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A CONVENIENT MICROWAVE INDUCED SYNTHESIS OF SOME NOVEL PYRAZOLINES CONTAINING SUBSTITUTED BENZYLOXY PHENYL RING SYSTEM

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Abstract
A convenient microwave assisted condensation of substituted chalcones with hydrazine hydrate using 2-methoxyethanol to yield novel substituted 2-pyrazoline derivatives. The method has several advantages in comparison with classical synthesis including clean reaction procedure, easy workup, and short reaction time giving excellent yields of product. Newly synthesized 2-pyrazolines were established on the basis of spectral technique.

Keywords: Pyrazolines, substituted chalcones, benzyloxy phenyl ring, microwave irradiation.

Introduction

Pyrazolines constitute an interesting class of heterocyclic compounds including various diverse chemical, pharmacological applications and great importance in heterocyclic chemistry. The aromatic compounds containing pyrazolines as basic nucleus have known to possess anti-inflammator[y], antimalarial[ii], analgesic[iii], antidepressant[iv], anticancer[v] and antimycobacterial[vi]. Various 2-pyrazolines exhibit good properties of photoluminescence, electroluminescence and as fluroescence[vii]. A classical synthesis of pyrazolines involes, the condensation of α,β- unsaturated carbonyl compounds with hydrazine hydrate is commonly used[viii]. In view of these applications of five membered heterocycles, it was thought worthwhile to synthesize some novel pyrazoline derivatives by the condensation of different substituted chalcones 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. A multimode microwave oven (2450 MHz, 300 W, Brand LG, India) were used for performing reaction.

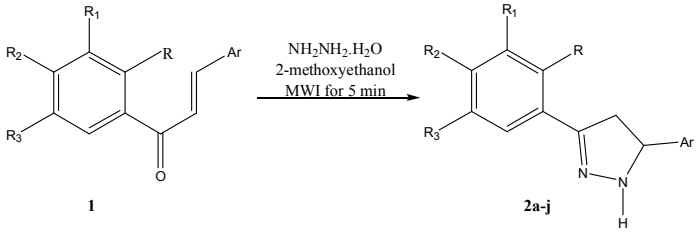
Typical procedure for synthesis of 2-pyrazolines derivatives

Preparation of 3-(2'-hydroxy-3',5'-dichloro phenyl)-5(2-benzyloxy phenyl)-pyrazoline (3a)

A mixture of 3-[2-Benzyloxy-phenyl]-1-[3,5-dichloro-2-hydroxy-phenyl]-propenone [0.01 mole] and hydrazine hydrate [0.02 mole] in 2-methoxyethanol [8 ml] were irradiated for 5 minutes in microwave oven. The progress of reaction monitored on TLC. The reaction mixture was cooled and poured in ice cold water. The solid was separated was filtered washed with ethanol and then with water, dried and crystallized from ethanol to give pure 2-pyrazoline derivative.

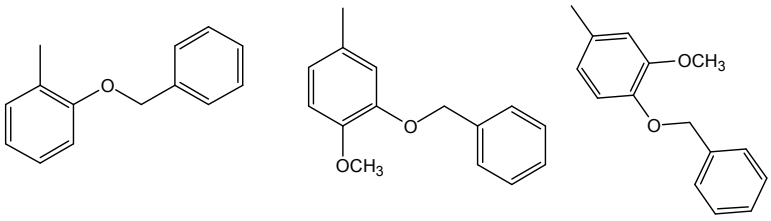
Similar other substituted derivatives were prepared by using same procedure. The physical and analytical data of **2a-j** pyrazolines are reported in table **1**.

Scheme 1

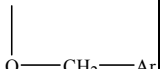
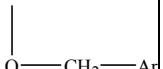


1 2a-j

Where Ar



3a 3b 3c

Entry	Substitutents				Ar
	R	R_1	R_2	R_3	
2a	OH	Cl	H	Cl	3a
2b	OH	Br	H	CH_3	3b
2c	OH	Cl	H	Cl	3b
2d	Cl	Cl	Cl	H	3b
2e	OH	H	CH_3	Cl	3c
2f	OH	Cl	H	Cl	3c
2g	H		H		3b
2h	OH	H	CH_3	Cl	3b
2i	OH	I	H	CH_3	3b
2j	OH	Br	CH_3	Cl	3b

