Spectral QSAR and QPR study of some (E)-4-(((2-hydroxy-6-(substituted phenyl)-1,6-dihydropyrimidin-4-yl)methyl)diazeneyl)benzoic acid derivatives

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ABSTRACT

A series of titled compounds were synthesized and recorded the infrared and NMR spectra. The assigned spectral group frequencies were correlated with Hammett substituent constants, F and R parameter. From the statistical analysis results, the effect of substituents on the spectral group frequencies has been studied.

Keywords: Dihydropyrimidines; Diazeneyl benzoic acids; IR spectra; NMR spectra; Hammett correlation; QSAR and QPR study

1. INTRODUCTION

Pyrimidine, hydroxy pyrimidine six membered heterocyclic derivatives are important bio-potent molecule as well as in artificial drug synthesis [1,2]. They possess valuable biological activities such as cardiovascular [3], anti-HIV [4], anti-tumour [5], anti-inflammatory [6], anti-tubercular [7], diuretic [8], antimicrobial [9] anti-cancer [9] and antimalarial [10]. Spectroscopic data was applied for predicting the ground state configuration and QSAR and QPR study of chalcones [11], oxazines [12], pyrazoline [13], imines [14], acyl halides, and it esters [15]. Using infrared functional group frequencies such as carbonyl absorptions, chemists studied the s-cis and s-trans conformers of chalcones [16], cis- and gauche- form of acyl esters [15]. From the proton NMR spectral chemical shift(ppm), the E and Z configuration was assigned in alkene [16], alkynes [17] and chalcones [18] derivatives. Recently, Mayavel et al have studied the effect of substituent on the (E)-N-(substituted benzylidene)-9-ethyl-9H-carbazole-3-amine derivatives [19] with IR and NMR spectral data through Hammet equation. Sathiyendiran et al., have studied the spectral correlations of some substituted styryl (E)-4-((2-oxopropyl) diazenyl) benzoic acids [20].

Kalyanasundaram and his coworkers have studied the spectral correlation analysis of Hammett substituent constants and biological activities of some (E)-1-(4-phenoxyphenyl)-3-phenylprop-2-en-1-ones [21]. Within the above view there is no report available in the literature for the study of effect of substituents through Hammett equation with spectral data
for the titled compounds. In the present study, the authors have taken effort for studying the QSAR and QPR of spectral data of the titled compounds by synthesis and recorded their infrared and NMR spectra.

2. EXPERIMENTAL

2.1. General

The infrared spectra of all compounds were recorded in SHIMADUZ Fourier Transform IR spectrophotometer using KBr disc technique. The NMR spectra of all compounds were recorded in BRUKER AV 400 type spectrometer, using CDCl$_3$ as a solvent, 400 MHz frequency was applied for recording $^1$H, 100 MHz for $^{13}$C NMR spectra, taking TMS as standard.

2.2. Synthesis of (E)-4-(((2-hydroxy-6-(substituted phenyl)-1,6-dihydropyrimidin-4-yl) methyl)diazenyl)benzoic acid derivatives

The titled pyrimidine derivatives were prepared and their purities were analyzed by the literature method [22]. The general structure of the chalcones is illustrated in Fig. 1.

![Chemical structure](image)

X= H, 3-Br, 2-Cl, 4-Cl, 2-OH, 4-OH, 4-OCH$_3$, 2-NO$_2$, 4-NO$_2$

Fig. 1. (E)-4-(((2-hydroxy-6-(substituted phenyl)-1,6-dihydropyrimidin-4-yl)methyl)diazenyl)benzoic acid derivatives.
3. RESULTS AND DISCUSSION

In the present investigations, the authors have evaluated the effect of substituents on the assigned spectral frequencies using Hammett equation with Hammett substituent constants and Swain-Lupton’s[23] constants by single and multi-linear regression analysis.

3.1. IR spectral study

In infrared spectral study, the Hammett equation is employed for evaluation of effect of substituents on the CO, N=N, CN, OH and NH stretches with Hammett substituent constants. In this correlation, the Hammett equation was utilized as,

\[ \nu = \rho \sigma + \nu_0 \]  

where \( \nu \) is the frequency for the substituted system, \( \rho \) is the reaction constants in terms of intercept, \( \sigma \) is the substituent constants and \( \nu_0 \) is the frequency for the parent member of the series.

