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Hammett spectral correlations in some aryl 1,3-oxazine-4-thione derivatives

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ABSTRACT

A series of some aryl 1,3-oxazine-4-thione derivatives have been synthesized by 1-methyl imidazole catalyzed three component one pot synthetic method in room temperature. The purities of these thiones were studied by their physical constants and spectroscopic data. The infrared and ^{13}C NMR spectral data of CN and CS were correlated with Hammett substituent constants, F and R parameters using single and multi-linear regression analysis. From the results of statistical analysis, the effect of substituent on the spectral data was studied.

***Keywords*:** 1,3-oxazine-4-thiones; IR spectra; ^{13}C NMR spectra; Hammett correlation

1. INTRDUCTION

Aryl 1,3-oxazine-4-thiones are pharmaceutical important heterocycles [1,2]. They possess various biological activities such as antimicrobial [3], hypolipidacmic [4], antidiabetic [5], anti-inflammatory [6], antimycobacterial [7], antithrombotic [8], antagonism to progesterone receptor [9], antitumor [10], antiviral [11], leucocyte clastase [12] and scrotonin reuptakes [13]. The ground state equilibration of organic compounds was established using spectroscopic data [14]. Infrared spectra was applied for prediction of *E s-cis* and *s-trans* conformers of styrenes[15], polyenes [16], chalcones [17], unsaturated aldehydes [18], acid chlorides [19], unsaturated esters [20], *gauche* and *anti*- form acyl halides and its esters [21]. The spatial arrangement of protons such as *cis* and *trans* of organic stereo chemical compounds [22] were studied using NMR spectra. Currently chemists and spectroscopic researchers [23-29] have paid much more interest for correlation of spectral data with Hammett substituent constants. Thirunarayanan and Ravi [30] have studied the effect of substituents of some pyrazoline-1-ethanones. Substituent effects on the spectral group frequencies of 9*H*-fluorenayl bromides were studied by Thirunarayanan [31]. Sakthinathan et al., have investigated the effect of substituents on naphthyl based pyrazoline derivatives [32]. Sasikala et al., [22] have evaluated the effect of substituents and antimicrobial activities of some 5-bromo-2-thienyl based pyrazolines. The spectral

correlation of infrared and nuclear magnetic resonance spectra of *E*-imines have been predicted by Sakthinathan et. al. and Suresh et al., [33,34]. Thirunarayanan and Sekar have investigated the substituent effects on the IR and NMR spectral frequencies of some 3-(3,4-dichlorophenyl)-pyrazoline carbothiomides [35]. Spectral correlation study was first reported on the Tröger's bases by Thirunarayanan and Suresh [36]. Janaki et al, Vanangamudi et al, Subramanian et al. and Thirunarayanan et al., [37-40] have been investigated the effects of substituents on the spectral data of various chalcones. Thirunarayanan have studied the effect of substituents on the oxazine 2-amines by IR and NMR spectral data [27]. Recently, Thirunarayanan et al., [28] have studied the effect of substituents on aryl hydrazides by their infrared and nmr spectral data. Within the above view, there is no report available for the study of spectral correlation analysis on 1, 3-oxazine-4-thiones. Therefore the authors have taken efforts to synthesis and recorded the IR and NMR spectra for studying spectral correlation of above title compounds.

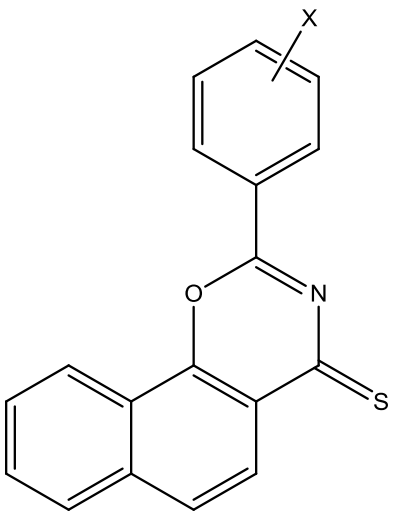
2. EXPERIMENTAL

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, 100 MHz frequency was applied for recording ^{13}C NMR spectra, taking TMS as standard.

2. 2. Synthesis of 1, 3-oxazine-4-thiones

The title 1,3-oxazine-4-thiones were synthesized and their purities were checked by literature method [41]. The general structure of the aryl 1,3-oxazine-4-thions are shown in Fig. 1.



