HL **ISSN: 2231 – 3087(print) / 2230 – 9632 (Online)**
http://heteroletters.org **Vol. 3: (4), 2013, 505-512**

2-METHOXYETHANOL AN EFFICIENT REACTION MEDIUM FOR SYNTHESIS OF SOME NOVEL 2*H*-PYRAZOLINES AND *N*-PHENYL PYRAZOLINES

Yogesh Nalwar, Sainath Zangade, Avinash Shinde and Yeshwant Vibhute*

Laboratory of Organic Synthesis, Department of Studies in Chemistry, Yeshwant Mahavidylaya, Nanded-431602, India.
E-mail address: drybv@rediffmail.com, drsbz@rediffmail.com
Tel.: +91.9960128307
Fax: +91.246.2253726

Abstract
An efficient and convenient thermal assisted condensation of substituted hydroxychalcones with hydrazine hydrate and phenyl hydrazine using 2-methoxyethanol in presence of mild basic condition to yield novel substituted 2-pyrazolines derivative. The method has several advantages in terms of clean reaction conditions, short reaction time giving excellent yields of product. Newly synthesized compounds were established on the basis of spectral technique.

Keywords: Synthesis; substituted hydroxychalcones; 2-pyrazolines; 2-methoxyethanol; thermal technique.

Introduction

Pyrazolines constitute an interesting class of organic compounds with diverse chemical, pharmacological applications and great importance in heterocyclic chemistry. The aromatic compounds containing pyrazolines as basic nucleus have known to possess antiinflammatory[i], antimalarial[ii], analgesic[iii], antidepressant[iv], anticancer[v] and antimycobacterial[vi]. 2-pyrazolines exhibit good properties of photoluminescence, electroluminescence and as fluroescence[vii]. Among the methods employed for the synthesis of pyrazolines, the condensation of α,β-unsaturated carbonyl compounds with hydrazine hydrate is commonly used[viii]. In view of these applications of five membered heterocycles and in continuation of earlier research work[ix], it was thought worthwhile to synthesize some novel pyrazoline derivatives by the condensation of different substituted hydroxychalcones with hydrazine hydrate and phenyl hydrazine in 2-methoxyethanol using conventional technique.

