



Spectral studies and antimicrobial activities of some (*E*)-*N*-(substituted benzylidene)-2,6- diisopropylanilines

G. Thirunarayanan^{1,*}, V. Manikandan², R. Aarulkumaran², R. Rarajan², V. Usha³

¹Department of Chemistry, Annamalai University, Annamalainagar - 608002, India

²PG and Research Department of Chemistry, Government Arts College, C-Mutlur - 608 102, India

³Department of Chemistry, University College of Engineering, Panruti - 607 106, India

E-mail address: drgrtnaryanan@gmail.com ,
thirunarayanan.g.10313@annamalaiuniversity.ac.in

ABSTRACT

A series of Schiff's base compounds were synthesized from 2,6-di(propan-2-yl) aniline with substituted aromatic aldehydes. The structures of all the synthesized compounds were characterized by physical constants, IR and NMR spectroscopic techniques. All the observed IR frequencies $\nu_{C=N}$ (cm^{-1}), NMR δ (ppm) of C-H & C=N chemical shifts have been correlated with Hammett substituent constants and *F* and *R* parameters using single and multi-linear regression analyses in order to study the effect of substituents on these spectral data has been studied. All the synthesized Schiff's base compounds were screened for their antimicrobial activity by disc diffusion method.

Keywords: Synthesis, 2,6-di(propan-2-yl)aniline, Schiff base, Spectral correlation and Antimicrobial studies

1. INTRODUCTION

Azomethines are generally known as Schiff's bases, to honour Hugo Schiff, who had synthesized such compounds earlier. Schiff's bases have been synthesized condensation

products of primary amines with carbonyl compounds such as aldehyde and ketones. Schiff's bases are characterized by the $-N=CH-$ (imine) group which finds importance in elucidating the mechanism of trans amination and racemization reactions in biological systems [1,2]. Schiff base compounds have been reported to play very important role in many microbial and chemical reactions, due to the presence of the imine group. Schiff's base compounds are generally bi- or tri- dentate ligands capable of forming very stable complexes with transition metals [3].

Schiff's bases have been attracted considerable attention of organic chemists due to their significant biological activities like anticancer [4], antitumor [5], anti-inflammatory agents [6], insecticidal [7], antibacterial [8], anti-tuberculosis [9], antimicrobial [10], anticonvulsant [11] activity. They are also used as versatile components in nucleophilic addition with organometallic reagents [12] and in cycloaddition reactions [13,14]. Schiff bases have been reported to play very important role in many biological and chemical reactions, due to the presence of the imine linkage. Schiff bases are generally bi or tri dentate ligands capable of forming very stable complexes with transition metals [15,16]. Schiff bases derived from aromatic amines and aromatic aldehydes are reported to be involved in the study of asymmetric catalysis [17], magnetic properties [18], phototropism [19], and binding with DNA [20].

Schiff's base are well known intermediates for the preparation of azetidinone [21], thiazolidinone [22], oxadiazoles [23], formazone [24], metal complexes [25-27] and many other derivatives [28,29]. Schiff bases have played an important role in the development of the chemical industry and biochemistry owing to their applications and their biological activities. They are also used as intermediates in the synthesis of medicinal products such as amino alkyl pyridine [30-32] and imines [33].

In recent years, correlation analysis has been applied by chemists [34-36] for assessing the effect of substituents of Schiff's bases through Hammett spectral correlations. Literature survey shows that there is a little information available regarding the study of IR and NMR spectral correlation and antimicrobial activities of substituted N-benzylidene-2,6-diisopropylanilines. Hence the authors have taken efforts for synthesizing N-benzylidene-2,6-diisopropylaniline compounds and studying the effect of substituents through the spectral data as well as their antimicrobial activities

2. EXPERIMENTAL

2.1. General

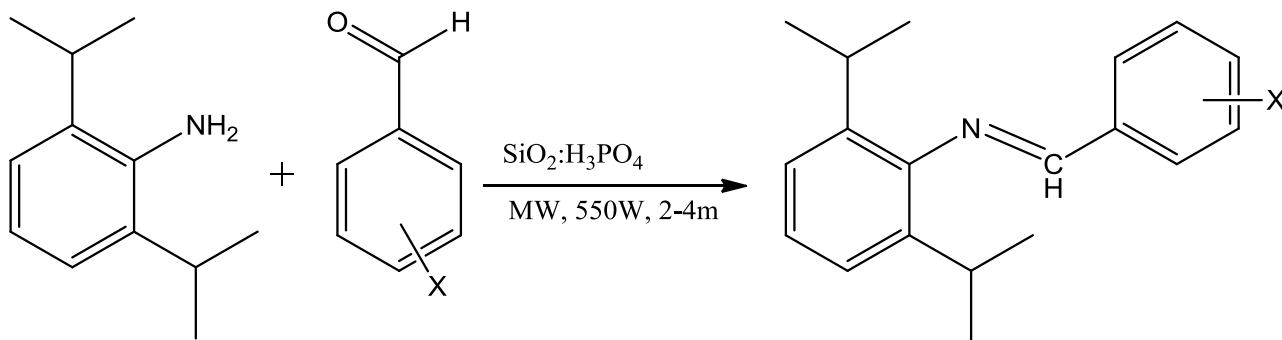
All chemicals were used in this investigation were purchased from Sigma-Aldrich and Merck Chemical companies. Mettler FP51 melting point apparatus was used for determining the melting point of all synthesized imines in open glass capillaries and are uncorrected. The AVATAR-300 Fourier transform spectrophotometer was used for recording infrared spectra (KBr, $4000-400\text{ cm}^{-1}$) of all imines in KBr disc. The Bruker AV400 series type NMR spectrometer was utilized for recording NMR spectra of all imines, operating at 400 MHz for ^1H and 100 MHz for ^{13}C spectra in CDCl_3 solvent using TMS as internal standard. Mass spectra of all synthesized imines were recorded on SHIMADZU mass spectrometer using chemical ionization technique.

2. 2. Synthesis of (*E*)-N-(substituted benzylidene)-2,6-diisopropylanilines

An appropriate equi-molar quantities of 2,6-diisopropylanilines (2 mmol), benzaldehydes (2 mmol) and 0.2 g of SiO₂-H₃PO₄ were taken in a 50 mL beaker, closed with the lid. This mixture was subjected to microwave irradiation for 2-4 minutes at 550 W (Scheme 1) (Samsung, Microwave Oven, 100-700 W). After completion of the reaction, dichloromethane (20 mL) was added, followed by simple filtration. The solution was concentrated and purified by re-crystallization. The synthesized imines were characterized by their physical constants, IR, ¹H and ¹³C NMR and Mass spectral data. The physical constants, analytical and spectroscopic data of synthesised imines are given in Table 1.

Table 1. The physical constants, analytical and spectroscopic data of synthesized imines.

No	X	M.F.	M.W	m.p (°C)	IR (ν, cm ⁻¹)	NMR (δ, ppm)		
					νCN	¹ H CH	¹³ C, CN	¹³ C, C _{ipso}
1	H	C ₁₉ H ₂₃ N	265	83-84 80[37]	1636.28	8.234	163.75	135.74
2	2-Br	C ₁₉ H ₂₂ BrN	344	98-99	1635.67	8.221	163.68	135.68
3	4-Br	C ₁₉ H ₂₂ BrN	344	116-117	1636.08	8.237	162.97	135.78
4	4-Cl	C ₁₉ H ₂₂ ClN	300	96-98 90[37]	1638.59	8.261	161.38	135.76
5	4-N(CH ₃) ₂	C ₂₁ H ₂₈ N ₂	308	112-113	1635.74	8.206	162.76	134.38
6	4-F	C ₁₉ H ₂₂ FN	283	92-94 88[37]	1648.32	8.196	163.68	136.96
7	3-OCH ₃	C ₂₀ H ₂₅ NO	295	101-102 98[37]	1638.11	8.131	161.97	133.44
8	4-CH ₃	C ₂₀ H ₂₅ N	279	98-99 95[37]	1639.66	8.177	162.29	133.62
9	2-NO ₂	C ₁₉ H ₂₂ N ₂ O ₂	310	115-116	1643.27	8.403	163.77	137.11
10	4-NO ₂	C ₁₉ H ₂₂ N ₂ O ₂	310	140-141 131[37]	1643.70	8.410	163.97	137.26



Scheme 1. Synthesis of (*E*)-*N*-(substituted benzylidene)-2,6-diisopropylanilines.

No	1	2	3	4	5	6	7	8	9	10
X	H	2-Br	4-Br	4-Cl	4-N(CH ₃) ₂	4-F	4-OCH ₃	4-CH ₃	2-NO ₂	4-NO ₂

3. RESULTS AND DISCUSSION

3. 1. Infrared spectral correlation

The assigned infrared frequencies (cm⁻¹) of νC=N of (*E*)-*N*-(substituted benzylidene)-2,6-diisopropylanilines are presented in Table 1.

The measured infrared frequency values are correlated [34-36] with Hammett substituent constants and *F* and *R* parameters using single and multi-linear regression analysis. Hammett equation employed for the correlation analysis, involving the absorption maxima is as shown below in equation (1).

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

where ν_0 is the frequency for the parent member of the series.

The results of statistical analysis of νC=N of (*E*)-*N*-(substituted benzylidene)-2,6-diisopropyl anilines with Hammett substituent constants and *F* and *R* parameters were presented in Table 2. From the Table 2, the correlation of νC=N of (*E*)-*N*-(substituted benzylidene)-2,6-diisopropyl anilines Hammett σ , σ_I and *F* parameters gave satisfactory correlations except 4-F and 4-CH₃ substituents. The Hammett σ^+ , σ_R and *R* parameters gave poor correlations. All the correlations have shown positive ρ values. This indicates the operation of normal substituent effect with respect to IR frequency νC=N(cm⁻¹) values in all substituted (*E*)-*N*-(substituted benzylidene)-2,6-diisopropylanilines. The failure in the correlation was due to the inability and weak polar and resonance effects of the substituents for predicting the reactivity on the νC=N(cm⁻¹) frequencies of all imines. Also this is associated with the resonance-conjugative structure as shown in Figure 1. Some of the single linear plots are shown in Figs. 2-4.

Table 2. The results of statistical analysis of infrared (ν_{CN} , cm^{-1}) and NMR chemical shifts (δ ppm) of (*E*)-*N*-(substituted benzylidene)-2,6-diisopropylanilines with Hammett σ , σ^+ , σ_{I} , σ_{R} and *F* and *R* parameters.

