SYNTHESIS OF SOME NEW BIOACTIVE 1-N-SUBTITUTED 3, 5-DIARYL-2-PYRAZOLINES

Sadaf Sadiq Khan and Aurangzeb Hasan*
Department of Chemistry, Quaid-i-Azam University, Islamabad 45320, Pakistan
E-mail: flavonoids@hotmail.com

Abstract : A group of four series (A-D) of 22 new bioactive 1-N-acid substituted 3, 5-diphenyl-2-pyrazolines were synthesized by cyclization of variably substituted chalcones and simple or substituted phenyl hydrazine and / or semicarbazide, using acetic acid as a solvent. The chemical structure of the compounds was characterized by FTIR, ^{1}HNMR, and EIMS spectroscopy and chemical analyses. The antifungal and antibacterial activities of these compounds were evaluated by agar tube dilution method and agar well diffusion method respectively.

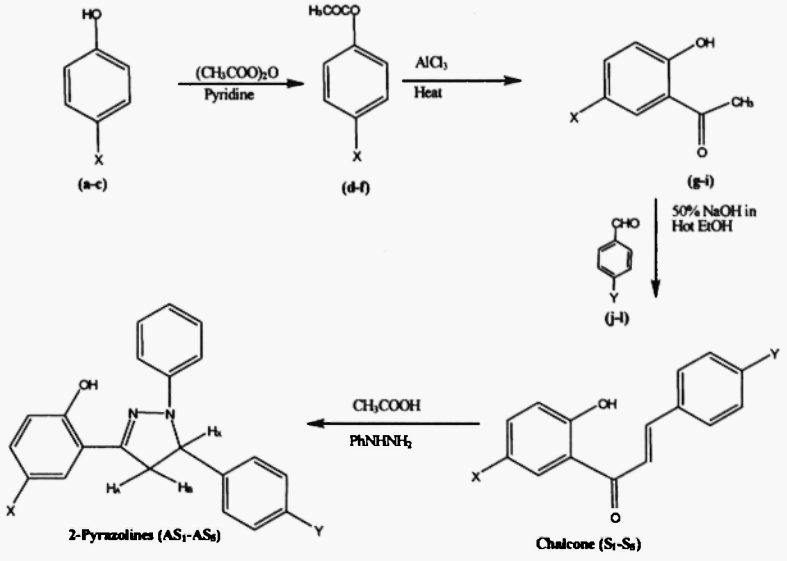
Introduction

In continuation of our previous work [1] on the synthesis of pyrazolines which have displayed various biological properties such as pesticidal, fungicidal, insecticidal, anti-inflammatory, antiarthritic, antidepressant and antiviral activities [2-4]. Considerable interest has been focused on the pyrazolines structure, which is known to possess a broad spectrum of biological activities such as transquillising, muscle relaxant, psychoanaleptic, anticonvulsant and antihypertensive activities [5-9]. Moreover, these heterocyclic compounds, in addition to biological activities have also shown some industrial applications like bleaching agent, dyes, optical brighteners and various fluorescent-whitening agents [2, 4, 10-13].

Earlier studies by E. Palaska, *et al.* [14] also demonstrated the antidepressant activities of some 3, 5-diphenyl-2-pyrazolines. The present study is therefore devoted to the synthesis of pyrazolines from variably substituted chalcones, which are also associated with diverse biological activities [15-20], and simple or substituted phenyl hydrazine and / or semicabazide. This study was carried out in the quest to prepare pyrazolines not synthesized earlier that may possess new and/or enhanced biological and other industrial properties. As part of our continuing efforts in this area a group of four series of 22 new 1-N- substituted 3, 5-diphenyl -2- pyrazolines have been synthesized and evaluated for their antifungal and antibacterial activities

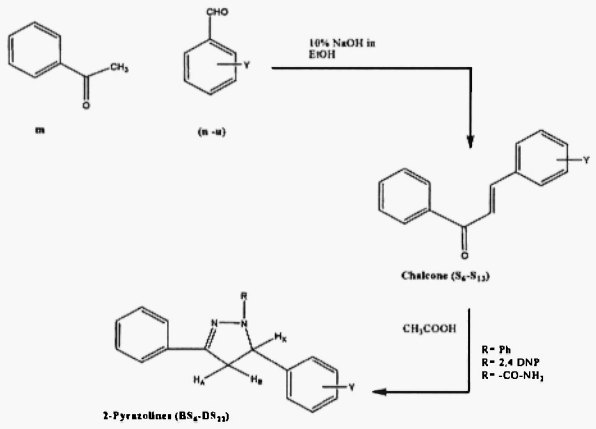
Results and Discussion

O-acetyl 4-halo-phenols (**d-f**) were prepared by reacting 4-halo-phenols (**a-c**) with acetic anhydride in the presence of pyridine. On Fries rearrangement with anhydrous $AlCl_3$ (**d-f**) yielded 5-halo-2-hydroxy acetophenones (**g-i**). Compounds (**g-i**) on further reaction with various aromatic aldehydes (**j-l**) in the presence of 50% NaOH and hot ethanol were converted into 2-hydroxy substituted chalcones (S_1-S_5), which on cyclization with phenyl hydrazine in acetic acid afforded 1- phenyl -3-(2-hydroxy -5-halo-phenyl)-5-(4-halo-phenyl)-2-pyrazolines (AS_1-AS_5) (Scheme 1).



