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Solid SiO_2:H_3PO_4 acid catalyzed solvent-free cyclization of aryl 2-propen-1-ones: Synthesis of some 1-thiocarbomyl pyrazolines and spectral correlations of some 3-phenyl-5-(substituted phenyl)-4,5-dihydro-1*H*-pyrazole-1-carbothioamides

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ABSTRACT

In the present study we have synthesized some 1-thiocarbomyl pyrazolines including 3-phenyl-5-(substitutedphenyl)-4,5-dihydro-[1]*H*-pyrazole-1-carbothioamides using solvent free SiO_2:H_3PO_4 catalyzed cyclization of chalcones with thiosemicarbazide under microwave irradiation. The yields of the [1]*H*-pyrazole-1-carbothioamides are more than 85%. The synthesised pyrazole-1-carbothioamides were characterized by their analytical, physical and spectral data. The infrared νC=N, C=S, NH (cm^{-1}) frequencies, NMR chemical shifts (δ, ppm) H_a, H_b, H_c, C=N, C=S of synthesised 3-phenyl-5-(substitutedphenyl)-4,5-dihydro-[1]*H*-pyrazole-1-carbothioamides were correlated with Hammett substituent constants, F and R parameters. From the results of statistical analyses the effects of substituent on the above functional group of pyrazole-1-carbothiamides.

KEYWORDS

1*H*-pyrazole-1-carbothioamides;
SiO_2:H_3PO_4;
Environmentally benign reaction;
IR and NMR spectra;
Hammett correlations.

INTRODUCTION

In the bi- nitrogen five membered heterocyclics, the 1-thiocarbomyl pyrazolines are important and they possess –CS-NH_2 group in N_1 atom of pyrazoline ring[1-4]. These thiocarbomyl pyrazoline derivatives possess numerous 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, anti-viral and cannabinoid CBI receptor antagonists[9]. Many solvent assisted or solvent-free synthetic methods were reported in literature for synthesis of thiocarbomyl pyrazoline derivatives[3,13,15-18]. In these synthetic techniques, many pyrazoline derivatives were synthesised by cyclization of chalcones with hydrazine hydrate[19] or phenylhydrazine[20] or phenyl hydrazine hydrochloride[21-23]. Similarly 1-pyrazoline-1-cabothioamides were synthesised by cyclization of chalcones with thiosemicarbazide[3,13,14,24] or substituted thiosemicarbazide[3,9,14] or hydrazenidium dithiocyanate[25]. Now-a-days organic chemists, scientists and researchers preferred solvent-free environmentally benign synthesis due to easy working procedure, shorter reaction time, higher yields, less hazardousness

and solvent usage[26-31]. Based on the above advantages, the greener synthetic methods such as, solvent-free microwave irradiation and ultrasonication were used for synthesis of 1-thiocarbomyl pyrazolines[23,32,33]. Numerous catalysts had been utilized for synthesis of 1-thiocarbomyl pyrazoline derivatives such as Lewis acids, bases and their salts[13,32,34], CH_3COOH/CH_3COONa[3], NaOH/EtOH[24,32,35], KOH/EtOH[20,33], neat reaction in ethanol[3,15] and Basic alumina/ K_2CO_3[36,37]. These thiocarbomyl pyrazolines are used as starting material for synthesis of thiazole substituted pyrazoles[18]. Recently 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 their 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 method and studied the anticancer activities by Mathew co-workers[13]. Ashok et al., 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 their antibacterial activities[15-17]. More than 60% yields of 1-thiocarbomyl-2-(2,4-dichloro-5-fluorophenyl)-5-(substitutedphenyl)-pyrazoline derivatives had been synthesised by Patil et al.,[37] using alumina/K_2CO_3 catalyzed cyclization of 2,4-dichloro-5-phenyl chalcones with thiosemicarbazide under microwave irradiation. Spectroscopic data are useful for prediction of the ground state equilibration of organic compounds. The ultraviolet spectral absorption maxima (λ max, nm) is also utilized for prediction of the effect of substituents[31]. In pyrazoline derivatives (^{1}H pyrazole), the infrared stretches were used for predicting the effects of substituents on the C=N, C-H, N-H[21] functional group. From NMR spectroscopic analysis of the pyrazoline derivatives, the spatial arrangement 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 predictable by their frequencies with multiplicities viz., 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 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 substituent constants, F and R parameters. In these correlations they observed satisfactory correlation coefficients. Recently Thirunarayanan et al.[23] have studied the solvent-free synthesis and spectral correlations of some 1-phenyl-3-(5-bromothiophen-2-yl)-5-(substituted phenyl)-2-pyrazolines. There is no information available for solvent-free synthesis of some thiocarbomyl pyrazolines including 3-phenyl-5-(substitutedphenyl)-4,5-dihydro-^{1}*H*-pyrazole-1-carbothioamides derivatives by cyclization of the respective chalcones and thiosemicarbazide in presence of solid SiO_2:H_3PO_4 catalyst in literature in the past. Therefore the authors have taken efforts to synthesize some thiocarbomyl pyrazolines including 3-phenyl-5-(substitutedphenyl)-4,5-dihydro-1*H*-pyrazole-1-carbothioamides by solvent free microwave assisted cyclization of chalcones and thiosemicarbazide in presence of SiO_2:H_3PO_4. The purities of these pyrazolines were persuaded by their physical constants

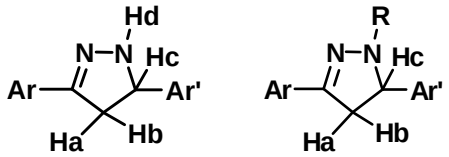


Figure 1 : General structure of 1*H*-pyrazoles

and spectral data published earlier in literature. Also the authors have recorded the infrared and NMR spectra of these synthesised thiocarbomyl pyrazoline derivatives for studying the Hammett spectral correlations.

