Hammett spectral correlations in benzofuranyl flavonols

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ABSTRACT

A series containing eleven benzofuranyl flavonols have been prepared by cyclization of 3-hydroxybenzofuranyl chalcones with 30 % hydrogen peroxide in the presence of sodium bicarbonate. The synthesized flavonols were characterized by their physical constants, analytical and spectroscopic data. The infrared spectral νOH, CO stretches(cm^{-1}), NMR chemical shifts of OH, CO(δ, ppm) of these flavonols were assigned and correlated with Hammett substituent constants, F and R parameters using single and multi linear regression analysis. From the results of statistical analyses, the effects of substituents on the above group frequencies were discussed.

*Keywords***:** Benzofuranyl flavonols; Hammett equation; IR spectra; NMR spectra; Regression analysis

1. INTRODUCTION

Hammett spectral correlation is useful for predicting the ground state equilibration of organic molecules such as unsaturated carbonyl compounds [1], alkenes [2], polyenes [3], acyl halides and its esters [4]. Infrared spectra are a good tool for analyzing the structure of organic molecules, qualitative and quantitative measurements, *s-cis* and *s-trans* equilibration of unsaturated ketones, *anti-* and *gauche-* form of acyl halides and esters [4,5]. The NMR spectroscopy was utilized for predicting spatial arrangements of the *E* or *Z* isomers and conformers in unsaturated ketones, pyrazolines and it derivatives [6,7]. The effect of substituents on the above molecular conformers and isomers also studied through Hammett substituent constants, F and R parameters [8]. Thirunarayanan have studied the effect of substituents on spectral frequencies in thiadiazole-2-amines [9].

Joseph et al have studied the effect of substituents on dimethyl phenyl chalcones by Hammett equation with spectral data [10]. Sekar and Thirunarayanan have studied the spectral correlation in pyrazoline derivatives [11]. The substituent effects on oxazine-2-amines were studied using spectral data using single and multi-regression analysis [12]. Kamalakkannan et al have studied the substituent effects on 2-indolyl chalcones by electrochemical redox potential with Hammett equation [13].

Within the above view there is no report available for the study of effect of substituents on the 3-hydroxy-2-(substituted phenyl)-4*H*-pyrano[3,2-b][1]benzofuron-4-ones through spectral data using regression analysis.

Therefore the authors have taken effort to prepare some 3-hydroxy-2-(substituted phenyl)-4*H*-pyrano[3,2-b][1]benzofuron-4-one derivatives and recorded the infrared and NMR spectra for studying the effect of substituents on the spectral frequencies.

2. EXPERIMENTAL

2. 1. General

All chemicals and solvents used in this present study were procured from Sigma-Aldrich and Merck companies. The infrared spectra of all oxazine imines have been recorded in SHIMADUZ Fourier Transform IR spectrophotometer using KBr disc. 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 ^1H, 100 MHz for ^{13}C NMR spectra, taking TMS as standard.

2. 2. General procedure for synthesis of 3-hydroxy-2-(substituted phenyl)-4*H*-pyrano [3, 2-b][1]benzofuron-4-one derivatives

About 2 mmol of 3-hydroxybenzofuranyl chalcones, 5 mL of 5 % sodium bicarbonate, 10 mL of ethanol were vigorously stirred in the three necked flask under cooling condition (Scheme 1). To this reaction mixture, added drop-wise 5 mL 30 % hydrogen peroxide through dropping funnel for half an hour duration and continued the stirring to one hour and it was kept overnight.

The mixture was diluted with 20 mL of water and acidified with concentrated H_2SO_4 (5-7 mL). The obtained solid product was filtered at the pump washed with water, dried and recrystallized with ethanol. The analytical, physical constants and spectroscopic data of synthesized substituted flavonols were presented in Table 1.

