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Synthesis and Biological Screening of Pyrazole Anchored Chromones

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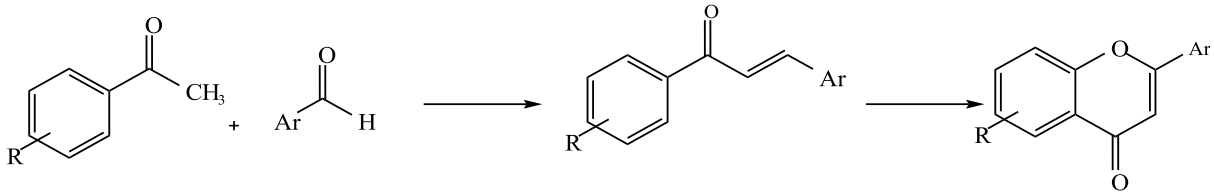
Abstract

In the recent work, we synthesized derivatives of chalcone from pyrazole aldehyde. In additionwe prepared chromone from chalcone derivatives.Herewe performed simple condensation reaction between acetophenone with novel pyrazole aldehyde to yield chalcone. further we synthesize chromone from chalcone. A series of chalcone and their chromone derivatives were successfully achieved with good yield. All the synthesized compounds are characterized and confirmed by spectral analysis like ^{1}H NMR, ^{13}CNMR, IR & Mass. Further synthesized derivatives were studied for biological screening.



Key Words: Pyrazole aldehyde, Chalcone, Chromone, Spectral analysis, Microbial Screening.

Introduction

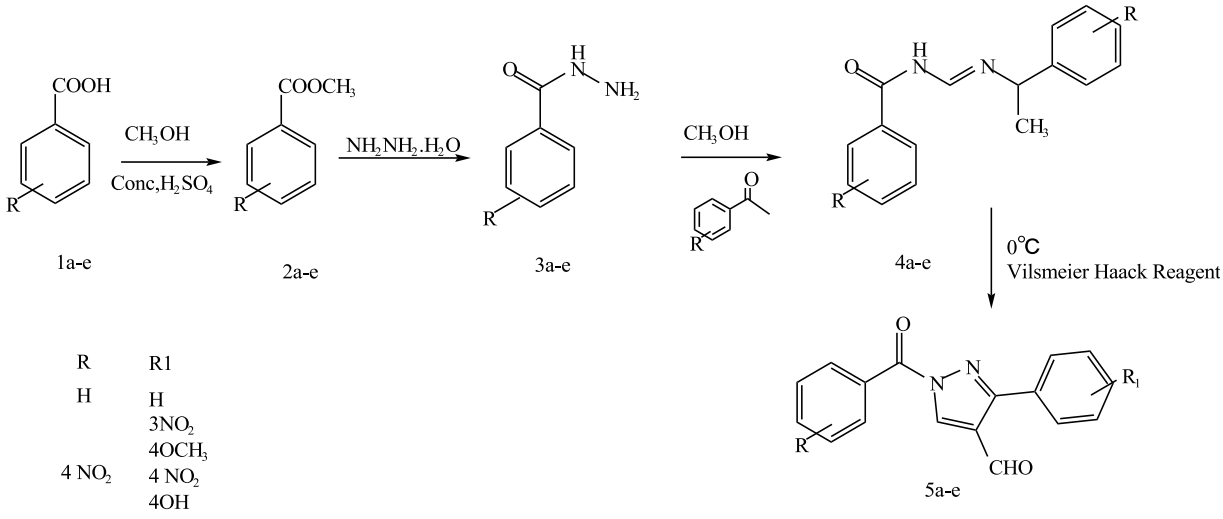
Pyrazoles are five-membered heterocycles that constitute a class of compounds helpful in organic synthesis. In fact, a number of methods of synthesis and synthetic analogues have been reported over the years. The presence of pyrazole moiety in various structures leads to the diversified applications in different areas such as technology, farming and medicine. In particular, they are specifically identified as inhibitors of protein glycation, antibacterial, antifungal, anticancer, antidepressant, anti-inflammatory, anti-tuberculosis, antioxidant as well as antiviral agents Nowadays, More attention have attracted towards pyrazole system, as biomolecules due to their unique pharmacological properties. This heterocycle can be traced in a number of well-established drugs belonging to some different categories with diverse therapeutic effects.

A literature survey revealed that several biological active compoundshave been synthesized by using pyrazole-3(4)-carbaldehydes. These compounds show activities like antimicrobial, anti-inflammatory, antitubercular, antitumor, anti-angiogenesis, anti-parasitic, and antiviral activity.

In the present review, we report descriptions and discussions on the most relevant synthesis methods and pharmacological properties of pyrazole-derived heterocyclic systems.