EXPERIMENTAL

Materials and methods

All chemicals used were purchased from Sigma-Aldrich and E-Merck chemical companies. 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.

Preparation of SiO_2:H_3PO_4 catalyst

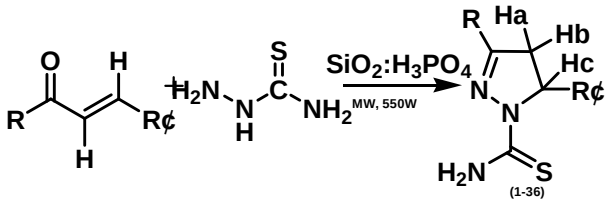
The SiO_2:H_3PO_4 catalyst was prepared by the procedure published in literature[38]. In a 50mL Borosil beaker, 2g of silica (10-20μ) 2mL of ortho phosphoric acid were taken and mixed thoroughly with glass rod. This mixture was heated on a hot air oven at 85°C for 1h, cooled to room temperature, stored in a borosil bottle and tightly capped. This was characterized by infrared spectra and SEM analysis.

Synthesis of substituted pyrazole-1-carbothioamide derivatives

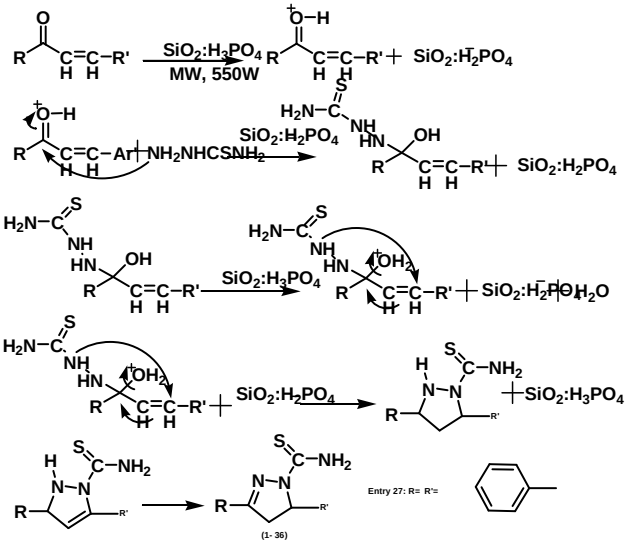
An appropriate equi-molar quantities of chalcones (2 mmol), thiosemicarbazide (2 mmol) and SiO_2:H_3PO_4 (0.5 g) were taken in a 50 mL borosil beaker and closed with lid. The mixture has been subjected to microwave irradiation for 4-6 minutes in a microwave oven at 550 watts, 2540 MHz frequency (Scheme 1) (Samsung Grill, GW73BD Microwave oven, 230V A/c, 50Hz, 2450Hz, 100-750W (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.

RESULTS AND DISCUSSION

In our organic chemistry research laboratory, we attempts to synthesize substituted pyrazoline-1-carbothioamides by cyclization of substituted chalcones and thiosemicarbazide in the presence of SiO_2:H_3PO_4 catalyst in microwave irradiation under solvent free conditions. Hence the authors have synthesized the substituted pyrazoline-1- carbothioamides by the cyclization of 2 mmol of chalcone, 2 mmol of thiosemicarbazide in microwave irradiation with 0.5 g of SiO_2:H_3PO_4 catalyst at 550 W, 4-6 minutes (Samsung Grill, GW73BD Microwave oven, 230V A/c, 50Hz, 2450Hz, 100-750W (IEC-705), (Scheme 1). During the course of this reaction SiO_2:H_3PO_4 catalyses and leads to cyclizes the chalcones with thiosemicarbazide to elimination of water followed by proton transfer gave the 1-pyrazolines-1-carbothioamides. The yields of the 1-pyrazolines-1-carbothioamides in this reaction are more than 85%. The proposed general mechanism of this reaction is shown in (Scheme 2). The chalcone containing electron donating substituent (OCH_3) gave higher yields than electron-withdrawing (halogens, NO_2) sub-



Scheme 1 : Synthesis of 1-thiocarbomyl pyrazolines by SiO_2:H_3PO_4 catalyzed solvent free cyclization of chalcones and thiosemicarbazide under microwave irradiation



Scheme 2 : The proposed mechanism for the synthesis of pyrazolines-1-carbothioamides by SiO_2: H_3PO_4 catalyzed solvent free cyclization of chalcones and thiosemicarbazide under microwave irradiation.

stituents. Further we have investigated this cyclization reaction with equimolar quantities of the styryl phenyl ketone (entry 25) and thiosemicarbazide under the same condition as above. In this reaction the obtained yield was 92%. 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 85 to 92%. Further increase the catalyst amount be-

