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Synthesis and Antimicrobial Activity of Some 3,5-diaryl-1-(ρ-sulfamylphenyl)-2-pyrazolines

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ABSTRACT
A series of 3,5-diaryl-1-(ρ-sulfamylphenyl)-2-pyrazolines derivatives were synthesized by refluxing from various substituted chalcones and 4-hydrazinobenzene sulfonamide hydrochloride in two steps. Compounds were confirmed by physical and spectral data by modern analytical techniques and were evaluated for anti-inflammatory activity. Few Compounds showed moderate activity as compared to standard drug.

Keywords: Pyrazolines, Chalcones, Antimicrobial, Synthesis, Antibacterial, Antifungal

INTRODUCTION

Despite the rapid progress of science, the treatment of infectious diseases still remains a serious problem of concern to the scientific community, mainly because of the wide range of factors leading to the emergence of these diseases and also the increased number of pathogenic microorganisms with resistance to multiple drugs, including the Gram positive bacteria. [1] The rapid emergence of multidrug resistant pathogenic bacteria has become a serious health threat worldwide. It has been postulated that the development of resistance to known antibiotics could be overcome by identifying new drug targets *via* genomics, improving existing antibiotics and by identifying new antibacterial agents with novel structure and mode of action.[2] Since in the last two decades the incidence of invasive fungal infections has risen sharply, it has become imperative to enlarge the number of antifungal drugs with more potent activity and less toxicity.[3-4] Pyrazolines and their derivatives have been found to possess a broad spectrum of biological activities such as antibacterial[5-6], antidepressant [7], anticonvulsant [8-9], antihypertensive [10], antioxidant[11], antitumor [12] and

anticancer activities [13-14]. Recently these classes of compounds are reported to possess potential antiviral activity against flavivirus [15] and HIV [16]. Therefore, a study was initiated to explore the activity of this class of compound. The present work reports the synthesis of new 3,5-diaryl-1-(ρ-sulfamylphenyl)-2-pyrazolines and their *in vitro* antibacterial and antifungal screening as a part of our program aimed at the development of new heterocyclic compounds with potential biological activities.

MATERIALS AND METHODS

Material

Melting points were determined by open capillary apparatus and were uncorrected. IR spectra were recorded on a FT-IR Shimadzu DZU 8400S spectrophotometer in KBr disks. Elemental analysis were done on a Perkin-Elmer 2400C, H, N analyzer and values were found to be within the acceptable limits of the calculated values.

The ^{1}H-NMR spectra of the synthesized compounds in $CDCl_3$/DMSO were recorded at 400 MHz by Bruker Advance II 400 NMR spectrometer. Chemical shift values are given in (ppm) scale using tetramethylsilane (TMS) as an internal standard. The FAB mass spectra (at room temperature) were recorded on TOF MS ES^+ mass spectrometer. The melting point of the synthesized compounds were determined using an open capillary and are uncorrected. Progress of reaction and purity of synthesized compounds was ascertained by thin layer chromatography (TLC) using Silica gel G and Iodine vapors as detecting agent.

Methods

The synthesis of all the compounds **4a-p** was performed in a manner as outlined in Fig.1 and Table 1.

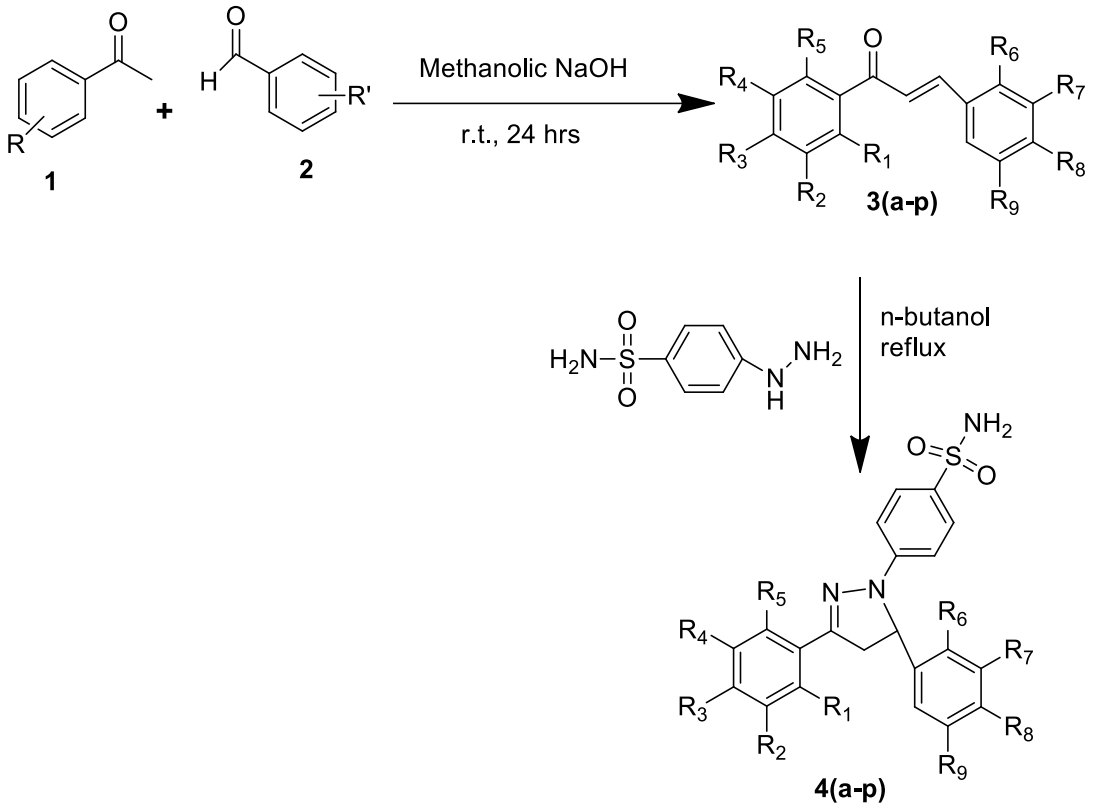

Fig 1. Scheme for the synthesis of 1, 3, 5-trisubstituted pyrazolines 4 (a-p).

Table 1: Different substitutions on synthesized 1, 3, 5-trisubstituted pyrazolines 4 (a-p)

S.No	Comp. No.		R_1	R_2	R_3	R_4	R_5	R_6	R_7	R_8	R_9
1	**3a**	**4a**	OH	-	OH	-	-	Cl	-	-	Cl
2	**3b**	**4b**	OH	-	OH	-	-	OCH_3	-	-	Cl
3	**3c**	**4c**	OH	-	OH	-	-	-	OH	-	-
4	**3d**	**4d**	OH	-	OH	-	-	-	OCH_3	OCH_3	-
5	**3e**	**4e**	Cl	-	Cl	-	-	Cl	-	-	Cl
6	**3f**	**4f**	Cl	-	Cl	-	-	OCH_3	-	-	Cl
7	**3g**	**4g**	Cl	-	Cl	-	-	-	OH	-	-
8	**3h**	**4h**	Cl	-	Cl	-	-	-	OCH_3	OCH_3	-
9	**3i**	**4i**	OCH_3	-	-	Cl	-	Cl	-	-	Cl
10	**3j**	**4j**	OCH_3	-	-	Cl	-	OCH_3	-	-	Cl
11	**3k**	**4k**	OCH_3	-	-	Cl	-	-	OH	-	-
12	**3l**	**4l**	OCH_3	-	-	Cl	-	-	OCH_3	OCH_3	-
13	**3m**	**4m**	-	Cl	OCH_3		OH	Cl	-	-	Cl
14	**3n**	**4n**	-	Cl	OCH_3	-	OH	OCH_3	-	-	Cl
15	**3o**	**4o**	-	Cl	OCH_3	-	OH	-	OH	-	-
16	**3p**	**4p**	-	Cl	OCH_3	-	OH	-	OCH_3	OCH_3	-

General procedure for the synthesis of chalcones (3a-p)

To a solution of substituted acetophenone (16 mmole) in 10 mL of methanol on an ice bath, freshly prepared 2 N methanolic NaOH solution (60 mL) was added and stirred for 10 min. To this, appropriate aldehyde (16 mmole) was added and stirred at room temperature for 12-24 hr. The reaction

mixture was cooled on an ice bath, neutralized with diluted HCl and the precipitate was washed three times with 50 mL distilled water to give the crude product.[17] The product was recrystallized from methanol or ethanol/ water. The purity of the product was checked by TLC using ethylacetate and hexane (4:6) as mobile phase and iodine vapors as detecting agent.