Spectral Analysis of compound 2a-j

2a. 2-[5-(2-Benzyloxy-phenyl)-4,5-dihydro-1H-pyrazol-3-yl]-4,6-dichloro-phenol: IR (KBr pellets): 3367 (N-H), 1592 (C=N), 1473, 1542 (C=C), 1232 (C-N) cm^{-1}. ^1H NMR (300 MH_Z, DMSO-d_6) δ 11.8 (s, 1H, OH), 6.8-7.6 (m, 11H, Ar-H), 6.8 (s, 1H, NH), 3.2 (dd, *J* = 5.0, 17.2 H_Z, 1H, H_A), δ 3.6 (dd, *J* = 12.0, 17.3 H_Z, 1H, H_B), δ 4.8 (dd, *J* = 5.1, 12.0 H_Z, 1H, H_X), 5.1 (s, 2H, OCH_2). MS (EI, *m/z*: 413 [M^+], 395, 377, 321, 291, 275, 257, 239, 165, 151, 120, 107, 91, 77, 65, 51.

2b. 2-[5-(3-Benzyloxy-4-methoxy-phenyl)-4,5-dihydro-1H-pyrazol-3-yl]-6-bromo-4-methyl-phenol: IR (KBr pellets): 3365 (N-H), 1590 (C=N), 1480, 1545 (C=C), 1238 (C-N) cm^{-1}. ^1H NMR (300 MH_Z, DMSO-d_6) δ 11.9 (s, 1H, OH), 6.8-7.7 (m, 10H, Ar-H), 6.7 (s, 1H, NH), 3.2 (dd, *J* = 5.1, 17.1 H_Z, 1H, H_A), δ 3.7 (dd, *J* = 12.0, 17.2 H_Z, 1H, H_B), δ 4.8 (dd, *J* = 5.1, 12.0 H_Z, 1H, H_X), 5.1 (s, 2H, OCH_2), 3.8 (s, 3H, OCH_3), 3.1 (s, 3H, CH_3). MS (EI, *m/z*: 467 [M^+].

2c. 2-[5-(3-Benzyloxy-4-methoxy-phenyl)-4,5-dihydro-1H-pyrazol-3-yl]-4,6-dichloro-phenol: IR (KBr pellets): 3364 (N-H), 1589 (C=N), 1478, 1549 (C=C), 1234 (C-N) cm^{-1}. ^1H NMR (300 MH_Z, DMSO-d_6) δ 11.9 (s, 1H, OH), 6.7-7.7 (m, 10H, Ar-H), 6.7 (s, 1H, NH), 3.2 (dd, *J* = 5.1, 17.1 H_Z, 1H, H_A), δ 3.6 (dd, *J* = 12.1, 17.1 H_Z, 1H, H_B), δ 4.8 (dd, *J* = 5.1, 12.1 H_Z, 1H, H_X), 5.1 (s, 2H, OCH_2), 3.7 (s, 3H, OCH_3). MS (EI, *m/z*: 442 [M^+].

2d. 5-(3-Benzyloxy-4-methoxy-phenyl)-3-(2,3,4-trichloro-phenyl)-4,5-dihydro-1H-pyrazole: IR (KBr pellets): 3365 (N-H), 1590 (C=N), 1470, 1546 (C=C), 1237 (C-N) cm^{-1}. ^1H NMR (300 MH_Z, DMSO-d_6) δ 6.6-7.7 (m, 10H, Ar-H), 6.8 (s, 1H, NH), 3.2 (dd, *J* = 5.1, 17.1 H_Z, 1H, H_A), δ 3.7 (dd, *J* = 12.1, 17.2 H_Z, 1H, H_B), δ 4.8 (dd, *J* = 5.1, 12.1 H_Z, 1H, H_X), 5.1 (s, 2H, OCH_2), 3.7 (s, 3H, OCH_3). MS (EI, *m/z*: 460 [M^+].

2e. 2-[5-(4-Benzyloxy-3-methoxy-phenyl)-4,5-dihydro-1H-pyrazol-3-yl]-4-chloro-5-methyl-phenol: IR (KBr pellets): 3367 (N-H), 1592 (C=N), 1480, 1545 (C=C), 1235 (C-N) cm^{-1}. ^1H NMR (300 MH_Z, DMSO-d_6) δ 11.8 (s, 1H, OH), 6.7-7.8 (m, 10H, Ar-H), 6.7 (s, 1H, NH), 3.2 (dd, *J* = 5.2, 17.1 H_Z, 1H, H_A), δ 3.7 (dd, *J* = 12.2, 17.1 H_Z, 1H, H_B), δ 4.8 (dd, *J* = 5.1, 12.1 H_Z, 1H, H_X), 5.1 (s, 2H, OCH_2), 3.7 (s, 3H, OCH_3), 3.1 (s, 3H, CH_3). MS (EI, *m/z*: 422 [M^+].