Freq.	Constants	r	I	ρ	s	n	Correlated derivatives
C=N	σ	0.904	1639.04	4.290	4.01	9	H, 2-Br, 4-Br, 4-Cl, 4-N(CH ₃) ₂ , 4-OCH ₃ , 4-CH ₃ , 2-NO ₂ , 4-NO ₂
	σ^+	0.831	1639.58	1.782	4.28	10	H, 2-Br, 4-Br, 4-Cl, 4-N(CH ₃) ₂ , 4-F, 4-OCH ₃ , 4-CH ₃ , 2-NO ₂ , 4-NO ₂
	σ_{I}	0.905	1636.42	8.823	3.87	8	H, 2-Br, 4-Br, 4-Cl, 4-N(CH ₃) ₂ , 4-OCH ₃ , 2-NO ₂ , 4-NO ₂
	σ_{R}	0.813	1639.98	2.398	4.47	10	H, 2-Br, 4-Br, 4-Cl, 4-N(CH ₃) ₂ , 4-F, 4-OCH ₃ , 4-CH ₃ , 2-NO ₂ , 4-NO ₂
	<i>F</i>	0.906	1635.34	1.027	3.29	9	H, 2-Br, 4-Br, 4-Cl, 4-N(CH ₃) ₂ , 4-F, 4-OCH ₃ , 2-NO ₂ , 4-NO ₂
	<i>R</i>	0.815	1640.04	1.854	4.46	10	H, 2-Br, 4-Br, 4-Cl, 4-N(CH ₃) ₂ , 4-F, 4-OCH ₃ , 4-CH ₃ , 2-NO ₂ , 4-NO ₂
CH	σ	0.985	8.227	0.170	0.05	9	H, 2-Br, 4-Br, 4-Cl, 4-F, 4-OCH ₃ , 4-CH ₃ , 2-NO ₂ , 4-NO ₂
	σ^+	0.966	8.249	0.178	0.07	9	H, 2-Br, 4-Br, 4-Cl, 4-F, 4-OCH ₃ , 4-CH ₃ , 2-NO ₂ , 4-NO ₂
	σ_{I}	0.963	8.169	0.222	0.07	7	2-Br, 4-Br, 4-Cl, 4-N(CH ₃) ₂ , 4-OCH ₃ , 2-NO ₂ , 4-NO ₂
	σ_{R}	0.971	8.300	0.285	0.06	10	H, 2-Br, 4-Br, 4-Cl, 4-N(CH ₃) ₂ , 4-F, 4-OCH ₃ , 4-CH ₃ , 2-NO ₂ , 4-NO ₂
	<i>F</i>	0.905	8.175	0.185	0.08	9	H, 2-Br, 4-Br, 4-Cl, 4-N(CH ₃) ₂ , 4-OCH ₃ , 4-CH ₃ , 2-NO ₂ , 4-NO ₂
	<i>R</i>	0.968	8.295	0.177	0.07	9	H, 2-Br, 4-Br, 4-Cl, 4-F, 4-OCH ₃ , 4-CH ₃ , 2-NO ₂ , 4-NO ₂
C=N	σ	0.904	162.91	0.941	0.83	9	H, 2-Br, 4-Br, 4-N(CH ₃) ₂ , 4-F, 4-OCH ₃ , 4-CH ₃ , 2-NO ₂ , 4-NO ₂
	σ^+	0.905	163.03	0.554	0.84	8	H, 2-Br, 4-Br, 4-Cl, 4-F, 4-OCH ₃ , 2-NO ₂ , 4-NO ₂
	σ_{I}	0.903	162.62	1.138	0.89	9	H, 2-Br, 4-Br, 4-N(CH ₃) ₂ , 4-F, 4-OCH ₃ , 4-CH ₃ , 2-NO ₂ , 4-NO ₂
	σ_{R}	0.837	163.27	1.364	0.88	10	H, 2-Br, 4-Br, 4-Cl, 4-N(CH ₃) ₂ , 4-F, 4-OCH ₃ , 4-CH ₃ , 2-NO ₂ , 4-NO ₂
	<i>F</i>	0.938	162.52	1.304	0.77	9	H, 2-Br, 4-Br, 4-N(CH ₃) ₂ , 4-F, 4-OCH ₃ , 4-CH ₃ , 2-NO ₂ , 4-NO ₂

	R	0.838	163.26	1.885	0.89	10	H, 2-Br, 4-Br, 4-Cl, 4-N(CH ₃) ₂ , 4-F, 4-OCH ₃ , 4-CH ₃ , 2-NO ₂ , 4-NO ₂
<i>C_{ipso}</i>	σ	0.908	135.28	2.429	0.61	10	H, 2-Br, 4-Br, 4-Cl, 4-N(CH ₃) ₂ , 4-F, 4-OCH ₃ , 4-CH ₃ , 2-NO ₂ , 4-NO ₂
	σ^+	0.907	135.60	1.302	0.64	9	H, 2-Br, 4-Br, 4-Cl, 4-F, 4-OCH ₃ , 4-CH ₃ , 2-NO ₂ , 4-NO ₂
	σ_I	0.907	134.14	4.068	0.64	10	H, 2-Br, 4-Br, 4-Cl, 4-N(CH ₃) ₂ , 4-F, 4-OCH ₃ , 4-CH ₃ , 2-NO ₂ , 4-NO ₂
	σ_R	0.904	136.07	2.738	0.69	8	H, 2-Br, 4-Br, 4-Cl, 4-N(CH ₃) ₂ , 4-OCH ₃ , 2-NO ₂ , 4-NO ₂
	F	0.907	134.04	4.013	0.64	10	H, 2-Br, 4-Br, 4-Cl, 4-N(CH ₃) ₂ , 4-F, 4-OCH ₃ , 4-CH ₃ , 2-NO ₂ , 4-NO ₂
	R	0.905	136.10	1.980	0.67	10	H, 2-Br, 4-Br, 4-Cl, 4-N(CH ₃) ₂ , 4-F, 4-OCH ₃ , 4-CH ₃ , 2-NO ₂ , 4-NO ₂
r = correlation coefficient; I = intercept; ρ = slope; s = standard deviation; n = number of correlated derivatives							

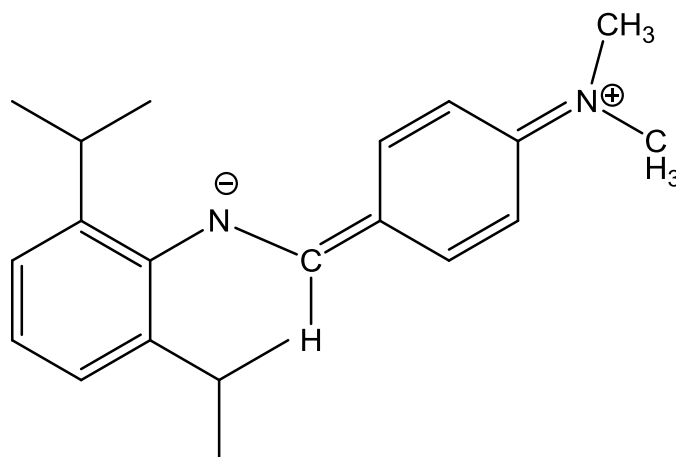


Fig. 1. The Resonance-conjugative structure

Some of the single regressions of (ν_{CN} , cm^{-1}) frequencies of (*E*)-*N*-(substituted benzylidene)-2,6-diisopropylanilines gave poor correlations. While seeking these frequencies in multi-regressions with Swain-Lupton constants [37], they produce satisfactory correlations.

The correlation equations are given in (2 and 3).

$$\nu_{C=N}(\text{cm}^{-1}) = 1636.28(\pm 2.744) + 9.035(\pm 0.540)\sigma_I + 0.493(\pm 0.571)\sigma_R \quad \dots(2)$$

(r = 0.954, n = 10, P > 95%)

$$\nu_{C=N}(\text{cm}^{-1}) = 1635.43(\pm 2.387) + 10.958(\pm 4.522)F + 0.266(\pm 0.034)R \quad \dots(3)$$

(r = 0.968, n = 10, P > 95%)

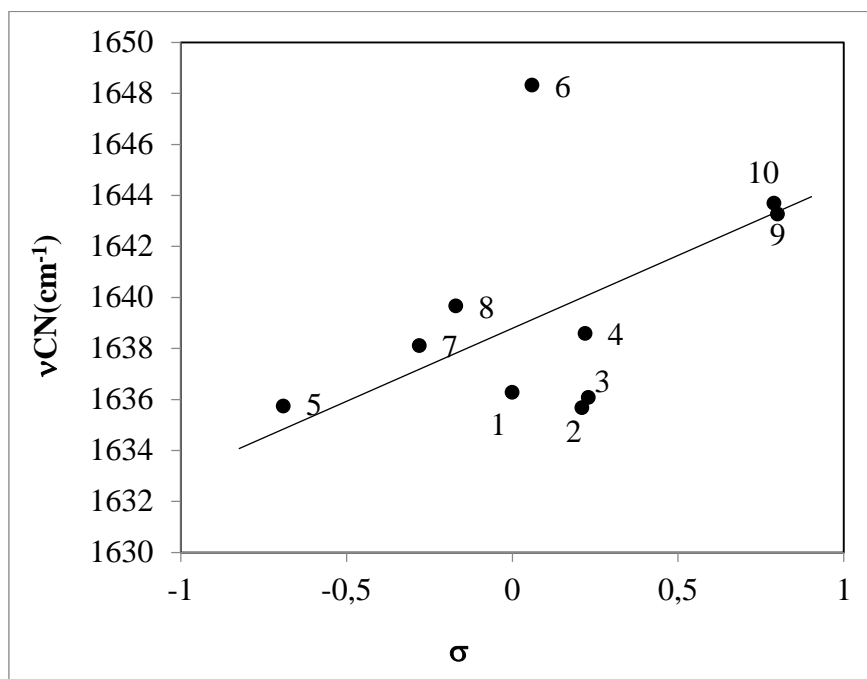


Fig. 2. Plot of ν_{CN} (cm⁻¹) frequencies of (*E*)-*N*-(substituted benzylidene)-2,6-diisopropylanilines Vs σ .

