Synthesis and spectral correlation study of some 3-(3,4-dichlorophenyl)-5-(substituted phenyl)-4,5-dihydro-^{1}*H*-pyrazole-1-yl-ethanones

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ABSTRACT

Some N-acetyl pyrazoles including 3-(3,4-dichlorophenyl)-5-(substituted phenyl)-4,5-dihydro-^{1}*H*-pyrazole-1-yl-ethanones have been synthesised by solvent free cyclization cum acetylation of chalcones including substituted styryl 3,4-dichlorophenyl ketones using hydrazine hydrate and acetic anhydride in presence of catalytic amount of fly-ash: H_2SO_4 catalyst. The yield of these N-acetyl pyrazole derivatives are more than 75 %. The synthesised N-acetyl pyrazoline derivatives were characterized by their physical constants and spectral data. The infrared spectral νC=N and C=O (cm^{-1}) frequencies, NMR chemical shifts (δ, ppm) of H_a, H_b, H_c, CH_3 protons, C=N, C=O and CH_3 carbons of 1-(3-(3,4-dichlorophenyl)-5-(substitutedphenyl)-4,5-dihydro-^{1}*H*-pyrazole-1-yl) ethanones have been assigned and correlated with Hammett substituent constants and Swain-Lupton's parameters using single and multi-regression analysis. From the results of statistical analyses the effect of substituents on the above group frequencies and chemical shifts of the acetylated pyrazoles were discussed.

Keywords: Solvent-free cyclization cum acetylation; N-acetyl pyrazoles; IR spectra; NMR spectra; Hammett correlations

1. INTRODUCTION

The [1]*N*-acetyl pyrazoline is a five membered bi-nitrogen compounds and one of the derivative of 4,5-dihydro-^{1}*H*-pyrazoles. These N-acetyl pyrazole derivatives are important precursor for synthesis of various pyrazoline based heterocycles such as cyanopyridine [1] indoxacarb [2] carbohydrazide hydrazine [3], pyrimidine [4]. There are numerous solvent-free or solvent assisted acetylation methods available for synthesis of N-acetylated pyrazoline derivatives in literature [5-8]. Glacial acetic acid and acetic anhydride were employed with solvent assistant conventional heating, solvent-free microwave and ultrasounds wave irradiation for acetylation of pyrazolines [5,6]. Osman et al., [1] have synthesised up to 75 % yield of 4,7-dimethoxy-5-(5-aryl-N-acetylpyrazolin-3-yl)benzofuran-6-ols by refluxation of Khellinone chalcones, hydrazine hydrate and glacial acetic acid. The 5-(*p*-tolyl)-4,5-dihydro-

1-acetyl-pyrazol-3-yl]-phenyl}-3H-quinazolin-4-ones were synthesised using refluxation method of corresponding chalcones with hydrazine acetic acid in ethanol by Mosaad et al [9]. More than 84 % yield of some series of new N[1]-cinnamoyl-3, 5-diaryl-2-pyrazolines has been synthesised using microwave as well as in conventional heating by Srivastava et al., [6]. Shah et al., have synthesised up to 75 % yield and studied the IR and ^{1}H NMR spectra of some new series of 4-(4-hydroxyphenyl)-3-chloro-1-{4-[5-(substituted phenyl)-1-acetyl-4,5-dihydro-pyrazol-3-yl]phenyl} azetidin-2-one are synthesized by reacting 3-chloro-1-{4-[5-(substitutedphenyl)-4,5-dihydro-pyrazol-3-yl]phenyl}-4-(4-hydroxyphenyl) azetidin-2-one with acetic acid [10]. N-acetyl-3-(2-naphthyl)-5-aryl pyrazoline derivatives were synthesised and studied their FTIR, NMR and HRMS data by Ethiraj et al., [11]. Many N-acetyl pyrazole derivatives such as N-acetyl-3,5-diphenyl pyrazolines[12], 1-acetyl-4-[5-(3-chloro-4-fluorophenyl)-2-furyl]-3-substituted phenyl-4,5-dihydro-1H-pyrazoles [13], 2,4-bis-(tetrahydro-1,4-oxazine)-6-[4"-{1"-acetyl-5"-(4"'-methoxyphenyl)-2"-pyrazoline-3"-yl} phenylamino]-*s*-triazine [14], fluorine containing arylfuryl N-acetylpyrazolines [7] and 4,6-dimethoxy-5-(1-acetyl-5-aryl-2-pyrazolin-3-yl)benzo[b]furans [15] were synthesised by synthetic organic chemists using conventional heating method and studied their spectral data.

These 1-acetyl pyrazoline derivatives possess important biological activities such as antibacterial [6,7,10,13], endogenous proteolysis [12], cytotoxicity [11], EGFR kinase [8] and anti-inflammatory activities [9]. Spectroscopic data are useful for studying the ground state equilibration of organic compounds. The ultraviolet spectroscopic data of absorption maxima (λ max, nm) is also applied for prediction of the effect of substituents [16]. In pyrazoline molecules (^{1}H pyrazoles), the infrared spectra is used for predicting the effects of substituents on the vibrations of C=N, C-H, N-H [17]. From NMR spectroscopy, the spatial arrangements of the protons H_a, H_b and H_c or H_a, H_b, H_c and H_d of the types shown in Fig. 1 were predictable by their frequencies with multiplicities viz.,
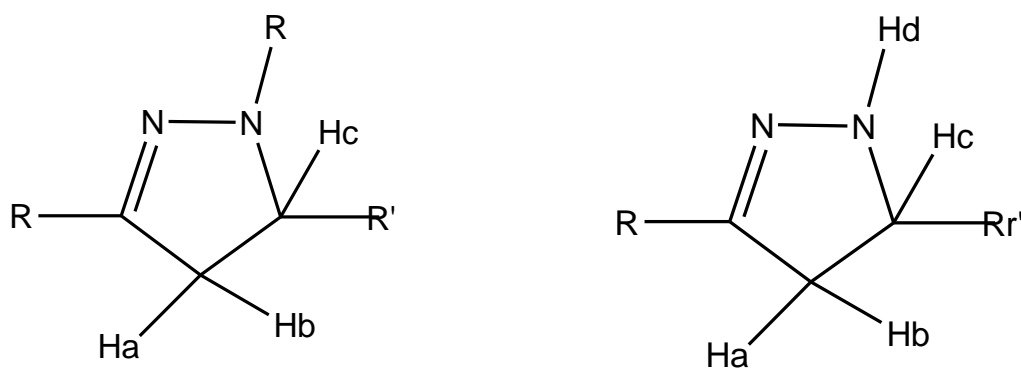

