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Montmorrilonite K10 catalyzed efficient synthesis of some 4'-nitrochalcones and their 1, 3, 5-triaryl-2-pyrazolines and *in vitro* antimicrobial evaluation

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Abstract: An expeditious synthesis of some 4'-nitrochalcones **(3a-n)** and their subsequent facile one-pot transformation to 1, 3, 5-triaryl-2-pyrazolines **(4a-n)** has been carried out using montmorrilonite K10 via microwave mediated solvent free protocol. An emphasis is given to highlighting the greenness of the processes, and a fair comparison is also provided between different inorganic solid supports as catalysts. Both conventional as well as non-conventional approaches have been explored by comparing the reaction conditions and yields. The newly synthesized pyrazolines were studied for their *in vitro* antimicrobial evaluation against bacterial strains *Bacillus pumilus* and *Escherichia coli* and fungal strains *Aspergillus niger and Penicillium chrysogenum.* Findings of biological evaluation highlighted **4b**, **4e**, **4j** and **4m** as potential new leads in the search of new antimicrobial agents. The structures of newly synthesized compounds have been established on the basis of elemental analysis and spectroscopic studies.

Keywords: Chalcones, Pyrazolines, Montmorrilonite K10, Microwave, Antibacterial activity, Antifungal activity.

Introduction

Infectious diseases are one of the major causes of death worldwide [1]. During the past decades, new infectious disease has appeared and old ones previously throughout to be controlled to have reemerged and thus, despite many significant developments in the antimicrobial therapy, many problems remain to be solved for most of the antimicrobial drugs available [2]. Hence the discovery of new antimicrobial agents will be better pharmaceutical profile and is still highly desirable. In recent decades, the problems of multi-drug resistant microorganism have reached an alarming stage in many countries around the world.

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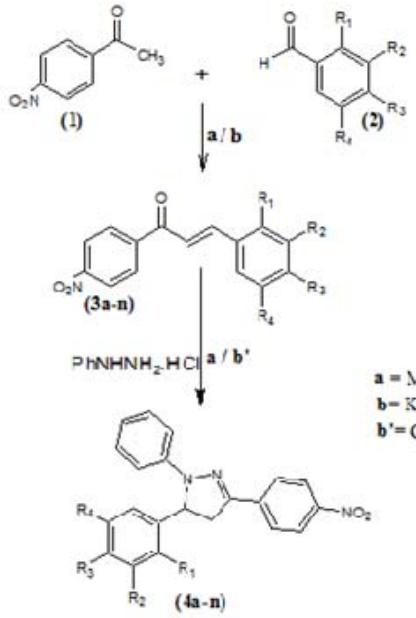
Infections caused by the microorganisms need for an effective therapy that has led to an escalating search for novel antimicrobial agents [3].

Small ring heterocycles containing nitrogen, sulphur and oxygen have been under investigation for a long time because of their pharmacological importance [4]. Chalcones possess a wide spectrum of biological activities [5-10] offers an unprecedented opportunity to synthetic chemists to design different bioactive heterocycles due to the presence of α, β-unsaturated carbonyl functionality. Nitrogen containing heterocycles like pyrazolines have received considerable attention in recent years due to their varied pharmacological activities such as antiviral [11], herbicidal [12], antimicrobial [13, 14], anti-inflammatory etc. [15]. On the other hand, non-conventional synthetic routes like inorganic solid supported microwave assisted organic reactions have

emerged as a new lead in organic synthesis with various advantages like highly accelerated rate of reaction, improvement of yield and quality of products [16-19]. In continuation of our earlier endeavor [20-22] to design and synthesis of novel bioactive heterocycles and keeping in view the advantages of heterogeneous catalysis for the synthesis of bioactive heterocycles; it was felt worth-while to synthesize some novel chalcones and their pyrazoline derivatives.

Firstly, a series of substituted 4′-nitrochalcones **(3a-n)** has been synthesized using montmorriolonite K10 as catalyst via Claisen-Schmidt condensation of 4-nitroactophenone and variously substituted aromatic aldehydes. Some of the starting chalcones have been reported by Sebti et al. [23, 24]. The synthesized chalcones on treatment with phenylhydrazine hydrochloride via clay catalysis afforded isomeric 1, 3, 5-triaryl-2-pyrazoline derivatives **(4a-n)** (Scheme 1).

Results and discussion



Entry 3 and 4	a	b	c	d	e	f	g	h	i	j	k	l	m	n
R_1	H	Cl	H	H	Cl	H	H	H	H	H	H	H	H	H
R_2	H	H	Cl	H	H	H	H	NO_2	H	H	OCH_3	OCH_3	OH	OCH_3
R_3	H	H	H	Cl	Cl	Br	F	H	CH_3	OCH_3	OCH_3	OCH_3	OCH_3	OH
R_4	H	H	H	H	H	H	H	H	H	H	H	OCH_3	H	Br

Scheme 1: Synthesis of 1,3,5-triaryl-2-pyrazolines.

For the said transformations, both conventional as well as non-conventional clay catalyzed microwave irradiation approaches have been explored and results have been shown in Table 1.

Table 1. Comparison of reaction time and yields of products **(3a-n and 4a-n)** under microwave and conventional method.

Compd.	Reaction time		yield/ %		Compd	Reaction time		yield/ %	
	MW/min	Conventional/h	MW	Conventional		MW/min	Conventional/h	MW	Conventional
3a	6	24	73	66	**4a**	5.5	9	74	65
3b	5	24	68	62	**4b**	5.5	8	79	68
3c	7	24	70	65	**4c**	6	10	78	65
3d	8	22	72	66	**4d**	6	10	80	67
3e	5	24	72	67	**4e**	6.5	9	76	61
3f	6	22	80	68	**4f**	7.5	8	77	63
3g	7	26	69	62	**4g**	6.5	11	79	65
3h	8	26	72	61	**4h**	6	10.5	80	67
3i	8	24	71	65	**4i**	8.0	10.5	82	65
3j	7	23	70	66	**4j**	5.5	10	83	66
3k	8	23	77	64	**4k**	7.5	11	84	68
3l	6	25	75	62	**4l**	6.0	10.5	80	67
3m	7	23	72	66	**4m**	7.0	11	82	67
3n	8	25	73	65	**4n**	8.0	12	79	65

In view of the immense utility of eco-friendly synthetic approaches, improved syntheses of pyrazolines were performed using different inorganic solid supports as heterogeneous catalysts under microwave irradiation. In this context, the suitability of different inorganic solid supports *i.e.*, acidic alumina, basic alumina, neutral alumina, montmorillonite K-10 and K_2CO_3 were examined in presence of microwave irradiation. According to (Table 2), the observed percentage yield of the products obtained with montmorrilonite K-10 clay as inorganic solid support is best than other solid supports and neat (without catalysts). This observation can be attributed to the more surface area and catalytic character in montmorrilonite K-10 than that of the other inorganic solids. Also, the clay possesses some advance properties like cation exchange capacity and swelling ability, thereby accommodating various guest species in its interlayers. An attempt has also been made to carried out the said transformation with different inorganic solid supports in the absentia of MW irradiation with conventional protocol resulted very poor yields (40-50%) confirms the MW irradiation as one of the best available energy sources.

