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Infrared and NMR spectral Hammett correlations in 4-(2-naphthyl)-5,6-dihydro-6-(substituted phenyl)-^4H-1,3-oxazine-2-amines

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ABSTRACT

A series containing ten titled compounds have been synthesised and recorded the IR and NMR spectra. From the spectra the infrared νNH, C=N, C-O-C stretches, NMR chemical shifts of (δ, ppm) NH and C=N were assigned and correlated with Hammett substituent constants, F and R parameters using single regression analysis. From the results, the effects of substituent on the above spectral frequencies were discussed.

***Keywords*:** Oxazine-2-amines; IR and NMR spectra; Hammett equation; Correlation analysis

1. INTRODUCTION

Hammett equation is one of the best tools for predicting the effect of substituents on the reaction centre of substrates through kinetic parameter or spectral data with linear regression analysis [1]. The spectral parameter is used for studying the effect of substituent on the substrate and ground state equilibration such as *E* and *Z* isomers, *s-cis* and *s-trans* conformers, *cis* and *gauche* conformers [2-4]. Correlation analysis was utilized for studying the transition state of the reaction mechanism [5], enol-enone tautomerism [6], structure-activity relationships of bio active molecules [7] and electrochemical redox behaviour of compounds [8]. The unsaturated cyclic oxazine-2-amines are important bioactive molecules. They possess many biologically activities such as antimicrobial [9], anti-plasmodial [10], anti-cancer [11], anti-depressants [12], cytotoxicity [13], anti-osteoplastic [14], anti-tumour [15], anti-oxidant [16], anti-tuberculosis [17], anti-neoplastic [18], antagonists [19], anti-inflammatory [20] anti-infectants [21], IKB kinase beta [22], PTP-1B inhibition [23] and insect antifeedant activities [24].

Recently, Thirunarayanan et al., have synthesised and evaluated the antimicrobial and insect antifeedant activities of some aryl oxazine derivatives [9,24]. The effect of substituent on the spectral group frequencies of some 4-(6-methoxy-2-naphthyl)-5,6-dihydro-6-(substituted phenyl)-^4H-1,3-oxazine-2-amines were studied by Thirunarayanan [25]. There is no report available for the study of effect of substituents on the spectral group frequencies of

titled compounds in literature in the past. Therefore the authors have taken efforts to synthesized some 4-(2-naphthyl)-5,6-dihydro-6-(substituted phenyl)-^4H-1,3-oxazine-2-amines and recorded the infrared and nuclear magnetic resonance spectra for studying the Hammett spectral correlations.

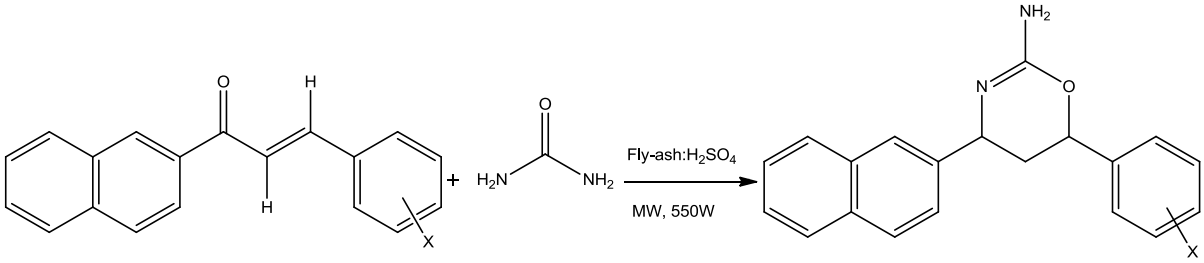
2. EXPERIMENTAL

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. Synthesis of 4-(2-naphthyl)-5,6-dihydro-6(substituted phenyl)-^4H-1,3-oxazine-2-amines

The titled oxazine-2-amines were synthesized and their purities were checked by literature method [26]. Substituted styryl 2-naphthyl ketones (2 mmol), urea (2 mmol) and 0.5 g of fly-ash:H_2SO_4 were subjected to microwave irradiation for 2-4 m at 650 W (Scheme 1) (Samsung, Microwave Oven, 100-700 W). Dichloromethane (10 mL) was added to the reaction-production mixture after completion of reaction, followed by simple filtration. Concentration of the extract afforded the crude product and this was purified by re-crystallization with ethanol.



