

IR and ¹H NMR spectral studies of some 2-Amino-4-isopropyl-6-methoxy-N-phenylpyrimidine-5-carboxamides: Assessment of substituent effects

R. Arulkumar¹, R. Sundararajan¹, V. Manikandan¹, V. Sathiyendiran²,
S. Pazhamalai³, G. Thirunarayanan^{4,*}

¹PG & Research Department of Chemistry, Government Arts College,
C-Mutlur, Chidambaram - 608 102, India

²Department of Chemistry, Sourashtra College, Madurai - 625 004, India

³DDE wing of Chemistry, Annamalai University, Annamalainagar - 608 002, India

⁴Department of Chemistry, Annamalai University, Annamalainagar - 608 002, India

*E-mail address: drgtnarayanan@gmail.com

ABSTRACT

A series of 2-Amino-4-isopropyl-6-methoxy-N-phenylpyrimidine-5-carboxamide compounds have been synthesized from various substituted dithioacetal and guanidine. The purities of these compounds were checked by their physical constants, UV, IR, NMR and MASS spectral data. The IR and ¹H NMR spectral data of these compounds have been correlated with Hammett sigma constants, F and R parameters using single and multi-linear regression analysis. From the results of statistical analysis, the effects of substituents on the spectral group frequencies have been discussed.

Keywords: 2-Amino-4-isopropyl-6-methoxy-N-phenylpyrimidine-5-carboxamides, IR spectra; NMR spectra; Substituent effects

1. INTRODUCTION

Heterocyclic chemistry comprises at least half of all organic chemistry research worldwide. In particular, heterocyclic structures form the basis of many pharmaceutical, agrochemical and medicinal products [1]. Nitrogen containing heterocyclic ring such as pyrimidine is a promising structural moiety for drug design. Pyrimidine derivatives form a component in a number of useful drugs and are associated with many biological and therapeutical activities [2]. Pyrimidine derivatives have been reported as anti-microbial [3], analgesic, anti-viral, anti-inflammatory [4], anti-HIV [5], anti-tubercular [6], anti-tumour [7], anti-malarial [8], cardiovascular [9] agents. Pyrimidine derivatives have been found to exhibit cytostatic [10-12], immune modulating [13,14] and antibacterial properties [15-21]. In particular, studies concerning the synthesis of pyrimido[4,5-d]-1,3-oxazines [22] showing

considerable similarity to quinoline chemotherapeutic agents with an antibacterial effect. The spectral data of these 2-Amino-4-isopropyl-6-methoxy-N-phenyl pyrimidine-5-carboxamide compounds were useful for prediction of ground state equilibration like various conformers.

The effects of substituent on the infrared group frequencies (ν , cm^{-1}) and NMR chemical shifts (δ , ppm) of 2-amino-4-isopropyl-6-methoxy-N-phenylpyrimidine-5-carboxamide compounds. In their studies, they observed satisfactory and good correlations for each spectral data with Hammett substituent constants, F and R parameters.

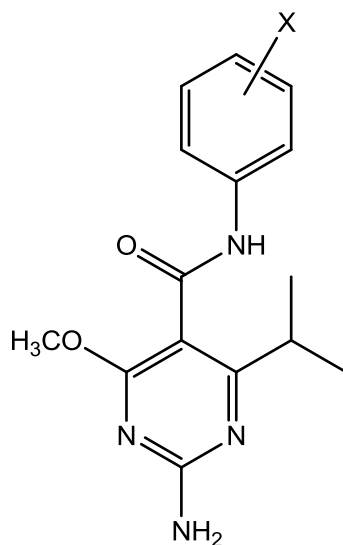
2. EXPERIMENTAL

2.1 General

All chemicals used were purchased from Sigma-Aldrich and E-Merck chemical companies. Melting points of all chalcones were determined in open glass capillaries on Mettler FP51 melting point apparatus and are uncorrected. Infrared spectra (KBr, 4000-400 cm^{-1}) were recorded AVATAR-300 Fourier transform spectrophotometer. Bruker AV400 NMR spectrometer was used for recording NMR spectra operating at 400 MHz for ^1H spectra and 125.46 MHz for ^{13}C spectra in CDCl_3 solvent using TMS as internal standard. Mass spectra of all chalcones were recorded on SHIMADZU spectrometer using chemical ionization technique.

2.2. Synthesis of substituted 2-amino-4-isopropyl-6-methoxy-N-phenylpyrimidine-5-carboxamides

All substituted 2-Amino-4-isopropyl-6-methoxy-N-phenylpyrimidine-5-carboxamide were synthesized and their purities were examined by procedure published in literature [23]. An equi-molar quantities of substituted dithioacetal (2 mmol) and guanidine (2 mmol), in the presence of sodium methoxide were refluxed for 6h and the completion of the reaction was monitored by thin layer chromatography.



