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Fly-ash:H$_2$O catalyzed aqueous phase cyclization of chalcones: Synthesis of some substituted pyrazole-1-carbothioamides and spectral correlations in 3-(3,4-dimethylphenyl)-5-(substituted phenyl)-4,5-dihydro-1*H*-pyrazole-1-carbothioamides

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ABSTRACT

Some substituted 1-thiocarbomyl pyrazolines including 3-(3,4-dimethylphenyl)-5-(substituted phenyl)-4,5-dihydro-1*H*-pyrazole-1-carbothioamides using solvent-free aqueous phase fly-ash catalyzed cyclization between chalcones and thiosemicarbazide. The yields of these thiocarbomyl pyrazolines are more than 75%. The purities of these synthesised pyrazoline derivatives are checked by their physical constants and spectral data earlier reported in the literature The spectral data of these 3-(3,4-dimethylphenyl)-5-(substituted phenyl)-4,5-dihydro-1*H*-pyrazole-1-carbothioamides had been correlated, using single and multi-linear regression analysis.   © 2013 Trade Science Inc. - INDIA

KEYWORDS

3-(3,4-dimethylphenyl)-5-(substituted phenyl)-4,5-dihydro-1*H*-pyrazole-1-carbothioamides;
Fly-ash:H$_2$O;
Solvent free synthesis;
Hammett correlations.

INTRODUCTION

There are numerous solvent-free[1,2] synthetic methods available and these methods had been applied for stereospecific, stereoselective and regioselective synthesis of organic compounds. These solvent free reactions involving the formation of carbon-carbon bond and carbon-heteroatom bond are important and interesting in green synthesis. In the five membered bi-nitrogen heterocyclics, the 1-thiocarbomyl pyrazoline derivatives are important compounds and they possess –CS-NH$_2$ group in N$_1$ atom of pyrazoline ring[3,4]. These substituted 1-thiocarbomyl pyrazoline derivatives possess many important biological activities such as, anti-bacterial[5], anti-fungal[6], anti-depressants[7], anti-convulsant[8], anti-inflammatory[9], anti-tumour[10], anaesthetic[11], analgesic[12], anti-cancer[13] MAO-B inhibitors[14], steroidal, nitric oxide synthase inhibitor, antiviral and cannabinoid CBI receptor antagonists[9]. Several solvent-free and thermal methods were reported in literature for synthesis of thiocarbomyl pyrazoline derivatives[3,13,15-18]. In these methods, many substituted pyrazoline derivatives were synthesised by cyclization of chalcones with hydrazine hydrate[19] or phenylhydrazine[20] or phenyl hydrazine hydrochloride[21-23]. Similarly substituted 1-thiocarbomyl pyrazoline derivatives were synthesised by cyclization of chalcones with thiosemicarbazide[3,13,14,24] or substituted thiosemicarbazide[3,9,14] or hydrazenidium dithiocyanate[25]. In recent years, synthetic organic chemists, scientists and

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researchers preferred greener synthesis due to easy working procedure, shorter reaction time, higher yields, less hazardousness and solvent usage[26-31]. Based on the above important advantages, the greener synthetic methods such as, solvent-free microwave irradiation and ultrasonication were used for synthesis of thiocarbomyl pyrazoline derivatives[23,32,33]. Several liquid and solid phase catalysts were utilized for synthesis of substituted 1-thiocarbomyl pyrazoline derivatives such as Lewis acids, bases and their salts[13,32,33], CH_3COOH/CH_3COONa[3], $NaOH/EtOH$[24,32,35], $KOH/EtOH$[20,33], neatreaction in ethanol[3,14] and Basic alumina/ K_2CO_3[36,37]. These thiocarbomyl pyrazolines are important as starting material for synthesis of thiazole substituted pyrazoles[18]. Chawla et al.,[36] have synthesised more than 80% yield of some 3-substituted phenyl-5-substitutedphenyl-4,5-dihydropyrazole-1-carbothioamides by microwave irradiation method and evaluated the antimicrobial activities. The same yield of 5-(1,3-benzodioxol-yl)-3-(substituted)phenyl-4,5-dihydro-1H-pyrazol-1-carbothioamides have been synthesised by microwave irradiation method and studied the anticancer activities by Mathew et al.,[13]. Ashok co-workers have been synthesised 80% yields of some 3-(3-benzoyl-6-hydroxy-3-methylbenzo[b]furon-5-yl)-5-(aryl)-4,5-dihydro-1H-pyrazole carbothioamides using microwave irradiation technique and studied the antibacterial activities[15-17]. Patil et al.,[37] have synthesised 60-85% yields of 1-thiocarbomyl-2-(2,4-dichloro-5-fluorophenyl)-5-(substitutedphenyl)-pyrazoline derivatives using microwave with alumina/ K_2CO_3 as catalyst. Spectroscopic data applied for predicting the ground state equilibrium of organic compounds. The uv absorption maxima (λ max, nm) is also applied for prediction of effect of substituents[31]. In pyrazoline molecules (¹H pyrazoles), the infrared spectra is utilized for predicting the effects of substituents on the vibrations of C=N, C-H, N-H[21]. 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 Figure 1 were assigned from their frequencies with multiplicities viz., doublet or triplet or doublet of doublets.

Based on the stereo chemical terms, the chemical shifts of the protons of respective pyrazoles have been assigned and the effects of substituent were studied.