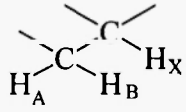
Scheme-1

Further more, by Claisen Schmidt condensation reaction; unsubtituted acetophenone (**m**) was converted to chalcones (S_6-S_{13}) by reacting it with variably substituted benzaldehydes (**n-u**) in the presence of 10% NaOH and ethanol. Chalcones (S_6-S_{13}) on cyclization with phenyl hydrazine gave 2-pyrazolines (BS_6-BS_{13}) , chalcones (S_6, S_8-S_{10}, S_{13}) with 2,4-dinitrophenylhyrdazine (2,4-DNP) gave 2-pyrazolines (CS_{14}-CS_{18}) and chalcones (S_6, S_8-S_{10}) on treatment with semicabazide in the presence of acetic acid give 2-pyrazolines (DS_{19}-DS_{22}) scheme 2.



Scheme-2

1-Phenyl-3-(2-hydroxy-5-bromophenyl)-5-(4-fluorophenyl)-2-pyrazoline (AS_1) was obtained as yellow grannuals. The molecular formula and molecular weight of (AS_1) are $C_{21}H_{16}N_2BrFO$ and 410 respectively. The FTIR spectrum showed stretching frequencies at 3493 cm^{-1}, 3028 cm^{-1}, 1584 cm^{-1}, 1493 cm^{-1} which are characteristics of OH, CH_2, C=N, C=C of the aromatic rings respectively (Table 2). The mass spectrum of 1-phenyl-3-(2-hydroxy-5-bromophenyl)-5-(4-fluorophenyl)-2-pyrazoline (AS_1) showed characteristics peaks of molecular ion peak M, M+2 at m/z 410, 412 respectively with relative isotopic abundance of Br which are found in good agreement with molecular weight. The characteristic peaks at m/z 329 and 331 appeared due to the loss of Br radical from molecular ion. The base peak in the mass spectrum appeared at m/z 410 which is also the molecular ion peak. Other peaks at 315 and 239 are formed from the loss of A, B and C ring from the molecule. The ^1H NMR spectrum of 1-phenyl-3-(2-hydroxy-5-bromo-phenyl)-5-(4-fluorophenyl)-2-pyrazoline (AS_1) showed three doublet of doublets at 3.20 ppm, 3.92 ppm, 5.25 ppm, with large coupling constant (7.40,17.2) Hz, (12.36,17.2) Hz and (7.41,12.2) Hz which are characteristic and showed following type of arrangement of protons.



The phenolic –OH of the ring at 3-position showed a broad singlet at 10.6 ppm. The aromatic protons are shown in the range of 6.76-7.35 ppm. The δ values, multiplicity and J values of all protons of 1-phenyl-3-(2-hydroxy-5-bromophenyl)-5-(4-fluoro-phenyl)-2-pyrazoline (AS_1) are presented in the experimental section. Similarly all other 2-prazolines (AS_2-DS_{22}) were characterized on the basis of their physical and spectral data.

For compounds BS_6-BS_{13} there is no much difference in ^1H NMR and FTIR spectral data from that of AS_1, except that in ^1H NMR spectra of B-series compounds, there is no peak due to O–H proton and also in FTIR spectra stretching vibration due to –OH absorption band is absent.

The difference between AS_1 and C-series (CS_{14} – CS_{18}) compounds lies in ^1H NMR and EIMS spectrum. In ^1H NMR spectrum there are downfield shift values due to 2,4-dinitrophenyl protons, which appear between 7.79-8.60 ppm. EIMS spectra of C-series compounds show fragments at [M-30] and [M-46] due to the loss of M-NO and M-NO_2 respectively.

D-series (DS_{19} – DS_{22}) 2-pyrazolines differs from AS_1 in their FTIR spectral data In D-series 2-pyrazolines there is a stretching band due to the carbonyl group and a sharp band due to the N–H group of semicarbazide. Similarly in ^1H NMR spectral analysis, δ values between 5.70-5.87 ppm appear which are characteristic of the $–NH_2$ protons. In

EIMS spectral analysis a fragment ion $[M-44]^+$ is prominent due to loss of $-NH_2-C=O$ moiety.Physical data of synthesized 2-pyrazolines (**AS_1-DS_{22}**) are listed in Table-1.

Table-1 : Structure and physical data of the compounds (AS1-DS23)

Compound #	X	Y	R	Formula	M.P ^{0}C	Yield (%)	R_f	Solvent*
AS_1	Br	F	Ph	$C_{21}H_{11}N_2BrFO$	180-182	83	94	Ethanol
AS_2	Cl	Cl	Ph	$C_{21}H_{11}N_2Cl_2O$	130-132	73	91	"
AS_3	F	Br	Ph	$C_{21}H_{11}N_2FBrO$	190-194	68	90	"
AS_4	Br	Br	Ph	$C_{21}H_{11}N_2Br_2O$	124-128	63	93	"
AS_5	Br	Cl	Ph	$C_{21}H_{11}N_2BrClO$	160-162	69	89	"
BS_6	H	H	Ph	$C_{21}H_{18}N_2$	138-140	84	92	"
BS_7	H	3-F	Ph	$C_{21}H_{17}N_2F$	122-126	63	92	"
BS_8	H	3-NO_2	Ph	$C_{21}H_{17}N_3O_2$	118-120	73	88	"
BS_9	H	4-Cl	Ph	$C_{21}H_{17}N_2Cl$	180-182	78	93	"
BS_{10}	H	4-OCH_3	Ph	$C_{21}H_{20}N_2O$	328-330	81	91	"
BS_{11}	H	2-Cl	Ph	$C_{21}H_{17}N_2Cl$	130-132	73	86	"
BS_{12}	H	4-CH_3	Ph	$C_{22}H_{20}N_2$	128-130	77	84	"
BS_{13}	H	4-$N(CH_3)_2$	Ph	$C_{23}H_{23}N_3$	136-138	59	89	"
CS_{14}	H	H	2,4-DNP	$C_{21}H_{16}N_4O_4$	260-262	79	90	"
CS_{15}	H	4-OCH_3	2,4-DNP	$C_{22}H_{18}N_4O_5$	190-192	69	96	"
CS_{16}	H	4-$N(CH_3)_2$	2,4-DNP	$C_{23}H_{21}N_5O_4$	210-212	68	98	"
CS_{17}	H	3-NO_2	2,4-DNP	$C_{21}H_{15}N_5O_6$	280-282	75	95	"
CS_{18}	H	4-Cl	2,4-DNP	$C_{21}H_{15}N_4O_4Cl$	268-270	79	92	"
DS_{19}	H	H	H_2N-CO	$C_{16}H_{15}N_3O$	168-170	77	85	"
DS_{20}	H	4-OCH_3	H_2N-CO	$C_{17}H_{17}N_3O$	210-212	86	97	"
DS_{21}	H	4-Cl	H_2N-CO	$C_{16}H_{14}N_3ClO$	220-222	89	96	"
DS_{22}	H	3-NO_2	H_2N-CO	$C_{16}H_{14}N_4O_3$	132-134	90	94	"

