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## QSAR study of infrared and nuclear magnetic resonance spectra of 1-(3-chloro-4-nitrophenyl)-2-(substituted benzylidene) hydrazines

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### ABSTRACT

Ten 1-(3-chloro-4-nitrophenyl)-2-(substituted benzylidene) hydrazines have been synthesized by FeCl<sub>3</sub>/Bentonite catalyzed solvent-free condensation of substituted phenyl hydrazine and aldehydes under microwave irradiation. The synthesized hydrazides are characterized by the physical constants, micro analysis and spectroscopic data. The assigned characteristic spectroscopic data of these 1-(3-chloro-4-nitrophenyl)-2-(substituted benzylidene) hydrazines were correlated with Hammett substituent constants, F and R parameters using Hammett equation through single and multi-regression analysis. With the results of statistical analysis results, the quantitative structure activity relationships were studied and finding the effect of substituents on the spectral data.

**Keywords:** 1-(3-chloro-4-nitrophenyl)-2-(substituted benzylidene) hydrazines, FeCl<sub>3</sub>/Bentonite, Solvent-free synthesis, IR and NMR spectra, Hammett equation, QSAR study

### 1. INTRODUCTION

Azines are nitrogenous compounds and they had azomethine >N=N= moieties in their structures. More over in addition they possess the skeletons' of amido –CO-NH-N= imines –

CO-NH-N=CH- and carbothioamides –CS-NH-N=CH–. These hydrazines were prepared by condensation of carbonyl compounds and hydrazine hydrates in presence of base or acid in organic medium or solvent-free methods. The geometry of these azines were confirmed by spectroscopic techniques such as UV-Visible, FT-IR [1], NMR [2], Mass and XRD [3-8]. From infrared spectral frequencies ( $\nu$ ,  $\text{cm}^{-1}$ ) of N-N and CH=N stretches used for confirmation for the formation of azines. Generally, the stretching vibrations ( $\nu$ ,  $\text{cm}^{-1}$ ) of  $\nu_{\text{NH}}$  is falls in the range of 3290-3390  $\text{cm}^{-1}$ ,  $\nu_{\text{C=N}}$  is falls in the range of 1500-1585  $\text{cm}^{-1}$ . From NMR spectra, the proton and carbon chemical shifts ( $\delta$ , ppm) of NH, CH groups are useful for establish the structure of azines [2-5]. The proton chemical shifts ( $\delta$ , ppm) of NH, CH were obtained at the range of 7-8 and 7-8.5 ppm as singlet's. The carbon chemical shifts ( $\delta$ , ppm) CN was obtained in the range of 148-155 ppm. These azine derivatives are important in medicinal and pharmaceutical fields. They shows important biological activities due to presence of polar groups in azomethine units in their structure. The important biological activities are antimicrobial [2-5,9-22], anticonvulsant [1,9,10,16,19,20], anticancer [16,17,19-21,23,24], antidepressant [9,10], antianalgesics [9,17,20,21], anti-inflammatory [1,9,10, 6,19-21,25], antioxidant [1,10,21,26], antiplatelet [10,17,25], antimalarial [9,20,21], antimycobacterial [10,21,27], antitumoural [9,10,16,20,21,28,29], vasodilator[10], antiviral [9,10,17,19-21], antischistosomiasis [10, 21], antiepileptic [9,21], antihypertensive [21,25], antianxiety [9, 21], antitubercular [9,10,16,21], herbicidal [20,21,30], cardiovascular [10,20,21], HIV-1inhibitors [20,21], CNS activity[16], pesticidal [10,16], antidiabetic [10,16,21,25], antihyperlipidemic [16] and nematicidel [31,32]. Thirunarayanan et. al., [33] have studied the Hammett spectral LFER of some antioxidant substituted benzylidene hydrazines. Synthesis, study of structure activity relationship and evaluation of biological activities of substituted (*E*)-2-benzylidene-*N*-methyl hydrazine carbothioamides was reported by Vijayakumar et. al., [34]. Within the above view, there is no report available for the study of QSAR of infrared and nuclear magnetic resonance spectral data with Hammett equation in literature in the past. Therefore the authors taken efforts for the synthesis of some 1-(3-chloro-4-nitrophenyl)-2-(substituted benzylidene) hydrazines and recorded their infrared and nuclear magnetic resonance spectra for evaluation of QSAR leads to assessing the effects of substituents.

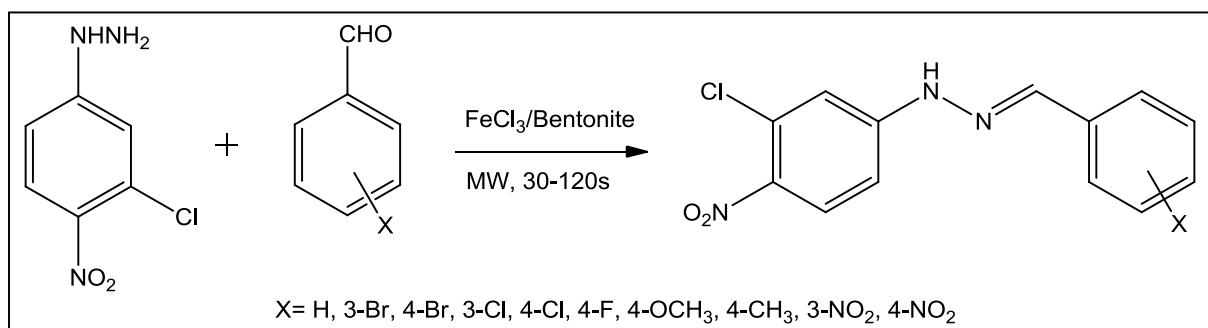
## 2. EXPERIMENTAL

### 2. 1. General

The melting points of all compounds were measured in Raga melting point apparatus using capillary tube and are uncorrected. IR spectra of all hydrazines under investigation were recorded using the SHIMADZU 8400 FT-IR spectrophotometer. The  $^1\text{H}$  and  $^{13}\text{C}$  NMR Spectra of all  $\alpha$ ,  $\beta$ -unsaturated ketones under investigation were recorded using the BRUKER, 400MHz model spectrometer operating at 400 MHz has been utilized for recording  $^1\text{H}$  NMR spectra and 100 MHz for  $^{13}\text{C}$  NMR spectra in  $\text{CDCl}_3$  and DMSO solvent using TMS as internal standard. The mass spectra of all compounds recorded as electron impact (70 eV) and chemical ionization mode FAB+ mass spectrum in VARIAN-SATURN 2200 GC-MS spectrometer (Varian Medical Systems, Palo Alto, CA, USA). Microanalyses of all the hydrazines were performed in Thermofinnigan CHN analyzer.

## 2. 2. General procedure for synthesis of 1-(3-chloro-4-nitrophenyl)-2-(3-substituted benzylidene) hydrazines [35]

An appropriate mixture of equimolar quantities of substituted hydrazine (0.01 mol), substituted benzaldehyde (0.01 mol) and 0.2 g of FeCl<sub>3</sub>/Bentonite catalyst were taken in a round bottomed flask, thoroughly mixed. Then these contents were subjected to microwave irradiation in a scientific microwave oven at 120 °C with the regular interval time 30-120 s (**Scheme 1**). The precipitate obtained, was filtered at the filter pump and washed several times with cold water. The crude product was recrystallized from ethanol to afforded glittering red orange solids.



**Scheme 1.** Synthesis of 1-(3-chloro-4-nitrophenyl)-2-(3-substituted benzylidene) hydrazines.

The physical constants, yields, micro analysis and mass spectral data of the synthesized 1-(3-chloro-4-nitrophenyl)-2-(3-substituted benzylidene) hydrazines are presented in Table 1. The infrared and nuclear magnetic resonance spectral data of prepared 1-(3-chloro-4-nitrophenyl)-2-(3-substituted benzylidene) hydrazines are presented in Table 2.

**Table 1.** The physical constants, yields, micro analysis and mass spectral data of the synthesized 1-(3-chloro-4-nitrophenyl)-2-(3-substituted benzylidene) hydrazines.