The assigned CO, N=N, CN, OH and NH stretches (\( \nu, \text{cm}^{-1} \)) of all (\( E \)-4-(((2-hydroxy-6-(substituted phenyl)-1,6-dihydropyrimidin-4-yl)methyl)diazenyl)benzoic acid derivatives are presented in Table 1.

**Table 1.** The infrared and NMR spectroscopic data of (\( E \)-4-(((2-hydroxy-6-(substituted phenyl)-1,6-dihydropyrimidin-4-yl)methyl)diazenyl)benzoic acid derivatives.

| Sl. No. | X  | IR (\( \nu, \text{cm}^{-1} \)) | \(^1^H (\delta, \text{ppm})\) | \(^{13}C (\delta, \text{ppm})\) |
|--------|----|-------------------------------|--------------------------|--------------------------|
|        |    | CO N=N CN OH NH CH=CH-CN CH=CH-CN CO CH-CN CO CH-CN | CO N=N CN OH NH CH=CH-CN CH=CH-CN CO CH-CN CO CH-CN | CO N=N CN OH NH CH=CH-CN CH=CH-CN CO CH-CN CO CH-CN |
| 1      | H  | 1683 1483 1594 3410 3214 | 2.617 2.641 4.521 6.271 | 170.41 61.641 156.72 |
| 2      | 3-Br | 1685 1484 1596 3415 3215 | 2.623 2.644 4.671 6.073 | 170.92 61.644 156.81 |
| 3      | 2-Cl | 1696 1486 1589 3419 3218 | 2.623 2.644 4.671 6.073 | 170.67 62.71 156.97 |
| 4      | 4-Cl | 1692 1485 1591 3417 3216 | 2.623 2.644 4.671 6.073 | 170.70 170.92 61.644 156.97 |
| 5      | 2-OH | 1688 1484 1595 3417 3216 | 2.623 2.644 4.671 6.073 | 171.73 170.70 62.457 156.81 |

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The results of statistical analysis [11-16,18-21] are shown in Table 2. From the table 2, the correlation of νCO stretches of all compounds gave satisfactory correlation for Hammett σ, σ-cancel, and σI constants. The Hammett σI constants, F and R parameters were fail in correlations. This due to the inability of effect of substituents on the carbonyl group and associated with the resonance-conjugative structure as shown in Fig. 2. All correlations gave positive ρ values. This may mean that the normal substituent effects operated in all system.

Fig. 2. The resonance-conjugative structure.

The N=N stretches (ν, cm⁻¹) of pyrimidine derivatives were produced satisfactory correlation coefficient with Hammett substituent constants and F and R parameters along with positive ρ values.
The C=N stretches (ν, cm⁻¹) of pyrimidine derivatives were produced poor correlation coefficient with Hammett substituent constants and F and R parameters along with positive ρ values. The reasons for the poor correlation of these stretches are stated earlier and associated with resonance-conjugated structure as shown in Fig. 2.

The OH stretches (ν, cm⁻¹) of pyrimidine derivatives were produced poor correlation coefficient with Hammett σ, σ⁺, σ₁ constants and F parameters. The resonance components of the substitutes were fail in correlation. All correlation gave positive ρ values. The reasons for the failure correlation of this stretches were stated earlier and associated with resonance-conjugated structure as shown in Fig. 2.

The NH stretches (ν, cm⁻¹) of pyrimidine derivatives were produced satisfactory correlation coefficient with Hammett substituent constants and F and R parameters along with positive ρ values.

Among these correlations some of the correlation gave poor coefficients. They are worthwhile when they are subjected to multi-regression analysis. In multi parameter correlation with Swain-Lupton’s [18] parameters, these stretches produced satisfactory correlations. The generated multi-regression analysis equations are shown in (2-11).