Where X = H, *o*-Br, *m*-Cl, *p*-Cl, *o*-F, *p*-F, *o*-OCH₃, *p*-OCH₃, *o*-CH₃, *p*-CH₃

Fig. 1. Substituted 2-Amino-4-isopropyl-6-methoxy-N-phenylpyrimidine-5-carboxamide

After completion of the reaction, the solid product was separated by filtration. Further the product was purified by column chromatography using dichloromethane and ethyl acetate mixture as eluent. The general structure of the carboxamides was shown in Fig. 1.

3. RESULTS AND DISCUSSION

In the present study the authors have studied the effects of substituents on the spectral data such as infrared spectral carbonyl and deformation modes (ν , cm^{-1}), the chemical shifts (δ , ppm) of $-\text{NH}_2$, $-\text{OCH}_3$ and $-\text{CONH}$ protons of synthesized 2-amino-4-isopropyl-6-methoxy-N-phenylpyrimidine-5-carboxamide compounds with Hammett substituent constants, F and R parameters using single and multi-linear regression analysis for predicting the reactivity on the group frequencies.

Table 1. The infrared absorptions (ν , cm^{-1}) and NMR chemical shifts (δ , ppm) of substituted 2-amino-4-isopropyl-6-methoxy-N-phenylpyrimidine-5-carboxamide compounds.

Entry	X	IR (ν , cm^{-1})				NMR(δ , ppm)		
		C=O	C=N	NH ₂	-C-O-C-	NH ₂	OCH ₃	CONH
1	H	1618.34	1538.46	3414.34	1430.40	5.702	3.802	9.508
2	<i>o</i> -Br	1648.52	1586.02	3459.12	1261.08	5.608	3.808	9.600
3	<i>m</i> -Cl	1649.04	1588.44	3460.86	1246.48	5.640	3.806	9.602
4	<i>p</i> -Cl	1651.30	1588.86	3462.56	1248.50	5.602	3.810	9.582
5	<i>o</i> -F	1654.45	1590.68	3444.24	1260.56	5.624	3.820	9.586
6	<i>p</i> -F	1650.96	1588.46	3448.50	1262.84	5.612	3.904	9.624
7	<i>o</i> -OCH ₃	1624.54	1508.34	3422.20	1151.46	5.694	3.782	9.504
8	<i>p</i> -OCH ₃	1630.00	1509.21	3454.48	1052.24	5.584	3.764	9.488
9	<i>o</i> -CH ₃	1620.98	1568.36	3440.27	1054.63	5.692	3.784	9.426
10	<i>p</i> -CH ₃	1618.46	1538.40	3414.21	1060.61	5.576	3.688	9.482

3. 1. IR spectral study

The synthesized compounds in the present study are shown in Fig. 1. The carbonyl C=N, NH₂ and -C-O-C- stretching frequencies (cm^{-1}) of substituted 2-amino-4-isopropyl-6-methoxy-N-phenylpyrimidine-5-carboxamides are tabulated in Table 1.

The infrared frequencies for carbonyl absorption are assigned based on the assignments made by Hays and Timmons [24] for CO at 1640, C=N at 1580, NH₂ at 3400 and -O-C-O- at 1200 cm^{-1} , respectively. The assigned infrared frequencies have been correlated with Hammett substituent constants and Swain-Lupton's constants [25]. In this correlation the structure parameter Hammett equation employed is as shown in the following equation:

$$v = \rho\sigma + v_0 \quad \dots(1)$$

Where v is the carbonyl frequencies of substituted system and v_0 is the corresponding quantity of unsubstituted system; σ is a Hammett substituent constant, which in principle is characteristics of the substituent and ρ is a reaction constant which is depend upon the nature of the reaction.

The results of statistical analysis [26-40] were shown in Table 2. From Table 2, The Hammett substituent constants and F parameters correlated satisfactorily with CO stretches. The resonance component was fail in correlation. All the correlations have positive ρ values. This is due to the inability of prediction of the reactivity through the resonance on the carbonyl stretches and associated with the resonance-conjugative structure as shown in Fig. 2.

The Hammett substituent constants and F parameters gave satisfactory correlation with C=N stretches. The remaining Hammett substituent constant σ_R and R parameter have given poor correlation. This is due to the reasons stated in earlier and associated with the resonance conjugative structure. And all the compounds have positive ρ values.

Except R parameter, the Hammett substituent constants and F parameters gave satisfactory correlation with NH₂ stretches. The reasons stated in earlier and associated with the resonance conjugative structure for the correlations fail with NH₂ stretches.

The Hammett substituent constants and F and R parameters gave satisfactory correlation with -C-O-C- stretches and all correlations gave positive ρ values.