No.	X	M.F.	Time (s)	Yield (%)	m.p. (°C)	M.W.	Micro analysis (%)			Mass (m/z)
							C	H	N	
1	H	C <sub>13</sub> H <sub>10</sub> ClN <sub>3</sub> O <sub>2</sub>	120	92	116-117	275	56.66 (56.64)	3.60 (3.66)	15.22 (15.24)	275[M <sup>+</sup> ], 277[M <sup>2+</sup> ]
2	3-Br	C <sub>13</sub> H <sub>9</sub> BrClN <sub>3</sub> O <sub>2</sub>	120	94	103-104	352	43.05 (43.03)	2.48 (2.56)	11.79 (11.85)	352[M <sup>+</sup> ], 355[M <sup>2+</sup> ], 357[M <sup>4+</sup> ]
3	4-Br	C <sub>13</sub> H <sub>9</sub> BrClN <sub>3</sub> O <sub>2</sub>	120	93	115-116	352	43.06 (43.03)	2.50 (2.56)	15.81 (11.85)	352[M <sup>+</sup> ], 355[M <sup>2+</sup> ], 357[M <sup>4+</sup> ]

4	3-Cl	C <sub>13</sub> H <sub>9</sub> Cl <sub>2</sub> N <sub>3</sub> O <sub>2</sub>	90	92	102-103	310	50.38 (50.53)	2.88 (2.92)	13.49 (13.55)	310[M <sup>+</sup> ], 312[M <sup>2+</sup> ], 314[M <sup>4+</sup> ]
5	4-Cl	C <sub>13</sub> H <sub>9</sub> Cl <sub>2</sub> N <sub>3</sub> O <sub>2</sub>	120	93	117-118	310	50.56 (50.53)	2.90 (2.92)	13.51 (13.55)	310[M <sup>+</sup> ], 312[M <sup>2+</sup> ], 314[M <sup>4+</sup> ]
6	4-F	C <sub>13</sub> H <sub>9</sub> ClFN <sub>3</sub> O <sub>2</sub>	120	93	121-122	294	53.17 (53.17)	3.06 (3.09)	14.29 (14.31)	294[M <sup>+</sup> ], 298[M <sup>2+</sup> ], 312[M <sup>4+</sup> ]
7	4-OCH <sub>3</sub>	C <sub>13</sub> H <sub>12</sub> ClN <sub>3</sub> O <sub>3</sub>	120	95	117-118	306	55.04 (55.01)	3.92 (3.96)	13.71 (13.74)	306[M <sup>+</sup> ], 308[M <sup>2+</sup> ]
8	4-CH <sub>3</sub>	C <sub>13</sub> H <sub>12</sub> ClN <sub>3</sub> O <sub>2</sub>	120	94	124-125	290	58.06 (58.04)	4.13 (4.17)	14.58 (14.50)	290[M <sup>+</sup> ], 292[M <sup>2+</sup> ]
9	3-NO <sub>2</sub>	C <sub>13</sub> H <sub>9</sub> ClN <sub>4</sub> O <sub>4</sub>	120	91	113-114	230	48.71 (48.69)	2.79 (2.83)	17.43 (17.47)	230[M <sup>+</sup> ], 232[M <sup>2+</sup> ]
10	4-NO <sub>2</sub>	C <sub>13</sub> H <sub>9</sub> ClN <sub>4</sub> O <sub>4</sub>	120	91	125-126	230	48.70 (48.69)	2.81 (2.83)	17.44 (17.47)	230[M <sup>+</sup> ], 232[M <sup>2+</sup> ]

**Table 2.** The infrared and NMR spectral data of synthesized 1-(3-chloro-4-nitrophenyl)-2-(3-substitutedbenzylidene) hydrazines

Entry	X	IR (ν, cm <sup>-1</sup> )			<sup>1</sup> H NMR (δ, ppm)			<sup>13</sup> C NMR (δ, ppm)		
		C=N	NH	CH (1H, s)	NH (1H, s)	Ar-H (m)	X	CH	Ar-C	X
1	H	1543.05	3300.20	7.706	7.943	7.065-7.983 (8H)	---	145.39	114.23- 154.38	---
2	3-Br	1523.76	3331.07	7.841	7.590	7.125-7.935 (7H)	---	148.84	115.02- 156.45	---

3	4-Br	1544.98	3294.42	7.822	7.571	7.203-7.925 (7H)	---	147.80	114.23- 155.67	---
4	3-Cl	1539.20	3309.85	7.973	7.934	7.312-7.901 (7H)	---	147.75	114.95- 156.23	---
5	4-Cl	1544.98	3300.20	7.945	7.720	7.526-7.896 (7H)	---	149.43	115.38- 155.90	---
6	3-F	1537.27	3311.78	7.949	7.844	7.462-7.759 (7H)	---	147.85	113.29- 155.08	---
7	4-OCH <sub>3</sub>	1517.98	3325.28	7.930	7.720	7.401-7.852 (7H)	3.675	149.40	113.11- 155.23	62.35
8	3-CH <sub>3</sub>	1546.91	3304.06	7.939	7.738	7.415-7.725 (7H)	2.364	143.42	113.28- 156.21	24.35
9	3-NO <sub>2</sub>	1527.62	3296.35	8.279	7.997	7.502-7.854 (7H)	---	147.78	115.36- 152.69	---
10	4-NO <sub>2</sub>	1527.62	3300.20	7.939	7.720	7.512-7.862 (7H)	---	145.57	115.97- 153.68	---

### 3. RESULTS AND DISCUSSION

#### 3. 1. Infrared Spectral study

The effect of substituents on the infrared spectral group frequencies ( $\nu$ ,  $\text{cm}^{-1}$ ) of hydrazines are very limited. Thirunarayanan et al., [33], Vijayakumar et al., [34] and Rajarajan et al. [36] have studied the effects of substituents. In the present investigation, the author have studied the effect of substituents on the infrared spectral group frequencies ( $\nu$ ,

$\text{cm}^{-1}$ ) of 1-(3-chloro-4-nitrophenyl)-2-(3-substituted benzylidene) hydrazines using Hammett substituent constants with single and multi-regression analysis. Infrared spectral correlations, the Hammett equation was employed as,

$$\nu = \rho\sigma + \nu_0 \quad \dots (1)$$

where  $\nu_0$  is the frequency of the parent compound.

The characteristic infrared frequencies ( $\nu$ ,  $\text{cm}^{-1}$ ) of synthesized hydrazines are NH and C=N. The absorption frequencies of NH and C=N stretching falls in the range of 3290-3340 and 1510-1550  $\text{cm}^{-1}$  for the synthesized hydrazine derivatives. The observed frequencies of NH and C=N ( $\nu$ ,  $\text{cm}^{-1}$ ) stretches of present investigation was presented in **Table 2**. These values are correlated with Hammett substituent constants, F and R parameters using single and multi-regression analysis [33,34,36,37]. The results of statistical analysis is presented in **Table 3**.

**Table 3.** Results of statistical analysis of IR spectral frequencies  $\nu_{\text{CN}}$  and  $\nu_{\text{NH}}$  ( $\text{cm}^{-1}$ ) and chemical shifts ( $\delta$ , ppm) of NH and CH=N protons and carbons of 1-(3-chloro-4-nitro phenyl)-2-(substituted benzylidene) hydrazines with Hammett  $\sigma$ ,  $\sigma^+$ ,  $\sigma_I$ ,  $\sigma_R$  constants, F and R parameters.

Freq.	Constt.	r	I	$\rho$	s	n	Correlated derivatives
Infrared spectral correlations							
$\nu_{\text{CN}}$ ( $\text{cm}^{-1}$ )	$\sigma$	0.901	1536.90	-5.742	10.71	8	H, 4-Br, 3-Cl, 4-Cl, 3-F, 3-CH <sub>3</sub> , 3-NO <sub>2</sub> , 4-NO <sub>2</sub>
	$\sigma^+$	0.906	1535.56	-1.322	10.88	8	H, 4-Br, 3-Cl, 4-Cl, 3-F, 3-CH <sub>3</sub> , 3-NO <sub>2</sub> , 4-NO <sub>2</sub>
	$\sigma_I$	0.839	1544.83	-16.562	11.36	10	H, 3-Br, 4-Br, 3-Cl, 4-Cl, 3-F, 4-OCH <sub>3</sub> , 3-CH <sub>3</sub> , 3-NO <sub>2</sub> , 4-NO <sub>2</sub>
	$\sigma_R$	0.805	1535.67	2.252	10.89	10	H, 3-Br, 4-Br, 3-Cl, 4-Cl, 3-F, 4-OCH <sub>3</sub> , 3-CH <sub>3</sub> , 3-NO <sub>2</sub> , 4-NO <sub>2</sub>
	F	0.836	1541.29	-14.449	10.17	10	H, 3-Br, 4-Br, 3-Cl, 4-Cl, 3-F, 4-OCH <sub>3</sub> , 3-CH <sub>3</sub> , 3-NO <sub>2</sub> , 4-NO <sub>2</sub>
	R	0.810	1536.14	4.253	10.85	10	H, 3-Br, 4-Br, 3-Cl, 4-Cl, 3-F, 4-OCH <sub>3</sub> , 3-CH <sub>3</sub> , 3-NO <sub>2</sub> , 4-NO <sub>2</sub>
$\nu_{\text{NH}}$ ( $\text{cm}^{-1}$ )	$\sigma$	0.903	3310.39	-11.211	12.42	9	H, 4-Br, 3-Cl, 4-Cl, 3-F, 4-OCH <sub>3</sub> , 3-CH <sub>3</sub> , 3-NO <sub>2</sub> , 4-NO <sub>2</sub>
	$\sigma^+$	0.933	3308.68	-7.683	12.31	9	H, 4-Br, 3-Cl, 4-Cl, 3-F, 4-OCH <sub>3</sub> , 3-CH <sub>3</sub> , 3-NO <sub>2</sub> , 4-NO <sub>2</sub>