Table 2. Different inorganic solid supports in non-conventional MW irradiated synthesis of (**4a**–**n).**

Exp. No.	Solid supports	MW Power, W	Time, min	Temp., °C	Yield, %
1.	Alumina acidic	700	9.0-10.0	73	59
2.	Alumina basic	700	11.0-12.0	79	70
3.	Alumina neutral	700	10.0-11.0	76	64
4.	Montmorillonite K 10	700	7.0-8.0	89	80
5.	K_2CO_3	700	12.5–13.5	72	65
6.	Nil	700	15	70	15

The products were identified by their spectral data, physical data (melting point, elemental analysis), and comparison with authentic ones FTIR spectra supported the above observation, a peak observed around at 1672-1695 (C=O stretching), 1631-1634 (-CH=CH stretching); ^{1}H NMR spectrum revealed the presence of a doublet at δ 7.49-7.62 corresponding to α hydrogen and doublet at δ 7.78-7.88 corresponding to for β hydrogen respectively **(3a-n)** and the structures of the newly synthesized compounds **(4a-n)** showed FTIR spectrum bands at 1570-1594 (C=C stretching), 1625-1650 (C=N stretching); ^{1}H NMR spectrum revealed the presence of a two double doublet at δ 3.01-3.28 and δ 3.49-3.78 corresponding to two hydrogen of -CH_2 of 2-pyrazolines and double doublet at δ 5.42- 5.88 corresponding to –CH- of 2-Pyrazolines.

Reusability is one of the important properties of this catalyst. In this study, due to the fact that the catalyst was insoluble in dichloromethane, it could therefore be recycled by a simple filtration. The separated catalyst was washed with dichloromethane, dried at 60°C under vacuum for 30 min. and reused in another reaction. The results show that there is no any significant loss of activity in using recycled catalyst after three times in the model reaction (Fig. 1).

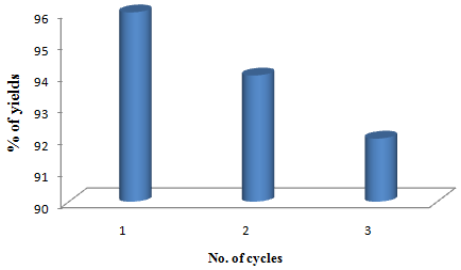


Figure 1. Recyclability of montmorrilonite clay K10

Antimicrobial evaluation:

All the newly synthesized pyrazolines **(4a-n)** were screened for their antimicrobial evaluation using chloramphenicol and fluconazole as positive controls. Table 3 shows that all the newly synthesized compounds **(4a-n)** were able to inhibit bacterial and fungal growth and create a zone of inhibition.

Table 3. Animicrobial activity of 1, 3, 5-triaryl-2-pyrazoline derivatives (**4a-n)**

Compounds	Zone of inhibition				Zone of inhibition			
	B. pumilis		*E. coli*		*A. niger*		*P.crysogenum*	
	0.05mL	0.1mL	0.05mL	0.1mL	0.05mL	0.1mL	0.05mL	0.1mL
4a	8	10	10	11	12	13	10	13
4b	10	13	11	12	15	18	15	17
4c	10	11	9	11	13	14	12	14
4d	9	10	9	10	12	14	13	15
4e	10	12	8	10	15	17	14	15
4f	9	11	8	10	13	15	9	11
4g	13	16	9	12	10	13	8	12
4h	12	13	11	13	9	11	9	13
4i	12	13	12	14	8	10	10	13
4j	14	16	12	13	9	10	11	14
4k	11	15	11	13	10	11	9	12
4l	13	14	10	12	10	11	12	15
4m	14	13	9	12	12	13	16	18
4n	13	14	8	11	11	13	12	14
Chloramphenicol	15	17	15	13	-	-	-	-
Fluconazole	-	-	-	-	15	16	15	17

The results revealed a significant inhibitory activity of all compounds against both fungal and bacterial strains. *Aspergillus* fungal strain shows higher susceptibility towards pyrazoline derivatives: ***(4b)*** and ***(4e)*** while growth of *Penicilium* fungal strain was maximum inhibited by ***(4m***). Growth of both bacterial strains *Bacillus* and *Escherichia* was inhibited maximum by ***(4j)***. The control plate did not exhibit inhibition on the tested fungi and bacteria where as positive controls Fluconazole and Chloramphenicol have antifungal and antibacterial activity even at 5µg/well respectively. The findings indicate that the newly synthesized pyrazoline derivatives can be used

as potent biocide as they showed maximum zone of inhibition nearly equal to the standard antifungal and antibacterial

Experimental Section

All melting points (m.ps.) were determined in open capillaries on Veego (VMP-PM) melting point apparatus and were uncorrected. The purity of the compounds was routinely checked by mixed mps and thin layer chromatography (TLC) with Silica Gel-G (Merck) plates using benzene: ethyl acetate (9:1 v/v) as eluent. The instruments used for spectroscopic data are; IR spectra was recorded in KBr on a Perkin-Elmer spectrophotometer model RX I (υ_{max} in cm^{-1}), ^1H NMR ($CDCl_3$) on 500 MHz and ^{13}C NMR ($CDCl_3$) on 125 MHz FT-NMR spectrometer Bruker AV III with tetramethylsilane (TMS) as an internal standard, Mass spectral analysis performed on JEOL GC mate and elemental analysis was carried out on a Carlo Erba 1108 analyzer and were within the ± 0.5 % of the theoretical values. Microwave assisted reactions were carried out on a MW synthesizer model CATA-R, operating 700W, generating 2450 MHz frequency. The compounds were evaluated for antibacterial activity against *Bacillus pumilus* and *Escherichia coli* and antifungal activity against *Aspergillus niger* and *Penicillium crysogenum*.

General procedures for the synthesis of chalcones (3a-n):

Both conventional as well as non-conventional protocols have been explored to synthesize compounds **(3a-n)** and **(4a-n)** and find the non-conventional montmorrilonite K10 catalyzed microwave assisted method as a better one with improved yield and shorter reaction time.

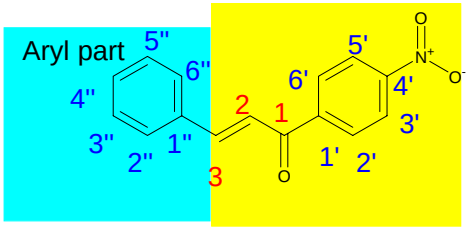
Solution phase conventional method:

A mixture of 4-nitroacetophenone **1** (1.65 g, 0.01 mol) and substituted aromatic aldehyde **2a** (1.02 ml, 0. 01 mol) was stirred in ethanol (30 mL) followed by the drop wise addition of aqueous solution of KOH (40%, 15 mL). The resulted reaction mixture was kept overnight at room temperature and then it was poured into crushed ice and acidified with dil. HCl. The solid separated was filtered off and recrystallized from ethanol afforded analytical samples of **(3a-n)**.

Solid phase non-conventional method

To a solution of 4-nitroacetophenone **1** (1.65 g, 0.01 mol) and substituted aromatic aldehyde **2a** (1.02 ml, 0. 01 mol) in DMF (1 mL) was taken in a 100 mL borosil flask, to this, montmorrilonite K10 (4g) was added and uniformly mixed with glass rod. The resulted slurry was air dried to become powder form by removing the solvent. Adsorbed powder was irradiated inside a microwave synthesizer for 5-8 min. at the medium power level (700 W). After the completion of the reaction (monitored by TLC), the reaction mixture was cooled at room temperature, and the product was extracted with dichloromethane (2 x 20 mL). Removal of the solvent and subsequent recrystallization with ethanol resulted analytical samples of **(3a-n)**.