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yond 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 phenyl ketone and thiosemicarbazide (entry 25) is presented in TABLE 2. From the TABLE 2, first two runs gave 92% product. The third, fourth and fifth runs of reactions gave the yields 91.5%, 91.5% and 91% of 1- pyrazoline-1-carbothiamide. There was no appreciable loss in its effect of catalytic activity were observed up to fifth run. The effect of solvents on the

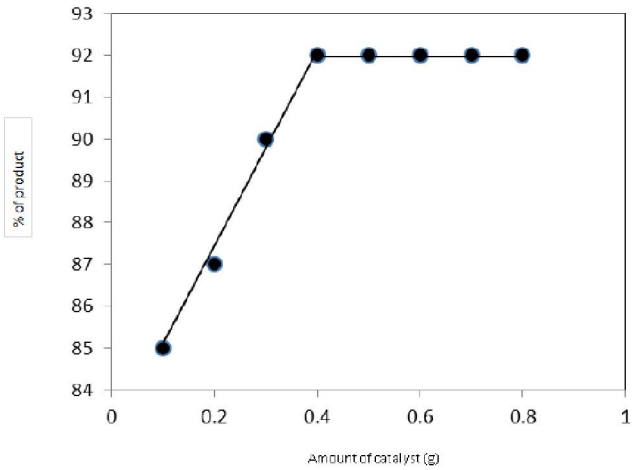
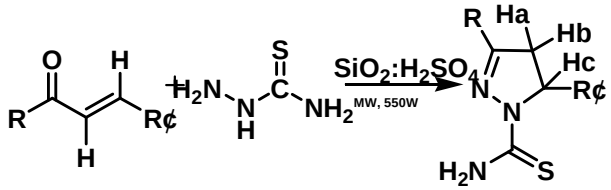


Figure 2 : Effect of catalyst loading

TABLE 1 : Analytical, physical constants, yields and mass fragments of pyrazolines-1- carbothioamides synthesised by SiO_2:H_3PO_4 catalyzed solvent-free cyclization of chalcones and thiosemicarbazide reaction of the type under microwave irradiation.



Entry	R	R'	Product	M.W.	Yield	m.p. (°C)	Mass (m/z)
1	CH_3	C_6H_5	$C_{11}H_{13}N_3S$	219	85	273-274 273[25]	219[M^+]
2	CH_3	4-$OCH_3C_6H_4$	$C_{12}H_{15}N_3OS$	249	90	182-183 182[25]	249[M^+]
3	CH_3	4-$N(CH_3)_2C_6H_4$	$C_{13}H_{18}N_4S$	263	86	238-239 238[25]	263[M^+]
4	CH_3	C_4H_3O(2-Furyl)	$C_9H_{15}N_3OS$	213	88	221-222 220-222[25]	213[M^+]
5	CH_3	C_4H_3S(2-Thienyl)	$C_9H_{15}N_3S_2$	229	87	119-220 220[25]	213[M^+]
6	C_4H_3S(2-Thienyl)	C_6H_5	$C_{14}H_{17}N_3S_2$	291	86	164-165 160-165[32]	291[M^+]
7	C_4H_3S(2-Thienyl)	4-BrC_6H_4	$C_{14}H_{16}BrN_3S_2$	370	87	254-255 250-255[32]	370[M^+], 372[M^{2+}],
8	C_4H_3S(2-Thienyl)	2,4,5-$(OCH_3)_3C_6H_2$	$C_{17}H_{23}N_3O_3S_2$	381	91	214-215 210-215[32]	381[M^+],
9	C_4H_3S(2-Thienyl)	4-$N(CH_3)_2C_6H_4$	$C_{16}H_{18}N_4S_2$	330	88	174-175 170-175[32]	330[M^+],
10	C_6H_5	2,4-Cl_2-C_6H_3	$C_{16}H_{13}Cl_2N_3S$	350	89	220-221 217-220[33]	350[M^+], 352[M^{2+}]
11	2,4-Br_2-C_6H_3	4-ClC_6H_4	$C_{16}H_{12}Br_2ClN_3S$	491	89	218-219 216-218[23]	491[M^+], 493[M^{2+}], 495[M^{4+}]
12	2,4-Br_2-C_6H_3	4-$OCH_3C_6H_4$	$C_{17}H_{15}Br_2N_3O_3S$	361	92	239-240 236-238[23]	361[M^+], 363[M^{2+}]