X=H, 3-Br, 3-Cl, 4-Cl, 4-NMe₂, 2-OH, 4-OH, 4-OMe, 3-NO₂, 4-NO₂
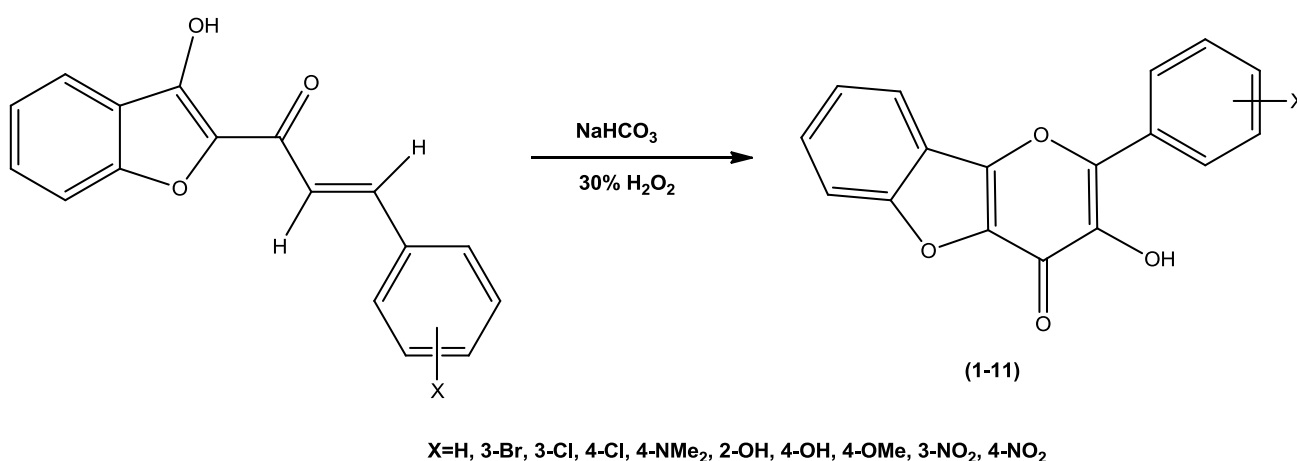
Scheme 1. Synthesis of 3-hydroxy-2-(substituted phenyl)-4*H*-pyrano[3,2-b][1]benzofuron-4-ones.

3. RESULTS AND DISCUSSION

In the present study, the author have investigated the effect of substituent on spectral frequencies of 3-hydroxy-2-(substituted phenyl)-4H-pyrano[3,2-b][1]benzofuron-4-ones using Hammett substituent constants, F and R parameters by linear regression analysis [15-19].

Table 1. Analytical, physical constants and spectroscopic data of 3-hydroxy-2-(substituted phenyl)-4H-pyrano[3,2-b][1]benzofuron-4-ones.

Entry	X	M.F.	M.W.	m.p. (°C)	Mass (m/z)	IR (ν, cm^{-1})		NMR (δ, ppm)	
						OH	CO	OH	CO
1	H	C$_{18}$H$_{12}$O$_4$	278	112-113	278[M$^+$]	3410	1689	7.143	171.26
2	3-Br	C$_{18}$H$_{11}$BrO$_4$	341	138-139	341[M$^+$], 343[M^{2+}]	3414	1689	7.032	170.26
3	3-Cl	C$_{18}$H$_{11}$ClO$_4$	297	127-128	297[M$^+$], 299[M^{2+}]	3413	1690	7.101	170.32
4	4-Cl	C$_{18}$H$_{11}$ClO$_4$	297	144-145 (142-144) [14]	297[M$^+$], 299[M^{2+}]	3413	1690	7.132	170.03
5	4-NMe$_2$	C$_{20}$H$_{17}$NO$_4$	305	125-127 (123-129) [14]	305[M$^+$]	3407	1688	7.093	171.68
6	2-OH	C$_{18}$H$_{12}$O$_5$	278	150-152 (153-156) [14]	278[M$^+$]	3409	1686	7.349	171.61
7	4-OH	C$_{18}$H$_{12}$O$_5$	278	123-125 (122-124) [14]	278[M$^+$]	3410	1691	7.214	171.24
8	4-OMe	C$_{19}$H$_{14}$O$_5$	292	145-146 (147-150) [14]	292[M$^+$]	3403	1682	7.008	170.16
9	4-Me	C$_{19}$H$_{14}$O$_4$	276	123-124 (119-122) [14]	276[M$^+$]	3406	1684	7.114	170.96
10	3-NO$_2$	C$_{18}$H$_{11}$NO$_6$	323	126-127	323[M$^+$]	3415	1691	7.395	171.96
11	4-NO$_2$	C$_{18}$H$_{11}$NO$_6$	323	144-146 (143-145) [14]	323[M$^+$]	3416	1693	7.413	173.76