	$\sigma_I$	0.805	3308.38	-2.650	13.03	10	H, 3-Br, 4-Br, 3-Cl, 4-Cl, 3-F, 4-OCH <sub>3</sub> , 3-CH <sub>3</sub> , 3-NO <sub>2</sub> , 4-NO <sub>2</sub>
	$\sigma_R$	0.905	3302.88	-33.235	10.80	9	H, 4-Br, 3-Cl, 4-Cl, 3-F, 4-OCH <sub>3</sub> , 3-CH <sub>3</sub> , 3-NO <sub>2</sub> , 4-NO <sub>2</sub>
	F	0.800	3307.50	-0.394	13.04	10	H, 3-Br, 4-Br, 3-Cl, 4-Cl, 3-F, 4-OCH <sub>3</sub> , 3-CH <sub>3</sub> , 3-NO <sub>2</sub> , 4-NO <sub>2</sub>
	R	0.905	3301.80	-29.159	10.88	9	H, 4-Br, 3-Cl, 4-Cl, 3-F, 4-OCH <sub>3</sub> , 3-CH <sub>3</sub> , 3-NO <sub>2</sub> , 4-NO <sub>2</sub>
<sup>1</sup> H NMR spectral correlations							
$\delta_{CH}$ (ppm)	$\sigma$	0.805	7.872	0.219	0.13	10	H, 3-Br, 4-Br, 3-Cl, 4-Cl, 3-F, 4-OCH <sub>3</sub> , 3-CH <sub>3</sub> , 3-NO <sub>2</sub> , 4-NO <sub>2</sub>
	$\sigma^+$	0.802	7.918	0.078	0.14	10	H, 3-Br, 4-Br, 3-Cl, 4-Cl, 3-F, 4-OCH <sub>3</sub> , 3-CH <sub>3</sub> , 3-NO <sub>2</sub> , 4-NO <sub>2</sub>
	$\sigma_I$	0.851	7.810	0.310	0.13	10	H, 3-Br, 4-Br, 3-Cl, 4-Cl, 3-F, 4-OCH <sub>3</sub> , 3-CH <sub>3</sub> , 3-NO <sub>2</sub> , 4-NO <sub>2</sub>
	$\sigma_R$	0.825	7.958	0.170	0.15	10	H, 3-Br, 4-Br, 3-Cl, 4-Cl, 3-F, 4-OCH <sub>3</sub> , 3-CH <sub>3</sub> , 3-NO <sub>2</sub> , 4-NO <sub>2</sub>
	F	0.805	7.812	0.290	0.13	10	H, 3-Br, 4-Br, 3-Cl, 4-Cl, 3-F, 4-OCH <sub>3</sub> , 3-CH <sub>3</sub> , 3-NO <sub>2</sub> , 4-NO <sub>2</sub>
	R	0.821	7.956	0.128	0.15	10	H, 3-Br, 4-Br, 3-Cl, 4-Cl, 3-F, 4-OCH <sub>3</sub> , 3-CH <sub>3</sub> , 3-NO <sub>2</sub> , 4-NO <sub>2</sub>
$\delta_{NH}$ (ppm)	$\sigma$	0.908	7.785	0.709	0.15	7	H, 3-Cl, 3-F, 4-OCH <sub>3</sub> , 3-CH <sub>3</sub> , 3-NO <sub>2</sub> , 4-NO <sub>2</sub>
	$\sigma^+$	0.915	7.770	0.041	0.15	7	H, 3-Cl, 3-F, 4-OCH <sub>3</sub> , 3-CH <sub>3</sub> , 3-NO <sub>2</sub> , 4-NO <sub>2</sub>
	$\sigma_I$	0.903	7.786	0.023	0.15	8	4-Br, 3-Cl, 4-Cl, 3-F, 4-OCH <sub>3</sub> , 3-CH <sub>3</sub> , 3-NO <sub>2</sub> , 4-NO <sub>2</sub>
	$\sigma_R$	0.822	7.798	0.157	0.16	10	H, 3-Br, 4-Br, 3-Cl, 4-Cl, 3-F, 4-OCH <sub>3</sub> , 3-CH <sub>3</sub> , 3-NO <sub>2</sub> , 4-NO <sub>2</sub>
	F	0.802	7.770	0.005	0.10	10	H, 3-Br, 4-Br, 3-Cl, 4-Cl, 3-F, 4-OCH <sub>3</sub> , 3-CH <sub>3</sub> , 3-NO <sub>2</sub> , 4-NO <sub>2</sub>

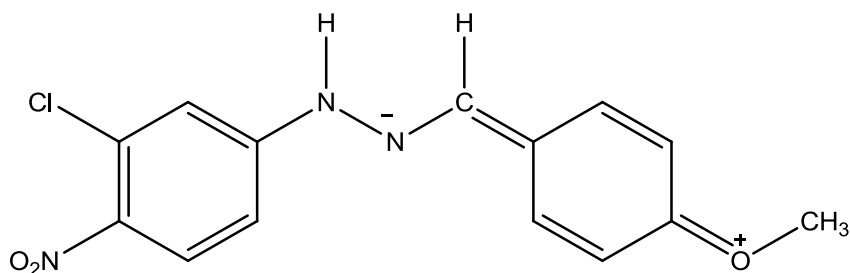
	R	815	7.808	0.196	0.18	10	H, 3-Br, 4-Br, 3-Cl, 4-Cl, 3-F, 4-OCH <sub>3</sub> , 3-CH <sub>3</sub> , 3-NO <sub>2</sub> , 4-NO <sub>2</sub>
<sup>13</sup> C NMR spectral correlations							
$\delta_{CH}$ (ppm)	$\sigma$	0.905	146.95	4.356	2.41	9	H, 3-Br, 4-Br, 3-Cl, 4-Cl, 3-F, 3-CH <sub>3</sub> , 3-NO <sub>2</sub> , 4-NO <sub>2</sub>
	$\sigma^+$	0.904	147.70	2.514	2.49	9	H, 3-Br, 4-Br, 3-Cl, 4-Cl, 3-F, 3-CH <sub>3</sub> , 3-NO <sub>2</sub> , 4-NO <sub>2</sub>
	$\sigma_I$	0.907	144.93	8.167	1.94	10	H, 3-Br, 4-Br, 3-Cl, 4-Cl, 3-F, 4-OCH <sub>3</sub> , 3-CH <sub>3</sub> , 3-NO <sub>2</sub> , 4-NO <sub>2</sub>
	$\sigma_R$	0.811	148.33	1.450	2.84	10	H, 3-Br, 4-Br, 3-Cl, 4-Cl, 3-F, 4-OCH <sub>3</sub> , 3-CH <sub>3</sub> , 3-NO <sub>2</sub> , 4-NO <sub>2</sub>
	F	0.906	145.35	6.675	2.18	8	H, 3-Br, 4-Br, 3-Cl, 4-Cl, 4-OCH <sub>3</sub> , 3-CH <sub>3</sub> , 4-NO <sub>2</sub>
	R	0.812	148.40	1.378	2.84	10	H, 3-Br, 4-Br, 3-Cl, 4-Cl, 3-F, 4-OCH <sub>3</sub> , 3-CH <sub>3</sub> , 3-NO <sub>2</sub> , 4-NO <sub>2</sub>

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

From the Table 2, the Hammett  $\sigma$ ,  $\sigma^+$  constants correlated satisfactorily with C=N stretches of 1-(3-chloro-4-nitrophenyl)-2-(substituted benzylidene) hydrazines except 3-Br and 4-OCH<sub>3</sub> substituents. If these substituted hydrazines stretches include, the correlation was reduced considerably. The remaining Hammett  $\sigma_I$ ,  $\sigma_R$  constants, F and R parameters gave poor correlations. The inductive and resonance effects were absent for prediction of effect of substituent on the C=N stretches of hydrazines. All correlations gave negative  $\rho$  values except resonance component. This implies that the electron donating substituents predicts the substituent effect on the frequencies. The failure in correlation was due to the inability of prediction of substituent electronic effects, weak inductive, field and resonance on the stretches associated with the resonance-conjugative structure as illustrated in **Figure 1**.

