | 132.69 | 155.2 | 119.55 | 162.03 | 150.69 | 163.87 |
| 5. | -Cl | 137.21 | 128.55 | 135.15 | 132.01 | 153.52 | 120.09 | 162.04 | 150.65 | 163.67 |
| 6. | -Br | 126.29 | 131.51 | 135.15 | 132.4 | 153.56 | 120.24 | 162.04 | 150.65 | 163.67 |
| 7. | -NO ₂ | 148.49 | 132.69 | 123.37 | 140.48 | 151.63 | 123.15 | 161.62 | 150.68 | 163.13 |

RESULTS AND DISCUSSIONS:

Correlations with Lynch-Equation:

The SCS of monosubstituted benzenes has been very useful in the signal assignment of polysubstituted compounds⁸⁻¹¹. However, in many published studies summarized by Craik¹² it has been apparent that the SCS values of X and Y at positions 4' and 1' in disubstituted benzenes Fig. (2) are non-additive. Lynch¹³ has proposed that the non-additivity of the chemical shifts of C-1' and C-4' is reflected in the relationship Eq. (5) where SCS_X(Y) is the substituent chemical shift of the carbon *para*-to X in the series of 1',4'-disubstituted benzenes (Fig. 2, X, Y \neq H),

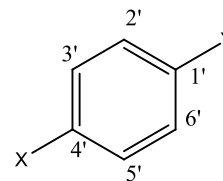


Figure -2

$$SCS_X(Y) = a + b [SCS_X(H)] \dots \dots \dots (5)$$

SCS_X(H) is the corresponding substituent chemical shift of the carbon *para*-to X in monosubstituted benzenes (Fig.2, Y=H), 'b' is the slope parameter and 'a' is the shift calculated for the parent species with X=Y. A wide range of successful correlations (using Lynch equation)

Spectra:

1H and ^{13}C spectra of substituted 5-benzylidenebarbituric acids were obtained on a Bruker AMX 400 MHz spectrometer. Chemical shifts of 1H were measured with the peak of DMSO at δ 2.51 as the internal reference, while those of ^{13}C were recorded with the central peak of DMSO at δ 39.90 as the internal reference. The 1H and ^{13}C chemical shifts of the substituted 5-benzylidenebarbituric acids are presented in Tables 1 and 2 respectively.

Assignment of 1H and ^{13}C chemical shifts:

Assignments of 1H chemical shifts were made using considerations of splitting patterns, spin decoupling and additivity of chemical shifts. The ^{13}C chemical shifts were assigned by intensity and SCS considerations.

Table 1: 1H NMR chemical shifts of substituted 5-benzylidenebarbituric acids

| S. No. | Substituent (X) | H _{2,2'} | H _{3,3'} | H ₅ | H ₈ | H ₁₀ |
|--------|-----------------|-------------------|-------------------|----------------|----------------|-----------------|
| 1 | 0 | 7.065 | 8.369 | 8.252 | 11.175 | 11.302 |
| 2 | -OH | 6.878 | 8.32 | 8.213 | 11.117 | 11.249 |
| 3 | 0 | 7.304 | 8.094 | 8.255 | 11.218 | 11.365 |
| 4 | -H | 7.485 | 8.073 | 8.285 | 11.238 | 11.397 |
| 5 | -Cl | 7.518 | 8.069 | 8.243 | 11.275 | 11.425 |
| 6 | -Br | 7.67 | 7.979 | 8.223 | 11.272 | 11.421 |
| 7 | 0 | 8.245 | 8.017 | 8.324 | 11.329 | 11.504 |

have been established for the SCS of carbons bearing Y in Fig. (2) with the value of 'b' ranging from 0.6 to 1.5¹⁴. When the slope is close to unity, experimental results could be reproduced by additivity relationship and when $b \neq 1$, the Lynch equation can be used to predict the SCS values through proportionality relationships. The slope b of the Lynch equation Eq. (5) is less than one, then the fixed substituent at C-1' Fig. (2) diminishes the substituent effect. When slope b is larger than one, showing that the fixed substituent undergoes an amplification of the substituent effect.

In case of C₁, there is a good correlation with (r=0.988) appropriate SCS (S_i) values, slope b is 0.97, which reveals that the fixed substituent Y=CH-C-C₃H₂N₂O₃,

has little effect on the additivity of this shifts¹⁴. A satisfactory correlation exists between SCS of C_{22'} and S_o with a correlation coefficient (r=0.828) and the slope value (b=0.84), indicating that the fixed substituent Y, significantly diminishes the substituent effect¹⁴. A poor correlation exists between SCS of C_{33'} and S_m with a correlation coefficient (r=0.113) and the slope value (b=0.71) which reveals that the fixed substituent Y diminishes the substituent effect¹⁴. The C₄ carbon affords a good correlation with S_p with correlation coefficient r=0.993 and the slope value b=0.94 demonstrates that the fixed substituent Y has little effect on the additivity of these shifts¹⁴. The results of Lynch correlations are given in table (3) and the plots of Lynch correlations shown in fig. (3).

Table (3): Results of Lynch correlations^a of ¹³C chemical shifts of substituted 5-benzylidenebarbituric acids Fig. (1) with SCS values for monosubstituted benzenes.