2f. 2-[5-(4-Benzyloxy-3-methoxy-phenyl)-4,5-dihydro-1H-pyrazol-3-yl]-4,6-dichloro-phenol: IR (KBr pellets): 3364 (N-H), 1594 (C=N), 1470, 1547 (C=C), 1236 (C-N) cm^{-1}. ^1H NMR (300 MH_Z, DMSO-d_6) δ 11.8 (s, 1H, OH), 6.7-7.6 (m, 10H, Ar-H), 6.7 (s, 1H, NH), 3.2 (dd, *J* = 5.1, 17.1 H_Z, 1H, H_A), δ 3.6 (dd, *J* = 12.1, 17.1 H_Z, 1H, H_B), δ 4.8 (dd, *J* = 5.1, 12.1 H_Z, 1H, H_X), 5.1 (s, 2H, OCH_2), 3.8 (s, 3H, OCH_3). MS (EI, *m/z*: 477 [M^+].

2g. 5-(3-Benzyloxy-4-methoxy-phenyl)-3-(3,5-bis-benzyloxy-phenyl)-4,5-dihydro-1H-pyrazole: IR (KBr pellets): 3367 (N-H), 1592 (C=N), 1478, 1549 (C=C), 1234 (C-N) cm^{-1}. ^1H NMR (300 MH_Z, DMSO-d_6) δ 11.8 (s, 1H, OH), 6.7-7.9 (m, 20H, Ar-H), 6.8 (s, 1H, NH), 3.3 (dd, *J* = 5.2, 17.3 H_Z, 1H, H_A), δ 3.7 (dd, *J* = 12.2, 17.2 H_Z, 1H, H_B), δ 4.8 (dd, *J* = 5.2, 12.1 H_Z, 1H, H_X), 5.1 (s, 2H, OCH_2), 5.3 (s, 4H, OCH_2), 3.8 (s, 3H, OCH_3). MS (EI, *m/z*: 570 [M^+].

2h. 4-Chloro-2-[5-(4-methoxy-3-phenoxy-phenyl)-4,5-dihydro-1H-pyrazol-3-yl]-5-methyl-phenol: IR (KBr pellets): 3368 (N-H), 1594 (C=N), 1468, 1540 (C=C), 1231 (C-N) cm^{-1}. ^1H NMR (300 MH_Z, DMSO-d_6) δ 11.8 (s, 1H, OH), 6.7-7.8 (m, 10H, Ar-H), 6.7 (s, 1H, NH), 3.2 (dd, *J* = 5.2, 17.1 H_Z, 1H, H_A), δ 3.7 (dd, *J* = 12.2, 17.1 H_Z, 1H, H_B), δ 4.8 (dd, *J* = 5.1, 12.1 H_Z, 1H, H_X), 5.1 (s, 2H, OCH_2), 3.7 (s, 3H, OCH_3), 3.1 (s, 3H, CH_3). MS (EI, *m/z*: 422 [M^+].

2i. 2-Iodo-6-[5-(4-methoxy-3-phenoxy-phenyl)-4,5-dihydro-1H-pyrazol-3-yl]-4-methyl-phenol: IR (KBr pellets): 3362 (N-H), 1590 (C=N), 1475, 1552 (C=C), 1235 (C-N) cm^{-1}. ^1H NMR (300 MH_Z, DMSO-d_6) δ 11.7 (s, 1H, OH), 6.7-7.6 (m, 10H, Ar-H), 6.7 (s, 1H, NH), 3.2 (dd, *J* = 5.1,

17.1 H_Z, 1H, H_A), δ 3.6 (dd, *J* = 12.1, 17.1 H_Z, 1H, H_B), δ 4.8 (dd, *J* = 5.1, 12.1 H_Z, 1H, H_X), 5.1 (s, 2H, OCH_2), 3.8 (s, 3H, OCH_3), 3.1 (s, 3H, CH_3). MS (EI, *m/z*: 514 [M^+].

2j. 2-Bromo-4-chloro-6-[5-(4-methoxy-3-phenoxy-phenyl)-4,5-dihydro-1H-pyrazol-3-yl]-3-methyl-phenol: IR (KBr pellets): 3367 (N-H), 1592 (C=N), 1476, 1545 (C=C), 1233 (C-N) cm^{-1}. ^1H NMR (300 MH_Z, DMSO-d_6) δ 11.8 (s, 1H, OH), 6.7-7.8 (m, 9H, Ar-H), 6.7 (s, 1H, NH), 3.2 (dd, *J* = 5.1, 17.1 H_Z, 1H, H_A), δ 3.7 (dd, *J* = 12.2, 17.1 H_Z, 1H, H_B), δ 4.8 (dd, *J* = 5.1, 12.2 H_Z, 1H, H_X), 5.1 (s, 2H, OCH_2), 3.8 (s, 3H, OCH_3), 3.1 (s, 3H, CH_3). MS (EI, *m/z*: 501 [M^+].