Entry	R	R'	Product	M.W.	Yield	m.p. (°C)	Mass (m/z)
13	2,4-Cl_2-C_6H_3	4-ClC_6H_4	$C_{16}H_{12}Cl_3N_3S$	323	88	212-213 211-213[24]	323[M^+], 325[M^{2+}], 327[M^{4+}]
14	2,4-Cl_2-C_6H_3	4-$OCH_3C_6H_4$	$C_{17}H_{17}Cl_2FN_3S$	381	93	210-211 209-210[24]	381[M^+], 383[M^{2+}]
15	4-$OCH_3C_6H_4$	C_6H_5	$C_{17}H_{17}N_3OS$	311	86	162-163 160-162[36]	311[M^+]
16	4-ClC_6H_4	C_6H_5	$C_{16}H_{14}ClN_3S$	315	85	123-124 122-123[36]	315[M^+], 317[M^{2+}]
17	3-$NO_2C_6H_4$	C_6H_5	$C_{16}H_{14}N_4O_2S$	326	85	129-130 128-130[36]	326[M^+]
18	4-$OCH_3C_6H_4$	4-ClC_6H_4	$C_{17}H_{16}ClN_3OS$	345	92	127-128 125-127[36]	360[M^+], 362[M^{2+}],
19	4-ClC_6H_4	4-ClC_6H_4	$C_{16}H_{13}Cl_2N_3S$	350	86	148-149 147-148[36]	350[M^+], 352[M^{2+}], 354[M^{2+4}],
20	3-$NO_2C_6H_4$	4-ClC_6H_4	$C_{16}H_{13}ClN_4O_3S$	237	87	150-151 148-150[36]	337[M^+], 396[M^{2+}]
21	2,4-$(CH_3)_2$-C_6H_3	4-FC_6H_4	$C_{18}H_{18}FN_3S$	327	90	225-226 223-225[24]	327[M^+], 329[M^{2+}]
22	2,4-$(CH_3)_2$-C_6H_3	4-$NO_2C_6H_4$	$C_{18}H_{18}N_4O_2S$	354	89	203-204 202-203[24]	354[M^+]
23	C_4H_3O(2-Furyl)	C_6H_5	$C_{14}H_{13}N_3OS$	271	92	177-178 176-177[34]	271[M^+]
24	C_4H_3O(2-Furyl)	C_4H_3O(2-Furyl)	$C_{12}H_{11}N_3O_2S$	293	92	164-165 163-164[34]	293[M^+]
25	2,4-Cl_2-5-F-C_6H_2	C_6H_5	$C_{16}H_{12}Cl_2FN_3S$	368	94	165-166 165[37]	368[M^+], 370[M^{2+}], 372[M^{+4}]
26	2,4-Cl_2-5-F-C_6H_2	2-ClC_6H_4	$C_{16}H_{11}Cl_3FN_3S$	402	90	145-146 145[37]	402[M^+], 404[M^{2+}], 408[M^{+4}], 410[M^{+6}]
27	C_6H_5	C_6H_5	$C_{16}H_{15}N_3S$	281	92	202-203 200-202[33]	281[M^+]
28	C_6H_5	2-BrC_6H_4	$C_{16}H_{14}BrN_3S$	361	88	173-174 170-174[33]	361[M^+], 363[M^{2+}]
29	C_6H_5	3-BrC_6H_4	$C_{16}H_{14}BrN_3S$	361	89	215-216 213-215[33]	361[M^+], 363[M^{2+}]
30	C_6H_5	4-BrC_6H_4	$C_{16}H_{14}BrN_3S$	361	89	196-197 195-197[33]	361[M^+], 363[M^{2+}]
31	C_6H_5	4-ClC_6H_4	$C_{16}H_{14}ClN_3S$	315	88	178-179 174-178[33]	315[M^+], 317[M^{2+}]
32	C_6H_5	4-FC_6H_4	$C_{16}H_{14}FN_3S$	299	89	236-237 235-237[33]	299[M^+], 301[M^{2+}]
33	C_6H_5	2-$OCH_3C_6H_4$	$C_{17}H_{17}N_3OS$	311	92	215-216 211-215[33]	311[M^+]
34	C_6H_5	4-$OCH_3C_6H_4$	$C_{17}H_{17}N_3OS$	311	92	166-167 165-167[33]	311[M^+]
35	C_6H_5	2-$CH_3C_6H_4$	$C_{17}H_{17}N_3S$	295	91	215-216 211-216[33]	395[M^+]
36	C_6H_5	2,4-$(OCH_3)_2C_6H_3$	$C_{18}H_{19}N_3O_2S$	341	90	160-161 159-160[33]	341[M^+]

TABLE 2 : Reusability of fly-ash:H_2SO_4 catalyst on cyclization of styryl phenyl ketone (2 mmol) and thiosemicarbazide (2 mmol) under microwave irradiation(entry 27).

Run	1	2	3	4	5
Yield	92	92	91.5	91.5	91

yield also studied with methanol, ethanol, dichloromethane and tetrahydrofuran from each component of the catalyst (entry 25). Similarly the effect of microwave irradiation was studied on the each component of the catalysts. The effect of solvents on the yields of pyrazoline-1-carbothioamide was presented in TABLE 3. From the table the highest yield of pyrazoline-1-carbothioamide obtained from the cyclization of chalcone and thiosemicarbazide with the catalyst SiO_2:H_3PO_4 in microwave irradiation.

IR spectral study

The synthesis of pyrazoline-1-carbothioamides are shown in Scheme 1. In the present study, the authors have chosen a series of pyrazoline-1-carbothioamide derivatives namely 3-phenyl-5-(substitutedphenyl)-4,5-dihydro-[1]*H*-pyrazole-1-carbothioamide (entries 25-33) for studying the substituent effects on the spectral data. The infrared νC=N, NH, C=S and CF stretching frequencies (cm^{-1}) of these pyrazoline-1-carbothioamides (entries 25-33) have been assigned and are presented in TABLE 4. These data were correlated[21,23,28-31,38-42]

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TABLE 3 : The effect of solvents in conventional heating and without solvent in microwave irradiation on yield of pyrazoline-1-carbothiamide (entry 27)

Solvents												Microwave irradiation		
MeOH			EtOH			DCM			THF					
SiO_2	PA	SPA	SiO_2	PA	SPA	SiO_2	PA	SPA	SiO_2	PA	SPA	SiO_2	PA	SPA
69	53	68	72	58	72	73	60	76	75	61	78	72	70	92

MeOH=Methanol; EtOH=Ethanol; DCM= Dichloromethane; THF=Tetrahydrofuran; PA=Phosphoric acid; SPA=SiO_2:H_3PO_4

TABLE 4 : The spectroscopic data of 1- thiocarbomyl pyrazolines (entries 27-35).