The effects of substituent on the 2-naphthyl based pyrazoline ring protons were studied first by Sakthinathan et. al.,[21]. 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. Recently Thirunarayanan et al.[23] have synthesised some 1-phenyl-3-(5-bromothiophen-2-yl)-5-(substituted phenyl)-2-pyrazolines by solvent free method and investigated the effect of substituents using spectral data with Hammett substituent constants and F and R parameters. The literature survey reveals that there is no information available for solvent-free synthesis of some substituted thiocarbomyl pyrazolines including 1-thiocarbomyl-3-(3,4-dimethylphenyl)-5-(substituted phenyl)-pyrazoline derivatives by cyclization of the respective chalcones and thiosemicarbazide in presence of fly-ash. Therefore the authors have taken efforts to prepared some thiocarbomyl pyrazolines including 1-thiocarbomyl-3-(3,4-dimethylphenyl)-5-(substituted phenyl)-pyrazoline derivatives by aqueous phase cyclization of chalcones and thiosemicarbazide in presence of fly-ash:H₂O. 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 3-(3,4-dimethylphenyl)-5-(substituted phenyl)-4,5-dihydro-1*H*-pyrazole-1-carbothioamides for studying the Hammett spectral correlations.
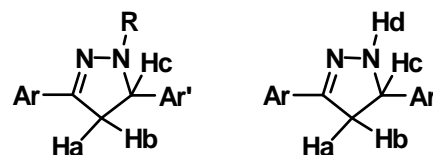

**Figure 1 : General structure of 1*H*-pyrazoles**

EXPERIMENTAL

General

All chemicals used were procured from Sigma-Aldrich and E-Merck. Fly-ash was collected from the Thermal Power Plant II, Neyveli Lignite Corporation, Tamilnadu, India. Melting points of all pyrazole-1-carbothioamides 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.

Synthesis of substituted pyrazole-1-carbothioamide derivatives

Appropriate equi-molar quantities of chalcones (2 mmol), thiosemicarbazide (2 mmol), fly-ash (0.5 g) and 15 mL of water were refluxed with 0.5g of fly-ash for 3-5h (Scheme 1). The completion of the reaction was monitored by TLC. After completion, the reaction mixture was cooled to room temperature. The product was isolated by adding 10mL of dichloromethane and 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.
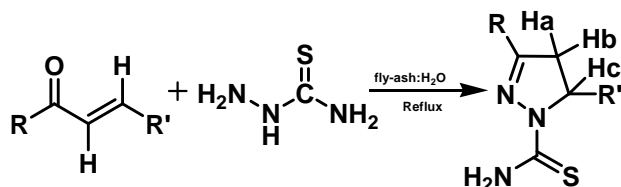
Scheme 1 : Synthesis of 1-thiocarbomyl pyrazolines by fly-ash:H$_2$O catalyzed solvent free cyclization of chalcones and thiosemicarbazide under thermal condition

RESULTS AND DISCUSSION

The waste air-pollutant fly-ash has many chemical species[27,38,40-42] SiO$_2$, Fe$_2$O$_3$, Al$_2$O$_3$, CaO, MgO and insoluble residues. The fly ash particles are in the silt-sized range of 2-50 microns[38]. Glass, mullite-quartz, and magnetic spinel are the three major mineralogical matrices identified in fly ash. Si, Al, Fe, Ca, C, Mg, K, Na, S, Ti, P, and Mn are the major elemental constituents of fly ash. The solubility of fly ash has been extensively investigated and it is largely dependent on factors

specific to the extraction procedure. Literature study reveals that the long-term leaching studies predict that fly ash will lose substantial amounts of soluble salts over time, but simulation models predict that the loss of trace elements from fly ash deposits through leaching will be very slow. Small amounts of radioisotopes are found to be the constituents of fly ash which do not appear to be hazardous.

In our research laboratory, we attempts to synthesize substituted pyrazoline-1- carbothioamides derivatives by cyclization of chalcones and thiosemicarbazide in the presence of fly-ash catalyst in aqueous phase thermal condition. Hence the authors have synthesized the substituted 1-thiocarbomyl pyrazoline derivatives by the cyclization of 2 mmole of chalcone, 2 mmole of thiosemicarbazide and 15mL of water were refluxed with 0.5g fly-ash for 3-5h (Scheme 1). During the course of this reaction fly-ash assisted for the cyclization between chalcones and thiosemicarbazide to elimination of water followed by proton transfer gave the 1-thiocarbomyl pyrazolines. The yields of the pyrazolines in this reaction are more than 70%. The chalcones containing electron donating substituent (-OCH$_3$) gave higher yields than electron-withdrawing halogens and -NO$_2$ substituents. Further we have investigated this cyclization reaction with equimolar quantities of the styryl 3,4-dimethylphenyl ketone (entry 25) and thiosemicarbazide under the same condition as above. In this reaction the obtained yield was 75%. The effect of catalyst on this reaction was studied by varying the catalyst quantity from 0.1 g to 1 g. As the catalyst quantity is increased from 0.1 g to 1 g, the percentage of yield of product is increased from 70 to 75%. Further increase the catalyst amount beyond 0.4 g, there is no significant increasing the percentage of the product. The effect of catalyst loading is shown in (Figure 2). The optimum quantity of catalyst loading was found to be 0.4g. The results, analytical and mass spectral data are summarized in TABLE 1.

The reusability of this catalyst was studied for the cyclization of styryl 2,4-dimethylphenyl ketone and thiosemicarbazide (entry 25) is presented in TABLE 2. From the TABLE 2, first run gave 75% product. The second, third, fourth and fifth runs of reactions gave the yields 70, 62, 55 and 50% of 1-thiocarbomyl pyrazolines. In this cyclization there was an appreciable