3-(2',5'-dichlorophenyl)-1-(2,4-dihydroxyphenyl)prop-2-en-1-one (3a)

Synthesized by above method from 2,4-dihydroxyacetophenone (16 mmol) and 2,5-dichlorobenzaldehyde (16 mmol); Yield 85%, White solid; mp 165–167°C; R_f (EtOAc/Hex 4:6) 0.45; IR (KBr) ν_{max}/cm^{-1} 3440 (O-H), 1669 (C=O), 1597 (Ar C=C), 750 (C–Cl), 3063, 2931, 1625, 1415, 1325, 1296, 1134, 1153, 1046, 982, 759, 737 (Ar) ; ^{1}H-NMR ($CDCl_3$, 400 MHz), δ (ppm) 11.62 (2H, s, OH-2,4), 7.76 (1H, d, *J* 16, H-b), 7.69 (2H, dd, *J* 6.8 and 4.5, H-6, 6'), 7.34 (1H, d, *J* 16.0, H-a), 7.21 (4H, m, *J* 4.8, H-3, 5, 3', 4'); FAB-MS *m/z* 308.14 $[M+H]^+$; Anal. Calcd for $C_{15}H_{10}Cl_2O_3$: C, 58.28; H, 3.26. Found: C, 58.98; H, 3.12

3-(5'-chloro-2'-methoxyphenyl)-1-(2,4-hydroxyphenyl)prop-2-en-1-one (3b)

Synthesized by above method from 4-Hydoxyacetophenone (16 mmol) and 2-methoxy,5-chlorobenzaldehyde (16 mmol); Yield 70%, yellow crystalline solid; mp 112–114°C; R_f (EtOAc/Hex 4:6) 0.47; IR (KBr) ν_{max}/cm^{-1} 3441 (O-H), 1645 (C=O), 1595 (Ar C=C), 760 (C–Cl), 3060, 2965, 1645, 1434, 1323, 1296, 982, 759 (Ar); ^{1}H-NMR ($CDCl_3$, 400 MHz), δ (ppm) 10.60 (2H, s, OH-2,4), 7.76 (1H, d, *J* 15.6, H-b), 7.69-7.60 (4H, m, H-3, 5, 6, 6'), 7.34 (1H, d, *J* 16.0, H-a), 6.81 (2H, dd, *J* 5.2, H-3', 4'), 3.81 (3H, s, OCH_3-2'); FAB-MS *m/z* 304.06 $[M+H]^+$; Anal. Calcd for $C_{16}H_{13}ClO_4$: C, 63.06; H, 4.30; Found: C, 63.41; H, 4.58.

3-(3'-hydroxyphenyl)-1-(2,4-hydroxyphenyl)prop-2-en-1-one (3c)

Synthesized by above method from 4-Hydroxyacetophenone (16 mmol) and 4-hydroxybenzaldehyde (16 mmol); Yield 65%, Yellow solid; mp 124–126°C; R_f (EtOAc/Hex 4:6) 0.36; IR (KBr) ν_{max}/cm^{-1} 3440 (O-H), 1661 (C=O), 1592 (Ar C=C), 750 (C–Cl), 3068, 2931, 1621, 1435, 1312, 1213, 1115, 1153, 1046, 982, 751(Ar); ^{1}H-NMR ($CDCl_3$, 400 MHz), δ (ppm) 9.95 (3H, s, OH-2,4, 3'), 7.71 (1H, d, *J* 15.3, H-b), 7.61-7.54 (4H, m, H-3, 5, 6, 6'), 7.31 (1H, d, *J* 16.0, H-a), 7.21-7.15 (4H, m, *J* 4.8, H-2, 2', 4', 5') FAB-MS *m/z* 256.08 $[M+H]^+$; Anal. Calcd for $C_{15}H_{12}O_4$: C, 70.31; H, 4.72; Found: C, 70.37; H, 4.12;

3-(3', 4'-dimethoxyphenyl)-1-(4-hydroxyphenyl)prop-2-en-1-one (3d)

Synthesized by above method from 4-Hydroxyacetophenone (16 mmol) and 4-hydroxybenzaldehyde (16 mmol); Yield 76%, White solid; mp 108–110°C; R_f (EtOAc/Hex 4:6) 0.34; IR (KBr) ν_{max}/cm^{-1} 3435 (O-H), 1661 (C=O), 1592 (Ar C=C), 760 (C–Cl), 3068, 2931, 1621, 1435, 1312, 1213, 1115, 1153, 1046, 982,

751(Ar); ^{1}H-NMR ($CDCl_3$, 400 MHz), δ (ppm) 11.55 (1H, s, OH-4, 2), 7.73 (1H, d, *J* 15.3, H-b), 7.66-7.55 (4H, m, H-3, 5, 6, 6'), 7.35 (1H, d, *J* 16.0, H-a), 7.25-7.21 (3H, m, *J* 4.4, H-2, 2', 5'), 3.74 (6H, s, OCH_3-3', 4'); FAB-MS *m/z* 300.08 $[M+H]^+$; Anal. Calcd for $C_{17}H_{16}O_5$: C, 67.99; H, 5.37; Found: C, 67.28; H, 5.70;

3-(2', 5'-dichlorophenyl)-1-(2, 5-dichlorophenyl)prop-2-en-1-one (3e)

Synthesized by above method from 2,5-dichloroacetophenone (16 mmol) and 2,5-dichlorobenzaldehyde (16 mmol); Yield 69%, White crystalline solid; mp 138–140°C; R_f (EtOAc/Hex 4:6) 0.38; IR (KBr) ν_{max}/cm^{-1} 1662 (C=O), 1598 (Ar C=C), 743 (C–Cl), 3064, 2930, 1627, 1415, 1325, 1296, 1134, 1117, 1047, 982, 819, 759, 737 (Ar); ^{1}H-NMR ($CDCl_3$, 400 MHz), δ (ppm) 7.76 (1H, d, *J* 15.7, H-b), 7.69 (2H, dd, *J* 6.8 and 4.5, H-6, 6'), 7.34 (1H, d, *J* 16.0, H-a), 7.21-7.15 (4H, m, *J* 4.8, H-3, 4, 3', 4') FAB-MS *m/z*: 345.93 $[M+H]^+$; Anal. Calcd for $C_{15}H_8Cl_4O$: C, 52.06; H, 2.33. Found: C, 52.59; H, 2.29.