Entry	X	IR(ν, cm-1)			^{1}H NMR(δ,ppm)				^{13}C NMR(δ,ppm)		
		C=N	C=S	NH	Ha (*dd*, 1H)	Hb (*dd*, 1H)	Hc (*dd*, 1H)	X	C=N	C=S	X
27	H	1578	1366	3558	3.123	3.917	5.971	---	156.48	176.19	---
28	2-Br	1590	1357	3528	3.291	3.871	6.017	---	155.72	177.13	---
29	3-Br	1583	1361	3534	3.326	3.971	6.107	---	155.15	176.92	---
30	4-Br	1582	1376	3394	3.150	3.899	5.996	---	155.54	177.91	---
31	4-Cl	1576	1375	3387	3.041	3.901	5.893	---	154.28	176.54	---
32	4-F	1548	1366	3356	3.214	3.971	5.904	---	154.79	175.97	---
33	2-OCH_3	1590	1375	3433	3.861	3.904	6.107	3.791	156.07	177.67	55.47
34	4-OCH_3	1598	1378	3365	3.795	3.807	5.917	3.071	156.78	177.17	56.72
35	2-CH_3	1585	1378	3448	3.017	3.617	6.197	2.471	155.49	176.59	21.73

with Hammett substituent constants and Swain-Lupton's[43] parameters. In this correlation the structure parameter Hammett equation employed is as shown in equation (1).

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

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

The observed νC=N stretching frequencies (cm^{-1}) are correlated with various Hammett substituent constants and F and R parameters through single and multi-regression analyses including Swain-Lupton's[43] parameters. The results of statistical analysis of single parameter correlation are shown in TABLE 5. The correlation of νC=N (cm^{-1}) frequencies of 3-phenyl-5-(substitutedphenyl)-4,5-dihydro-1*H*-pyrazole-1-carbothioamide with Hammett substituent constants, F and R parameters were satisfactory, excluding H, 4-F and 2-CH_3 substituents. When these substituents were included in the regression, they reduced the correlation considerably. A satisfactory correlation was obtained for νC=S (cm^{-1}) frequencies of 3-phenyl-5-(substitutedphenyl)-4,5-dihydro-1*H*-pyrazole-1-carbothioamide with Hammett σ and σ^+ substituent constants excluding 4-Br and 4-Cl substituents. Hammett σ_R constant and R parameters has shown satisfactory correlation for the νNH stretches (cm^{-1}) of these of 3-phenyl-5-(substitutedphenyl)-4,5-dihydro-1*H*-pyrazole-1-carbothioamides. The remaining Hammett substituent constants and F parameters shown poor correlation. The failure in correlation was due to the inability of transmittance of inductive and field effects of the substituent on the spectral group frequencies νC=N, C=S, NH and (cm^{-1}) and is associated with the resonance-conjugative structure shown in Figure 3. Some of the single parameter correlations of νC=S and NH (cm^{-1}) frequencies of 3-phenyl-5-(substitutedphenyl)-4,5-dihydro-1*H*-pyrazole-1-carbothioamides with Hammett substituent constants, F and R parameters were fail. So, the authors think that it is worthwhile to seek the multi-regression analysis of these frequencies with Swain-Lupton's[40] 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).

$$\nu_{CN}(cm^{-1}) = 1587.85(\pm11.142)-24.329\sigma_I\ (\pm7.812)-4.549\ \sigma_R\ (\pm1.125) \quad (2)$$

(*R*=0.934, *P*> 90%, n=9)

$$\nu_{CN}(cm^{-1}) = 1590.38(\pm9.269)-30.842F\ (\pm2.398)-12.312R\ (\pm6.257) \quad (3)$$

(*R*=0.955, P > 95%, n=9)

TABLE 5 : Results of statistical analysis of infrared ν(cm^{-1}) C=N, C=S, NH, NMR chemical shifts (δ ppm) of H_a, H_b, H_c, C=N and C=S of pyrazoline- 1-varbothioamides with Hammett σ, σ$^+$, σ_I σ_R constants and F and R parameters(entries 27-35).