Table 2. Results of statistical analysis of infrared $\nu(cm^{-1})$ OH, CO stretches, NMR chemical shifts of OH and CO (δ, ppm) of 3-hydroxy-2-(substituted phenyl)-4*H*-pyrano[3,2-b][1]benzofuron-4-ones with Hammett constants σ, σ^+, σ_I, σ_R and F and R parameters.

Frequency	Constants	r	I	ρ	s	n	Correlated derivatives
νOH	σ	0.998	3410.02	7.372	2.28	11	H, 3-Br, 3-Cl, 4-Cl, 4-NMe$_2$, 2-OH, 4-OH, 4-OMe, 4-Me, 3-NO$_2$, 4-NO$_2$
	σ^+	0.997	3411.18	4.223	2.63	11	H, 3-Br, 3-Cl, 4-Cl, 4-NMe$_2$, 2-OH, 4-OH, 4-OMe, 4-Me, 3-NO$_2$, 4-NO$_2$
	σ_I	0.977	3406.39	13.103	2.69	11	H, 3-Br, 3-Cl, 4-Cl, 4-NMe$_2$, 2-OH, 4-OH, 4-OMe, 4-Me, 3-NO$_2$, 4-NO$_2$
	σ_R	0.976	3412.65	9.870	3.39	11	H, 3-Br, 3-Cl, 4-Cl, 4-NMe$_2$, 2-OH, 4-OH, 4-OMe, 4-Me, 3-NO$_2$, 4-NO$_2$
	F	0.967	3405.92	11.746	2.96	11	H, 3-Br, 3-Cl, 4-Cl, 4-NMe$_2$, 2-OH, 4-OH, 4-OMe, 4-Me, 3-NO$_2$, 4-NO$_2$
	R	0.906	3412.77	7.081	3.31	11	H, 3-Br, 3-Cl, 4-Cl, 4-NMe$_2$, 2-OH, 4-OH, 4-OMe, 4-Me, 3-NO$_2$, 4-NO$_2$
νCO	σ	0.905	1688.16	4.123	2.77	9	H, 3-Br, 3-Cl, 4-Cl, 2-OH, 4-OMe, 4-Me, 3-NO$_2$, 4-NO$_2$
	σ^+	0.904	1688.77	2.101	2.99	9	H, 3-Br, 3-Cl, 4-Cl, 2-OH, 4-OMe, 4-Me, 3-NO$_2$, 4-NO$_2$
	σ_I	0.906	1685.88	8.119	2.74	10	H, 3-Br, 3-Cl, 4-Cl, 4-NMe$_2$, 2-OH, 4-OMe, 4-Me, 3-NO$_2$, 4-NO$_2$
	σ_R	0.904	1689.76	6.118	2.99	9	H, 3-Br, 3-Cl, 4-Cl, 4-NMe$_2$, 2-OH, 4-OH, 4-Me, 3-NO$_2$, 4-NO$_2$
	F	0.905	1685.51	8.741	2.78	10	H, 3-Br, 3-Cl, 4-Cl, 4-NMe$_2$, 2-OH, 4-OH, 4-Me, 3-NO$_2$, 4-NO$_2$
	R	0.874	1689.62	3.704	3.12	11	H, 3-Br, 3-Cl, 4-Cl, 4-NMe$_2$, 2-OH, 4-OH, 4-OMe, 4-Me, 3-NO$_2$, 4-NO$_2$
δOH	σ	0.804	7.171	0.141	0.13	11	H, 3-Br, 3-Cl, 4-Cl, 4-NMe$_2$, 2-OH, 4-OH, 4-OMe, 4-Me, 3-NO$_2$, 4-NO$_2$
	σ^+	0.884	7.192	0.077	0.13	11	H, 3-Br, 3-Cl, 4-Cl, 4-NMe$_2$, 2-OH, 4-OH, 4-OMe, 4-Me, 3-NO$_2$, 4-NO$_2$
	σ_I	0.846	7.095	0.270	0.13	11	H, 3-Br, 3-Cl, 4-Cl, 4-NMe$_2$, 2-OH, 4-OH, 4-OMe, 4-Me, 3-NO$_2$, 4-NO$_2$