3-(5'-chloro-2'-methoxyphenyl)-1-(2,5-dichlorophenyl)prop-2-en-1-one (3f)

Synthesized by above method from 2,5-dichloroacetophenone (16 mmol) and 5-chloro, 2-methoxybenzaldehyde (16 mmol); Yield 67%, Creamy-coloured fine needles; mp 148–150°C; R_f (EtOAc/Hex 4:6) 0.79; IR (KBr) ν_{max}/cm^{-1} 1662, 1216 (C=O), 1594 (C=C), 1261, 1026 (C–O), 742 (C–Cl), 3061, 1591, 1457, 1384, 1296, 1194, 980, 854, 756 (Ar); ^{1}H-NMR ($CDCl_3$, 400 MHz), δ (ppm) 7.74 (1H, d, *J* 15.7, H-b), 7.65 (1H, d, *J* 6.8, H-6), 7.34 (1H, d, *J* 15.9, H-a), 7.26-7.30 (4H, m, H-3, 4, 4', 6'), 6.81 (1H, d, *J* 5.2, H-3'), 3.89 (3H, s, OCH_3-2'); FAB-MS *m/z*: 341.27 $[M+H]^+$; Anal. Calcd for $C_{16}H_{11}Cl_3O_2$: C 56.25, H 3.25 Found C 56.23, H 3.92.

1-(2,5-dichlorophenyl)-3-(3'-hydroxyphenyl)prop-2-en-1-one (3g)

Synthesized by above method from 2,5-dichloroacetophenone (16 mmol) and 3-hydroxybenzaldehyde (16 mmol); Yield 60%, White amorphous solid; mp 141–144°C; R_f (EtOAc/Hex 4:6) 0.42; IR (KBr) ν_{max}/cm^{-1} 3441 (O-H), 1663 (C=O), 1589 (Ar C=C), 745 (C–Cl), 3060, 2945, 1620, 1320, 1298, 1139, 1153, 1046, 982, 759, 737 (Ar); ^{1}H-NMR ($CDCl_3$, 400 MHz), δ (ppm) 11.62 (1H, s, OH-3'), 7.70 (1H, d, *J* 15.7, H-b), 7.61 (2H, dd, *J* 6.5 and 4.4, H-6, 6'), 7.32 (1H, d, *J* 16.0, H-a), 7.21-7.11 (4H, m, H-3, 4, 2', 4', 5'); FAB-MS *m/z* 292.01 $[M+H]^+$; Anal. Calcd for $C_{15}H_{10}Cl_2O_2$: C, 61.46; H, 3.44. Found: C C, 61.98; H, 3.12

1-(2,5-dichlorophenyl)-3-(3',4'-dimethoxyphenyl)prop-2-en-1-one (3h)

Synthesized by above method from 2,5-dichloroacetophenone (16 mmol) and 3, 4-dimethoxybenzaldehyde (16 mmol); Yield 69%, white amorphous solid; mp 115-118°C; R_f (EtOAc/Hex 4:6) 0.67; IR (KBr) ν_{max}/cm^{-}

[1] 1653 (C=O), 1605 (Ar C=C), 1547 (COC=C), 1261, 1025 (C-O), 1150 (C-Cl), 3051 (Ar C-H), 2932, 2841 (C-H), 1524, 1472, 1147, 969 (Ar); ^{1}H-NMR ($CDCl_3$, 400 MHz), δ (ppm) 7.81 (1H, d, *J* 15.5, H-b), 7.75 (1H, d, *J* 8.5, H-6), 7.61 (1H, d, *J* 15.1, H-a), 7.40 (1H, d, *J* 6.8, H-4), 7.15 (1H, dd, *J* 2.3 and 8.5, H-6, 6'), 7.01 (1H, d, *J* 2.3, H-2'), 6.98 (1H, d, *J* 5.1 H-3), 6.84 (1H, d, *J* 8.1, H-5'), 3.82 (6H, s, OCH_3-3', 4'). FAB-MS *m/z* 322.02 $[M+H]^+$; Anal. Calcd for $C_{16}H_{12}Cl_2O_3$: C, 59.46; H, 3.74;. Found: C, 59.23; H, 3.42;

1-(5-chloro-2-methoxyphenyl)-3-(2',5'-dichlorophenyl)prop-2-en-1-one (3i)

Synthesized by above method from 2- methoxy, 5-chloro-acetophenone (16 mmol) and 2, 5-dichlorobenzaldehyde (16 mmol); Yield 66%, Yellow solid; mp 105-107°C; R_f (EtOAc/Hex 4:6) 0.32; IR (KBr) ν_{max} /cm^{-1} 1650 (C=O), 1585 (Ar C=C), 1517 (COC=C), 1268, 1029 (C-O), 1150 (C-Cl), 3058 (Ar C-H), 2933 (C-H), 1619, 1512, 969, 810, (Ar); ^{1}H-NMR ($CDCl_3$, 400 MHz), δ (ppm) 7.81 (1H, d, *J* 15.7, H-b), 7.71 (1H, d, *J* 8.3, H-6), 7.60 (1H, d, *J* 15.4, H-a), 7.56 (1H, d, *J* 6.4, H-4), 7.40 (1H, d, *J* 5.9, H-3), 7.10 (1H, dd, *J* 2.6 and 8.4, H-6'), 7.06 (1H, d, *J* 1.9, H-3'), 6.90 (1H, d, *J* 8.8, H-4'), 3.76 (3H, s, OCH_3-2). FAB-MS *m/z* 339.38 $[M+H]^+$; Anal. Calcd for $C_{16}H_{11}Cl_3O_2$: C, 56.25; H, 3.25; Found: C, 56.68; H, 3.39

1-(5-chloro-2-methoxyphenyl)-3-(5'-chloro-2'-methoxyphenyl)prop-2-en-1-one (3j)

Synthesized by above mentioned method A from 2- methoxy, 5-chloroacetophenone (16 mmol) and 2-methoxy, 5-chlorobenzaldehyde (16 mmol); Yield 3.7 g, 69%, Yellow solid; mp 107-109°C; R_f (EtOAc/Hex 4:6) 0.35; IR (KBr) ν_{max} /cm^{-1} 1655 (C=O), 1580 (Ar C=C), 1519 (COC=C), 1264, 1025 (C-O), 1157 (C-Cl), 3052 (Ar C-H), 2930 (C-H), 1611, 1517, 960, 815, (Ar); ^{1}H-NMR ($CDCl_3$, 400 MHz), δ (ppm) 7.86 (1H, d, *J* 15.7, H-b), 7.74 (1H, d, *J* 8.3, H-6), 7.61 (1H, d, *J* 15.4, H-a), 7.54 (1H, d, *J* 6.4, H-4), 7.46 (1H, d, *J* 5.9, H-3), 7.10 (1H, dd, *J* 2.6 and 8.4, H-6'), 7.04 (1H, d, *J* 1.9, H-3'), 6.92 (1H, d, *J* 8.8, H-4'), 3.80 (3H, s, OCH_3-2), 3.85 (3H, s, OCH_3-2'), FAB-MS *m/z* 339.38 $[M+H]^+$; Anal. Calcd for $C_{17}H_{14}Cl_2O_3$: C, 60.55; H, 4.18; Found: C, 60.29; H, 4.57

1-(5-chloro-2-methoxyphenyl)-3-(3'-hydroxyphenyl)prop-2-en-1-one (3k)