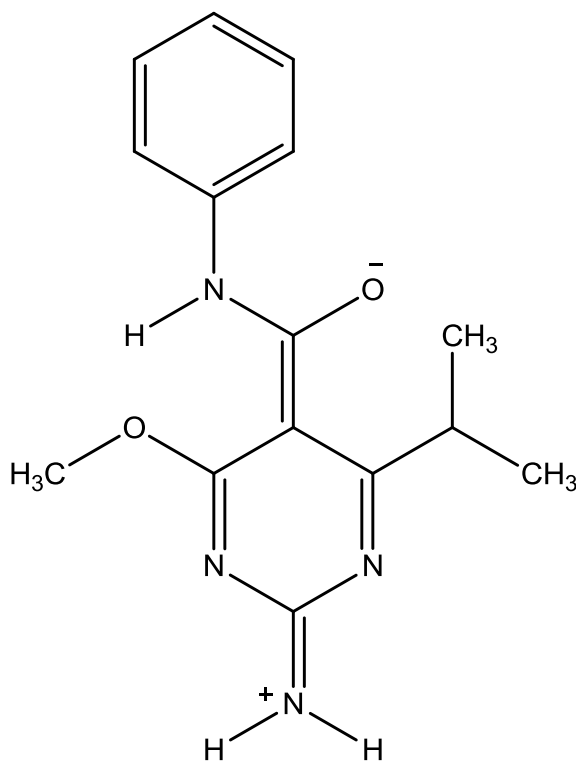


Fig. 2. The resonance-conjugative structure.

Table 2. Results of statistical analysis of infrared absorptions (ν , cm^{-1}) and NMR chemical shifts (δ , ppm) of substituted α -Amino-4-isopropyl-6-methoxy-N-phenylpyrimidine-5-carboxamide compounds with Hammett σ , σ^+ , σ_I , σ_R and F and R parameters.

Frequency	Constants	r	I	ρ	s	n	Correlated derivatives
vCO	σ	0.907	1636.22	48.039	9.99	10	H, <i>o</i> -Br, <i>m</i> -Cl, <i>p</i> -Cl, <i>o</i> -F, <i>p</i> -F, <i>o</i> -OCH ₃ , <i>p</i> -OCH ₃ , <i>o</i> -CH ₃ , <i>p</i> -CH ₃
	σ^+	0.906	1637.34	24.045	11.82	10	H, <i>o</i> -Br, <i>m</i> -Cl, <i>p</i> -Cl, <i>o</i> -F, <i>p</i> -F, <i>o</i> -OCH ₃ , <i>p</i> -OCH ₃ , <i>o</i> -CH ₃ , <i>p</i> -CH ₃
	σ_I	0.991	1618.21	63.181	5.65	10	H, <i>o</i> -Br, <i>m</i> -Cl, <i>p</i> -Cl, <i>o</i> -F, <i>p</i> -F, <i>o</i> -OCH ₃ , <i>p</i> -OCH ₃ , <i>o</i> -CH ₃ , <i>p</i> -CH ₃
	σ_R	0.832	1629.26	-25.960	15.43	10	H, <i>o</i> -Br, <i>m</i> -Cl, <i>p</i> -Cl, <i>o</i> -F, <i>p</i> -F, <i>o</i> -OCH ₃ , <i>p</i> -OCH ₃ , <i>o</i> -CH ₃ , <i>p</i> -CH ₃
	F	0.990	1619.56	50.717	6.85	10	H, <i>o</i> -Br, <i>m</i> -Cl, <i>p</i> -Cl, <i>o</i> -F, <i>p</i> -F, <i>o</i> -OCH ₃ , <i>p</i> -OCH ₃ , <i>o</i> -CH ₃ , <i>p</i> -CH ₃
	R	0.883	1629.20	-22.736	15.39	10	H, <i>o</i> -Br, <i>m</i> -Cl, <i>p</i> -Cl, <i>o</i> -F, <i>p</i> -F, <i>o</i> -OCH ₃ , <i>p</i> -OCH ₃ , <i>o</i> -CH ₃ , <i>p</i> -CH ₃
vC=N	σ	0.988	1559.46	17.593	17.03	8	H, <i>o</i> -Br, <i>m</i> -Cl, <i>p</i> -Cl, <i>o</i> -F, <i>p</i> -F, <i>o</i> -CH ₃ , <i>p</i> -CH ₃
	σ^+	0.983	1562.34	63.999	19.77	10	H, <i>o</i> -Br, <i>m</i> -Cl, <i>p</i> -Cl, <i>o</i> -F, <i>p</i> -F, <i>o</i> -OCH ₃ , <i>p</i> -OCH ₃ , <i>o</i> -CH ₃ , <i>p</i> -CH ₃
	σ_I	0.955	1536.58	81.973	29.90	8	H, <i>o</i> -Br, <i>m</i> -Cl, <i>p</i> -Cl, <i>o</i> -F, <i>p</i> -F, <i>o</i> -CH ₃ , <i>p</i> -CH ₃
	σ_R	0.815	1568.22	27.019	35.47	10	H, <i>o</i> -Br, <i>m</i> -Cl, <i>p</i> -Cl, <i>o</i> -F, <i>p</i> -F, <i>o</i> -OCH ₃ , <i>p</i> -OCH ₃ , <i>o</i> -CH ₃ , <i>p</i> -CH ₃
	F	0.905	1536.87	70.158	29.48	8	H, <i>o</i> -Br, <i>m</i> -Cl, <i>p</i> -Cl, <i>o</i> -F, <i>p</i> -F, <i>o</i> -CH ₃ , <i>p</i> -CH ₃
	R	0.813	1567.25	20.525	35.57	10	H, <i>o</i> -Br, <i>m</i> -Cl, <i>p</i> -Cl, <i>o</i> -F, <i>p</i> -F, <i>o</i> -OCH ₃ , <i>p</i> -OCH ₃ , <i>o</i> -CH ₃ , <i>p</i> -CH ₃
vNH ₂	σ	0.958	3441.68	43.701	16.21	10	H, <i>o</i> -Br, <i>m</i> -Cl, <i>p</i> -Cl, <i>o</i> -F, <i>p</i> -F, <i>o</i> -OCH ₃ , <i>p</i> -OCH ₃ , <i>o</i> -CH ₃ , <i>p</i> -CH ₃
	σ^+	0.938	3442.54	16.354	18.49	9	H, <i>o</i> -Br, <i>m</i> -Cl, <i>p</i> -Cl, <i>o</i> -F, <i>p</i> -F, <i>o</i> -OCH ₃ , <i>o</i> -CH ₃ , <i>p</i> -CH ₃
	σ_I	0.973	3424.30	60.861	15.53	10	H, <i>o</i> -Br, <i>m</i> -Cl, <i>p</i> -Cl, <i>o</i> -F, <i>p</i> -F, <i>o</i> -OCH ₃ , <i>p</i> -OCH ₃

