International Journal for Pharmaceutical Research Scholars (IJPRS)
ISSN No: 2277-7873
RESEARCH ARTICLE
V-1, I-4, 2012

Synthesis and Antimicrobial Activities of Some Pyrazoline Derivatives

Ganguly SS, Gami SP, Vilapara KV, Naliapara YT*

Department of Chemistry, Saurashtra University, Rajkot-360005, Gujarat, India

Manuscript No: IJPRS/V1/I4/00193, Received On: 20/10/2012, Accepted On: 29/10/2012

ABSTRACT

An efficient synthesis of 3, 5-disubstituted-2-pyrazoline was carried out by the condensation of chalcones with hydrazine hydrate in ethanol in presence of piperidine. The newly synthesized compounds were characterized by ^{1}H NMR spectroscopy, IR spectroscopy, MS, elemental analysis and screened for their antimicrobial activity against various strains of bacteria and fungi.

KEYWORDS

Pyrazoline, Antibacterial activity, Chalcone, Benzenesulfonamide.

INTRODUCTION

Heterocyclic compounds are a group of organic compounds containing rings in which one or more of the carbon atom is replaced by an atom other than carbon, usually nitrogen, oxygen sulphur or other hetero atoms. Heterocycles containing nitrogen are most abundant and great biological applicability than those containing oxygen or sulphur. Pyrazolines as a class of nitrogen containing heterocyclic compounds have many medicinal application such as antimicrobial[10,11], antitubercular[4], anticonvulsant[8], anti-inflammatory[9], antinociceptive[7] and some of the Pyrazolines derivatives are used in therapy of neurodegenerative disorders[12]. The standard procedure for the preparation of the 2-pyrazolines involves the cyclocondensation of α,β-unsaturated compound and hydrazine derivatives[1-3]. The microwave assisted synthesis under solvent free condition are also reported[5,6].

We have synthesize N-(2-(5-Aryl-4,5-dihydro pyrazoline)phenyl)Benzenesulfonamide derive-atives by the refluxing Chalcone with hydrazine derivatives in the presence of piperidine in ethanol.

The structures of the newly synthesized compounds were characterized by the elemental analyses, IR, ^{1}H NMR and mass spectral data. The antimicrobial activity was assayed by using the cup-plate agar diffusion method[10] by measuring the zone of inhibition in mm. All the compounds were screened against varieties of bacterial strains such *Bacillus megaterium, Proteus vulgaris, Escherichia coli, Staphylo coccus aureus* and fungi *Aspergillus niger* at 40 μg/ml concentration. Standard drugs like Ampicillin, Chloramphenicol, Norfloxacin and Griseofulvin were used for the comparison purpose.

EXPERIMENTAL

Melting points were determined in open capillary tubes and are uncorrected. Thin layer chromatography using silica gel G (E. Merck) plates was used to access the reactions and purity of the synthesized compounds. All the products have been characterized by elemental analysis, IR, ^{1}H NMR and mass spectral study. IR spectra were recorded on Shimadzu FTIR-8400 spectrophotometer in KBr disc and noteworthy absorption levels (cm^{-1}) are listed. ^{1}H NMR spectra were recorded on Bruker

***Address for Correspondence:**
Naliapara Yogesh T
Department of Chemistry, Saurashtra University,
Rajkot-360005
Gujarat,
India.
E-Mail Id: naliaparachem@yahoo.co.in

spectrometer (400 MHz) using TMS as an internal standard, chemical shift in δ ppm. Mass spectra were determined using direct inlet probe on a GCMS-QP2010 mass spectrometer, Elemental analysis were performed on a Carlo Erba EA 1108 elemental analyzer.

of N-(2-acetylphenyl) benzenesulfonamide (0.01M, 3.63g) in ethanol (95%, 20 ml) aqueous sodium hydroxide (40%, 8 ml) and stirred at 20-30°C for 12 hours. The contents were poured into crushed ice and isolated by acidification and recrystallised from ethanol: dioxane (2:1) mixture.