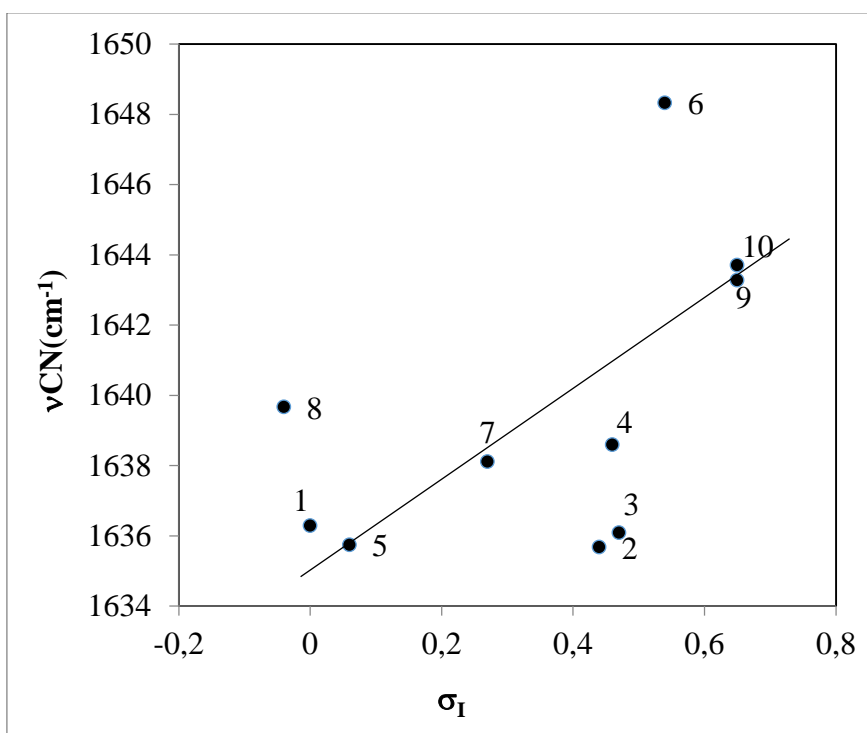


Fig. 3. Plot of ν_{CN} (cm⁻¹) frequencies of (*E*)-*N*-(substituted benzylidene)-2,6-diisopropylanilines Vs σ_1 .

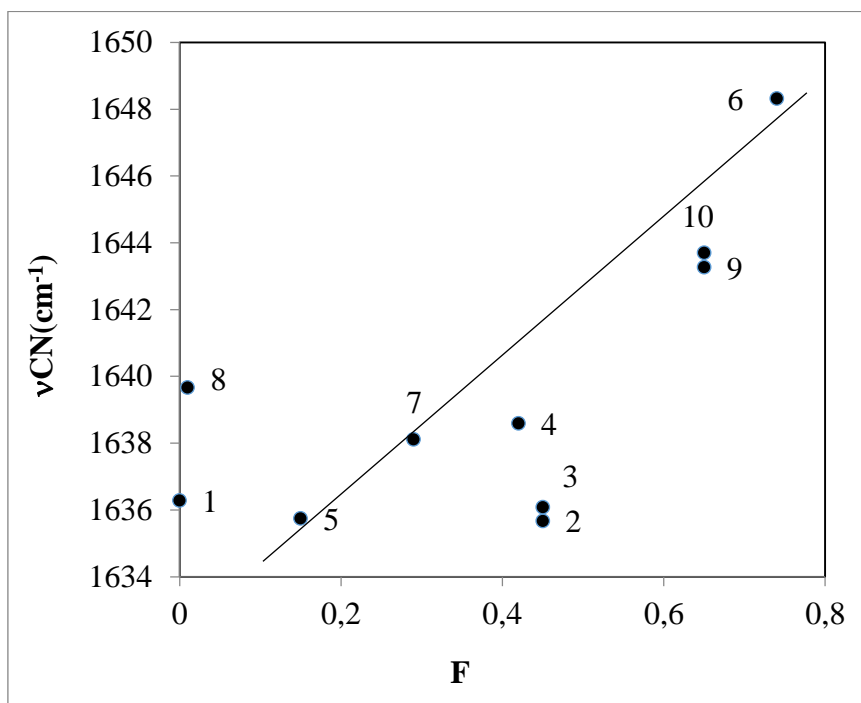


Fig. 4. Plot of ν_{CN} (cm^{-1}) frequencies of (*E*)-*N*-(substituted benzylidene)-2,6-diisopropylanilines Vs *F*.

3. 2. NMR Spectral Correlation

In nuclear magnetic resonance spectra, the ^1H and the ^{13}C chemical shifts (δ) depends on the electronic environment of the nuclei concerned. The assigned chemical shifts (ppm) have been correlated with reactivity parameters using Hammett equation [34-36] in the form of equation (6)

$$\delta = \rho\sigma + \delta_0 \quad \dots(4)$$

where δ_0 is the frequency for the parent member of the series.

3. 2. 1. ^1H NMR spectral correlation

The assigned ^1H chemical shifts (δ , ppm) of $\text{CH}=\text{N}$ protons of (*E*)-*N*-(substituted benzylidene)-2,6-diisopropylanilines are presented in Table 1. These ^1H chemical shifts (δ , ppm) are correlated [34-36] with Hammett substituent constants and *F* and *R* parameters using single and multi-linear regression analysis. The results of statistical analysis is presented in Table 2. From the table 2, the ^1H chemical shifts (δ , ppm) of $\text{CH}=\text{N}$ protons of (*E*)-*N*-(substituted benzylidene)-2,6-diisopropylanilines produced satisfactory correlation except 4- $\text{N}(\text{CH}_3)_2$, 4-F and 4- CH_3 substituents. The Hammett σ constants seems better. All correlations gave positive ρ values. The single parameter correlations are shown in Figs. 5-10. Similarly, the multi-regressions of these chemical shifts (δ , ppm) with Swain-Lupton constants [37] produce satisfactory correlations. The correlation equations are given in (5 and 6).

$$\delta_{\text{CH}}(\text{ppm}) = 8.237(\pm 0.032) + 0.154(\pm 0.065)\sigma_{\text{I}} + 0.240(\pm 0.067)\sigma_{\text{R}} \quad \dots(5)$$

($r = 0.988$, $n = 10$, $P > 95\%$)

$$\delta_{\text{CH}}(\text{ppm}) = 8.234(\pm 0.041) + 0.145(\pm 0.079)F + 0.156(\pm 0.062)R \quad \dots(6)$$

($r = 0.979$, $n = 10$, $P > 95\%$)

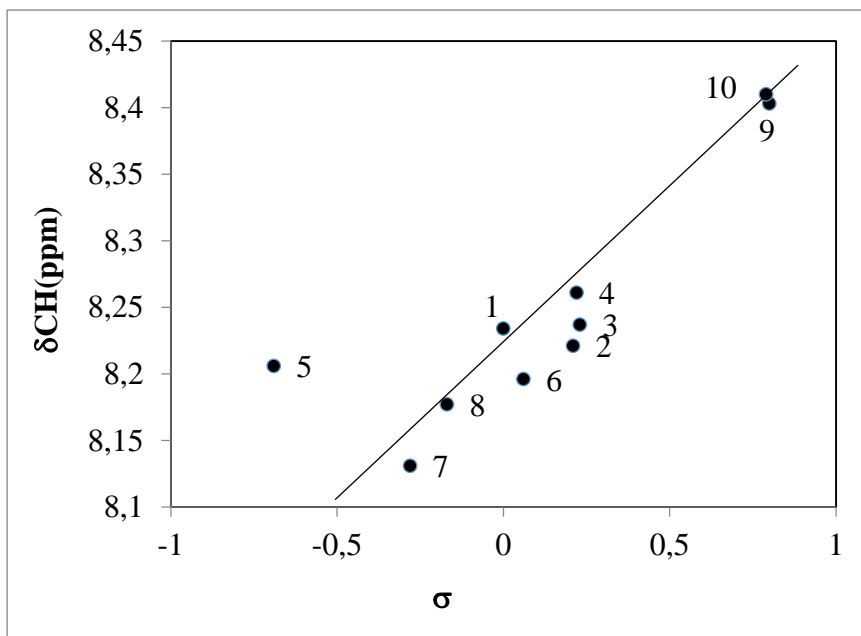


Fig. 5. Plot of ^1H chemical shifts (δ , ppm) of $\text{CH}=\text{N}$ of (*E*)-*N*-(substituted benzylidene)-2,6-diisopropylanilines Vs σ .

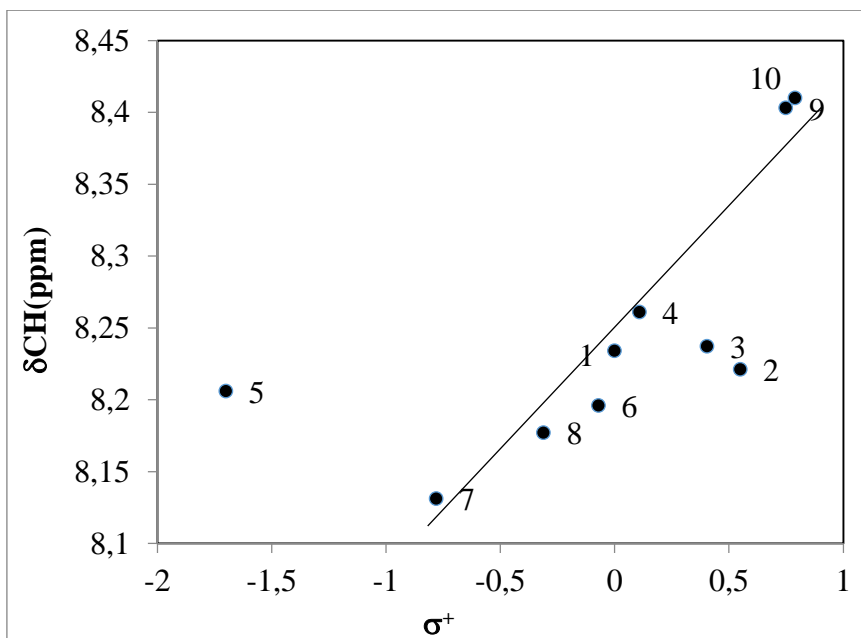


Fig. 6. Plot of ^1H chemical shifts (δ , ppm) of $\text{CH}=\text{N}$ of (*E*)-*N*-(substituted benzylidene)-2,6-diisopropylanilines Vs σ^+ .