Synthesized by above method from 2-methoxy,5-chloroacetophenone (16 mmol) and 3-hydroxybenzaldehyde (16 mmol); Yield 69%, yellow cryastalline solid; mp 135–137°C; R_f (EtOAc/Hex 4:6) 0.34; IR (KBr) ν_{max}/cm^{-1} 3445 (O-H), 1665 (C=O), 1568 (Ar C=C), 748 (C–Cl), 3063, 2941, 1625, 1291, 1134, 1150, 980, 754 (Ar); ^{1}H-NMR ($CDCl_3$, 400 MHz), δ (ppm) 11.54 (1H, s, OH-2'), 7.71 (1H, d, *J* 15.7, H-b), 7.65 (2H, dd, *J* 6.5 and 4.4, H-6, 6'), 7.30 (1H, d, *J* 16.0, H-a), 7.24-7.15 (4H, m, H-3, 4, 2', 4'), 6.94 (1H, d, *J* 8.0, H-5'); 3.70 (3H, s, OCH_3-2) FAB-MS *m/z* 288.06 $[M+H]^+$; Anal. Calcd for $C_{16}H_{13}ClO_3$: C, 66.56; H, 4.54. Found: C, 66.39; H, 4.40

1-(5-chloro-2-methoxyphenyl)-3-(3',4'-dimethoxyphenyl)prop-2-en-1-one (3l)

Synthesized by above method from 2-methoxy, 5-chloroacetophenone (16 mmol) and 3,4-dimethoxybenzaldehyde (16 mmol); Yield 71%, Pale yellow solid; mp 117-119°C; R_f (EtOAc/Hex 4:6) 0.49; IR (KBr) ν_{max} /cm^{-1} 1645 (C=O), 1589 (Ar C=C), 1512 (COC=C), 1265, 1025 (C-O), 1151 (C-Cl), 3064 (Ar C-H), 2941 (C-H), 1611, 1518, 967, 811 (Ar); ^{1}H-NMR ($CDCl_3$, 400 MHz), δ (ppm) 7.84 (1H, d, *J* 15.9, H-b), 7.58 (1H, d, *J* 15.6, H-a), 7.54 (1H, d, *J* 6.4, H-4), 7.48 (1H, d, *J* 5.4, H-3), 7.10 (2H, dd, *J* 2.6 and 8.4, H-6,6'), 7.22 (1H, d, *J* 4.3, H-2'), 6.91 (1H, d, *J* 8.1, H-5') 3.79 (3H, s, OCH_3-2), 3.71 (6H, s, OCH_3-3',4').. FAB-MS *m/z* 332.08 [M +H]$^+$; Anal. Calcd for $C_{18}H_{17}ClO_4$: C, 64.97; H, 5.15. Found: C, 64.36; H, 5.45

1-(5-chloro-2-hydroxy-4-methylphenyl)-3-(2',5'-dichlorophenyl)prop-2-en-1-one (3m)

Synthesized by above method from 3-chloro, 6-hydoxy, 4-methylacetophenone (16 mmol) and 2,5-dichlorobenzaldehyde (16 mmol); Yield 71%, White amorphous solid; mp 94–97°C; R_f (EtOAc/Hex 4:6) 0.67; IR (KBr) ν_{max}/cm^{-1} 3447 (O-H), 1660 (C=O), 1596 (Ar C=C), 740 (C–Cl), 3064, 2965, 1647, 1434, 1320, 980, 759 (Ar, CH_3); ^{1}H-NMR ($CDCl_3$, 400 MHz), δ (ppm) 11.57 (1H, s, OH-2), 7.75 (1H, d, *J* 15.5, H-b), 7.68 (2H, dd, *J* 6.8, 7.8 , H-6, 6'), 7.34 (1H, d, *J* 16.0, H-a), 7.62-7.53 (2H, m, H-4', 2), 7.41-7.23 (2H, m, H-3',6'), 6.71 (1H, d, *J* 8.1, H-5), 2.31 (3H, s, CH_3-4); FAB-MS *m/z* 339.98 [M +H]$^+$; Anal. Calcd for $C_{16}H_{11}Cl_3O_2$: C, 56.25; H, 3.25; Found: C, 56.54; H, 3.65.

1-(5-chloro-2-hydroxy-4-methylphenyl)-3-(5'-chloro-2'-methoxyphenyl)prop-2-en-1-one (3n)

Synthesized by above method from 3-chloro, 6-hydoxy, 4-methylacetophenone (16 mmol) and 2-methoxy, 5-dichlorobenzaldehyde (16 mmol); Yield 68%, White solid; mp 137–139°C; R_f (EtOAc/Hex 4:6) 0.48; IR (KBr) ν_{max}/cm^{-1} 3431 (O-H), 1657 (C=O), 1586 (Ar C=C), 760 (C–Cl), 3064, 2964, 1643, 1434, 985, 753 (Ar); ^{1}H-NMR ($CDCl_3$, 400 MHz), δ (ppm) 10.35 (1H, s, OH), 7.70 (1H, d, *J* 15.2, H-b), 7.69 (2H, dd, *J* 6.8, 7.8 , H-6', 2), 7.32 (1H, d, *J* 16.0, H-a), 7.24 (1H, d, *J* 4.2, H-5), 6.82 (2H, dd, *J* 5.3,7.1 H-3', 4'), 2.84 (3H, s, OCH_3-2'), 2.34 (3H, s, CH_3-4); FAB-MS *m/z* 336.03 [M +H]$^+$; Anal. Calcd for $C_{17}H_{14}Cl_2O_3$: 60.55; H, 4.18;; Found: C, 60.67; H, 4.38.

1-(5-chloro-2-hydroxy-4-methylphenyl)-3-(3'-hydroxyphenyl)prop-2-en-1-one (3o)

Synthesized by above mentioned method from 3-chloro, 6-hydoxy, 4-methylacetophenone (16 mmol) and 3-hydroxybenzaldehyde (16 mmol); Yield 69%, yellow solid; mp 183–185°C; R_f (EtOAc/Hex 4:6) 0.31; IR (KBr) ν_{max}/cm^{-1} 3445 (O-H), 1665 (C=O), 1568 (Ar C=C), 760 (C–Cl), 3063, 2941, 1625, 1291, 1134, 1150, 980, 754 (Ar); ^{1}H-NMR ($CDCl_3$, 400 MHz), δ (ppm) 11.54 (1H, s, OH), 7.71 (1H, d, *J* 15.7, H-b), 7.65 (2H, dd,

J 6.5 and 4.4, H-6, 6'), 7.30 (1H, d, *J* 16.0, H-a), 7.24 (4H, m, *J* 4.5, H-3, 4, 2', 4'), 6.94 (1H, d, *J* 8.0, H-5'), 2.37 (3H, s, CH_3-4); FAB-MS *m/z* 288.38 $[M+H]^+$; Anal. Calcd for $C_{16}H_{13}ClO_3$: C, 66.56; H, 4.54; Found: C, 63.29; H, 4.73

1-(5-chloro-2-hydroxy-4-methylphenyl)-3-(3',4'-dimethoxyphenyl)prop-2-en-1-one (3p)