Characterization of the synthesized 4'-nitrochalcones



*(2E)-1-(4-nitrophenyl)-3-phenylprop-2-en-1-one(**3a**)* Light red solid; m.p. 159-160°C; IR (KBr, cm^{-1}): 1360 (Ar-NO_2), 1632 (-CH=CH str.), 1693 (-C=O str.), 3432 (O-H str.); ^{13}C NMR (100 MHz, $CDCl_3$): δ 121.2(C2), 145.6(C3), 189.4(C1), 122.4(C3'/5'), 129.6(C2'/6'), 141.4(C1'), 150.2(C4'), 127.9(C4"), 128.2(C2"/ C6"), 131.3(C3"/C5"), 133.4(C1"); ^1H NMR (500 MHz, $CDCl_3$): δ 7.00-7.42 (m, 4H, ArH), 7.50 (d, αH, *J*=15.3Hz), 7.80 (d, βH, *J*=15.3Hz), 7.82-8.10 (m, 5H, ArH); MS: (*m/z*): 253.00 [M^+]. Anal.Calcd.for $C_{15}H_{11}O_3N$: C, 71.15; H, 4.35; N, 5.53 %. Found: C, 71.45; H, 4.10; N, 5.90%.

*(2E)-3-(2-chlorophenyl)-1-(4-nitrophenyl)prop-2-en-1-one(**3b**)***:*** Light yellow solid; m.p. 167-168°C; IR (KBr, cm^{-1}): 825 (C-Cl str.), 1355 (Ar-NO_2), 1615 (-CH=CH str.), 1672 (-C=O str.), 3434 (O-H str.); ^{13}C-NMR (100 MHz, $CDCl_3$): δ124.2(C2), 136.4(C3), 191.2(C1), 121.3(C3'/5'), 128.7(C2'/6'), 142.2(C1'), 151.4(C4'),126.1(C4"), 128.7(C2"/ C6"), 130.1(C3"/C5"), 132.3(C1"), 132.4(C4"), 132.8(C2"); ^1H-NMR (500 MHz, $CDCl_3$): δ 7.08-7.50 (m, 4H, ArH), 7.60 (d, αH, *J*=15.3Hz), 7.85 (d, βH, *J*=15.3Hz), 7.87-8.12 (m, 4H, ArH); MS: *m/z*) 287.50 [M^+]. Anal.Calcd.for $C_{15}H_{10}O_3NCl$: C, 62.61; H, 3.48; N, 4.87 %. Found: C, 62.30; H, 3.78; N, 4.50%.

*(2E)-3-(3-chlorophenyl)-1-(4-nitrophenyl)prop-2-en-1-one (**3c**):* Dark yellow solid; m.p. 130-131°C; IR (KBr, cm^{-1}): 815 (C-Cl str.), 1355 (Ar-NO_2), 1632 (-CH=CH str.), 1692 (-C=O str.), 3429 (O-H str.); ^{13}C-NMR (100 MHz, $CDCl_3$): δ 123.6(C2), 141.3(C3), 190.4(C1), 122.8(C3'/C5'), 128.6(C2'/C6'), 141.5(C1'), 149.9(C4'), 127.4(C6"), 128.4(C2"/C4"), 131.8(C5"), 133.7(C1"), 135.4(C3"); ^{1}H-NMR (500 MHz, $CDCl_3$): δ 7.02-7.48 (m, 4H, ArH), 7.62 (d, αH, *J*=15.3Hz), 7.83 (d, βH, *J*=15.3Hz), 7.86-8.10 (m, 4H, ArH); MS: (*m/z*) 287.50 [M^+]. Anal.Calcdfor $C_{15}H_{10}O_3NCl$: C, 62.61; H, 3.48; N, 4.87 %. Found: C, 62.89; H, 3.23; N, 5.20%.

*(2E)-3-(4-chlorophenyl)-1-(4-nitrophenyl)prop-2-en-1-one(**3d**):* Orange solid; m.p. 159-160°C; IR (KBr, cm^{-1}): 818 (C-Cl str.), 1358 (Ar -NO_2), 1634 (-CH=CH str.), 1693 (-C=O str.), 3432 (O-H str.); ^{13}C-NMR (100 MHz, $CDCl_3$): δ 119.9(C2), 141.6(C3), 188.8(C1), 121.2(C3'/C5'), 129.3(C2'/C6'), 142.7(C1'), 150.6(C4'),128.6(C3"/C5"), 130.1(C2"/C6"), 131.2(C1"), 138.(C4"); ^{1}H-NMR (500 MHz, $CDCl_3$): δ 7.05-7.48 (m, 4H, ArH), 7.61 (d, αH, *J*=15.3Hz), 7.81 (d, βH, *J*=15.3Hz), 7.86-8.10 (m, 4H, ArH); MS: (*m/z*) 287.50 [M^+]. Anal.Calcd.for $C_{15}H_{10}O_3NCl$: C, 62.61; H, 3.48; N, 4.87 %. Found: C, 62.30; H, 3.80; N, 4.70%.

*(2E)-3-(2,4-dichlorophenyl)-1-(4-nitrophenyl)prop-2-en-1-one(**3e**)*:Dark yellow solid; m.p. 151-152°C; IR (KBr, cm^{-1}): 816 (C-Cl str.), 1360 (Ar-NO_2), 1631 (-CH=CH str.), 1692 (-C=O str.), 3435 (O-H str.) ; ^{13}C-NMR (100 MHz, $CDCl_3$): δ123.7(C2), 136.6(C3), 189.7(C1), 122.5(C3'/C5'), 128.7(C2'/C6'), 142.5(C1'), 151.4(C4'), 127.4(C5"), 127.9(C3"), 128.7(C4"), 130.4(C6"), 130.7(C1"), 135.3(C2"); ^{1}H-NMR (500 MHz, $CDCl_3$): δ 7.08-7.43 (m, 4H, ArH), 7.52 (d, αH, *J*=15.3Hz), 7.80 (d, βH, *J*=15.3Hz), 7.82-8.10 (m, 3H, ArH); MS: (*m/z*) 322.00 [M^+]. Anal.Calcd.for $C_{15}H_9O_3NCl_2$: C, 55.90; H, 2.79; N, 4.35 %. Found: C, 55.53; H, 2.45; N, 4.65%.

*(2E)-3-(4-bromophenyl)-1-(4-nitrophenyl)prop-2-en-1-one(**3f**):*Yellow solid; m.p. 155-156°C; IR (KBr, cm^{-1}): 748 (C-Br), 1362 (Ar-NO_2), 1633 (-CH=CH str.), 1693 (-C=O str.), 3429 (O-H str.); ^{13}C-NMR (100 MHz, $CDCl_3$): δ118.9(C2), 141.8(C3), 187.6(C1), 121.2(C3'/C5'), 129.2(C2'/C6'), 141.8(C1'), 150.3(C4'), 123.8(C4"), 129.9(C2"/C6"), 130.2(C3"/C5"), 131.2(C1"); ^{1}H-NMR (500 MHz, $CDCl_3$) δ 6.95-7.35 (m, 4H, ArH), 7.49 (d, αH, *J*=15.3Hz), 7.78 (d, βH, *J*=15.3Hz), 7.82-8.08 (m, 4H, ArH); MS: (*m/z*) 331.90 [M^+]. Anal.Calcd.for $C_{15}H_{10}O_3NBr$: C, 54.23; H, 3.01; N, 4.22 %. Found: C, 54.43; H, 3.30; N, 3.89%.