*** = Recrystallization solvent**

Antibacterial Activity Analysis

Synthesized compound were tested for their antibacterial activity by adopting agar well diffusion method [21] Bacteria cultures used were *Escherichia coli, Bacillus subtillus, Pseudomona pickitii,* Enterobacter *aerogenes* and *Micrococcus luteus* Roxithromycin was used as standard drug. Using micropipette, 100 µl of test solution was poured in respective well. Different concentrations of test samples, a solution for positive control (Roxithromycin) and one for negative control (DMSO) was applied to each Petri plate. These plates were incubated at 37°C. After 24 hours and 48 hours of incubation the diameter of the clear zones, showing no bacterial growth, around each well was measured. Triplicate plates were prepared for each sample compound. Mean clear zone of these plates was calculated in mm with standard deviation.

Antifungal Activity Analysis

Synthesized compound were tested for their antibacterial activity by adopting agar tube dilution method [22]. Fungal cultures used were *Trichphyton longifusus, Candida albicans, Aspergillus flavus, Microsporum canis, Fusarium solani and Candida glabrata.* Amphotericin B for *Aspergillus flavus* and Miconazole for rest of fungal species were used as standard drugs. Tubes are allowed to cool to 50c and non solidified sabourtaud agar media were poisoned with 66.6 ml of compound pipetted from the stock solution. This will give the final of concentration of 400 µg /ml and 200 µg /ml of the sample and pure compound respectively in media. Tubes were then allowed to solidify in stated position at room temperature. Each tube is inoculated with a 4mm diameter piece of inoculums removed from a seven day old culture of fungi. For non-mycelia growth an agar surface streak is employed. Other media supplemented with, DMSO and reference antifungal drug serving as negative and positive control respectively. The tubes incubated at 27 – 29 c for 7 – 10 days. Growth in compound amended media is determined by measuring linear growth (mm) and growth inhibition calculated with reference of negative control.

Percentage inhibition of fungal growth = 100- (linear growth in test (mm)/ Linear growth in control (mm)) ×100

Structure Activity Relationship

It is observed that among different pyrazolines the presence of various substituents and their positions are very important from biological activity point of view. It was observed that almost all pyrazolines show significant antibacterial activity. Pyrazolines **CS_{16}, CS_{17} & CS_{19}** were found to be significantly active against *Micrococcus luteus* and *Enterobacter aerogenes* bacterial strains **(Table-2)**.

Table-2 : Antibacterial activity of pyrazolines (AS1-DS23) against five strains.

Compound	Zone of Inhibition (mm)					Remarks/ Activity
	E.coli	*B. subtillus*	*P. pickitii*	*M.luteus*	*E. aerogenes*	
ROX	25	22	33	22.5	20	Significant
AS_1	-	-	12	-	-	-
AS_2	-	-	-	-	-	-
AS_3	-	-	10	-	-	-
AS_4	-	-	-	12.5	13.5	-
AS_5	-	-	-	-	-	-
BS_6	-	-	11.5	-	-	-
BS_7	-	-	12	-	-	-
BS_8	-	13	12	13.5	-	-
BS_9	10.35	-	-	-	-	-
BS_{10}	-	-	-	-	-	-
BS_{11}	-	-	11	-	11.75	-
BS_{12}	-	-	-	-	-	-
BS_{13}	-	-	-	-	-	-
CS_{14}	-	-	12	-	-	-
CS_{15}	10.5	10	12.5	13.5	11.5	-
CS_{16}	13	11	16.25	14.5	12.5	-
CS_{17}	-	-	11.5	-	11	-
CS_{18}	-	11	11.5	12.5	11.5	-
DS_{19}	-	-	11	-	11.25	-
DS_{20}	-	-	-	-	-	-
DS_{21}	-	-	11.5	-	-	-
DS_{22}	-	-	-	-	-	-

However, the same pyrazolines exhibited significant antibacterial activity against *Escherichia coli, Bacillus subtillus* and *Pseudomonas pickitti* as compared to standard drug Roxithromycin. All of other pyrazolines showed mild activity only against *Pseudomonas pickitti.* The antibacterial exhibited by 2-pyrazolines **CS_{16}, CS_{17}** and **CS_{19}** is probably due to the presence of the nitro groups of the 2,4-dinitrophenylhydrazine as well as the presence of a substituents at position 4 of the phenyl ring attached at position 5 of the 2-pyrazoline.However, significant antifungal activity was recorded against two fungal strains i.e. *T.longifusus* and *M.canis* **(Table-3)**

Table-3 : Antifungal activity of pyrazolines (2f-o) against six fungal strains.