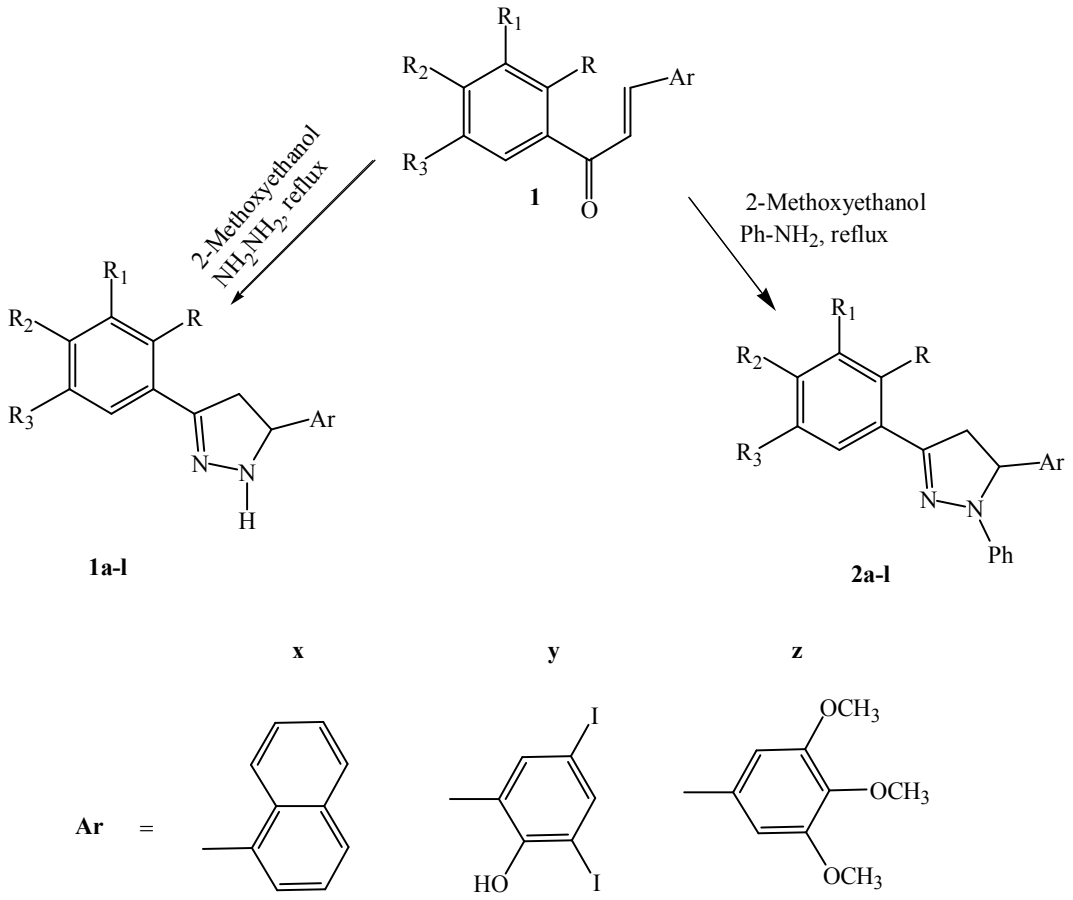
Methods

Melting points were determined in an open capillary tube and are uncorrected. IR spectra were recorded in KBr on a Perkin-Elmer spectrometer. ^{1}H NMR spectra were recorded on a Gemini 300-MHZ instrument in DMSO as solvent and TMS as an internal standard. The mass spectra were recorded on EISHIMADZU-GC-MS spectrometer. Elemental analyses were performed on a Perkin-Elmer 240 CHN elemental analyzer.

Typical Procedure for synthesis of pyrazolines

Mixture of different substituted hydroxychalcones (0.01 mol) and hydrazine hydrate (0.02 mol) / phenyl hydrazine (0.02 mol) was dissolved in 10 ml of 2-methoxyethanol. To this 0.001 mmol of piperidine was added to reaction mixture and refluxed for 10-15 min (TLC). Then reaction mixture was cooled to room temperature. Solid separated was isolated by simple Buchner filtration; final purification was achieved by crystallization from ethanol to give 2-pyrazolines **1**,**2a-l**.

Scheme 1



1a,2a: R=OH; R_1=Br; R_2=H; R_3=Cl; Ar= **x**
1b,2b: R=OH; R_1=I; R_2=CH_3; R_3= Cl; Ar= **x**
1c,2c: R=OH; R_1=Br; R_2=CH_3; R_3=Cl; Ar= **x**
1d,2d: R=OH; R_1=I; R_2= H; R_3= Cl; Ar= **x**
1e,2e: R=H; R_1=CH_3; R_2=OH; R_3=Br; Ar= **x**
1f,2f: R=H; R_1=CH_3; R_2=OH; R_3=I; Ar= **x**
1g,2g:R=H; R_1=Cl; R_2=OH; R_3=Cl; Ar= **x**
1h,2h:R=OH; R_1=Cl; R_2=OH; R_3=Cl; Ar= **x**
1i,2i:R=OH; R_1=Br; R_2=CH_3; R_3=Cl; Ar= **y**
1j,2j:R=OH; R_1=Br; R_2=H; R_3=Cl; Ar= **y**
1k,2k:R=OH; R_1=Br; R_2=H; R_3=Cl; Ar= **z**
1l,2l:R=OH; R_1=Br; R_2=CH_3; R_3=Cl; Ar= **z**

Spectral analysis of some compounds

2-Bromo-4-chloro-6-(5-naphthalen-1-yl-4,5-dihydro-1*H*-pyrazol-3-yl)-phenol. 1a: IR (KBr Pellets): 1594 (C=N), 1448, 1520 (C=C), 1208, 1145 (C-N) cm^{-1}. ^1H NMR (300 MHz, DMSO-d_6) δ 12.10 (s, 1H, OH), 7.28-8.32 (m, 9H, ArH), 6.79 (s, 1H, NH), 3.0 (dd, *J* = 5.2, 18.2 Hz, 1H, H_A), 3.89 (dd, *J* = 12.2, 18.2 Hz, 1H, H_B), 5.62 (dd, *J* = 5.2, 12.1, 1H, H_X). ^{13}C NMR (DMSO): 158.08 (C *of* Ar-OH), 154.25 (C *of* C=N), 139.42-115.73 (C *of Aromatic ring*), 58.32 (C *of* CH), 43.52 (C of CH_2). MS m/z: 401 (M^+). Anal. Cacl for $C_{19}H_{14}N_2OBrCl$: C, 56.85; H, 6.10; X (*Halogen*), 28.67. Found: C, 56.92; H, 6.12; X (*Halogen*), 28.62.