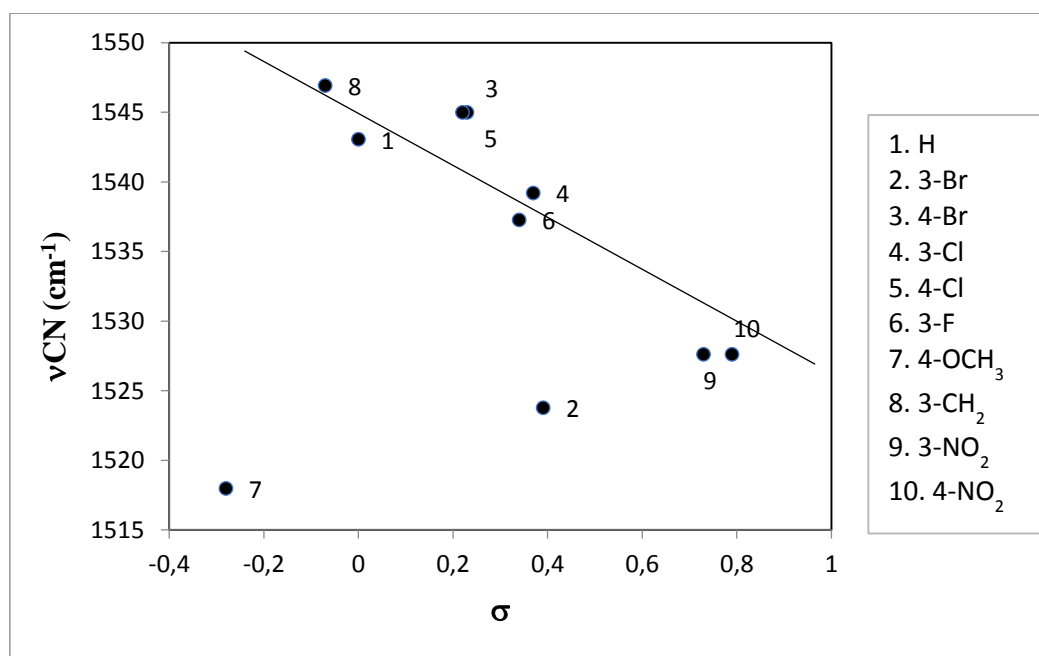
The correlation of NH stretches of 1-(3-chloro-4-nitrophenyl)-2-(substituted benzylidene) hydrazines produced satisfactory correlation coefficients with Hammett  $\sigma$ ,  $\sigma^+$  constants excluding 3-Br substituent. The poor correlation was observed for the remaining Hammett  $\sigma_I$ ,  $\sigma_R$  constants, F and R parameters with NH stretches of prepared hydrazines. All correlations gave negative  $\rho$  values except. This implies that the electron donating substituents predicts the substituent effect on the frequencies. The reason for obtaining poor correlation was stated earlier and associated with the resonance-conjugative structure as shown in **Figure 1**. Satisfactory correlation plots are shown in **Figures 2-5**.



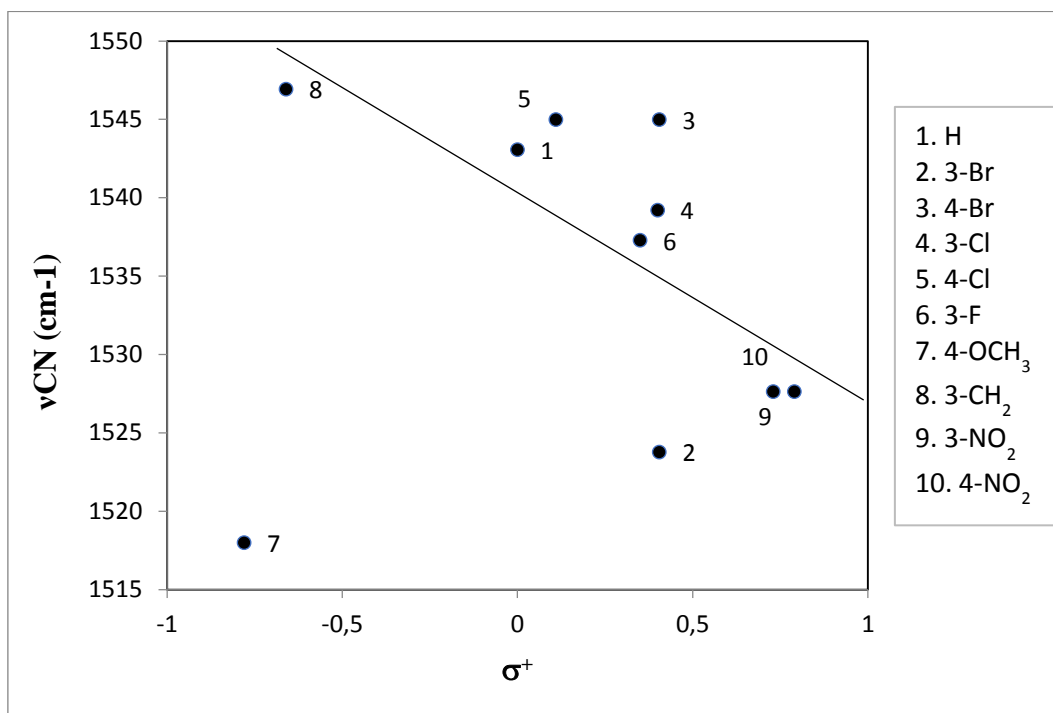


**Figure 1.** The resonance-conjugative structure of 1-(3-chloro-4-nitrophenyl)-2-(4-methoxy benzylidene) hydrazine

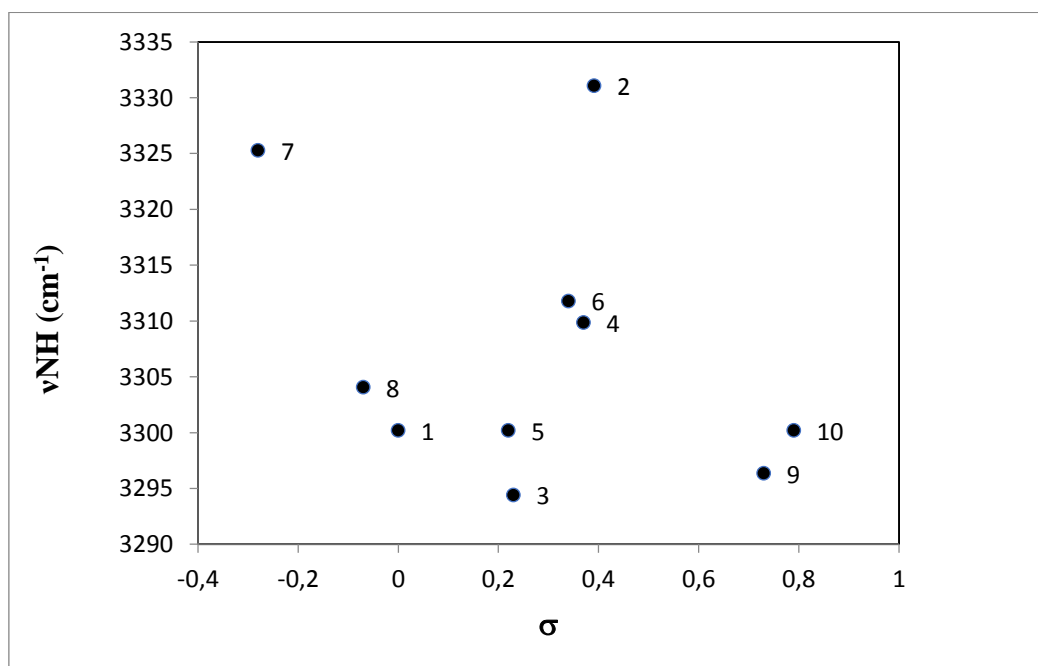
The correlation of NH stretches of 1-(3-chloro-4-nitrophenyl)-2-(substituted benzylidene) hydrazines produced satisfactory correlation coefficients with Hammett  $\sigma$ ,  $\sigma^+$  constants excluding 3-Br substituent. The poor correlation was observed for the remaining Hammett  $\sigma_I$ ,  $\sigma_R$  constants, F and R parameters with NH stretches of prepared hydrazines. All correlations gave negative  $\rho$  values except. This implies that the electron donating substituents predicts the substituent effect on the frequencies. The reason for obtaining poor correlation was stated earlier and associated with the resonance-conjugative structure as shown in **Figure 1**. Satisfactory correlation plots are shown in **Figures 2-5**.