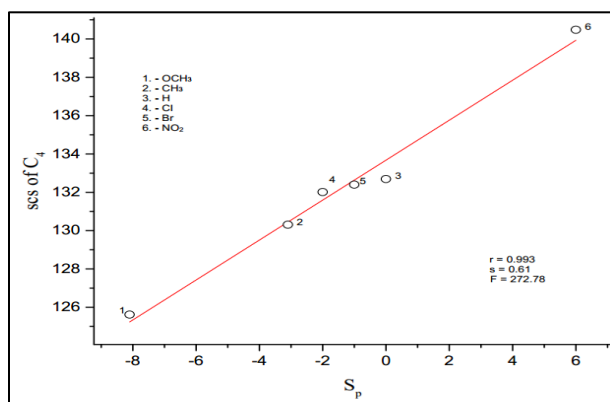
| S. No. | Nucleus | Benzene SCS | Slope (b) | Intercept (a) | r ^b | n ^c | s ^d |
|--------|------------------|----------------|-----------|---------------|----------------|----------------|----------------|
| 1. | C ₁ | S _i | 0.97 | 132.23 | 0.988 | 6 | 2.17 |
| 2. | C _{22'} | S _o | 0.84 | 129.73 | 0.828 | 6 | 4.14 |
| 3. | C _{33'} | S _m | 0.71 | 132.69 | 0.113 | 6 | 5.63 |
| 4. | C ₄ | S _p | 0.94 | -126.43 | 0.993 | 6 | 0.61 |

Where, 'a' is SCSX (Y) = a + b SCSX (H); 'b' is Correlation coefficient; 'c' is Number of data points; 'd' is Standard deviations

Table (4): Results of statistical treatment of ¹³C – Chemical shift with $\sigma_p, \sigma_p^o, \sigma_p^+, \sigma_p^-, \sigma_p^+/\sigma_p, \sigma_p^+/\sigma_p^-, \sigma_p^+/\sigma_p^+, \sigma_p^+/\sigma_p^-$ substituent constants using single parameter equation (2)

| S.No. | Carbons | Scale | ρ | R | s | F | log δ^o | n |
|-------|------------------|------------------------------------|--------------|-------|--------|--------|----------------|---|
| 1 | C ₄ | σ_p | 0.043±0.006 | 0.949 | 0.006 | 43.33 | 2.115±0.002 | 7 |
| | | σ_p^o | 0.038±0.010 | 0.882 | 0.008 | 13.99 | 2.114±0.004 | 6 |
| | | σ_p^+ | 0.029±0.002 | 0.986 | 0.003 | 179.37 | 2.121±0.001 | 7 |
| | | σ_p^+/σ_p | 0.033±0.006 | 0.924 | 0.007 | 29.11 | 2.117±0.003 | 7 |
| | | σ_p^+/σ_p^- | 0.024±0.002 | 0.989 | 0.003 | 226.34 | 2.118±0.001 | 7 |
| | | $\sigma_p^+/\sigma_p^+/\sigma_p^-$ | 0.026±0.004 | 0.938 | 0.006 | 37.12 | 2.115±0.002 | 7 |
| 2 | C ₅ | σ_p | -0.011±0.001 | 0.984 | 0.001 | 152.18 | 2.189±0.001 | 7 |
| | | σ_p^o | -0.015±0.001 | 0.988 | 0.001 | 163.39 | 2.190±0.001 | 6 |
| | | σ_p^+ | -0.007±0.001 | 0.916 | 0.002 | 25.94 | 2.187±0.001 | 7 |
| | | σ_p^+/σ_p | -0.008±0.002 | 0.887 | 0.002 | 18.40 | 2.188±0.001 | 7 |
| | | σ_p^+/σ_p^- | -0.006±0.001 | 0.938 | 0.002 | 36.47 | 2.188±0.001 | 7 |
| | | $\sigma_p^+/\sigma_p^+/\sigma_p^-$ | -0.006±0.001 | 0.917 | 0.002 | 26.68 | 2.189±0.001 | 7 |
| 3 | C ₆ | σ_p | 0.025±0.004 | 0.950 | 0.004 | 45.95 | 2.073±0.001 | 7 |
| | | σ_p^o | 0.021±0.005 | 0.900 | 0.004 | 17.16 | 2.073±0.002 | 6 |
| | | σ_p^+ | 0.018±0.001 | 0.995 | 0.001 | 508.52 | 2.077±0.001 | 7 |
| | | σ_p^+/σ_p | 0.019±0.003 | 0.917 | 0.005 | 26.46 | 2.075±0.002 | 7 |
| | | σ_p^+/σ_p^- | 0.014±0.002 | 0.970 | 0.003 | 80.18 | 2.075±0.001 | 7 |
| | | $\sigma_p^+/\sigma_p^+/\sigma_p^-$ | 0.015±0.003 | 0.902 | 0.005 | 21.75 | 2.075±0.002 | 7 |
| 4 | C ₇ | σ_p | -0.004±0.002 | 0.722 | 0.001 | 5.43 | 2.211±0.001 | 7 |
| | | σ_p^o | -0.004±0.002 | 0.620 | 0.002 | 2.51 | 2.211±0.001 | 6 |
| | | σ_p^+ | -0.003±0.001 | 0.820 | 0.001 | 10.24 | 2.210±0.001 | 7 |
| | | σ_p^+/σ_p | -0.004±0.001 | 0.917 | 0.001 | 26.41 | 2.210±0.001 | 7 |
| | | σ_p^+/σ_p^- | -0.002±0.001 | 0.775 | 0.001 | 7.51 | 2.210±0.001 | 7 |
| | | $\sigma_p^+/\sigma_p^+/\sigma_p^-$ | -0.003±0.001 | 0.836 | 0.001 | 11.63 | 2.210±0.001 | 7 |
| 5 | C ₁₁ | σ_p | -0.003±0.001 | 0.979 | 0.0003 | 116.72 | 2.24±0.001 | 7 |
| | | σ_p^o | -0.003±0.001 | 0.945 | 0.0004 | 33.30 | 2.215±0.001 | 6 |
| | | σ_p^+ | -0.002±0.001 | 0.996 | 0.0001 | 640.41 | 2.214±0.001 | 7 |
| | | σ_p^+/σ_p | -0.002±0.001 | 0.935 | 0.0005 | 34.80 | 2.214±0.001 | 7 |
| | | σ_p^+/σ_p^- | -0.002±0.001 | 0.983 | 0.0003 | 145.26 | 2.214±0.001 | 7 |
| | | $\sigma_p^+/\sigma_p^+/\sigma_p^-$ | -0.002±0.001 | 0.930 | 0.0005 | 32.23 | 2.215±0.001 | 7 |
| 6 | C _{22'} | σ_o | 0.044±0.024 | 0.632 | 0.020 | 3.33 | 2.094±0.008 | 7 |
| | | σ_o^* | 0.038±0.020 | 0.691 | 0.020 | 3.66 | 2.095±0.009 | 6 |
| | | E _s | -0.042±0.013 | 0.825 | 0.016 | 10.69 | 2.103±0.006 | 7 |