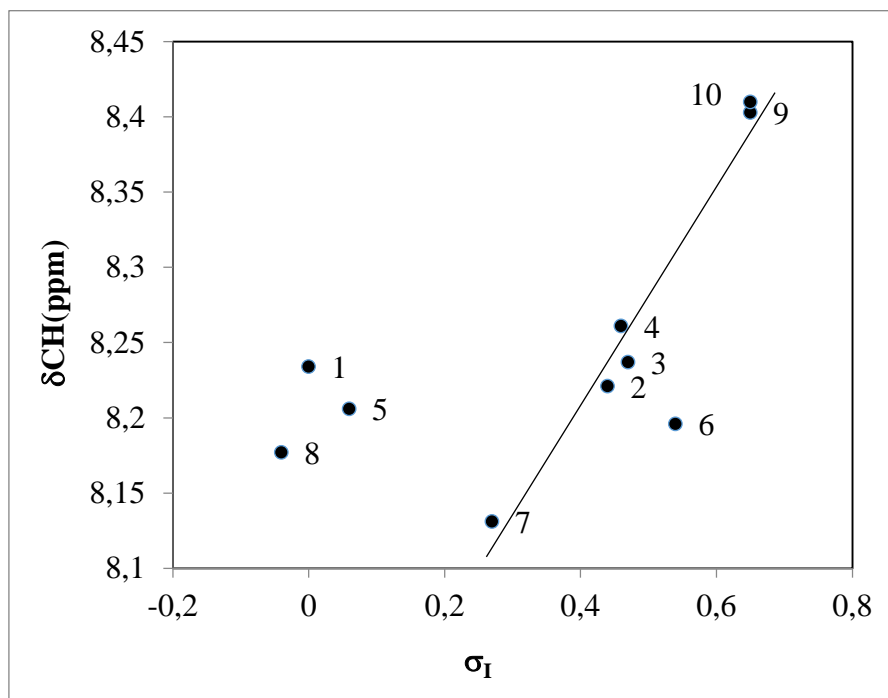


Fig. 7. Plot of ^1H chemical shifts (δ , ppm) of $\text{CH}=\text{N}$ of (*E*)-*N*-(substituted benzylidene)-2,6-diisopropylanilines Vs σ_I .

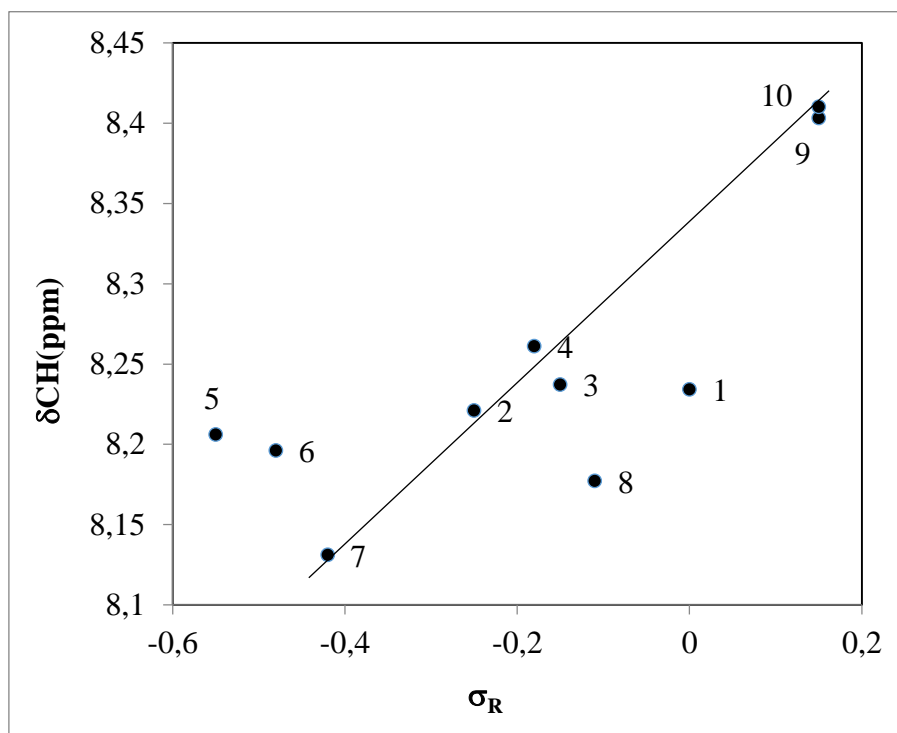


Fig. 8. Plot of ^1H chemical shifts (δ , ppm) of $\text{CH}=\text{N}$ of (*E*)-*N*-(substituted benzylidene)-2,6-diisopropylanilines Vs σ_R .

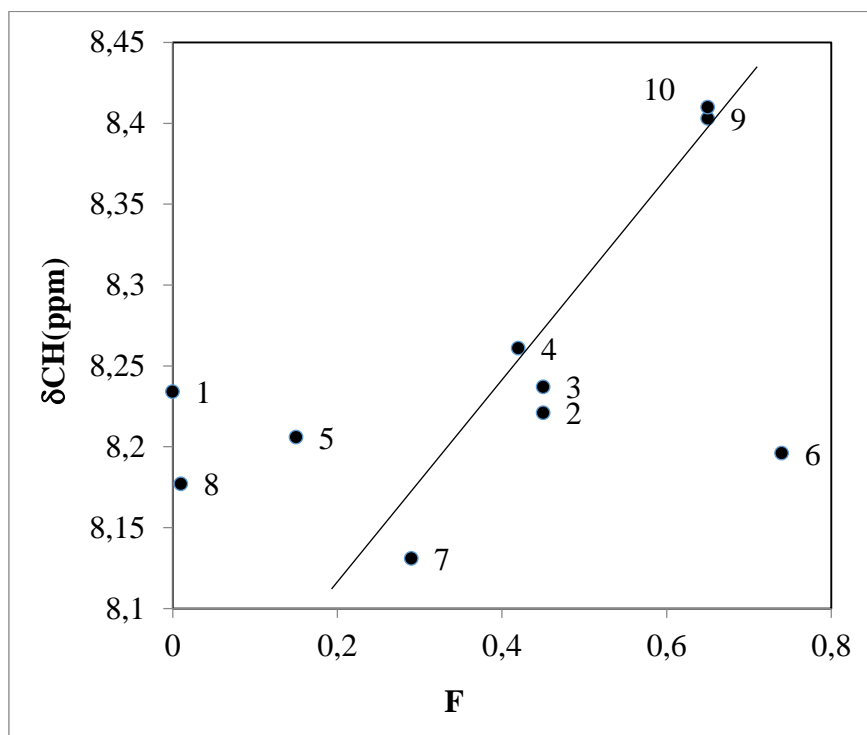


Fig. 9. Plot of ^1H chemical shifts (δ , ppm) of $\text{CH}=\text{N}$ of (*E*)-*N*-(substituted benzylidene)-2,6-diisopropylanilines Vs F.

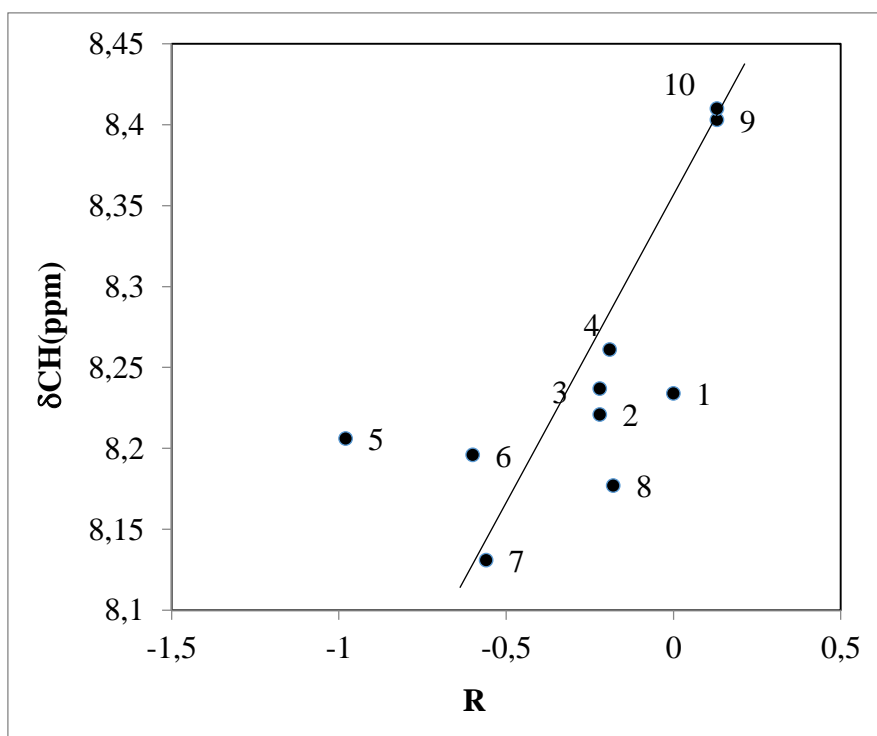


Fig. 10. Plot of ^1H chemical shifts (δ , ppm) of $\text{CH}=\text{N}$ of (*E*)-*N*-(substituted benzylidene)-2,6-diisopropylanilines Vs R.

3. 2. 2. ^{13}C NMR spectral correlation

The assigned ^{13}C chemical shifts (δ , ppm) of CH=N and ipso carbons of (*E*)-N-(substituted benzylidene)-2,6-diisopropylanilines are presented in Table 1. These chemical shifts (δ , ppm) are correlated [34-36] with Hammett substituent constants and *F* and *R* parameters using single and multi-linear regression analysis. The results of statistical analysis are presented in Table 2. From the table 2, the ^{13}C chemical shifts (δ , ppm) of CH=N carbons of (*E*)-N-(substituted benzylidene)-2,6-diisopropylanilines produced satisfactory correlation with Hammett σ_{R} , σ^+ , σ_{I} constant and *F* parameters excluding 4-Cl, 4-N(CH₃)₂, and 4-CH₃ substituents. When these substituents included in the correlations, they reduced the correlation coefficient considerably. The Hammett σ_{R} constant and *R* parameters gave poor correlations. All correlations gave positive ρ values. The failure in correlations is due to the reasons stated earlier and associated with the resonance-conjugative structure as shown in the Figure 1. The single parameter correlations are shown in Figs. 11-14. The failure in single regressions are worthwhile when seeking they are involving the multi-regressions of these chemical shifts (δ , ppm) with Swain-Lupton constants [37] produce satisfactory correlations. The correlation equations are given in (7 and 8).

$$\delta_{\text{CN}} (\text{ppm}) = 162.93(\pm 0.621) + 0.819(\pm 0.012)\sigma_{\text{I}} + 1.102(\pm 0.130)\sigma_{\text{R}} \quad \dots(7)$$

($r = 0.943$, $n = 10$, $P > 90\%$)

$$\delta_{\text{CN}} (\text{ppm}) = 162.78(\pm 0.606) + 1.119(\pm 0.115) F + 0.722(\pm 0.086) R \quad \dots(8)$$

($r = 0.947$, $n = 10$, $P > 90\%$)