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loss in its effect of catalytic activity were observed up to fifth run. The effect of solvents on the yield also studied with methanol, ethanol, dichloromethane and tetrahydrofuran from each component of the catalyst (entry 25). The effect of solvents on the yields of 1-thiocarbomyl pyrazolines was presented in TABLE 3. From the table, the highest yield of 1-thiocarbomyl pyrazolines obtained from the aqueous phase cyclization of chalcone and thiosemicarbazide with fly-ash:H₂O catalyst.
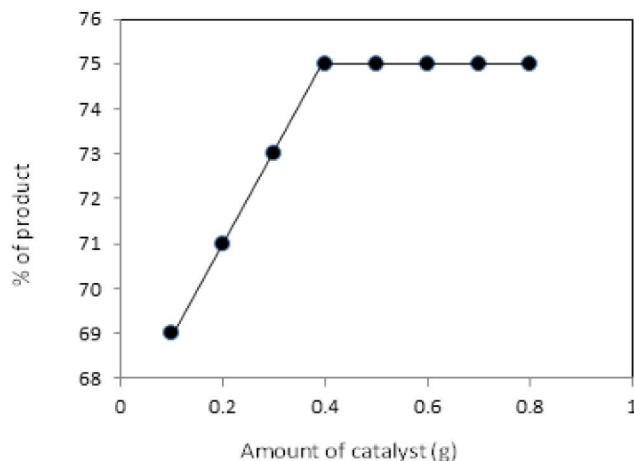

Figure 2 : Effect of catalyst loading

IR spectral study

The synthesis of substituted 1-thiocarbomyl pyrazoline derivatives are shown in Scheme 1. In the present study, the authors have chosen a series of 1-thiocarbomyl pyrazoline derivatives namely 3-(3,4-dimethylphenyl)-5-(substituted phenyl)-4,5-dihydro-1*H*-pyrazole-1-carbothioamides (entries 25-35) for studying the effects of substituent on the spectral data. The infrared νC=N, NH and C=S stretching frequencies (cm⁻¹) of 3-(3,4-dimethylphenyl)-5-(substituted phenyl)-4,5-dihydro-1*H*-pyrazole-1-carbothioamides (entries 25-35) have been assigned and are presented in TABLE 4. These data have been correlated[1,2,21,23,28,31,43] with Hammett substituent constants and Swain-Lupton's[44] parameters. In this correlation the structure parameter Hammett equation employed is as shown in equation (1).

$$\nu = \rho\sigma + \nu_o \qquad (1)$$

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

The observed νC=N stretching frequencies (cm⁻¹) of these 3-(3,4-dimethylphenyl)-5-(substituted phenyl)-4,5-dihydro-1*H*-pyrazole-1-carbothioamides are cor-

TABLE 1 : Analytical, physical constants, yields and mass fragments of 1-thiocarbomyl pyrazolines synthesised by fly-ash:H₂O catalyzed solvent-free cyclization of chalcones and thiosemicarbazide reaction of the following type under thermal condition

Entry	R	R'	Product	M.W.	Yield	m.p. (°C)	Mass (m/z)
1	CH₃	C₆H₅	C₁₁H₁₃N₃S	219	85	273-274 273[25]	219[M⁺]
2	CH₃	4-OCH₃C₆H₄	C₁₂H₁₅N₃OS	249	84	182-183 182[25]	249[M⁺]
3	CH₃	4-N(CH₃)₂C₆H₄	C₁₃H₁₈N₄S	263	86	238-239 238[25]	263[M⁺]
4	CH₃	C₄H₃O(2-Furyl)	C₉H₁₅N₃OS	213	80	221-222 220-222[25]	213[M⁺]
5	CH₃	C₄H₃S(2-Thienyl)	C₉H₁₅N₃S₂	229	81	119-220 220[25]	213[M⁺]
6	C₄H₃S(2-Thienyl)	C₆H₅	C₁₄H₁₇N₃S₂	291	83	164-165 160-165[32]	291[M⁺]
7	C₄H₃S(2-Thienyl)	4-BrC₆H₄	C₁₄H₁₆BrN₃S₂	370	82	254-255 250-255[32]	370[M⁺], 372[M²⁺]
8	C₄H₃S(2-Thienyl)	2,4,5-(OCH₃)₃C₆H₂	C₁₇H₂₃N₃O₃S₂	381	83	214-215 210-215[32]	381[M⁺]
9	C₄H₃S(2-Thienyl)	4-N(CH₃)₂C₆H₄	C₁₆H₁₈N₄S₂	330	80	174-175 170-175[32]	330[M⁺]
10	C₆H₅	2,4-Cl₂-C₆H₃	C₁₆H₁₃Cl₂N₃S	350	80	220-221 217-220[33]	350[M⁺], 352[M²⁺]
11	2,4-Cl₂-5-F-C₆H₂	C₆H₅	C₁₆H₁₂Cl₂FN₃S	368	81	165-166 165[37]	368[M⁺], 370[M²⁺], 372[M⁺⁴]