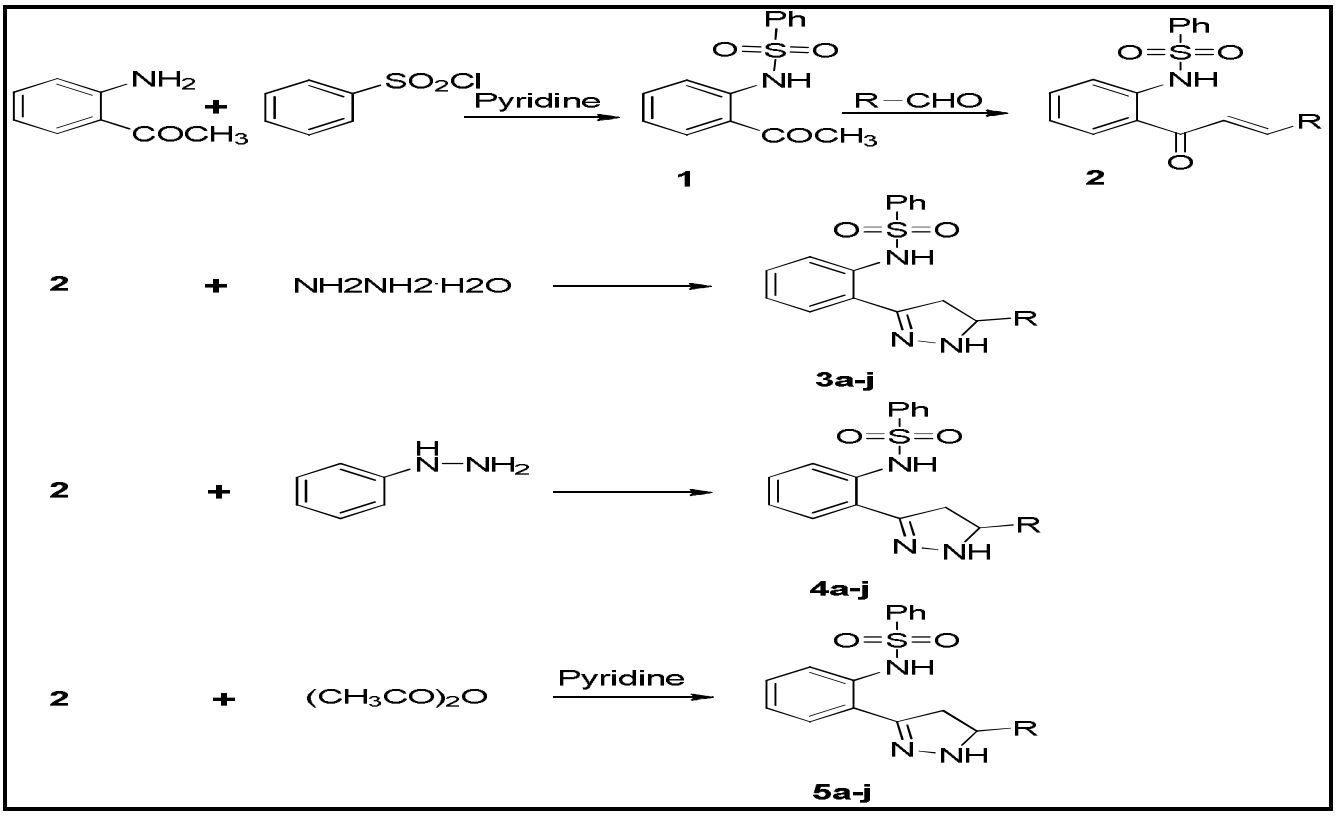

Figure 2: Reaction Scheme

General synthesis for N-(2-acetylphenyl)benzenesulfonamide (1)

To a mixture of 2-aminoacetophenone (0.01 M; 1.35g) and pyridine (0.01 M; 0.96 ml) benzenesulphonylchloride (0.015 M, 1.93 ml) were added drop wise with constant stirring. The mixture was refluxed for 3-4 hrs in ethanol. The contents were poured into crushed ice and concentrated HCl mixture. The product was isolated and crystallized from dioxane, ethanol (1:1).