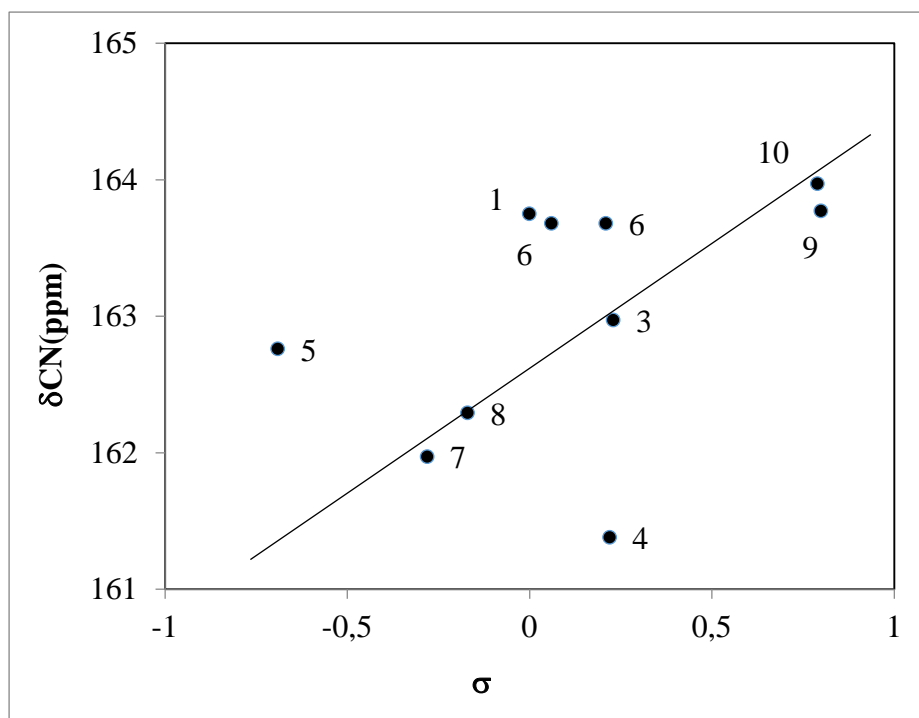


Fig. 11. Plot of ^{13}C chemical shifts (δ , ppm) of C=N of (*E*)-N-(substituted benzylidene)-2,6-diisopropylanilines Vs σ .

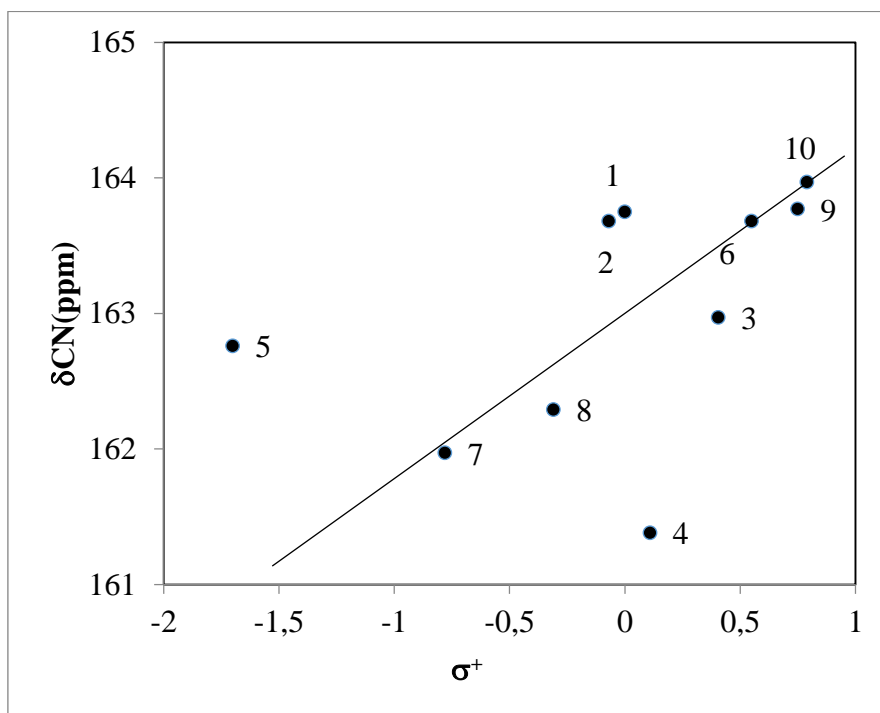


Fig. 12. Plot of ^{13}C chemical shifts (δ , ppm) of C=N of (*E*)-N-(substituted benzylidene)-2,6-diisopropylanilines Vs σ^+ .

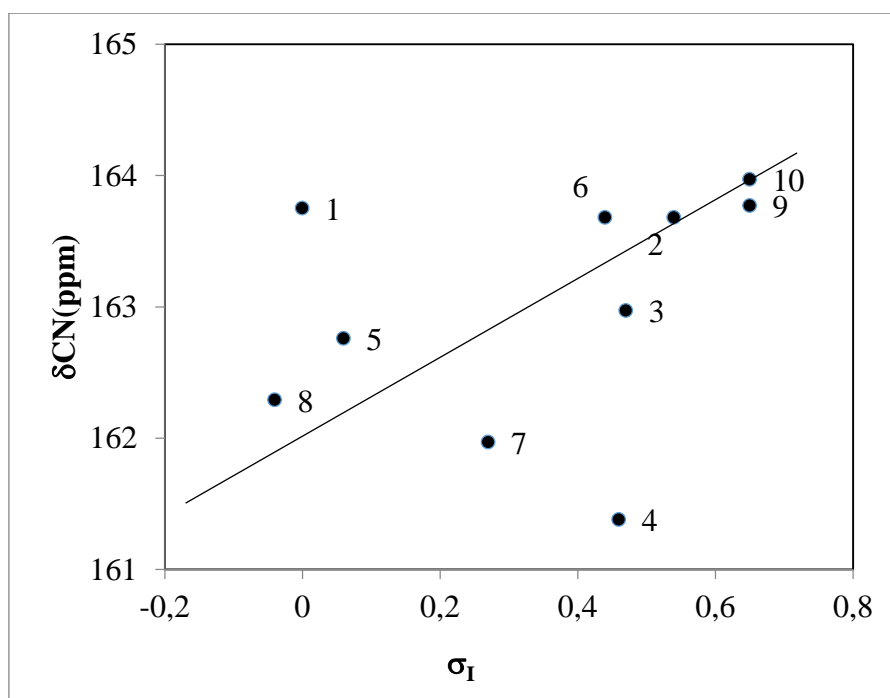


Fig. 13. Plot of ^{13}C chemical shifts (δ , ppm) of C=N of (*E*)-N-(substituted benzylidene)-2,6-diisopropylanilines Vs σ_I .

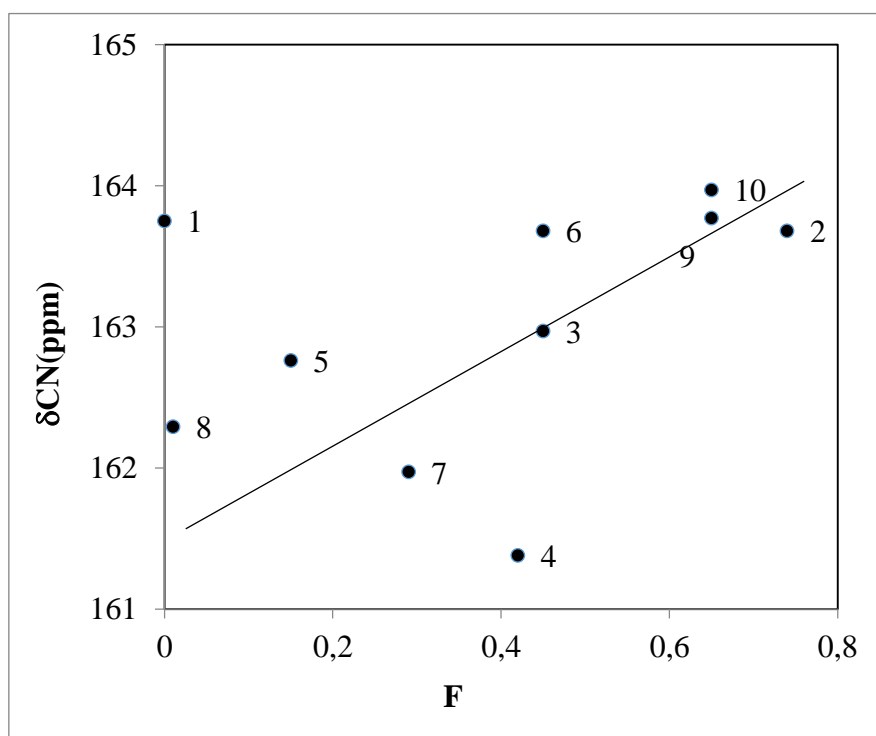


Fig. 14. Plot of ^{13}C chemical shifts (δ , ppm) of C=N of (*E*)-N-(substituted benzylidene)-2,6-diisopropylanilines Vs F.

The assigned ^{13}C chemical shifts (δ , ppm) of Cipso carbons of (*E*)-N-(substituted benzylidene)-2,6-diisopropylanilines are presented in Table 1. From the Table 2, the ^{13}C chemical shifts (δ , ppm) of Cipso carbons of (*E*)-N-(substituted benzylidene)-2,6-diisopropylanilines produced satisfactory correlation with Hammett substituent constants, F and R parameters excluding 4-N(CH₃)₂, 4-F and 4-CH₃ substituents. When these substituents included in the correlations, they reduced the correlation coefficient considerably. The inductive effect of the dimethylamine substituents does not cooperate and not obey for predicting the correlation through reactivity at the reaction center. The methyl group also behaves like dimethylamine group. The fluorine substituent also not cooperate for predicting the reactivity at the reaction center. Among these correlations σ constants seems slightly better. The resonance components gave least correlation coefficient. Some of the single parameter correlations are shown in Figs. 15-20. Similarly, the multi-regressions of these chemical shifts (δ , ppm) with Swain-Lupton constants [37] produce satisfactory correlations.