Entry	R	R'	Product	M.W.	Yield	m.p. (°C)	Mass (m/z)
12	2,4-Cl$_2$-5-F-C$_6$H$_2$	2-ClC$_6$H$_4$	C$_{16}$H$_{11}$Cl$_3$FN$_3$S	402	80	145-146 145[37]	402[M$^+$], 404[M^{2+}], 408[M^{+4}], 410[M^{+6}]
13	2,4-Br$_2$-C$_6$H$_3$	4-C$_6$H$_4$	C$_{16}$H$_{13}$Br$_2$N$_3$S	439	80	132-133	439[M$^+$], 441[M^{2+}], 443[M^{4+}]
14	2,4-Br$_2$-C$_6$H$_3$	2-BrC$_6$H$_4$	C$_{16}$H$_{12}$Br$_3$N$_3$S	519	81	217-218 214-216[24]	519[M$^+$], 521M^{2+}], 523[M^{4+}]
15	4-OCH$_3$C$_6$H$_4$	C$_6$H$_5$	C$_{17}$H$_{17}$N$_3$OS	311	84	162-163 160-162[36]	311[M$^+$]
16	4-ClC$_6$H$_4$	C$_6$H$_5$	C$_{16}$H$_{14}$ClN$_3$S	315	80	123-124 122-123[36]	315[M$^+$], 317[M^{2+}]
17	3-NO$_2$C$_6$H$_4$	C$_6$H$_5$	C$_{16}$H$_{14}$N$_4$O$_2$S	326	80	129-130 128-130[36]	326[M$^+$]
18	4-OCH$_3$C$_6$H$_4$	4-ClC$_6$H$_4$	C$_{17}$H$_{16}$ClN$_3$OS	345	84	127-128 125-127[36]	360[M$^+$], 362[M^{2+}],
19	4-ClC$_6$H$_4$	4-ClC$_6$H$_4$	C$_{16}$H$_{13}$Cl$_2$N$_3$S	350	82	148-149 147-148[36]	350[M$^+$], 352[M^{2+}], 354[M^{2+4}],
20	3-NO$_2$C$_6$H$_4$	4-ClC$_6$H$_4$	C$_{16}$H$_{13}$ClN$_4$O$_3$S	237	81	150-151 148-150[36]	337[M$^+$], 396[M^{2+}]
21	2,4-Cl$_2$-C$_6$H$_3$	C$_6$H$_5$	C$_{16}$H$_{13}$Cl$_2$N$_3$S	351	85	135-136	351[M$^+$], 353M^{2+}], 355[M^{4+}]
22	2,4-Cl$_2$-C$_6$H$_3$	2-BrC$_6$H$_4$	C$_{16}$H$_{12}$BrCl$_2$N$_3$S	426	81	230-231 229-230[24]	429[M$^+$], 431M^{2+}], 433[M^{4+}]
23	C$_4$H$_3$O(2-Furyl)	C$_6$H$_5$	C$_{14}$H$_{13}$N$_3$OS	271	82	177-178 176-177[34]	271[M$^+$]
24	C$_4$H$_3$O(2-Furyl)	C$_4$H$_3$O(2-Furyl)	C$_{12}$H$_{11}$N$_3$O$_2$S	293	82	164-165 163-164[34]	293[M$^+$]
25	3,4-(CH$_3$)$_2$-C$_6$H$_3$	C$_6$H$_5$	C$_{18}$H$_{19}$N$_3$S	309	75	135-136	309[M$^+$], 353M^{2+}], 355[M^{4+}]
26	3,4-(CH$_3$)$_2$-C$_6$H$_3$	2-BrC$_6$H$_4$	C$_{18}$H$_{18}$BrN$_3$S	388	71	219-220 217-219[24]	388[M$^+$], 390M^{2+}]
27	3,4-(CH$_3$)$_2$-C$_6$H$_3$	4-BrC$_6$H$_4$	C$_{18}$H$_{18}$BrN$_3$S	388	72	234-235 231-333[24]	388[M$^+$], 390M^{2+}]
28	3,4-(CH$_3$)$_2$-C$_6$H$_3$	2-ClC$_6$H$_4$	C$_{18}$H$_{18}$ClN$_3$S	343	72	210-211 208-210[24]	343[M$^+$], 345[M^{2+}]
29	3,4-(CH$_3$)$_2$-C$_6$H$_3$	4-ClC$_6$H$_4$	C$_{18}$H$_{18}$ClN$_3$S	343	72	217-218 216-217[24]	343[M$^+$], 345[M^{2+}]
30	3,4-(CH$_3$)$_2$-C$_6$H$_3$	2-FC$_6$H$_4$	C$_{18}$H$_{18}$FN$_3$S	327	70	213-214 211-213[24]	327[M$^+$], 329[M^{2+}]
31	3,4-(CH$_3$)$_2$-C$_6$H$_3$	4-FC$_6$H$_4$	C$_{18}$H$_{18}$FN$_3$S	327	71	224-225 223-225[24]	327[M$^+$], 329[M^{2+}]
32	3,4-(CH$_3$)$_2$-C$_6$H$_3$	4-OHC$_6$H$_4$	C$_{18}$H$_{19}$N$_3$OS	325	72	219-220 218-219[24]	325[M$^+$]
33	3,4-(CH$_3$)$_2$-C$_6$H$_3$	4-OCH$_3$C$_6$H$_4$	C$_{19}$H$_{21}$N$_3$OS	339	75	209-210 207-209[24]	339[M$^+$]
34	3,4-(CH$_3$)$_2$-C$_6$H$_3$	4-CH$_3$C$_6$H$_4$	C$_{19}$H$_{21}$N$_3$S	323	74	200-201 198-200[24]	323[M$^+$]
35	3,4-(CH$_3$)$_2$-C$_6$H$_3$	4-NO$_2$C$_6$H$_4$	C$_{18}$H$_{28}$N$_4$O$_2$S	354	70	203-204 202-203[24]	354[M$^+$]

TABLE 2 : Reusability of fly-ash:H$_2$O catalyst on cyclization of styryl 3,4-dimethylphenyl ketone (2 mmol) and thiosemicarbazide (2 mmol) under reflux condition (entry 25)

Run	1	2	3	4	5
Yield	75	70	62	50	53

TABLE 3 : The effect of solvents on the yield of 1-thiocarbomyl pyrazoline (entry 25)

Solvents				Fly-ash:H$_2$O
MeOH	EtOH	DCM	THF	
73	73	68	65	75

MeOH=Methanol; EtOH=Ethanol; DCM= Dichloromethane; THF=Tetrahydrofuran

related with various Hammett substituent constants and F and R parameters through single and multi-regression analyses including Swain-Lupton's[44] parameters. The results of statistical analyses of single parameter correlations are shown in TABLE 5.