Compound	% Inhibition						Remarks/ Activity
	T.longifusus	*C.albicans*	*A.flavus*	*M.canis*	*F.solani*	*C.glabrata*	
AS_1	85	0	75	80	50	0	**Significant**
AS_3	20	0	90	60	50	0	"
BS_6	90	0	70	20	85	0	"
BS_7	85	0	0	80	75	0	"
BS_9	70	0	50	85	0	0	"
CS_{14}	80	0	20	60	0	0	"
DS_{19}	85	0	0	80	70	0	"

*** % inhibition of standard drug (Miconazole) is 100%**

In addition, pyrazolines (**AS_1, AS_3** and **BS_6**) were found significantly active against *A.flavus.* Similarly pyrazolines (**BS_6, BS_7** and **DS_{19}**) showed considerable activity against *F.solani.* On the other hand, all pyrazolines did not show

any activity against *C.albicans* and *C.glabrata* fungal strains. In view of structure activity relationship, it can be said that all pyrazolines with any substitution pattern will always show significant antifungal activity against *T.longifusus* and *M.canis*. Against *A.flavus* 1,3,5 triphenyl pyrazoline (**BS_6**) shows moderate activity. When hydrogen atom at position x, y and z are replaced by Br, F and OH (**AS_1**) respectively, no significant change in antifungal activity occurs. But, when the positions of Br and F are altered (AS_3) the activity enhances substantially. Against *F.solani* pyrazoline **BS_6** showed slightly more activity than against *A.flavus*.

Conclusions

Synthesis of 2-pyrazolines was carried out with the substitutions of various halogens, hydrazines, hydrazides and semicarbazides at various positions. The ten synthesized pyrazolines were checked for their antibacterial and antifungal activities. It is concluded from the results that 2-pyrazolines are significantly active against all fungal strains accept *C.albican* and *C.glabrata*. In contrast to this Pyrazolines CS_{16}, CS_{17} & CS_{19} were found to be significantly active against *Micrococcus luteus* and *Enterobacter aerogenes* bacterial strains. However, the same pyrazolines exhibited significant antibacterial activity against *Escherichia coli, Bacillus subtillus* and *Pseudomonas pickitti* as compared to standard drug Roxithromycin. All of other pyrazolines showed mild activity only against *Pseudomonas pickitti*. The antibacterial exhibited by 2-pyrazolines **CS_{16}**, **CS_{17}** and **CS_{19}** is probably due to the presence of the nitro groups of the 2,4-dinitrophenylhydrazine as well as the presence of a substituents at position 4 of the phenyl ring attached at position 5 of the 2-pyrazoline.

Experimental Protocol

All melting points were determined in open capillaries using Gallenkemp melting point apparatus and are uncorrected. All chemicals were supplied by Sigma-Aldarich (Germany). R_f values were calculated by using precoated silica gel aluminum backed thin layer chromatographic (TLC) plates Kieselgel 60 F_{254} Merck (Germany), in ethyl acetate: pet-ether (1:9). FTIR spectra were recorded on Bio-Rad Merlin using KBr discs. ^{1}H NMR spectra were recorded on GEQE 3400, 400 MHz Spectrometer (Oxford Magnet) using TMS as internal standard. EIMS were recorded on VG: 70 SE Mass Spectrometer. Purity of each compound was monitored by TLC. Chemical analyses were carried out on Leco CHNS-932 instrument.

Synthesis of 1, 3 diphenyl-2-propen-1-ones (S_1-S_{13})

1, 3-Diphenyl-2-propen-1-one (chalcone) derivatives were synthesized by condensing acetophenone (0.01mol) with appropriate benzaldehyde derivatives (0.01mol) according to claisen Schmidt condensation [23-25].

General procedure for the Synthesis of 2-pyrazolines (AS_1-DS_{22})

Phenyl hydrazine and /or hydrazide (0.013 mol) 1.33 ml was added to 1-(5-X-2'-hydroxyphenyl)-3-(4-halo)-2-propene-1-one (S_1) (0.01 mol) 3.21g in acetic acid (15 ml) and the mixture was refluxed under constant stirring for 3 hours at 100-110°C until the cyclization is completed and a deep orange colour developed. The reaction mixture was diluted with ice-cold water. The new thing in this method is the use of extraction step which has been done in ethyl acetate. Removal of the solvent under reduced pressure afforded the product which was purified by crystallization from ethanol. Spectroscopic data of the compounds (**AS_1-DS_{22}**) are given below.

1-Phenyl-3-(2-hydroxy-5-bromo-phenyl)-5-(4-flouro-phenyl)-2-pyrazolines (**AS_1**) IR (KBr) (υ_{max}/cm^1): 1584 (C=N), 3028 (CH_2), 1285 (C-N), 1493 (C=C Ar.), 3493 (OH), 630 (C-Br), 1160 (C-F); ^{1}HNMR ($CDCl_3$) δH: 3.20(dd, 1H,*J*=7.40,17.2 Hz, H_A), 3.92(dd,1H,*J* =12.36,17.2 Hz, H_B), 5.25(dd,1H,*J*=7.41,12.2 Hz, H_X), 6.76-7-35 (m,12H, $H_{arom.}$), 10.6 (s,1H,OH); EIMS (m/z, %):410(M^+, 100), 239 (22), 315* (20), 77 (16.5), 91 (43.4);Anal. Calcd for $C_{21}H_{11}N_2BrFO$ (406.24): C, 62.09; H, 2.73; N, 6.90. Found: C, 62.05; H, 2.75; N, 6.93.