*(2E)-3-(4-fluorophenyl)-1-(4-nitrophenyl)prop-2-en-1-one(**3g**):*Red solid; m.p. 146-147°C; IR (KBr, cm^{-1}): 1156 (C-F), 1362 (Ar-NO_2), 1633 (-CH=CH str.), 1693 (-C=O str.), 3429 (O-H str.); ^{13}C-NMR (100 MHz, $CDCl_3$): δ121.5(C2), 142.2(C3), 191.5(C1), 122.8(C3'/C5'), 128.6(C2'/C6'), 142.2(C1'), 151.8(C4'), 115.1(C3"/C5"), 130.2(C1"), 130.6(C2"/C6"), 162.4(C4"); ^{1}H-NMR (500 MHz, $CDCl_3$): δ 7.02-7.48 (m, 4H, ArH), 7.53 (d, αH, *J*=15.3Hz), 7.79 (d, βH, *J*=15.3Hz), 7.82-8.06 (m, 4H, ArH); MS: (*m/z*) 271.00 [M^+]. Anal.Calcd.for $C_{15}H_{10}O_3NF$: C, 66.42; H, 3.69; N, 5.16 %. Found: C, 66.20; H, 3.94; N, 5.47%.

*(2E)-3-(3-nitrophenyl)-1-(4-nitrophenyl)prop-2-en-1-one(**3h**):*Light yellow solid; m.p. 171-172°C; IR (KBr, cm^{-1}): 1360, 1505 (Ar-NO_2), 1632 (-CH=CH str.), 1699 (-C=O str.), 3431 (O-H str.) ; ^{13}C-NMR (100 MHz, $CDCl_3$): δ124.1(C2), 141.3(C3), 188.3(C1), 121.7(C3'/C5'), 129.3(C2'/C6'), 141.4(C1'), 150.8(C4'), 121.4(C4"), 123.4(C2"), 129.1(C5"), 135.7(C6"), 136.5(C1"), 150.5(C3"); ^{1}H-NMR (500 MHz, $CDCl_3$): δ 6.96-7.40 (m, 4H, ArH), 7.55 (d, αH, *J*=15.3Hz), 7.80 (d, βH, *J*=15.3Hz), 7.88-8.05 (m, 4H, ArH); MS: (*m/z*) 250.00 [M^+]. Anal.Calcd.for $C_{15}H_{10}O_5N_2$: C, 72.00; H, 4.00; N, 11.20 %. Found: C, 72.35; H, 3.80; N, 11.51%.

*(2E)-3-(4-methylphenyl)-1-(4-nitrophenyl)prop-2-en-1-one(**3i**)*:Dark Red solid; m.p. 208-209°C; IR (KBr, cm^{-1}): 1359 (Ar-NO_2), 1631 (-CH=CH str.), 1691 (-C=O str.), 2913 (aliphatic C-H str.), 3433 (O-H str.); ^{13}C-NMR (100 MHz, $CDCl_3$): δ121.3(C2), 143.8(C3), 189.4(C1), 122.7 (C3'/C5'), 129.7(C2'/C6'), 142.8(C1'), 151.5(C4'), 129.2(C2"/C6"), 130.6(C3"/C5"), 131.2(C1"), 138.6(C4"); ^{1}H-NMR (500 MHz, $CDCl_3$): δ 2.63 (3H, s, -CH_3), 6.92-7.42 (m, 4H, ArH), 7.51 (d, αH, *J*=15.3Hz), 7.82 (d, βH, *J*=15.3Hz), 7.83-8.02 (m, 4H, ArH); MS: (*m/z*) 267.00 [M^+]. Anal.Calcd.for $C_{16}H_{13}O_3N$: C, 71.91; H, 4.87; N, 5.24 %. Found: C, 71.70; H, 4.40; N, 5.59%.

*(2E)-3-(4-methoxyphenyl)-1-(4-nitrophenyl)prop-2-en-1-one(**3j**):* Orange solid; m.p. 149-150°C; IR (KBr, cm^{-1}): 1355 (Ar-NO_2), 1631 (-CH=CH str.), 1693 (-C=O str.), 2820 (OCH_3), 3435 (O-H str.); ^{13}C-NMR (100 MHz, $CDCl_3$): δ119.9(C2), 143.7(C3), 191.3(C1), 121.4(C3'/C5'), 128.9(C2'/C6'), 141.9(C1'), 150.6(C4'), 116.1(C3"/C5"), 126.3(C1"), 130.7(C2"/C6"), 162.6(C4"), OMe(55.4); ^{1}H-NMR (500 MHz, $CDCl_3$):

δ 3.87 (s, 3H, OCH_3), 6.98-7.52 (m, 4H, ArH), 7.57 (d, αH, *J*=15.3Hz), 7.80 (d, βH, *J*=15.3Hz), 7.83-7.98 (m, 4H, ArH); MS: (*m/z*) 283.00 [M^+]. Anal.Calcd.for $C_{16}H_{13}O_4N$: C, 67.84; H, 4.59; N, 4.95 %. Found: C, 68.10; H, 4.89; N, 4.70%.

*(2E)-3-(3,4-dimethoxyphenyl)-1-(4-nitrophenyl)prop-2-en-1-one(**3k**)*:Orange solid; m.p. 182-183°C; IR (KBr, cm^{-1}): 1358 (Ar-NO_2), 1633 (-CH=CH str.), 1695 (-C=O str.), 2815 (OCH_3), 3435 (O-H str.); ^{13}C-NMR (100 MHz, $CDCl_3$): δ121.8(C2), 143.9(C3), 190.1(C1), 122.4(C3'/C5'), 129.4(C2'/C6'), 142.4(C1'), 152.2(C4'), 112.1(C5"), 113.8(C2"), 120.8(C6"), 127.8(C1"), 150.2(C4"), 151.2(C3"), OMe (56.6, 59.7); ^{1}H-NMR (500 MHz, $CDCl_3$): δ 3.95 (s, 6H, 2 x OCH_3), 6.93-7.42 (m, 4H, ArH), 7.54 (d, αH, *J*=15.3Hz), 7.85 (d, βH, *J*=15.3Hz), 7.88-8.16 (m, 3H, ArH); MS: (*m/z*) 313.00 [M^+]. Anal.Calcd.for $C_{17}H_{15}O_5N$: C, 65.17; H, 4.79; N, 4.47 %. Found: C, 65.37; H, 4.55; N, 4.69%.

*(2E)-3-(3,4,5-trimethoxyphenyl)-1-(4-nitrophenyl) prop-2-en-1-one(**3l**)*:Dark red solid; m.p. 153-154°C; IR (KBr, cm^{-1}): 1360 (Ar-NO_2), 1631 (-CH=CH str.), 1692 (-C=O str.), 2825 (OCH_3), 3438 (O-H str.); ^{13}C-NMR (100 MHz, $CDCl_3$): δ122.5(C2), 142.8(C3), 188.5(C1), 121.5(C3'/C5'), 128.9(C2'/C6'), 141.1(C1'), 151.6(C4'), 105.5(C2"/C6"), 130.5(C1"), 140.3(C4"), 154.7(C3"/C5"), OMe (56.7, 60.3); ^{1}H-NMR (500 MHz, $CDCl_3$): δ 3.97 (s, 9H, 3 x OCH_3), 6.95-7.49 (m, 4H, ArH), 7.53 (d, αH, *J*=15.3Hz), 7.82 (d, βH, *J*=15.3Hz), 7.85-8.12 (m, 2H, ArH); MS: (*m/z*) 343.00 [M^+]. Anal.Calcd.for $C_{18}H_{17}O_6N$: C, 62.97; H, 4.96; N, 4.08 %. Found: C, 62.72; H, 4.70; N, 4.23%.