**Table 2.** Results of statistical analysis of IR, ¹H NMR and ¹³C-NMR spectral values of (E)-4-(((2-hydroxy-6-(substituted phenyl)-1,6-dihydropyrimidin-4-yl)methyl) diazenyl)benzoic acid derivatives with Hammett σ, σ⁺, σ₁, σᵣ constants, F and R parameters.

| Frequency | Constant | r  | ν (cm⁻¹) | I   | ρ  | s  | n  | Correlated derivatives                  |
|-----------|----------|----|----------|-----|----|----|----|-----------------------------------------|
| ν CO      | σ        | 0.905 | 1688.55  | 9.440 | 5.77 |    | 9 | H, 3-Br, 2-Cl, 4-Cl, 2-OH, 4-OH, 4-OCH₃, 2-NO₂, 4-NO₂ |
|           | σ⁺       | 0.905 | 1689.87  | 6.052 | 5.95 |    |   |                                         |
|           | σ₁       | 0.907 | 1681.30  | 22.777 | 5.01 |    |   |                                         |
|           | σᵣ       | 0.844 | 1692.11  | 10.260 | 6.55 |    |   |                                         |
|           | F        | 0.917 | 1680.45  | 24.553 | 4.98 |    |   |                                         |
|           | R        | 0.832 | 1692.23  | 8.185  | 6.58 |    |   |                                         |
| ν N=N     | σ        | 0.986 | 1483.46  | 6.655 | 1.73 |    | 9 | H, 3-Br, 2-Cl, 4-Cl, 2-OH, 4-OH, 4-OCH₃, 2-NO₂, 4-NO₂ |
|           | σ⁺       | 0.986 | 1484.37  | 4.562 | 1.72 |    |   |                                         |
|           | σ₁       | 0.917 | 1480.13  | 11.444 | 2.31 |    |   |                                         |
|           | σᵣ       | 0.908 | 1486.18  | 8.343  | 2.51 |    |   |                                         |
|           | F        | 0.972 | 1479.87  | 11.889 | 2.01 |    |   |                                         |
|           | R        | 0.907 | 1486.42  | 7.181  | 2.39 |    |   |                                         |
| ν C=N     | σ        | 0.849 | 1592.25  | 6.566 | 5.24 |    | 9 | H, 3-Br, 2-Cl, 4-Cl, 2-OH, 4-OH, 4-OCH₃, 2-NO₂, 4-NO₂ |
|           | σ⁺       | 0.843 | 1593.17  | 3.954 | 5.42 |    |   |                                         |
|           | σ₁       | 0.830 | 1590.16  | 8.197 | 5.73 |    |   |                                         |
|           | σᵣ       | 0.843 | 1595.10  | 9.057  | 5.43 |    |   |                                         |
|           | F        | 0.837 | 1589.14  | 10.652 | 5.59 |    |   |                                         |
|       | R           | νOH (cm⁻¹) | νNH (cm⁻¹) | δNH (ppm) | δCH₂ (ppm) | δCH-N (ppm) | δCH=Σ (ppm) |
|-------|-------------|------------|------------|-----------|------------|-------------|--------------|
|       | 0.836       | 1594.96    | 6.270      | 5.61      | 9          | 9           | 9            |
| σ     | 0.906       | 3413.84    | 9.742      | 5.32      | H, 3-Br, 2-Cl, 4-Cl, 2-OH, 4-OH, 4-OCH₃, 2-NO₂, 4-NO₂ |
| σ⁺    | 0.915       | 3415.17    | 6.789      | 5.24      | H, 3-Br, 2-Cl, 4-Cl, 2-OH, 4-OH, 4-OCH₃, 2-NO₂, 4-NO₂ |
| σ₀    | 0.916       | 3407.70    | 20.026     | 5.22      | H, 3-Br, 2-Cl, 4-Cl, 2-OH, 4-OH, 4-OCH₃, 2-NO₂, 4-NO₂ |
| σᵣ    | 0.831       | 3417.28    | 9.416      | 6.36      | H, 3-Br, 2-Cl, 4-Cl, 2-OH, 4-OH, 4-OCH₃, 2-NO₂, 4-NO₂ |
| F     | 0.966       | 3406.87    | 21.777     | 5.19      | H, 3-Br, 2-Cl, 4-Cl, 2-OH, 4-OH, 4-OCH₃, 2-NO₂, 4-NO₂ |