^an=6 means calculated without -OH group

Fig. (3). Lynch plot of SCS of C₄ vs S_p

Hammett and dual substituent parameter correlations:

The ¹³C chemical shifts of the carbon atoms of the 5-benzylidenebarbituric acid series afford several reasonable correlations using Hammett substituent parameters Eq.(1) and the data are given in Table (4). The results of the correlations of ¹³C SCS values of 5-benzylidenebarbituric acid series with σ_I and σ_R constants according to equation (2) are presented in Table (5). The results of multiple regression analysis of ¹³C chemical shifts with σ_p , ($\sigma_p^+ - \sigma_p$) and σ_p^o , ($\sigma_p^+ - \sigma_p^o$) constants using Yukava – Tsuno equation (3) are presented in Table (6).

Table 5: DSP analysis of chemical shift data with dual parameter equation (3)

| S.No | Carbons | Scale | ρ_I | ρ_R | R | SE | F | log δ^o | n | $\lambda = \rho_R/\rho_I$ |
|------|------------------|------------------------|--------------|--------------|-------|--------|--------|----------------|---|---------------------------|
| 1 | C ₄ | σ_I, σ_R | 0.024±0.003 | 0.051±0.003 | 0.995 | 0.002 | 154.44 | 2.122±0.001 | 6 | 0.25 |
| | | σ_I, σ_R^o | 0.032±0.017 | 0.036±0.017 | 0.849 | 0.01 | 3.89 | 2.118±0.007 | 6 | 1.33 |
| | | σ_I, σ_R^+ | 0.010±0.030 | 0.018±0.016 | 0.640 | 0.016 | 1.39 | 2.122±0.015 | 7 | 1.80 |
| | | σ_I, σ_R^- | 0.019±0.011 | 0.037±0.009 | 0.943 | 0.007 | 12.10 | 2.120±0.005 | 6 | 2.00 |
| | | F, R | 0.025±0.003 | 0.054±0.002 | 0.996 | 0.002 | 279.61 | 2.123±0.001 | 7 | 2.00 |
| 2 | C ₅ | σ_I, σ_R | -0.013±0.001 | -0.007±0.001 | 0.998 | 0.0003 | 349.25 | 2.191±0.001 | 6 | 0.70 |
| | | σ_I, σ_R^o | -0.014±0.003 | -0.005±0.002 | 0.956 | 0.002 | 16.09 | 2.191±0.001 | 6 | 0.36 |
| | | σ_I, σ_R^+ | -0.011±0.006 | -0.002±0.001 | 0.838 | 0.003 | 4.74 | 2.191±0.003 | 7 | 0.20 |
| | | σ_I, σ_R^- | -0.012±0.002 | -0.005±0.001 | 0.980 | 0.001 | 36.20 | 2.191±0.001 | 6 | 0.42 |
| | | F, R | -0.014±0.001 | -0.009±0.001 | 0.993 | 0.001 | 146.55 | 2.191±0.001 | 7 | 0.71 |
| 3 | C ₆ | σ_I, σ_R | 0.016±0.002 | 0.026±0.002 | 0.996 | 0.001 | 176.46 | 2.077±0.001 | 6 | 1.63 |
| | | σ_I, σ_R^o | 0.019±0.010 | 0.016±0.010 | 0.810 | 0.006 | 2.86 | 2.074±0.004 | 6 | 0.80 |
| | | σ_I, σ_R^+ | 0.008±0.019 | 0.010±0.009 | 0.636 | 0.01 | 1.36 | 2.076±0.009 | 7 | 1.25 |
| | | σ_I, σ_R^- | 0.014±0.008 | 0.017±0.007 | 0.885 | 0.005 | 5.43 | 2.075±0.003 | 6 | 1.21 |
| | | F, R | 0.015±0.003 | 0.032±0.002 | 0.990 | 0.002 | 105.40 | 2.078±0.001 | 7 | 2.13 |
| 4 | C ₇ | σ_I, σ_R | -0.001±0.001 | -0.008±0.002 | 0.928 | 0.001 | 9.34 | 2.209±0.001 | 6 | 2.00 |
| | | σ_I, σ_R^o | -0.002±0.003 | -0.004±0.003 | 0.550 | 0.002 | 0.649 | 2.210±0.002 | 6 | 2.00 |
| | | σ_I, σ_R^+ | 0.001±0.002 | -0.003±0.002 | 0.669 | 0.002 | 1.618 | 2.208±0.002 | 7 | 0.21 |
| | | σ_I, σ_R^- | -0.001±0.001 | -0.004±0.003 | 0.648 | 0.002 | 1.087 | 2.210±0.001 | 6 | 4.00 |
| | | F, R | -0.001±0.002 | -0.005±0.002 | 0.806 | 0.001 | 3.719 | 2.209±0.001 | 7 | 5.00 |
| 5 | C ₁₁ | σ_I, σ_R | -0.003±0.001 | -0.003±0.001 | 0.998 | 0.0001 | 341.86 | 2.214±0.001 | 6 | 1.50 |
| | | σ_I, σ_R^o | -0.003±0.001 | -0.002±0.001 | 0.859 | 0.0007 | 4.22 | 2.214±0.001 | 6 | 0.66 |
| | | F, R | -0.002±0.001 | -0.004±0.001 | 0.993 | 0.002 | 152.18 | 2.214±0.001 | 7 | 2.00 |
| 6 | C _{22'} | σ_I, σ_R | 0.010±0.022 | 0.079±0.020 | 0.891 | 0.01 | 5.81 | 2.115±0.010 | 6 | 8.00 |
| | | σ_I, σ_R^o | 0.020±0.001 | 0.031±0.042 | 0.438 | 0.03 | 0.35 | 2.104±0.018 | 6 | 1.50 |
| | | F, R | 0.006±0.019 | 0.081±0.024 | 0.903 | 0.01 | 8.85 | 2.117±0.010 | 7 | 1.33 |

