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Solid acidic Bentonite/$FeCl_3$ catalysed solvent-free cyclization of some aryl enones: Synthesis and assessment of antimicrobial potentials of some aryl pyrazolines

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ABSTRACT

Some aryl pyrazolines including 3-(substituted phenyl)-5-(naphthalen-1-yl)-1-phenyl-4,5-dihydro-1*H*-pyrazoles were prepared by microwave irradiation promoted cyclization of aryl enones and phenylhydrazine in the presence of solid acidic bentonite/$FeCl_3$ catalyst under solvent-free conditions. In this cyclization the obtained yields are more than 75%. The structural analysis of these pyrazoline derivatives were confirmed through analytical and spectral techniques. The effect of catalyst and solvent on this cyclization also investigated through the obtained yields. The antimicrobial activities of these pyrazoline derivatives were assessed through measurement of mm of zone of inhibition against their micro stains using well known Bauer-Kirby disc diffusion method.

***Keywords*:** 1,3,5-Substituted pyrazolines, Bentonite/$FeCl_3$, Solvent-free synthesis, IR and NMR Spectra, Antimicrobial activities

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1. INTRODUCTION

Pyrazoline derivatives constitutes an interesting class of 5-membered nitrogen heterocycles. Pyrazoline and their derivatives have been attracting a lot of interest amongst researchers in the field of medicinal chemistry because of their bioactivity [1]. The pyrazoline ring system contain N-N bond linkage have been shown to possess a broad range of physiological activities such as anti-bacterial [2], antioxidant [3], molluscicidal [4], antidepressant [5], antitumor [6], anticancer [7], anticonvulsant [8], anti-inflammatory [9], insecticides [10], hypoglycemic [11], antiamoebic [12], fungicide [13], anti-tuberculosis [14] and antidepressant [15] activities. Some 1-[(Benzoxazole/benzimidazole-2-yl)thioacetyl] pyrazoline derivatives were obtained by reacting 3,5-diaryl-1-(2-chloroacetyl)pyrazolines with 2-marcaptobenzoxazole to investigate their potential antinociceptive activities [16]. Pyrazoline derivatives widely used as optical brightening agents for paper, fabrics and textiles [17]. They also act as a hole-conveying medium in photoconductive materials [18]. Specifically, 2-Pyrazolines containing electron donors and acceptors at 1-and 3-positions have intrinsically large molecular hyper polarizability which suggests the photo reactivity of the two-dimensional array constructed with its nanoparticles in applied optical field [19]. Shi *et al.* [20] had synthesized two novel pyrazoline derivatives, named 2,8-bis(1,3-diphenyl-pyrazoline-5-yl) dibenzofuran and 2,8-bis(1-(4-bromophenyl)-3-phenyl-pyrazoline-5-yl) dibenzofuran.

The absorbed absorption and emission spectra of the synthesized compounds were determined by experimental methods in different polar solvents and were computed using the DFT and the TDDFT also studied.

At present, scientists have paid more interest to solvent-free synthesis, QSAR, QPR and QSR studies by correlation of UV, IR and NMR spectral data with Hammett substituent constants and assessment of biological activities of organic substrates [21]. From the correlation analysis they investigated the effect of substituents on chalcones [21], flavanones [22], sulfanamides [23], oxazines [24], ω-bromo esters [25], aryl imine [26] and hydrazone [27] compounds. The effects of substituents on the pyrazoline ring protons were studied first by Sakthinathan *et al.* [28]. Recently Thirunarayanan and Sekar had synthesized a series of 1-acetyl pyrazolines including 1-(3-(3,4-dimethylphenyl)-5-(substituted phenyl)-4,5-dihydro-^{1}H-pyrazole-1-yl) ethanones and studied spectral correlation analysis [29]. From the past and present, literature survey shows no information regarding the synthesis of above pyrazoline derivatives through solvent-free process in the presence of the Bentonite/$FeCl_3$ catalyst and their antimicrobial activities. Hence, the authors have taken efforts for the synthesis of the above titled pyrazolines and studied the effect of catalyst, solvent and assessed their antimicrobial activities using Bauer-Kirby disc diffusion technique.

2. EXPERIMENTAL

2. 1. Materials and methods

The chemicals and reagents utilized in this investigation was bought from Sigma-Aldrich, E-Merck, CDH and Alfa-Aser chemical companies. Samsung, Grill GW73BD Model, 100–750 W, 2450 MHz, 230 A/c type microwave oven was used for synthesis of all pyrazolines. The melting points of all pyrazolines were measured in Guna electrical melting point apparatus. The infrared spectra of all pyrazolines were recorded in AVATAR-300 FT-IR spectrophotometer.