X= H, 3-Br, 4-Br, 3-Cl, 4-Cl, 4-OCH_3, 4-CH_3, 3-NO_2, 4-NO_2

Fig. 1. 2-(substituted phenyl)-4H-naphtho[2,1-e][1,3]oxazine-4-thiones.

3. RESULTS AND DISCUSSION

In the present study, the authors have evaluated the effect of substituents on the infrared νC=N, C=S (cm^{-1}) stretches, ^{13}C NMR δC=N and C=S (ppm) chemical shifts of 2-(substituted phenyl)-4H-naphtho[2,1-e][1,3]oxazine-4-thiones by Hammett correlation (Table 1).

Table 1. The infrared and ^{13}C NMR spectral data of 2-(substituted phenyl)-4*H*-naphtho[2,1-e] (1,3) oxazine-4-thiones.

Sl. No.	X	IR (ν, cm^{-1})		^{13}C NMR (δ, ppm)	
		CN	CS	CN	CS
1	H	1655	1194	164.23	197.76
2	3-Br	1658	1189	164.55	197.08
3	4-Br	1666	1176	164.97	198.92
4	3-Cl	1656	1178	164.76	197.16
5	4-Cl	1662	1182	164.48	199.14
6	4-OCH_3	1648	1169	164.26	197.02
7	4-CH_3	1672	1174	165.49	198.09
8	3-NO_2	1668	1198	165.96	198.06
9	4-NO_2	1663	1206	165.54	197.97

In infrared spectral correlation study, the Hammett equation was taken as,

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

where ν is the frequency for the substituted system, ρ is the reaction constants in terms of intercept, σ is the substituent constants and ν_o is the frequency for the parent member of the series.

The results of statistical analysis [14-17,21-28,31-46] were presented in Table 2. From the Table 2, the correlation of νC=N, C=S (cm^{-1}) stretches with Hammett substituent constants and F and R values are satisfactory along with positive ρ values. Comparatively, the C=S stretches were gave significant correlation than νC=N stretches.

In ^{13}C nuclear magnetic resonance spectral correlations, the Hammett equation was used in the form as shown in (2):

$$\text{Log } \delta = \text{Log } \delta_0 + \rho\sigma \quad \ldots\ldots (2)$$

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

The results of statistical analysis of chemical shifts (ppm) of δC=N, C=S [21-40,42-46] thiones were presented in Table 2. From the Table 2, the correlation of chemical shifts (ppm) of δC=N with Hammett substituent constants and F and R values are satisfactory. The correlation of δC=S with Hammett substituent constants and F and R values seems poor. This is due to the inability of effects of substituents on the chemical shifts through resonance or conjugation as shown in the Fig. 2. All correlations gave positive ρ values. This inferred the normal substituent effects operates in all systems.

Some of the individual correlations were fail in the statistical analysis for the correlation of chemical shifts (ppm) of δC=N, C=S. while seeking this with multi-parameter correlation with Swain-Lupton's [42] parameters, they gave satisfactory correlations. The generated multi-regression analysis equations are shown in (3-10).

Table 2. Results of statistical analysis of IR and ^{13}C NMR spectral values of 2-(substituted phenyl)-4*H*-naphtho[2,1-e] (1,3) oxazine-4-thione with Hammett σ, σ^+, σ_I, σ_R constants, F and R parameters.

Frequency	Constant	r	I	ρ	s	n	Correlated derivatives
νCN (cm^{-1})	σ	0.903	1659.22	6.553	7.40	9	H, 3-Br, 4-Br, 3-Cl, 4-Cl, 4-OCH_3, 4-CH_3, 2-NO_2,4-NO_2
	σ^+	0.904	1659.68	6.200	7.18		
	σ_I	0.902	1659.86	2.717	7.88		
	σ_R	0.905	1663.18	23.173	6.56		
	F	0.901	1659.41	3.980	7.85		
	R	0.905	1663.54	18.407	6.72		
νCS (cm^{-1})	σ	0.978	1178.42	26.381	8.22	9	H, 3-Br, 4-Br, 3-Cl, 4-Cl, 4-OCH_3, 4-CH_3, 2-NO_2,4-NO_2
	σ^+	0.973	1181.58	18.116	8.93		
	σ_I	0.904	1177.02	21.461	11.88		
	σ_R	0.988	1191.18	61.419	6.09		
	F	0.904	1176.37	23.528	11.88		
	R	0.988	1192.51	51.251	6.26		
δCN (ppm)	σ	0.958	164.66	0.981	0.53	9	H, 3-Br, 4-Br, 3-Cl, 4-Cl, 4-OCH_3, 4-CH_3, 2-NO_2, 4-NO_2
	σ^+	0.954	164.78	0.669	0.55		
	σ_I	0.903	164.56	0.919	0.61		
	σ_R	0.969	165.15	2.414	0.47		
	F	0.904	164.49	1.144	0.59		
	R	0.962	165.18	1.832	0.51		
δCS (ppm)	σ	0.812	197.84	0.241	0.80	9	H, 3-Br, 4-Br, 3-Cl, 4-Cl, 4-OCH_3, 4-CH_3, 2-NO_2,4-NO_2
	σ^+	0.882	197.84	0.347	0.81		
	σ_I	0.810	197.76	0.375	0.80		
	σ_R	0.825	198.01	1.069	0.78		
	F	0.811	197.77	0.355	0.81		
	R	0.828	198.05	1.008	0.78		