Fig. 1. General structure of 1*H*-pyrazoles.

doublet or triplet or doublet of doublets. Based on the geometry, the chemical shift of the protons of respective pyrazoles has been assigned and the effects of substituent will be studied. The effects of substituent on the 2-naphthyl based pyrazoline ring protons were studied first by Sakthinathan et. al., [17]. In their study, they assigned infrared νC=N (cm^{-1}), NMR chemical shifts (δ, ppm) of H_a, H_b, H_c, C=N values and correlated with Hammett

substituents. In these correlations they observed satisfactory r values. Thirunarayanan et al. [18] have studied the solvent free synthesis, spectral correlations of some 1-phenyl-3-(5-bromothiophen-2-yl)-5-(substituted phenyl)-2-pyrazolines. Recently Thirunarayanan and Sekar have studied the microwave assisted synthesis and spectral correlation of some substituted 1-thiocarbomyl pyrazolines including 3-(3,4-dichlorophenyl)-5-(substituted phenyl)-4,5-dihydro-[1]*H*-pyrazole-1-carbothioamides [19].

The literature survey reveals that there is no information available for solvent-free synthesis of some N-acetyl pyrazolines including 3-(3,4-dichlorophenyl)-5 (substitutedphenyl)-4,5-dihydro-[1]*H*-pyrazole) derivatives by cyclization of the respective chalcones and acetic anhydride in presence of solid fly-ash: H_2SO_4 catalyst. Therefore the authors have taken efforts to synthesis some N-acetyl pyrazolines including 3-(3,4-dichlorophenyl)-5-(substitutedphenyl)-4,5-dihydro-[1]*H*-pyrazole) derivatives by solvent free microwave assisted cyclization of chalcones, hydrazine hydrate and acetic anhydride in presence of catalytic quantity of fly-ash: H_2SO_4.

The purities of these pyrazolines were checked by their physical constants and spectral data published earlier in literature. Also the authors have recorded the infrared and NMR spectra of these synthesised N-acetyl pyrazoline derivatives for studying the Hammett spectral correlations.

## 2. EXPERIMENTAL

2. 1. Materials and methods

All chemicals used were procured from Sigma-Aldrich and E-Merck. Melting points of all pyrazoles have been determined in open glass capillaries on Mettler FP51 melting point apparatus and are uncorrected. Infrared spectra (KBr, 4000-400 cm^{-1}) have been recorded on BRUKER (Thermo Nicolet) Fourier transform spectrophotometer.

The NMR spectra of all pyrazolines have been recorded on Bruker AV400 spectrometer operating at 400 MHz for recording ^{1}H and 100 MHz for ^{13}C spectra in CDCl$_3$ solvent using TMS as internal standard. Mass spectra have been recorded on SHIMADZU spectrometer using chemical ionization technique.

2. 2. Synthesis of N-acetyl substituted pyrazole derivatives [20]

An appropriate equi-molar quantities of 3,4-dichloro phenyl chalcones (2 mmol) [20], hydrazine hydrate (2 mmol), acetic anhydride (1 mmol) and fly-ash: H_2SO_4 (0.5 g) were taken in a 50 mL borosil beaker and closed with lid. The mixture has been subjected to microwave irradiation for 4-6 minutes in a microwave oven at 550 watts, 2540 MHz frequency (Scheme 1) (Samsung Grill, GW73BD Microwave oven, 230 V A/c, 50 Hz, 2450 Hz, 100-750 W (IEC-705), and then cooled to room temperature. After separating the organic layer with dichloromethane, the solid product has been obtained on evaporation.

The solid, on recrystallization from benzene-hexane mixture afforded glittering product. The insoluble catalyst has been recycled by washing with ethyl acetate (8 mL) followed by drying in an oven at 100 °C for 1h and reused for further reactions. The analytical, physical constants and mass fragments of the synthesised 1-acetylpyrazolines were presented in Table1.
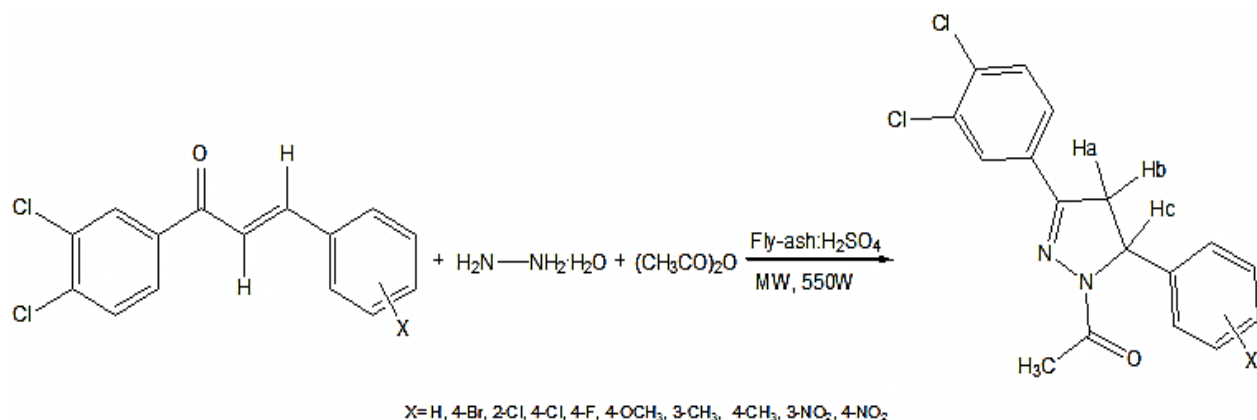
Scheme 1. Synthesis of 3-(3,4-dichlorophenyl)-5-(substituted phenyl)-4,5-dihydro-[1]*H*-pyrazole-1-yl-ethanones.