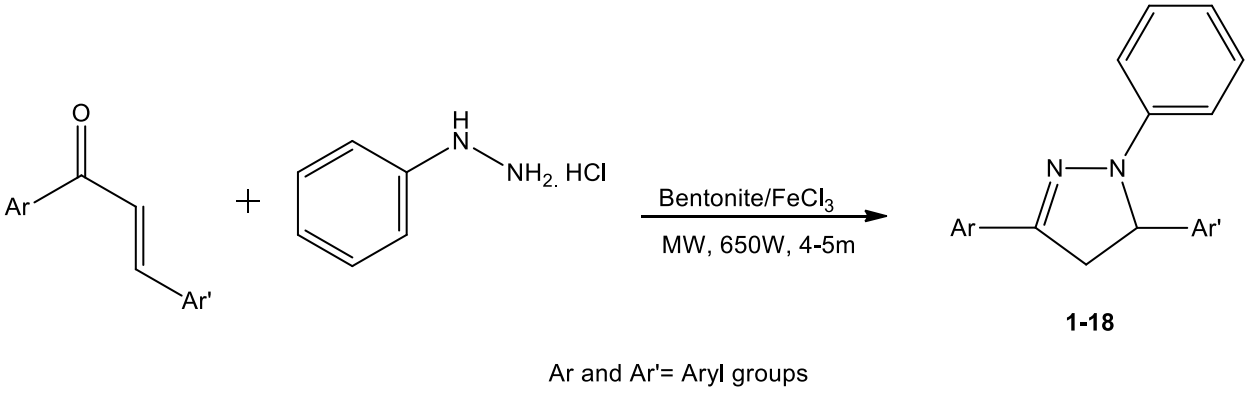
The BRUKER-400 MHz NMR spectrometers were used for recording proton and ^{13}C spectra in $CDCl_3$-d_6 solvent using tetramethyl silane as internal standard. Mass spectral fragments of all compounds were recorded in SHIMADZU mass spectrometer by means of chemical ionization system.

2. 1. Synthesis of chalcones

The chalcones taken in this investigation was prepared by the procedure reported in literature [30].

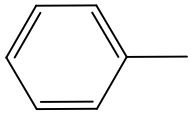
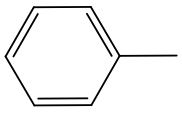
2. 2. Synthesis of pyrazolines

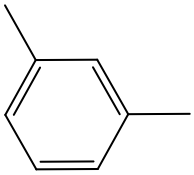
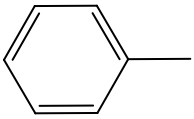
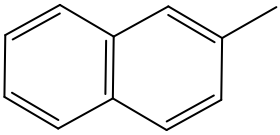
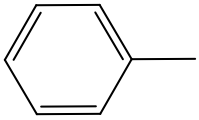
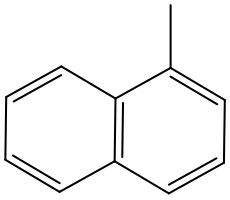
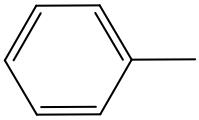
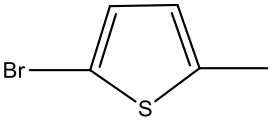
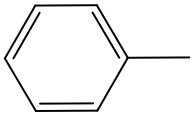
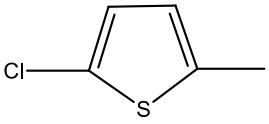
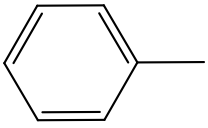
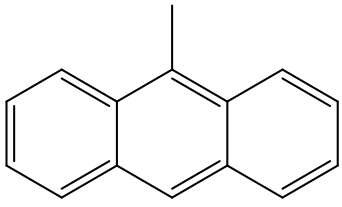
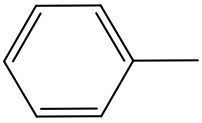
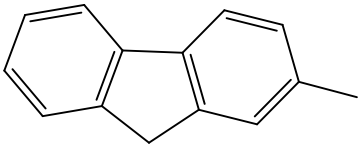
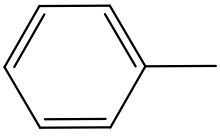
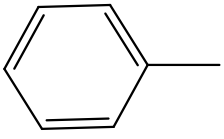
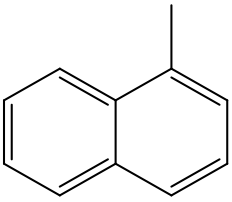
An appropriate equi-molar quantity of chalcones (0.20 mmol), phenyl hydrazine hydrochloride (0.20 mmol) with 0.4 g $FeCl_3$/Bentonite (3 mmol) catalyst were mixed thoroughly in a 50 mL Borosil beaker and closed with lid. This mixture was subjected to microwave irradiation in microwave oven (Samsung, Grill GW73BD Model, 100–750 W, 2450 MHz, 230 A/c) at 650 W for 4–5 min (Scheme 1).

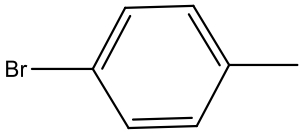
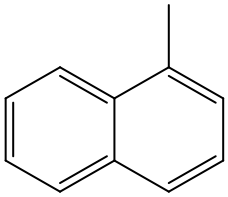
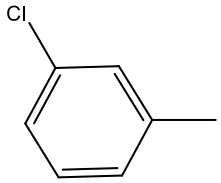
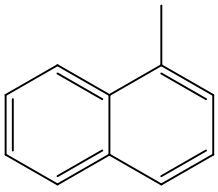
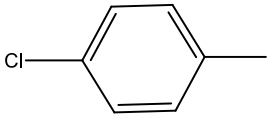
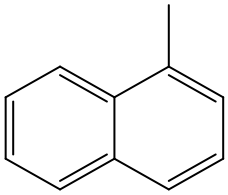
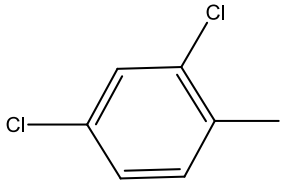
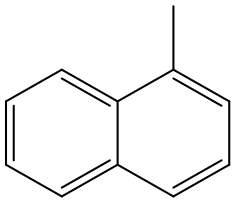
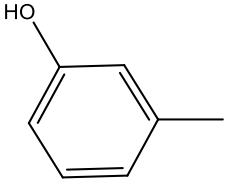
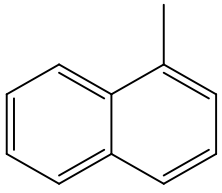
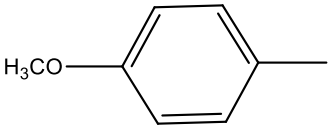
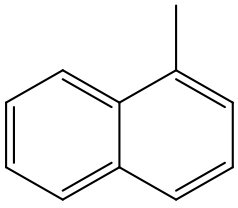
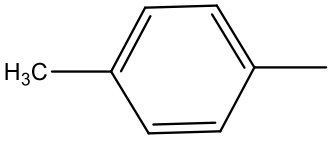
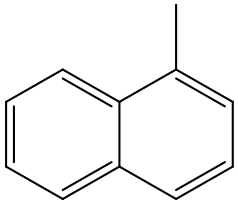