Entry	1	2	3	4	5	6	7	8	9	10
X	H	3-NH_2	3-Cl	4-Cl	4-$N(CH_3)_2$	4-OH	4-OCH_3	4-CH3	3-NO_2	4-NO_2

Scheme 1. Synthesis of 4-(2-naphthyl)-5,6-dihydro-6-(substituted phenyl)-^4H-1,3-oxazine-2-amines by fly-ash:H_2SO_4 catalyzed cyclization of aryl chalcones and urea under microwave irradiation.

3. RESULTS AND DISCUSSION

In the present study, the author have investigated the effect of substituents on the infrared νNH, C=N, C-O-C (cm^{-1}) stretches, ^1H NMR δNH, ^{13}C NMR δC=N (ppm) chemical shifts of 4-(2-naphthyl)-5,6-dihydro-6(substituted phenyl)-^4H-1,3-oxazine-2-amines by Hammett correlation.

3. 1. Infrared spectral study

In infrared spectral study, the νNH, C=N and C-O-C (cm^{-1}) stretches of synthesized amines were correlated by the Hammett equation as shown in equation (1).

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

where ν_o is the frequency for the parent member of the series.

The assigned νNH, C=N (cm^{-1}) stretches, ^{1}H NMR δNH, ^{13}C NMR δC=N (ppm) chemical shifts of 4-(2-naphthyl)-5,6-dihydro-6(substituted phenyl)-^{4}*H*-1,3-oxazine-2-amines were presented in Table1. These data were correlated with Hammett substituent constants, F and R parameters linear regression analysis [1-4,8,27-29]. The result of statistical analysis was presented in Table 2.

Table 1. The infrared νNH, C=N, C-O-C (cm^{-1}) stretches, ^{1}H NMR δNH, ^{13}C NMR δC=N (ppm) chemical shifts of 4-(2-naphthyl)-5,6-dihydro-6-(substituted phenyl)-^{4}*H*-1,3-oxazine-2-amines.

Entry	X	IR (ν, cm^{-1})			^{1}H (δ, ppm)	^{13}C (δ, ppm)
		NH	C=N	C-O-C	NH	C=N
10	H	3526	1598	1215	2.291	165.02
11	3-NH_2	3548	1592	1210	2.112	165.25
12	3-Cl	3545	1605	1215	2.225	164.25
13	4-Cl	3535	1589	1222	2.125	165.28
14	4-$N(CH_3)_2$	3552	1621	1214	2.091	164.57
15	4-OH	3545	1596	1221	2.204	165.33
16	4-OCH_3	3532	1613	1215	2.220	164.72
17	4-CH_3	3535	1622	1221	2.212	164.47
18	3-NO_2	3555	1625	1215	2.321	165.41
19	4-NO_2	3555	1648	1217	2.182	165.32

The correlation of infrared νNH (cm^{-1}) stretches of 4-(2-naphthyl)-5,6-dihydro-6-(substituted phenyl)-^{4}*H*-1,3-oxazine-2-amines were satisfactorily with Hammett σ, σ^+, σ_I constants and F parameters excluding 3-NH_2 and 4-$N(CH_3)_2$. When these substituents were included in the correlation, the correlation was reduced considerably. The Hammett σ_R constant and R parameter were fail in correlation. This is due to the inability of transmittance of effect of substituent on the group frequencies and associated with resonance-conjugative structure as shown in Figure 1. All correlations gave positive ρ values. This implies that the normal substituent effects operates in all systems.