	σ_R	0.832	7.218	0.175	0.14	11	H, 3-Br, 3-Cl, 4-Cl, 4-NMe₂, 2-OH, 4-OH, 4-OMe, 4-Me, 3-NO₂, 4-NO₂
	F	0.854	7.062	0.353	0.12	11	H, 3-Br, 3-Cl, 4-Cl, 4-NMe₂, 2-OH, 4-OH, 4-OMe, 4-Me, 3-NO₂, 4-NO₂
	R	0.832	7.221	0.126	0.14	11	H, 3-Br, 3-Cl, 4-Cl, 4-NMe₂, 2-OH, 4-OH, 4-OMe, 4-Me, 3-NO₂, 4-NO₂
δCO	σ	0.829	171.15	0.690	1.08	11	H, 3-Br, 3-Cl, 4-Cl, 4-NMe₂, 2-OH, 4-OH, 4-OMe, 4-Me, 3-NO₂, 4-NO₂
	σ^+	0.819	171.41	0.273	1.11	11	H, 3-Br, 3-Cl, 4-Cl, 4-NMe₂, 2-OH, 4-OH, 4-OMe, 4-Me, 3-NO₂, 4-NO₂
	σ_I	0.823	170.86	1.062	1.10	11	H, 3-Br, 3-Cl, 4-Cl, 4-NMe₂, 2-OH, 4-OH, 4-OMe, 4-Me, 3-NO₂, 4-NO₂
	σ_R	0.833	171.49	1.347	1.07	11	H, 3-Br, 3-Cl, 4-Cl, 4-NMe₂, 2-OH, 4-OH, 4-OMe, 4-Me, 3-NO₂, 4-NO₂
	F	0.832	170.65	1.614	1.07	11	H, 3-Br, 3-Cl, 4-Cl, 4-NMe₂, 2-OH, 4-OH, 4-OMe, 4-Me, 3-NO₂, 4-NO₂
	R	0.822	171.40	0.652	1.11	11	H, 3-Br, 3-Cl, 4-Cl, 4-NMe₂, 2-OH, 4-OH, 4-OMe, 4-Me, 3-NO₂, 4-NO₂

r = correlation co-efficient; ρ = slope; I = intercept; s = standard deviation; n = number of substituents

3. 1. Infrared spectral study

Infrared spectra of all synthesized 3-hydroxy-2-(substituted phenyl)-4*H*-pyrano[3,2-b][1]benzofuron-4-ones were recorded in KBr disc technique. From the spectra, the authors have expected the doublet for the carbonyl stretches (cm⁻¹) due to presence of cyclic α, β-unsaturated moiety. But the doublet was not observed. It may happened by the suppression of hydroxyl group attached in α- position. The assigned νCO and OH stretches (cm⁻¹) were presented in Table 1. These data are correlated with Hammett substituent constants, F and R parameters by linear regression analysis. In the infrared spectral correlation, the Hammett equation was taken in the form as:

$$\nu = \rho\sigma + \nu_o \qquad\qquad \ldots(1)$$

where ν_o is the frequency for the parent member of the series, ν is the frequency for the substituted member of the series, ρ is the reaction constants and it depends on reaction conditions such as temperature and concentration, σ is the substituent constants.