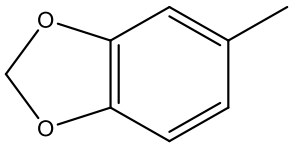
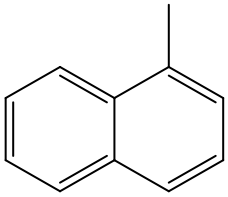
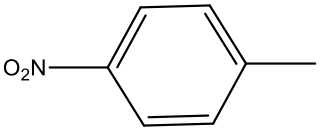
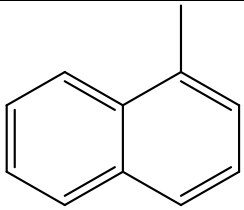
Scheme 1. Synthesis of pyrazolines

Table 1. The physical constants and analytical data of 1,3,5-triaryl-4,5-dihydro-^1H-pyrazole derivatives.

Entry	Ar	Ar'	Yield (%)	Time (m)	m.p. (°C)	M. W
1			83	4	139-141 [6]	298

2			80	4	123-124	312
3			85	4.5	116-117[7]	348
4			84	4.5	112-113	348
5			80	4	151-152[8]	384
6			81	4	132-133	338
7			76	5	126-127[9]	322
8			79	5	121-122	386
9			86	4	103-104	348

10			85	4.5	116-117	427
11			84	4.5	124-125	382
12			82	4.5	114-115	382
13			80	5	132-133	417
14			81	4	112-113	364
15			86	4	117-118	378
16			87	4	125-126	362

17			82	5	134-136	392
18			79	5	147-148	393

The completion of reaction was checked by thin layer chromatography (TLC). The reaction mixture was extracted with 10 mL of dichloromethane. After separating the organic layer with dichloromethane, the solid product was obtained on evaporation. Further this purified by column chromatogram (DCM:EtOAc), evaporation of solvent by rotary vacuum evaporator afforded glittering product.

The catalyst was washed with ethanol and dried in oven at 110 °C, before it is used for further runs. The synthesized pyrazoline derivative were characterized by their physical constants and spectroscopic data. The physical constants and the yields of the pyrazolines are given in **Table 1**. The spectroscopic data of selective compounds are presented in Table 2.

Table 2. The infrared and nuclear magnetic resonance spectral data of selective ^{1}H pyrazoline derivatives.

Entry	**IR (ν, cm^{-1})**	**^{1}H NMR (δ, ppm)**				
	CN	**H_4 (dd)**	**H_5 (dd)**	**$H_{5'}$ (dd)**	**Ar-H**	**Substt.**
9	1598.33	5.324	4.832	3.962	6.988-7.321	---
10	1602.43	5.076	4.231	4.011	7.346-7.902	---
11	1599.34	5.108	4.243	3.851	6.897-7.436	---
12	1598.23	5.340	4.109	3.790	7.324-7.962	---
13	1599.11	5.211	3.908	3.521	6.973-7.801	---
14	1601.23	5.340	4.327	4.021	6.607-7.347	---
15	1598.39	5.210	4.732	3.402	7.324-8.102	2.041 (OCH_3)

16	1597.04	5.127	4.621	3.804	7.102-7.923	2.123 (CH_3)
17	1603.02	5.203	4.391	4.112	7.042-8.023	---
18	1604.93	5.315	4.490	3.906	7.119-8.201	---
^{13}C NMR(δ, ppm)						**Mass (m/z)**
Entry	**C=N**	C_4	**C_5**	**Ar-C**	**Substt.**	
9	154.37	57.98	44.32	126.34-138.26	---	348[M^+]
10	156.31	55.90	43.22	123.65-139.43	---	427[M^+], 429[M^{2+}]
11	153.98	54.39	44.25	124.98-149.80	---	382[M^+], 384[M^{2+}]
12	156.34	52.09	43.81	123.06-148.39	---	382[M^+], 384[M^{2+}]
13	154.32	55.38	44.28	124.23-149.53	---	417[M+], 419[M^{2+}], 421[M^{4+}]
14	156.91	59.34	46.30	121.37-147.91	---	364[M^+]
15	157.01	57.70	44.62	124.80-149.51	64.97(OCH_3)	378[M^+]
16	152.76	54.98	46.81	123.80-148.92	24.86 (CH_3)	362[M^+]
17	156.92	58.90	48.32	122.93-149.57	---	392[M^+]
18	157.36	59.02	48.98	124.90-151.34	---	393[M^+]

3. RESULTS AND DISCUSSION

In our research laboratory the authors have attempts to synthesis of some pyrazoline derivatives by the cyclization of chalcones and phenyl hydrazine hydrochloride in the presence of solid catalyst Bentonite-$FeCl_3$ using microwave irradiation promoted solvent-free conditions. As described in the experimental section an equi-molar quantities of chalcones containing electron-donating and electron withdrawing groups (0.20 mmol), phenyl hydrazine hydrochloride (0.20 mmol) with 0.4 g $FeCl_3$/Bentonite (3 mmol) catalyst were mixed thoroughly in a 50 mL Borosil beaker and closed with lid. This mixture was subjected to microwave irradiation in microwave oven (Samsung, Grill GW73BD Model, 100–750 W, 2450 MHz, 230 A/c) at 650 W for 4–5 min (**Scheme 1**).