Frequency	Constants	r	I	ρ	s	n	Correlated derivatives
νC=N	σ	0.902	1581.78	-14.074	14.18	8	H, 2-Br, 3-Br, 4-Br, 4-Cl, 2-OCH_3, 4-OCH_3, 2-CH_3
	σ$^+$	0.902	1581.41	-6.875	14.74	8	H, 2-Br, 3-Br, 4-Br, 4-Cl, 4-F, 2-OCH_3, 4-OCH_3, 2-CH_3
	σ_I	0.903	1588.60	-22.938	14.21	7	2-Br, 3-Br, 4-Br, 4-Cl, 4-F, 2-OCH_3, 4-OCH_3
	σ_R	0.905	1582.21	4.173	15.07	8	H, 2-Br, 3-Br, 4-Br, 4-Cl, 2-OCH_3, 4-OCH_3, 2-CH_3
	F	0.905	1592.18	-32.138	12.80	7	2-Br, 3-Br, 4-Br, 4-Cl, 4-F, 2-OCH_3, 4-OCH_3
	R	0.901	1583.76	8.693	14.96	8	H, 2-Br, 3-Br, 4-Br, 4-Cl, 2-OCH_3, 4-OCH_3, 2-CH_3
νC=S	σ	0.904	1370.87	-13.565	7.30	7	H, 2-Br, 3-Br, 4-F, 2-OCH_3, 4-OCH_3, 2-CH_3
	σ$^+$	0.906	1370.08	-11.752	6.35	7	H, 2-Br, 3-Br, 4-F, 2-OCH_3, 4-OCH_3, 2-CH_3
	σ_I	0.813	1374.11	-11.908	7.99	9	H, 2-Br, 3-Br, 4-Br, 4-Cl, 4-F, 2-OCH_3, 4-OCH_3, 2-CH_3
	σ_R	0.819	1368.09	-8.044	8.25	9	H, 2-Br, 3-Br, 4-Br, 4-Cl, 4-F, 2-OCH_3, 4-OCH_3, 2-CH_3
	F	0.833	1374.12	-11.382	7.92	9	H, 2-Br, 3-Br, 4-Br, 4-Cl, 4-F, 2-OCH_3, 4-OCH_3, 2-CH_3
	R	0.823	1367.56	-8.706	8.17	9	H, 2-Br, 3-Br, 4-Br, 4-Cl, 4-F, 2-OCH_3, 4-OCH_3, 2-CH_3
νNH	σ	0.823	3441.71	63.781	80.54	9	H, 2-Br, 3-Br, 4-Br, 4-Cl, 4-F, 2-OCH_3, 4-OCH_3, 2-CH_3
	σ$^+$	0.884	3445.73	83.146	73.05	9	H, 2-Br, 3-Br, 4-Br, 4-Cl, 4-F, 2-OCH_3, 4-OCH_3, 2-CH_3
	σ_I	0.835	3487.80	-131.702	77.55	9	H, 2-Br, 3-Br, 4-Br, 4-Cl, 4-F, 2-OCH_3, 4-OCH_3, 2-CH_3
	σ_R	0.905	3305.09	228.096	68.53	9	H, 2-Br, 3-Br, 4-Br, 4-Cl, 4-F, 2-OCH_3, 4-OCH_3, 2-CH_3
	F	0.886	3493.99	-142.889	74.83	9	H, 2-Br, 3-Br, 4-Br, 4-Cl, 4-F, 2-OCH_3, 4-OCH_3, 2-CH_3
	R	0.906	3519.48	244.49	61.48	9	H, 2-Br, 3-Br, 4-Br, 4-Cl, 4-F, 2-OCH_3, 4-OCH_3, 2-CH_3
δH_a	σ	0.906	3.345	-0.667	0.26	7	H, 2-Br, 3-Br, 4-Br, 4-Cl, 4-F, 2-CH_3
	σ$^+$	0.906	3.308	-0.426	0.26	7	H, 2-Br, 3-Br, 4-Br, 4-Cl, 4-F, 2-CH_3
	σ_I	0.871	3.296	0.112	0.33	9	H, 2-Br, 3-Br, 4-Br, 4-Cl, 4-F, 2-OCH_3, 4-OCH_3, 2-CH_3
	σ_R	0.907	2.996	-1.213	0.21	9	H, 2-Br, 3-Br, 4-Br, 4-Cl, 4-F, 2-OCH_3, 4-OCH_3, 2-CH_3
	F	0.855	3.283	0.070	0.33	9	H, 2-Br, 3-Br, 4-Br, 4-Cl, 4-F, 2-OCH_3, 4-OCH_3, 2-CH_3
	R	0.907	2.999	-1.037	0.23	9	H, 2-Br, 3-Br, 4-Br, 4-Cl, 4-F, 2-OCH_3, 4-OCH_3, 2-CH_3
δH_b	σ	0.904	3.864	0.171	0.10	8	H, 2-Br, 3-Br, 4-Br, 4-Cl, 4-F, 2-OCH_3, 4-OCH_3
	σ$^+$	0.903	3.871	0.094	0.10	8	H, 2-Br, 3-Br, 4-Br, 4-Cl, 4-F, 2-OCH_3, 4-OCH_3
	σ_I	0.906	3.761	0.342	0.08	8	2-Br, 3-Br, 4-Br, 4-Cl, 4-F, 2-OCH_3, 4-OCH_3, 2-CH_3
	σ_R	0.811	3.855	-0.067	0.11	9	H, 2-Br, 3-Br, 4-Br, 4-Cl, 4-F, 2-OCH_3, 4-OCH_3, 2-CH_3
	F	0.906	3.772	0.261	0.08	9	H, 2-Br, 3-Br, 4-Br, 4-Cl, 4-F, 2-OCH_3, 4-OCH_3, 2-CH_3
	R	0.813	3.851	-0.069	0.11	9	H, 2-Br, 3-Br, 4-Br, 4-Cl, 4-F, 2-OCH_3, 4-OCH_3, 2-CH_3
δH_c	σ	0.817	6.015	-0.066	0.11	9	H, 2-Br, 3-Br, 4-Br, 4-Cl, 4-F, 2-OCH_3, 4-OCH_3, 2-CH_3
	σ$^+$	0.803	6.021	0.007	0.11	9	H, 2-Br, 3-Br, 4-Br, 4-Cl, 4-F, 2-OCH_3, 4-OCH_3, 2-CH_3
	σ_I	0.904	6.082	-0.214	0.10	8	2-Br, 3-Br, 4-Br, 4-Cl, 4-F, 2-OCH_3, 4-OCH_3, 2-CH_3
	σ_R	0.809	6.025	0.050	0.11	9	H, 2-Br, 3-Br, 4-Br, 4-Cl, 4-F, 2-OCH_3, 4-OCH_3, 2-CH_3
	F	0.904	6.084	-0.209	0.10	8	2-Br, 3-Br, 4-Br, 4-Cl, 4-F, 2-OCH_3, 4-OCH_3, 2-CH_3
	R	0.829	0.042	0.099	0.11	9	H, 2-Br, 3-Br, 4-Br, 4-Cl, 4-F, 2-OCH_3, 4-OCH_3, 2-CH_3
δCN	σ	0.905	155.661	-1.566	0.70	9	H, 2-Br, 3-Br, 4-Br, 4-Cl, 4-F, 2-OCH_3, 4-OCH_3, 2-CH_3
	σ$^+$	0.904	155.57	-0872	0.74	9	H, 2-Br, 3-Br, 4-Br, 4-Cl, 4-F, 2-OCH_3, 4-OCH_3, 2-CH_3
	σ_I	0.905	156.29	-2.163	0.69	7	2-Br, 3-Br, 4-Br, 4-Cl, 4-F, 2-OCH_3, 4-OCH_3
	σ_R	0.889	155.49	-0.374	0.84	9	H, 2-Br, 3-Br, 4-Br, 4-Cl, 4-F, 2-OCH_3, 4-OCH_3, 2-CH_3
	F	0.905	156.24	-1.829	0.70	8	H, 2-Br, 3-Br, 4-Br, 4-Cl, 4-F, 2-OCH_3, 4-OCH_3
	R	0.808	155.49	-0.311	0.84	9	H, 2-Br, 3-Br, 4-Br, 4-Cl, 4-F, 2-OCH_3, 4-OCH_3, 2-CH_3
δCS	σ	0.900	176.89	-0.004	0.96	7	H, 2-Br, 3-Br, 4-Br, 4-Cl, 4-F, 2-CH_3
	σ$^+$	0.903	176.89	0.046	0.68	7	H, 2-Br, 3-Br, 4-Br, 4-Cl, 4-F, 2-CH_3
	σ_I	0.902	176.68	0.667	0.67	7	2-Br, 3-Br, 4-Br, 4-Cl, 4-F, 2-OCH_3, 4-OCH_3
	σ_R	0.882	176.69	-0.761	0.67	9	H, 2-Br, 3-Br, 4-Br, 4-Cl, 4-F, 2-OCH_3, 4-OCH_3, 2-CH_3
	F	0.802	176.87	0.068	0.68	9	H, 2-Br, 3-Br, 4-Br, 4-Cl, 4-F, 2-OCH_3, 4-OCH_3, 2-CH_3
	R	0.801	176.45	-0.580	0.68	9	H, 2-Br, 3-Br, 4-Br, 4-Cl, 4-F, 2-OCH_3, 4-OCH_3, 2-CH_3