Synthesized by above mentioned method from 3-chloro, 6-hydoxy, 4-methylacetophenone (16 mmol) and 3,4-methoxy benzaldehyde (16 mmol); Yield 78%, white solid; mp 123-125°C; R_f (EtOAc/Hex 4:6) 0.76; IR (KBr) ν_{max} /cm^{-1} 1650 (C=O), 1589 (Ar C=C), 1517 (COC=C), 1265, 1024 (C-O), 1155 (C-Cl), 3055 (Ar C-H), 2939 (C-H), 1612, 1519, 975, 818, (Ar); ^{1}H-NMR ($CDCl_3$, 400 MHz), δ (ppm) 7.82 (1H, d, *J* 16, H-b), 7.54 (1H, d, *J* 16, H-a), 7.54 (1H, d, *J* 6.4, H-4), 7.48 (1H, d, *J* 5.4, H-3), 7.10 (2H, dd, *J* 2.6 and 8.4, H-6, 6'), 7.22 (1H, d, *J* 4.3, H-2'), 6.91 (1H, d, *J* 8.1, H-5'), 3.70 (6H, s, OCH_3-3', 4'), 2.32 (3H, s, CH_3-4). FAB-MS *m/z* 332.07 $[M+H]^+$; Anal. Calcd for $C_{18}H_{17}ClO_4$: C, 64.97; H, 5.15; Found: C, 64.23; H, 5.67

General method for the synthesis of 3,5-diaryl-1-(p-sulfamylphenyl)-2-pyrazolines (4a- 4p):

Appropriate chalcones **3a – 3p** (0.001 mol) and 4-hydrazinobenzene sulfonamide hydrochloride (0.001 mol) were dissolved in ethanol (25 ml) and refluxed for 24 h. After completion of the reaction, refluxing condenser was removed and the reaction solution was concentrated to 10–15 ml. It was left at room temperature to give crystalline compound. It was filtered and recrystallised to give pure compound .[18] For preparing pyrazoline a small amount of NaOAc was added to refluxing alcohol.

3-(2",4" -hydroxyphenyl)-5-(2',5'-dichlorophenyl)-1-(ρ-sulfamylphenyl)-Δ^2-

Pyrazoline (4a)

Synthesized by above method from chalcone **3a**; Recrystallized from methanol; Yield 46%, off white amorphous solid; mp 210-213°C; R_f = 0.74, (toluene/ethyl acetate/formic acid, 5:4:1); IR (KBr) ν_{max}/cm^{-1} 3254 (O-H), 3315 & 3252 (NH_2), 1605 (C=N), 1159 ($SO_2N<$), 1107 (C–Cl), 3045, 2950 (C-H), 1505, 1467, 922, 815, 798 (Ar); ^{1}H-NMR ($CDCl_3$, 400 MHz), δ (ppm) 10.05 (2H, s, 2",4"-OH), 7.87 (1H, d, *J 12.3* H-6"), 7.65 (2H, m, H-8, 10), 7.40-7.48 (3H, m, H-3', 4', 6'), 7.10 (2H, s, SO_2NH_2), 6.82-6.86 (4H, m, H-7, 11, 3", 5"), 5.68 (1H, m, H-5), 3.96 (1H, m, 4-H_y), 3.10 (1H, m, 4-H_x); FAB-MS *m/z*: 477.72 $[M+H]^+$; Anal. Calcd for $C_{21}H_{17}Cl_2N_3O_4S$: C, 52.73; H, 3.58; N, 8.78; Found: C, 52.49; H, 3.26; N, 8.36.

3-(2",4" -hydroxyphenyl)-5-(2'-methoxy, 5'-chlorophenyl)-1-(ρ-sulfamylphenyl)-Δ^2-Pyrazoline (4b)

Synthesized by above method from chalcone **3b**; Recrystallized from methanol; Yield 35%, off white amorphous solid; mp 219-222°C; R_f = 0.75, (toluene/ethyl acetate/formic acid, 5:4:1); IR (KBr) ν_{max}/cm^{-1}

3254 (O-H), 3315 & 3252 (NH_2), 1605 (C=N), 1159 (SO_2N<), 1107 (C–Cl), 3045, 2950 (C-H), 1505, 1467, 922, 815, 798 (Ar); ^{1}H-NMR ($CDCl_3$, 400 MHz), δ (ppm) 10.05 (2H, s, 2",4"-OH), 7.87 (1H, d, *J 12.3* H-6"), 7.65 (2H, m, H-8, 10), 7.40-7.48 (3H, m, H-3', 4', 6'), 7.10 (2H, s, SO_2NH_2), 6.82-6.86 (4H, m, H-7, 11, 3", 5"), 5.68 (1H, m, H-5), 3.96 (1H, m, 4-H_y), 3.73 (3H, s, OCH_3-2'), 3.10 (1H, m, 4-H_x); FAB-MS *m/z*: 461.72 $[M+H]^+$; Anal. Calcd for $C_{22}H_{20}ClN_3O_4S$: C, 57.70; H, 4.40; N, 9.18 Found: C, 57.29; H, 4.73; N, 9.83.

3-(2",4" -hydroxyphenyl)-5-(3'-hydroxyphenyl)-1-(ρ-sulfamylphenyl)-Δ^2-Pyrazoline (4c)

Synthesized by above method from chalcone **3c**; Yield 38%, Pale yellow solid; mp 265-267°C; IR (KBr) ν_{max}/cm^{-1} 3212 (O-H), 3334 & 3278 (NH_2), 1612 (C=N), 1151 (SO_2N<), 1110 (C–Cl), 3041, 2954 (C-H), 1501, 1462, 923, 811, 794 (Ar); ^{1}H-NMR ($CDCl_3$, 400 MHz), δ (ppm) 11.05 (3H, s, 2",4", 3'-OH), 7.82 (1H, d, *J 10.3* H-6"), 7.20-7.15 (1H, m, H-2', 5'), 7.10 (2H, s, SO_2NH_2), 7.61 (2H, dd, *J 12.3* and 6.2, H-8, 10), 6.94 (2H, d, *J* 7.1, H-2'), 6.85-6.76 (6H, m, H-7, 11, 4',6', 3", 5"), 5.92 (1H, dd, *J 12.5* and 6.2, H-5), 3.85 (1H, dd, *J 17.5* and 11.6, 4-H_y), 3.08 (1H, dd, *J 17.5* and 4.6, 4-H_x); FAB-MS *m/z*: 425.39 $[M+H]^+$; Anal. Calcd for $C_{21}H_{19}N_3O_5S$: C, 59.28; H, 4.50; N, 9.88; Found: C, 59.10; H, 4.29; N, 9.98;

3-(2",4"-hydroxyphenyl)-5-(3',4'-dimethoxyphenyl)-1-(ρ-sulfamylphenyl)-Δ^2 Pyrazoline (4d)

Synthesized by above method from chalcone **4d**; Yield 42%, white amorphous solid; mp 256-258°C; IR (KBr) ν_{max}/cm^{-1} 3245 (O-H), 3334 & 3278 (NH_2), 1612 (C=N), 1151 (SO_2N<), 1110 (C–Cl), 3041, 2954 (C-H), 1501, 1462, 923, 811, 794 (Ar); ^{1}H-NMR ($CDCl_3$, 400 MHz), δ (ppm) 10.65 (2H, s, 2",4"-OH), 7.87 (1H, d, *J 10.4* H-6"), 7.67 (2H, dd, *J 10.3* and 4.2, H-8, 10), 7.10 (2H, s, SO_2NH_2), 6.92-6.85 (7H, m, H-7, 11, 2', 4',6', 3", 5"), 5.92 (1H, t, H-5), 3.89 (1H, dd, *J 17.5* and 11.3, 4-H_y), 3.75 (6H, s, OCH_3-3', 4'), 3.01 (1H, dd, *J 17.4* and 4.9, 4-H_x); FAB-MS *m/z*: 469.79 $[M+H]^+$; Anal. Calcd for $C_{23}H_{23}N_3O_6S$: C, 58.84; H, 4.94; N, 8.95 Found: C, 58.27; H, 4.93; N, 8.45