| R     | 0.884       | 3417.56    | 8.150      | 6.29      | H, 3-Br, 2-Cl, 4-Cl, 2-OH, 4-OH, 4-OCH₃, 2-NO₂, 4-NO₂ |
| σ     | 0.908       | 3214.99    | 13.567     | 3.18      | H, 3-Br, 2-Cl, 4-Cl, 2-OH, 4-OH, 4-OCH₃, 2-NO₂, 4-NO₂ |
| σ⁺    | 0.900       | 3216.87    | 8.871      | 3.72      | H, 3-Br, 2-Cl, 4-Cl, 2-OH, 4-OH, 4-OCH₃, 2-NO₂, 4-NO₂ |
| σ₀    | 0.907       | 3208.32    | 23.011     | 4.55      | H, 3-Br, 2-Cl, 4-Cl, 2-OH, 4-OH, 4-OCH₃, 2-NO₂, 4-NO₂ |
| σᵣ    | 0.907       | 3220.56    | 17.098     | 4.81      | H, 3-Br, 2-Cl, 4-Cl, 2-OH, 4-OH, 4-OCH₃, 2-NO₂, 4-NO₂ |
| F     | 0.907       | 3207.79    | 23.961     | 4.71      | H, 3-Br, 2-Cl, 4-Cl, 2-OH, 4-OH, 4-OCH₃, 2-NO₂, 4-NO₂ |
| R     | 0.907       | 3221.03    | 14.677     | 4.61      | H, 3-Br, 2-Cl, 4-Cl, 2-OH, 4-OH, 4-OCH₃, 2-NO₂, 4-NO₂ |
| σ     | 0.833       | 2.489      | 0.831      | 0.10      | H, 3-Br, 2-Cl, 4-Cl, 2-OH, 4-OH, 4-OCH₃, 2-NO₂, 4-NO₂ |
| σ⁺    | 0.905       | 2.500      | 0.085      | 0.09      | H, 3-Br, 2-Cl, 4-Cl, 2-OH, 4-OH, 4-OCH₃, 2-NO₂, 4-NO₂ |
| σ₀    | 0.711       | 2.500      | 0.115      | 0.11      | H, 3-Br, 2-Cl, 4-Cl, 2-OH, 4-OH, 4-OCH₃, 2-NO₂, 4-NO₂ |
| σᵣ    | 0.831       | 2.532      | 0.148      | 0.10      | H, 3-Br, 2-Cl, 4-Cl, 2-OH, 4-OH, 4-OCH₃, 2-NO₂, 4-NO₂ |
| F     | 0.806       | 2.516      | 0.033      | 0.11      | H, 3-Br, 2-Cl, 4-Cl, 2-OH, 4-OH, 4-OCH₃, 2-NO₂, 4-NO₂ |
| R     | 0.840       | 2.537      | 0.129      | 0.10      | H, 3-Br, 2-Cl, 4-Cl, 2-OH, 4-OH, 4-OCH₃, 2-NO₂, 4-NO₂ |
| σ     | 0.838       | 2.513      | 0.070      | 0.07      | H, 3-Br, 2-Cl, 4-Cl, 2-OH, 4-OH, 4-OCH₃, 2-NO₂, 4-NO₂ |
| σ⁺    | 0.844       | 2.522      | 0.056      | 0.07      | H, 3-Br, 2-Cl, 4-Cl, 2-OH, 4-OH, 4-OCH₃, 2-NO₂, 4-NO₂ |
| σ₀    | 0.809       | 2.538      | 0.034      | 0.08      | H, 3-Br, 2-Cl, 4-Cl, 2-OH, 4-OH, 4-OCH₃, 2-NO₂, 4-NO₂ |
| σᵣ    | 0.905       | 2.554      | 0.156      | 0.06      | H, 3-Br, 2-Cl, 4-Cl, 2-OH, 4-OH, 4-OCH₃, 2-NO₂, 4-NO₂ |
| F     | 0.813       | 2.547      | 0.056      | 0.08      | H, 3-Br, 2-Cl, 4-Cl, 2-OH, 4-OH, 4-OCH₃, 2-NO₂, 4-NO₂ |
| R     | 0.905       | 2.557      | 0.123      | 0.07      | H, 3-Br, 2-Cl, 4-Cl, 2-OH, 4-OH, 4-OCH₃, 2-NO₂, 4-NO₂ |
| σ     | 0.906       | 4.551      | 0.093      | 0.05      | H, 3-Br, 2-Cl, 4-Cl, 2-OH, 4-OH, 4-OCH₃, 2-NO₂, 4-NO₂ |
| σ⁺    | 0.904       | 4.562      | 0.051      | 0.06      | H, 3-Br, 2-Cl, 4-Cl, 2-OH, 4-OH, 4-OCH₃, 2-NO₂, 4-NO₂ |
| σ₀    | 0.905       | 4.504      | 0.162      | 0.05      | H, 3-Br, 2-Cl, 4-Cl, 2-OH, 4-OH, 4-OCH₃, 2-NO₂, 4-NO₂ |
| σᵣ    | 0.839       | 4.858      | 0.095      | 0.06      | H, 3-Br, 2-Cl, 4-Cl, 2-OH, 4-OH, 4-OCH₃, 2-NO₂, 4-NO₂ |
| F     | 0.905       | 4.459      | 0.192      | 0.05      | H, 3-Br, 2-Cl, 4-Cl, 2-OH, 4-OH, 4-OCH₃, 2-NO₂, 4-NO₂ |
| R     | 0.831       | 4.583      | 0.063      | 0.06      | H, 3-Br, 2-Cl, 4-Cl, 2-OH, 4-OH, 4-OCH₃, 2-NO₂, 4-NO₂ |
| σ     | 0.828       | 6.143      | 0.151      | 0.22      | H, 3-Br, 2-Cl, 4-Cl, 2-OH, 4-OH, 4-OCH₃, 2-NO₂, 4-NO₂ |
| σ⁺    | 0.846       | 6.166      | 0.167      | 0.21      | H, 3-Br, 2-Cl, 4-Cl, 2-OH, 4-OH, 4-OCH₃, 2-NO₂, 4-NO₂ |
$\nu \text{C}=\text{O} (\text{cm}^{-1}) = 1682.09(\pm 5.392) + 21.644(\pm 10.417)\sigma_I + 1.803(\pm 0.812)\sigma_R$ 
\hspace{10cm} ...(2) 
\hspace{10cm} (r = 0.971, n = 9, P > 95 \%) 