Table 1. Analytical, physical constants and Mass fragments data of 3-(3,4-dichlorophenyl)-5-(substituted phenyl)-4,5-dihydro-[1]*H*-pyrazole-1-yl-ethanones.

Entry	X	M. F.	M.W.	m.p. (°C)	Mass (m/z)
1	H	$C_{17}H_{14}Cl_2N_2O$	334	121-122(121-122) [20]	$334M^+$, $336M^{2+}$, $338M^{4+}$
2	4-Br	$C_{17}H_{13}BrCl_2N_2O$	412	135-136(135-136) [20]	$412M^+$, $414M^{2+}$, $416M^{4+}$
3	2-Cl	$C_{17}H_{13}Cl_3N_2O$	368	119-120(119-120) [20]	$368M^+$, $370M^{2+}$, $372M^{4+}$
4	4-Cl	$C_{17}H_{13}Cl_3N_2O$	368	131-132(131-132) [20]	$368M^+$, $370M^{2+}$, $372M^{4+}$
5	4-F	$C_{17}H_{13}Cl_2FN_2O$	350	147-148(147-148) [20]	$350M^+$, $352M^{2+}$, $354M^{4+}$
6	4-OCH_3	$C_{18}H_{16}Cl_2N_2O_2$	364	112-113(112-113) [20]	$364M^+$, $366M^{2+}$, $368M^{4+}$
7	3-CH_3	$C_{18}H_{16}Cl_2N_2O$	348	125-126(125-126) [20]	$348M^+$, $350M^{2+}$, $352M^{4+}$
8	4-CH_3	$C_{18}H_{16}Cl_2N_2O$	348	116-117(116-117) [20]	$348M^+$, $350M^{2+}$, $352M^{4+}$
9	3-NO_2	$C_{17}H_{13}Cl_2N_3O_3$	378	152-153(152-153) [20]	$378M^+$, $380M^{2+}$, $382M^{4+}$
10	4-NO_2	$C_{17}H_{13}Cl_2N_3O_3$	378	147-148(147-148) [20]	$378M^+$, $380M^{2+}$, $382M^{4+}$

3. RESULTS AND DISCUSSION

3. 1. Spectral correlations

In the present investigation, the spectral linearity of 1-(3-(3,4-dichlorophenyl)-5-(substituted phenyl)-4,5-dihydro-[1]*H*-pyrazole-1-yl) ethanones has been studied by assessment of the substituent effects [16-19,21-26] on the absorption group frequencies. The infrared carbonyl stretches νCO, CN (cm^{-1}) and NMR chemical shifts δ(ppm) of H_a, H_b, H_c, CH_3 protons, C=N, C=O and CH_3 carbons were assigned and these frequencies were correlated with Hammett substituent constants, F and R parameters.

3. 1. 1. IR spectral study

The νC=N and CO stretching frequencies (cm^{-1}) of 1-(3-(3,4-dichlorophenyl)-5-(substituted phenyl)-4,5-dihydro-^1H-pyrazole-1-yl) ethanones of the present study are presented in Table 2. These data have been correlated with Hammett substituent constants and Swain-Lupton's constants [27]. The results of statistical analyses were shown in Table 3. In this correlation the structure parameter Hammett equation employed is as shown in the following equation (1).

$$\nu = \rho\sigma + \nu_0 \qquad \qquad …(1)$$

Where ν is the carbonyl frequencies of substituted system and ν_0 is the corresponding quantity of unsubstitued system; σ is a Hammett substituent constant, which is characteristics of the substituent and ρ is a reaction constant which depends upon the nature of the reaction.

The νC=N and C=O stretching frequencies (cm^{-1}) with Hammett σ, σ^+, σ_I constants and F parameters has shown satisfactory correlation excluding 4-Cl, 4-OCH$_3$, 4-CH$_3$ and nitro substituents. If these substituents included in the correlations, they reduced the correlations considerably. All correlations gave positive ρ value. This means that the normal substituent effects operate in all systems. The Hammett σ_R constant and R parameters were fail in correlation. This is due to the weak resonance effect of the substituents, unable to transmit their effects on the stretching frequencies and is associated with the resonance – conjugative structure shown in Fig. 2.
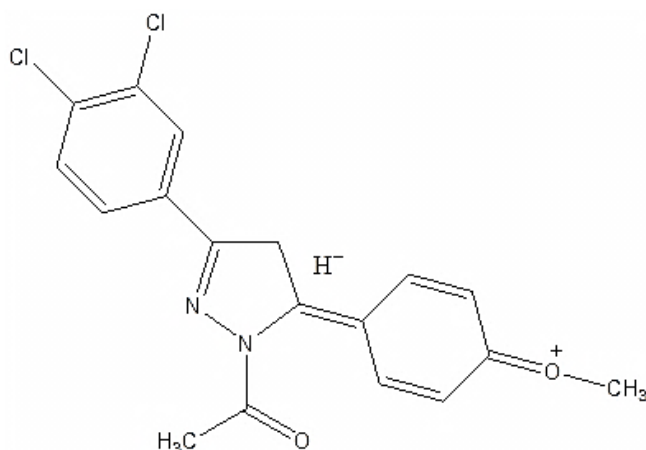

Fig. 2. The resonance-conjugative structure.