1-Phenyl-3-(2-hydroxy-5-chloro-phenyl)-5-(4-chloro-phenyl)-2-pyrazolines (**AS_2**) IR (KBr) (υ_{max}/cm^1): 1590 (C=N), 3010 (CH_2), 1280 (C-N), 1475 (C=C Ar.), 3500 (OH), 730 (C-Cl); ^{1}HNMR ($CDCl_3$) δH: 3.17(dd, 1H,*J*=7.40,17.2 Hz, H_A), 3.87(dd,1H,*J*= 12.30,17.21Hz, H_B), 5.20(dd,1H,*J* =7.40,12.1 Hz, H_X), 6.56-7.71 (m,12H, $H_{arom.}$), 10.6 (s,1H,OH); EIMS (m/z, %): 382* (M^+, 100), 255* (30), 271* (18), 77 (18), 91 (40) :Anal. Calcd for $C_{21}H_{11}N_2Cl_2O$ (378.24): C, 66.69; H, 2.93; N, 7.41. Found: C, 66.66; H, 2.95; N, 7.43.

1-Phenyl-3-(2-hydroxy-5-fluoro-phenyl)-5-(4-bromo-phenyl)-2-pyrazolines (**AS_3**) IR (KBr) (υ_{max}/cm^1): 1580 (C=N), 3015 (CH_2), 1290 (C-N), 1480 (C=C Ar.), 3495 (OH), 1170 (C-F), 640 (C-Br); ^{1}HNMR ($CDCl_3$) δH: 3.21(dd, 1H,*J* =7.39,17.2 Hz, H_A), 3.94(dd,1H,*J* =12.34,17.2 Hz, H_B), 5.27(dd,1H,*J* =7.41,12.2 Hz, H_X), 6.62-7.54

(m,12H, $H_{arom.}$), 10.7 (s,1H,OH); EIMS (m/z, %):410* (100), 299* (40), 255 (20), 77 (19), 91 (35) ;Anal. Calcd for $C_{21}H_{11}N_2FBrO$ (406.24): C, 62.06; H, 2.74; N, 6.91. Found: C, 62.04; H, 2.72; N, 6.94.

1-Phenyl-3-(2-hydroxy-5-bromo-phenyl)-5-(4-bromo-phenyl)-2-pyrazolines (AS_4) IR (KBr) (υ_{max}/cm^{1}) 1583 (C=N), 3019 (CH_2), 1282 (C-N), 1495 (C=C Ar.), 3480 (OH), 650 (C-Br); ^{1}HNMR ($CDCl_3$) δH: 3.18(dd, 1H,*J*=7.41,17.2 Hz, H_A), 3.90(dd,1H,*J*=12.35,17.1 Hz, H_B), 5.23(dd,1H,*J* =7.41,12.2 Hz, H_X), 6.70-7.32 (m,12H, $H_{arom.}$), 10.6 (s,1H,OH); EIMS (m/z, %):470** ((M^+, 100), 299* (38), 315* (22), 77 (22), 91 (40) ;Anal. Calcd for $C_{21}H_{11}N_2Br_2O$ (467.14): C, 54.00; H, 2.37; N, 6.00. Found: C, 54.05; H, 2.35; N, 6.03.

1-Phenyl-3-(2-hydroxy-5-bromo-phenyl)-5-(4-chloro-phenyl)-2-pyrazolines (AS_5) IR (KBr) (υ_{max}/cm^{1}): 1595 (C=N), 3035 (CH_2), 1292 (C-N), 1494 (C=C Ar.), 3520 (OH), 660 (C-Br), 750 (C-Cl); ^{1}HNMR ($CDCl_3$) δH: 3.19(dd, 1H,*J* =7.40, 17.21Hz, H_A), 3.89(dd,1H,*J* =12.36,17.2 Hz, H_B), 5.21(dd,1H,*J* =7.41,12.1 Hz, H_X), 6.69-7.60 (m,12H, $H_{arom.}$), 10.4 (s,1H,OH); EIMS (m/z, %): 426** (M^+, 100), 255* (30), 315* (32), 77 (16), 91 (60) ;Anal. Calcd for $C_{21}H_{11}N_2BrClO$ (422.69): C, 59.67; H, 2.62; N, 6.63. Found: C, 59.65; H, 2.65; N, 6.60.

1, 3, 5-Triphenyl-2-pyrazolines (BS_6) IR (KBr) (υ_{max}/cm^{1}): 1595 (C=N), 2908 (CH_2), 1239 (C-N), 1491 (C=C Ar.); ^{1}HNMR ($CDCl_3$) δH: 3.16(dd, 1H,*J* = 7.24,17.02 Hz, H_A), 3.86(dd, 1H,*J*= 12.3,17.02 Hz, H_B), 5.28(dd, 1H,*J* = 7.24,12.33 Hz, HX), 6.76-7.71 (m, 15H, $H_{arom.}$); EIMS (m/z, %): 298 (M^+, 100), 221 (45.2), 194 (10.6), 91 (42.6), 77 (13.4) ;Anal. Calcd for $C_{21}H_{18}N_2$ (298.39): C, 84.53; H, 6.08; N, 9.39. Found: C, 84.55; H, 6.10; N, 9.36.