"n=6 means calculated without -OH group"

Table (6): Results of multiple regression analysis of ¹³C chemical shifts with σ_p , ($\sigma_p^+ - \sigma_p$) and σ_p^o , ($\sigma_p^+ - \sigma_p^o$) constants using Yukava – Tsuno equation (3).

| S.No. | Carbon | scale | ρ | r | R | SE | F | n |
|-------|-----------------|---|--------------|--------------|-------|-------|--------|---|
| 1. | C ₄ | $\sigma_p, (\sigma_p^+ - \sigma_p)$ | 0.028±0.006 | 0.032±0.009 | 0.986 | 0.003 | 72.76 | 7 |
| | | $\sigma_p^o, (\sigma_p^+ - \sigma_p^o)$ | 0.027±0.009 | 0.020±0.009 | 0.954 | 0.006 | 15.15 | 6 |
| 2. | C ₅ | $\sigma_p, (\sigma_p^+ - \sigma_p)$ | -0.013±0.001 | 0.004±0.002 | 0.994 | 0.001 | 167.30 | 7 |
| | | $\sigma_p^o, (\sigma_p^+ - \sigma_p^o)$ | -0.012±0.001 | -0.001±0.001 | 0.988 | 0.001 | 61.27 | 6 |
| 3. | C ₆ | $\sigma_p, (\sigma_p^+ - \sigma_p)$ | 0.016±0.002 | 0.021±0.003 | 0.996 | 0.001 | 274.61 | 7 |
| | | $\sigma_p^o, (\sigma_p^+ - \sigma_p^o)$ | 0.014±0.002 | 0.012±0.003 | 0.989 | 0.002 | 65.94 | 6 |
| 4. | C ₇ | $\sigma_p, (\sigma_p^+ - \sigma_p)$ | -0.007±0.002 | -0.006±0.003 | 0.866 | 0.001 | 6.01 | 7 |
| | | $\sigma_p^o, (\sigma_p^+ - \sigma_p^o)$ | -0.001±0.001 | -0.005±0.001 | 0.937 | 0.001 | 10.76 | 6 |
| 5. | C ₁₁ | $\sigma_p, (\sigma_p^+ - \sigma_p)$ | -0.003±0.001 | -0.002±0.001 | 0.998 | 0.001 | 518.04 | 7 |
| | | $\sigma_p^o, (\sigma_p^+ - \sigma_p^o)$ | -0.002±0.001 | -0.001±0.001 | 0.994 | 0.001 | 133.10 | 6 |

"n=6 means calculated without -OH group"

Substituent effects on the ^{13}C NMR chemical shifts of the substituted 5-benzylidenearbituric acids:

The use of ^{13}C NMR SCS is to monitor the transmission of electronic effects in the molecular frame works in general and to understand the mode of transmission of long-range substituent effects in extended π -electron systems, in particular, are topics of current interest. Thus long-range ^{13}C SCS have been reported for N-benzylideneanilines¹⁵, N-benzylidenebenzylamines¹⁶, chalcones¹⁷, benzophenones¹⁸, phenylacetylenes¹⁹, β -nitrostyrenes^{20,21}, cinnamic acids^{22,23}, cinnamates²⁴, benzonitrile²⁵, cyanopyridine²⁶, (E)-1-benzylidene-2-(diphenyl methylene) hydrazines²⁷, aryl hydrazides²⁸, (E)-1-benzylidene-2-(4-bromophenyl) hydrazines²⁹, N-(substituted phenyl)-2-cyanoacetamides³⁰, 4-bromo-1-naphthyl chalcones³¹ and symmetrical diimines³². The ^{13}C chemical shift data of several carbon atoms of substituted 5-benzylidenearbituric acids has been correlated with SSP equation (Eq.1.), DSP equations (Eq.2.) and Yukawa-Tsuno equation (Eq.3.).

C₄ - Carbon atom.

The Chemical shift of C₄ carbon appeared over a relatively narrow range of 16.24 ppm. The result of SSP analysis shown in the table (4), an excellent correlation affords by σ_p^+ / σ_p^- constant given in equation (6), and the plot of $\log \delta C_4$ vs σ_p^+ / σ_p^- as shown in Fig. (4).

$$\log \delta C_4 = 0.024 \sigma_p^+ / \sigma_p^- + 2.118 \dots \dots \dots (6)$$

(±0.002) (±0.001)

$$r = 0.989; s = 0.003; n = 7$$

The result of DSP analysis in the table (5), afford an excellent correlation are shown in equations (7) and (8)

$$\log \delta C_4 = 0.024 \sigma_I + 0.051 \sigma_R + 2.12 \dots \dots \dots (7)$$