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

$\nu_{C=S}(cm^{-1})$ = 1371.83(±9.623)-16.317σ_I (±4.761)-13.830 σ_R (±5.991) (4)

(*R*=0.944, *P*> 90%, n=9)

$\nu_{C=S}(cm^{-1})$ =1371.81(±5.064)-20.695F (±3.107) – 20.191R (±4.346) (5)

(*R*=0.957, P > 95%, n=9)

$\nu_{NH}(cm^{-1})$ = 3321.23(±52.588)-69.581σ_I (±31.265)+20.150σ_R (±4.212) (6)

(*R*=0.958, *P*> 95%, n=9)

$\nu_{NH}(cm^{-1})$ =3526.45(±44.889)-39.854F (±11.609)+22.236R (±12.706) (7)

(*R*=0.967, P > 95%, n=9)

^{1}H NMR spectral study

The ^{1}H NMR spectra of synthesised 3-phenyl-5-(substitutedphenyl)-4,5-dihydro-1*H*-pyrazole-1-carbothioamide derivatives (entries 25-33) under investigation have been recorded in deuteriochloroform solution 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-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 ^{1}H or the ^{13}C 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).

$\log \delta = \log \delta_0 + \rho\sigma$ (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-phenyl-5-(substitutedphenyl)-4,5-dihydro-1*H*-pyrazole-1-carbothioamides have been correlated with various Hammett sigma constants. The results of statistical analysis[21,23,28-31,38-42] are presented in TABLE 5. The H_a proton chemical shifts (δ, ppm) with Hammett σ, σ^+, σ_R constants and F parameters gave satisfactory correlations. The Hammett σ_I constant and R parameter has shown poor correlations. The failure in correlation is associated with the conjugative structure shown in Figure 3.