1, 3-Diphenyl-5-(3-fluoro-phenyl)-2-pyrazolines (BS_7) IR (KBr) (υ_{max}/cm^{1}): 1570 (C=N), 3010 (CH_2), 1241 (C-N), 1470 (C=C Ar.), 1125 (C-F); ^{1}HNMR ($CDCl_3$) δH: 3.12(dd, 1H,*J* =7.14,17.05 Hz, H_A), 3.85(dd, 1H,*J* =12.32,17.04 Hz, H_B), 5.27(dd, 1H,*J* =7.1,12.2 Hz, HX), 6.77-7.71 (m, 14H, $H_{arom.}$); EIMS (m/z, %): 316 (M^+, 100), 221 (57), 194 (19.7), 91 (83.4), 77 (19.9) ;Anal. Calcd for $C_{21}H_{17}N_2F$ (316.38): C, 79.72; H, 5.42; N, 8.85. Found: C, 79.75; H, 5.45; N, 8.82.

1, 3-Diphenyl-5-(3-nitro-phenyl)-2-pyrazolines (BS_8) IR (KBr) (υ_{max}/cm^{1}): 1580 (C=N), 3025 (CH_2), 1250 (C-N), 1495 (C=C Ar.), 1325 (C-N); ^{1}HNMR ($CDCl_3$) δH: 3.13(dd, 1H,*J* =7.14,17.04 Hz, H_A), 3.89(dd, 1H,*J* =12.3,17.03 Hz, H_B), 5.29(dd, 1H,*J* =7.1,12.2 Hz, HX), 6.79-7.71 (m, 14H, $H_{arom.}$); EIMS (m/z, %): 343 (M^+, 100), 221 (52), 194 (20), 91 (74), 77 (12.2) ;Anal. Calcd for $C_{21}H_{17}N_3O_2$ (343.39): C, 73.45; H, 4.99; N, 12.24. Found: C, 73.42; H, 4.95; N, 12.22.

1, 3-Diphenyl-5-(4-chloro-phenyl)-2-pyrazolines (BS_9) IR (KBr) (υ_{max}/cm^{1}): 1590 (C=N), 3010 (CH_2), 1237 (C-N), 1475 (C=C Ar.), 692 (C-Cl); ^{1}HNMR ($CDCl_3$) δH: 3.11(dd, 1H,*J* =7.3,17.03 Hz, H_A), 3.86(dd, 1H,*J* =12.3,17.02 Hz, H_B), 5.25(dd, 1H,*J* =7.13,12.2 Hz, HX), 6.78-8.03 (m, 14H, $H_{arom.}$); EIMS (m/z, %): 332* (M^+, 100), 221 (27.8), 194 (9.6), 91 (36.3), 77 (11.3) ;Anal. Calcd for $C_{21}H_{17}N_2Cl$ (332.84): C, 75.78; H, 5.15; N, 8.42. Found: C, 75.76; H, 5.13; N, 8.45.

1, 3-Diphenyl-5-(4-methoxy-phenyl)-2-pyrazolines (BS_{10}) IR (KBr) (υ_{max}/cm^{1}): 1595 (C=N), 3020 (CH_2), 1252 (C-N), 1477 (C=C Ar.), 1155 (C-O-C); ^{1}HNMR ($CDCl_3$) δH: 3.13(dd, 1H,*J* =7.20,17.05Hz, H_A), 3.83(dd,1H,*J* =12.37,17.04 Hz, H_B), 5.24(dd,1H,*J* =7.18,12.2 Hz, H_X), 6.75-7.71 (m,14H, $H_{arom.}$), 3.75 (s, 3H, -OCH_3); EIMS (m/z, %): 328 (M^+, 100), 221 (16.6), 194 (13.1), 91 (40.8) ;Anal. Calcd for $C_{21}H_{20}N_2O$ (316.41): C, 79.72; H, 6.37; N, 8.85. Found: C, 79.75; H, 6.35; N, 8.80.

1, 3-Diphenyl-5-(2-chloro-phenyl)-2-pyrazolines (BS_{11}) IR (KBr) (υ_{max}/cm^{1}): 1585 (C=N), 3022 (CH_2), 1247 (C-N), 1480 (C=C Ar.), 690 (C-Cl); ^{1}HNMR ($CDCl_3$) δH: 3.07(dd, 1H,*J* =6.7,17.20 Hz, H_A), 3.99(dd, 1H,*J* =12.4,17.1 Hz, H_B), 5.65(dd, 1H,*J* =6.7,12.3 Hz, HX), 6.79-7.72 (m, 14H, $H_{arom.}$); EIMS (m/z, %): 332* (M^+, 100), 221 (84.7), 194 (18.1), 91 (70.3), 77 (22.3) ;Anal. Calcd for $C_{21}H_{17}N_2Cl$ (332.84): C, 75.77; H, 5.14; N, 8.41. Found: C, 75.79; H, 5.16; N, 8.40.

1, 3-Diphenyl-5-(4-methyl-phenyl)-2-pyrazolines (BS_{12}) IR (KBr) (υ_{max}/cm^{1}): 1595 (C=N), 3035 (CH_2), 1292 (C-N), 1494 (C=C Ar.), 2900(CH_2); ^{1}HNMR ($CDCl_3$) δH: 3.13(dd, 1H,*J* =7.23,17.04 Hz, H_A), 3.84(dd,1H,*J* =12.32,17.01 Hz, H_B), 5.25(dd,1H,*J* =7.22,12.2 Hz,H_X), 6.71-7.71 (m,14H, $H_{arom.}$), 2.30 (s, 3H, -CH_3); EIMS (m/z, %): 312 (M^+, 100), 221 (29), 194 (11.6), 91 (38.1), 77 (21.6) ;Anal. Calcd for $C_{22}H_{20}N_2$ (312.42): C, 84.58; H, 6.45; N, 8.97. Found: C, 84.56; H, 6.44; N, 8.95.