In view of the inability of some of the Hammett σ constants to produce individually satisfactory correlations, it was thought as worthwhile to seek multiple correlations involving either σ_I and σ_R constants or Swain-Lupton's [27] F and R parameters. The correlation equations for CN and CO are given in equations (2-5).

Table 2. The infrared, NMR spectral data of 3-(3,4-dichlorophenyl)-5-(substitutdphenyl)-4,5-dihydro-[1]*H*-pyrazole-1-yl-ethanones.

Entry	X	IR		^{1}H NMR					[13]C			
		C=N	C=O	H_a	H_b	H_c	CH_3	X	C=N	C=O	CH_3	X
1	H	1574.18	1641.20	3.297	3.819	5.568	2.934	---	159.06	168.67	24.46	---
2	4-Br	1578.21	1644.65	3.197	3.857	5.565	2.401	---	159.66	173.56	24.61	---
3	2-Cl	1576.84	1643.82	3.195	3.879	5.594	2.295	---	158.97	172.96	25.87	---
4	4-Cl	1577.71	1647.41	3.851	2.996	5.671	2.265	---	158.67	169.80	25.81	---
5	4-F	1576.21	1644.17	3.201	3.846	6.071	2.401	---	159.71	168.12	24.16	---
6	4-OCH$_3$	1570.07	1638.74	3.117	3.701	5.457	2.249	3.845	158.58	168.80	22.74	58.45
7	3-CH$_3$	1571.19	1640.94	3.153	3.794	5.497	2.310	2.401	157.67	172.05	24.77	24.68
8	4-CH$_3$	1570.27	1639.71	3.167	3.807	5.943	2.287	2.316	158.09	171.94	23.79	24.35
9	3-NO$_2$	1575.16	1644.97	3.208	3.943	5.973	2.441	---	159.87	174.91	26.97	---
10	4-NO$_2$	1575.97	1645.08	3.217	3.997	5.997	2.531	---	159.97	174.96	26.87	---

Table 3. Results of statistical analysis of infrared ν(cm^{-1}) C=N, C=O, NMR chemical shifts (δ,ppm) of H_a, H_b, H_c, C=N, C=O, and CH$_3$ of 3-(3,4-dichlorophenyl)-5-(substituted phenyl)-4,5-dihydro-[1]*H*-pyrazole-1-yl-ethanones with Hammett σ, σ^+, σ_I σ_R constants and F and R parameters.

Frequency	Constants	r	I	ρ	s	n	Correlated derivatives
νC=N	σ	0.907	1573.69	5.193	2.88	8	H, 4-Br, 2-Cl, 4-Cl, 4-F, 4-OCH$_3$, 3-CH$_3$, 4-CH$_3$
	σ^+	0.907	1574.29	4.297	2.08	8	H, 4-Br, 2-Cl, 4-Cl, 4-F, 4-OCH$_3$, 3-CH$_3$, 4-CH$_3$
	σ_I	0.907	1571.88	7.879	2.24	7	H, 4-Br, 2-Cl, 4-Cl, 4-F, 3-CH$_3$, 4-NO$_2$
	σ_R	0.880	1574.74	1.202	3.22	10	H, 4-Br, 2-Cl, 4-Cl, 4-F, 4-OCH$_3$, 3-CH$_3$, 4-CH$_3$, 3-NO$_2$, 4-NO$_2$
	F	0.906	1572.01	7.063	2.45	8	H, 4-Br, 2-Cl, 4-Cl, 4-F, 4-OCH$_3$, 3-CH$_3$, 4-CH$_3$
	R	0.818	1575.04	2.330	3.17	10	H, 4-Br, 2-Cl, 4-Cl, 4-F, 4-OCH$_3$, 3-CH$_3$, 4-CH$_3$, 3-NO$_2$, 4-NO$_2$
νC=O	σ	0.907	1642.08	5.744	1.99	8	H, 4-Br, 2-Cl, 4-Cl, 4-F, 4-OCH$_3$, 3-CH$_3$, 4-CH$_3$