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

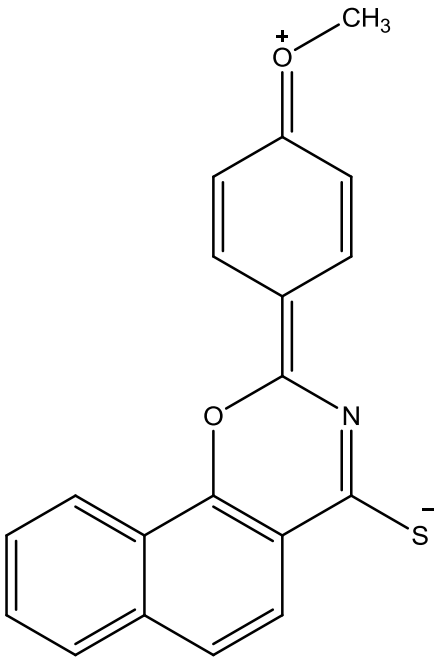


Fig. 2. The resonance-conjugative structure.

$$\nu CN(cm^{-1}) = 1664.36(\pm5.169) + 2.810(\pm1.043)\sigma_I + 24.455(\pm10.7176)\sigma_R \quad ...(3)$$
(r = 0.956, n = 9, P > 95 %)

$$\nu CN(cm^{-1}) = 1664.18(\pm5.688) + 1.509(\pm0.114)F + 18.949(\pm7.120)R \quad ...(4)$$
(r = 0.952, n = 9, P > 95 %)

$$\nu CS(cm^{-1}) = 1187.62(\pm4.516) + 8.447(\pm0.911)\sigma_I + 57.623(\pm12.853)\sigma_R \quad ...(5)$$
(r = 0.990, n = 9, P > 95 %)

$$\nu CS(cm^{-1}) = 1188.41(\pm4.927) + 9.687(\pm0.991)F + 47.777(\pm11.046)R \quad ...(6)$$
(r = 0.989, n = 9, P > 95 %)

$$\delta CN(ppm) = 164.97(\pm0.366) + 0.417(\pm0.073)\sigma_I + 2.223(\pm1.043)\sigma_R \quad ...(7)$$
(r = 0.949, n = 9, P > 90 %)

$$\delta CN(ppm) = 164.89(\pm0.427) + 6.684(\pm0.083)F + 1.586(\pm0.062)R \quad ...(8)$$
(r = 0.967, n = 9, P > 95 %)

$$\delta CS(ppm) = 197.95(\pm0642) + 0.149(\pm0.012)\sigma_I + 1.002(\pm0.177)\sigma_R \quad ...(9)$$
(r = 0.925, n = 9, P > 90 %)

$$\delta CS(ppm) = 198.02(\pm0.637) + 0.070(\pm0.001)F + 0.982(\pm0.148)R \quad ...(10)$$
(r = 0.928, n = 9, P > 90 %)

4. CONCLUSIONS

There are nine aryl 1,3-oxazine-4-thione derivatives have been synthesized by 1-methyl imidazole catalyzed three component one pot synthetic method in room temperature. The purities of these thiones were studied by their physical constants and spectroscopic data. The infrared and ^{13}C NMR spectral data of CN and CS were correlated with Hammett substituent constants, F and R parameters using single and multi-linear regression analysis. The infrared νCN and νCS stretches (cm^{-1}) were correlated satisfactorily with Hammett substituent constants, F and R parameters. Satisfactory correlation was obtained for the ^{13}C chemical shifts of δCN(ppm) of thiones with Hammett substituent constants, F and R parameters. The δCS(ppm) of thiones were failed in correlation. In multiple correlation all spectral frequencies gave satisfactorily correlation with Swain-Lupton's constants.

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