							<i>o</i> -CH ₃ , <i>p</i> -CH ₃
	σ_R	0.916	3437.37	-16.489	19.73	8	<i>o</i> -Br, <i>m</i> -Cl, <i>p</i> -Cl, <i>o</i> -F, <i>p</i> -F, <i>o</i> -OCH ₃ , <i>p</i> -OCH ₃ , <i>o</i> -CH ₃
	F	0.959	3428.24	41.052	16.01	10	H, <i>o</i> -Br, <i>m</i> -Cl, <i>p</i> -Cl, <i>o</i> -F, <i>p</i> -F, <i>o</i> -OCH ₃ , <i>p</i> -OCH ₃ , <i>o</i> -CH ₃ , <i>p</i> -CH ₃
	R	0.815	3437.17	-14.956	16.69	10	H, <i>o</i> -Br, <i>m</i> -Cl, <i>p</i> -Cl, <i>o</i> -F, <i>p</i> -F, <i>o</i> -OCH ₃ , <i>p</i> -OCH ₃ , <i>o</i> -CH ₃ , <i>p</i> -CH ₃
ν_{C-O-C}	σ	0.960	1200.27	289.665	103.14	9	<i>o</i> -Br, <i>m</i> -Cl, <i>p</i> -Cl, <i>o</i> -F, <i>p</i> -F, <i>o</i> -OCH ₃ , <i>p</i> -OCH ₃ , <i>o</i> -CH ₃ , <i>p</i> -CH ₃
	σ^+	0.962	1207.80	173.508	100.49	9	Br, <i>m</i> -Cl, <i>p</i> -Cl, <i>o</i> -F, <i>p</i> -F, <i>o</i> -OCH ₃ , <i>p</i> -OCH ₃ , <i>o</i> -CH ₃ , <i>p</i> -CH ₃
	σ_I	0.931	1153.87	167.833	122.65	9	Br, <i>m</i> -Cl, <i>p</i> -Cl, <i>o</i> -F, <i>p</i> -F, <i>o</i> -OCH ₃ , <i>p</i> -OCH ₃ , <i>o</i> -CH ₃ , <i>p</i> -CH ₃
	σ_R	0.921	1241.57	135.777	126.18	8	H, <i>o</i> -Br, <i>m</i> -Cl, <i>p</i> -Cl, <i>o</i> -F, <i>p</i> -F, <i>o</i> -OCH ₃ , <i>p</i> -OCH ₃
	F	0.929	1158.87	130.579	123.47	9	Br, <i>m</i> -Cl, <i>p</i> -Cl, <i>o</i> -F, <i>p</i> -F, <i>o</i> -OCH ₃ , <i>p</i> -OCH ₃ , <i>o</i> -CH ₃ , <i>p</i> -CH ₃
	R	0.926	1249.63	142.541	124.66	8	H, <i>o</i> -Br, <i>m</i> -Cl, <i>p</i> -Cl, <i>o</i> -F, <i>p</i> -F, <i>o</i> -OCH ₃ , <i>p</i> -OCH ₃
δ_{NH_2}	σ	0.921	5.633	-0.404	0.04	7	<i>o</i> -Br, <i>m</i> -Cl, <i>p</i> -Cl, <i>o</i> -F, <i>p</i> -F, <i>p</i> -OCH ₃ , <i>p</i> -CH ₃
	σ^+	0.902	5.633	-0.003	0.04	7	<i>o</i> -Br, <i>m</i> -Cl, <i>p</i> -Cl, <i>o</i> -F, <i>p</i> -F, <i>p</i> -OCH ₃ , <i>p</i> -CH ₃
	σ_I	0.933	5.653	-0.068	0.04	8	H, <i>o</i> -Br, <i>m</i> -Cl, <i>p</i> -Cl, <i>o</i> -F, <i>p</i> -F, <i>o</i> -OCH ₃ , <i>o</i> -CH ₃
	σ_R	0.909	5.639	0.022	0.04	8	H, <i>o</i> -Br, <i>m</i> -Cl, <i>p</i> -Cl, <i>o</i> -F, <i>p</i> -F, <i>p</i> -OCH ₃ , <i>o</i> -CH ₃
	F	0.935	0.653	-0.060	0.04	8	H, <i>o</i> -Br, <i>m</i> -Cl, <i>p</i> -Cl, <i>o</i> -F, <i>p</i> -F, <i>o</i> -OCH ₃ , <i>o</i> -CH ₃
	R	0.823	5.649	0.048	0.04	10	H, <i>o</i> -Br, <i>m</i> -Cl, <i>p</i> -Cl, <i>o</i> -F, <i>p</i> -F, <i>o</i> -OCH ₃ , <i>p</i> -OCH ₃ , <i>o</i> -CH ₃ , <i>p</i> -CH ₃
δ_{OCH_3}	σ	0.946	3.795	0.097	0.05	8	H, <i>o</i> -Br, <i>m</i> -Cl, <i>p</i> -Cl, <i>o</i> -F, <i>o</i> -OCH ₃ , <i>p</i> -OCH ₃ , <i>o</i> -CH ₃
	σ^+	0.940	3.798	0.048	0.05	8	H, <i>o</i> -Br, <i>m</i> -Cl, <i>p</i> -Cl, <i>o</i> -F, <i>o</i> -OCH ₃ , <i>p</i> -OCH ₃ , <i>o</i> -CH ₃ , <i>p</i> -CH ₃
	σ_I	0.968	3.749	0.161	0.04	10	H, <i>o</i> -Br, <i>m</i> -Cl, <i>p</i> -Cl, <i>o</i> -F, <i>p</i> -F, <i>o</i> -OCH ₃ , <i>p</i> -OCH ₃ , <i>o</i> -CH ₃ , <i>p</i> -CH ₃
	σ_R	0.935	3.769	-0.097	0.05	10	H, <i>o</i> -Br, <i>m</i> -Cl, <i>p</i> -Cl, <i>o</i> -F, <i>p</i> -F, <i>o</i> -OCH ₃ , <i>p</i> -OCH ₃ , <i>o</i> -CH ₃ , <i>p</i> -CH ₃
	F	0.972	3.749	0.140	0.03	10	H, <i>o</i> -Br, <i>m</i> -Cl, <i>p</i> -Cl, <i>o</i> -F, <i>p</i> -F, <i>o</i> -OCH ₃ , <i>p</i> -OCH ₃ ,