	σ^+	0.907	1642.81	3.864	1.92	8	H, 4-Br, 2-Cl, 4-Cl, 4-F, 4-OCH$_3$, 3-CH$_3$, 4-CH$_3$
	σ_I	0.907	1640.46	7.603	1.88	8	H, 4-Br, 2-Cl, 4-F, 3-CH$_3$, 4-CH$_3$, 3-NO$_2$, 4-NO$_2$
	σ_R	0.832	1643.48	3.024	2.85	10	H, 4-Br, 2-Cl, 4-Cl, 4-F, 4-OCH$_3$, 3-CH$_3$, 4-CH$_3$, 3-NO$_2$, 4-NO$_2$
	F	0.907	1640.54	6.924	2.08	8	H, 4-Br, 2-Cl, 4-F, 3-CH$_3$, 4-CH$_3$, 3-NO$_2$, 4-NO$_2$
	R	0.831	1643.73	3.490	2.78	10	H, 4-Br, 2-Cl, 4-Cl, 4-F, 4-OCH$_3$, 3-CH$_3$, 4-CH$_3$, 3-NO$_2$, 4-NO$_2$
δH_a	σ	0.901	3.246	0.080	0.22	8	4-Br, 2-Cl, 4-Cl, 4-F, 4-OCH$_3$, 3-CH$_3$, 3-NO$_2$, 4-NO$_2$
	σ^+	0.901	3.256	0.058	0.22	8	4-Br, 2-Cl, 4-Cl, 4-F, 4-OCH$_3$, 3-CH$_3$, 3-NO$_2$, 4-NO$_2$
	σ_I	0.816	3.217	0.125	0.22	10	H, 4-Br, 2-Cl, 4-Cl, 4-F, 4-OCH$_3$, 3-CH$_3$, 4-CH$_3$, 3-NO$_2$, 4-NO$_2$
	σ_R	0.803	3.264	0.031	0.22	10	H, 4-Br, 2-Cl, 4-Cl, 4-F, 4-OCH$_3$, 3-CH$_3$, 4-CH$_3$, 3-NO$_2$, 4-NO$_2$
	F	0.907	3.238	0.060	0.22	8	4-Br, 2-Cl, 4-F, 4-OCH$_3$, 3-CH$_3$, 4-CH$_3$, 3-NO$_2$, 4-NO$_2$
	R	0.811	3.277	0.102	0.22	10	H, 4-Br, 2-Cl, 4-Cl, 4-F, 4-OCH$_3$, 3-CH$_3$, 4-CH$_3$, 3-NO$_2$, 4-NO$_2$
δH_b	σ	0.922	3.732	0.181	0.29	10	H, 4-Br, 2-Cl, 4-Cl, 4-F, 4-OCH$_3$, 3-CH$_3$, 4-CH$_3$, 3-NO$_2$, 4-NO$_2$
	σ^+	0.907	3.755	0.125	0.29	10	H, 4-Br, 2-Cl, 4-Cl, 4-F, 4-OCH$_3$, 3-CH$_3$, 4-CH$_3$, 3-NO$_2$, 4-NO$_2$
	σ_I	0.905	3.745	0.258	0.29	8	H, 4-Br, 2-Cl, 4-Cl, 4-F, 3-CH$_3$, 4-CH$_3$, 3-NO$_2$,
	σ_R	0.825	3.810	0.342	0.28	10	H, 4-Br, 2-Cl, 4-Cl, 4-F, 4-OCH$_3$, 3-CH$_3$, 4-CH$_3$, 3-NO$_2$, 4-NO$_2$
	F	0.901	3.726	0.111	0.29	8	H, 4-Br, 2-Cl, 4-Cl, 3-CH$_3$, 4-CH$_3$, 3-NO$_2$, 4-NO$_2$

	R	0.902	3.807	0.228	0.29	9	H, 4-Br, 2-Cl, 4-Cl, 4-OCH$_3$, 3-CH$_3$, 4-CH$_3$, 3-NO$_2$, 4-NO$_2$
δH$_c$	σ	0.905	5.675	0.339	0.21	8	H, 4-Br, 2-Cl, 4-Cl, 4-OCH$_3$, 3-CH$_3$, 3-NO$_2$, 4-NO$_2$
	σ^+	0.904	5.720	0.200	0.22	8	H, 4-Br, 2-Cl, 4-Cl, 4-OCH$_3$, 3-CH$_3$, 3-NO$_2$, 4-NO$_2$
	σ_I	0.904	5.604	0.378	0.22	7	4-Br, 2-Cl, 4-Cl, 4-F, 4-OCH$_3$, 3-NO$_2$, 4-NO$_2$
	σ_R	0.852	5.799	0.248	0.24	10	H, 4-Br, 2-Cl, 4-Cl, 4-F, 4-OCH$_3$, 3-CH$_3$, 4-CH$_3$, 3-NO$_2$, 4-NO$_2$
	F	0.905	5.564	0.741	0.20	7	4-Br, 2-Cl, 4-Cl, 4-F, 4-OCH$_3$, 3-NO$_2$, 4-NO$_2$
	R	0.819	5.769	0.189	0.24	10	H, 4-Br, 2-Cl, 4-Cl, 4-F, 4-OCH$_3$, 3-CH$_3$, 4-CH$_3$, 3-NO$_2$, 4-NO$_2$
δCH$_3$	σ	0.902	2.391	0.117	0.21	9	H, 4-Br, 2-Cl, 4-F, 4-OCH$_3$, 3-CH$_3$, 4-CH$_3$, 3-NO$_2$, 4-NO$_2$
	σ^+	0.902	2.404	0.107	0.20	9	H, 4-Br, 2-Cl, 4-F, 4-OCH$_3$, 3-CH$_3$, 4-CH$_3$, 3-NO$_2$, 4-NO$_2$
	σ_I	0.901	2.444	0.909	0.21	7	4-Br, 2-Cl, 4-Cl, 4-F, 4-OCH$_3$, 3-NO$_2$, 4-NO$_2$
	σ_R	0.904	2.471	0.435	0.19	9	H, 2-Cl, 4-Cl, 4-F, 4-OCH$_3$, 3-CH$_3$, 4-CH$_3$, 3-NO$_2$, 4-NO$_2$
	F	0.901	2.450	-0.106	0.21	7	4-Br, 2-Cl, 4-Cl, 4-F, 4-OCH$_3$, 3-NO$_2$, 4-NO$_2$
	R	0.904	2.485	0.390	0.19	9	H, 4-Br, 2-Cl, 4-Cl, 4-OCH$_3$, 3-CH$_3$, 4-CH$_3$, 3-NO$_2$, 4-NO$_2$
δC=N	σ	0.907	158.74	1.640	0.55	8	H, 4-Br, 2-Cl, 4-Cl, 3-CH$_3$, 4-CH$_3$, 3-NO$_2$, 4-NO$_2$
	σ^+	0.907	158.94	1.153	0.50	8	H, 4-Br, 2-Cl, 4-Cl, 3-CH$_3$, 4-CH$_3$, 3-NO$_2$, 4-NO$_2$
	σ_I	0.908	158.22	2.333	0.46	9	4-Br, 2-Cl, 4-Cl, 4-F, 4-OCH$_3$, 3-CH$_3$, 4-CH$_3$, 3-NO$_2$, 4-NO$_2$
	σ_R	0.821	159.15	0.825	0.81	10	H, 4-Br, 2-Cl, 4-Cl, 4-F, 4-OCH$_3$, 3-CH$_3$, 4-CH$_3$, 3-NO$_2$, 4-NO$_2$
	F	0.908	158.18	2.307	0.46	9	4-Br, 2-Cl, 4-Cl, 4-F,