General synthesis for 2'-phenylsulphonamido chalcone (2)

Substituted benzaldehyde (0.02 M, 2.02 ml) in ethanol (95%, 15 ml) was added to the mixture

General synthesis for N-(2-(5-aryl-4, 5-dihydro-1H-pyrazol-3-yl)phenyl) benzene sulfonamide (3a-j)

Chalcone (0.01M, 3.97 g) in 25 ml ethanol, hydrazine hydrate (0.01M, 0.5 ml) and piperidine (2 ml) was refluxed for 12 hrs. The refluxing mixture was poured into acidified ice. The product was isolated and recrystallised from R.S., acetic acid (5:1) mixture.

Compound (3e); Yield: 62 %; m.p. 80 °C; Anal. Calcd. for $C_{21}H_{18}ClN_3O_2S$: C, 61.23; H, 4.40; Cl, 8.61; N, 10.20; O, 7.77; S, 7.78. Found: C, 61.15; H, 4.48; N, 10.12; O, 7.80; Cl, 8 .64; S,7.74. IR (KBr, cm^{-1}) spectra of the compounds showed bands at 3095 (Ar-H str.), 3450 (N-H str.), 1300 (C-N str.), 1330 (S=O

str.), 775 (-C-Cl str.); ^{1}H NMR (400 MHz $CDCl_3$+DMSO-d6, δ/ppm): 3.0-3.42 (2H, dd, -CH_2 pyrazoline), 4.6-5.01 (1H, dd, -CH Pyrazoline), 7.14-7.55 (13H, m, Ar-H). MS (m/z): 412, 364, 300, 270, 256, 179, 111, 92, 77.

Compound (3f); Yield: 65 %; m.p. 181 °C; Anal. Calcd. for $C_{21}H_{18}ClN_3O_2S$: C, 61.23; H, 4.40; Cl, 8.61; N, 10.20; O, 7.77; S, 7.78. Found: C, 61.15; H, 4.48; N, 10.12; O, 7.80; Cl, 8 .64; S,7.74. IR (KBr, cm^{-1}) spectra of the compounds showed bands at 3082 (Ar-H str.), 3442 (N-H str.), 1315 (C-N str.), 1340 (S=O str.), 762 (-C-Cl str.); ^{1}H NMR (400 MHz $CDCl_3$+DMSO-d6, δ/ppm): 2.90-3.47 (2H, dd, -CH_2 pyrazoline), 4.45-5.11 (1H, dd, -CH Pyrazoline), 7.54-7.85 (13H, m, Ar-H). MS (m/z): 412, 364, 300, 270, 256, 179, 111, 92, 77, 67.

Compound (3i); Yield: 63 %; m.p. 121 °C; Anal. Calcd. for $C_{22}H_{21}N_3O_3S$: C, 64.85; H, 5.19; N, 10.31; O,11.78; S, 7.87. Found: C, 64.83; H, 5.25; N, 10.20; O, 11.82; S,7.89. IR (KBr, cm^{-1}) spectra of the compounds showed bands at 3080 (Ar-H str.), 3400 (N-H str.), 1330 (C-N str.), 1350 (S=O str.), 1250 (C-O-C str.); ^{1}H NMR (400 MHz $CDCl_3$+DMSO-d6, δ/ppm): 3.71-4.42 (2H, dd, -CH_2 pyrazoline), 4.16 (3H, s, -OCH_3), 5.64-5.89 (1H, dd, -CH Pyrazoline), 7.28-8.19 (13H, m, Ar-H), 8.54 (1H , s, SO_2-NH-). MS (m/z): 405, 374, 298, 264, 232, 173, 107, 92, 77.

Similarly, other compounds **3a-j** was prepared. Their characterization data are recorded in Table I.

General synthesis for N-(2-(1-phenyl-5-aryl-4, 5-dihydro pyrazol-3-yl)phenyl) benzene sulfonamide 4(a-j)

Chalcone (0.01M, 2.53 g) in 25 ml ethanol, phenyl hydrazine (0.01M, 0.98 ml) and piperidine (2 ml) were refluxed for 12 hrs. The resulting mixture was poured into acidified ice. The product was isolated and recrystallised from R.S., dioxane (2:1) mixture.