3-(2",5"-dichorophenyl)-5-(2',5'-dichlorophenyl)-1-(ρ-sulfamylphenyl)-Δ^2-Pyrazoline (5e)

Synthesized by above method from chalcone **5e**; Yield 42%, white solid; mp 226-228°C; IR (KBr) ν_{max}/cm^{-1} 3312 & 3261 (NH_2), 1630 (C=N), 1159 (SO_2N<), 1101 (C–Cl), 3031, 2934 (C-H), 1462, 923, 818, 794 (Ar); ^{1}H-NMR ($CDCl_3$, 400 MHz), δ (ppm) 7.87 (2H, dd, *J 10.4* and 4.1, H-2", 6"), 7.67 (2H, dd, *J 10.3* and 4.2, H-8, 10), 7.10 (2H, s, SO_2NH_2), 6.92-6.85 (7H, m, H-7, 11, 2', 4',6', 3", 5"), 5.92 (1H, t, H-5), 3.89 (1H, dd, *J 17.5* and 11.3, 4-H_y), 3.01 (1H, dd, *J 17.4* and 4.9, 4-H_x); FAB-MS *m/z*: 453.79 $[M+H]^+$; Anal. Calcd for $C_{21}H_{15}Cl_4N_3O_2S$: C, 60.91; H, 5.11; N, 9.27; Found: C, 60.27; H, 5.93; N, 9.45

3-(2",5"-dichorophenyl)-5-(5'-chloro-2'-methoxyphenyl)-1-(ρ-sulfamylphenyl)-Δ^2-Pyrazoline (5f)

Synthesized by above method from chalcone **3f**; Yield 44%, Pale yellow solid; mp 218-220°C; IR (KBr) ν_{max}/cm^{-1} 3301 & 3258 (NH_2), 1637 (C=N), 1151 (SO_2N<), 1105 (C–Cl), 3036, 2926 (C-H), 1461, 926, 794 (Ar); ^{1}H-NMR ($CDCl_3$, 400 MHz), δ (ppm) 7.87 (2H, dd, *J 10.4* and 4.1, H-2", 6"), 7.67 (2H, dd, *J 10.3* and 4.2, H-8, 10), 7.10 (2H, s, SO_2NH_2), 6.90-6.83 (7H, m, H-7, 11, 3', 4', 6', 3", 5"), 5.87 (1H, t, H-5), 3.80 (1H, m, 4-H_y), 3.70 (3H, s, OCH_3-2'), 3.04 (1H, m, 4-H_x); FAB-MS *m/z*: 511.35 $[M+H]^+$; Anal. Calcd for $C_{22}H_{18}Cl_3N_3O_3S$: C, 51.73; H, 3.55; N, 8.23; Found: C, 51.10; H, 3.39; N, 8.37

3-(2",5"-dichorophenyl)-5-(3'-hydroxyphenyl)-1-(ρ-sulfamylphenyl)-Δ^2-Pyrazoline (4g)

Synthesized by above method from chalcone **3g**; Yield 41%, white solid; mp 224-227°C; IR (KBr) ν_{max}/cm^{-1} 3223 (O-H), 3330 & 3276 (NH_2), 1617 (C=N), 1157 (SO_2N<), 1130 (C–Cl), 3046, 2923 (C-H), 1501, 1462, 923, 810, 794 (Ar); ^{1}H-NMR ($CDCl_3$, 400 MHz), δ (ppm) 10.65 (1H, s, 4"-OH), 7.87 (2H, dd, *J 10.4* and 4.1, H-2", 6"), 7.67 (2H, dd, *J 10.3* and 4.2, H-8, 10), 7.10 (2H, s, SO_2NH_2), 6.90-6.83 (7H, m, H-7, 11, 3', 4', 6', 3", 5"), 5.87 (1H, t, H-5), 3.80 (1H, m, 4-H_y), 3.04 (1H, m, 4-H_x); FAB-MS *m/z*: 511.35 $[M+H]^+$; Anal. Calcd for $C_{21}H_{17}Cl_2N_3O_3S$: C, 54.55; H, 3.71; N, 9.09; Found: C, 54.62; H, 3.45; N, 9.63

3-(2",5"-dichorophenyl)-5-(3',4'-dimethoxyphenyl)-1-(ρ-sulfamylphenyl)-Δ^2-Pyrazoline (4h)

Synthesized by above method from chalcone **3h** Yield 38%, white solid; mp 287-289°C; IR (KBr) ν_{max}/cm^{-1} 3323 & 3267 (NH_2), 1610 (C=N), 1150 (SO_2N<), 1139 (C–Cl), 3041, 2925 (C-H), 1520, 1461, 923, 790 (Ar); ^{1}H-NMR ($CDCl_3$, 400 MHz), δ (ppm) 6.98-6.85 (7H, m, H-7, 11, 2', 5', 6'), 7.45 (2H, d, J 3.2 H-3", 4"), 7.69 (2H, dd, *J 10.3* and 4.1, H-8, 10), 7.16 (2H, s, SO_2NH_2), 5.81 (1H, t, H-5), 3.82 (1H, m, 4-H_y), 3.72 (3H, s, OCH_3-3', 4'), 3.04 (1H, m, 4-H_x); FAB-MS *m/z*: 505.76 $[M+H]^+$; Anal. Calcd for $C_{23}H_{21}Cl_2N_3O_4S$: C, 54.55; H, 4.18; N, 8.30; Found: C, 54.83; H, 4.57; N, 8.07.

3-(2"methoxy, 5"-chorophenyl)-5-(2',5'-dichlorophenyl)-1-(ρ-sulfamylphenyl)-Δ^2-Pyrazoline (4i)

Synthesized by above method from chalcone **3i,** Yield 44%, Pale yellow solid; mp 240-242°C; IR (KBr) ν_{max}/cm^{-1} 3326 & 3260 (NH_2), 1613 (C=N), 1145 (SO_2N<), 1130 (C–Cl), 3046, 2920 (C-H), 1522, 1456, 920, 794 (Ar); ^{1}H-NMR ($CDCl_3$, 400 MHz), δ (ppm) 7.75-7.40 (7H, m, H-8, 10, 3', 4', 6', 4", 6"), 7.12 (2H, s, SO_2NH_2), 6.95-6.89 (3H, m, H-7, 11, 3") 5.87 (1H, t, H-5), 3.80 (1H, m, 4-H_y), 3.04 (1H, m, 4-H_x); FAB-MS *m/z*: 511.23 $[M+H]^+$; Anal. Calcd for $C_{22}H_{18}Cl_3N_3O_3S$: C, 51.72; H, 3.50; N, 8.27; Found: C, 51.46; H, 3.83; N, 8.53

3-(2"methoxy,5"-chorophenyl)-5-(2'-methoxy,5'-chlorophenyl)-1-(ρ-sulfamylphenyl)-Δ^2-Pyrazoline (4j)

Synthesized by above method from chalcone **3j**; Yield: 39%, brownish yellow amorphous solid; mp 261-263°C; IR (KBr) ν_{max}/cm^{-1} 3321 & 3245 (NH_2), 1610 (C=N), 1149 ($SO_2N<$), 1156 (C–Cl), 3048, 2928 (C-H), 1520, 1452, 928, 799 (Ar); ^{1}H-NMR ($CDCl_3$, 400 MHz), δ (ppm) 7.72-7.42 (7H, m, H-8, 10, 3', 4', 6', 4", 6"), 7.14 (2H, s, SO_2NH_2), 6.96-6.88(3H, m, H-7, 11, 3") 5.82 (1H, t, H-5), 3.85 (1H, m, 4-H_y), 3.71 (3H, s, OCH_3-2'), 3.08 (1H, m, 4-H_x); FAB-MS *m/z*: 505.84 $[M+H]^+$; Anal. Calcd for $C_{23}H_{21}Cl_2N_3O_4S$: C, 54.55; H, 4.18; N, 8.30; Found: C, 54.30; H, 4.29; N, 8.84