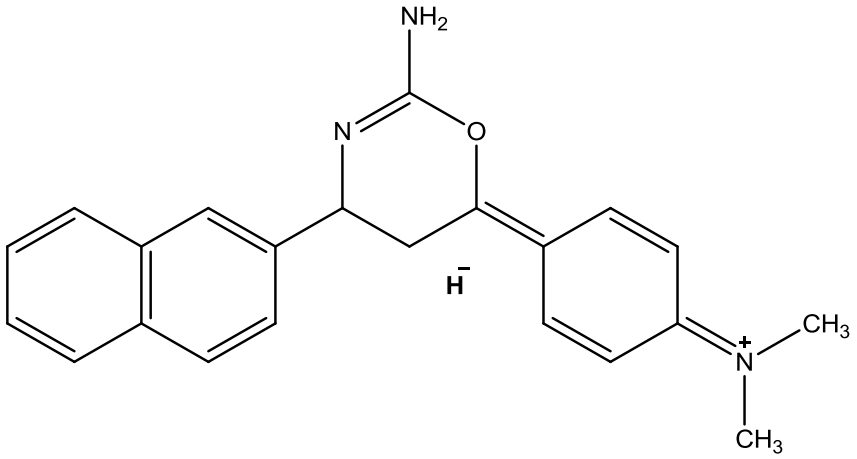


Figure 1. The resonance-conjugative structure.

The correlation of infrared νCN (cm^{-1}) stretches of 4-(2-naphthyl)-5,6-dihydro-6-(substituted phenyl)-^{4}*H*-1,3-oxazine-2-amines were satisfactorily with Hammett σ, σ^+ and σ_R constants excluding 4-$N(CH_3)_2$ substituent. The Hammett σ_I constant, F and R parameters have shown poor correlations. All correlations gave positive ρ values. This implies that the normal substituent effect operates in all systems. The failure in correlation was due to the reason stated earlier and associated with the conjugative-structure as shown in Figure 1.

Table 2. Results of statistical analysis of IR, ^{1}H NMR and ^{13}C-NMR spectral values of 4-(2-naphthyl)-5,6-dihydro-6-(substituted phenyl)-^{4}*H*-1,3-oxazine-2-amines with Hammett σ, σ^+, σ_I, σ_R constants, F and R parameters.

Frequency	Constant	r	I	ρ	s	n	Correlated derivatives
νNH (cm^{-1})	σ	0.903	3542.35	7.359	10.18	10	H, 3-NH_2, 3-Cl, 4-Cl, 4-$N(CH_3)_2$, 4-OH, 4-OCH_3, 4-CH_3, 3-NO_2, 4-NO_2
	σ^+	0.901	3543.16	1.999	10.71	10	H, 3-NH_2, 3-Cl, 4-Cl, 4-$N(CH_3)_2$, 4-OH, 4-OCH_3, 4-CH_3, 3-NO_2, 4-NO_2
	σ_I	0.905	3546.70	21.009	9.20	8	H, 3-Cl, 4-Cl, 4-OH, 4-OCH_3, 4-CH_3, 3-NO_2, 4-NO_2
	σ_R	0.805	3543.28	2.344	10.81	10	H, 3-NH_2, 3-Cl, 4-Cl, 4-$N(CH_3)_2$, 4-OH, 4-OCH_3, 4-CH_3, 3-NO_2, 4-NO_2
	F	0.905	3535.04	24.663	8.81	8	H, 3-Cl, 4-Cl, 4-OH, 4-OCH_3, 4-CH_3, 3-NO_2, 4-NO_2
	R	0.807	3542.15	1.976	1080	10	H, 3-NH_2, 3-Cl, 4-Cl, 4-$N(CH_3)_2$, 4-OH, 4-OCH_3, 4-CH_3, 3-NO_2, 4-NO_2
νC=N (cm^{-1})	σ	0.903	1610.03	14.132	18.24	9	H, 3-NH_2, 3-Cl, 4-Cl, 4-OH, 4-OCH_3,4-CH_3, 3-NO_2, 4-NO_2
	σ^+	0.902	1611.88	5.372	19.06	9	H, 3-NH_2, 3-Cl, 4-Cl, 4-OH, 4-OCH_3,4-CH_3, 3-NO_2, 4-NO_2
	σ_I	0.803	1603.59	2.194	18.33	10	H, 3-NH_2, 3-Cl, 4-Cl,