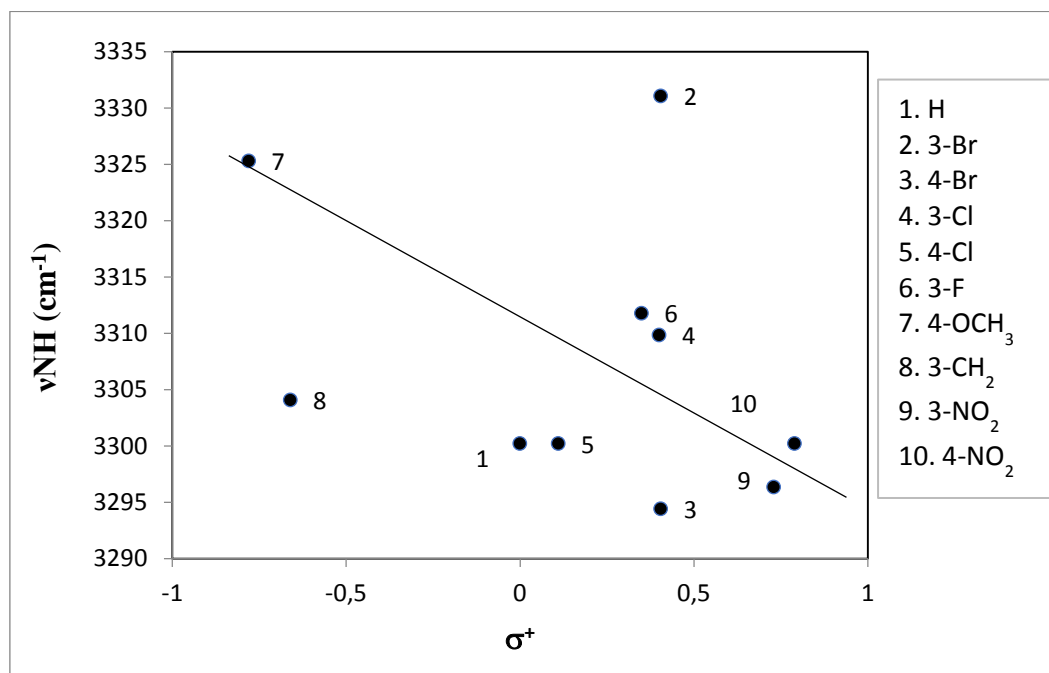
**Figure 2.** The plot of  $\nu_{C=N}$  ( $\text{cm}^{-1}$ ) of 1-(3-chloro-4-nitrophenyl)-2-(substituted benzylidene) hydrazines with  $\sigma$ .



**Figure 3.** The plot of  $\nu_{C=N}$  (cm<sup>-1</sup>) of 1-(3-chloro-4-nitrophenyl)-2-(substituted benzylidene) hydrazines with  $\sigma^+$ .



**Figure 4.** The plot of  $\nu_{NH}$  (cm<sup>-1</sup>) of 1-(3-chloro-4-nitrophenyl)-2-(substituted benzylidene) hydrazines with  $\sigma$ .



**Figure 5.** The plot of  $\nu_{\text{NH}}$  ( $\text{cm}^{-1}$ ) of 1-(3-chloro-4-nitrophenyl)-2-(substituted benzylidene) hydrazines with  $\sigma^+$ .

Some of the single regression analysis produced poor correlations for C=N and NH stretches of 1-(3-chloro-4-nitrophenyl)-2-(substituted benzylidene) hydrazines. When these correlation was worthwhile, while seeking in multi-regression analysis with Field, Resonance and Swain-Lupton's constants [37]. They produced satisfactory correlations. The obtained multi-regression equations are presented in (2-5).

$$\nu_{\text{CH}=\text{N}} = 1542.57(\pm 7.207) - 16.936(\pm 1.437)\sigma_{\text{I}} + 4.488(\pm 1.719)\sigma_{\text{R}} \quad \dots(2)$$

(R = 0.940, n = 10, P > 90%)

$$\nu_{\text{CH}=\text{N}} = 1541.85(\pm 7.130) - 14.241(\pm 5.764)F + 3.265(\pm 1.467)R \quad \dots(3)$$

(R = 0.937, n = 10, P > 90%)

$$\nu_{\text{NH}} = 3302.70(\pm 7.435) - 2.257(\pm 1.464)\sigma_{\text{I}} - 29.315(\pm 1.598)\sigma_{\text{R}} \quad \dots(4)$$

(R = 0.958, n = 10, P > 95%)

$$\nu_{\text{NH}} = 3305.81(\pm 3.711) - 4.714(\pm 2.317)F - 14.717(\pm 1.378)R \quad \dots(5)$$

(R = 0.956, n = 10, P > 95%)

### 3. 2. NMR Spectral study

#### 3. 2. 1. $^1\text{H}$ NMR Spectral correlation

The  $^1\text{H}$  NMR Spectral chemical shifts ( $\delta$ , ppm) of synthesized hydrazines was subjected to analyses the effect of substituents on the chemical shifts for predicting the reactivity using Hammett equation. In NMR spectral correlation, the Hammett equation was employed as (6)

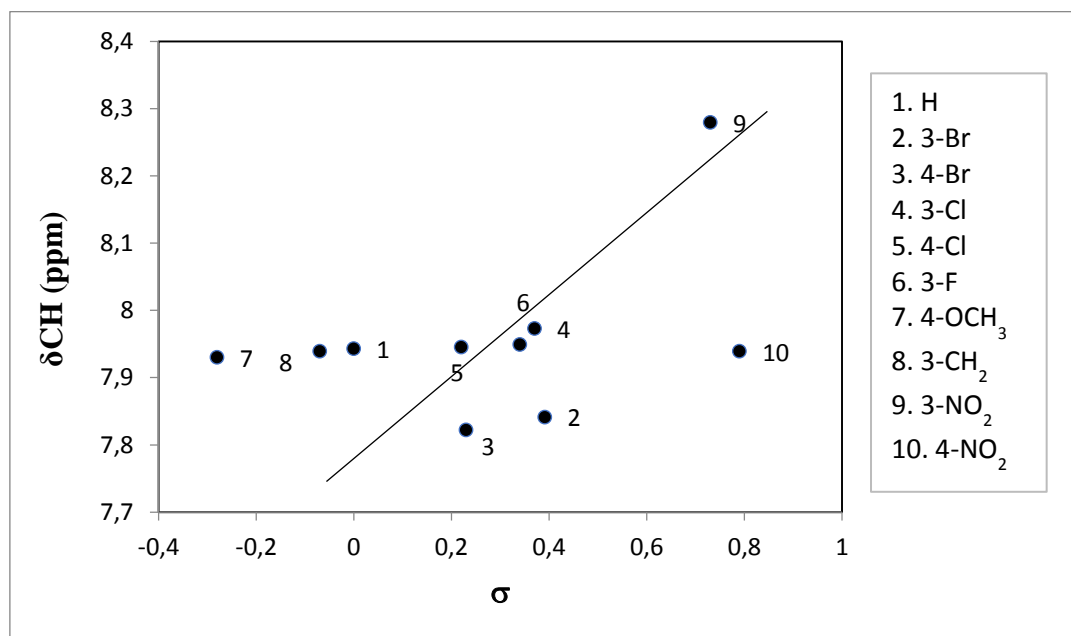
$$\delta = \delta_0 + \rho\sigma \quad \dots (6)$$

where  $\delta_0$  is the chemical shift of un substituted system.