The correlation of νC=N and C=S(cm^{-1}) frequencies of 3-(3,4-dimethylphenyl)-5-(substituted phenyl)-4,5-dihydro-1*H*-pyrazole-1-carbothioamides with Hammett substituent constants, F and R parameters has shown satisfactory correlation coefficients excluding H, and 4-CH$_3$ substituents. If these substituents are included

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TABLE 4 : The spectroscopic data of 1- thiocarbomyl pyrazolines (entries 25-35)

Entry	X	IR(ν, cm⁻¹)			¹H NMR(δ,ppm)			¹³C NMR(δ,ppm)	
		C=N	NH	C=S	H$_a$ (dd, 1H)	H$_b$ (dd, 1H)	H$_c$ (dd, 1H)	C=N	C=S
25	H	1593	3462	1380	3.021	3.652	6.358	158.25	176.58
26	2-Br	1588	3454	1368	3.353	3.871	6.301	161.33	174.72
27	4-Br	1584	3451	1366	3.405	3.712	5.961	163.84	178.10
28	2-Cl	1583	3449	1362	3.107	3.914	7.194	162.11	177.11
39	4-Cl	1581	3455	1363	3.421	3.814	5.972	159.61	173.21
30	2-F	1580	3453	1365	3.108	3.108	6.353	159.92	174.18
31	4-F	1576	3450	1368	3.147	3.767	5.947	163.71	176.93
32	4-OH	1578	3454	1364	3.105	3.705	5.966	164.23	177.16
33	4-OCH₃	1574	3447	1360	3.145	3.791	6.017	158.71	174.07
34	4-CH₃	1575	3453	1363	3.165	3.796	5.981	159.07	174.14
35	4-NO₂	1588	3457	1371	3.316	3.841	5.971	163.21	178.10

TABLE 5 : Results of statistical analysis of infrared ν(cm⁻¹) C=N, C=S, NH, CF, NMR chemical shifts (δ ppm) of Ha, Hb, Hc, C=N and C=S of 1-thiocarbamyl pyrazolines with Hammett σ, σ^+, σ_I, σ_R constants and F and R parameters (entries 25-35)

Frequency	Constants	r	I	ρ	s	n	Correlated derivatives
νC=N	σ	0.905	1580.58	10.446	5.22	10	2-Br, 2-Cl, 4-Cl, 2-F, 4-OH, 4-OCH₃, 4-CH₃, 4-NO₂
	σ^+	0.906	1581.35	6.697	5.02	10	2-Br, 2-Cl, 4-Cl, 2-F, 4-OH, 4-OCH₃, 4-CH₃, 4-NO₂
	σ_I	0.907	1581.04	2.121	6.30	9	2-Br, 2-Cl, 4-Cl, 2-F, 4-OH, 4-OCH₃, 4-NO₂
	σ_R	0.906	1586.43	19.442	4.78	10	H, 2-Br, 2-Cl, 4-Cl, 2-F, 4-OH, 4-OCH₃, 4-NO₂
	F	0.908	1582.67	-2.089	6.36	11	H, 2-Br, 4-Br, 2-Cl, 4-Cl, 2-F, 4-F, 4-OH, 4-OCH₃, 4-CH₃, 4-NO₂
	R	0.907	1586.75	16.120	4.45	10	H, 2-Br, 4-Br, 2-Cl, 4-Cl, 2-F, 4-F, 4-OH, 4-OCH₃, 4-NO₂
νNH	σ	0.823	3452.38	2.771	4.19	11	H, 2-Br, 4-Br, 2-Cl, 4-Cl, 2-F, 4-F, 4-OH, 4-OCH₃, 4-CH₃, 4-NO₂
	σ^+	0.822	3454.06	1.667	4.20	11	H, 2-Br, 4-Br, 2-Cl, 4-Cl, 2-F, 4-F, 4-OH, 4-OCH₃, 4-CH₃, 4-NO₂
	σ_I	0.882	3455.13	-5.316	4.13	11	H, 2-Br, 4-Br, 2-Cl, 4-Cl, 2-F, 4-F, 4-OH, 4-OCH₃, 4-CH₃, 4-NO₂
	σ_R	0.906	3456.12	12.404	3.36	11	H, 2-Br, 4-Br, 2-Cl, 4-Cl, 2-F, 4-F, 4-OH, 4-OCH₃, 4-CH₃, 4-NO₂
	F	0.838	3455.22	-4.999	4.10	11	H, 2-Br, 4-Br, 2-Cl, 4-Cl, 2-F, 4-F, 4-OH, 4-OCH₃, 4-CH₃, 4-NO₂
	R	0.905	3455.86	8.747	3.52	11	H, 2-Br, 4-Br, 2-Cl, 4-Cl, 2-F, 4-F, 4-OH, 4-OCH₃, 4-CH₃, 4-NO₂
νC=S	σ	0.929	1365.77	4.960	5.05	10	2-Br, 4-Br, 2-Cl, 4-Cl, 2-F, 4-F, 4-OH, 4-OCH₃, 4-CH₃, 4-NO₂
	σ^+	0.903	1366.15	3.035	5.51	10	2-Br, 4-Br, 2-Cl, 4-Cl, 2-F, 4-F, 4-OH, 4-OCH₃, 4-CH₃, 4-NO₂
	σ_I	0.901	1367.92	-4.263	5.71	9	2-Br, 4-Br, 2-Cl, 4-Cl, 2-F, 4-F, 4-OH, 4-OCH₃, 4-NO₂
	σ_R	0.905	1369.69	14.088	4.92	10	2-Br, 4-Br, 2-Cl, 4-Cl, 2-F, 4-F, 4-OH, 4-OCH₃, 4-CH₃, 4-NO₂
	F	0.901	1367.74	-3.371	5.72	10	2-Br, 4-Br, 2-Cl, 4-Cl, 2-F, 4-F, 4-OH, 4-OCH₃, 4-CH₃, 4-NO₂
	R	0.905	1369.58	10.499	4.97	10	2-Br, 4-Br, 2-Cl, 4-Cl, 2-F, 4-F, 4-OH, 4-OCH₃, 4-CH₃, 4-NO₂
δH$_a$	σ	0.905	3.108	0.240	0.12	11	H, 2-Br, 4-Br, 2-Cl, 4-Cl, 2-F, 4-F, 4-OH, 4-OCH₃, 4-CH₃, 4-NO₂
	σ^+	0.904	3.201	0.106	0.13	11	H, 2-Br, 4-Br, 2-Cl, 4-Cl, 2-F, 4-F, 4-OH, 4-OCH₃, 4-CH₃, 4-NO₂
	σ_I	0.904	3.095	0.309	0.12	11	H, 2-Br, 4-Br, 2-Cl, 4-Cl, 2-F, 4-F, 4-OH, 4-OCH₃, 4-CH₃, 4-NO₂
	σ_R	0.833	3.282	0.216	0.13	11	H, 2-Br, 4-Br, 2-Cl, 4-Cl, 2-F, 4-F, 4-OH, 4-OCH₃, 4-CH₃, 4-NO₂
	F	0.822	3.145	0.154	0.14	11	H, 2-Br, 4-Br, 2-Cl, 4-Cl, 2-F, 4-F, 4-OH, 4-OCH₃, 4-CH₃, 4-NO₂
	R	0.875	8.265	0.185	0.15	11	H, 2-Br, 4-Br, 2-Cl, 4-Cl, 2-F, 4-F, 4-OH, 4-OCH₃, 4-CH₃, 4-NO₂
δH$_b$	σ	0.808	3.729	0.005	0.23	11	H, 2-Br, 4-Br, 2-Cl, 4-Cl, 2-F, 4-F, 4-OH, 4-OCH₃, 4-CH₃, 4-NO₂
	σ^+	0.810	3.729	-0.041	0.22	11	H, 2-Br, 4-Br, 2-Cl, 4-Cl, 2-F, 4-F, 4-OH, 4-OCH₃, 4-CH₃, 4-NO₂