3-(2"methoxy,5"-chorophenyl)-5-(3'-hydroxyphenyl)-1-(ρ-sulfamylphenyl)-Δ^2-Pyrazoline (4k)

Synthesized by above method from chalcone **3k**; Yield 45%, reddish brown amorphous solid; mp 258-260°C; IR (KBr) ν_{max}/cm^{-1} 3282 (O-H), 3329 & 3240 (NH_2), 1617 (C=N), 1141 ($SO_2N<$), 1150 (C–Cl), 3040, 2921 (C-H), 1524, 921, 770 (Ar); ^{1}H-NMR ($CDCl_3$, 400 MHz), δ (ppm) 10.25 (1H, s, 2'-OH), 7.72-7.42 (7H, m, H-8, 10, 2', 4', 6', 4", 6"), 6.95-6.85 (3H, m, H-7, 11, 3", 5') 7.10 (2H, s, SO_2NH_2), 5.84 (1H, t, H-5), 3.86 (1H, m, 4-H_y), 3.09 (1H, m, 4-H_x); FAB-MS *m/z*: 457.64 $[M+H]^+$; Anal. Calcd for $C_{22}H_{20}ClN_3O_4S$: C, 57.70; H, 4.40; N, 9.18; Found: C, 57.07; H, 4.94; N, 9.75

3-(2"methoxy,5"-chorophenyl)-5-(3',4'-dimethoxyphenyl)-1-(ρ-sulfamylphenyl)-Δ^2-Pyrazoline (4l)

Synthesized by above method from chalcone **3l**; Yield 30%, white solid; mp 222-224°C; IR (KBr) ν_{max}/cm^{-1} 3322 & 3246 (NH_2), 1610 (C=N), 1146 ($SO_2N<$), 1155 (C–Cl), 3041, 2934 (C-H), 1525, 932, 789 (Ar);; ^{1}H-NMR ($CDCl_3$, 400 MHz), δ (ppm) 7.70-7.46 (7H, m, H-8, 10, 2', 5', 6', 4", 6"), 6.93-6.86 (3H, m, H-7, 11, 3") 7.15 (2H, s, SO_2NH_2), 5.88 (1H, t, H-5), 3.82 (1H, m, 4-H_y), 3.70 (3H, s, OCH_3-3', 4'), 3.04 (1H, m, 4-H_x); FAB-MS *m/z*: 501.49 $[M+H]^+$; Anal. Calcd for $C_{24}H_{24}ClN_3O_5S$: C, 57.42; H, 4.82; N, 8.37; Found: C, 57.28; H, 4.58; N, 8.43

3-(5"-chloro-2"-hydroxy-4"-methylphenyl)-5-(2',5'-dichlorophenyl)-1-(ρ-sulfamylphenyl)-Δ^2-Pyrazoline (4m)

Synthesized by above method from chalcone **3m**; Yield 43%, off white amorphous solid; mp 282-284°C; IR (KBr) ν_{max}/cm^{-1} 3223 (O-H), 3330 & 3276 (NH_2), 1617 (C=N), 1157 ($SO_2N<$), 1130 (C–Cl), 3046, 2923 (C-H), 1501, 1462, 923, 810, 794 (Ar); ^{1}H-NMR ($CDCl_3$, 400 MHz), δ (ppm) 11.09 (1H, s, 2"-OH), 7.77-7.45 (6H, m, H-8, 10, 3', 4', 6', 6"), 7.15 (2H, s, SO_2NH_2), 6.94-6.89 (3H, dd, J 5.4 and 2.4, H-7, 11) 5.83(1H, t,

H-5), 3.81 (1H, m, 4-H_y), 3.06 (1H, m, 4-H_x), 2.89 (3H, s, CH_3-4"); FAB-MS *m/z*: 511.47 $[M+H]^+$; Anal. Calcd for $C_{22}H_{18}Cl_3N_3O_3S$: C, 51.73; H, 3.55; N, 8.23; Found: C, 51.08; H, 3.78; N, 8.34

3-(5"-chloro-2"-hydroxy-4"-methylphenyl)-5-(5'-chloro-2'-methoxyphenyl)-1-(ρ-sulfamylphenyl)-Δ^2-Pyrazoline (4n)

Synthesized by above method from chalcone **3n**; Yield 40%, off white solid; mp 287-289°C; IR (KBr) ν_{max}/cm^{-1} 3245 (O-H), 3334 & 3278 (NH_2), 1612 (C=N), 1151 ($SO_2N<$), 1110 (C–Cl), 3041, 2954 (C-H), 1501, 1462, 923, 811, 794 (Ar); ^{1}H-NMR ($CDCl_3$, 400 MHz), δ (ppm) 10.56 (1H, s, 2"-OH), 7.71-7.47 (6H, m, H-8, 10, 3', 4', 6', 6"), 7.10 (2H, s, SO_2NH_2), 6.91-6.85 (3H, dd, J 5.4 and 2.4, H-7, 11) 5.85(1H, t, H-5), 3.81 (1H, m, 4-H_y), 3.78 (3H, s, OCH_3-2'), 3.06 (1H, m, 4-H_x), 2.91 (3H, s, CH_3-4"); FAB-MS *m/z*: 505.39 $[M+H]^+$; Anal. Calcd for $C_{23}H_{21}Cl_2N_3O_4S$: C, 54.55; H, 4.18; N, 8.30 Found: C, 54.28; H, 4.82; N, 8.47

3-(5"-chloro-2"-hydroxy-4"-methylphenyl)-5-(3'-hydroxyphenyl)-1-(ρ-sulfamylphenyl)-Δ^2-Pyrazoline (4o)

Synthesized by above method from chalcone **3o**; Yield 31%, off white solid; mp 296-298°C; IR (KBr) ν_{max}/cm^{-1} 3267 (O-H), 3330 & 3278 (NH_2), 1612 (C=N), 1151 ($SO_2N<$), 1110 (C–Cl), 3041, 2954 (C-H), 1501, 1462, 923, 794 (Ar); ^{1}H-NMR ($CDCl_3$, 400 MHz), δ (ppm) 10.25 (2H, s, 2", 3'-OH), 7.60-7.63 (3H, m, H-8, 10, 6"), 6.85-6.40 (4H, m, H-2', 4', 6', 5"), 7.12 (2H, s, SO_2NH_2), 6.88-6.82 (3H, dd, J 5.4 and 2.4, H-7, 11) 5.85 (1H, t, H-5), 3.83 (1H, m, 4-H_y), 3.12 (1H, m, 4-H_x), 2.84 (3H, s, CH_3-4"); FAB-MS *m/z*: 457.39 $[M+H]^+$; Anal. Calcd for $C_{22}H_{20}ClN_3O_4S$: C, 57.70; H, 4.40; N, 9.18; Found: C, 57.75; H, 4.25; N, 9.87

3-(5"-chloro-2"-hydroxy-4"-methylphenyl)-5-(3',4'-dimethoxyphenyl)-1-(ρ-sulfamylphenyl)-Δ^2-Pyrazoline (4p)