*(2E)-3-(3-hydroxy-4-methoxyphenyl)-1-(4-nitrophenyl)prop-2-en-1-one(**3m**)*: Dark yellow solid; m.p. 158-159°C; IR (KBr, cm^{-1}): 1357 (Ar-NO_2), 1632 (-CH=CH str.), 1693 (-C=O str.), 2827 (OCH_3), 3440 (O-H str.); ^{13}C-NMR (100 MHz, $CDCl_3$): δ123.9(C2), 143.1(C3), 189.3(C1), 122.2(C3'/C5'), 129.4(C2'/C6'), 142.6(C1'), 150.2(C4'), 110.8(C5"), 113.8(C2"), 120.6(C6"), 127.2(C1"), 145.7(C3"), 153.4(C4"), OMe (55.9, 61.2); ^{1}H-NMR (500 MHz, $CDCl_3$): δ 3.93 (s, 3H, OCH_3), 6.99-7.50 (m, 4H, ArH), 7.55 (d, αH, *J*=15.3Hz), 7.88 (d, βH, *J*=15.3Hz), 7.95-8.15 (m, 3H, ArH), 11.92 (s, 1H, Ar-OH); MS: (*m/z*) 303.00 [M^+]. Anal.Calcd.for $C_{16}H_{13}O_5N$: C, 63.37; H, 4.29; N, 4.62 %. Found: C, 63.64; H, 4.03; N, 4.93%.

*(2E)-3-(3-bromo-4-hydroxy-5-methoxyphenyl)-1-(4-nitrophenyl)prop-2-en-1-one(**3n**)*: Orange solid; m.p. 143-144°C; IR (KBr, cm^{-1}): 737 (C-Br), 1360 (Ar-NO_2), 1631 (-CH=CH str.), 1694 (-C=O str.), 2823 (OCH_3), 3435 (O-H str.); ^{13}C-NMR (100 MHz, $CDCl_3$): δ122.3(C2), 142.9(C3), 190.4(C1), 121.3(C3'/C5'), 128.3(C2'/C6", 141.4(C1'), 149.5(C4'), 108.8(C2"), 111.8(C5"), 130.6(C1"), 133.7(C6"), 149.3(C3"), 151.6(C4"), OMe (56.6); ^{1}H-NMR (500 MHz, $CDCl_3$): δ 3.94 (s, 3H, OCH_3), 6.92-7.38 (m, 4H, ArH), 7.53 (d, αH, *J*=15.3Hz), 7.85 (d, βH, *J*=15.3Hz), 7.92-8.11 (m, 2H, ArH), 11.97 (s, 1H, Ar-OH); MS: (*m/z*) 381.90 [M^+]. Anal.Calcd.for $C_{16}H_{12}O_5NBr$: C, 50.27; H, 3.14; N, 3.66 %. Found: C, 50.56; H, 2.95; N, 3.91%.

General procedure for the synthesis of 1, 3, 5-triaryl-2-pyrazolines (4a-n)

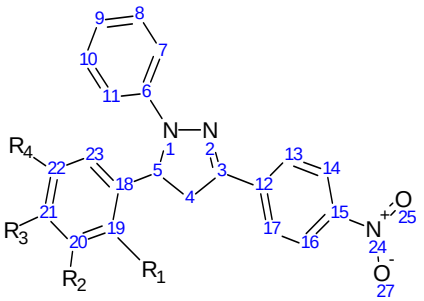
Solution phase conventional method:

A solution of substituted chalcones **3a-n** (1.265 g, 0.005 mol) and phenylhydrazine hydrochloride (0.72 g, 0.015 mol) in glacial acetic acid (30 mL) was refluxed for about 10-12 hrs. Excess of solvent was removed under reduced pressure, and the reaction mixture was poured into ice-cold water. The product obtained was, filtered, washed with water and recrystallized from ethanol resulted analytical samples of **(4a-n)**.

Solid phase non-conventional method

To a solution of substituted chalcones **3a** (1.265 g, 0.005 mol) and phenylhydrazine hydrochloride (0.72 g, 0.015 mol) in DMF (1 mL) taken in a 100 mL borosil flask, to this montmorrilonite K10 (4gm) was added. The resulted slurry was air dried to become powder form by removing the solvent. Adsorbed powder was irradiated inside a microwave synthesizer for 5-8 min. at the medium power level (700 W). After the completion of the reaction (monitored by TLC), the reaction mixture was cooled at room temperature, and the product was extracted with ethanol (2 x 20 mL). Removal of the solvent and subsequent recrystallization with ethanol resulted analytical samples of isomeric mixture 1, 3, 5-triaryl-2-pyrazoline derivatives **(4a-n)**. Comparison of reaction time and yields of the products under microwave and classical methods are shown in (Table. 2).

Characterization of the synthesized pyrazolines



*3-(4-nitrophenyl)-1, 5-diphenyl-4,5-dihydro-1H-pyrazole (**4a**):* Orange solid, m.p. 165-166°C; IR (KBr, cm^{-1}): 1363 (Ar-NO_2), 1590 (C=C str.), 1645 (C=N str.), 2921 (aliphatic C-H str.), 3009, 3067 (Ar- CH str.), 3399 (O-H str.); ^{13}C NMR (100 MHz, $CDCl_3$): δ: 43.1(C4), 68.7(C5), 149.8(C3), 112.4(C7/C11), 118.3(C9), 128.4(C8/C10), 146.3(C6), 122.7(C14/C16), 128.3(C13/17), 140.3(C12), 146.2(C15), 127.3(C20/C22), 128.1(C19/C23), 128.5(C21), 144.6(C18); ^1H NMR (500 MHz, $CDCl_3$): δ 3.01 (1H, dd, *J*= 15.5Hz, *J*= 5.5Hz, CHH_A), 3.65 (1H, dd, *J*= 15.5Hz, *J*= 6.1Hz, CH_BH), 5.48 (1H, dd, *J*= 12.6 Hz, *J*= 5.1Hz, CHAr), 7.10-7.38 (5H, m, ArH), 7.48-7.77 (4H, m, ArH), 7.99-8.34 (5H, m, ArH); MS: (*m/z*) 343.00 [M^+]. Anal.Calcd.for $C_{21}H_{17}O_2N_3$: C, 73.47; H, 4.96; N, 12.24 %. Found: C, 73.67; H, 4.71; N, 12.59%.

*5-(2-chlorophenyl)-3-(4-nitrophenyl)-1-phenyl-4,5-dihydro-1H-pyrazole(**4b**):*Light red solid, m.p. 153-154°C; IR (KBr, cm^{-1}): 753 (C-Cl str.), 1362 (Ar-NO_2), 1584 (C=C stretching),1650 (C=N str.), 2920 (aliphatic C-H str.), 3007, 3060 (Ar-CH str.), 3419 (O-H str.); ^{13}C NMR (100 MHz, $CDCl_3$): δ:44.3(C4), 67.6(C5), 148.5(C3), 113.6(C7/C11), 117.4(C9), 128.6(C8/C10), 145.8(C6), 121.3(C14/C16), 129.5(C13/C17), 139.6(C12), 147.2(C15), 126.3(C23), 127.7(C20), 128.2(C21), 128.7(C22), 134.2(C19), 138.3(C18); ^1H NMR (500 MHz, $CDCl_3$): δ 3.10 (1H, dd, *J*= 15.8Hz, *J*= 6.5Hz, CHH_A), 3.58 (1H, dd, *J*= 15.8Hz, *J*= 5.9Hz, CH_BH), 5.42 (1H, dd, *J*= 12.5Hz, *J*= 6.1Hz, CHAr), 7.08-7.42 (5H, m, ArH), 7.58-7.72 (4H, m, ArH), 7.89-8.24 (4H, m, ArH); MS: (*m/z*) 377.50 [M^+]. Anal.Calcd.for $C_{21}H_{16}O_2N_3Cl$: C, 66.75; H, 4.24; N, 11.12 %. Found: C, 66.97; H, 4.04; N, 11.52%.