in the regression, they reduced the correlation considerably. The νNH stretches (cm⁻¹) of these 3-(3,4-dimethylphenyl)-5-(substituted phenyl)-4,5-dihydro-1*H*-pyrazole-1-carbothioamides has shown satisfactory correlation for Hammett σR a substituent and R parameters excluding 4-F and 4-OH substituents. The remaining Hammett substituent constant gave poor correlation. The failure in correlation was due to the absence of transmittance of polar, inductive, and field effects of the substituent on the spectral group frequencies νNH (cm⁻¹) and is associated with the resonance-conjugative structure shown in Figure 3.

Some of the Hammett single parameter correlations of νNH (cm⁻¹) frequencies of 3-(3,4-dimethylphenyl)-5-(substituted phenyl)-4,5-dihydro-1*H*-pyrazole-1-carbothioamides were fail individually. So, the authors think that, it is worthwhile to seek the multi-regression

Frequency	Constants	r	I	ρ	s	n	Correlated derivatives
	σ_I	0.820	3.733	-0.023	0.22	11	H, 2-Br, 4-Br, 2-Cl, 4-Cl, 2-F, 4-F, 4-OH, 4-OCH$_3$, 4-CH$_3$, 4-NO$_2$
	σ_R	0.837	3.818	0.394	0.21	11	H, 2-Br, 4-Br, 2-Cl, 4-Cl, 2-F, 4-F, 4-OH, 4-OCH$_3$, 4-CH$_3$, 4-NO$_2$
	F	0.829	3.823	-0.252	0.22	11	H, 2-Br, 4-Br, 2-Cl, 4-Cl, 2-F, 4-F, 4-OH, 4-OCH$_3$, 4-CH$_3$, 4-NO$_2$
	R	0.839	3.823	0.321	0.21	11	H, 2-Br, 4-Br, 2-Cl, 4-Cl, 2-F, 4-F, 4-OH, 4-OCH$_3$, 4-CH$_3$, 4-NO$_2$
δH_c	σ	0.809	6.171	0.105	0.39	11	H, 2-Br, 4-Br, 2-Cl, 4-Cl, 2-F, 4-F, 4-OH, 4-OCH$_3$, 4-CH$_3$, 4-NO$_2$
	σ^+	0.873	6.167	0.238	0.36	11	H, 2-Br, 4-Br, 2-Cl, 4-Cl, 2-F, 4-F, 4-OH, 4-OCH$_3$, 4-CH$_3$, 4-NO$_2$
	σ_I	0.805	6.147	0.091	0.39	11	H, 2-Br, 4-Br, 2-Cl, 4-Cl, 2-F, 4-F, 4-OH, 4-OCH$_3$, 4-CH$_3$, 4-NO$_2$
	σ_R	0.812	6.171	-0.051	0.39	11	H, 2-Br, 4-Br, 2-Cl, 4-Cl, 2-F, 4-F, 4-OH, 4-OCH$_3$, 4-CH$_3$, 4-NO$_2$
	F	0.802	6.198	-0.336	0.39	11	H, 2-Br, 4-Br, 2-Cl, 4-Cl, 2-F, 4-F, 4-OH, 4-OCH$_3$, 4-CH$_3$, 4-NO$_2$
	R	0.812	6.324	0.119	0.39	11	H, 2-Br, 4-Br, 2-Cl, 4-Cl, 2-F, 4-F, 4-OH, 4-OCH$_3$, 4-CH$_3$, 4-NO$_2$
δCN	σ	0.903	161.02	2.086	2.26	10	H, 2-Br, 4-Br, 2-Cl, 4-Cl, 2-F, 4-F, 4-OCH$_3$, 4-CH$_3$, 4-NO$_2$
	σ^+	0.901	161.23	0.598	2.35	10	H, 2-Br, 4-Br, 2-Cl, 4-Cl, 2-F, 4-F, 4-OCH$_3$, 4-CH$_3$, 4-NO$_2$
	σ_I	0.905	159.02	6.135	1.90	10	H, 2-Br, 4-Br, 2-Cl, 4-Cl, 2-F, 4-F, 4-OCH$_3$, 4-CH$_3$, 4-NO$_2$
	σ_R	0.880	160.97	-1.230	2.36	11	H, 2-Br, 4-Br, 2-Cl, 4-Cl, 2-F, 4-F, 4-OH, 4-OCH$_3$, 4-CH$_3$, 4-NO$_2$
	F	0.905	159.24	4.954	1.19	9	H, 2-Br, 4-Br, 2-Cl, 4-Cl, 2-F, 4-OCH$_3$, 4-CH$_3$, 4-NO$_2$
	R	0.881	160.81	-1.507	2.38	11	H, 2-Br, 4-Br, 2-Cl, 4-Cl, 2-F, 4-F, 4-OH, 4-OCH$_3$, 4-CH3, 3-NO$_2$
δCS	σ	0.903	175.61	1.972	1.76	10	H, 2-Br, 4-Br, 2-Cl, 4-Cl, 2-F, 4-F, 4-OCH$_3$, 4-CH3, 3-NO$_2$
	σ^+	0.902	175.95	0.672	1.85	10	H, 2-Br, 4-Br, 2-Cl, 4-Cl, 2-F, 4-F, 4-OCH$_3$, 4-CH3, 3-NO$_2$
	σ_I	0.828	175.00	2.299	1.18	11	H, 2-Br, 4-Br, 2-Cl, 4-Cl, 2-F, 4-F, 4-OH, 4-OCH$_3$, 4-CH$_3$, 4-NO$_2$
	σ_R	0.878	176.44	2.514	1.18	11	H, 2-Br, 4-Br, 2-Cl, 4-Cl, 2-F, 4-F, 4-OH, 4-OCH$_3$, 4-CH$_3$, 4-NO$_2$
	F	0.861	175.78	1.358	1.85	11	H, 2-Br, 4-Br, 2-Cl, 4-Cl, 2-F, 4-F, 4-OH, 4-OCH$_3$, 4-CH$_3$, 4-NO$_2$
	R	0.821	176.26	1.352	1.85	11	H, 2-Br, 4-Br, 2-Cl, 4-Cl, 2-F, 4-F, 4-OH, 4-OCH$_3$, 4-CH$_3$, 4-NO$_2$