							<i>o</i> -CH ₃ , <i>p</i> -CH ₃
	R	0.833	3.770	-0.079	0.05	10	H, <i>o</i> -Br, <i>m</i> -Cl, <i>p</i> -Cl, <i>o</i> -F, <i>p</i> -F, <i>o</i> -OCH ₃ , <i>p</i> -OCH ₃ , <i>o</i> -CH ₃ , <i>p</i> -CH ₃
δCON H	σ	0.925	9.157	-1.232	1.26	10	H, <i>o</i> -Br, <i>m</i> -Cl, <i>p</i> -Cl, <i>o</i> -F, <i>p</i> -F, <i>o</i> -OCH ₃ , <i>p</i> -OCH ₃ , <i>o</i> -CH ₃ , <i>p</i> -CH ₃
	σ ⁺	0.907	9.140	-0.205	1.30	10	H, <i>o</i> -Br, <i>m</i> -Cl, <i>p</i> -Cl, <i>o</i> -F, <i>p</i> -F, <i>o</i> -OCH ₃ , <i>p</i> -OCH ₃ , <i>o</i> -CH ₃ , <i>p</i> -CH ₃
	σ _I	0.921	9.482	-1.150	1.27	10	H, <i>o</i> -Br, <i>m</i> -Cl, <i>p</i> -Cl, <i>o</i> -F, <i>p</i> -F, <i>o</i> -OCH ₃ , <i>p</i> -OCH ₃ , <i>o</i> -CH ₃ , <i>p</i> -CH ₃
	σ _R	0.920	8.773	-1.306	1.27	10	H, <i>o</i> -Br, <i>m</i> -Cl, <i>p</i> -Cl, <i>o</i> -F, <i>p</i> -F, <i>o</i> -OCH ₃ , <i>p</i> -OCH ₃ , <i>o</i> -CH ₃ , <i>p</i> -CH ₃
	F	0.906	9.238	-0.275	1.30	10	H, <i>o</i> -Br, <i>m</i> -Cl, <i>p</i> -Cl, <i>o</i> -F, <i>p</i> -F, <i>o</i> -OCH ₃ , <i>p</i> -OCH ₃ , <i>o</i> -CH ₃ , <i>p</i> -CH ₃
	R	0.922	8.734	-1.256	1.27	10	H, <i>o</i> -Br, <i>m</i> -Cl, <i>p</i> -Cl, <i>o</i> -F, <i>p</i> -F, <i>o</i> -OCH ₃ , <i>p</i> -OCH ₃ , <i>o</i> -CH ₃ , <i>p</i> -CH ₃