*5-(3-chlorophenyl)-3-(4-nitrophenyl)-1-phenyl-4,5-dihydro-1H-pyrazole(**4c**):* Red solid, m.p. 142-143°C; IR (KBr, cm^{-1}): 760 (C-Cl str.), 1580 (C=C str.), 1638 (C=N str.), 2931 (aliphatic C-H str.), 3011, 3067 (Ar-CH str.), 3423 (O-H str.); ^{13}C NMR (100 MHz, $CDCl_3$): δ 44.8(C4), 66.4(C5), 150.7(C3), 113.1(C7/C11), 117.3(C9), 127.2(C8/C10), 146.1(C6),123.8(C14/C16), 128.6(C13/17), 139.4(C12), 146.5(C15), 124.6(C23), 126.4(C19), 127.8(C21), 133.6(C22), 137.6(C20), 138.7(C18); ^1H NMR (500 MHz, $CDCl_3$): δ 3.02 (1H, dd, *J*= 15.5Hz, *J*= 6.7Hz, CHH_A), 3.58 (1H, dd, *J*= 15.5Hz, *J*= 6.1Hz, CH_BH), 5.52 (1H, dd, *J*= 12.6Hz, *J*= 6.3Hz, CHAr), 7.05-7.39 (5H, m, ArH)), 7.42-7.78 (4H, m, ArH)), 7.82-8.12 (4H, m, ArH)); MS: (*m/z*) 377.50 [M^+]. Anal.Calcd.for $C_{21}H_{16}O_2N_3Cl$: C,66.75; H, 4.24; N, 11.12 %. Found: C, 66.96; H, 4.01; N, 11.37%.

*5-(4-chlorophenyl)-3-(4-nitrophenyl)-1-phenyl-4,5-dihydro-1H-pyrazole(**4d**):*Red solid, m.p. 139-140°C; IR (KBr, cm^{-1}): 752 (C-Cl str.), 1355 (Ar-NO_2), 1575 (C=C str.), 1640 (C=N str.), 2922 (aliphatic C-H str.), 3011, 3067 (Ar-CH str.), 3422 (O-H str.); ^{13}C NMR (100 MHz, $CDCl_3$): δ 43.3(C4), 67.1(C5), 149.2(C3), 112.2(C7/C11), 118.7(C9), 128.5(C8/C10), 145.5(C6), 122.2(C14/C16), 128.2(C13/C17), 140.3(C12), 147.7 (C15),128.5(C19/C23), 130.2 (C20/C22), 134.9(C21), 140.2(C18); ^1H NMR (500 MHz, $CDCl_3$): δ 3.20 (1H, dd, *J*= 15.6Hz, *J*= 7.1Hz, CHH_A), 3.52 (1H, dd, *J*= 15.6Hz, *J*= 7.4Hz, CH_BH), 5.58 (1H, dd, *J*= 12.5, *J*= 6.9Hz, ArCH), 7.22-7.33 (5H, m, ArH), 7.42-7.68 (4H, m, ArH), 7.88-8.06 (4H, m, ArH); MS: (*m/z*) 377.50 [M^+]. Anal.Calcd.for $C_{21}H_{16}O_2N_3Cl$: C,66.75; H, 4.24; N, 11.12 %. Found: C, 66.96; H, 4.59; N, 10.90%.

*5-(2,4-chlorophenyl)-3-(4-nitrophenyl)-1-phenyl-4,5-dihydro-1H-pyrazole(**4e**)***:*** Orange solid; m.p. 183-184°C; IR (KBr, cm^{-1}): 758, 820 (C-Cl str.), 1362 (Ar-NO_2), 1580 (C=C str.), 1635 (C=N str.), 2935 (aliphatic C-H str.), 3009, 3069 (Ar- CH str.), 3419 (O-H str.); ^{13}C NMR (100 MHz, $CDCl_3$): δ 44.1(C4), 64.8(C5), 148.4(C3), 113.6(C7/C11), 116.4(C9), 127.2(C8/C10), 147.2(C6), 123.3(C14/16), 129.4(C13/C17), 140.8(C12), 148.3(C15), 126.3(C22), 129.5(C20), 130.4(C21), 133.1(C23), 133.8(C19), 136.7(C18); ^1H NMR (500 MHz, $CDCl_3$, δ / ppm): 3.08 (1H, dd, *J*= 15.7Hz, *J*= 7.2Hz, CHH_A), 3.62 (1H, dd, *J*= 15.7Hz, *J*= 7.7Hz, CH_BH), 5.52 (1H, dd, *J*= 12.6, *J*= 7.1Hz, CHAr), 7.12-7.38 (5H, m, ArH), 7.42-7.72 (4H, m, ArH), 7.82-7.96 (3H, m, ArH); MS: (*m/z*) 412.00 [M^+]. Anal.Calcd.for $C_{21}H_{15}O_2N_3Cl_2$: C,61.16; H, 3.64; N, 10.19 %. Found: C, 61.40; H, 3.89; N, 9.90%.

*5-(4-bromophenyl)-3-(4-nitrophenyl)-1-phenyl-4,5-dihydro-1H-pyrazole(**4f**):*Dark red solid; m.p. 107-108°C; IR (KBr, cm^{-1}): 862 (C-Br), 1359 (Ar-NO_2), 1580 (C=C str.), 1628 (C=N str.), 2920 (aliphatic C-H str.), 3011, 3068 (Ar-CH str.), 3411 (O-H str.); ^{13}C NMR (100 MHz, $CDCl_3$): δ43.8(C4), 66.3(C5), 147.1(C3),113.2(C7/C11), 118.8(C9), 127.8(C8/C10), 146.5(C6),121.4(C14/C16), 129.1(C13/C17), 139.5(C12), 147.5(C15),123.4(C21), 130.6(C19/C23), 134.9(C20/C22), 141.8(C18); ^1H NMR (500 MHz, $CDCl_3$): δ 3.20 (1H, dd, *J*= 15.8Hz, *J*= 7.2Hz, CHH_A), 3.78 (1H, dd, *J*= 15.8Hz, *J*= 7.5Hz, CH_BH), 5.42 (1H, dd, *J*= 12.5, *J*= 7.4Hz, CHAr), 7.12-7.35 (5H, m, ArH), 7.42-7.69 (4H, m, ArH), 7.78-7.98 (4H, m, ArH); MS: (*m/z*) 421.90 [M^+]. Anal.Calcd.for $C_{21}H_{16}O_2N_3Br$: C,59.73; H, 3.79; N, 9.95 %. Found: C, 59.96; H, 3.53; N, 9.70%.

*5-(4-fluorophenyl)-3-(4-nitrophenyl)-1-phenyl-4,5-dihydro-1H-pyrazole(**4g**)*: Red solid; m.p. 174-175°C; IR (KBr, cm^{-1}): 1244 (C- F), 1362 (Ar-NO_2), 1575 (C=C str.), 1625 (C=N str.), 2920 (aliphatic C-H str.), 3011, 3051 (Ar-CH str.), 3418 (O-H str.); ^{13}C NMR (100 MHz, $CDCl_3$): δ43.3(C4), 67.1(C5), 150.8(C3), 112.9(C17/C11), 117.3(C9), 128.8(C8/C10), 46.8(C6),122.5(C14/C16), 129.2(C13/C17), 139.8 (C12), 147.4 (C15),117.3 (C20/C22), 127.3(C19/C23), 137.8(C18), 158.3(C21); ^1H NMR (500 MHz, $CDCl_3$): δ 3.24 (1H, dd, *J*= 16.0Hz, *J*= 7.7Hz, CHHA), 3.76 (1H, dd, *J*= 16.0Hz, *J*= 7.9Hz, CH_BH), 5.54 (1H, dd, *J*= 12.7, *J*= 7.1Hz, CHAr), 7.03-7.28 (5H, m, ArH), 7.51-7.68 (4H, m, ArH), 7.83-8.24 (4H, m, ArH); MS: (*m/z*) 316.00 [M^+]. Anal.Calcd.for $C_{21}H_{16}O_2N_3F$: C,79.75; H, 5.06; N, 13.30 %. Found: C, 79.40; H, 5.31; N, 13.55%.