$v \text{C}=\text{O} (\text{cm}^{-1}) = 1682.04(\pm 5.134) + 22.607(\pm 10.183)F + 3.180(\pm 0.612)R$ 
\hspace{10cm} ...(3) 
\hspace{10cm} (r = 0.973, n = 9, P > 95 \%) 

$v \text{N}=\text{N} (\text{cm}^{-1}) = 1482.38(\pm 2.063) + 8.221(\pm 4.092)\sigma_I + 5.313(\pm 3.178)\sigma_R$ 
\hspace{10cm} ...(4) 
\hspace{10cm} (r = 0.983, n = 9, P > 95 \%) 

$v \text{N}=\text{N} (\text{cm}^{-1}) = 1482.54(\pm 1.775) + 8.667(\pm 5.521)F + 5.216(\pm 2.118)R$ 
\hspace{10cm} ...(5) 
\hspace{10cm} (r = 0.987, n = 9, P > 95 \%) 

\[ \begin{array}{|c|c|c|c|c|} 
\hline
\text{Variable} & \sigma_I & 0.816 & 6.104 & 0.177 & 0.23 \\
\hline
\sigma_R & 0.830 & 6.221 & 0.258 & 0.22 \\
F & 0.801 & 6.164 & 0.021 & 0.23 \\
R & 0.841 & 6.247 & 0.287 & 0.21 \\
\hline
\end{array} \]

\[ \begin{array}{|c|c|c|c|c|} 
\hline
\text{Variable} & \sigma & 0.907 & 170.81 & 1.698 & 0.66 \\
\hline
\sigma^+ & 0.906 & 171.05 & 1.024 & 0.75 \\
\sigma_I & 0.906 & 169.93 & 2.994 & 0.75 \\
\sigma_R & 0.905 & 171.44 & 1.803 & 0.87 \\
F & 0.907 & 169.70 & 3.531 & 0.68 \\
R & 0.905 & 171.48 & 1.058 & 0.86 \\
\hline
\end{array} \]