The results of statistical analysis are shown in Table 2. From Table 2, the νOH stretches(cm⁻¹) gave good correlation with Hammett σ and σ⁺ constants. The Hammett σ_I, σ_R substituent constants, F and R parameters have shown satisfactory correlation with νOH stretches (cm⁻¹) of 3-hydroxy-2-(substituted phenyl)-4*H*-pyrano[3,2-b][1]benzofuron-4-ones. All correlations gave positive ρ values. This supports that the normal substituent effects

operates in all systems. Similarly the multi-regression analysis gave good correlation with Swain-Lupton's [20] σ_I, σ_R substituent constants, F and R parameters. The generated multi-regression analysis equations are given in (2) and (3).

$$\nu OH(cm^{-1}) = 3408.44(\pm 1.764) + 10.354(\pm 3.611)\sigma_I + 5.503(\pm 0.531)\sigma_R \qquad ...(2)$$
$$(R = 0.984, \quad n = 11, P > 95\ \%)$$

$$\nu OH(cm^{-1}) = 3408.38(\pm 1.887) + 10.817(\pm 3.901)F + 4.673(\pm 0.223)R \qquad ...(3)$$
$$(R = 0.983, \quad n = 11, P > 95\ \%)$$

The νCO stretches (cm^{-1}) of 3-hydroxy-2-(substituted phenyl)-4*H*-pyrano[3,2-b][1] benzofuron-4-ones gave satisfactory correlations with Hammett substituent constants and F parameter. The R parameter was failed in correlation. All correlations gave positive ρ values.

This supports that the normal substituent effects operates in all systems. The failure in correlation for R parameters is due to the inability of transmittance of substituent effects of substituents on the νCO stretches and associated with the resonance conjugative structure as shown in Fig. 1.
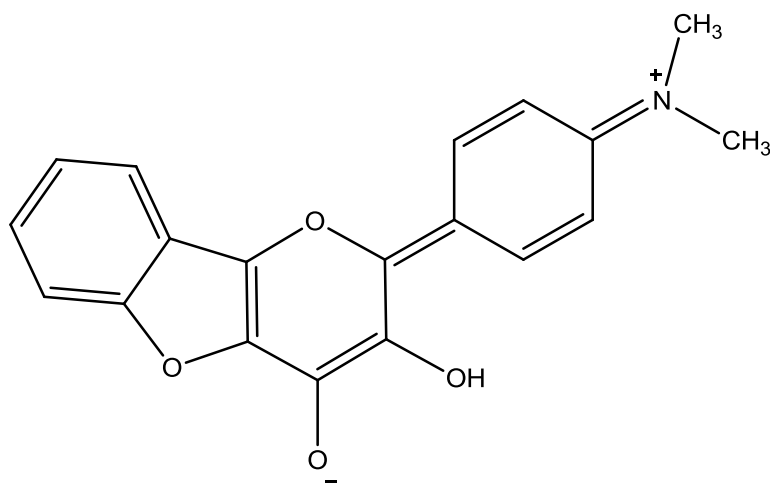

Figure. 1. The resonance-conjugative structure.