*5-(3-nitrophenyl)-3-(4-nitrophenyl)-1-phenyl-4,5-dihydro-1H-pyrazole(**4h**)*: Brown solid; m.p. 97-98°C; IR (KBr, cm^{-1}): 1366 (Ar-NO_2), 1575 (C=C str.), 1628 (C=N str.), 2931 (aliphatic C-H str.), 3009, 3069 (Ar-CH str.), 3421 (O-H str.); ^{13}C NMR (100 MHz, $CDCl_3$): δ: 44.3(C4), 65.3(C5), 149.3(C3), 112.7(C7/C11), 117.3(C9), 127.9(C8/C10), 145.7(C6), 123.2(C14/16), 129.4(C13/C17), 140.4(C12), 146.8(C15),123.6(C23), 125.2(C21), 129.3(C20), 132.7(C19), 139.7(18), 151.3(C22); ^1H NMR (500 MHz, $CDCl_3$): δ 3.15 (1H, dd, *J*= 15.7Hz, *J*= 7.2Hz, CHH_A), 3.64 (1H, dd, *J*= 15.7Hz, *J*= 7.5Hz, CH_BH), 5.56 (1H, dd, *J*= 12.8, *J*= 7.0Hz, CHAr), 7.10-7.34 (5H, m, ArH), 7.48-7.72 (4H, m, ArH), 7.88-8.15 (4H, m, ArH); MS: (*m/z*) 388.00 [M^+]. Anal.Calcd.for $C_{21}H_{16}O_4N_4$: C,64.95; H, 4.12; N, 14.43 %. Found: C, 64.71; H, 4.37; N, 14.10%.

*5-(4-methylphenyl)-3-(4-nitrophenyl)-1-phenyl-4,5-dihydro-1H-pyrazole(**4i**):*Red solid; m.p. 140-141°C; IR (KBr, cm^{-1}): 1350 (aromatic-NO_2), 1580 (C=C str.), 1640 (C=N str.), 2930 (aliphatic C-H str.), 3011, 3060 (Ar-CH str.), 3420 (O-H str.); ^{13}C NMR (100 MHz, $CDCl_3$): δ: 43.6(C4), 65.7(C5), 148.6(C3),113.6(C7/C11), 118.5(C9), 128.3(C8/C10), 147.8(C6), 123.2(C14/C16), 128.5(C13/C17), 140.8(C12), 147.2(C15),125.3(C19/C23), 131.4(C20/C22), 137.7(C21), 139.4(C18); ^1H NMR (500 MHz, $CDCl_3$): δ 2.91 (3H, s, CH_3), 3.22 (1H, dd, *J*= 15.8Hz, *J*= 4.5Hz, CHH_A), 3.53 (1H, dd, *J*= 15.8Hz, *J*= 4.7Hz, CH_BH), 5.63 (1H, dd, *J*= 12.8, *J*= 4.6Hz, CHAr), 7.10-7.38 (5H, m, ArH), 7.45-7.78 (4H, m ArH), 7.92-8.21 (4H, m, ArH); MS: (*m/z*) 357.00 [M^+]. Anal.Calcd.for $C_{22}H_{19}O_2N_3$: C,73.95; H, 5.32; N, 11.76 %. Found: C, 73.71; H, 5.57; N, 11.99%.

*5-(4-methoxyphenyl)-3-(4-nitrophenyl)-1-phenyl-4,5-dihydro-1H-pyrazole(**4j**)*: Orange solid; m.p. 176-177°C; IR (KBr, cm^{-1}): 1358 (Ar-NO_2), 1574 (C=C str.), 1635 (C=N str.), 2820 (OCH_3), 2934 (aliphatic C-H str.), 3011, 3071 (Ar-CH str.), 3415 (O-H str.); ^{13}C NMR (100 MHz, $CDCl_3$): δ44.8(C4), 65.7(C5), 150.1(C3),112.3(C7/C11), 117.4(C9), 127.5(C8/C10), 147.9(C6),122.5(C14/C16), 128.3 (C13/C17), 139.6 (C12), 148.2(C15),116.5(C20/C22), 126.5(C23/C19), 134.5(C18), 160.3(C21), 55.5(OMe); ^1H NMR (500 MHz, $CDCl_3$): δ 3.16 (1H, dd, *J*= 15.8Hz, *J*= 4.5Hz, CHH_A), 3.67 (1H, dd, *J*= 15.8Hz, *J*= 4.7Hz, CH_BH), 3.97 (3H, s, OCH_3), 5.88 (1H, dd, *J*= 12.7, *J*= 4.6Hz, CHAr), 7.12-7.35 (5H, m, ArH), 7.45-7.82 (4H, m, ArH), 7.95-8.16 (4H, m, ArH); MS: (*m/z*) 373.00 [M^+]. Anal.Calcd.for $C_{22}H_{19}O_3N_3$: C,70.78; H, 5.09; N, 11.26 %. Found: C, 70.43; H, 5.24; N, 11.51%.

*5-(3,4-dimethoxyhenyl)-3-(4-nitrophenyl)-1-phenyl-4,5-dihydro-1H-pyrazole (**4k**)*: Orange solid; m.p. 145-146°C; IR (KBr, cm^{-1}): 1362 (Ar-NO_2), 1580 (C=C str.), 1640 (C=N str.), 2925 (OCH_3), 2931 (aliphatic C-H str.), 3011, 3067 (Ar-CH str.), 3418 (O-H str.); ^{13}C NMR (100 MHz, $CDCl_3$): δ: 43.2(C4), 66.1(C5), 149.5(C3), 113.3(C7/C11), 118.5(C9), 128.3(C8/C10), 146.3(C6), 121.7(C14/C16), 129.3(C13/17), 140.7(C12), 148.8(C15), 109.6(C19), 113.1(C22), 121.3(C23), 133.2(C18), 149.1(C21), 151.2(C20), 55.9(OMe); ^1H NMR (500 MHz, $CDCl_3$): δ 3.17 (1H,

dd, *J*= 15.7Hz, *J*= 4.4Hz, CHH_A), 3.49 (1H, dd, *J*= 15.7Hz, *J*= 4.7Hz, CH_BH), 3.93 (6H, s, 2 x OCH_3), 5.83 (1H, dd, *J*= 12.8, *J*= 4.4Hz, CHAr), 7.06-7.38 (5H, m, ArH), 7.48-7.86 (4H, m, ArH), 7.92-8.11 (3H, m, ArH); MS: (*m/z*) 403.00 [M^+]. Anal.Calcd.for $C_{23}H_{21}O_4N_3$: C,68.49; H, 5.21; N, 10.42 %. Found: C, 68.71; H, 5.53; N, 10.16%.