(±0.003) (±0.003) (±0.001)

$$R = 0.995; SE = 0.002; n = 6; F = 154.44$$

$$\log \delta C_4 = 0.025 F + 0.054 R + 2.12 \dots \dots \dots (8)$$

(±0.003) (±0.002) (±0.001)

$$R = 0.996; SE = 0.002; n = 7; F = 279.61$$

The sign of ρ_I and ρ_R are positive reveals that the normal substituent effect operates on C₄ carbon atom, i.e., an electron withdrawing substituent decrease the C₄ carbon atom shielding and an electron releasing substituent increase it. Examination of chemical shift of data in table (2), electron-withdrawing substituent causes downfield shift and electron releasing substituent causes up field. The magnitude of ρ_R is greater than ρ_I indicate that the predominance of resonance effect over inductive effect in the chemical shift of C₄ carbon atom. This result is also shown from Yukawa-Tsuno equation (3) is given in table (6). The result of best fit eq. (3) is given in equation (9)

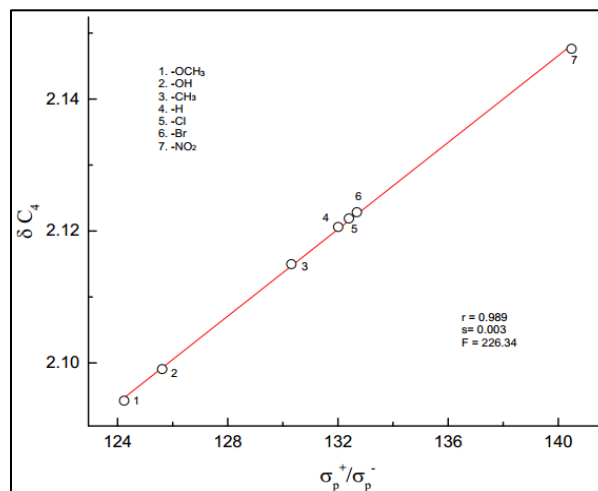


Fig. 4. The plot of $\log \delta C_4$ vs σ_p^+ / σ_p^-

$$\log \delta C_4 = 0.028 \sigma_p + 0.032 (\sigma_p^+ - \sigma_p^-) + 2.121 \dots \dots \dots (9)$$

(±0.006) (±0.009) (±0.002)

$$R = 0.986; SE = 0.003; n = 7; F = 72.76$$

C₅ - Carbon atom:

The chemical shift of C₅ carbon appeared over a relatively narrow range of 4.42 ppm. The SSP analysis with various σ parameters, σ_p^0 gave satisfactory correlation, results shown in the table (4). It gave negative correlation (Eq.10) and negative slope indicates that a reverse substituent effect operates on the carbonyl carbon. The Hammett plot of $\log \delta C_5$ vs σ_p^0 gives,

$$\log \delta C_5 = -0.015 \sigma_p^0 + 2.189 \dots \dots \dots (10)$$

(±0.001) (±0.001)

$$r = 0.988; s = 0.001; n = 6$$

Examination of chemical shift data (table 2) of C₅ carbon, electron releasing group caused downfield shift by increasing the shielding and electron withdrawing group cause upfield shift by decreasing the shielding.

The DSP analysis of C₅ carbon with various σ_R scale is given in table (8), the best fit is given in equations (11) and (12)

$$\log \delta C_5 = -0.013 \sigma_I - 0.007 \sigma_R + 2.191 \dots \dots \dots (11)$$

(±0.001) (±0.0003) (0.003)

$$R = 0.998; SE = 0.0003; n = 6; F = 349.25$$

$$\log \delta C_5 = -0.014 F - 0.009 R + 2.077 \dots \dots \dots (12)$$

(±0.001) (±0.001) (±0.001)

$$R = 0.993; SE = 0.001; n = 7; F = 146.55$$

The sign of slopes ρ_I and ρ_R are negative, reveals that the reverse substituent effect operates on C₅ carbon atom. The results of Yukawa-Tsuno equation (13), also indicate that the magnitude of 'r' is very low (<1).

$$\log \delta C_5 = -0.013\sigma_p + 0.004(\sigma_p^+ - \sigma_p) + 2.190 \dots \dots \dots (13)$$

(±0.001) (±0.002) (±0.004)

$$R = 0.994; SE = 0.001; n = 7; F = 167.30$$

C₆ – Carbon atom

The chemical shift of C₆ carbon atom appeared over a relatively narrow range of 7.15 ppm. The results of SSP analysis shown in table (4), excellent correlation afford by σ_p^+ constant given in equation (14).

$$\log \delta C_6 = 0.018\sigma_p^+ + 2.077 \dots \dots \dots (14)$$

(±0.001) (±0.001)

$$r = 0.995; s = 0.001; n = 7; F = 508.52$$

The results of DSP analysis in table (5), afford an excellent correlation are shown in equations (15) and (16).

$$\log \delta C_6 = 0.016\sigma_I + 0.026\sigma_R + 2.077 \dots \dots \dots (15)$$

(±0.002) (±0.002) (0.001)

$$R = 0.996; SE = 0.001; F = 176.46; n = 6$$

$$\log \delta C_6 = 0.015F + 0.032R + 2.078 \dots \dots \dots (16)$$

(±0.003) (±0.002) (0.001)

$$R = 0.990; SE = 0.002; F = 105.40; n = 7$$

The sign of ρ_I and ρ_R are positive reveals that the normal substituent effect operates on C₆ carbon atom, i.e., an electron withdrawing substituent decrease the C₇ carbon atom shielding and an electron releasing substituent increase it. Examination of chemical shift data in table (2), electron withdrawing substituent causes downfield shift and electron releasing substituent causes upfield. The magnitude of ρ_R greater than ρ_I indicate that the predominance of resonance effect over inductive effect in the chemical shift of C₆ carbon atom.