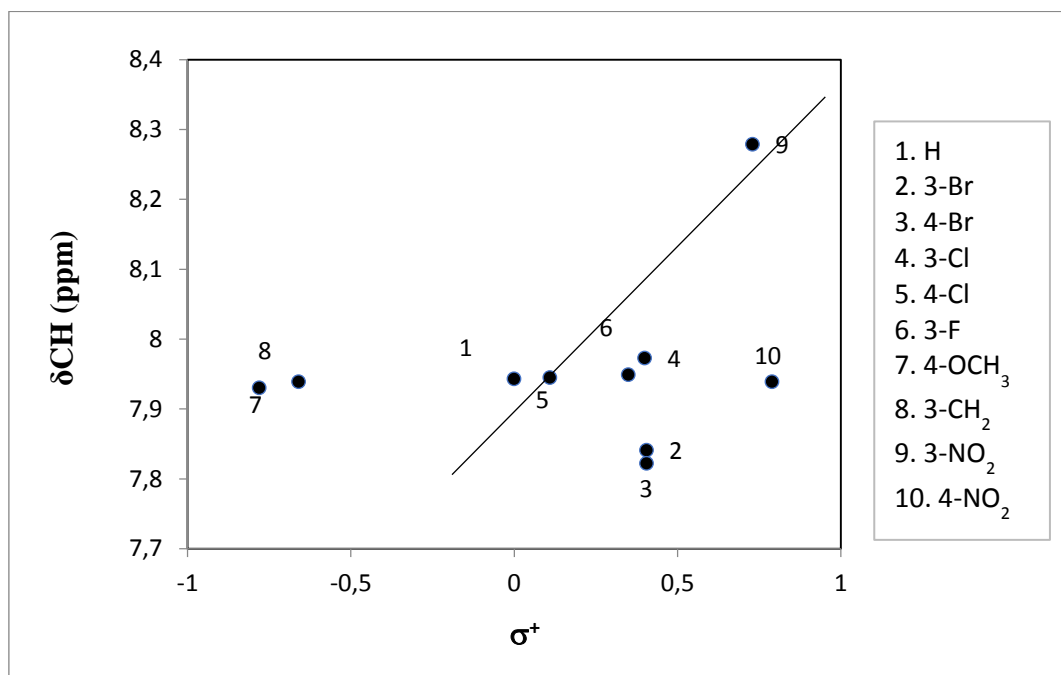
In the present investigation, the proton chemical shifts ( $\delta$ , ppm) of NH and CH=N of synthesized hydrazine derivatives were assigned. These protons gave singlet at 7.5 to 8 ppm range. The assigned chemical shifts ( $\delta$ , ppm) of NH and CH=N 1-(3-chloro-4-nitrophenyl)-2-(substituted benzylidene) hydrazines were presented in **Table 2**. These chemical shifts were correlated with Hammett substituent constants, F and R parameter using single and multi-regression analysis [33,34,36,37] The results of statistical analysis was presented in **Table 3**.

From Table 3, the correlation of CH=N chemical shifts ( $\delta$ , ppm) of 1-(3-chloro-4-nitrophenyl)-2-(substituted benzylidene) hydrazines with Hammett  $\sigma$ ,  $\sigma^+$ ,  $\sigma_I$ ,  $\sigma_R$  constants, F and R parameters gave poor correlations. Even though the inductive and resonance effect of substituents also fails for predicting the reactivity on the CH=N proton chemical shifts. This failure was already stated the reason and along with the resonance conjugative structure as illustrated in **Figure 1**. All correlation gave positive  $\rho$  values. This means that the normal substituent effect operates in all systems.

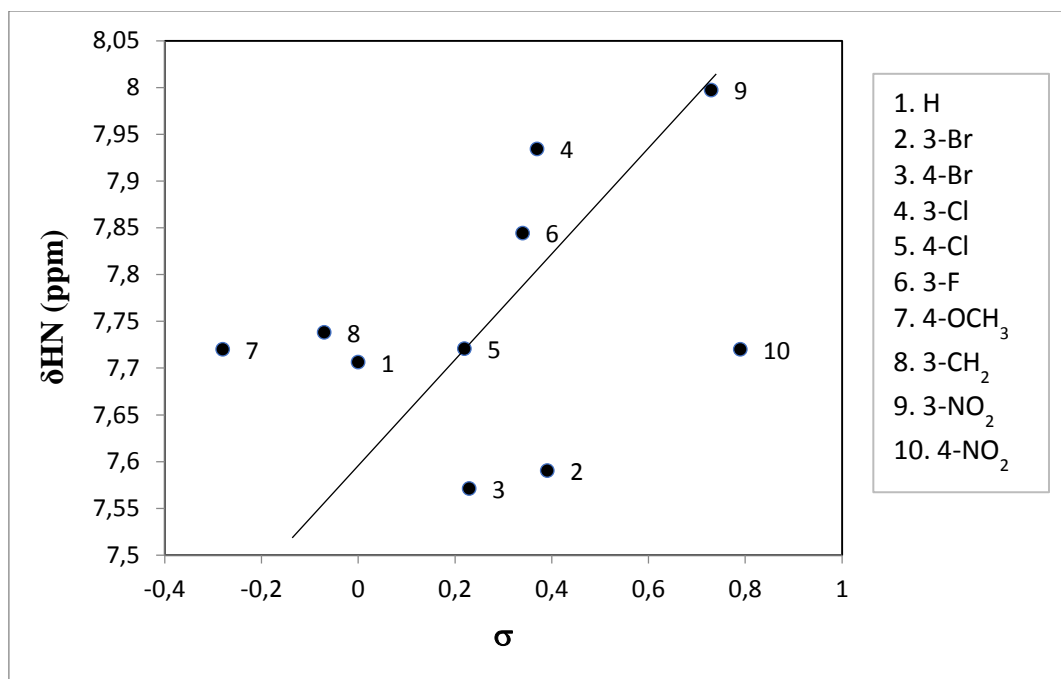
A satisfactory correlation was observed for the regression NH chemical shifts ( $\delta$ , ppm) of 1-(3-chloro-4-nitrophenyl)-2-(substituted benzylidene) hydrazines with Hammett  $\sigma$ ,  $\sigma^+$  and  $\sigma_I$  constants excluding H, 3-Br, 4-Br and 4-Cl substituents. During If they will included in the correlations, the correlation coefficients was reduced considerably. The  $\sigma_R$  constants, F and R parameters were fail in correlation. This is due to the resonance and field effects of the substituents were unable to find the reactivity through the magnetic shielding and it is associated with the resonance-conjugative structure as illustrated in **Figure 1**. All correlations gave positive  $\rho$  values. This means that the normal substituent effect operates in all systems. Some of Hammett plots are shown in **Figures 6-9**.



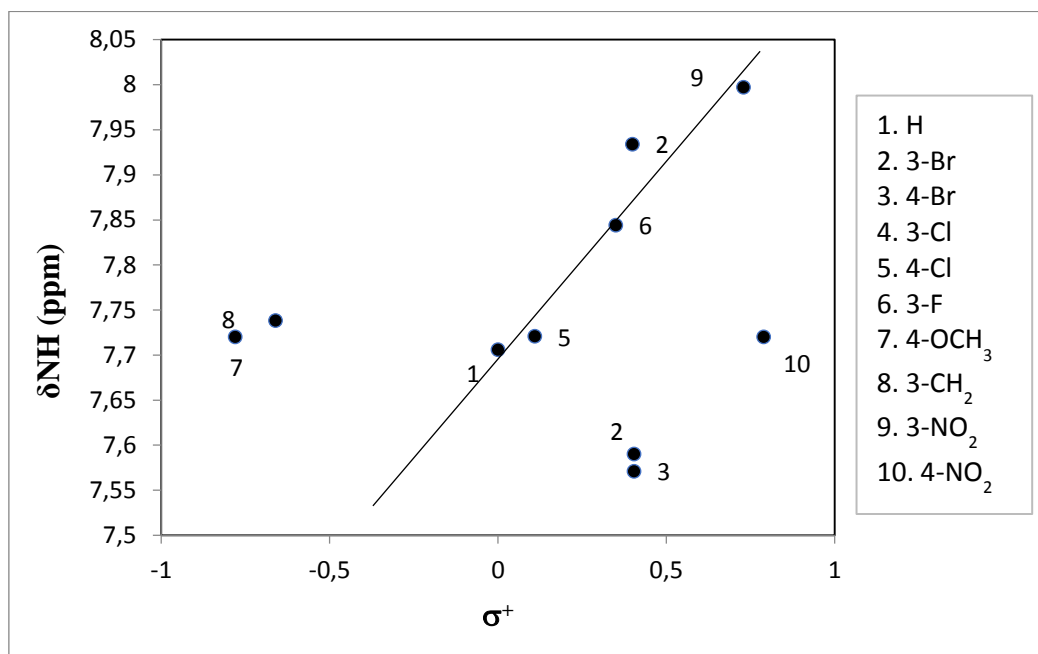
**Figure 6.** Plot of CH=N chemical shifts ( $\delta$ , ppm) of 1-(3-chloro-4-nitrophenyl)-2-(substituted benzylidene)hydrazines Vs  $\sigma$



**Figure 7.** Plot of CH=N chemical shifts ( $\delta$ , ppm) of 1-(3-chloro-4-nitrophenyl)-2-(substituted benzylidene) hydrazines Vs  $\sigma^+$



**Figure 8.** Plot of NH chemical shifts ( $\delta$ , ppm) of 1-(3-chloro-4-nitrophenyl)-2-(substituted benzylidene) hydrazines Vs  $\sigma$



**Figure 9.** Plot of NH chemical shifts ( $\delta$ , ppm) of 1-(3-chloro-4-nitrophenyl)-2-(substituted benzylidene) hydrazines Vs  $\sigma^+$