*5-(3,4,5-trimethoxyhenyl)-3-(4-nitrophenyl)-1-phenyl-4,5-dihydro-1H-pyrazole(**4l**):* Red solid; m.p. 176-177°C; IR (KBr, cm^{-1}): 1365 (Ar-NO_2), 1583 (C=C str.), 1642 (C=N str.), 2929 (OCH_3), 2933 (aliphatic C-H str.), 3011, 3067, (Ar-CH str.), 3420 (O-H str.); ^{13}C NMR (100 MHz, $CDCl_3$): *δ*: 44.9(C4), 67.6(C5), 148.4(C3), 112.3(C7/C11), 117.9(C9), 127.1(C8/C10), 145.2(C6),122.8 (C14/C16), 129.2(C13/C17), 140.2(C12), 147.3(C15),103.8(C19/C23), 134.7(C18), 138.3(C21), 155.4(C22), 55.9(OMe); ^1H NMR (500 MHz, $CDCl_3$, *δ* / ppm): 3.20 (1H, dd, *J*= 15.8Hz, *J*= 4.2Hz, CHH_A), 3.51 (1H, dd, *J*= 15.8Hz, *J*= 4.6Hz, CH_BH), 3.97 (9H, s, 3 x OCH_3), 5.80 (1H, dd, *J*= 12.7, *J*= 4.4Hz, CHAr), 7.06-7.33 (5H, m, ArH), 7.45-7.83 (4H, m, ArH), 7.95-8.14 (2H, m, ArH); MS: (*m/z*) 433.00 [M^+]. Anal.Calcd.for $C_{24}H_{23}O_5N_3$: C, 66.51; H, 5.31; N, 9.70 %. Found: C, 66.26; H, 5.52; N, 9.99%.

*2-methoxy-5-[3-(4-nitrophenyl)-1-phenyl-4,5-dihydro-1H-pyrazol-5-yl]phenol(**4m**):*Orange solid; m.p.134-135°C; IR (KBr, cm^{-1}): 1366 (Ar-NO_2), 1590 (C=C str.), 1642 (C=N str.), 2915 (OCH_3), 2928 (aliphatic C-H str.), 3009, 3050 (Ar-CH str.), 3422 (O-H str.); ^{13}C NMR (100 MHz, $CDCl_3$): *δ*43.4(C4), 66.9(C5), 148.2(C3),113.4(C7/C11), 117.4(C9), 127.8(C8/C10), 145.6(C6), 123.8(C14/C16), 128.8(C13/C17), 139.4(C12), 148.2(C15),116.7(C22), 117.6(C19), 122.3(C23), 133.2(C18), 146.5(C21), 151.5(C20), 56.4 (OMe); ^1H NMR (500 MHz, $CDCl_3$): *δ* 3.28 (1H, dd, *J*= 15.6Hz, *J*= 4.1Hz, CHH_A), 3.72 (1H, dd, *J*= 15.6Hz, *J*= 4.4Hz, CH_BH), 3.95 (3H, s, OCH_3), 5.46 (1H, dd, *J*= 12.5, *J*= 4.3Hz, CHAr), 7.11-7.40 (5H, m, ArH), 7.52-7.84 (4H, m, ArH), 7.92-8.15 (3H, m, ArH), 10.97 (1H, s, Ar-OH); MS: (*m/z*) 389.00 [M^+]. Anal.Calcd.for $C_{22}H_{19}O_4N_3$: C, 67.87; H, 4.88; N, 10.80 %. Found: C, 67.51; H, 4.73; N, 11.05%.

2-bromo-6-methoxy-4-[3-(4-nitrophenyl)-1-phenyl-4,5-dihydro-1H-pyrazol-5-yl]phenol ***(4n):*** Red solid; mp. 90-91°C; IR (KBr, cm^{-1}): 862 (C-Br), 1359 (Ar-NO_2), 1593 (C=C str.), 1660 (C=N str.), 2830 (OCH_3), 2919 (aliphatic C-H str.), 3009, 3061 (Ar-CH str.), 3392 (O-H str.); ^{13}C NMR (100 MHz, $CDCl_3$): *δ*44.3(C4), 65.3(C5), 150.1(C3), 113.4(C7/C11), 118.4(C9), 128.3(C8/C10), 144.8(C6), 123.4(C14/C16), 129.5(C13/C17), 139.8(C12), 147.1(C15), 111.4(C19), 117.3(C22), 124.4(C23), 135.3(C18), 147.4(C21), 149.2(C20), 56.7(OMe); ^1H NMR (500 MHz, $CDCl_3$): *δ* 3.20 (1H, dd, *J*= 15.7Hz, *J*= 5.2Hz, CHH_A), 3.52 (1H, dd, *J*= 15.7Hz, *J*= 5.5Hz, CH_BH), 5.69 (1H, dd, *J*= 12.6, *J*= 5.4Hz, CHAr), 3.89 (3H, s, OCH_3), 7.11-7.49 (5H, m, ArH), 7.85-7.94 ((2H, m, ArH), 7.99-8.34 (4H, m, ArH), 10.80 (1H, s, Ar-OH); MS: (*m/z*) 467.90 [M^+]. Anal.Calcd.for $C_{22}H_{18}O_4N_3Br$: C, 56.42; H, 3.85; N, 8.98 %. Found: C, 56.17; H, 3.61; N, 9.14%.

Antimicrobial evaluation

Antibacterial and antifungal evaluation of newly synthesized pyrazoline derivatives were carried out by agar well diffusion method and mycelium inhibition method [25, 26], respectively with some modifications. Each compound (5 mg) was dissolved in 5 mL of dimethyl sulfoxide (1000 µg / mL). Volumes of 0.05 mL and 0.1 mL of each compound were used for the antimicrobial evaluation.

For antibacterial activity tests, 1.0 mLof 24h old bacterial broth culture was homogeneously spread on solidified agar plates. After 5-10 mm wells were made by using gel puncture and filled with 500 µl of test compound solution (homogenized using an ultrasonic cleaner). The plates were incubated at 37°C for 24h. The zone size was determined by measuring the radius of the zone of inhibition by scale and divider.

For antifungal activity, about 15 mL of the Potato Dextrose Agar (PDA) medium was poured into petri plates and allowed to solidify. After solidification, 500 uL of test compound was spread on them with the help of sterilized swab. Five mm disc of 7-day-old culture of the test fungi was placed at the centre of the petri plates and incubated at 25±2 ºC for seven days. After incubation the colony diameter was measured in millimeter. Dimethyl Sulphoxide was used as a control which did not reveal any inhibition. Chloramphenicol for antibacterial and fluconazole for antifungal were used as the standard drugs. Each experiment was carried out in triplicate.

Statistical calculations

For statistical analysis, SPSS Statistics 17.0 software was used and all tests were performed in triplicate, and the results were expressed as the mean ± the standard errors of the mean. *P* values lower than 0.05 were considered significant.

Conclusion

Two important features are apparent to our present study. Firstly, a new series of substituted 1, 3, 5-triaryl-2-pyrazolines have been synthesized and concluded that montmorrilonite K-10 clay catalyzed microwave assisted method as a better one with improved yields and shorter reaction time. By comparing different inorganic solid supports, it was concluded that montmorillonite K-10 was the most suitable support for the synthesis of title compounds. Secondly, it was observed from the results obtained by the antimicrobial evaluation that compounds **4b, 4e** and **4m** were found to be the most potent compound of the series with antifungal activity nearly equal to that of the standard drug, i.e. fluconazole against *A. niger* and *P. crysogenium,* respectively, while compound **(4j)** have exhibited antibacterial activity nearly equal to reference drug i.e chloramphenicol whereas the other compounds show moderate to good activity. These results suggest that the chalcone derivatives *i.e.* 1, 3, 5-trriaryl-2-pyrazolines derivatives have excellent scope for further development as new class of antimicrobial agents.

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