The correlation equations are given in (9 and 10).

$$\delta_{\text{Cipso}} (\text{ppm}) = 134.56(\pm 0.607) + 3.621(\pm 1.195)\sigma_{\text{I}} + 1.599(\pm 0.217)\sigma_{\text{R}} \quad \dots(9)$$

(r = 0.981, n = 10, P > 95%)

$$\delta_{\text{Cipso}} (\text{ppm}) = 134.57(\pm 0.550) + 3.641(\pm 1.047) F + 1.452(\pm 0.788) R \quad \dots(10)$$

(r = 0.985, n = 10, P > 90%)

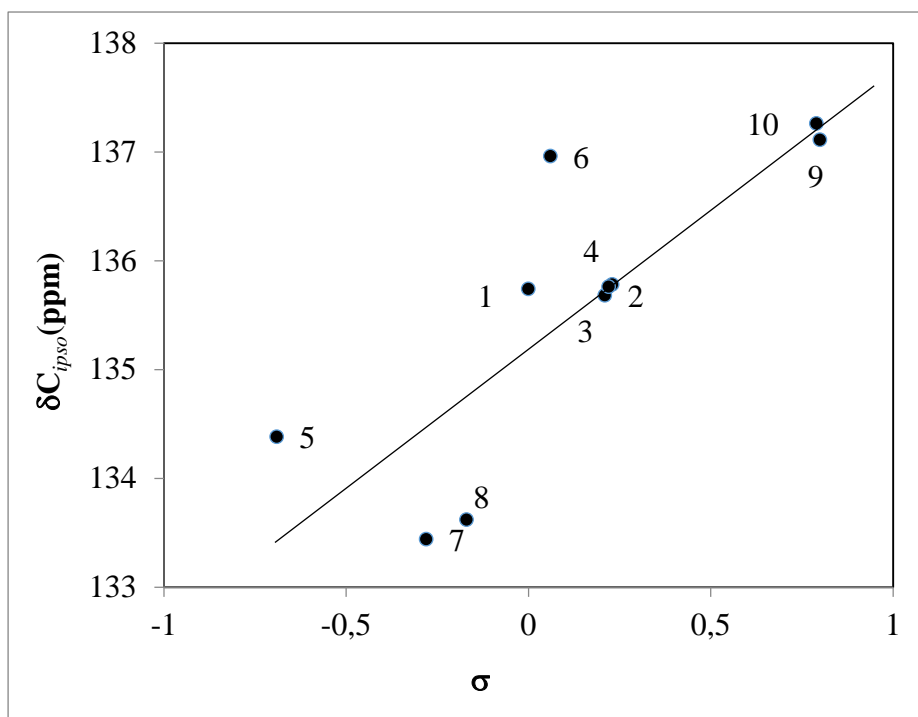


Fig. 15. Plot of ^{13}C chemical shifts (δ , ppm) of C_{ipso} of (*E*)-*N*-(substituted benzylidene)-2,6-diisopropylanilines Vs σ .

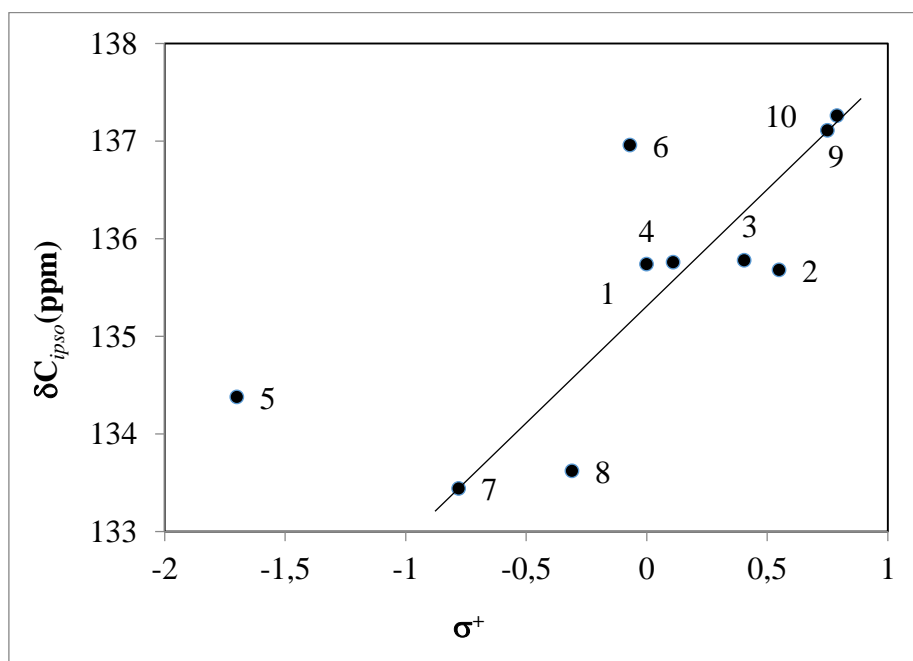


Fig. 16. Plot of ^{13}C chemical shifts (δ , ppm) of C_{ipso} of (*E*)-*N*-(substituted benzylidene)-2,6-diisopropylanilines Vs σ^+ .

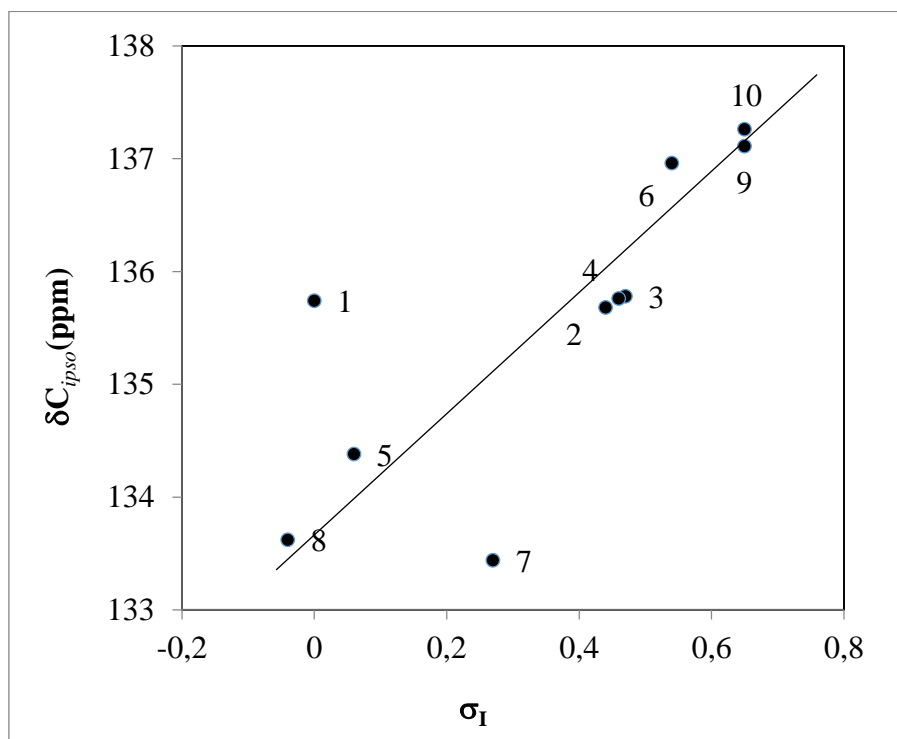


Fig. 17. Plot of ^{13}C chemical shifts (δ , ppm) of Cipso of (*E*)-N-(substituted benzylidene)-2,6-diisopropylanilines Vs σ_I .

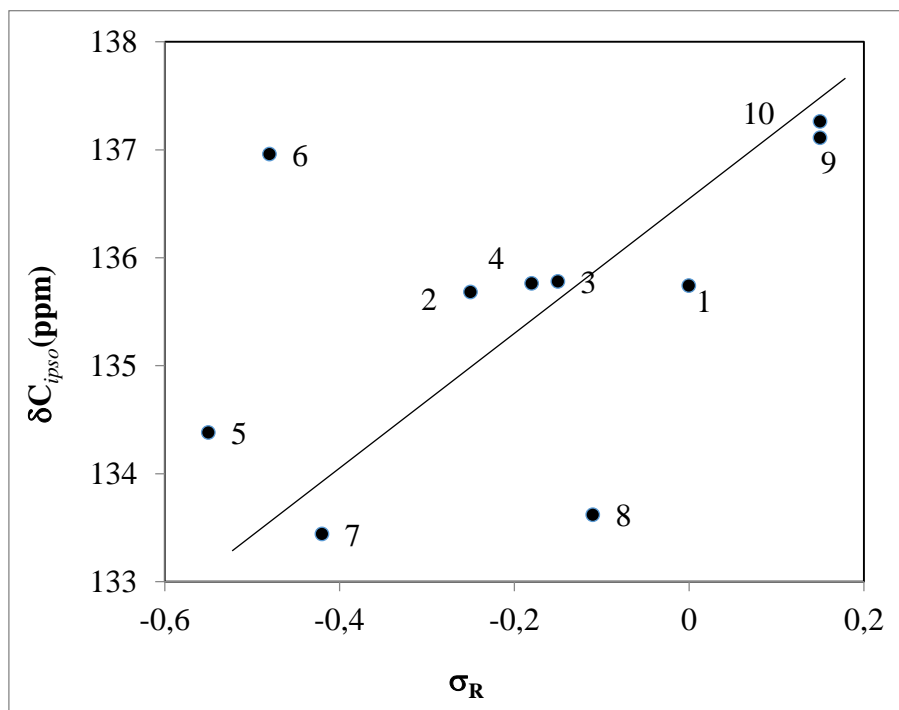


Fig. 18. Plot of ^{13}C chemical shifts (δ , ppm) of Cipso of (*E*)-N-(substituted benzylidene)-2,6-diisopropylanilines Vs σ_R .

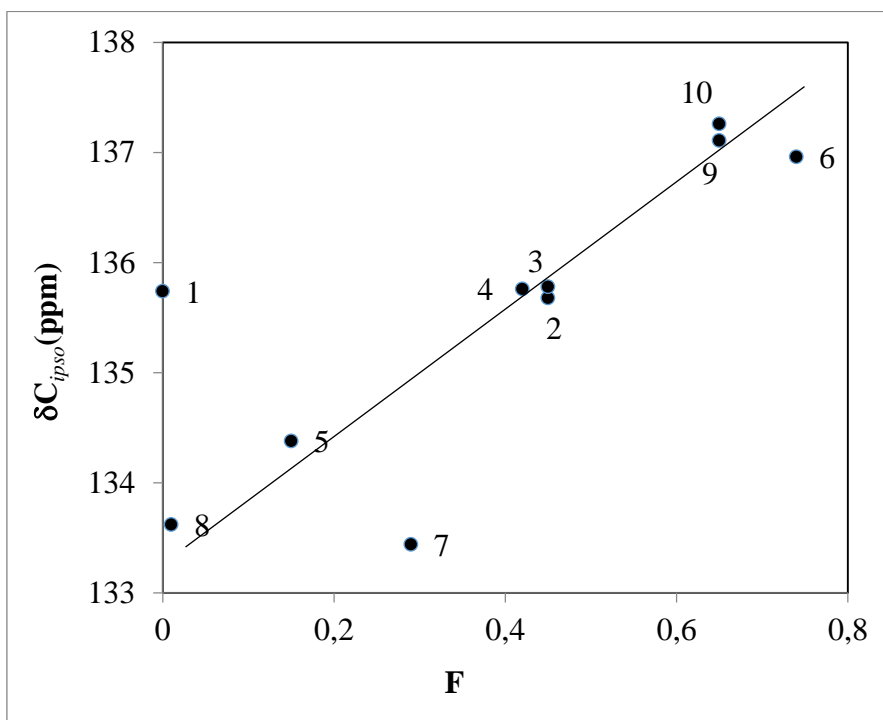


Fig. 19. Plot of ^{13}C chemical shifts (δ , ppm) of Cipso of (*E*)-*N*-(substituted benzylidene)-2,6-diisopropylanilines Vs F.