4-Chloro-2-iodo-3-methyl-6-(5-naphthalen-1-yl-4,5-dihydro-1*H*-pyrazol-3-yl)-phenol. 1b: IR (KBr Pellets): 1590 (C=N), 1432, 1518 (C=C), 1216, 1130 (C-N) cm^{-1}. ^1H NMR (300 MHz, DMSO-d_6) δ 12.14 (s, 1H, OH),7.22-8.28 (m, 8H, ArH), 6.81 (s, 1H, NH), 3.0 (dd, *J* = 5.2, 18.2 Hz, 1H, H_A), 3.89 (dd, *J* = 12.2, 18.2 Hz, 1H, H_B), 5.62 (dd, *J* = 5.2, 12.1, 1H, H_X), 2.21 (s, 3H, CH_3). ^{13}C NMR (DMSO): 157.92 (C *of* Ar-OH), 153.87 (C *of* C=N), 137.29-112.64 (C *of Aromatic ring*), 57.92 (C *of* CH), 42.82 (C of CH_2), 12.11 (C *of* CH_3). MS m/z: 462 (M^+).Anal. Cacl for $C_{20}H_{16}N_2OICl$: C, 51.94; H, 3.40; X (*Halogen*), 35.06. Found: C, 51.97; H, 3.42; X (*Halogen*), 35.10.

2-Bromo-4-chloro-3-methyl-6-(5-naphthalen-1-yl-4,5-dihydro-1*H*-pyrazol-3-yl)-phenol. 1c:IR (KBr Pellets): 1592 (C=N), 1426, 1521 (C=C), 1214, 1128 (C-N) cm^{-1}. ^1H NMR (300 MHz, DMSO-d_6) δ 12.12 (s, 1H, OH),6.79 (s, 1H, NH), 7.23-8.34 (m, 8H, Ar-H), 3.03 (dd, *J* = 5.1, 18.0 Hz, 1H, H_A), 3.88 (dd, *J* = 12.1, 18.1 Hz, 1H, H_B), 5.63 (dd, *J* = 5.1, 12.0, 1H, H_X), 2.12 (s, 3H, CH_3) ^{13}C NMR (DMSO): 157.19 (C *of* Ar-OH), 152.94 (C *of* C=N), 138.42-113.76 (C *of Aromatic ring*), 57.54 (C *of* CH), 42.13 (C of CH_2), 12.08 (C *of* CH_3).MS m/z: 416 (M^+). Anal. Cacl for $C_{20}H_{16}N_2OBrCl$: C, 57.69; H, 3.84; X (*Halogen*), 27.76. Found: C, 57.65; H, 3.86; X (*Halogen*), 27.80.

4-Chloro-2-iodo-6-(5-naphthalen-1-yl-4,5-dihydro-1*H*-pyrazol-3-yl)-phenol. 1d:IR (KBr Pellets): 1594 (C=N), 1426, 1520 (C=C), 1226, 1120 (C-N) cm^{-1}. ^1H NMR (300 MHz, DMSO-d_6) δ 12.10 (s, 1H, OH), 6.80 (s, 1H, NH), 7.20-8.31 (m, 9H, Ar-H), 3.04 (dd, *J* = 5.1, 18.1 Hz, 1H, H_A), 3.86 (dd, *J* = 12.2, 18.1 Hz, 1H, H_B), 5.60 (dd, *J* = 5.1, 12.2, 1H, H_X). ^{13}C NMR (DMSO): 157.86 (C *of* Ar-OH), 154.37 (C *of* C=N), 138.47-115.32 (C *of Aromatic ring*), 58.43 (C *of* CH), 43.68 (C of CH_2). MS m/z: 448 (M^+). Anal. Cacl for $C_{19}H_{14}N_2OICl$: C, 50.89; H, 3.12; X (*Halogen*), 36.16. Found: C, 50.83; H, 3.15; X (*Halogen*), 36.12.

2-Bromo-6-methyl-4-(5-naphthalen-1-yl-4,5-dihydro-1*H*-pyrazol-3-yl)-phenol. 1e:IR (KBr Pellets): 1596 (C=N), 1430, 1524 (C=C), 1222, 1116 (C-N) cm^{-1}. ^1H NMR (300 MHz, DMSO-d_6) δ 10.24 (s, 1H, OH),6.84 (s, 1H, NH), 7.16-8.21 (m, 9H, Ar-H), 3.03 (dd, *J* = 5.2, 18.2 Hz, 1H, H_A), 3.87 (dd, *J* = 12.1, 18.1 Hz, 1H, H_B), 5.63 (dd, *J* = 5.2, 12.2, 1H, H_X), 2.10 (s, 3H, CH_3) ^{13}C NMR (DMSO): 157.59 (C *of* Ar-OH), 153.73 (C *of* C=N), 139.34-114.81 (C *of Aromatic ring*), 56.98 (C *of* CH), 42.73 (C of CH_2), 12.14 (C *of* CH_3).MS m/z: 381 (M^+). Anal. Cacl for $C_{20}H_{17}N_2OBr$: C, 62.99; H, 4.46; X (*Halogen*), 20.99. Found: C, 62.97; H, 4.50; X (*Halogen*), 20.96.