The completion of reaction was checked by thin layer chromatography (TLC). The reaction mixture was extracted with 10 mL of dichloromethane. After separating the organic layer with dichloromethane, the solid product was obtained on evaporation. Further this purified by column chromatogram with dichloromethane and ethyl acetate as eluents. Evaporation of solvent by rotary vacuum evaporator afforded glittering product. The catalyst was washed with ethanol and dried in oven at 110 °C, before it is used for further runs. In this cyclization the

obtained yields are more than 75%. The synthesized pyrazoline derivative were characterized by their physical constants and spectroscopic data. The physical constants and the yields of the pyrazolines are given in **Table 1.** The spectroscopic data of selective compounds are presented in **Table 2.**

From the infrared spectra, the C stretches were obtained in the range of 1597.04-1604.93 cm^{-1}. From the proton NMR spectral data, the H_4, H_5, $H_{5'}$, Aromatic and substituent proton chemical shifts (δ, ppm) have been assigned. From the ^{13}C NMR spectra the CN, C_1, C_4, C_5, Aromatic ring and substituent carbon chemical shifts (δ, ppm) were assigned. These data are supported for the formation of pyrazoline derivatives. This cyclization process followed the acidic catalyzed reaction mechanism. The plausible mechanism was illustrated in **Figure 1.**

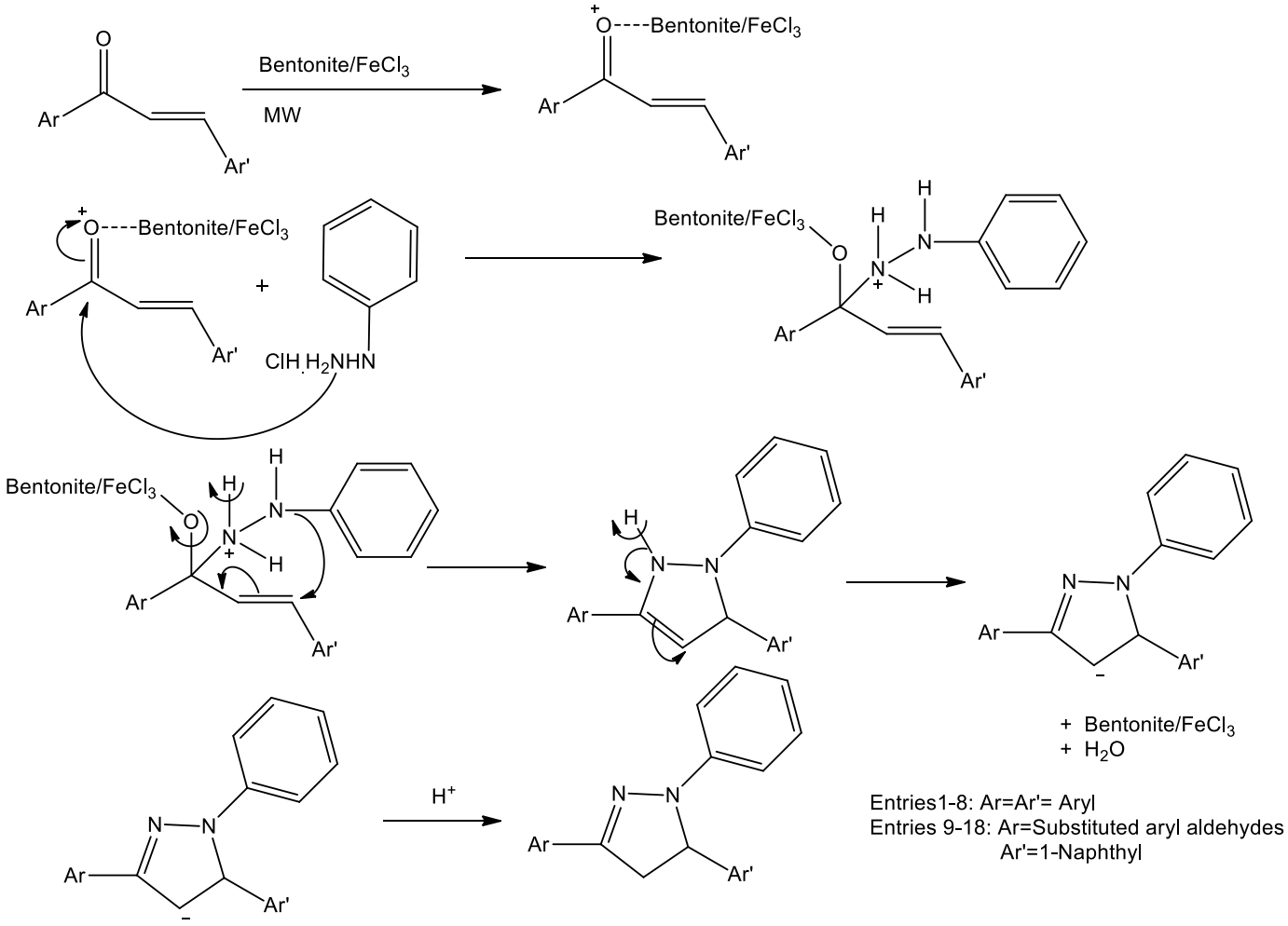


Figure 1. Mechanism of formation of pyrazoline.