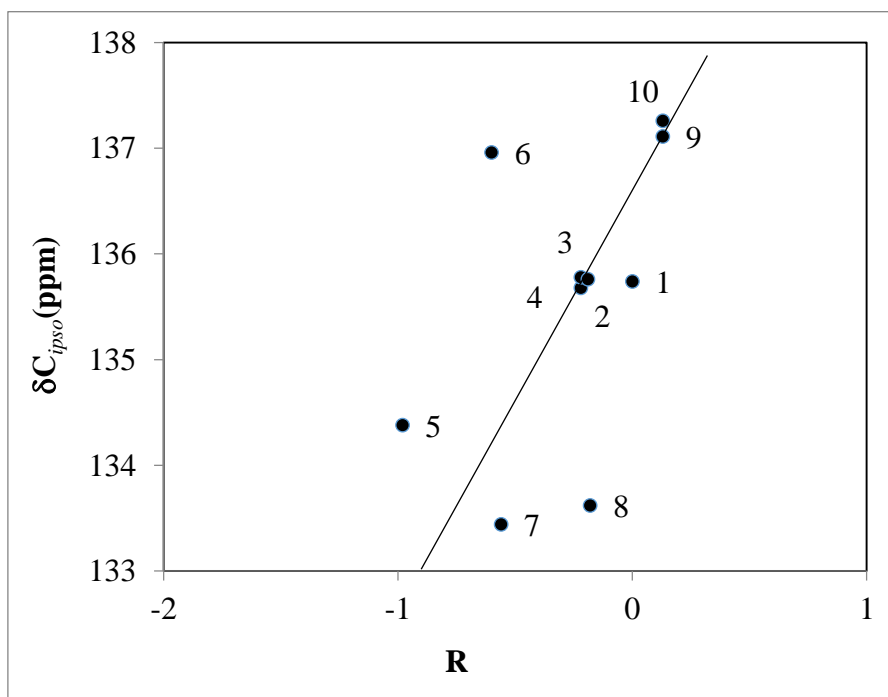


Fig. 20. Plot of ^{13}C chemical shifts (δ , ppm) of Cipso of (*E*)-*N*-(substituted benzylidene)-2,6-diisopropylanilines Vs R.

3. 3. Antimicrobial activities

The antimicrobial activities such as antibacterial and antifungal activities of synthesized (*E*)-*N*-(substituted benzylidene)-2,6-diisopropylanilines were measured using disc diffusion method from the literature procedure [36,38]. In this method the maximum zone of inhibition of imines against their bacterial and fungi strains were measured. This disc-diffusion experiment was conducted with the dilution of 250 mg/mL, Ampicillin and Miconazole was standard drug and DMSO was the control solvent. In the present investigation there are two gram positive *B. subtilis* and *M. luteus* strains and two gram negative bacterial *E. coli* and *P. aeruginosa* strains were employed for evaluation of antibacterial and antifungal activities of synthesized imine derivatives. The fungal strains *A. niger* and *T. viride* were used for evaluation of antifungal activities of synthesized imine derivatives.

3. 3. 1. Antibacterial activity

The observed antibacterial activity of synthesized (*E*)-*N*-(substituted benzylidene)-2,6-diisopropylanilines by means of measurement of mm of zone of inhibition was presented in Table 3. The disc diffusion zone of inhibition of (*E*)-*N*-(substituted benzylidene)-2,6-diisopropylanilines through the correlation-clustered column chart was shown in Figure 21. From the Table 3, the imine derivatives 4 showed better antibacterial activities against *B. subtilis* strains. The imine derivatives 1-3, 6 and 7-9 were showed good antibacterial activities against *B. subtilis* strains. The imines 5 and 10 show satisfactory bacterial activity against *B. subtilis* strains. The imine compounds 4 show better antibacterial activities against *M. luteus* bacterial strains. Compounds 1-3 and 6-8 were showed good antibacterial activities against *M. luteus* bacterial strain. The imines 5, 9 and 10 show satisfactory antibacterial activity against *M. luteus* bacterial strain. Imine 4 show excellent and the compound 3 show better antibacterial activities against *E. coli* bacterial strain. The imine derivatives 1, 6-8 and 10 were shown good antibacterial activities against *E. coli* bacterial strain. The imine derivatives 2, 5 and 9 were shown satisfactory antibacterial activities against *E. coli* bacterial strain. Compound 4 show better antibacterial activities against *P. aeruginosa* bacterial strain.

The remaining imine compounds show good antibacterial activities against *P. aeruginosa* bacterial strain.

Table 3. Zone of inhibition (mm) values of antibacterial activity of I-N-(substituted benzylidene)-2,6-diisopropylanilines.

Entry	X	Zone of inhibition (mm)			
		Gram positive bacteria		Gram negative bacteria	
		<i>B. subtilis</i>	<i>M. luteus</i>	<i>E. coli</i>	<i>P. aeruginosa</i>
1	H	12	12	10	10
2	2-Br	15	13	9	12
3	4-Br	13	15	16	11
4	4-Cl	16	16	17	16

5	4-N(CH ₃) ₂	9	8	9	10
6	4-F	10	12	15	10
7	3-OCH ₃	10	12	13	12
8	4-CH ₃	11	10	12	14
9	2-NO ₂	10	9	9	14
10	4-NO ₂	9	8	12	13
Standard	Ampicillin	16	16	16	16
Control	DMSO	---	---	---	---

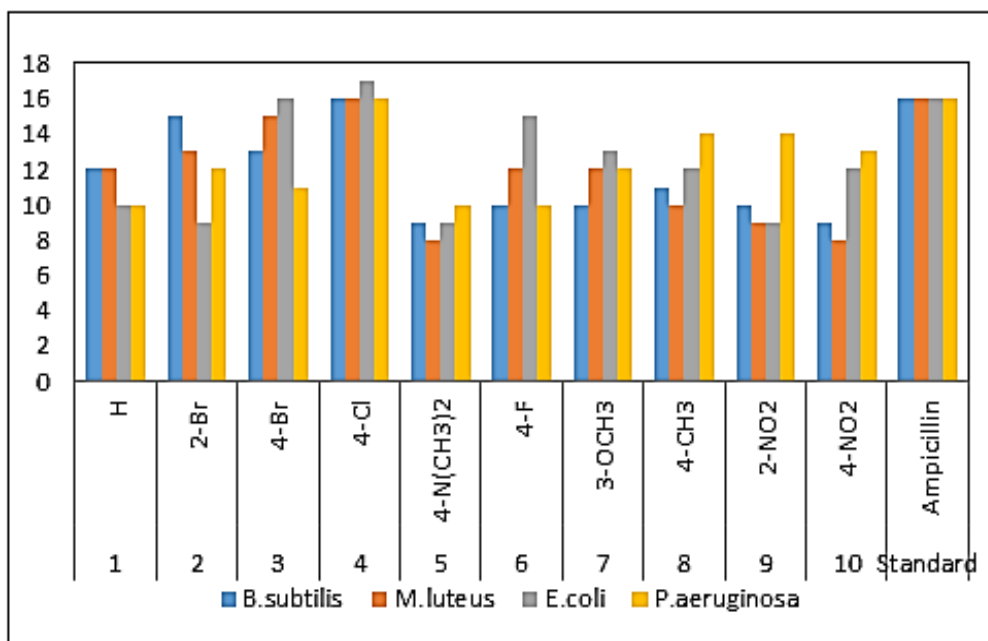


Fig. 21. Zone of inhibition (mm) values of antibacterial activity of I-N-(substituted benzylidene)-2,6-diisopropylanilines-clustered column chart.

3. 3. 2. Antifungal activity

The observed antifungal activity of synthesized (*E*)-N-(substituted benzylidene)-2,6-diisopropylanilines by means of measurement of mm of zone of inhibition was presented in Table 4. The disc diffusion of zone of mm of inhibition of I-N-(substituted benzylidene)-2,6-diisopropylanilines through correlation-clustered column chart was illustrated in Figure 22. From the table 4, the imine derivative 10 show better antifungal activities against *A. niger* strain. The compounds 1 and 3-8 showed good antifungal activities against *A. niger* strain. The imine derivative 2 show least antifungal activities against *A. niger* strain. The imine

compound 9 show excellent antifungal activities against *T. viride* fungal strains. The imine compound 10 show better antifungal activities against *T. viride* fungal strain. Compounds 1-5, 7 and 8 were showed good antifungal activity against *T. viride* fungal strains. The imine compound 9 show least antifungal activity against *T. viride* fungal strains.

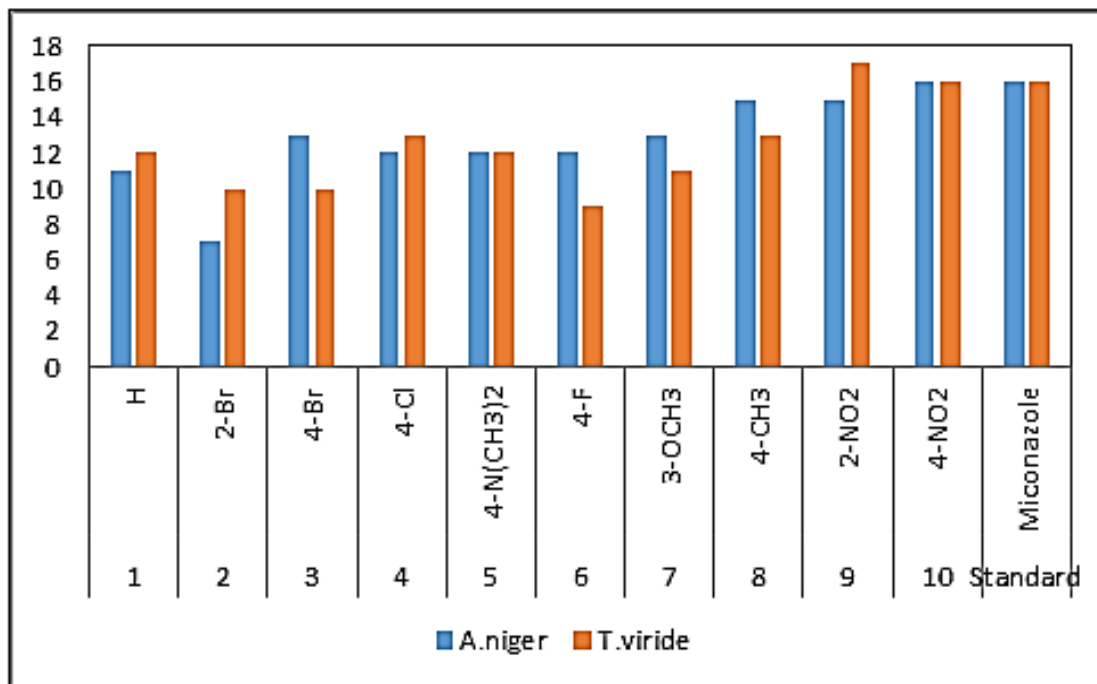


Fig. 22. Zone of inhibition (mm) values of antifungal activity of I-N-(substituted benzylidene)-2,6-diisopropylanilines-clustered column chart.