Table 1: Analytical and physical data of 2-pyrazoline derivatives

Entry	Mol. Formula	Mol. Wt.	M.P. ^0C	Yield (%)	Elemental Analysis found (Calc.)			
					C	H	N	X Cl, Br, I
4a	$C_{22}H_{18}O_2N_2Cl_2$	413	104	78	64.25 (64.07)	4.12 (4.63)	6.66 (6.79)	17.23 (17.33)
4b	$C_{24}H_{23}O_3N_2Br$	467	126	75	61.23 (61.67)	4.50 (4.92)	5.80 (5.99)	17.13 (16.98)
4c	$C_{23}H_{20}O_3N_2Cl_2$	443	214	80	62.01 (62.30)	4.44 (4.51)	6.02 (6.32)	16.02 (16.23)
4d	$C_{23}H_{19}O_2N_2Cl_3$	461.5	74	84	59.22 (59.8)	4.15 (4.11)	6.35 (6.06)	23.07 (23.34)
4e	$C_{24}H_{23}O_3N_2Cl$	422.5	172	78	68.53 (68.16)	5.11 (5.44)	6.34 (6.62)	8.40 (8.01)
4f	$C_{23}H_{20}O_3N_2Cl_2$	443	140	67	62.40 (62.30)	4.32 (4.51)	6.14 (6.32)	16.02 (16.22)
4g	$C_{37}H_{34}O_4N_2$	570	114	76	77.93 (77.89)	5.80 (5.96)	4.80 (4.91)	-
4h	$C_{24}H_{23}O_3N_2Cl$	422.5	108	82	68.01 (68.16)	5.52 (5.44)	6.58 (6.62)	8.40 (8.11)
4i	$C_{24}H_{22}O_3N_2I$	514	105	85	56.14 (56.03)	4.63 (4.47)	4.41 (5.44)	24.70 (24.12)
4j	$C_{24}H_{22}O_3N_2ClBr$	501.5	182	80	57.13 (57.42)	4.16 (4.38)	5.44 (5.58)	23.14 (23.03)

Result and discussion

Reported synthesis for 2-pyrazolines by the reaction between 2'-hydroxychalcones and hydrazine hydrate using 2-methoxyethanol under irradiation of tungsten light gives 92 % yield of desired the product [ix]. In view of theses, we reported the condensation of substituted chalcones with hydrazine hydrate using 2-methoxyethanol to yield novel substituted 2-pyrazoline derivatives under microwave irradiation (Scheme **1**). Microwave irradiation has been used to accelerate organic reactions because of high heating efficiency, providing remarkable rate enhancement, dramatic reduction in reaction times with improvement in yield and quality of products. Reactions that require hours or even days by conventional heating can often be accomplished in second or minutes by microwave heating [x]. Use of 2-methoxyethanol under

conventional technique has several advantages including clean reaction procedure, no need of catalyst, short reaction time and high yields of product.
The obtained 2-pyrazolines were characterized using spectroscopic technique, their IR spectra show absence of carbonyl absorption band and the appearance of characteristic absorption band for ν C=N at 1592-1588 cm^{-1} and a band at 1130 cm^{-1} for C-N. In the ^1H NMR spectrum, an ABX pattern was observable, H_A, H_B and H_X appear as double doublets at δ 3.10–3.30, 3.75–3.80 and 4.90–5.0 ppm with J_{AB} = 17.5 Hz, J_{AX} = 4.8 Hz, and J_{BX} = 11.8 Hz and singlet of 2-*H* pyrazolines around at δ 6.85 ppm respectively.

Conclusion

In summary we reported the synthesis of novel 2-pyrazolines containing benzyloxy phenyl ring system. The combination of microwave with 2-methoxyethanol found to be excellent and convenient reaction route in terms of simple reaction procedure, quick reaction time giving percent yield of product.

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. Zangade S., Shinde A., Patil A., Vibhute Y. Eur.J.Chem. 3 (2012) 208.
x. Shinde A., Zangade S., Chavan S., Vibhute Y. Org.Commun. 7 (2014) 60.

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