In the first step, Bentonite/$FeCl_3$ catalyst bonded with carbonyl oxygen atom of the chalcone and oxygen getting positive charge. The second step consist of the attach of carbonyl carbon by the amino group of phenyl hydrazine molecule, the carbonyl oxygen positive charge was balanced and the amino group nitrogen getting positive charge. The N atom nearby phenyl

group in hydrazine was bonded to beta carbon of vinyl part and the double bond was moved to alpha carbon of vinyl part and carbonyl carbon leads to cyclization occur. Then the removal of proton from N atom leads to double bonded between carbonyl carbon and N atom and the alpha carbon getting negative charge. Finally, the alpha carbon was protonated, and the positive charge was neutralized gave the desired pyrazolines. Further the authors have studied the effect of catalyst on the yield by increment of catalyst in the cyclization for the entry of compound **9**. As increased the catalyst quantity from 0.5 to 0.5 g, the obtained yields increased from 65 to 86%. In this cyclization the optimum quantity of catalyst is 0.4 g. Beyond 0.4 g of catalyst, there is no increment in the yield. The statistical correlation diagram for increment of catalyst with respect to the obtained yields for the entry of compound **9** is shown in **Figure 2**.

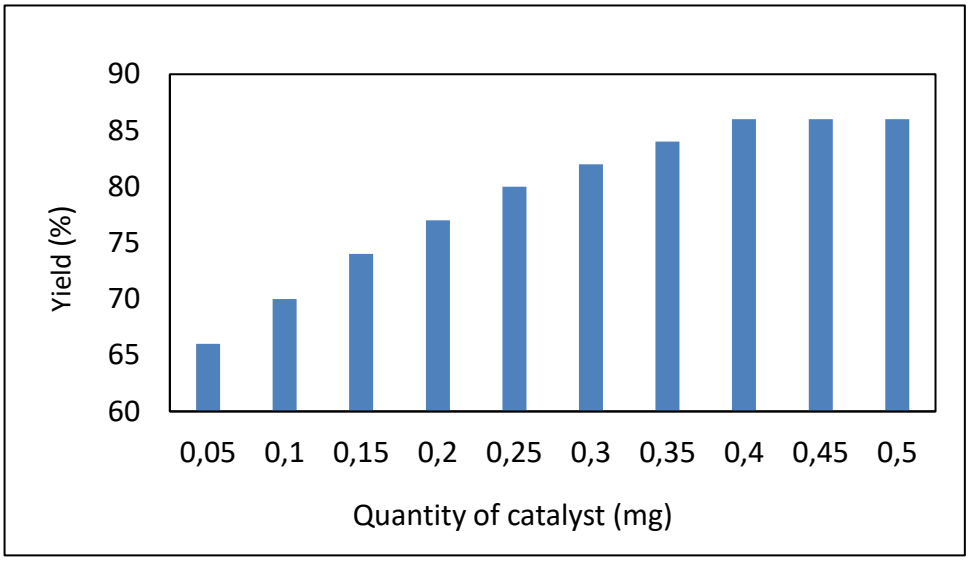


Figure 2. Effect of catalyst on the yield of pyrazoline **9**.

The authors also investigated the effects of solvent on the cyclisation by means of percentage of product (**entry 9**) such as styryl-1-naphthyl ketone and phenyl hydrazine hydrochloride in the same quantities in conventional heating. This experiment was conducted with methanol, methyl cyanide, ethanol, ethyl acetate, dichloromethane, dioxane, n-propanol and tetrahydrofuran. Among the solvents, ethanol medium gave more than 50% yield. The obtained yield of the pyrazolines in solvent-free microwave heating and solvent-assisted conventional heating methods of synthesis of pyrazoline **(entry 9)** is presented in **Table 3.**

Table 3. Yield of product **(entry 9)** in conventional heating and microwave heating method.

Conventional heating									MW
Solvent	MeOH	ACN	EtOH	EtOAc	DCM	DO	n-Prop	THF	
Yield (%)	45	46	53	32	48	35	47	38	86

MeOH = Methanol; CAN = Acetonitrile; EtOH = Ethanol; EtOAc = Ethylacetate;
DCM = Dichloromethane; n-Prop = n-Propanol; THF = Tetrahydrofuran

3. 1. Antimicrobial activities

Antimicrobial activities of the prepared 3-(substituted phenyl)-5-(naphthalen-1-yl)-1-phenyl-4,5-dihydro-1*H*-pyrazoles **(Entries 9-18)** were assessed by Bauer-Kirby[31] Disc diffusion technique. In this experiment the authors taken to each two gram positive and negative antimicrobial microbes such as *S. pyogenes, B. subtilis, E. coli and P. aeruginosa.*

Ciprofloxacin was taken as standard drug and DMSO used as a solvent. Measurement of antifungal activities of these pyrazolines, the authors applied the Bauer-Kirby [31] disc diffusion method using PDA medium with antifungal stains such as *A. flavus*, *A, niger*, *F. oxysporum* and *P. chrysogenum.* Amphotericin-B was used as standard and DMSO as solvent.