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

Some of the single parameter correlations with Hammett substituent constants were not obeyed in the regression. While seeking these parameters in multi-regression, with F and R Swain-Lupton's [25] constants, they gave satisfactory correlations with the infrared group frequencies. The multi correlation equations are given in (2-9).

$$\nu\text{CO}(\text{cm}^{-1}) = 1621.72(\pm 2.525) + 74.938(\pm 7.341)\sigma_{\text{I}} + 24.360(\pm 8.660)\sigma_{\text{R}} \quad \dots(2)$$

$(R = 0.997, n = 10, P > 95 \%)$

$$\nu\text{CO}(\text{cm}^{-1}) = 1624.31(\pm 2.271) + 68.336(\pm 6.205)F + 32.565(\pm 7.589)R \quad \dots(3)$$

$(R = 0.997, n = 10, P > 95 \%)$

$$\nu\text{C=N}(\text{cm}^{-1}) = 1554.07(\pm 14.189) + 140.567(\pm 41.252)\sigma_{\text{I}} + 121.410(\pm 48.659)\sigma_{\text{R}} \quad \dots(4)$$

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

$$\nu\text{C=N}(\text{cm}^{-1}) = 1556.91(\pm 10.225) + 144.556(\pm 27.933)F + 137.51(\pm 34.163)R \quad \dots(5)$$

$(R = 0.989, n = 10, P > 95 \%)$

$$\nu\text{NH}_2(\text{cm}^{-1}) = 3429.50(\pm 7.877) + 78.267(\pm 22.902)\sigma_{\text{I}} + 36.066(\pm 27.015)\sigma_{\text{R}} \quad \dots(6)$$

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

$$\nu\text{NH}_2(\text{cm}^{-1}) = 3432.97(\pm 9.430) + 58.631(\pm 25.762)F + 32.491(\pm 31.508)R \quad \dots(7)$$

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

$$\nu_{\text{C-O-C}}(\text{cm}^{-1}) = 1206.83(\pm 68.971) + 345.244(\pm 200.521)\sigma_{\text{I}} + 367.608(\pm 236.529)\sigma_{\text{R}} \quad \dots(8)$$

$$(R = 0.957, n = 10, P > 95 \%)$$

$$\nu_{\text{C-O-C}}(\text{cm}^{-1}) = 1223.19(\pm 59.862) + 369.467(\pm 163.537)F + 441.53(\pm 200.009)R \quad \dots(9)$$

$$(R = 0.967, n = 10, P > 95 \%)$$

3. 2. ¹H NMR Spectral study

From the ¹H NMR spectra of compounds of the chemical shifts (δ, ppm) NH₂, -OCH₃ and -CONH are assigned and tabulated in Table 2. These chemical shifts were correlated with Hammett substituent constants, F and R parameters. The statistical analysis [26-40] of these chemical shifts is presented in Table 2.

From Table 2, the chemical shifts values of -NH₂ and -OCH₃ (δ, ppm) correlated with Hammett substituent constants and F parameter gave satisfactory correlation except R parameter.

From Table 2, the chemical shifts values of -CONH (δ, ppm) correlated with Hammett substituent constants and F and R parameter gave satisfactory correlation. The other correlations were fail. This is due to the reasons stated earlier and associated with the resonance conjugative structure as shown in Fig. 2.

Some of the single parameter correlations with Hammett substituent constants were not obeyed in the regression. While seeking these parameters in multi-regression, with F and R Swain-Lupton's [33] constants, they gave satisfactory correlations with the chemical shifts of (δ, ppm) H_α and H_β. The multi correlation equations are given in (10-15).