2-Iodo-6-methyl-4-(5-naphthalen-1-yl-4,5-dihydro-1*H*-pyrazol-3-yl)-phenol. 1f:IR (KBr Pellets): 1592 (C=N), 1438, 1528 (C=C), 1227, 1122 (C-N) cm^{-1}. ^1H NMR (300 MHz, DMSO-d_6) δ 10.21 (s, 1H, OH),6.80 (s, 1H, NH), 7.19-8.25 (m, 9H, Ar-H), 3.01 (dd, *J* = 5.1, 18.2 Hz, 1H, H_A), 3.85 (dd, *J* = 12.0, 18.1 Hz, 1H, H_B), 5.68 (dd, *J* = 5.1, 12.1, 1H, H_X), 2.12 (s, 3H, CH_3). ^{13}C NMR (DMSO): 158.12 (C *of* Ar-OH), 153.41 (C *of* C=N), 138.30-114.72 (C *of Aromatic ring*), 56.80 (C *of* CH), 42.67 (C of CH_2),12.12 (C *of* CH_3).MS m/z: 428 (M^+). Anal. Cacl for $C_{20}H_{17}N_2OI$: C, 56.07; H, 3.97; X (*Halogen*), 29.67. Found: C, 56.12; H, 3.95; X (*Halogen*), 29.70.

2,6-Dichloro-4-(5-naphthalen-1-yl-4,5-dihydro-1*H*-pyrazol-3-yl)-phenol. 1g:IR (KBr Pellets): 1590 (C=N), 1425, 1523 (C=C), 1230, 1122 (C-N) cm^{-1}. ^1H NMR (300 MHz, DMSO-d_6) δ 10.24 (s, 1H, OH),6.78 (s, 1H, NH), 7.16-8.20 (m, 9H, Ar-H), 3.02 (dd, *J* = 5.0, 18.1 Hz, 1H, H_A), 3.87 (dd, *J* = 12.1, 18.0 Hz, 1H, H_B), 5.57 (dd, *J* = 5.1, 12.1, 1H, H_X). ^{13}C NMR (DMSO): 158.79 (C *of* Ar-OH), 153.66 (C *of* C=N), 136.21-113.53 (C *of Aromatic ring*), 57.13 (C *of* CH), 42.83 (C of CH_2).MS m/z: 356 (M^+).Anal. Cacl for $C_{19}H_{14}N_2Cl_2O$: C, 64.04; H, 3.93; X (*Halogen*), 19.66. Found: C, 64.10; H, 3.97; X (*Halogen*), 19.71.

2,4-Dichloro-6-(5-naphthalen-1-yl-4,5-dihydro-1*H*-pyrazol-3-yl)-benzene-1,3-diol. 1h:IR (KBr Pellets): 1592 (C=N), 1428, 1528 (C=C), 1226, 1123 (C-N) cm^{-1}. ^1H NMR (300 MHz, DMSO-d_6) δ 12.14 (s, 1H, OH),10.21 (s, 1H, OH), 6.80 (s, 1H, NH), 7.21-8.24 (m, 8H, Ar-H), 3.04 (dd, *J* = 5.1, 18.0 Hz, 1H, H_A), 3.85 (dd, *J* = 12.1, 18.0 Hz, 1H, H_B), 5.58 (dd, *J* = 5.1, 12.0, 1H, H_X). ^{13}C NMR (DMSO): 158.83 (C *of* Ar-OH), 153.69 (C *of* C=N), 139.32-115.57 (C *of Aromatic ring*), 57.17 (C *of* CH), 42.79 (C of CH_2).MS m/z: 373 (M^+).Anal. Cacl for $C_{19}H_{14}N_2O_2Cl_2$: C, 61.29; H, 3.76; X (*Halogen*), 18.81. Found: C, 61.34; H, 3.74; X (*Halogen*), 18.85.

2-Bromo-4-chloro-3-methyl-6-(5-naphthalen-1-yl-4,5-dihydro-1*H*-pyrazol-3-yl)-phenol. 1i:IR (KBr Pellets): 1592 (C=N), 1432, 1528 (C=C), 1229, 1120 (C-N) cm^{-1}. ^1H NMR (300 MHz, DMSO-d_6) δ 12.28 (s, 1H, OH),11.13 (s, 1H, OH), 6.80 (s, 1H, NH), 7.23-8.28 (m, 3H, Ar-H), 3.04 (dd, *J* = 5.1, 18.0 Hz, 1H, H_A), 3.85 (dd, *J* = 12.1, 18.0 Hz, 1H, H_B), 5.58 (dd, *J* = 5.1, 12.0, 1H, H_X),2.14 (s, 3H, CH_3). ^{13}C NMR (DMSO): 157.96 (C *of* Ar-OH), 153.74 (C *of* C=N), 140.18-116.46 (C *of Aromatic ring*), 57.23 (C *of* CH), 42.65 (C of CH_2), 12.17 (C *of* CH_3).MS m/z: 633 (M^+). Anal. Cacl for $C_{16}H_{12}N_2O_2I_2ClBr$: C, 30.33; H, 1.89; X (*Halogen*), 58.29. Found: C, 30.29; H, 1.92; X (*Halogen*), 58.35.