3. 1. 1. Antibacterial activities

The measured antibacterial activities by means of measurement of mm of zone of inhibition of these pyrazolines were presented in **Table 4.** The statistical correlation clustered column chart of the activities was illustrated in **Figure 3.** From the table 4, substituted pyrazoline derivatives **10-14** shows good antibacterial activity. Among these the compound **14** have dichloro substitution shows maximum activity against *S. pyogenes* stain.

Table 4. The antibacterial screening effect of synthesized pyrazoline derivatives.

Entry	X	Zone of inhibition (mm)			
		Gram positive bacteria		Gram negative bacteria	
		S. pyogenes	***B. subtilis***	***E. coli***	***P. aeruginosa***
9	H	4	6	9	9
10	4-Br	13	12	7	10
11	3-Cl	14	15	7	7
12	4-Cl	11	11	6	8
13	4-F	12	13	7	7
14	2,4-Cl_2	15	16	9	11
15	4-OCH_3	6	8	6	5
16	4-CH_3	8	7	8	7
17	5-Ph.B.	7	7	7	7

18	4-NO_2	8	8	8	7
Standard	Ciprofloxacin	16	18	10	12
Control	DMSO	---	---	---	---

Pyrazolines **15-18** showed moderate antibacterial against the *S. pyogenes* stain. The parent compound **9** had least antibacterial activity. Substituted pyrazoline derivatives **10-14** shows good activity against *B. subtilis* antibacterial stain. Among these the compound **14** have dichloro substitution shows maximum activity against *B. subtilis* stain. Pyrazolines **15-18** showed moderate antibacterial against the *B. subtilis* stain. The parent compound **9** had least antibacterial activity. All 3-(substituted phenyl)-5-(naphthalen-1-yl)-1-phenyl-4,5-dihydro-1*H*-pyrazoles have showed satisfied and good antibacterial activity against *E. coli* bacterial stain. The dichloro substituted pyrazoline **14** have significant antibacterial activity. Methoxy substituted pyrazoline **15** shows satisfactory antibacterial activity against *E. coli* stain. All the 3-(substituted phenyl)-5-(naphthalen-1-yl)-1-phenyl-4,5-dihydro-1*H*-pyrazoles have showed satisfied and good antibacterial activity against *P. aeruginosa* bacterial stain. The dichloro substituted pyrazoline **14** have significant antibacterial activity. Methoxy substituted pyrazoline **15** shows satisfactory antibacterial activity against *P. aeruginosa* stain.

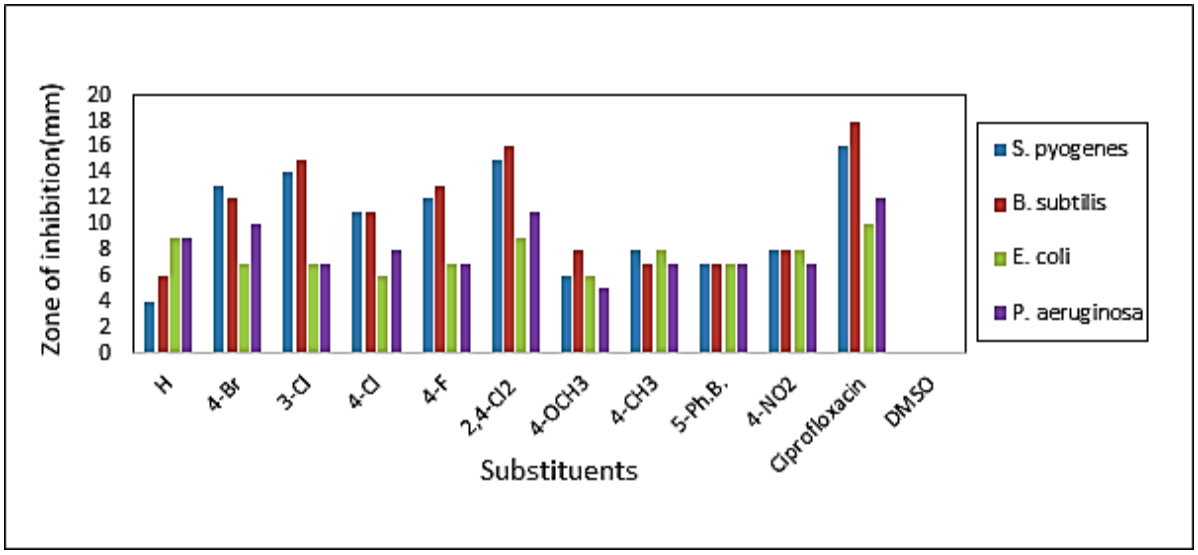


Figure 3. Antibacterial activities-clustered column chart of the pyrazolines (**entries 9-18**).

3. 1. 2. Antifungal activity

The measured antifungal activities of 3-(substituted phenyl)-5-(naphthalen-1-yl)-1-phenyl-4,5-dihydro-1*H*-pyrazoles (**entries 9-18**) were presented in Table 5 and the statistical correlation cluster column chart was illustrated in Figure 4. From the Table 5, the halogen, methyl and nitro substituted pyrazolines **10-14, 16** and **18** showed good antibacterial activities against *A.flavus* fungal stain. The Parent, 5-benzo[d][1,3]dioxole substituted compounds show

moderate antifungal activities. The methoxy substituted compound shows least antifungal activity against *A. flavus* stain. The compounds have 4-Br, 4-F and dichloro substitutions **14** shows good and better antifungal activities against *A. niger* fungal stain. The 3-Cl, 4-Cl, methoxy, methyl, 5-benzo[d][1,3]dioxole and nitro substituted pyrazolines were shown moderate antifungal activities. The parent pyrazoline show least antifungal activity.