		r	ρ	I	s	n	
							4-OCH$_3$, 3-CH$_3$, 4-CH$_3$, 3-NO$_2$, 4-NO$_2$
	R	0.824	159.17	0.771	0.80	10	H, 4-Br, 2-Cl, 4-Cl, 4-F, 4-OCH$_3$, 3-CH$_3$, 4-CH$_3$, 3-NO$_2$, 4-NO$_2$
δC=O	σ	0.908	173.02	2.633	0.66	10	H, 4-Br, 2-Cl, 4-Cl, 4-F, 4-OCH$_3$, 3-CH$_3$, 4-CH$_3$, 3-NO$_2$, 4-NO$_2$
	σ$^+$	0.901	173.37	1.568	0.67	10	H, 4-Br, 2-Cl, 4-Cl, 4-F, 4-OCH$_3$, 3-CH$_3$, 4-CH$_3$, 3-NO$_2$, 4-NO$_2$
	σ$_I$	0.907	172.46	2.985	0.68	10	H, 4-Br, 2-Cl, 4-Cl, 4-F, 4-OCH$_3$, 3-CH$_3$, 4-CH$_3$, 3-NO$_2$, 4-NO$_2$
	σ$_R$	0.904	173.83	2.639	1.02	8	H, 4-Br, 2-Cl, 4-Cl, 4-F, 4-OCH$_3$, 3-NO$_2$, 4-NO$_2$
	F	0.906	172.56	2.583	0.92	8	4-Br, 2-Cl, 4-Cl, 4-OCH$_3$, 3-CH$_3$, 4-CH$_3$, 3-NO$_2$, 4-NO$_2$
	R	0.905	173.94	2.470	0.99	8	4-Br, 2-Cl, 4-Cl, 4-OCH$_3$, 3-CH$_3$, 4-CH$_3$, 3-NO$_2$, 4-NO$_2$
δCH$_3$	σ	0.906	24.15	0.900	0.39	7	H, 4-Br, 4-F, 4-OCH$_3$, 4-CH$_3$, 3-NO$_2$, 4-NO$_2$
	σ$^+$	0.904	23.27	0.426	0.45	7	H, 4-Br, 4-F, 4-OCH$_3$, 4-CH$_3$, 3-NO$_2$, 4-NO$_2$
	σ$_I$	0.822	25.53	0.368	0.50	10	H, 4-Br, 2-Cl, 4-Cl, 4-F, 4-OCH$_3$, 3-CH$_3$, 4-CH$_3$, 3-NO$_2$, 4-NO$_2$
	σ$_R$	0.907	24.16	1.654	0.35	10	H, 4-Br, 2-Cl, 4-Cl, 4-F, 4-OCH$_3$, 3-CH$_3$, 4-CH$_3$, 3-NO$_2$, 4-NO$_2$
	F	0.822	26.31	0.388	0.50	10	H, 4-Br, 2-Cl, 4-Cl, 4-F, 4-OCH$_3$, 3-CH$_3$, 4-CH$_3$, 3-NO$_2$, 4-NO$_2$
	R	0.906	23.54	1.274	0.39	10	H, 4-Br, 2-Cl, 4-Cl, 4-F, 4-OCH$_3$, 3-CH$_3$, 4-CH$_3$, 3-NO$_2$, 4-NO$_2$

r = correlation co-efficient; ρ = slope; I = intercept; s = standard deviation; n = number of substituents

$$\nu C=N \ (cm^{-1}) = 1571.98(\pm 1.365) + 7.845(\pm 2.873)\ \sigma_I + 0.642(\pm 0.037)\ \sigma_R \qquad \ldots(2)$$
$$(R = 0.972,\ n = 10,\ P > 95\ \%)$$

$$\nu C=N \ (cm^{-1}) = 1572.48(\pm 1.479) + 7.156(\pm 2.998)\ F + 2.653(\pm 0.035)\ R \qquad \ldots(3)$$
$$(R = 0.968,\ n = 10,\ P > 95\ \%)$$

$$\nu C=O \ (cm^{-1}) = 1642.84 \ (\pm 1.099) + 7.051 \ (\pm 2.313) \ \sigma_I + 2.489 \ (\pm 0.305) \ \sigma_R \qquad \dots(4)$$
$$(R = 0.978, \ n = 10, \ P > 95 \ \%)$$

$$\nu C=O \ (cm^{-1}) = 1641.22 \ (\pm 1.152) + 7.058 \ (\pm 1.338) \ F + 3.809 \ (\pm 2.651) \ R \qquad \dots(5)$$
$$(R = 0.977, \ n = 10, \ P > 95 \ \%)$$

3. 1. 2. ^{1}H NMR spectral study

The ^{1}H NMR spectra of synthesized 1-(3-(3,4-dichlorophenyl)-5-(substituted phenyl)-4,5-dihydro-[1]H-pyrazole-1-yl) ethanones were recorded in deuteriochloroform solutions employing tetramethylsilane (TMS) as internal standard. The signals of the pyrazoline ring protons have been assigned. They have been calculated as AB or AA' systems respectively. The chemical shifts (ppm) of H_a are at higher fields than those of H_b and H_c in this series of 1-acetyl pyrazolines. This is due to the deshielding of H_b and H_c which are in different chemical as well as magnetic environment. These H_a protons gave an AB pattern and the H_b proton doublet of doublet in most cases was well separated from the signals H_c and the aromatic protons. The assigned chemical shifts (ppm) of the pyrazoline ring H_a, H_b and H_c protons are presented in Table 2.