							4-$N(CH_3)_2$, 4-OH, 4-OCH_3, 4-CH_3, 3-NO_2, 4-NO_2
	σ_R	0.904	1618.05	34.379	17.10	9	H, 3-NH_2, 3-Cl, 4-Cl, 4-OH, 4-OCH_3,4-CH_3, 3-NO_2, 4-NO_2
	F	0.804	1600.85	33.493	17.61	10	H, 3-NH_2, 3-Cl, 4-Cl, 4-$N(CH_3)_2$, 4-OH, 4-OCH_3, 4-CH_3, 3-NO_2, 4-NO_2
	R	0.883	1616.45	16.942	18.27	10	H, 3-NH_2, 3-Cl, 4-Cl, 4-$N(CH_3)_2$, 4-OH, 4-OCH_3, 4-CH_3, 3-NO_2, 4-NO_2
νC-O-C (cm^{-1})	σ	0.817	1216.56	1.278	4.00	10	H, 3-NH_2, 3-Cl, 4-Cl, 4-$N(CH_3)_2$, 4-OH, 4-OCH_3, 4-CH_3, 3-NO_2, 4-NO_2
	σ^+	0.808	1216.50	0.042	4.00	10	H, 3-NH_2, 3-Cl, 4-Cl, 4-$N(CH_3)_2$, 4-OH, 4-OCH_3, 4-CH_3, 3-NO_2, 4-NO_2
	σ_I	0.810	1216.06	1.501	3.98	10	H, 3-NH_2, 3-Cl, 4-Cl, 4-$N(CH_3)_2$, 4-OH, 4-OCH_3, 4-CH_3, 3-NO_2, 4-NO_2
	σ_R	0.821	1217.14	3.122	3.91	10	H, 3-NH_2, 3-Cl, 4-Cl, 4-$N(CH_3)_2$, 4-OH, 4-OCH_3, 4-CH_3, 3-NO_2, 4-NO_2
	F	0.852	1215.79	2.341	3.96	10	H, 3-NH_2, 3-Cl, 4-Cl, 4-$N(CH_3)_2$, 4-OH, 4-OCH_3, 4-CH_3, 3-NO_2, 4-NO_2
	R	0.872	1217.75	2.365	3.88	10	H, 3-NH_2, 3-Cl, 4-Cl, 4-$N(CH_3)_2$, 4-OH, 4-OCH_3, 4-CH_3, 3-NO_2, 4-NO_2
δNH (ppm)	σ	0.904	2.194	0.066	0.05	10	H, 3-NH_2, 3-Cl, 4-Cl, 4-$N(CH_3)_2$, 4-OH, 4-OCH_3, 4-CH_3, 3-NO_2, 4-NO_2
	σ^+	0.947	2.206	0.045	0.05	10	H, 3-NH_2, 3-Cl, 4-Cl, 4-$N(CH_3)_2$, 4-OH, 4-OCH_3, 4-CH_3, 3-NO_2, 4-NO_2
	σ_I	0.920	2.176	0.063	0.06	10	H, 3-NH_2, 3-Cl, 4-Cl, 4-$N(CH_3)_2$, 4-OH, 4-OCH_3, 4-CH_3, 3-NO_2, 4-NO_2
	σ_R	0.965	2.236	0.185	0.05	10	H, 3-NH_2, 3-Cl, 4-Cl, 4-$N(CH_3)_2$, 4-OH, 4-OCH_3, 4-CH_3, 3-NO_2, 4-NO_2
	F	0.802	2.178	0.067	0.08	10	H, 3-NH_2, 3-Cl, 4-Cl, 4-$N(CH_3)_2$, 4-OH, 4-OCH_3, 4-CH_3, 3-NO_2, 4-NO_2
	R	0.966	2.239	0.125	0.04	10	H, 3-NH_2, 3-Cl, 4-Cl, 4-$N(CH_3)_2$, 4-OH, 4-OCH_3, 4-CH_3, 3-NO_2, 4-NO_2
δC=N (ppm)	σ	0.904	164.94	0.349	0.41	10	H, 3-NH_2, 4-Cl, 4-$N(CH_3)_2$, 4-OH, 4-OCH_3,4-CH_3, 3-NO_2, 4-NO_2
	σ^+	0.903	164.99	0.180	0.42	10	H, 3-NH_2, 4-Cl, 4-$N(CH_3)_2$, 4-OH, 4-OCH_3,4-CH_3,