Table 5. The antifungal screening effect of 3-(substituted phenyl)-5-(naphthalen-1-yl)-1-phenyl-4,5-dihydro-1*H*-pyrazoles (**entries 9-18**).

Entry	**X**	**Zone of inhibition (mm)**			
		A. flavus	***A. niger***	***F. oxysporum***	***P. chrysogenum***
9	H	4	3	2	4
10	4-Br	8	7	5	6
11	3-Cl	9	5	6	7
12	4-Cl	7	6	6	8
13	4-F	9	7	7	7
14	2,4-Cl_2	12	11	10	11
15	4-OCH_3	2	5	6	5
16	4-CH_3	7	5	8	9
17	5-Ph.B.	6	5	4	5
18	4-NO_2	8	6	5	6
Standard	Amphotericin-B	14	15	12	15
Control	DMSO	---	---	---	---

The disubstituted halo compounds **14** and showed good antifungal activities against *F. oxysporum* fungal stain. The remaining mono substituted pyrazolines 10-13, and methoxy, methyl, 5-benzo[d][1,3]dioxole and nitro substituted pyrazolines shows moderate antifungal activity. The parent compound **9** showed least antifungal activity against *F. oxysporum* fungal stain. The dichloro substituted pyrazoline **14** shows good antifungal activity against *P. chrysogenum* fungal stain. The mono halo, methoxy, methyl, 5-benzo[d][1,3]dioxole and nitro substituted pyrazolines **6-19** and **15-18** shows moderate antifungal activity. The parent compound 9 shows least antifungal activity against *P. chrysogenum* fungal stain.

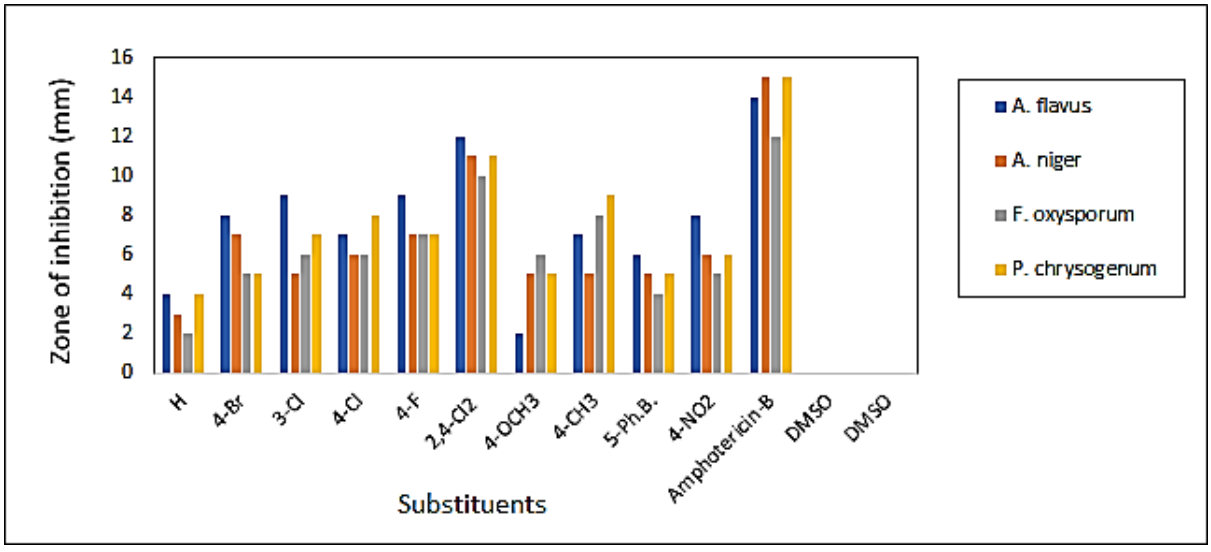


Figure 4. Antifungal activities-clustered column chart of the pyrazolines (**entries 9-18**).

4. CONCLUSIONS

There are eighteen aryl pyrazolines including 3-(substituted phenyl)-5-(naphthalen-1-yl)-1-phenyl-4,5-dihydro-1*H*-pyrazoles (**9-18**) were synthesised by microwave irradiation promoted cyclization of aryl enones and phenylhydrazine in the presence of solid acidic bentonite/$FeCl_3$ catalyst under solvent-free conditions. In this cyclization the obtained yields are more than 75%. The structural analysis of these pyrazoline derivatives were confirmed through analytical and spectral techniques. The effect of catalyst and solvent on this cyclization also investigated through the obtained yield for the compound **9.** The antimicrobial activities of these pyrazoline derivatives were assessed through measurement of mm of zone of inhibition against their micro stains using well known Bauer-Kirby disc diffusion method.

The compound dichloro substituted pyrazoline **14** have dichloro substitution shows maximum activity against all fungal stain. The remaining compounds shows moderate and least antifungal activities. The halogen, methyl and nitro substituted pyrazolines **10-14, 16 and 18** showed good antibacterial activities against *A. flavus* fungal stain. The compounds have 4-Br, 4-F and dichloro substitutions **14** shows good and better antifungal activities against *A. niger* fungal stain. The disubstituted halo compounds **14** and showed good antifungal activities against *F. oxysporum* fungal stain. The dichloro substituted pyrazoline **14** shows good antifungal activity against *P. chrysogenum* fungal stain. The mono halo, methoxy, methyl, 5-benzo[d][1,3]dioxole and nitro substituted pyrazolines **6-19** and **15-18** shows moderate antifungal activity.