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

$$\text{Log } \delta = \text{Log } \delta_0 + \rho\sigma \qquad \dots(6)$$

where δ_0 is the chemical shift of unsubstitued ketones.

The assigned H_a, H_b and H_c proton chemical shifts (ppm) of synthesized 1-(3-(3,4-dichlorophenyl)-5-(substituted phenyl)-4,5-dihydro-[1]H-pyrazole-1-yl) ethanones have been correlated with various Hammett sigma constants. The results of statistical analysis [16-19,21-26] are presented in Table 3. The H_a proton chemical shifts (δ, ppm) with Hammett σ, σ^+ constants and F parameters gave satisfactory correlations excluding H, 4-Cl and 4-CH$_3$ substituents. All correlations gave positive ρ values and it implies that there is a normal substituent effect operates in all systems. The resonance effect and R parameter were fail in correlation. The failure in correlation is associated with the conjugative structure shown in Fig. 2.

The results of statistical analysis of H_b proton chemical shifts (δ, ppm) with Hammett substituent constants, F and R parameters were shown in Table 3. The H_b proton chemical shifts (δ, ppm) with Hammett substituent constants, F and R parameters gave satisfactory correlation excluding 4-F, 4-OCH$_3$ and 4-NO$_2$ substituents. Hammett σ_R constant has shown poor correlation. All correlation gave positive ρ values. The poor correlation is due to the absence or incapability of transmittance of resonance effect of substituent on the H_b proton chemical shifts and it is associated with the conjugative structure shown in Fig. 2.

The results of statistical analysis of H_c proton chemical shifts (δ, ppm) with Hammett substituents are presented in Table 3. The H_c proton chemical shifts with Hammett σ, σ^+, σ_I, constants and F parameters gave satisfactory correlation excluding 4-F, 3-CH$_3$ and 4-CH$_3$ substituents. All correlations produce positive ρ values. This means that the normal substituent effect operates in all systems. The Hammett σ_I constant and R parameter has shown poor correlation with H_c chemical shifts (δ, ppm) of the synthesised 1-(3-(3,4-dichlorophenyl)-5-(substituted phenyl)-4,5-dihydro-[1]H-pyrazole-1-yl) ethanones. The failure

in correlation was the reasons stated earlier and associated with conjugative structure shown in Fig. 2.

The methyl proton singlet was assigned for the synthesised 1-(3-(3,4-dichlorophenyl)-5-(substituted phenyl)-4,5-dihydro-[1]*H*-pyrazole-1-yl) ethanones and these chemical shifts were correlated with Hammett substituent constants and Swain-Lupton's [27] parameters. The results of the statistical analyses were shown in Table 3. The chemical shift of the methyl protons singlet were satisfactory correlated with Hammett substituent constants, F and R parameters excluding H, 4-Br, 4-Cl, 4-F, 3-CH$_3$ and 4-CH$_3$ substituents. If these substituents were included in the regression, they reduced the correlations considerably.

In view of the inability of the Hammett σ constants to produce satisfactory correlation individually, the authors think that it is worthwhile to seek multiple correlations involving either σ$_I$ and σ$_R$ constants or Swain-Lupton's[27] F and R parameters. The correlation equations for H$_{a-c}$ proton chemical shifts (δ, ppm) are given in (7-14).

$$\delta H_a^{(ppm)} = 3.220\ (\pm 0.135) + 0.124\ (\pm 0.025)\ \sigma_I + 0.022\ (\pm 0.004)\ \sigma_R \qquad \ldots(7)$$
$$(R = 0.916, P > 90\ \%,\ n = 10)$$

$$\delta H_a^{(ppm)} = 3.2457\ (\pm 0.140) + 0.063(\pm 0.024)\ F + 0.105\ (\pm 0.003\ R \qquad \ldots(8)$$
$$(R = 0.914, P > 90\ \%,\ n = 10)$$

$$\delta H_b^{(ppm)} = 3.797\ (\pm 0.175) + 0.038\ (\pm 0.020)\ \sigma_I + 0.340\ (\pm 0.041)\ \sigma_R \qquad \ldots(9)$$
$$(R = 0.925, P > 90\ \%,\ n = 0)$$

$$\delta H_b^{(ppm)} = 3.764\ (\pm 0.182) + 0.119\ (\pm 0.369)\ F + 0.238\ (\pm 0.001)\ R \qquad \ldots(10)$$
$$(R = 0.923, P > 90\ \%,\ n = 10)$$

$$\delta H_c^{(ppm)} = 5.636\ (\pm 0.132) + 0.369\ (\pm 0.023)\sigma_I + 0.217\ (\pm 0.002)\ \sigma_R \qquad \ldots(11)$$
$$(R = 0.948, P > 90\ \%,\ n = 10)$$

$$\delta H_c^{(ppm)} = 5.598\ (\pm 0.128) + 0.481\ (\pm 0.074)\ F + 0.218(\pm 0.026)\ R \qquad \ldots(12)$$
$$(R = 0.960, P > 95\ \%,\ n = 10)$$

$$\delta CH_3^{(ppm)} = 2.512\ (\pm 0.116) - 0.117\ (\pm 0.021)\ \sigma_I + 0.444\ (\pm 0.032)\ \sigma_R \qquad \ldots(13)$$
$$(R = 0.947, P > 90\ \%,\ n = 10)$$

$$\delta CH_3^{(ppm)} = 2.518\ (\pm 0.128) - 0.092\ (\pm 0.024)\ F + 0.386\ (\pm 0.037)\ R \qquad \ldots(14)$$
$$(R = 0.948, P > 90\ \%,\ n = 10)$$