\[ \begin{array}{|c|c|c|c|c|} 
\hline
\text{Variable} & \delta \text{C}O & \text{ppm} & \sigma & 0.834 & 62.513 & 0.072 & 0.07 \\
\hline
\sigma^+ & 0.844 & 62.522 & 0.056 & 0.07 \\
\sigma_I & 0.709 & 62.538 & 0.088 & 0.08 \\
\sigma_R & 0.905 & 62.558 & 0.157 & 0.06 \\
F & 0.813 & 62.413 & 0.087 & 0.07 \\
R & 0.824 & 62.173 & 0.411 & 0.07 \\
\hline
\end{array} \]

\[ \begin{array}{|c|c|c|c|c|} 
\hline
\text{Variable} & \delta \text{CH}_2 & \text{ppm} & \sigma & 0.903 & 156.68 & 0.506 & 0.10 \\
\hline
\sigma^+ & 0.909 & 156.74 & 0.370 & 0.05 \\
\sigma_I & 0.906 & 156.46 & 0.778 & 0.18 \\
\sigma_R & 0.907 & 156.88 & 0.645 & 0.17 \\
F & 0.906 & 156.47 & 0.736 & 0.20 \\
R & 0.908 & 156.91 & 0.587 & 0.14 \\
\hline
\end{array} \]

\[ \begin{array}{|c|c|c|c|c|} 
\hline
\text{Variable} & \delta \text{CN} & \text{ppm} & \sigma & 0.903 & 156.68 & 0.506 & 0.10 \\
\hline
\sigma^+ & 0.909 & 156.74 & 0.370 & 0.05 \\
\sigma_I & 0.906 & 156.46 & 0.778 & 0.18 \\
\sigma_R & 0.907 & 156.88 & 0.645 & 0.17 \\
F & 0.906 & 156.47 & 0.736 & 0.20 \\
R & 0.908 & 156.91 & 0.587 & 0.14 \\
\hline
\end{array} \]

\[ \begin{array}{|c|c|c|c|c|} 
\hline
\text{Variable} & \delta \text{CN} & \text{ppm} & \sigma & 0.903 & 156.68 & 0.506 & 0.10 \\
\hline
\sigma^+ & 0.909 & 156.74 & 0.370 & 0.05 \\
\sigma_I & 0.906 & 156.46 & 0.778 & 0.18 \\
\sigma_R & 0.907 & 156.88 & 0.645 & 0.17 \\
F & 0.906 & 156.47 & 0.736 & 0.20 \\
R & 0.908 & 156.91 & 0.587 & 0.14 \\
\hline
\end{array} \]

$r = \text{correlation coefficient}; I = \text{intercept}; \rho = \text{slope}; s = \text{standard deviation}; n = \text{number of correlated derivatives}$
\[ v_{\text{C=N}}(\text{cm}^{-1}) = 1593.56(\pm 5.760) + 3.324(\pm 11.248)\sigma_I + 7.715(\pm 0.818)\sigma_R \] 
\hspace{2cm} ...(6)

\[ v_{\text{C=N}}(\text{cm}^{-1}) = 1591.40(\pm 5.683) + 7.882(\pm 1.125)\sigma_I + 4.527(\pm 1.654)\sigma_R \] 
\hspace{2cm} ...(7)

\[ v_{\text{OH}}(\text{cm}^{-1}) = 3408.82(\pm 5.550) + 18.700(\pm 10.838)\sigma_I + 2.109(\pm 0.854)\sigma_R \] 
\hspace{2cm} ...(8)

\[ v_{\text{OH}}(\text{cm}^{-1}) = 3408.80(\pm 5.281) + 19.420(\pm 10.474)\sigma_I + 3.580(\pm 1.304)\sigma_R \] 
\hspace{2cm} ...(9)

\[ v_{\text{NH}}(\text{cm}^{-1}) = 3213.58(\pm 3.931) + 16.292(\pm 7.673)\sigma_I + 10.744(\pm 6.055)\sigma_R \] 
\hspace{2cm} ...(10)

\[ v_{\text{NH}}(\text{cm}^{-1}) = 3213.22(\pm 3.295) + 17.326(\pm 6.536)\sigma_I + 10.841(\pm 3.931)\sigma_R \] 
\hspace{2cm} ...(11)