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References

[1] V.H. Babu, C.H. Sridevi, A. Joseph, K.K. Srinivasan, *Indian J. Pharm. Sci.* 69, 2007, 470.

[2] G. Thirunarayanan and K. G. Sekar, *J. Taibah Univ. Sci.* 8, 2014, 124.

[3] K. Hazra, L. V. G. Nargund, P. Rashmi, J. N. NarendraSharath Chandra and B. Nandha, *Der Chemica Sinica,* 2(2), 2011, 149.

[4] M. F. EI Shehry, R. H. Swellem, Sh. M. Abu- Bakr, E. M. Ei-Telbani, *Eur. J. Med. Chem.* 45, 2010, 4783.

[5] E. Palaska, M. Aytemir, I. TayfunUzbay, D. Erol, *Eur. J. Med. Chem.* 36, 2001, 539.

[6] H. J. Park, K. Lee, S. Park, B. Ahn, J. C. Lee, H. Y. Cho, K. E. Lee, *Bio Org. Med. Chem. Lett.* 15, 2005, 3307.

[7] V.K. Ahluwalia, L. Nayal, N. Kalia, S. Bala and A. K. Tahim, *Indian J. Chem.* 26B, 1987, 384.

[8] A. Anees, Md. Siddiqui, M.d. Azizur Rahman, Md. Shaharyar, R, Mishra, *Chem. Sci. J.* 8, 2010, 1.

[9] S. Mukherjee, V. Kumar, A. K. Prasad, H. G. Raj, M. E. Brakhe, C. E. Olsen, S. C. Jain and V. S. Parmar, *Med. Chem.* 9, 2001, 337.

[10] C. K. Chu and J. J. Cutler, *Heterocycl. Chem.* 23, 1986, 289.

[11] C. Sridevi, K. Balaji, A. Naidu, S. Kavimani, D. Venkappayya, R. Suthakaran, R. Parimala. *Int. J. Pharm. Tech. Res.* 1, 2009, 816.

[12] K. Naik, Y. N. Spoorthy, L. R. K. R. Ravindranath and A. R. G. Prasad, *J. Appl. Pharm.* 4(1), 2013, 720.

[13] A. A. Siddiqui, M. A. Rahman, M. Shaharyar and R. Mishra, *Chem. Sci. J.* 1, 2010, 1.

[14] A. K. Bhatt, R. P. Bhamaria, M. R. Patel, R. A. Bellare and C. A. Deliwala, *Indian J. Chem.* 10, 1972, 694.

[15] D. M. Bailey, P. E. Hansen, A. G. Hlavac, E. R. Baizman, J. Pearl, A. F. Defelice and M. E. Feigenson, *J. Med. Chem.* 28, 1985, 256

[16] Z. Asim Kaplancikli, G. Turan-Zitouni, A. Ozdemir, O. Devrim Can, P. Chevallet, *Eur. J. Med. Chem.* 44(6), 2009, 2606.

[17] Z. Brozozowski and F. Saczewski; *Eur. J. Med. Chem.* 2002, 37, 709.

[18] T. S. Jeong, K.S. Kim, S. J. An, K. H. Cho, S. Lee, W.S. Lee. *Bioorg Med Chem Lett.* 14, 2004, 2715.

[19] B. A. Bhat, K. L. Dhar, S. C. Puri, M. Shanmugavel and G. N. Qazi, *Bioorg. Med. Chem. Lett.* 15(22), 2005, 5030.

[20] P.T. Chovatia, J. D. Akabari, P. K. Kachhadia, P. D. Zalavadia and H. S. Joshi, *J. Serb. Chem. Soc.* 71, 2007, 713.

[21] G. Vanangamudi, M. Subramanian, P. Jayanthi, R. Arulkumaran, D. Kamalakkannan, G. Thirunarayanan, *Arab. J. Chem.* 9(1), 2016, S717.

[22] G. Thirunarayanan, K. G. Sekar, *Int. Lett. Chem. Phy. Astro.* 25, 2014, 39.

[23] K. G. Sekar, G. Thirunarayanan, *Int. Lett. Chem. Phy. Astro.* 13, 2013, 249,

[24] G. Thirunarayanan, K. G. Sekar, *Int. Lett. Chem. Phy. Astro.* 36, 2014,193.

[25] G. Thirunarayanan, G. Vanangamudi, V. Sathiyendiran, K. Ravi, *Indian J. Chem.* 59B, 2011, 593.

[26] R. Senbagam, R. Vijayakumar, M. Rajarajan, S. Balaji, V. Manikandan, G. Vanangamudi and G. Thirunarayanan, *Kar. Int. Jour. Mod. Sci.* 2, 2016, 56.

[27] M. Rajarajan, R. Senbagam, R. Vijayakumar, S. Balaji, V. Manikandan, G. Vanangamudi, G. Thirunarayanan, *Indian J. Chem.* 55B, 2016, 197.

[28] S. P. Sakthinathan, G. Vanangamudi, G. Thirunarayanan, *Spectrochim. Acta* 95A, 2012, 693.

[29] G. Thirunarayanan and K.G. Sekar, *Arab. J. Chem.* 20, 2016, 661.

[30] G. Thirunarayanan and N. Dinesh Kumar, *World Scientific News* 74, 2017, 251.

[31] A. W. Bauer, W. M. M. Kirby, J. C. Sherris and M. Truck, *Am. J. Clin. Pathol*, 45, 1966, 493.