1, 3-Diphenyl-5-(4-N-N dimethyl phenyl)-2-pyrazolines (BS_{13}) IR (KBr) (υ_{max}/cm^{-1}): 1575 (C=N), 3000 (CH_2), 1240 (C-N), 1492 (C=C Ar.), 1300(N-CH_3); ^{1}HNMR ($CDCl_3$) δH: 3.14(dd, 1H,J =7.29,16.9 Hz, H_A), 3.80(dd,1H,J =12.2,17.02 Hz, H_B), 5.20(dd,1H,J =7.28,12.1 Hz,H_X), 6.65-7.71 (m,14H, $H_{arom.}$), 2.90 (s, 6H, N $(CH_3)_2$); EIMS (m/z, %): 341 (M^+,100), 221 (13.8), 194 (12.2), 91 (22.4), 147 (37.3) ;Anal. Calcd for $C_{23}H_{23}N_3$ (341.46): C, 80.90; H, 6.79; N, 12.31. Found: C, 80.95; H, 6.75; N, 12.33.

1-(2, 4-Dinitro phenyl)-3, 5-diphenyl-2-pyrazolines (CS_{14}) IR (KBr) (υ_{max}/cm^{-1}): 1587 (C=N), 3104 (CH_2), 1300 (C-N), 1497 (C=C Ar.); ^{1}HNMR ($CDCl_3$) δH: 3.38(dd, 1H,J =5.06,17.1 Hz, H_A), 3.95(dd,1H,J =12.1,17.6 Hz, H_B), 5.87(dd,1H,J =5.07,11.7 Hz,H_X), 7.22-7.25 (m,10H, $H_{arom.}$), 7.79-8.60 (m,3H, $H_{2\,4\text{-}DNP}$); EIMS (m/z, %): 388 (M^+, 100), 358 (80), 342 (40), 77 (70), 51 (40) ;Anal. Calcd for $C_{21}H_{16}N_4O_4$ (388.39): C, 64.94; H, 4.15; N, 14.43. Found: C, 64.95; H, 4.18; N, 14.46.

1-(2, 4-Dinitro phenyl) 3-phenyl-5-(4-methoxy-phenyl)-2-pyrazolines (CS_{15}) IR (KBr) (υ_{max}/cm^{-1}): 1585 (C=N), 3105 (CH_2), 1299 (C-N), 1496 (C=C Ar.), 1154 (C-O-C); ^{1}HNMR ($CDCl_3$) δH: 3.39(dd, 1H,J =5.06,17.1 Hz, H_A), 3.90(dd,1H,J =12.2,17.6 Hz, H_B), 5.87(dd,1H,J =5.08,11.7 Hz,H_X), 7.27-7.29 (m,9H, $H_{arom.}$), 7.79-8.69 (m, 3H, $H_{2\,4\text{-}DNP}$), 3.70(s,3H,OCH_3); EIMS (m/z, %):418(M^+, 100), 388 (78), 372 (42), 77 (60), 51 (30) ;Anal. Calcd for $C_{22}H_{18}N_4O_5$ (418.41): C, 63.15; H, 4.34; N, 13.39. Found: C, 63.17; H, 4.36; N, 13.36.

1-(2, 4-Dinitro phenyl) 3-phenyl-5-(4-N-N dimethyl-phenyl)-2-pyrazolines (CS_{16}) IR (KBr) (υ_{max}/cm^{-1}): 1570 (C=N), 3010 (CH_2), 1285 (C-N), 1490 (C=C Ar.), 1325 (CH_3); ^{1}HNMR ($CDCl_3$) δH: 3.37(dd, 1H,J =5.06,17.1 Hz, H_A), 3.89(dd,1H,J =12.2,17.6 Hz, H_B), 5.82(dd,1H,J =5.09,11.7 Hz,H_X), 7.79-7.35 (m,9H, $H_{arom.}$), 7.79-8.59 (m, 3H, $H_{2\,4\text{-}DNP}$), 2.91(s,6H,N$(CH_3)_2$); EIMS (m/z, %):431(M^+, 100), 401 (82), 385 (38), 77 (72), 51 (40) ;Anal. Calcd for $C_{23}H_{21}N_5O_4$ (431.45): C, 64.03; H, 4.91; N, 16.23. Found: C, 64.05; H, 4.95; N, 16.25.

1-(2, 4-Dinitro phenyl) 3-phenyl-5-(3-nitro-phenyl)-2-pyrazolines (CS_{17}) IR (KBr) (υ_{max}/cm^{-1}): 1583 (C=N), 3125 (CH_2), 1302 (C-N), 1486 (C=C Ar.); ^{1}HNMR ($CDCl_3$) δH: 3.35(dd, 1H,J =5.06,17.1 Hz, H_A), 3.92(dd,1H,J =12.2,17.6 Hz, H_B), 5.86(dd,1H,J =5.09,11.7 Hz,H_X), 7.27-7.37 (m,9H, $H_{arom.}$), 7.70-8.65(m, 3H, $H_{2\,4\text{-}DNP}$); EIMS (m/z, %):433(M^+, 100), 403 (76), 387 (46), 77 (66), 51 (30) ;Anal. Calcd for $C_{21}H_{15}N_5O_6$ (433.38): C, 58.20; H, 3.49; N, 16.16. Found: C, 58.25; H, 3.45; N, 16.19.