The H_b proton chemical shifts (δ, ppm) of 3-phenyl-5-(substitutedphenyl)-4,5-dihydro-1*H*-pyrazole-1-carbothioamide derivatives with Hammett σ, σ^+, σ_I constants and F parameters had shown satisfactory correlation. All correlation gave positive ρ values. excluding Hammett σ^+ constants. The poor correlation is due to the absence or incapability The resonance component

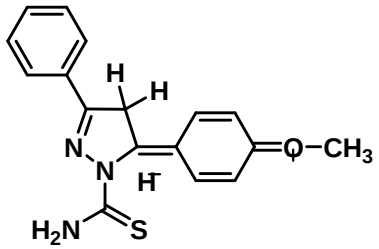

Figure 3 : The resonance-conjugative structure

of the substituents were fail in correlation. This is due to the inability of transmittance of resonance effects of substituent on the H_b proton chemical shifts and it is associated with the conjugative structure shown in Figure 3.

The results of statistical analysis of H_c proton chemical shifts (δ, ppm) with Hammett substituents are presented in TABLE 5. The H_S proton chemical shifts with Hammett σ_I, and F parameters gave satisfactory correlation excluding H substituent. The remaining Hammett substituent constants and R parameter has shown poor correlation with H_c chemical shifts (δ, ppm) of the pyrazoline-1-carbothioamides. The failure in correlation was the reasons stated earlier and associated with 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[43] F and R parameters. The correlation equations for H_{a-c} proton chemical shifts (δ, ppm) are given in (9)-(14).

$\delta H_a^{(ppm)}$ = 3.059(±0.165) - 0.298(±0.041σ_I – 1.319 (±0.448)σ_R (9)

(*R*=0.977, *P*> 95%, n=9)

$\delta H_a^{(ppm)}$ = 3.092(±0.147) - 0.552(±0.321) F – 1.344 (±0.418) R (10)

(*R*=0.979, *P* > 95%, n=9)

$\delta H_b^{(ppm)}$ = 3.777(±0.067) + 0.361 (±0.160) σ_I+0.062

$(\pm 0.011)\sigma_R$ (11)
(R=0.966, P> 95%, n=9)

$\delta H_b^{(ppm)} = 3.790(\pm 0.063) + 0.349\ (\pm 0.0165)\ F + 0.214\ (\pm 0.018)\ R$ (14)
(R=0.966, P > 95%, n=9)

$\delta H_c^{(ppm)} = 6.077(\pm 0.080) - 0.223(\pm 0.020)\sigma_I - 0.029\ (\pm 0.002)\sigma_R$ (13)
(R=0.942, P> 90%, n=9)

$\delta H_c^{(ppm)} = 6.081(\pm 0.073) - 0.220\ (\pm 0.091)\ F + 0.022\ (\pm 0.020)\ R$ (14)
(R=0.946, P > 90%, n=9)

^{13}C NMR spectra

Chemists and physical organic chemistry researchers[21,23,28-31,38-42] have made extensive study of ^{13}C NMR spectra for a large number of ketones, styrenes and keto-epoxides. In their investigations, they studied the linear Hammett correlation of the chemical shifts (ppm) of vinyl and carbonyl carbons with Hammett σ constants, F and R parameters using single and multi-linear regression analyses. In the present investigation, the chemical shifts (δ, ppm) of pyrazoline-1-carbothioamide ring 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 chemical shifts (δ, ppm) observed for the C=N and C=S of synthesised pyrazoline-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 substituent constants and F parameters excluding 2-CH_3 substituents. The resonance components of the substituents were fail in correlations. This 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 pyrazoline-1-carothioamides has been correlated satisfactorily with Hammett σ, σ^+ and σ_I constants excluding H, 2-OCH_3, 4-OCH_3 and 2-CH_3 substituents. The remaining Hammett substituent constant, F and R parameters were failing in correlations. 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 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[43]. The generated correlation equations are given in (15) to (18).

$\delta_{C=N}^{(ppm)} = 156.08(\pm 0.513) - 2.558(\pm 0.128)\sigma_I - 1.29\ (\pm 0.138)\sigma_R$ (15)
(R=0.963, P> 95%, n=9)

$\delta_{C=N}(ppm) = 155.97(\pm 0.446) - 2.471(\pm 0.115)\ F - 1.832\ (\pm 0.162)R$ (16)
(R=0.969, P> 95%, n=9)

$\delta_{C=S}^{(ppm)} = 176.588(\pm 0.521) + 0.448(\pm 0.132)\sigma_I - 0.568\ (\pm 0.143)\sigma_R$ (17)
(R=0.926, P> 90%, n=9)

$\delta_{C=S}^{(ppm)} = 176.784(\pm 0.500) - 0.223\ (\pm 0.029)\ F - 0.662\ (\pm 0.14)R$ (18)
(R=0.956, P> 95%, n=10)

CONCLUSION

Some pyrazolines-1-carbothioamides including 3-phenyl-5-(substitutedphenyl)-4,5-dihydro-[1]*H*-pyrazole-1-carbothioamides have been synthesised by microwave assisted SiO_2:H_3PO_4 catalyzed solvent free cyclization of chalcones and thiosemicarbazide. The yields of the synthesized pyrazolines-1-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} and C=N, C=S, of 3-phenyl-5-(substitutedphenyl)-4,5-dihydro-[1]*H*-pyrazole-1-carbothioamides have shown satisfactory correlations in both single and multi-regression analyses.

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