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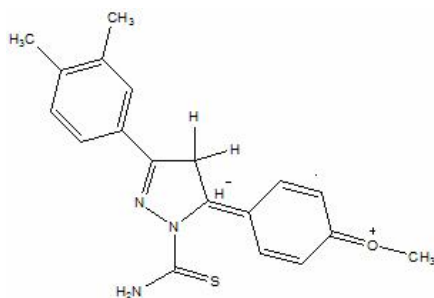

Figure 3 : The resonance-conjugative structure

analysis of these frequencies with Swain-Lupton's[44] constants. The multi-regressions gave satisfactory correlation with inductive, resonance and field effects of the substituents. The corresponding multi-regression equations are given in (2) –(7).

v_{CN}(cm^{-1}) = 1584.96(±3.3714)+4.366σ_I(±0.726) -2.002 σ_R (±0.066)   (2)

(*R*=0.968, *P*> 95%, n=11)

v_{CN}(cm^{-1}) =1585.72(±2.964)+3.166F (±0.133) +16.968R (±5.702)   (3)

(*R*=0.972, P > 95%, n=11)

$v_{C=S}$(cm^{-1}) = 1370.61(±3.518)-2.725σ_I (±0.755) +13.712 σ_R (±2.668)   (4)

(*R*=0.953, *P*> 95%, n=11)

$v_{C=S}$(cm^{-1}) =1369.62(±3.360) -0.129 F (±0.062) +10.465R (±0.0.064)   (5)

(*R*=0.951, P > 95%, n=11)

v_{NH}(cm^{-1}) = 3457.46(±2.334)-13.981σ_I(±0.498) +11.899σ_R (±5.30)   (6)

(*R*=0.966, *P*> 95%, n=11)

v_{NH}(cm^{-1}) =3456.67(±2.346)-2.496F (±0.264) +8.854R (±2.514)   (7)

(*R*=0.959, P > 95%, n=11)

1H NMR spectral study

The 1H NMR spectra of synthesised 3-(3,4-dimethylphenyl)-5-(substituted phenyl)-4,5-dihydro-1*H*-pyrazole-1-carbothioamide derivatives (entries 25-35) under investigation have been recorded in deuteriochloroform solution employing tetramethylsilane (TMS) as internal standard. The signals of the 3-(3,4-dimethylphenyl)-5-(substituted phenyl)-4,5-dihydro-1*H*-pyrazole-1-carbothioamides 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

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series of 1-thiocarbomyl 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 4.

In nuclear magnetic resonance spectra, the ¹H or the ¹³C chemical shifts (δ, ppm) depend on the electronic environment of the nuclei concerned. These chemical shifts have been correlated with reactivity parameters. Thus the Hammett equation may be used in the form as shown in (8).

$$\textbf{Log } \delta = \textbf{Log } \delta_0 + \rho\sigma \tag{8}$$

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

The assigned H_a, H_b and H_c proton chemical shifts (ppm) of synthesized 3-(3,4-dimethylphenyl)-5-(substituted phenyl)-4,5-dihydro-1*H*-pyrazole-1-carbothioamides have been correlated with various Hammett sigma constants. The results of statistical analysis[1,2,21,23,28-31,43] are presented in TABLE 5. The H_a proton chemical shifts chemical shifts (ppm) correlated satisfactorily with Hammett σ, σ^+, and σ_I constants. The remaining Hammett substituent constants, F and R parameters were fail in correlation. All correlations gave positive ρ values. This implies that the normal substituent effects operates in all system. The H_b and H_c proton chemical shifts (δ, ppm) with Hammett substituent constants, F and R parameters gave poor correlations. The failure in correlation is associated with the conjugative structure shown in Figure 3.