2-Bromo-4-chloro-6-(5-naphthalen-1-yl-1-phenyl-4,5-dihydro-1*H*-pyrazol-3-yl)-phenol. 2a:IR (KBr Pellets): 1598 (C=N), 1428, 1518 (C=C), 1230, 1122 (C-N) cm^{-1}. ^1H NMR (300 MHz, DMSO-d_6) δ 12.14 (s, 1H, OH), 7.38-8.20 (m, 14H, Ar-H),3.10 (dd, *J* = 5.3, 18.2 Hz, 1H, H_A), 3.84 (dd, *J* = 12.2, 18.2 Hz, 1H, H_B), 5.58 (dd, *J* = 5.2, 12.2, 1H, H_X).^{13}C NMR (DMSO): 157.65 (C *of* Ar-OH), 155.21 (C *of* C=N), 137.16-116.18 (C *of Aromatic ring*), 58.62 (C *of* CH), 42.65 (C of CH_2).MS m/z: 478(M^+). Anal. Cacl for $C_{25}H_{18}N_2OBrCl$: C, 62.76; H, 3.76; X (*Halogen*), 24.16. Found: C, 62.79; H, 3.74; X (*Halogen*), 24.20.

4-Chloro-2-iodo-3-methyl-6-(5-naphthalen-1-yl-1-phenyl-4,5-dihydro-1*H*-pyrazol-3-yl)-phenol. 2b:IR (KBr Pellets): 1592 (C=N), 1432, 1567 (C=C), 1228, 1127 (C-N) cm^{-1}. ^1H NMR (300 MHz, DMSO-d_6) δ 12.10 (s, 1H, OH), 7.25-8.34 (m, 13H, Ar-H),3.08 (dd, *J* = 5.2, 18.1 Hz, 1H, H_A), 3.82 (dd, *J* = 12.2, 18.1 Hz, 1H, H_B), 5.59 (dd, *J* = 5.1, 12.2, 1H, H_X), 2.11 (s, 3H, CH_3).^{13}C NMR (DMSO): 158.18 (C *of* Ar-OH), 154.86 (C *of* C=N), 139.24-114.23 (C *of Aromatic ring*), 58.47 (C *of* CH), 43.23 (C of CH_2), 12.29 (C *of* CH_3).MS m/z: 539 (M^+). Anal. Cacl for $C_{26}H_{20}N_2OICl$: C, 57.88; H, 3.71; X (*Halogen*), 30.14. Found: C, 57.81; H, 3.74; X (*Halogen*), 30.20.

2-Bromo-4-chloro-3-methyl-6-(5-naphthalen-1-yl-1-phenyl-4,5-dihydro-1*H*-pyrazol-3-yl)-phenol. 2c:IR (KBr Pellets): 1590 (C=N), 1445, 1527 (C=C), 1224, 1133 (C-N) cm^{-1}. ^1H NMR (300 MHz, DMSO-d_6) δ 12.08 (s, 1H, OH), 7.28-8.30 (m, 13H, Ar-H),3.08 (dd, *J* = 5.2, 18.1 Hz, 1H, H_A), 3.80 (dd, *J* = 12.2, 18.2 Hz, 1H, H_B), 5.60 (dd, *J* = 5.2, 12.2, 1H, H_X), 2.10 (s, 3H, CH_3).^{13}C NMR (DMSO): 157.98 (C *of* Ar-OH), 154.79 (C *of* C=N), 139.27-114.19 (C *of Aromatic ring*), 58.44 (C *of* CH), 43.27 (C of CH_2), 12.27 (C *of* CH_3).MS m/z: 492 (M^+). Anal. Cacl for $C_{26}H_{20}N_2OBrCl$: C, 63.41; H, 4.06; X (*Halogen*), 23.47. Found: C, 63.45; H, 4.08; X (*Halogen*), 23.50.

4-Chloro-2-iodo-6-(5-naphthalen-1-yl-1-phenyl-4,5-dihydro-1*H*-pyrazol-3-yl)-phenol. 2d: IR (KBr Pellets): 1596 (C=N), 1424, 1522 (C=C), 1234, 1127 (C-N) cm^{-1}. ^1H NMR (300 MHz, DMSO-d_6) δ 12.13 (s, 1H, OH), 7.36-8.24 (m, 14H, Ar-H),3.09 (dd, *J* = 5.2, 18.2 Hz, 1H, H_A), 3.82 (dd, *J* = 12.1, 18.2 Hz, 1H, H_B), 5.59 (dd, *J* = 5.2, 12.2, 1H, H_X),^{13}C NMR (DMSO): 157.69 (C *of* Ar-OH), 155.17 (C *of* C=N), 137.21-116.12 (C *of Aromatic ring*), 58.65 (C *of* CH), 42.67 (C of CH_2).MS m/z:525 (M^+). Anal. Cacl for $C_{25}H_{18}N_2OICl$: C, 57.14; H, 3.42; X (*Halogen*), 30.95. Found: C, 57.18; H, 3.45; X (*Halogen*), 30.98.