							3-NO_2, 4-NO_2
	σ_I	0.841	164.76	0.987	0.40	10	H, 3-NH_2, 3-Cl, 4-Cl, 4-$N(CH_3)_2$, 4-OH, 4-OCH_3, 4-CH_3, 3-NO_2, 4-NO_2
	σ_R	0.825	165.04	0.142	0.43	10	H, 3-NH_2, 3-Cl, 4-Cl, 4-$N(CH_3)_2$, 4-OH, 4-OCH_3, 4-CH_3, 3-NO_2, 4-NO_2
	F	0.840	164.74	0.709	0.41	10	H, 3-NH_2, 3-Cl, 4-Cl, 4-$N(CH_3)_2$, 4-OH, 4-OCH_3, 4-CH_3, 3-NO_2, 4-NO_2
	R	0.821	165.03	0.230	0.43	10	H, 3-NH_2, 3-Cl, 4-Cl, 4-$N(CH_3)_2$, 4-OH, 4-OCH_3, 4-CH_3, 3-NO_2, 4-NO_2

r = correlation coefficient; I = intercept; ρ = slope; s = standard deviation;
n = number of correlated derivatives

The correlation of infrared νC-O-C (cm^{-1}) stretches of 4-(2-naphthyl)-5,6-dihydro-6-(substituted phenyl)-^4H-1,3-oxazine-2-amines were shown poor r values with Hammett substituent constants, F and R parameters. All correlations gave positive ρ values. This implies that the normal substituent effects operate in all systems. The failure in correlation was due to the reason stated earlier and associated with the conjugative-structure as shown in Figure 1.

Some of the infrared stretches were fail in correlation with Hammett constants, F and R parameters in single linear regression analysis. They are worthwhile when seeking in multi parameter correlation with σ_I and σ_R or F and R Swain-Lupton [30] parameters. The generated multi-regression analysis equations are given in (2-7).

$$\nu NH(cm^{-1}) = 3532.88(\pm 6.864) + 27.022(\pm 14.285)\sigma_I + 11.428(\pm 1.406)\sigma_R \quad ...(2)$$
$$(r = 0.958, n = 10, P > 95\ \%)$$

$$\nu NH(cm^{-1}) = 3529.03(\pm 6.193) + 33.222(\pm 12.980)F + 11.482(\pm 1798)R \quad ...(3)$$
$$(r = 0.969, n = 10, P > 95\ \%)$$

$$\nu C{=}N(cm^{-1}) = 1614.20(\pm 13.228) + 9.708(\pm 2.753)\sigma_I + 29.431(\pm 2.709)\sigma_R \quad ...(4)$$
$$(r = 0.949, n = 10, P > 90\ \%)$$

$$\nu C{=}N(cm^{-1}) = 1606.06(\pm 13.791) + 26.394(\pm 2.840)F + 0.413(\pm 1.777)R \quad ...(5)$$
$$(r = 0.947, n = 10, P > 90\ \%)$$

$$\nu C\text{-}S\text{-}C(cm^{-1}) = 1217.22(\pm 3.078) + 0.192(\pm 0.001)\sigma_I + 3.220(\pm 0.625)\sigma_R \quad ...(6)$$
$$(r = 0.921, n = 10\ P > 90\ \%)$$
$$\nu C\text{-}S\text{-}C(cm^{-1}) = 1216.98(\pm 3.100) + 0.742(\pm 0.064)F + 2.153(\pm 0.399)R \quad ...(7)$$
$$(r = 0.924, n = 10, P > 90\ \%)$$

3. 2. NMR spectral study

In nuclear magnetic resonance spectra, the ^1H or the ^{13}C chemical shifts (δ)(ppm) depend on the electronic environment of the nuclei concerned. These chemical shifts have

been correlated with reactivity parameters. Thus the Hammett equation may be used in the form as shown in (8).

$$\text{Log } \delta = \text{Log } \delta_0 + \rho\sigma \qquad \text{... (8)}$$

where δ_0 is the chemical shift of the corresponding parent compound.