The results of Yukawa-Tsuno equation (17), also indicate that the magnitude of 'r' is very low (<1).

$$\log \delta C_6 = 0.016\sigma_p + 0.021(\sigma_p^+ - \sigma_p) + 2.078 \dots \dots \dots (17)$$

(±0.002) (±0.003) (±0.001)

$$R = 0.996; SE = 0.001; F = 274.61; n = 7$$

C₇ – Carbon atom

The chemical shift of C₇ carbon atom appeared over a range of about 2.3 ppm. The result of SSP analysis shown in table (4), fairly well correlation afford by

σ_p^+/σ_p constant is given in equation (18), and the plot of $\log \delta C_7$ vs σ_p^+/σ_p is shown in Fig. (31). The result is shown in equation (18).

$$\log \delta C_7 = -0.004 \sigma_p^+/\sigma_p + 2.210 \dots \dots \dots (18)$$

(±0.001) (±0.003)

$$r = 0.917; s = 0.001; F = 26.41; n = 7$$

The examination of chemical shift data (table 2) of C₇ carbon electron-releasing group causes downfield shift by increasing the shielding and electron withdrawing group cause upfield shift by decreasing the shielding. The DSP analysis of C₇ carbon with various σ_R scale is shown in table (5), the best fit is given in Eq. (19).

$$\log \delta C_7 = -0.001\sigma_I - 0.008\sigma_R + 2.209 \dots \dots \dots (19)$$

(±0.001) (±0.002) (±0.001)

$$R = 0.928; SE = 0.001; F = 9.34; n = 6$$

The result of Yukawa-Tsuno equation (3), is given in table (6). The result of best fit of Eq. (3) is given in Eq. (20).

$$\log \delta C_7 = -0.001\sigma_p^0 - 0.005(\sigma_p^+/\sigma_p^0) + 2.208 \dots \dots \dots (20)$$

(±0.001) (±0.001) (±0.001)

$$R = 0.937; SE = 0.001; F = 10.76; n = 6$$

C₁₁ – Carbon atom

The chemical shift of C₁₁ carbon appeared over a relatively narrow range of 1.46 ppm. The SSP analysis with various σ parameters, σ_p^+ gave excellent correlation, results shown in table (4). It gave negative correlation (Eq. 21) and negative slope indicates that a reverse substituent effect operates on the C₁₁ carbon.

$$\log \delta C_{11} = -0.002 \sigma_p^+ + 2.214 \dots \dots \dots (21)$$

(±0.001) (±0.001)

$$r = 0.996; s = 0.0001; F = 640.41; n = 7$$

Examination of chemical shift data in table (2) shows that the electron-releasing substituent causes downfield shift while electron-withdrawing substituent causes upfield shift. The DSP analysis of C₁₁ carbon with various σ_R scale is given in table (5), the best fit is given in equations (22) and (23).

$$\log \delta C_{11} = -0.003\sigma_I - 0.003\sigma_R + 2.214 \dots \dots \dots (22)$$

(±0.001) (±0.001) (±0.001)

$$R = 0.998; SE = 0.0001; F = 341.86; n = 6$$

$$\log \delta C_{11} = -0.002F - 0.004R + 2.214 \dots \dots \dots (23)$$

(±0.001) (±0.001) (±0.001)

$$R = 0.993; SE = 0.002; F = 152.18; n = 7$$

The result of Yukawa-Tsuno equation (3), is given in table (6) also indicate that the magnitude of 'r' is very low (<1).

$$\log \delta C_{11} = -0.003 \sigma_p - 0.002(\sigma_p^+ - \sigma_p) + 2.214 \dots \dots \dots (24)$$

$$(\pm 0.001) \quad (\pm 0.001) \quad (\pm 0.001)$$

$$R = 0.993; SE = 0.002; F = 152.18; n = 7$$

C_{22'}-Carbon atoms

The chemical shift of C_{22'} carbon atom appeared over a relatively narrow range of about 2.116 ppm. In the SSP analysis of C_{22'}σ_o and σ_o* gave poor correlation coefficients (r) 0.632 and 0.691 respectively. The results of SSP analysis are given in Eqs. (25) and (26).

$$\log \delta C_{22'} = 0.044 \sigma_o + 2.094 \dots \dots \dots (25)$$

$$(\pm 0.024) \quad (\pm 0.008)$$

$$r = 0.632; s = 0.02; n = 7$$

$$\log \delta C_{22'} = 0.038 \sigma_o^* + 2.095 \dots \dots \dots (26)$$

$$(\pm 0.020) \quad (\pm 0.009)$$

$$r = 0.691; s = 0.02; n = 6$$

But the same parameter for E_s, gave satisfactory

correlation, given in Eq. (27).

$$\log \delta C_{22'} = -0.042 E_s + 2.10 \dots \dots \dots (27)$$

$$(\pm 0.013) \quad (\pm 0.006)$$

$$r = 0.825; s = 0.016; n = 7$$

The best fit of DSP analysis is given in Eqs. (28) and (29).

$$\log \delta C_{22'} = 0.010 \sigma_I + 0.079 \sigma_R + 2.115 \dots \dots \dots (28)$$

$$(\pm 0.020) \quad (\pm 0.020) \quad (\pm 0.010)$$

$$R = 0.891; SE = 0.01; n = 6$$

$$\log \delta C_{22'} = 0.006 F + 0.081 R + 2.117 \dots \dots \dots (29)$$

$$(\pm 0.020) \quad (\pm 0.019) \quad (\pm 0.010)$$

$$R = 0.903; SE = 0.01; n = 7$$

The sign of slopes ρ_I and ρ_R are positive reveals that the normal substituent effects operate on C_{22'} carbon atom. The magnitude of ρ_R is higher than the magnitude of ρ_I indicate that the resonance effect is predominant over resonance effect on C_{22'} carbon atom. The TSP analysis of Charton steric parameter (v) gave poor correlations that are given in table (7).