Synthesized by above method from chalcone **3p**; Yield 53%, white solid; mp 231-234°C; IR (KBr) ν_{max}/cm^{-1} 3438 (O-H), 3330 & 3276 (NH_2), 1151 ($SO_2N<$), 1581(Ar C=C), 1610 (C=N), 1238, 999 (C–O), 1212 (C-N), 1121 (C–Cl), 3049, 2945(C-H), 1565, 812, 773 (Ar); ^{1}H-NMR ($CDCl_3$, 400 MHz), δ (ppm) 10.12 (1H, s, 2"-OH), 7.72-7.50 (6H, m, H-8, 10, 2', 5', 6', 6"), 7.14 (2H, s, SO_2NH_2), 6.92-6.87 (3H, dd, J 5.4 and 2.4, H-7, 11) 5.81(1H, t, H-5), 3.84 (1H, m, 4-H_y), 3.79 (6H, s, OCH_3-3', 4'), 3.10 (1H, m, 4-H_x), 2.79 (3H, s, CH_3-4"); FAB-MS *m/z*: 501.96 $[M+H]^+$; Anal. Calcd for $C_{24}H_{24}ClN_3O_5S$: C, 57.42; H, 4.82; Cl, 7.06; N, 8.37 Found: C, 57.54; H, 4.87; N, 8.56

In vitro anti-inflammatory activity

Carrageenan induced hind paw edema method was used for evaluating anti-inflammatory activity.26 Wistar rats (either sex) weighing 150–175 g were kept in animal house of SRK University Bhopal. The experiments were performed in accordance with the guidelines of Committee for the Purpose of Control and Supervision of Experiments in Animals (CPCSEA). Overnight fasted rats (16 h) were divided into groups of 6 animals each. One group of rats, which served as control was given vehicle (1% CMC in water in a volume of 10 mL/kg) only. Test compounds (100 mg/kg b.w.) and celecoxib (100 mg/kg b.w.) suspended in vehicle (10 mL/kg) were administered orally to respective groups. After 30 min, all animals were injected with 0.1 mL of 1% carrageenan solution (prepared in normal saline) in the subplantar aponeurosis of left hind paw to induce inflammation and the volume of injected paw was measured by using plethysmometer immediately (at 0 h). The paw volume was again measured after 0.5, 1, 2, 3, 4 and 6 hr. The average paw volume in a group of treated rats was compared with vehicle (control group) and the percentage inhibition of edema was calculated by using the formula:

Percent inhibition = (1-Vt/Vc)

where Vt is the mean paw volume of the test drug treated rats and

Vc is the mean paw volume of the control.

RESULTS AND DISCUSSIONS

Chemistry

The procedure used to synthesize a series of 16 designed compounds (pyrazoline derivatives) is outlined in Figure 1 and Table 1. Structures of compounds **3(a-p)** and **4(a–p)** were confirmed by IR, NMR data as well as their distinct R_f values in TLC analysis. The IR spectra of synthesized compounds showed absorption bands which are characteristic of the anticipated structure of the synthesized compounds. Carbonyl stretching band of aldehydes and methyl ketones which generally occurs in 1680-1700 cm^{-1} range, is absent in the infrared spectra of products and a new band appears in 1630-1655 cm^{-1} region could be assigned to α, β-unsaturated ketonic group in the synthesized compounds. The signal at 1350-1300 (asymmetric) and 1120-1100 (symmetric) arise due to SO_2 group in sulfonamide chalcones. Two strong bands between 3321-3382 cm^{-1} and 3413-3485 cm^{-1} regions ascribe to amide –NH- stretching in sulfonamide chalcones. Other characteristic bands of substituted groups, viz, $\nu_{C\text{-}Cl}$, $\nu_{O\text{-}H}$, $\nu_{C\text{-}O\text{-}C}$, and $\nu_{C=N}$ in product chalcones are displayed in 725-750 cm^{-1}, 3550-3200 cm^{-1}, 1260-1000 cm^{-1} and 1260-1000 cm^{-1} regions of infrared spectra, respectively. The ^{1}H-NMR spectra of the synthesized compounds show signals for both aliphatic and aromatic protons, characteristic of the anticipated structure of the synthesized compounds. A singlet arising in 8.34-9.68 ppm region could be attributed to amide (-NH-) proton. Two doublets appearing in 7.25-7.77

ppm (*J* ~16 Hz, Ha) and 7.22-7.49 ppm (*J* ~16 Hz, Hb) regions may be due to trans-olifinic protons. The large J value (17 Hz) clearly reveals the trans geometry for the chalcones. Signals around δ value 3.1 and 3.9 ppm recorded as doublet of doublets (dd) were assigned to 4-H_x and 4-H_y protons of pyrazoline derivatives. The fragmentation pattern obtained in the mass spectra was also according to the anticipated structures. All the above results confirmed the formation of the synthesized compounds.

Anti-inflammatory activity

Synthesized twelve compounds were screened for anti-inflammatory activity by in-vitro method on Wister albino rats. The actions of synthesized compounds were done on paw of Wister albino rats and compared with Phenyl Butazone as a standard drug. The paw volumes are recorded with in 0.1, 1, 2, 3, 4, 6 hr interval time duration and the SEM values are calculated by using SPSS software.

Table 2 . Anti-inflammatory activity of synthesized hybrid compounds

Comd	**Percent inhibition** + **SEM at various time** intervals					
	0.5 hr	1 hr	2 hr	3 hr	4 hr	6 hr
21	36.45±1.65	41.65±.01*	45.85±0.45*	54.61±2.96**	42.97±2.32*	35.61±1.71
22	24.21±1.21	30.20±0.45	36.45±3.25	38.91±2.41	32.65±1.95	28.31±1.65
27	37.13±1.65	43.85±2.01*	47.01±0.01*	55.21±0.45**	44.15±2.60*	38.42±1.62
28	18.65±2.12	22.41±2.35	27.12±1.85	35.21±1.29	30.16±0.95	25.45±1.81
30	38.45±1.06	44.01±2.32*	50.21±1.42**	55.61±3.25**	47.21±1.09*	39.45±1.74
31	20.31±.32	26.15±1.95	3l.26±1.45	37.65±2.15	30.49±1.65	26.29±1.23
33	34.45±3.01	41.65±1.90*	44.21±0.10*	56.21±1.85**	49.26±1.21*	46.95±4.31*
34	12.14±1.65	16.61±0.01	21.35±0.01	34.64±3.02	32.45±2.12	26.45±2.65
37	22.65±3.95	28.14±0.30	34.65±0.91	41.95±1.86*	38.20±3.01	34.86±2.45
38	38.09±1.65	45.91±1.45*	48.45±0.10*	59.91±1.85**	52.75±2.10**	49.63±1.90*
Phenyl butazone	46.29±1.29*	59.65±2.32**	76.91±1.45***	93.23±1.50***	89.15±2.45***	87.45±2.05***

Dose:Standard and sample solution is 100 mg/kg body weight. Values are expressed as mean ± SEM (n=6).* $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$ compared to control. Student's i-test

The study indicated that **few compounds** exhibited moderate anti-inflammatory activity as compared to standard drug.

CONCLUSION

A novel series of 3,5-diaryl-1-(p-sulfamylphenyl)-2-pyrazolines (**4a-4p**), obtained from appropriate chalcones **3a – 3p** and 4-hydrazinobenzene sulfonamide hydrochloride were synthesized and characterized based on their physical, analytical, and spectral data. The compounds **4a-4p** were evaluated anti-inflammatory activity, showing significant anti-inflammatory activities.

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