### 3.2. \(^1\text{H}\) NMR Spectral study

In nuclear magnetic resonance spectra, the \(^1\text{H}\) or the \(^{13}\text{C}\) chemical shifts (\(\delta\), ppm) depend on the electronic environment of the nuclei concerned. These chemical shifts of hydrazide have been correlated with reactivity parameters. Thus the Hammett equation was used in the form as shown in (12).

\[
\log \delta = \log \delta_0 + \rho \sigma \]
\hspace{2cm} ... (12)

where \(\delta_0\) is the chemical shift of the corresponding parent compound.

The \(\text{NH}_2\), \(\text{CH}_2\), \(\text{CH-NH}\) and \(\text{CH=C}\) proton chemical shifts (\(\delta\), ppm) of pyrimidines have been assigned and correlated with Hammett substituent constants using single and multi-linear regression analysis [11-16,18-21]. The results of statistical analysis are shown in Table 2. From Table 2, the correlation of NH proton chemical shifts (\(\delta\), ppm) of pyridines with Hammett \(\sigma^+\) constant only satisfactory. The Hammett \(\sigma\), \(\sigma_I\), \(\sigma_R\) constant, F and R parameters were fail in correlations.

A satisfactory correlation were obtained for \(\text{CH}_2\) proton chemical shifts (\(\delta\), ppm) of pyridines with Hammett \(\sigma_R\) constant and R parameter. The remaining Hammett sigma constants and F parameters were fail in correlation.

The correlation of \(\text{CH-N}\) proton chemical shifts (\(\delta\), ppm) of pyridines gave satisfactory coefficients with Hammett \(\sigma\), \(\sigma^+\), \(\sigma_I\) constant and F parameter. The resonance components of the substituents were fail in correlation.

A poor correlation were observed for the correlation of \(\text{CH=C}\) proton chemical shifts (\(\delta\), ppm) of pyridines with Hammett substituent constants F and R parameters. All correlations gave positive \(\rho\) values. This is implies that the normal substituent effect operates in all system. The reason for failure in correlations of assigned proton chemical shifts were already stated earlier and is associated with the resonance-conjugative structure as shown in Fig. 2.

Some of the chemical shifts of assigned \(\text{NH}_2\), \(\text{CH}_2\), \(\text{CH-NH}\) and \(\text{CH=C}\) proton chemical shifts (\(\delta\), ppm) of pyrimidines have shown poor correlation in single parameter analysis. While seeking these chemical shifts are worthwhile, they are indulged in multi-parameter correlation. They produced satisfactory correlation either inductive and resonance
components or field and resonance components combined. The generated multi-regression equations are shown in (13-20).

\[
\delta_{\text{NH}}(\text{ppm}) = 2.592(\pm 0.107) + 0.103(\pm 0.021)\sigma_I + 0.198(\pm 0.106)\sigma_R \\
(\text{r} = 0.943, \text{n} = 9, \text{P} > 90 \%)
\]

\[
\delta_{\text{NH}}(\text{ppm}) = 2.959(\pm 0.105) + 0.103(\pm 0.020)F + 0.158(\pm 0.102)R \\
(\text{r} = 0.946, \text{n} = 9, \text{P} > 90 \%)
\]

\[
\delta_{\text{CH}_2}(\text{ppm}) = 2.634(\pm 0.069) + 0.172(\pm 0.134)\sigma_I + 0.219(\pm 0.101)\sigma_R \\
(\text{r} = 0.943, \text{n} = 9, \text{P} > 90 \%)
\]

\[
\delta_{\text{CH}_2}(\text{ppm}) = 2.625(\pm 0.070) + 0.152(\pm 0.109)F + 0.156(\pm 0.084)R \\
(\text{r} = 0.961, \text{n} = 9, \text{P} > 95 \%)
\]