All correlation of CH=N chemical shifts ( $\delta$ , ppm) of 1-(3-chloro-4-nitrophenyl)-2-(substituted benzylidene) hydrazines with Hammett  $\sigma$ ,  $\sigma^+$ ,  $\sigma_I$ ,  $\sigma_R$  constants, F and R parameters gave poor correlation coefficients. Some of the correlations of NH chemical shifts ( $\delta$ , ppm) of 1-(3-chloro-4-nitrophenyl)-2-(substituted benzylidene) hydrazines with Hammett substituent constant, F and R parameters were failed. They are worthwhile when seeking to multi-regressions of these data with Swain-Lupton's parameters [37]. All multi-regression analysis of CH=N and NH chemical shifts ( $\delta$ , ppm) of 1-(3-chloro-4-nitrophenyl)-2-(substituted benzylidene) hydrazines gave satisfactory correlations. The obtained multi-regression equations are given in (7-10).

$$\delta\text{CH=N (ppm)} = 7.833 (\pm 0.093) + 0.298 (\pm 0.189)\sigma_I + 0.135 (\pm 0.017)\sigma_R \quad \dots(7)$$

(R = 0.955, n = 10, P > 95%)

$$\delta\text{CH=N (ppm)} = 7.836 (\pm 0.090) + 0.300 (\pm 0.170)F + 0.496 (\pm 0.081)R \quad \dots(8)$$

(R = 0.956, n = 10, P > 95%)

$$\delta\text{NH (ppm)} = 7.818 (\pm 0.109) + 0.037 (\pm 0.002)\sigma_I + 0.161 (\pm 0.002)\sigma_R \quad \dots(9)$$

(R = 0.923, n = 10, P > 95%)

$$\delta\text{NH (ppm)} = 7.802 (\pm 0.105) + 0.016 (\pm 0.002)F + 0.166 (\pm 0.021)R \quad \dots(10)$$

(R = 0.927, n = 10, P > 95%)

### 3. 2. 2. <sup>13</sup>C NMR Spectral correlation

The <sup>13</sup>C NMR spectral chemical shifts ( $\delta$ , ppm) of C=N of synthesized hydrazines was subjected to analyses the effect of substituents on the chemical shifts for predicting the reactivity using Hammett equation. In the present investigation, the carbon chemical shifts

( $\delta$ , ppm) CH=N of synthesized hydrazine derivatives were assigned. These carbon chemical shifts falls in the range of 145-150 pp. The assigned chemical shifts ( $\delta$ , ppm) of CH=N of 1-(3-chloro-4-nitrophenyl)-2-(substituted benzylidene) hydrazines were presented in **Table 2**. These chemical shifts were correlated with Hammett substituent constants, F and R parameter using single and multi-regression analysis [33,34,36,37]. The results of statistical analysis were presented in **Table 3**. From Table 3, There is satisfactory correlation was observed for the  $^{13}\text{C}$  NMR spectral chemical shifts ( $\delta$ , ppm) of CH=N of 1-(3-chloro-4-nitrophenyl)-2-(substituted benzylidene) hydrazines with Hammett  $\sigma$ ,  $\sigma^+$ ,  $\sigma_1$  constants and F parameters excluding 3-F, 4-OCH<sub>3</sub> and 3-NO<sub>2</sub> substituents. When they will be included in the correlations, they reduced the correlation coefficient considerably. The Hammett  $\sigma_R$  constant R parameters were failed in correlations. This is due to the reasons stated earlier and associated with the resonance-conjugative structure as illustrated in **Figure 1**. All correlations gave positive  $\rho$  values. This implied that there is normal substituent effects operates in all systems. A satisfactory single regression plots are shown in Figures 10 and 11.

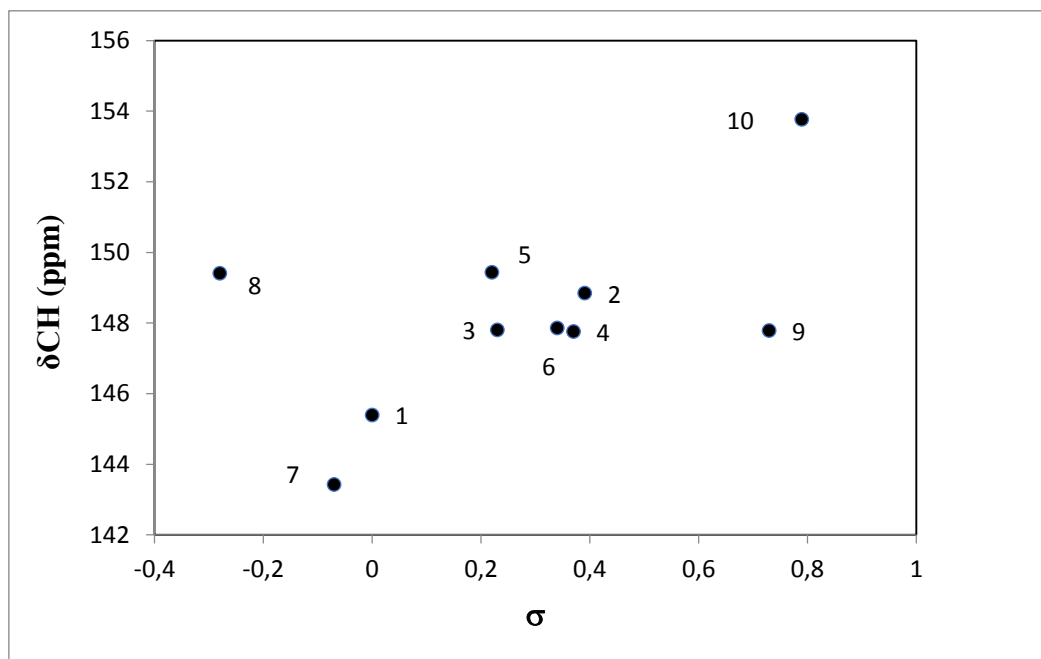
Some of the single parameter correlations were failed for producing satisfactory correlation coefficients. When these are produced satisfactory correlations in multi-parameter correlations.<sup>123</sup>. All multi-regression analysis of CH=N chemical shifts ( $\delta$ , ppm) of 1-(3-chloro-4-nitrophenyl)-2-(substituted benzylidene) hydrazines gave satisfactory correlations. The obtained multi-regression equations are given in (11 and 12).

$$\delta\text{CH=N (ppm)} = 145.02(\pm 1.387) + 8.126(\pm 2.173)\sigma_1 + 0.507(\pm 0.036)\sigma_R \quad \dots(11)$$

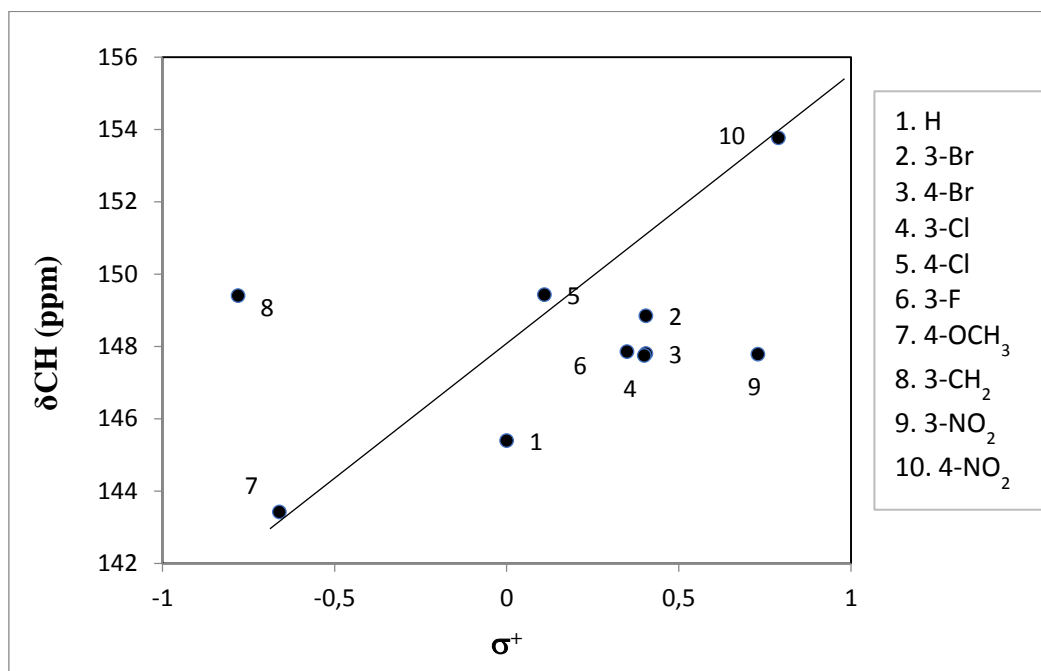
(R = 0.974, n = 10, P > 95%)

$$\delta\text{CH=N (ppm)} = 145.66(\pm 1.505) + 6.878(\pm 2.956)F + 1.856(\pm 0.308)R \quad \dots(12)$$