The R parameter was failed in single regression analysis. This is worthwhile, when seeking in the multi-regression analysis with Swain-Lupton's [20] σ_I, σ_R substituent constants, F and R parameters. The generated multi-regression analysis equations are given in (4) and (5).

$$\nu CO(cm^{-1}) = 1687.48(\pm 1.982) + 6.414(\pm 4.057)\sigma_I + 3.441(\pm 1.378)\sigma_R \qquad ...(4)$$
$$(R = 0.965, n = 11, P > 95\ \%)$$

$$\nu CO(cm^{-1}) = 1686.59(\pm 2.142) + 7.459(\pm 4.435)F + 2.046(\pm 1.125)R \qquad ...(5)$$
$$(R = 0.962, n = 11, P > 95\ \%)$$

3. 2. NMR spectral study

The NMR chemical shifts (δ, ppm) of OH and CO protons and carbons of 3-hydroxy-2-(substituted phenyl)-4*H*-pyrano[3, 2-b][1]benzofuron-4-ones were assigned and presented in Table 1. These chemical shifts (δ, ppm) were correlated with Hammett substituent constants, F and R parameters using single and multi-parameter correlations. In this NMR spectral correlation, the Hammett equation was employed as,

$$\delta = \rho\sigma + \delta_o \qquad \qquad ...(6)$$

where δ_o is the chemical shift (δ, ppm) for the parent member of the series, δ is the chemical shift (δ, ppm) for the substituted member of the series, ρ is the reaction constants and it depends on reaction conditions such as temperature and concentration, σ is the substituent constants.

The results of statistical analyses were presented in Table 2. From the Table 2, the correlation of OH and CO protons and carbon chemical shifts (δ, ppm) of 3-hydroxy-2-(substituted phenyl)-4*H*-pyrano[3,2-b][1]benzofuron-4-ones were failed with Hammett substituent constants, F and R parameters. All correlations gave positive ρ values. This supports that the normal substituent effects operates in all systems. The reason for failure of correlation was stated earlier and associated with resonance conjugative structure as shown in Fig. 1. In view of the inability of prediction of effect of substituents on the OH and CO protons and carbon chemical shifts (δ, ppm), they are worthwhile and produce satisfactory correlations when seeking in multi-regression analysis with Swain-Lupton's [20] σ_I, σ_R substituent constants, F and R parameters. The generated multi-regression analysis equations are given in (7-10)

$$\delta OH(ppm) = 7.124(\pm 0.100) + 0.321(\pm 0.021)\sigma_I + 0.078(\pm 0.001)\sigma_R \qquad ...(7)$$
$$(R = 0.974, \text{n} = 11, P > 95\ \%)$$

$$\delta OH(ppm) = 7.091(\pm 0.092) + 0.319(\pm 0.021)F + 0.055(\pm 0.012)R \qquad ...(8)$$
$$(R = 0.955, \text{n} = 11, P > 95\%)$$

$$\delta CO(ppm) = 171.29(\pm 0.812) + 0.491(\pm 0.066)\sigma_I + 1.142(\pm 0.152)\sigma_R \qquad ...(9)$$
$$(R = 0.934, \text{n} = 11, P > 95\ \%)$$

$$\delta CO(ppm) = 170.83(\pm 0.852) + 1.405(\pm 0.176)F + 0.338(\pm 0.105)R \qquad ...(10)$$
$$(R = 0.934, \text{n} = 11, P > 95\ \%)$$

4. CONCLUSION

Totally eleven benzofuranyl flavonols [3-hydroxy-2-(substituted phenyl)-4*H*-pyrano[3,2-b][1]benzofuron-4-ones] have been prepared by cyclization of 3-hydroxybenzofuranyl chalcones with 30 % hydrogen peroxide in the presence of sodium bicarbonate. The synthesized flavonols were characterized by their physical constants, analytical and spectroscopic data. The infrared spectral νOH, CO stretches(cm^{-1}), NMR chemical shifts of OH, CO(δ, ppm) proton and carbons of these flavonols were assigned and correlated with Hammett substituent constants, F and R parameters using single and multi

linear regression analysis. From the results of statistical analyses, νOH, CO stretches (cm^{-1}), gave good and satisfactory correlation in single and multi-regression analysis.

The NMR chemical shifts of OH, CO (δ, ppm) proton and carbons of these flavonols were failed in single parameter correlation and satisfactory in multi-parameter correlation.

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