3. 1. 3. ^{13}C NMR spectra

Chemists, physical organic chemists and spectral analysts [16-19,21-26] have made extensive study of ^{13}C NMR spectra for a large number of ketones, styrenes keto-epoxides and pyrazolines. In their study, they investigated the linear correlation of the chemical shifts (ppm) of vinyl, C=N and carbonyl carbons with Hammett σ constants, F and R parameters. In the present study, the ^{13}C chemical shifts (δ, ppm) of C=N, C=O and CH$_3$ carbon of 1-(3-(3,4-Dichlorophenyl)-5-(substituted phenyl)-4,5-dihydro-[1]*H*-pyrazole-1-yl) ethanones have been assigned and are presented in Table 2. Attempts have been made to correlate the above assigned carbon chemical shifts (δ, ppm) with Hammett substituent constants, field and

resonance parameters with the help of single and multi-regression analyses to study the reactivity through the effect of substituents.

The chemical shifts (δ,ppm) observed for the C=N, C=O and CH$_3$ have been correlated with Hammett substituent constants and the results of statistical analysis are presented in Table 3. The C=N chemical shifts (δ, ppm) has shown satisfactory correlation with Hammett σ, σ$^+$, σ$_I$ constants and F parameters excluding H, 4-F and 4-OCH$_3$ substituents. The resonance components were fail in correlation. All correlations gave positive ρ values. The failure in the correlation is due to incapability of transmittance of resonance effects of the substituents on the C=N carbon chemical shifts (δ, ppm). The chemical shifts (δ, ppm) observed for the C=O carbon of the 1-(3-(3,4-dichlorophenyl)-5-(substituted phenyl)-4,5-dihydro-^{1}H-pyrazole-1-yl) ethanones have been correlated satisfactorily with Hammett substituent constants, F and R parameters excluding H, 4-F, 3-CH$_3$ and 4-CH$_3$ substituents. All correlation produced positive ρ values. This implies that the normal substituent effect operates in all systems.

The assigned methyl carbon chemical shifts of the 1-(3-(3,4-dichlorophenyl)-5-(substituted phenyl)-4,5-dihydro-^{1}H-pyrazole-1-yl) ethanones have been correlated with Hammett substituent constants, F and R parameters and the results of statistical analyses were shown in Table 3. From the table, the Hammett σ, σ$^+$, σ$_R$ constants and R parameters gave satisfactory correlations excluding 2-Cl. 4-Cl and 3-CH$_3$ substituents. The Hammett σI constant and F parameters were fail in correlation. All correlations gave positive ρ values. This means that the normal substituent effect operates in all systems. The failure in the correlation was due to the reason stated earlier and it is associated with the resonance - conjugative structure shown in Fig. 2.

In view of the inability of some of the σ constants to produce individually satisfactory correlation, the authors think that, it is worthwhile to seek multiple correlation involving all either σ$_I$, σ$_R$ or F and R parameters [27]. The generated correlation equations are given in (15-20).

$$\delta C{=}N^{(ppm)} = 158.32\ (\pm0.268) + 2.308\ (\pm0.865)\ \sigma_I + 0.635\ (\pm0.074)\ \sigma_R \qquad \ldots(15)$$
$$(R = 0.984,\ P > 95\ \%,\ n = 10)$$

$$\delta C{=}N(ppm) = 158.34\ (\pm\ 0.253) + 2.338\ (\pm0.518)\ F + 0.877\ (\pm0.014)\ R \qquad \ldots(16)$$
$$(R = 0.987,\ P > 95\ \%,\ n = 10)$$

$$\delta C{=}O^{(ppm)} = 180.83\ (\pm0.364) + 2.850\ (\pm0.767)\sigma_I + 2.430\ (\pm1.012)\ \sigma_R \qquad \ldots(17)$$
$$(R = 0.986,\ P > 95\ \%,\ n = 10)$$

$$\delta C{=}O^{(ppm)} = 183.01\ (\pm\ 0.393) + 2.606\ (\pm0.979)\ F + 2.588\ (\pm1.010)\ R \qquad \ldots(18)$$
$$(R = 0.984,\ P > 95\ \%,\ n = 10)$$

$$\delta CH_3^{(ppm)} = 27.41\ (\pm0.211) + 0.330\ (\pm0.444)\ \sigma_I + 1.633\ (\pm0.052)\ \sigma_R \qquad \ldots(19)$$
$$(R = 0.974,\ P > 95\ \%,\ n = 10)$$

$$\delta CH_3^{(ppm)} = 27.39\ (\pm0.233) + 0.0433\ (\pm0.473)\ F + 1.093\ (\pm0.036)\ R \qquad \ldots(20)$$
$$(R = 0.969,\ P > 95\ \%,\ n = 10)$$

4. CONCLUSIONS

A series of some 1-acetyl pyrazolines including 3-(3,4-dichlorophenyl)-5-(substituted phenyl)-4,5-dihydro-[1]*H*-pyrazole-1-yl-ethanones have been synthesised by microwave assisted fly-ash:H_2SO_4 catalyzed solvent free cyclization cum acetylation of chalcones and hydrazine hydrate and acetic anhydride [28-31]. The yields of the synthesized carbothioamides are more than 85 %. The correlation study of infrared ν(cm[-1]) of C=N, C=S frequencies, ^{1}H and ^{13}C NMR chemical shifts (δ, ppm) of H_{a-c}, -CH_3, C=N, and C=S, have shown satisfactory correlation co-efficient in both single and multi-regression analyses.

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