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[44] F and R parameters. The correlation equations for H_{a-c} proton chemical shifts (δ, ppm) are given in (9)-(14).

$$\delta H_a^{(ppm)} = 3.145(\pm0.082) - 0.338(\pm0.175)\sigma_I$$
$$+ 0.259\ (\pm0.018)\sigma_R \tag{9}$$
$$(\textbf{\textit{R}=0.962, \textit{P}> 95\%, n=11})$$
$$\delta H_a^{(ppm)} = 3.189(\pm0.083) + 0.237(\pm0.017)$$
$$F + 0.247\ (\pm0.018)\ R \tag{10}$$
$$(\textbf{\textit{R}=0.953, \textit{P} > 95\%, n=11})$$
$$\delta H_b^{(ppm)} = 3.811(\pm0.153) - 0.052\ (\pm0.031)\ \sigma_I$$

$$+ 0.396\ (\pm0.032)\sigma_R \tag{11}$$
$$(\textbf{\textit{R}=0.937, \textit{P}> 90\%, n=11})$$
$$\delta H_b^{(ppm)} = 3.877(\pm0.139) - 0.166\ (\pm0.021)$$
$$F + 0.0278\ (\pm0.021)\ R \tag{12}$$
$$(\textbf{\textit{R}=0.938, \textit{P} > 90\%, n=11})$$
$$\delta H_c^{(ppm)} = 6.143(\pm0.284) + 0.096(\pm0.066)\sigma_I$$
$$- 0.365\ (\pm0.024)\sigma_R \tag{13}$$
$$(\textbf{\textit{R}=0.906, \textit{P}> 90\%, n=11})$$
$$\delta H_c^{(ppm)} = 6.230(\pm0.261) + 0.199(\pm0.021)\ F$$
$$+0.178\ (\pm0.052)\ R \tag{14}$$
$$(\textbf{\textit{R}=0.912, \textit{P} > 90\%, n=11})$$

¹³C NMR spectra

Chemists, Organic and physical organic chemistry researchers[1,2,21,23,28-31,43] have made extensive study of ¹³C NMR spectra for a large number of ketones, styrenes and keto-epoxides. In their study, they investigated the linear correlation of the chemical shifts (ppm) of vinyl and carbonyl carbons with Hammett σ constants, F and R parameters in alkenes, alkynes, acid chlorides and styrenes. In the present study, the chemical shifts (δ, ppm) of 3-(3,4-dimethylphenyl)-5-(substituted phenyl)-4,5-dihydro-1*H*-pyrazole-1-carbothioamides C=N and C=S carbon have been assigned and are presented in TABLE 4. 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 observed C=N and C=S chemical shifts (δ,ppm) of synthesised 3-(3,4-dimethylphenyl)-5-(substituted phenyl)-4,5-dihydro-1*H*-pyrazole-1-carbothioamides have been correlated with Hammett substituent constants and the results of statistical analysis are presented in TABLE 5. The C=N chemical shifts (δ, ppm) has shown satisfactory correlation with Hammett σ, σ^+, σ_I, constants and F parameters excluding 4-F and 4-OH substituents. The remaining Hammett substituent constants and R parameter were fail in correlation. The failure in the correlation is due to incapability of transmittance of the resonance effect of the substituents on the C=N carbon chemical shifts (δ, ppm). The chemical shifts (δ, ppm) observed for the C=S carbon of the 3-(3,4-dimethylphenyl)-5-(substituted phenyl)-4,5-dihydro-1*H*-pyrazole-1-carbothioamides have been shown poor correlation with Hammett σ and σ^+ constants. The remaining Hammett

substituent constants, F and R parameters were fail in correlation. All correlations gave positive ρ values. This shows that the normal substituent effects 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 Figure 3.

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 either σ_I, σ_R or F and R parameters[45]. The generated correlation equations are given in (15) to (18).

$$\delta_{C=N}^{(ppm)} = 158.93(\pm1.371) + 6.084\ (\pm2.035)\sigma_I$$
$$-0.458\ (\pm0.037)\sigma_R \tag{15}$$
$$(R=0.959, P>95\%, n=11)$$

$$\delta_{C=N}^{(ppm)} = 159.20(\pm1.341) + 4.895\ (\pm2.714)$$
$$F-0.196\ (\pm0.275)R \tag{16}$$
$$(R=0.955, P>95\%, n=11)$$

$$\delta_{C=S}^{(ppm)} = 175.56(\pm1.230) + 2.615(\pm0.201)\sigma_I$$
$$+2.852\ (\pm0.245)\sigma_R \tag{17}$$
$$(R=0.948, P>90\%, n=11)$$

$$\delta_{C=S}^{(ppm)} = 175.61(\pm1.206) + 1.968\ (\pm0.248)$$
$$F+2.320\ (\pm0.158)R \tag{18}$$
$$(R=0.933, P>90\%, n=11)$$

CONCLUSION

Some 1-thiocarbomyl pyrazolines including 3-(3,4-dimethylphenyl)-5-(substituted phenyl)-4,5-dihydro-1*H*-pyrazole-1-carbothioamides have been synthesised by fly-ash:H_2O catalyzed aqueous phase cyclization of chalcones and thiosemicarbazide. The yields of the synthesized carbothioamides are more than 75%. The correlation study of infrared ν(cm^{-1}) of C=N, C=S frequencies, ^1H and ^{13}C NMR chemical shifts (δ, ppm) of H_{a-c} and C=N, C=S, of 3-(3,4-dimethylphenyl)-5-(substitutedphenyl)-4,5-dihydro-1*H*-pyrazole-1-carbothioamides have shown satisfactory correlation coefficient in both single and multi-regression analyses.

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