2-Bromo-6-methyl-4-(5-naphthalen-1-yl-1-phenyl-4,5-dihydro-1*H*-pyrazol-3-yl)-phenol. 2e: IR (KBr Pellets): 1592 (C=N), 1428, 1529 (C=C), 1237, 1123 (C-N) cm^{-1}. ^1H NMR (300 MHz, DMSO-d_6) δ 10.13 (s, 1H, OH), 7.42-8.21 (m, 14H, Ar-H),3.12 (dd, *J* = 5.3, 18.2 Hz, 1H, H_A), 3.86 (dd, *J* = 12.2, 18.2 Hz, 1H, H_B), 5.57 (dd, *J* = 5.2, 12.2, 1H, H_X), 2.13 (s, 3H, CH_3).^{13}C NMR (DMSO): 157.73 (C *of* Ar-OH), 155.24 (C *of* C=N), 139.82-115.37 (C *of Aromatic ring*), 58.68 (C *of* CH), 42.70 (C of CH_2), 12.17 (C *of* CH_3).MS m/z:457 (M^+). Anal. Cacl for $C_{26}H_{21}N_2OBr$: C, 68.27; H, 4.59; X (*Halogen*), 17.50. Found: C, 68.23; H, 4.63; X (*Halogen*), 17.44.

2-Iodo-6-methyl-4-(5-naphthalen-1-yl-1-phenyl-4,5-dihydro-1*H*-pyrazol-3-yl)-phenol. 2f:IR (KBr Pellets): 1593 (C=N), 1426, 1529 (C=C), 1235, 1121 (C-N) cm^{-1}. ^1H NMR (300 MHz, DMSO-d_6) δ 10.11 (s, 1H, OH), 7.40-8.18 (m, 14H, Ar-H),3.10 (dd, *J* = 5.1, 18.1 Hz, 1H, H_A), 3.84 (dd, *J* = 12.1, 18.1 Hz, 1H, H_B), 5.56 (dd, *J* = 5.2, 12.1, 1H, H_X), 2.10 (s, 3H, CH_3).^{13}C NMR (DMSO): 157.65 (C *of* Ar-OH), 155.29 (C *of* C=N), 137.20-112.31 (C *of Aromatic ring*), 58.65 (C *of* CH), 42.65 (C of CH_2), 12.13 (C *of* CH_3).MS m/z:504 (M^+). Anal. Cacl for $C_{26}H_{21}N_2OIl$: C, 61.90; H, 4.16; X (*Halogen*), 25.19. Found: C, 61.92; H, 4.14; X (*Halogen*), 25.24.

2,6-Dichloro-4-(5-naphthalen-1-yl-1-phenyl-4,5-dihydro-1*H*-pyrazol-3-yl)-phenol. 2g:IR (KBr Pellets): 1595 (C=N), 1429, 1532 (C=C), 1230, 1124 (C-N) cm^{-1}. ^1H NMR (300 MHz, DMSO-d_6) δ 10.15 (s, 1H, OH), 7.36-8.21 (m, 14H, Ar-H),3.12 (dd, *J* = 5.2, 18.2 Hz, 1H, H_A), 3.86 (dd, *J* = 12.1, 18.2 Hz, 1H, H_B), 5.54 (dd, *J* = 5.2, 12.1, 1H, H_X).^{13}C NMR (DMSO): 157.73 (C *of* Ar-OH), 155.26 (C *of* C=N), 135.24-115.49 (C *of Aromatic ring*), 58.68 (C *of* CH), 42.63 (C of CH_2).MS m/z:432 (M^+). Anal. Cacl for $C_{25}H_{18}N_2Cl_2O$: C, 69.44; H, 4.16; X (*Halogen*), 16.20. Found: C, 69.40; H, 4.18; X (*Halogen*), 16.25.