$$\delta_{\text{NH}_2} (\text{ppm}) = 5.648(\pm 0.030) - 0.085(\pm 0.088)\sigma_{\text{I}} - 0.035(\pm 0.103)\sigma_{\text{R}} \quad \dots(10)$$

$$(R = 0.935, n = 10, P > 90 \%)$$

$$\delta_{\text{NH}_2} (\text{ppm}) = 5.653(\pm 0.029) - 0.060(\pm 0.080)F - 0.0003(\pm 0.098)R \quad \dots(11)$$

$$(R = 0.935, n = 10, P > 90 \%)$$

$$\delta_{\text{OCH}_3} (\text{ppm}) = 3.752(\pm 0.026) + 0.009(\pm 0.038)\sigma_{\text{I}} + 0.152(\pm 0.073)\sigma_{\text{R}} \quad \dots(12)$$

$$(R = 0.969, n = 10, P > 95 \%)$$

$$\delta_{\text{OCH}_3} (\text{ppm}) = 3.756(\pm 0.024) + 0.053(\pm 0.091)F + 0.164(\pm 0.064)R \quad \dots(13)$$

$$(R = 0.976, n = 10, P > 95 \%)$$

$$\delta_{\text{CONH}} (\text{ppm}) = 9.039(\pm 0.761) - 2.635(\pm 2.212)\sigma_{\text{I}} - 3.075(\pm 2.610)\sigma_{\text{R}} \quad \dots(14)$$

$$(R = 0.945, n = 10, P > 90 \%)$$

$$\delta_{\text{CONH}} (\text{ppm}) = 8.855(\pm 0.768) - 1.698(\pm 2.099)F - 2.630(\pm 2.567)R \quad \dots(15)$$

$$(R = 0.936, n = 10, P > 90 \%)$$

4. CONCLUSIONS

Totally ten substituted 2-amino-4-isopropyl-6-methoxy-N-phenylpyrimidine-5-carboxamide compounds have been synthesized and their purities were examined by literature method. The IR and ¹H NMR spectral data of these chalcones have been assigned and correlated with Hammett sigma constants, F and R parameters using single and multi-linear

regression analysis. From the results of statistical analysis, the effects of substituents on the spectral group frequencies have been discussed. Satisfactory correlations coefficients(r) obtained for many single and all multi parameter correlations.

References

- [1] T. Panneer Selvam, C. Richa James, P. Vijaysarathy Dniandev, S. Karyn Valzita, *Res. in Phar.* 2(4) (2012) 01-09.
- [2] L. W. Hertel, G. B. Boder, J. S. Kroin, et al., *Cancer Res.* 50 (1990) 4417- 4422.
- [3] K. Desai, R. Patel, K. Chikhalia, *J. Ind. Chem.* 45(B) (2006) 773-778.
- [4] A. E. Amr, M. S. Nermien, M. M. Abdulla, *Monatsh. Chem.*, 138 (2007) 699-707.
- [5] N. Fujiwara, T. Nakajima, Y. Ueda, H. Fujita, H. Kawakami, *Bioorg. Med. Chem.* 16 (2008) 9804-9816.
- [6] L. Ballell, R. A. Field, G. A. C. Chung, R. J. Young, *Bioorg. Med. Chem. Lett.* 17 (2007) 1736-1740.
- [7] E. Wagner, K. Al-Kadasi, M. Zimecki, W. Sawka-Dobrowolska, *Eur. J. Med. Chem.* 43 (2008) 2498-2504.
- [8] K. Gorlitzer, S. Herbig, R. D. Walter, *Pharmazie.* 52 (1997) 670-672.
- [9] W. ShenJeu, L. Cheng Tsung, T. Lo Ti, W. Jing Ru, K. Hrogn Huey. W. JihPyang, and L. C. Nan, *Eur. J. Med. Chem.* 40 (2005) 103-112
- [10] Z. Machon, J. Cieplik, *Synthesis.* 2 (1986) 142-144.
- [11] Z. Machon, J. Cieplik, *J. Pharmacol. Pharm.* 40 (1988) 201-208.
- [12] N. R. Mohamed, M. M. El-Saidi, Y. M. Ali, M. H. Elnagdi, *Sci. Pharm.* 75 (2007) 9-28.
- [13] J. Cieplik, Z. MachoN, M. Zimecki, Z. Wiecek, *Arch. Immunol. Ther. Exp.* 41(1993)11-15.
- [14] J. Cieplik, Z. MachoN, M. Zimecki, Z. Wiecek, *Farmaco.* 50 (1993) 131-132
- [15] J. Pluta, M. Flendrich, J. Cieplik, *Boll. Chim. Farm.* 135 (1996) 459-464
- [16] Y. A. Mostafa, M. A. Husein, A. A. Radwan, A. H. Kfayy, *Arch. Pharm. Res. Soc. Korea.* 31 (2008) 279-293
- [17] G. T. Kim, R. J. Ryu, S. Lee Ch, H. Youn, Y. R. Cho, H. Y. Joo, *J. Antibio. Jap. Res.* (2004) 468-471.
- [18] J. Cieplik, J. Pluta, A. Meler, *Arch. Pharm. Pharm. Med. Chem.* 330 (1997) 237-241.
- [19] N. S. Habib, R. Soliman, A. A. El-Tombary, S. A. El-Hawash, O. G. Shaaban, *Arch. Pharm. Res. Soc. Korea.* 30 (2007) 1511-1520.
- [20] J. Cieplik, J. Pluta, O. Gubrynowicz, *Sci. Pharm.* 68 (2000) 333-336.
- [21] J. Cieplik, M. Raginia, J. Pluta, O. Gubrynowicz, I. Bryndal, T. Lis, *Acta. Pol. Pharm. Drug. Res.* 65 (2008) 427-434.
- [22] Z. Macho, J. Cieplik, *Eur. J. Med. Chem., Chim. Ther.* 19 (1984) 359-363.