1-(2, 4-Dinitro phenyl) 3-phenyl-5-(4-chloro-phenyl)-2-pyrazolines (CS_{18}) IR (KBr) (υ_{max}/cm^{-1}): 1599 (C=N), 3115 (CH_2), 1310 (C-N), 1500 (C=C Ar.), 690(C-Cl); ^{1}HNMR ($CDCl_3$) δH: 3.35(dd, 1H,J =5.08,17.2 Hz, H_A), 3.92(dd,1H,J =12.1,17.3 Hz, H_B), 5.86(dd,1H,J =5.08,11.6 Hz,H_X), 7.27-7.37 (m,9H, $H_{arom.}$), 7.70-8.65(m, 3H, $H_{2,4\text{-}DNP}$); EIMS (m/z, %): 422.5* (100), 392* (80), 376* (50), 77 (74), 51 (46) ;Anal. Calcd for $C_{21}H_{15}N_4O_4Cl$ (422.33): C, 59.65; H, 3.58; N, 13.25. Found: C, 59.62; H, 3.54; N, 13.22.

1-Carboxamide-3, 5-diphenyl-2-pyrazolines (DS_{19}) IR (KBr) (υ_{max}/cm^{-1}): 1584 (C=N), 3023 (CH_2), 1285 (C-N), 1493 (C=C Ar.), 1686 (C=O), 3493 (N-H); ^{1}HNMR ($CDCl_3$) δH: 3.19(dd, 1H,J =5.30,17.6 Hz, H_A), 3.81(dd,1H,J =12.02,17.5 Hz, H_B), 5.54(dd,1H,J =5.02,11.9 Hz,H_X), 7.22-7.69 (m,10H, $H_{arom.}$), 5.87(br.s,2H,NH_2); EIMS (m/z, %): 265 (M^+, 15.6), 222 (81.9), 144 (100), 118 (39.2), 104 (72.8), 77 (74), 51(33) ;Anal. Calcd for $C_{16}H_{15}N_3O$ (265.32): C, 72.43; H, 5.70; N, 15.84. Found: C, 72.45; H, 5.75; N, 15.80.

1-Carboxamide-3-phenyl-5-(4-methoxy-phenyl)-2-pyrazolines (DS_{20}) IR (KBr) (υ_{max}/cm^{-1}): 1590 (C=N), 3030 (CH_2), 1280 (C-N), 1490 (C=C Ar.), 1690 (C=O), 3455 (N-H), 1136 (C-O-C); ^{1}HNMR ($CDCl_3$) δH: 3.15(dd, 1H,J =5.30,17.6 Hz, H_A), 3.80(dd,1H,J =12.06,17.5 Hz, H_B), 5.52(dd,1H,J =5.08,12.1 Hz,H_X), 718-7.78 (m,9H, $H_{arom.}$), 5.70(br.s,2H,NH_2), 3.90 (s,3H,OCH_3); EIMS (m/z, %): 295 (M^+,20), 251 (70), 144 (100), 118 (42), 104 (70), 77 (60), 51 (32) ;Anal. Calcd for $C_{17}H_{17}N_3O$ (279.34): C, 73.10; H, 6.13; N, 15.04. Found: C, 70.12; H, 6.15; N, 15.06.

1-Carboxamide-3-phenyl-5-(4-chloro-phenyl)-2-pyrazolines (DS_{21}) IR (KBr) (υ_{max}/cm^{-1}): 1587 (C=N), 3035 (CH_2), 1279 (C-N), 1495 (C=C Ar.), 1691(C=O), 3491(N-H),693(C-Cl); ^{1}HNMR ($CDCl_3$) δH: 3.14(dd, 1H,J =5.30,17.6 Hz, H_A), 3.81(dd,1H,J =12.09,17.5 Hz, H_B), 5.50(dd,1H, ,J =5.26,12.04 Hz,H_X), 7.16-7.98 (m,9H, $H_{arom.}$), 5.72 (br.s,2H,NH_2); EIMS (m/z, %): 299* (M^+,16.3), 255* (67), 144 (100), 118 (45), 104 (68), 77 (45), 55 (16) ;Anal. Calcd for $C_{16}H_{14}N_3ClO$ (299.76): C, 64.11; H, 4.71; N, 14.02. Found: C, 64.15; H, 4.75; N, 14.03.

1-Carboxamide-3-phenyl-5-(3-nitro-phenyl)-2-pyrazolines (DS_{22}) IR (KBr) (υ_{max}/cm^{-1}): 1592 (C=N), 3021 (CH_2), 1282 (C-N), 1489 (C=C Ar.), 1689 (C=O), 3470 (N-H); ^{1}HNMR ($CDCl_3$) δH: 3.17(dd, 1H,J =8,4 Hz, H_A), 3.79(dd,1H,J =12,12 Hz, H_B), 5.51(dd,1H,J =8,8 Hz,H_X), 7.21-7.90 (m,9H, $H_{arom.}$), 5.77 (br.s,2H,NH_2); EIMS (m/z,

%):310 (M^+, 20.2), 266 (72), 144 (100), 118 (46), 104 (74), 77 (46), 55 (18) ;Anal. Calcd for $C_{16}H_{14}N_4O_3$ (310.31): C, 61.93; H, 4.55; N, 18.05. Found: C, 61.95; H, 4.53; N, 18.06.

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Received on February 18, 2997.