2,4-Dichloro-6-(5-naphthalen-1-yl-1-phenyl-4,5-dihydro-1H-pyrazol-3-yl)-benzene-1,3-diol. 2h: IR (KBr Pellets): 1593 (C=N), 1428, 1530 (C=C), 1232, 1125 (C-N) cm^{-1}. ^1H NMR (300 MHz, DMSO-d_6) δ 10.15 (s, 1H, OH), 12.17 (s, 1H, OH), 7.43-8.19 (m, 13H, Ar-H),3.08 (dd, *J* = 5.1, 18.1 Hz, 1H, H_A), 3.84 (dd, *J* = 12.1, 18.1 Hz, 1H, H_B), 5.56 (dd, *J* = 5.1, 12.1, 1H, H_X).^{13}C NMR (DMSO): 157.79 (C *of* Ar-OH), 155.29 (C *of* C=N), 139.81-116.42 (C *of Aromatic ring*), 58.69 (C *of* CH), 42.65 (C of CH_2).MS m/z: 448 (M^+)Anal. Cacl for $C_{25}H_{18}N_2O_2Cl_2$: C, 66.96; H, 4.01; X (*Halogen*), 15.62. Found: C, 66.90; H, 4.07; X (*Halogen*), 15.66.

2-Bromo-4-chloro-6-[1-phenyl-5-(3,4,5-trimethoxy-phenyl)-4,5-dihydro-1H-pyrazol-3-yl]-phenol. 2k: IR (KBr Pellets): 1595 (C=N), 1432, 1534 (C=C), 1236, 1128 (C-N) cm^{-1}. ^1H NMR (300 MHz, DMSO-d_6) δ 12.13 (s, 1H, OH), 7.23-8.07 (m, 9H, Ar-H),3.11 (dd, *J* = 5.2, 18.1 Hz, 1H, H_A), 3.82 (dd, *J* = 12.0, 18.1 Hz, 1H, H_B), 5.53 (dd, *J* = 5.1, 12.0, 1H, H_X), 3.76 (s, 9H, OCH_3).^{13}C NMR (DMSO): 157.79 (C *of* Ar-OH), 155.29 (C *of* C=N), 139.81-116.42 (C *of Aromatic ring*), 58.69 (C *of* CH), 42.65 (C of CH_2).MS m/z:518 (M^+)Anal.Cacl for $C_{24}H_{22}O_4N_2ClBr$: C, 55.59; H, 4.24; X (*Halogen*), 22.29. Found: C, 55.64; H, 4.19; X (*Halogen*), 22.33.

Table-1: Physical data of some novel 2*H*-pyrazolines

Compound No.	Time in min.[a]	Yield in %[b]	Melting point (^{0}C)
1a	08	78	126-128
1b	10	72	105-107
1c	11	80	190-192
1d	10	74	138-140
1e	12	77	120-122
1f	14	80	140-142
1g	10	82	126-127
1h	09	85	142-145
1i	12	90	146-147
1j	10	83	184-186
1k	14	76	180-181
1l	14	89	198-199

Table-2: Physical data of some novel *N*-phenylpyrazolines

Compound No.	Time in min.[a]	Yield in %[b]	Melting point (^{0}C)
2a	**10**	83	200-201
2b	**14**	74	198-200
2c	**12**	72	220-221
2d	**10**	76	195-196
2e	**13**	83	115-117
2f	**16**	79	196-197
2g	**14**	75	140-141
2h	**12**	81	110-112
2i	**10**	80	120-122
2j	**13**	73	122-123
2k	**15**	95	182-184
2l	**10**	90	196-197

Result and discussion

In continuation of our earlier research work towards novel methodology in organic synthesis using 2-methoxyethanol[x], we report herein first time the synthesis of some new series of pyrazolines by the reaction of substituted hydroxychalcones with hydrazine hydrate and phenyl hydrazine in 2-methoxyethanol under mild basic condition using conventional heating method (Scheme **1**).

The required starting chalcones were prepared by classical aldol condensation involving base-catalyzed condensation of the desired carbonyl compounds with aldehyde followed by dehydration forming α,β-unsaturated carbonyl compounds[xi]. The resulted substituted

hydroxychalcones 0.01 mol and hydrazine hydrate 0.02 mol in 10 ml 2-methoxyethanol using piperidine 0.001 mmol were refluxed for 8-14 minutes as indicated by TLC to yield 2-pyrazoline. Recently the formation of 2-pyrazoline was reported by the reaction of chalcones with hydrazine hydrate take place in various conditions using ethanol, acetic acid, formic acid, or pyridine as solvent[xii]. However, many of these reported procedures have one or more disadvantages such as use of expensive catalyst, low selectivity, harsh reaction conditions, low yield, relatively long reaction time and environmental concern. After some preliminary observation we found that 2-methoxyethanol as an efficient reaction medium in terms of clean reaction conditions, not expensive, short reaction time giving high yields of desired product. In view of these findings, we turned our attention towards variety substituted hydroxychalcones. In all cases, reaction proceeds efficiently in high yields using 2-methoxyethanol (Table-**3**).