Compound (4e); Yield: 70 %; m.p. 157 °C; Anal. Calcd. for $C_{27}H_{22}ClN_3O_2S$: C, 66.45; H, 4.54; N, 8.61; Cl, 7.26; O, 6.56; S, 6.57. Found: C, 66.51; H, 4.58; N, 8.50; Cl, 7.22; O, 6.58; S, 6.59. IR (KBr, cm^{-1}) spectra of the compounds showed bands at 3009 (Ar-H str.), 3420 (N-H str.), 1315 (C-N str.), 1342 (S=O str.), 769 (-C-Cl str.). ^{1}H NMR (400 MHz $CDCl_3$+DMSO-d6, δ/ppm): 4.06-4.12 (2H, dd, -CH_2, Pyrazoline), 5.97 (1H, dd, -CH, Pyrazoline), 7.10-7.63 (18H, m, Ar-H), 8.28 (1H, s, -SO_2-NH-). MS (m/z): 488,452, 376, 255, 232, 156, 141, 154, 77, 35.

Compound (4f); Yield: 75 %; m.p. 68 °C; Anal. Calcd. for $C_{27}H_{22}ClN_3O_2S$: C, 66.45; H, 4.54; N, 8.61; Cl, 7.26; O, 6.56; S, 6.57. Found: C, 66.48; H, 4.68; N, 8.50; Cl, 7.18; O, 6.57; S, 6.58. IR (KBr, cm^{-1}) spectra of the compounds showed bands at 3039 (Ar-H str.), 3456 (N-H str.), 1305 (C-N str.), 1352 (S=O str.), 779 (-C-Cl str.). ^{1}H NMR (400 MHz $CDCl_3$+DMSO-d6, δ/ppm): 4.02-4.16 (2H, dd, -CH_2, Pyrazoline), 5.79 (1H, dd, -CH, Pyrazoline), 7.24-7.83 (18H, m, Ar-H), 8.58 (1H, s, -SO_2-NH-). MS (m/z): 488,452, 376, 255, 232, 156, 141, 154, 77, 35.

Compound (4i); Yield: 63 %; m.p. 164 °C; Anal. Calcd. for $C_{28}H_{25}N_3O_3S$: C, 69.54; H, 5.21; N, 8.69; O,9.93; S, 6.63. Found: C, 69.58; H, 5.21; N, 8.60; O, 9.98; S,6.66. IR (KBr, cm^{-1}) spectra of the compounds showed bands at 3065 (Ar-H str.), 3445 (N-H str.), 1305 (C-N str.), 1364 (S=O str.), 1230 (C-O-C str.); ^{1}H NMR (400 MHz $CDCl_3$+DMSO-d6, δ/ppm): 3.64-4.02 (2H, dd, -CH_2 pyrazoline), 4.18 (3H, s, -OCH_3), 5.58-5.78 (1H, dd, -CH Pyrazoline), 7.32-8.14 (13H, m, Ar-H), 8.4 (1H , s, SO_2-NH-). MS (m/z): 481, 404, 374, 325 249, 264, 232, 141, 107, 91, 77, 31.

Similarly, other compounds **4a-j** was prepared. Their characterization data are recorded in Table-I.

General synthesis for N-(2-(1-acetyl-5-aryl-4, 5-dihydro pyrazol-3-yl)phenyl) benzenesulfonamide 5(a-j)

Chalcone (0.01M, 3.97 g) in 25 ml ethanol, hydrazine hydrates (0.01M, 0.5ml) and piperidine (2 ml) was refluxed for 12 hrs. The product was poured into acidified ice and isolated. To this product acetic anhydride (2.5

ml) and pyridine (0.5 ml) were added and refluxed again for 10 hrs. The product was isolated and recrystallised from R.S., dioxane (2:1) mixture.

Table 1**:** Physical Data of Compounds **3a-j**, **4a-j** and **5a-j**.