(R = 0.966, n = 10, P > 95%)



**Figure 10.** The plot of  $\delta\text{CH}$  of 1-(3-chloro-4-nitrophenyl)-2-(substituted benzylidene) hydrazines Vs  $\sigma$



**Figure 11.** Plot of  $\delta_{CH}$  of 1-(3-chloro-4-nitrophenyl)-2-(substituted benzylidene) hydrazines Vs  $\sigma^+$

#### 4. CONCLUSIONS

About ten 1-(3-chloro-4-nitrophenyl)-2-(substituted benzylidene) hydrazine derivatives have been synthesized and characterized by their physical constants, microanalysis, infrared, NMR and Mass spectroscopic data. The assigned infrared characteristic stretches ( $\nu$ ,  $\text{cm}^{-1}$ ) of CN and NH of and the NMR proton and carbon chemical shifts ( $\delta$ , ppm) NH and  $\text{CH}=\text{N}$  of 1-(3-chloro-4-nitrophenyl)-2-(substituted benzylidene) hydrazines were correlated with Hammett  $\sigma$ ,  $\sigma^+$ ,  $\sigma_I$ ,  $\sigma_R$  constants, F and R parameters. From the results of statistical analysis, the effect of substituent on the spectral data was studied. In infrared spectral correlations, the Hammett  $\sigma$ ,  $\sigma^+$ ,  $\sigma_R$  constants and R parameters gave satisfactory correlations along with negative  $\rho$  values. In NMR spectral correlations, Hammett  $\sigma$ ,  $\sigma^+$ ,  $\sigma_I$  constants and F parameters gave satisfactory correlations along with positive  $\rho$  values. From the signs of  $\rho$  values, infrared correlations depends with electron donating substituents and NMR correlations depends with electron withdrawing substituents.

#### References

- [1] G. Rajitha, N. Saideepa and P. Praneetha, *Indian J. Chem.* 50 (2011) 729.
- [2] R. Vijayakumar, M. Rajarajan, S. Balaji, V. Manikandan, R. Senbagam, G. Vanangamudi and G. Thirunarayanan, *World Scientific News* 3 (2015) 81.



- [3] M. Rajarajan, R. Senbagam, R. Vijayakumar, S. Balaji, R. Manikandan, G. Vanangamudi and G. Thirunarayanan, *Indian J. Chem.* 55B (2016) 197.
- [4] M. Rajarajan, R. Senbagam, R. Vijayakumar, V. Manikandan, S. Balaji, G. Vanangamudi and G. Thirunarayanan. *World Scientific News* 3 (2015) 155.
- [5] M. Rajarajan, S. Balaji, R. Vijayakumar, R. Senbagam, V. Manikandan, G. Vanangamudi and G. Thirunarayanan, *JSM Chem.* 4(1) (2016) 1021.
- [6] I. Asri, M. H. S. A. Hamid, A. H. Mirza, M. A. Alia and M.zaul Karimb, *Acta Cryst.* E70 (2014) o633.
- [7] J. P. Jasinski, A. N. Braley, C. S. C. Kumar, H. S. Yathirajan and A. N. Mayekarc, *Acta Cryst.* E67(2011) o1200.
- [8] M. González, Y. Alvarado, J. Restrepo and J. B. Colmenárez, *Avances en Química* 8(3) (2013) 167.
- [9] R. Kumar, M. S. Yar, S. Chaturvedi and A. Srivastava, *Pharm. Tech.* 5 (2013) 1844.
- [10] S. Rollas and Ş. G. Küçükgülzel, *Molecules* 12 (2007) 1910.
- [11] S. R. Desai, U. V. Laddi, R. S. Bennur and S. C. Bennur, *Indian J. Pharm. Sci.* 2 (2011) 478.
- [12] R. Dua and S. K. Srivatsava, *Int. J. Pharm. Bio. Sci.* 6 (2010) 1.
- [13] A. E. H. M. Hussein, A. A. E. Adasy, I. S. A. Hafi, E. A. Ishak, E. H. Gawish and M. S. A. E. Gaby, *J. App. Pharm.* 6 (2014) 296
- [14] B. N. Prasanna Kumar, K. N. Mohanaa, L. Malleshab and N. D. Rekhac, *Curr. Chem. Lett.* 2(2013) 176
- [15] B. Parashar, S. Bharadwaj, V. K. Sharma and P. B. Punjabi, *Der Pharma Chemica* 2(2) (2010) 229
- [16] D. S. Salunkhe and P. B. Piste. *Int. J. Pharm. Sci. Res.* 5 (2014) 666
- [17] K. Padmini, P. Jaya Preethi, M. Divya, P. Rohini, M. Lohita, K. Swetha and P. Kaladar, *Int. J. Pharm. Res. Rev.* 2 (2013) 43.
- [18] M. Cacic, M. Trkovnik, F. Cacic and E. H. Schon, *Molecules* 11(2016) 134
- [19] M. Rudrapal and B. De, *Int. Res. J. Pure Appl. Chem.* 3 (2013) 232
- [20] M. S. Saini, R. Singh, J. Dwivedi and Aran kumar, *Int. J. Sci. Nature* 3 (2012) 925
- [21] M. Asif, *Int. J. Adv. Chem.* 2 (2014) 85
- [22] O. Prakash, K. Hussain, D. K. Aneja, C. Sharma and K. R. Aneja, *Org. Med. Chem. Lett.* 1, 1, 2011, DOI: <http://www.orgmedchemlett.com/content/1/1/1>
- [23] S. Nain, A. Sharma, H. Singh and S. Paliwal, *J. Biomed. Ther. Sci.* 2 (2015) 1
- [24] S. M. Patil, N. K. Tadge, P. S. Hargunani, V. J. Kadam and M. P. Toraskar, *Indo Am. J. Pharm. Res.* 4 (2014) 3188
- [25] K. Sheeja Devi, Y. Swapna, S. Bhagya Lakshmi, M. Suchitra, G. Sivakumar, K. Srinivasulu, *A. J. Res. Pharm. Sci. Biotech.* 1 (2013) 1.

- [26] M. Asif and A. Husain, *Journal of Applied Chemistry*, 2013, Article ID 247203, 7 pages, DOI: <http://dx.doi.org/10.1155/2013/247203>
- [27] M. Molnar and M. Cacic, *Croat. J. Food Sci. Technol.* 4 (2012) 54.
- [28] A. Almasirad, S. S. Sadr and A. Shafiee, *Iranian J. Pharm. Res.* 10 (2011) 727.
- [29] G. H. Elgemeie, N. M. Fathy, A. B. Farag, O. M. E. Badry, G. S. Hassan, K. M. Amin and F. Halaweish, *Med. Chem.* 2014, 4:4; DOI: <http://dx.doi.org/10.4172/2161-0444.1000171>
- [30] L. P. Lv, X. F. Zhou, H. B. Shic, J. R. Gaoa and W. X. Hu, *J. Chem. Res.* 38 (2014) 368
- [31] A. M. Mocanu, C. Cernatescu, *Sci. Res.* 8 (2007) 437
- [32] K. Eloho, M. Demurtas, A. Deplano, A. N. Mfopa, A. Murgia, A. Maxia, V. Onnis, and P. Caboni, *J. Agric. Food Chem.* 63 (2015) 9970
- [33] G. Thirunarayanan, V. Manikandan, R. Arulkumaran, M. Rajarajan, V. Sathiyendiran, *World Scientific News* 69 (2017) 201
- [34] R. Vijayakumar, M. Rajarajan, R. Senbagam, V. Manikandan, S. Balaji, G. Vanangamudi, G. Thirunarayanan. *Malasiyan J Fund. Appl. Sci.* 12(4) (2016) 130.
- [35] V. Ananthi, K. Rajalakshmi, I. Muthuvel, G. Thirunarayanan, *Annales - UMCS*, Accepted and in Press, 2017
- [36] M. Rajarajan, R. Vijayakumar, S. Balaji, R. Senbagam, V. Manikandan, G. Vanangamudi, and G. Thirunarayanan, *Orbital: The electronic J. Chem.* 8(5) (2016) 288
- [37] Swain C. G., Lupton E. C., *J. Am. Chem. Soc.* 90 (1968) 4328

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