Table (7): TSP analysis of SCS data of C_{22'} carbon atom of substituted 5-benzylidenebarbituric acids employing equation (4).

| S.No. | Scale | α | β | φ | R | s | F | P _R | P _S | n |
|-------|--|----------------|---------------|----------------|-------|-------|------|----------------|----------------|---|
| 1. | σ _I , σ _R , v | 0.019(±0.045) | 0.084(±0.034) | -0.007(±0.029) | 0.895 | 0.016 | 2.68 | 76.4 | 6.4 | 6 |
| 2. | σ _I , σ _R ^o , v | -0.008(±0.092) | 0.019(±0.060) | 0.022(±0.058) | 0.492 | 0.03 | 0.21 | 39.0 | 43.8 | 6 |
| 3. | σ _I , σ _R ⁺ , v | -0.093(±0.071) | 0.035(±0.023) | 0.057(±0.035) | 0.760 | 0.155 | 1.37 | 19.2 | 31.3 | 7 |
| 4. | σ _I , σ _R ⁻ , v | 0.006(±0.085) | 0.039(±0.058) | 0.001(±0.063) | 0.595 | 0.03 | 0.36 | 84.7 | 2.17 | 6 |
| 5. | F, R, v | -0.001(±0.050) | 0.078(±0.027) | 0.005(±0.030) | 0.904 | 0.016 | 4.47 | 92.0 | 5.95 | 7 |

"n=6 means calculated without -OH group"

The best fit of TSP analysis is taken from high correlation coefficient (R) and least standard error (SE) of the regression equation and the results are given in Eqs. (30) and (31).

$$\log \delta C_{22'} = 0.019 \sigma_I + 0.084 \sigma_R - 0.007 v + 2.117 \dots \dots \dots (30)$$

$$(\pm 0.045) \quad (\pm 0.034) \quad (\pm 0.029) \quad (\pm 0.015)$$

$$R = 0.895; SE = 0.016; n = 6$$

$$\log \delta C_{22'} = -0.001 F + 0.078 R - 0.005 v + 2.116 \dots \dots \dots (31)$$

$$(\pm 0.050) \quad (\pm 0.027) \quad (\pm 0.030) \quad (\pm 0.014)$$

$$R = 0.904, s = 0.016, n = 7$$

A better description of the composition of the electrical effect³³ is given by the equation,

$$P_R = \frac{\beta 100}{\alpha + \beta + \phi}$$

P_R is the percentage of delocalized effect. The result of TSP analysis is given in table (10) shows that the delocalized effect is predominant over the localized effect. The magnitude (%) of the steric factor³³ is given

by the equation,

$$P_S = \frac{\phi 100}{\alpha + \beta + \phi}$$

The results of table (7) shows that steric effect is also operating to some extent.

CONCLUSIONS:

A series of seven numbers of substituted 5-benzylidenebarbituric acids have been synthesized by condensation of barbituric acid with substituted benzaldehydes. These synthesized substituted 5-benzylidenebarbituric acids have been characterized by ¹H and ¹³C spectral data. The ¹³C NMR spectral data of these substituted 5-benzylidenebarbituric acids have been correlated with Hammett substituent constants and F and R parameters. From the results of statistical analysis, the effects of the substituent on the spectral data have been studied. The ¹³C NMR spectral correlations produced the most number of satisfactory correlations.

ACKNOWLEDGEMENTS:

One of the authors (P. Mohandass) is grateful to the University Grants Commission (UGC), Hyderabad for the award of Faculty Development Programme. Authors are also thankful to the Principal and Managing Board of Saraswathi Narayanan College, Madurai for providing research facilities.

CONFLICT OF INTEREST STATEMENT:

We declare that we have no conflict of interest.

REFERENCES:

- Craik DJ. and. Brownlee RTC. Substituent effects on chemical shifts in the side chains of aromatic systems, Progress in Physical Organic Chemistry . John Wiley & sons Inc., New York, 1983;pp 1-74.
- Slater CD, Robinson CN, Bies R, Bryan DW, Chang K, Hill AW, Moore WH.Jr. Otey TG, Popperireiter ML, Reisser JR, Stablein GE, Waddy VP, III Wilkinson WO, Wray WA. A comparison of single- and dual- parameter equations in the correlation of carbon-13 shifts in substituted styrene. Journal of Organic Chemistry. 1985; 50(21): 4125-4130.
- Suezawa H, Yuzuri T, Hirota M, Ito Y. Hanada. Substituent effects on the ^1H and ^{13}C and ^{15}N NMR spectra of substituted benzanilides. Bulletin of the Chemical Society of Japan.1990; 60(2):328-334.
- Yuzuri T, Suezawa H, Hirota M. Further investigations on polar substituent effects on the NMR chemical shifts of N-Acylanilines and related compounds. Correlation analytical approach and solvent effects. Bulletin of the Chemical Society of Japan. 1994;67(6):1664-1673.
- Radhakrishnan K, Mohandass P, Sankaralingam S, Chandramohan S. Synthesis and antimicrobial activity of 2-benzylidene-1,3-indandiones: A structure reactivity study. Der Chemica Sinica,2016;7(4): 1-7.
- Radhakrishnan K, Mohandass P, Sankaralingam S, Chandramohan S. Synthesis and antibacterial activity of 5-benzylidenebarbituric acids: A structure -reactivity study. International Journal of Chemtech Research. 2017;10(7):1019-1027.
- Branko S, Jursic A simple method for knoevenagel condensation of α,β -conjugated and aromatic aldehydes with barbituric acid. Journal of Heterocyclic Chemistry. 2001;38(3):655-657.
- Gronowitz S, Johnso A. Maholanyinov,S.Tomo and Sokaniov. Org. Magn. Reson. 1975;7:732.
- Dana G. Convert JP. Girault and Mathoz E. Effect of nuclear magnetic resonance of ^{13}C . Study of derivatives of 2-phenanthryl furan and 2- phenylpyrrole. Canadian Journal of Chemistry. 1976; 54(11): 1827-1836.
- Ray GJ, Kurland RJ, Colter AK. Magnetic resonance studies of triphenylcarbonium ions -II; Carbon-13 magnetic resonance studies of charge delocalization in *para*-substituted triphenyl carbonium ions. Tetrahedron.1971; 27(4): 735-752.
- Hinton JF, Layton B. Natural abundance of ^{13}C NMR investigation of substituted bromobenzene using noise decoupling of proton resonances. Organic Magnetic Resonance.1972;4:353-360.
- Craik DJ. Annual Reports on NMR spectroscopy. Edited by Webb GA. Academic Press. London. 1983; 15:1.
- Lynch BM. Proportionality relationships in the carbon-13 nuclear magnetic resonance spectra of *para*-disubstituted benzenes; a new interpretation of non-additive behavior. Canadian Journal of Chemistry. 1977; 55:541-547.
- Perumal S, Chandrasekaran R, Vijayabaskar V, David A. Wilson. ^1H and ^{13}C NMR study of substituted effects in 2- and 3-substituted diphenyl sulphides and sulphones and 4-substituted 2'6'-Dimethyldiphenyl sulphides. Magnetic Resonance in Chemistry. 1995; 33:779-790.
- InamotoN, Kushida K, Masuda H, Ohta S, Satoh Y, Tamwa. K, Tokomara K, Tori M Yoshida. Novel substituent effects in ^1H and ^{13}C NMR spectra of 4- and 4'-substituted N-benzylideneanilines. Tetrahedron Letters. 1974;15(41):3617-3620.
- Arrowsmith JE, Cook MJ, Hardstone DJ. Long range substituent-induced chemical shifts in the ^{13}C NMR spectra of N-Benzylidenebenzylamines. Organic Magnetic Resonance. 1978; 11(3): 160-161.
- SolcaniovaE, Toma, Gronowitz. Investigation of substituted effects of chalcones by ^{13}C nmr spectroscopy. Organic Magnetic Resonance.1976; 8: 439-443.
- Shapiro MJ. Carbon-13 NMR substituted effects in *para*-substituted benzophenones.Tetrahedron. 1977; 33(10):1091-1094.
- Dawson DA. and Reynolds WF. Canadian Journal of Chemistry.1975; 53(3): 373-382.
- Happer DAR. Australian Journal of Chemistry. 1976; 53: 373.
- Happer,D.A.R.; McKerrow, S.M. and Wilkinson, A. L Australian Journal of Chemistry.1977; 2:1479.
- Gunthor H, Prestein J, Watan PJ. Carbon-13 NMR spectra of coumarin and methoxy coumarin-A reinvestigation of charge density/chemical shift relations. Organic Magnetic resonance. 1975; 7: 339-344.
- Modro TA, Renolds WF,Kovupowa ES. Journal of the Chemical Society Perkin Transaction 2. 1977; 11:479-1483.
- Happer DAR. and Steenson BE. The determination of inductive effects by ^{13}C nuclear magnetic resonance spectrometry. Journal of the Chemical Society Perkin Transaction 2. 1983; 6: 843-848.
- Fadhil GF, Essa AH. Substituent effects in the ^{13}C NMR chemical shifts of *para*-(*para*-substituted benzylidene amino) benzonitrile and *para*-(*ortho*-substituted benzylidene amino)benzonitrile. Journal of the Iranian Chemical Society. 2009;6(4):808-811.
- Arulkumaran R, ManikandanV, Thirunarayanan G. Synthesis and Hammett spectral correlation studies of some substituted cyanopyridine compounds. World Scientific News. 2017; 80:239-255.
- Arulkumaran R, Manikandan V, Christhuraj P, Thirunarayanan G. Synthesis and spectral correlation studies of some substituted (E)-1-benzylidene-2-(diphenylmethylene) hydrazines. World Scientific News. 2017; 62:93-110.
- Thirunarayanan G. Sekar KG. and Lakshmi narayanan R. infrared and ^{13}C NMR spectral studies of some Aryl hydrazides; assessment substituent effects. International Letters of Chemistry, Physics and Astronomy. 2014; 32: 88-94.
- Rajarajan M, Senbagam R, Vijayakumar V, Manikandan V, Balaji S, Vanangamudi G, Thirukumaran G. Synthesis, spectral studies and antimicrobial a activities of some substituted (E)-1-benzylidene-2-(4-bromophenyl)-hydrazines. World Scientific News. 2015; 9: 155-171.
- Marinkovic AD, Brkic D, JelenaMS, Mijin DZ. Milcic M, Petrovic SD. Influence of substituents on IR, ^1H - and ^{13}C - NMR spectral data of N-(substituted phenyl)-2-cyanoacetamide-correlation analysis. Chemical Industry and Chemical Engineering Quarterly. 2013; 19(1): 67-78.
- Thirunarayanan G, Gopalakrishnan M. and Vanangamudi G. IR and NMRspectral studies of 4-bromo-1-naphthyl chalcones- assessment of substituent effects. Spectra Chimica Acta. Part A. 2007; 67(3-4):1106-1112.
- Thirunarayanan G. Synthesis, IR and NMR spectral correlations in some symmetrical diimines. Bulletin of Chemical Society of Ethiopia. 2014; 28(1): 73-79.
- ChartonM. Nature of the ortho effect. Reaction rates of carboxylic acids with diazodiphenylmethane. Journal of Organic Chemistry. 1975; 40(4): 407-411.