Compd.	R	M.F	M.W	M.P (°C)	Yield (%)
3a	-C_6H_5	$C_{21}H_{19}N_3O_2S$	377	220	60
3b	3-NH_2-C_6H_4	$C_{21}H_{20}N_4O_2S$	392	114	58
3c	5-Br-4-OH-3-OMe-C_6H_2	$C_{22}H_{20}BrN_3O_4S$	502	85	68
3d	5-Br-2-OH-C_6H_3	$C_{21}H_{18}BrN_3O_3S$	472	205	70
3e	2-Cl-C_6H_4	$C_{21}H_{18}ClN_3O_2S$	412	80	62
3f	4-Cl-C_6H_4	$C_{21}H_{18}ClN_3O_2S$	412	181	65
3g	3,5-Br_2-2-OH-C_6H_2	$C_{21}H_{17}Br_2N_3O_3S$	551	110	68
3h	3,4-$(OCH_3)_2$-C_6H_3	$C_{23}H_{23}N_3O_4S$	438	245	61
3i	4-OCH_3-C_6H_4	$C_{22}H_{21}N_3O_3S$	405	121	61
3j	2-C_4H_3O-C_6H_2	$C_{19}H_{17}N_3O_3$	335	107	52
3a	-C_6H_5	$C_{27}H_{23}N_3O_2S$	454	155	81
4b	3-NH_2-C_6H_4	$C_{27}H_{24}N_4O_2S$	469	120	62
4c	5-Br-4-OH-3-OMe-C_6H_2	$C_{28}H_{24}BrN_3O_4S$	578	87	68
4d	5-Br-2-OH-C_6H_3	$C_{27}H_{22}BrN_3O_3S$	548	167	67
4e	2-Cl-C_6H_4	$C_{27}H_{22}ClN_3O_2S$	488	157	70
4f	4-Cl-C_6H_4	$C_{27}H_{22}ClN_3O_2S$	488	68	75
4g	3,5-Br_2-2-OH-C_6H_2	$C_{27}H_{21}Br_2N_3O_3S$	627	151	68
4h	3,4-$(OCH_3)_2$-C_6H_3	$C_{28}H_{27}N_3O_4S$	502	153	65
4i	4-OCH_3-C_6H_4	$C_{28}H_{25}N_3O_3S$	484	164	63
4j	2-C_4H_3O-C_6H_2	$C_{25}H_{21}N_3O_3S$	445	85	48
5a	-C_6H_5	$C_{23}H_{21}N_3O_3S$	419	159	48
5b	3-NH_2-C_6H_4	$C_{23}H_{22}N_4O_3S$	435	175	52
5c	5-Br-4-OH-3-OMe-C_6H_2	$C_{24}H_{22}BrN_3O_5S$	544	171	55
5d	5-Br-2-OH-C_6H_3	$C_{23}H_{20}BrN_3O_4S$	514	175	52
5e	2-Cl-C_6H_4	$C_{23}H_{20}ClN_3O_3S$	454	96	83
5f	4-Cl-C_6H_4	$C_{23}H_{20}ClN_3O_3S$	454	209	45
5g	3,5-Br_2-2-OH-C_6H_2	$C_{23}H_{19}Br_2N_3O_4S$	593	157	43
5h	3,4-$(OCH_3)_2$-C_6H_3	$C_{25}H_{25}N_3O_5S$	480	172	50
5i	4-OCH_3-C_6H_4	$C_{24}H_{23}N_3O_4S$	450	162	55
5j	2-C_4H_3O-C_6H_2	$C_{21}H_{19}N_3O_4S$	409	113	49

Table 2: Antimicrobial Screening Results of Compounds **3a-j, 4a-j** and **5a-j**.