- [23] H. R. Khunt, P. P. Pipaliya, S. M. Ghelani, J. S. Babariya, Y. T. Naliapara, *International Letters of Chemistry, Physics and Astronomy* 5 (2014) 134-121.
- [24] W.P. Hays, C. J. Timmons., *Spectrochim. Acta.* 24A (1968) 323-334.
- [25] C.G. Swain, E. C. Lupton Jr., *J. Am. Chem. Soc.* 90 (1968) 4328-4337.
- [26] R. Ranganathan, R. Arulkumaran, D. Kamalakkannan, G. Vanangamudi, G. Thirunarayanan., *IUP J. Chem.* 4(2) (2011) 60-70.
- [27] K. Sathiyamoorthi, V. Mala, R. Suresh, S. P. Sakthinathan, D. Kamalakkannan, K. Ranganathan, R. Arulkumaran, R. Sundararajan, S. Vijayakumar, G. Vanangamudi, G. Thirunarayanan, *International Letters of Chemistry, Physics and Astronomy* 7 (2013) 102-119.
- [28] V. Mala, K. Sathiyamoorthi, S. P. Sakthinathan, D. Kamalakkannan, R. Suresh, G. Vanangamudi, G. Thirunarayanan, *Q. Science Connect.* (2013) 7, DOI:<http://dx.doi.org/10.5339/connect.2013.7>
- [29] S. P. Sakthinathan, R. Suresh, V. Mala, K. Sathiyamoorthi, D. Kamalakkannan, K. Ranganathan, R. Arulkumaran, S. Vijayakumar, R. Sundararajan, G. Vanangamudi, G. Thirunarayanan, *International Letters of Chemistry, Physics and Astronomy* 6 (2013) 77-90.
- [30] R. Suresh, D. Kamalakkannan, K. Ranganathan, R. Arulkumaran, R. Sundararajan, S.P. Sakthinathan, S. Vijayakumar, K. Sathiyamoorthi, V. Mala, G. Vanangamudi, K. Thirumurthy, P. Mayavel, G. Thirunarayanan, *Spectrochim. Acta Part A*, 101 (2013) 239-248.
- [31] K. Sathiyamoorthi, V. Mala, S.P. Sakthinathan, D. Kamalakkannan, R. Suresh, G. Vanangamudi, G. Thirunarayanan., *Spectrochim. Acta Part A*, 112 (2013) 245-256
- [32] P. Janaki, K. G Sekar, G. Thirunarayanan., *Organic Chem: An Indian J.*, 9 (2013) 68-80.
- [33] R. Arulkumaran, R. Sundararajan, G. Vanangamudi, M. Subramanian, K. Ravi, V. Sathiyendiran, S. Srinivasan, G. Thirunarayanan., *IUP J. Chem.*, 3 (2010) 82-98.
- [34] S. Vijayakumar, R. Arulkumaran, R. Sundararajan, S. P. Sakthinathan, R. Suresh, D. Kamalakkannan, K. Ranganathan, K. Sathiyamoorthi, V. Mala, G. Vanangamudi, G. Thirunarayanan, *International Letters of Chemistry, Physics and Astronomy* 9 (2013) 68-86.
- [35] G. Thirunarayanan, K. G. Sekar, *International Letters of Chemistry, Physics and Astronomy* 17(2)(2014) 193-200.
- [36] G. Thirunarayanan, K. G. Sekar, *International Letters of Chemistry, Physics and Astronomy* 17(1) (2014) 10-20
- [37] G. Thirunarayanan, K.G. Sekar, R. Lakshmi Narayanan, *International Letters of Chemistry, Physics and Astronomy* 13(1) (2014) 88-94.
- [38] P. Mayavel, K. Thirumurthy, S. Dinesh Kumar, G. Thirunarayanan, *Q-Science Connect.* (2014). DOI: <http://dx.doi.org/10.5339/connect.2014.10>
- [39] G. Thirunarayanan, K. G. Sekar, *J. Taibah Univ. Sci.* 8(2014) 124-136.

- [40] V. Sathiyendiran, K. G. Sekar, G. Thirunarayanan, R. Arulkumaran, R. Sundararajan, D. Kamalakkannan, R. Suresh, V. Manikanadan, R. Vijayakumar, G. Vanangamudi, *International Letters of Chemistry, Physics and Astronomy* 11(1) (2014) 33-43.

(Received 01 August 2014; accepted 10 August 2014)