The assigned ^{1}H NMR δNH, ^{13}C NMR δC=N (ppm) chemical shifts of 4-(2-naphthyl)-5,6-dihydro-6-(substituted phenyl)-^{4}*H*-1,3-oxazine-2-amines were presented in Table 1. These data were correlated with Hammett substituent constants, F and R parameters linear regression analysis [1-4,8,27-29]. The result of statistical analysis was presented in Table 2. From Table 2, the δNH (ppm) chemical shifts of 4-(2-naphthyl)-5,6-dihydro-6-(substituted phenyl)-^{4}*H*-1,3-oxazine-2-amines were satisfactorily correlated with Hammett substituent constants and R parameters. The Field effect of the substituents were fail in correlation and it unable to predict the reactivity on the NH chemical shifts. This is due to the reason stated earlier and associated with Figure 1. All correlations gave positive ρ values. This means that then normal substituent effects operates in all systems.

From Table 2, the ^{13}C NMR δC=N (ppm) chemical shifts of 4-(2-naphthyl)-5,6-dihydro-6-(substituted phenyl)-^{4}*H*-1,3-oxazine-2-amines were satisfactorily correlated with Hammett σ and σ^+ constants produce satisfactory correlations excluding 3-Cl substituent. The Hammett σ_I, σ_R substituent constants, F and R parameters were fail in correlation. This is due to the inability of substituent constants for prediction of reactivity on the chemical shifts of oxazine amines and associated with resonance conjugative structure shown in Fig. 1. All correlations gave positive ρ values. This means that then a normal substituent effect operates in all systems.

In view of the inability of prediction of effect of substituents by single regression analysis with Hammett substituent constants, F and R parameters, they are worthwhile when seeking in multi-regression analysis for ^{1}H NMR δNH, ^{13}C NMR δC=N (ppm) chemical shifts of 4-(6-methoxy-2-naphthyl)-5,6-dihydro-6-(substituted phenyl)-^{4}*H*-1,3-oxazine-2-amines. The generated multi-regression [30] analysis equations are given in (9-12):

$$\delta\text{NH(ppm)} = 2.255(\pm0.045) + 0.046(\pm0.002)\sigma_I + 0.208(\pm0.094)\,\sigma_R \qquad \text{...(9)}$$
$$(r = 0.966,\ n = 10,\ P > 95\ \%)$$

$$\delta\text{NH(ppm)} = 2.253(\pm0.046) + 0.035(\pm0.002)F + 0.136(\pm0.060)R \qquad \text{…(10)}$$
$$(r = 0.967,\ n = 10,\ P > 95\ \%)$$

$$\delta\text{C=N(ppm)} = 164.79(\pm0.317) + 0.634(\pm0.066)\sigma_I + 0.098(\pm0.006)\,\sigma_R \qquad \text{...(11)}$$
$$(r = 0.941,\ n = 10,\ P > 90\ \%)$$

$$\delta\text{C=N(ppm)} = 164.76(\pm0.327) + 0.682(\pm0.068)F + 0.036(\pm0.004)R \qquad \text{…(12)}$$
$$(r = 0.940,\ n = 10,\ P > 90\ \%)$$

4. CONCLUSIONS

Totally ten 4-(2-naphthyl)-5,6-dihydro-6-(substituted phenyl)-^{4}*H*-1,3-oxazine-2-amine compounds were synthesized and recorded IR and NMR spectra. The infrared νNH, C=N, C-O-C (cm^{-1}) stretches, ^{1}H NMR δNH, ^{13}C NMR δC=N (ppm) chemical shifts of synthesized

oxazine amines were assigned and correlated with Hammett substituent constants, F and R parameters. From the single parameter correlation analyses, the infrared νNH, C=N (cm^{-1}) stretches and NMR δNH and δC=N (ppm) chemical shifts correlated satisfactorily with Hammett substituent constants, F and R parameters. All the above spectral frequencies were satisfactorily correlated with σ_I and σ_R or F and R Swain-Lupton parameters in multi-regression analysis.

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