compd.	Zones of inhibition in mm				
	Antibacterial activity				Antifungal activity
	S. citrus	***E.coli***	***B.mega***	***S.typhose***	***A. niger***
3a	15	18	12	11	12
3b	12	21	11	12	12
3c	14	18	12	12	11
3d	16	23	11	11	11
3e	17	15	16	11	16
3f	13	24	11	14	12
3g	15	24	12	11	11
3h	11	18	12	11	11
3i	16	20	17	11	11
3j	15	23	12	11	12
4a	15	21	11	11	10
4b	11	23	12	10	11
4c	12	20	11	10	11
4d	12	21	12	11	12
4e	13	20	15	11	12
4f	14	24	11	11	13
4g	13	26	12	11	13
4h	14	23	13	13	16
4i	13	24	12	11	15
4j	13	22	11	11	11
5a	11	21	12	11	11
5b	13	18	12	12	11
5c	14	23	11	12	13
5d	11	19	12	11	13
5e	12	23	13	12	14
5f	12	20	11	11	11
5g	12	22	12	11	11
5h	12	26	11	11	11
5i	13	21	11	11	13
5j	12	24	11	12	11
Ampicillin	25	23	16	12	-
Chloramphenicol	17	23	22	13	-
Norfloxacin	23	24	23	25	-
Griseofulvin	-	-	-	-	25

Compound (5e); Yield: 83 %; m.p. 96 °C; Anal. Calcd. for $C_{23}H_{20}ClN_3O_3S$: C, 60.86; H, 4.44; N, 9.26; Cl, 7.81; O, 10.57; S, 7.06. Found: C, 60.90; H, 4.62; N, 9.15; Cl, 7.69; O, 10.61; S, 7.51. IR (KBr, cm^{-1}) spectra of the compounds showed bands at 3070 (Ar-H str.), 3400 (N-H str.), 1360 (C-N str.), 1330 (S=O str.), 1665 (-C=O Str.), 750 (-C-Cl str.). ^1H NMR (400 MHz $CDCl_3$+DMSO-d6, δ/ppm): 2.78 (3H, s, $-COCH_3$), 3.41-4.39 (2H, dd, $-CH_2$, Pyrazoline), 5.58-5.9 (1H, dd, -CH Pyrazoline), 7.26-8.12 (13H, m, Ar-H), 8.35 (1H, s, SO_2-NH-). MS (m/z): 454,418, 376, 297, 232, 221, 156, 77, 43, 35.

Compound (5f); Yield: 45 %; m.p. 209 °C; Anal. Calcd. for $C_{23}H_{20}ClN_3O_3S$: C, 60.86; H, 4.44; N, 9.26; Cl, 7.81; O, 10.57; S, 7.06. Found: C, 60.88; H, 4.66; N, 9.15; Cl, 7.67; O, 10.63; S, 7.50. IR (KBr, cm^{-1}) spectra of the compounds showed bands at 3060 (Ar-H str.), 3425 (N-H str.), 1326 (C-N str.), 1345 (S=O str.), 1680 (-C=O Str.), 767 (-C-Cl str.). ^1H NMR (400 MHz $CDCl_3$+DMSO-d6, δ/ppm): 2.68 (3H, s, $-COCH_3$), 3.51-4.41 (2H, dd, $-CH_2$, Pyrazoline), 5.53-5.88 (1H, dd, -CH Pyrazoline), 7.22-8.16 (13H, m, Ar-H), 8.61 (1H, s, SO_2-NH-). MS (m/z): 448,404, 306, 340, 291, 232, 173, 156, 141, 107, 77, 43.

Compound (5i); Yield: 55 %; m.p. 162 °C; Anal. Calcd. for $C_{24}H_{23}N_3O_4S$: C, 64.13; H, 5.16; N, 9.35; O,14.24; S, 7.13. Found: C, 64.20; H, 5.18; N, 9.26; O, 14.26; S,7.15. IR (KBr, cm^{-1}) spectra of the compounds showed bands at 3080 (Ar-H str.), 3400 (N-H str.), 1330 (C-N str.), 1350 (S=O str.), 1250 (C-O-C str.); ^1H NMR (400 MHz $CDCl_3$+DMSO-d6, δ/ppm): 2.87 (3H, s, $-COCH_3$), 3.75-4.45 (2H, dd, $-CH_2$ pyrazoline), 4.12 (3H, s, $-OCH_3$), 5.62-5.9 (1H, dd, -CH Pyrazoline), 7.26-8.12 (13H, m, Ar-H), 8.5 (1H , s, SO_2-NH-). MS (m/z): 446, 414, 338, 298, 289, 232, 156, 141, 107,77, 66, 31.