Table 12. Zone of inhibition (mm) values of antifungal activity of I-N-(substituted benzylidene)-2,6-diisopropylanilines.

Entry	X	Zone of Inhibition (mm)	
		<i>A. niger</i>	<i>T. viride</i>
1	H	11	12
2	2-Br	7	10
3	4-Br	13	10
4	4-Cl	12	13
5	4-N(CH ₃) ₂	12	12
6	4-F	12	9
7	3-OCH ₃	13	11
8	4-CH ₃	15	13

9	2-NO ₂	15	17
10	4-NO ₂	16	16
Standard	Miconazole	16	16
Control	DMSO	---	---

4. CONCLUSIONS

More than ten (*E*)-*N*-(substituted benzylidene)-2,6-diisopropylanilines have been synthesized by solvent-free microwave irradiation method. The structures of all the synthesized compounds were characterized by physical constants, IR and NMR spectroscopic techniques. All the observed IR frequencies $\nu_{C=N}$ (cm⁻¹), NMR δ (ppm) of C-H & C=N chemical shifts have been correlated with Hammett substituent constants and *F* and *R* parameters using single and multi-linear regression analyses in order to study the effect of substituents on these spectral data has been studied.

The correlation of $\nu_{C=N}$ of *I-N*-(substituted benzylidene)-2,6-diisopropyl anilines Hammett σ , σ_1 and *F* parameters gave satisfactory correlations except 4-F and 4-CH₃ substituents. The ¹H chemical shifts (δ , ppm) of CH=N protons of *I-N*-(substituted benzylidene)-2,6-diisopropylanilines produced satisfactory correlation except 4-N(CH₃)₂, 4-F and 4-CH₃ substituents. The ¹³C chemical shifts (δ , ppm) of CH=N carbons of *I-N*-(substituted benzylidene)-2,6-diisopropylanilines produced satisfactory correlation with Hammett σ_R , σ^+ , σ_1 constant and *F* parameters excluding 4-Cl, 4-N(CH₃)₂, and 4-CH₃ substituents.

The ¹³C chemical shifts (δ , ppm) of Cipso carbons of *I-N*-(substituted benzylidene)-2,6-diisopropylanilines produced satisfactory correlation with Hammett substituent constants, *F* and *R* parameters excluding 4-N(CH₃)₂, 4-F and 4-CH₃ substituents. Overall the multi-regressions of these infrared $\nu_{C=N}$ (cm⁻¹) frequencies and chemical shifts (δ , ppm) C-H protons, C=N and Cipso carbons with Swain-Lupton constants produce satisfactory correlations. All synthesized Schiff's base compounds were screened for their antimicrobial activity by disc diffusion method.

The imine compounds 4 shows better antibacterial activities against *M. luteus* bacterial strains. Compounds 1-3 and 6-8 were showed good antibacterial activities against *M. luteus* bacterial strain. Imine 4 showed excellent and the compound 3 show better antibacterial activities against *E. coli* bacterial strain. The imine derivatives 1, 6-8 and 10 were shown good antibacterial activities against *E. coli* bacterial strain. Compound 4 show better antibacterial activities against *P. aeruginosa* bacterial strain.

The remaining imine compound shows good antibacterial activities against *P. aeruginosa* bacterial strain. The imine derivative 10 show better antifungal activities against *A. niger* strain. The compounds 1 and 3-8 showed good antifungal activities against *A. niger* strain. The imine compound 9 show excellent antifungal activities against *T. viride* fungal strains. The imine compound 10 show better antifungal activities against *T. viride* fungal strain. Compounds 1-5, 7 and 8 were showed good antifungal activity against *T. viride* fungal strain.

References

- [1] K. Y. Lau, A. Mayr, K. K. Cheung, *Inorg. Chim. Acta* 285 (1999) 223.
- [2] A. S. Shawali, N. M. S. Harb, K. O. Badahdah, *J. Heterocycl. Chem.* 22 (1985) 1397.
- [3] M. Mustapha, B. R. Thorat, R. G. Sudhir Sawant, R. Atram, J. Yamgar, *Chem. Pharm. Res.* 3 (4) (2011) 5.
- [4] F. D. Popp, *J. Org. Chem.* 26 (1961) 1566.
- [5] D. Kong, X. Zhang, Q. Zhu, J. Xie, X. Zhou, *Zhongguo Yaowu Huaxue Zazhi*, 8(4) (1998) 245.
- [6] D. J. Hadjipavlou-litina, A. A. Geronikaki, *Drug Des. Discov.*, 15 (1996) 199.
- [7] S. S. Murthy, A. Kaur, B. Sreenivasalu, R. N. Sarma, *Indian J. Exp. Biol.* 36 (1998) 724.
- [8] K. N. Venugopala, V.A. Jayashree, *Indian J. Pharm. Sci.* 70 (2008) 88.
- [9] N. Solak, S. Rollas, *Arkivoc.* Xii (2006) 173.
- [10] S. J. Wadher, M.P. Puranik, N. A. Karande, P. G. Yeole, *Int. J. Pharm. Tech. Res.*, 1 (2009) 22.
- [11] A. L. Cates, S. M. Rasheed, *Pharm. Res.* 6 (1984) 271.
- [12] V. V. Kuznetsov, A. R. Palma, A. E. Aliev, A. V. Varlamov, N. S. Prostakov, *Zh. Org. Khim.*, 127 (1991) 1579.
- [13] A. E. Taggi, A. M. Hafez, H. Wack, B. Young, D. Ferraris, T. Lectka, *J. Am. Chem. Soc.*, 124 (2002) 6626.
- [14] (a) O. Tsuge, R. Kanemasa, *Adv. Heterocycl. Chem.* 45 (1989) 231.
(b) M. F. Aly, M. I. Younes, S. A. M. Metwally, *Tetrahedron.* 50 (1994) 3159.
- [15] M. Mustapha, B. R. Thorat, SudhirSawant, R. G. Atram, R. Yamgar, *J. Chem. Pharm. Res.* 3(4) (2011) 5.
- [16] R. Yamgar, P. Kamat, D. Khandekar, S. Sawant, *J. Chem. Pharm. Res.* 3 (2011)188.
- [17] K. C. Gupta and A. K. Sutar. *Coord. Chem. Rev.* 252 (2008) 1420.
- [18] M. Yuan, F. Zhao, W. Zhang, Z. M. Wang and S. Gao, *Inorg. Chem.* 46 (2007)11235.
- [19] H. Fukuda, K. Amimoto, H. Koyama and T. Kawato, *Tetrahedron Lett.* 50 (2009) 5376.
- [20] Y.C. Liu and C.Y. Yang, *Inorg. Chem. Commun.* 12 (2009) 704.
- [21] A. Bongini, M. Panunzio, G. Piersanti, E. Bandini, G. Martelli, G. Spunta and A. Venturini, *Euro. J. Org. Chem.*, 13 (2000) 2379.
- [22] V. V. Mulwad and J. M. Shirodkar, *Indian J. Het. Chem.*, 11(2002)199.
- [23] C. Ainsworth, *J. American Chem. Soc.*, 77 (1995)1148.
- [24] G. Weber and J. Messerschmidt, *Ana. Chimi. Acta.*, 545 (2005) 166.

- [25] R. Singh and N. K. Kaushik, *Main. Gro. Met. Chemi.*, 30 (2007)333
- [26] S. Zhu, Z. Zhou and B. Zhao Huaxue, *Yu Shengwu Gong Cheng.*, 25 (2008) 34.
- [27] C. F. Zhu, G. Z. Yuan, E. H. Sheng and Y. Cui, *Jiegou Huaxue.*, 28 (2009) 1304.
- [28] J. Wang, Y. Song and X. Gao, *Hecheng Huaxue.*, 16 (2008) 225.
- [29] Q. F. Cheng, X. Y. Xu, Q. F. Wang, B. H. Qian, W. J. Liu and X. J. Yang, *Jie. Hua.*, 28 (2009) 1281.
- [30] J. H. Xie, S. F. Zhu, Q. L. Zhou, *Chem. Rev.*, 111 (2011) 1713.
- [31] J. E. Robertson, H. J. Biel and T. F. Mitchell, *J. Med. Chem.*, 6 (1963)805.
- [32] H. J. Biel, W. K. Hoya and H. A. Leiser, *J. Am. Chem. Soc.*, 81 (1959) 2527.
- [33] K. Neuvonen, F. Fulop, H. Neuvonen, A. Koch, E. Kleinpeter and K. Pihlaja, *J. Org. Chem.*, 68 (2002) 2151.
- [34] R. Senbagam, G. Vanangamudi and G. Thirunarayanan, *Annales Umcs Chemia.*, 70(2), (2015) 169.
- [35] R. Suresh, D. Kamalakkannan, V. Mala, K. Sathiyamoorthiy, R. Sndararajan, S. P. Sakthinathan, R. Arulkumaran, G. Vanangamudi, G. Thirunarayanan, *Adv. Appl. Res.*, 7(1) (2015) 27.
- [36] R. Senbagam, R. Vijayakumar, M. Rajarajan, S. Balaji, V. Manikandan, G. Vanangamudi and G. Thirunarayanan, *Kar. Int. Jour. Mod. Sci.*, 2 (2016) 56.
- [37] C. G. Swain and E. C. Lupton, *J. Am. Chem. Soc.* 90 (1968) 4328.
- [38] A. W. Bauer, W. M. M. Kirby, J. C. Sherris and M. Truck, *Am. J. Clin. Pathol.*, 45 (1966) 493

(Received 28 December 2016; accepted 16 January 2017)