\[
\delta_{\text{CH}-\text{N}}(\text{ppm}) = 4.522(\pm 0.062) + 0.135(\pm 0.012)\sigma_I + 0.042(\pm 0.001)\sigma_R \\
(\text{r} = 0.954, \text{n} = 9, \text{P} > 95 \%)
\]

\[
\delta_{\text{CH}-\text{N}}(\text{ppm}) = 4.503(\pm 0.059) + 0.177(\pm 0.117)F + 0.024(\pm 0.007)R \\
(\text{r} = 0.959, \text{n} = 9, \text{P} > 95 \%)
\]

\[
\delta_{\text{CH}=\text{C}}(\text{ppm}) = 6.214(\pm 0.242) + 0.020(\pm 0.004)\sigma_I + 0.250(\pm 0.037)\sigma_R \\
(\text{r} = 0.930, \text{n} = 9, \text{P} > 90 \%)
\]

\[
\delta_{\text{CH}=\text{C}}(\text{ppm}) = 6.328(\pm 0.225) + 0.179(\pm 0.044)F + 0.326(\pm 0.026)R \\
(\text{r} = 0.944, \text{n} = 9, \text{P} > 95 \%)
\]

3. 3. $^{13}$C NMR Spectral study

The CO, CH$_2$, and CN carbon chemical shifts ($\delta$, ppm) of pyrimidine derivatives have been assigned and correlated with Hammett substituent constants using single and multi-linear regression analysis [11-16,18-21].

The results of statistical analysis are shown in Table 2. From Table 2, the correlation of CO carbon chemical shifts ($\delta$, ppm) of hydrazides with Hammett substituent constants and F and R parameters were satisfactory. The correlation of CH$_2$ carbon chemical shifts ($\delta$, ppm) were fail in correlation with Hammett substituent constants and F and R parameters. The CN carbon chemical shifts ($\delta$, ppm) pyrimidines were shows satisfactory correlation with Hammett substituent constants and f and R parameters. The failure in correlation is due to the reasons stated earlier and was associated with the resonance-conjugative structure as shown in Figure 2.

The chemical shifts ($\delta$, ppm) of CH$_2$ pyrimidines have shown poor correlation in single parameter analysis. While seeking these chemical shifts ($\delta$, ppm) CO, CH$_2$, and CN are worthwhile, they are indulged in multi-parameter correlation. They produced satisfactory correlation either inductive and resonance components or field and resonance components combined. The generated multi-regression equations are shown in (21-26)

\[
\delta_{\text{CO}}(\text{ppm}) = 170.303(\pm 0.772) + 2.468(\pm 1.508)\sigma_I + 0.839(\pm 0.011)\sigma_R \\
(\text{r} = 0.969, \text{n} = 9, \text{P} > 95 \%)
\]
\[ \delta_{CO}(\text{ppm}) = 170.125(\pm 0.663) + 3.017(\pm 0.131)F + 0.840(\pm 0.079)R \quad ...(22) \]
\[ \delta_{CH_2}(\text{ppm}) = 62.625(\pm 0.070) + 0.152(\pm 0.013)\sigma_I + 0.156(\pm 0.081)\sigma_R \quad ...(23) \]
\[ \delta_{CH_2}(\text{ppm}) = 62.613(\pm 0.172) + 0.817(\pm 0.032)F + 0.217(\pm 0.013)R \quad ...(24) \]
\[ \delta_{CN}(\text{ppm}) = 156.66(\pm 0.153) + 0.491(\pm 0.219)\sigma_I + 0.453(\pm 0.236)\sigma_R \quad ...(25) \]
\[ \delta_{CN}(\text{ppm}) = 156.719(\pm 0.127) + 0.436(\pm 0.021)F + 0.491(\pm 0.015)R \quad ...(26) \]

4. CONCLUSIONS

A series of dihydropyrimidine methyl diazenyl benzoic acid derivatives have been prepared and recorded their IR and NMR spectra. The assigned spectral group frequencies were correlated with Hammett substituent constants, F and R parameters. From the results of statistical analysis, almost all frequencies were shown satisfactorily correlations in both single and multi-parameter correlation analysis. There is a normal substituent effect operates in all systems evident with positive \( p \) values.

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