Similarly, other compounds **5a-j** was prepared. Their characterization data are recorded in Table-I.

RESULT AND DISCUSSION

The antimicrobial activity was assayed by using the cup-plate agar diffusion method[10] by measuring the zone of inhibition in mm. All the compounds were screened *in vitro* for their antimicrobial activity against varieties of bacterial strains such *Bacillus megaterium*, *Proteus vulgaris*, *Escherichia coli*, *Staphylo coccus aureus* and fungi *Aspergillus niger* at 40 μg/ml concentration. The antimicrobial activity exhibited by the compounds was quiet comparable with that of the antimicrobial activity exhibited by known antibiotics like Ampicillin, Chloramphenicol, Norfloxacin and Griseofulvin.

REFERENCES

1. Parham WE, Dooley JF, "1, 3-Bridged Aromatic Systems. I. A New Synthesis of Pyrazoles", Journal of the American Chemical Society, 1967, 89(4), 985-988.
2. Parham WE, Dooley JF, "1, 3-Bridged Aromatic Systems. III. Ring-Opening Reactions of gem-Dihaloacetoxycyclopropanes", Journal of Organic Chemistry, 1968, 33(4), 1476-1480.
3. Gaoa C, Haya AS, "A New Simple Method for the Synthesis of Hydroxy Substituted 1,2-Diphenylcyclopropanes", Synthetic Communication, 25(12), 1877-1883.
4. Chovatia YS, "Synthesis and evaluation of certain pyrazolines and related compounds for their antitubercular, antibacterial and antifungal activities" Indian Journal of Heterocyclic Chemistry (2004), 13(3), 225-228.
5. Ju Y, Varma RS, "Microwave-assisted cyclocondensation of hydrazine derivatives with alkyl dihalides or ditosylates in aqueous media: syntheses of pyrazole, pyrazolidine and phthalazine derivatives", Tetrahedron Letters, 2005, 46, 6011-6014.
6. Ju Y, Varma RS, "Aqueous N-Heterocyclization of Primary Amines and Hydrazines with Dihalides: Microwave-Assisted Syntheses of N-Azacycloalkanes,

Isoindole, Pyrazole, Pyrazolidine, and Phthalazine Derivatives", Journal of Organic Chemistry, 2006, 71(1), 135-141.

7. Kaplancikli ZA, Turan-Zitouni G, Ozdemir A, Can OD, Chevallet P, "Synthesis and antinociceptive activities of some pyrazoline derivatives", European Journal of Medicinal Chemistry, 2009, 44, 2606-2610.
8. Siddiqui N, Alam P, Ahsan W, "Design, Synthesis, and In-vivo harmacological Screening of N,3-(Substituted Diphenyl)-5-phenyl-1H-pyrazoline-1- carbothioamide Derivatives", Arch. Pharm. Chem. Life Sci., 2009, 342, 173 – 181.
9. Malhotra P, Pattan S, Nikalje AP, "Microwave Assisted Synthesis and Antiinflammatory Activity of 3, 5-diaryl substituted-2-pyrazolines", International Journal of Pharmacy and Pharmaceutical Sciences, 2010, 2(2), 21-26.
10. Divekar K, Swamy S, Kavitha N, Murugan V, Devgun M, "Synthesis and Evaluation of Some New Pyrazole Derivatives as Antimicrobial Agents", Research Journal of Pharmacy and Technology, 2010, 3(4), 1039-1043.
11. Chovatia YS, "Synthesis and Antibacterial Activity of some Pyrazoline derivatives" Oriental Journal of Chemistry, 2010, 26(1), 275-278.
12. Jagrat M, Behera J, Yabanoglu S, Ercan Y, Ucar G, "Pyrazoline based MAO inhibitors: Synthesis, biological evaluation and SAR studies", Bioorganic & Medicinal Chemistry Letters, 2011, 1, 4236-4300.