Table-3: The effect of various solvent on synthesis of 2-Bromo-4-chloro-6-[1-phenyl-5-(3,4,5-trimethoxy-phenyl)-4,5-dihydro-1H-pyrazol-3-yl]-phenol. 2k:

Entry	Solvent Used	Time required for completion of reaction	Yield (%)
1	EtOH	2 and ½ hr.	72
2	Acetic acid	3 hr.	65
3	DMF	3 and ½ hr	70
4	Dioxane	2 hr.	63
5	2-methoxyethanol	10 min.	94

The formation of products were assumed to proceed through the Micheal-type addition of hydrazine to activated double bond followed by intramolecular cyclization with the elimination of water molecule[xiv]. The reaction went to completion within 4 min and corresponding product obtained in 93 % yield. The IR spectra of title compounds show absence of carbonyl absorption band and appearance of characteristic absorption band near 1592 cm^{-1} for C=N. In the ^1H NMR spectrum, an ABX pattern was observable for three proton of pyrazoline nucleus. H_A, H_B and H_X appear as double doublets at δ 3.04, 3.85 and 5.58 ppm respectively. Similarly other analog derivatives are prepared by using same procedure, in all cases the reaction proceeds smoothly in high yields of product.

Conclusion

We have reported simple and efficient synthetic protocol for synthesis of 2-pyrazoline derivatives using 2-methoxyethanol under microwave irradiation. Method has several advantages such as, simple reaction procedure with easy isolation of product, short reaction time period and higher yields.

Acknowledgement

The authors gratefully acknowledge UGC-New Delhi for sanctioning major research grant (No. 38-267/2009). The authors are also thankful to principal, Yeshwant Mahavidyalaya, Nanded, for

providing laboratory facilities and Director of Indian Institute of Chemical Technology (IICT), Hyderabad, for providing necessary instrumental facilities.

References

i. Rathish I.G., Javed K., Ahmad S., Bano S., Alam M. S., Pillai K. K.,Singh S., Bagchi V. Bioorg.Med.Chem.Lett. 19 (2009) 255.

ii. Acharya B.N., Saraswat D., Tiwari M., Shivastava A.K., Ghorpade R., Bapna S., Kaushik M.P. Eur.J.Med.Chem. 45 (2010) 430.

iii. Manna F., Chimenti F., Bolasco A., Rossi F. Cenicola M.L., D'Amico M., Parrillo C. Pharmacological research 26 (1992) 267.

iv. Prasad Y.R., Rao A.L., Prasoona L., Murali K., Ravi Kumar P. Bioorg.Med.Chem.Lett. 15 (2005) 5030.

v. Banday A.H., Mir B.P., Lone I.H., Suri K.A. Steroids 75 (2010) 805.

vi. Mohammad S., Anees Ahamed S., Mohamed Ashraf A., Dharmarajan S., Perumal Y. Bioorg. Med.Chem.Lett. 16 (2006) 3947.

vii. Geeta J. P., Pramod Singh; Rawat B. S., Mohan Rawat S. M., Joshi G.C. Spectrochim Acta. Part: A 78 (2011). 1075.

viii. Werner S., Gunther M., Ferdinand B., Reto B., Robert S., Robert W. Tetrahedron 59 (2003) 2811.

ix. (a) Zangade S.B., Mokle S.S., Shinde A.T., Vibhute Y.B. Green Chem.Lett.Rev. 6 (2013) 123; (b) Chavan S., Zangade S., Vibhute A., Vibhute Y. Eur.J.Chem. 4 (2013) 98; (c) Zangade S., Mokle S., Shinde A.; Vibhute Y. Eur.J.Chem. 3 (2012) 314.

x. (a) Zangade S., Shinde A., Patil A., Vibhute Y. Eur.J.Chem. 3 (2012) 208; (b) Zangade S., Mokle S., Chavan S., Vibhute Y. Orbital: Electron.J.Chem. 3(2011) 144; (c) Zangade S., Shinde A., Sundge S., Vibhute Y. Analele Universitatii din Bucuresti. 20 (2011) 141. (d) Zangade S.B., Shinde A.T., Vibhute A.Y., Vibhute Y.B. Pak.J.Chem. 2 (2012) 18.

xi. Nalwar Y.S., Sayyed M.A., Mokle S.S., Zanwar P.R. Vibhute Y.B. World J.Chem. 4 (2009) 123.

xii. (a) Pramod Singh; Negi J.S.; Pant G.J.; Rawant Mohan S. M.; Budakoti A. Molbank. (2009) M 61; (b) Raiford L. C.; Peterson W. J. J. Org. Chem. 1 (1937) 544; (c) Levai A. J. Heterocyl. Chem. 35 (1998) 13; (c) Sharma T. C.; Pawar S. R.; Reddy N. J. Acta a Chim. Hung. 112 (1983) 159.

xiv. ElGaby M.S.A.; Sayed A. Z.; Abu-Shanab F. A.; Hes-sein A. M. Phosphorous Sulphur Silicon 164 (2000), 1.

Received on July 3, 2013