ManchalaMahalakshmi et al developed a series of substituted acetophenones are condensed with hydrazides to the corresponding hydrazones which are then cyclized by using Vilsmier-Hack reaction to give the final series of 1-Benzoyl-3-phenyl-1H-pyrazole-4-carbaldehyde derivatives respectively. In addition these derivatives had significant antioxidant and anti-inflammatory activity.

Scheme 1

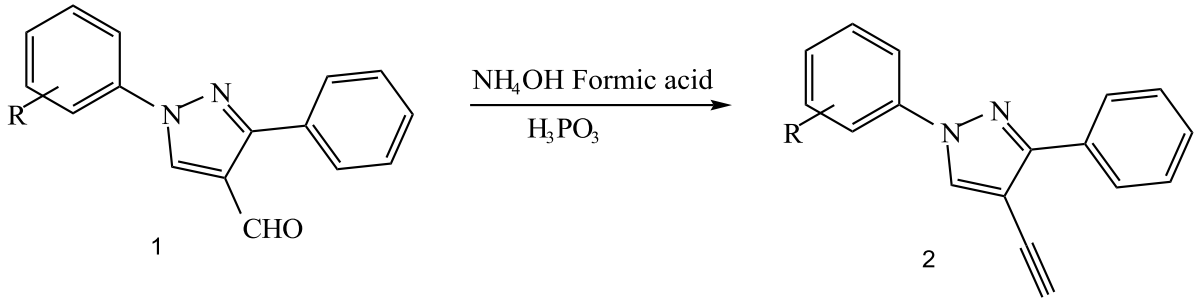


Scheme- Conventional method for synthesis of 1-Benzoyl-3-phenyl-1H-Pyrazole-4-carbaldehyde.

Tukaram Choudhary and co-workers performed One-pot condensation of pyrazole-4-aldehydes and hydroxylamine hydrochloride to form the corresponding oxime by using formic acid as a medium which was on dehydrated to produce newof pyrazole-4-carbonitrile. This method converts aldehyde to nitrile in a single pot under the catalysis of orthophosphoric acid. Most remarkable features of this method are metal-free, cost-effective, atom efficiency with great yield (98–99%). For the synthesis of useful and adaptable precursors, this procedure will serve as a scalable and reliable method (nitriles). This

compound will make way for the production of numerous useful compounds with medical applications.

Scheme 2:

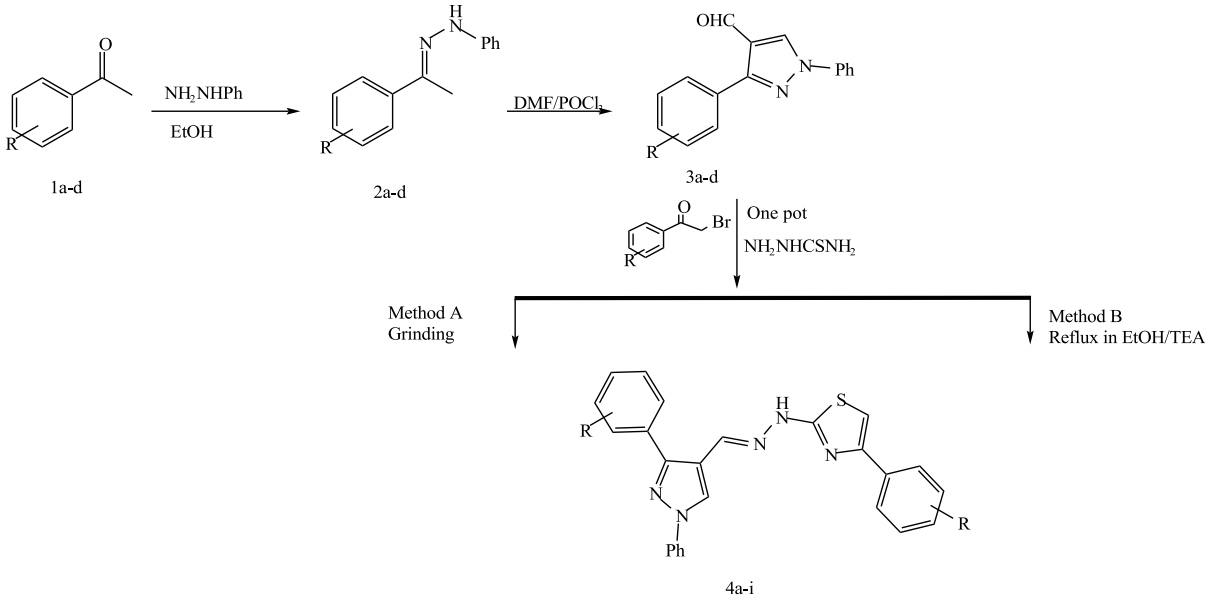


Scheme- Transformation of pyrazole carbaldehyde to novel pyrazole nitrile

Sachin V. Patil et al development one pot synthesis of new 2,4-disubstitued thiazolyl pyrazole derivatives was carried out. the target compounds were produced by a reaction between various pyrazole 4-carbalaldehydes, thiosemicarbazide, and α-haloketones. Both the standard approach, which involved refluxing pyrazole 4-carbaldehyde, thiosemicarbazide, and -haloketones in ethanol, and the second method, which involved grinding the reaction mixture at room temperature, were used to carry out the synthesis. Comparisons were made between the two processes for reaction rate, product yield, and product purity. Every of the producedcompounds had their antibacterial properties evaluated. The majority of the compounds had good to moderate antibacterial and antifungal properties.

Scheme 3:

ISSN 2063-5346 *Section A-Research paper*



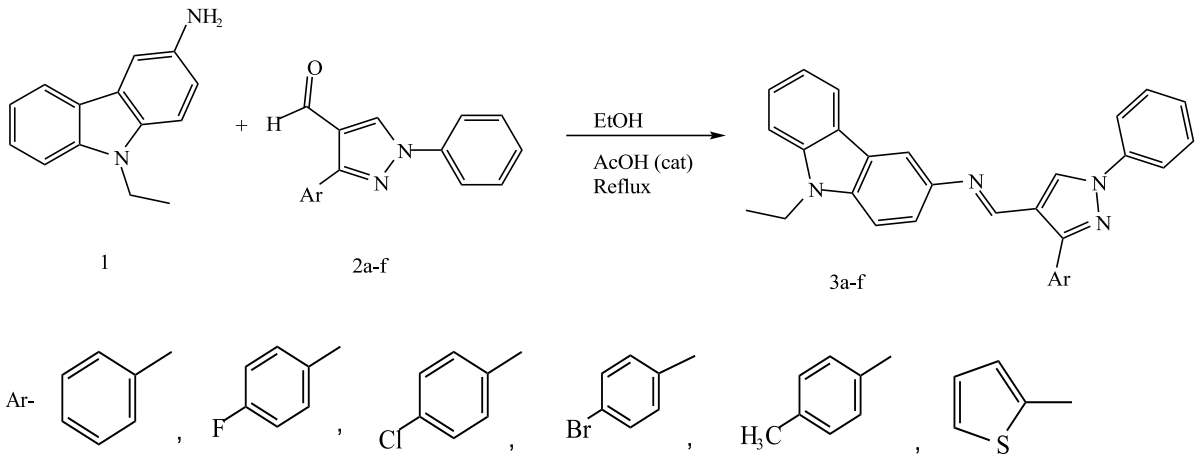
1a-d 2a-d 3a-d 4a-i

Compound	R	R’	Compound	R	R’
4a	3,5-bis(CF_3)	4-NO_2	4g	3-NO_2	4-NO_2
4b	3,5-bis(CF_3)	3-NO_2	4h	3-NO_2	4-NO_2
4c	3,5-bis(CF_3)	4-Cl	4i	3-NO_2	4-Cl
4d	4-NO_2	3-NO_2	4j	4-Br	4-NO_2
4e	4-NO_2	4-NO_2	4k	4-Br	3-NO_2
4f	4-NO_2	4-Cl	4l	4-Br	4-Cl

Gopinath D. Shirole et al, prepared Carbazole Schiff bases in accordance with the literature procedure, starting from the condensation of 9-ethyl-9H-carbazol-3-amine 1 with substituted 1,3-diaryl pyrazole aldehyde in ethanol and a catalytic amount of glacial acetic acid. The substituted 1, 3-diaryl pyrazole aldehydes were prepared by the well-known Vilsmeier Haack reaction.

Scheme 4:

ISSN 2063-5346 *Section A-Research paper*

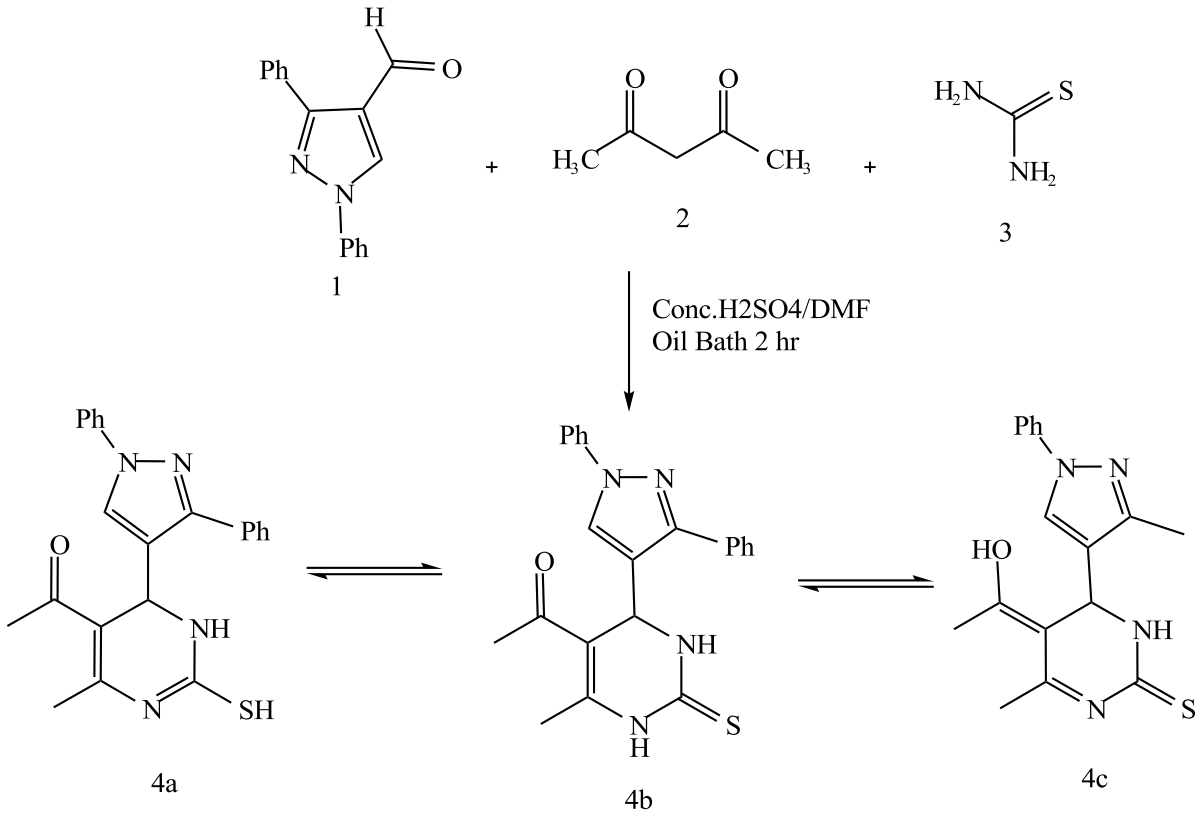


It was reported that all the derivatives among showed stronger antibacterial efficacies and broader bioactive spectrum against E. coli, S. faecalis, and B. subtilis with the MIC values in the range of 10.5–15.5 µg/mL comparable to that of the positive control.

K. N. M. Halim et al, preparedtetrahydropyrimidinethione was efficiently prepared via Biginellicyclocondensation reaction of pyrazole aldehyde, acetylacetone and thiourea and it was then used as crucial building block synthon for creation of valuable N-heterocycles. The structure of pyrimidine was established on the basis of its analytical and spectral data. There are three possible tautomerconfigurations for pyrimidine.

Scheme-5

ISSN 2063-5346 *Section A-Research paper*

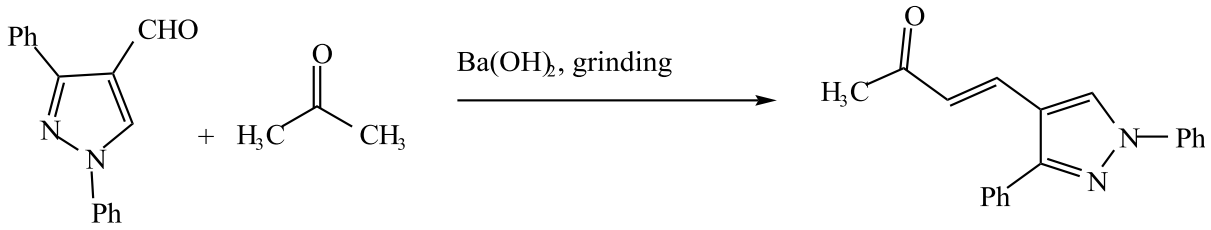


Scheme-Synthesis of tetrahydropyrimidiethione

Pravin Kumar et al,provides a method for the synthesis of pyrazole chalcones under solvent free conditions at room temperature pyrazole-substituted chalcones has been achieved by grinding pyrazole aldehydes and acetophenones in the presence of activated barium hydroxide in 5–10 min with the yield above 90% yield. It is annon-toxic, solvent free, Claisen Schmidt condensation.

Scheme 6:

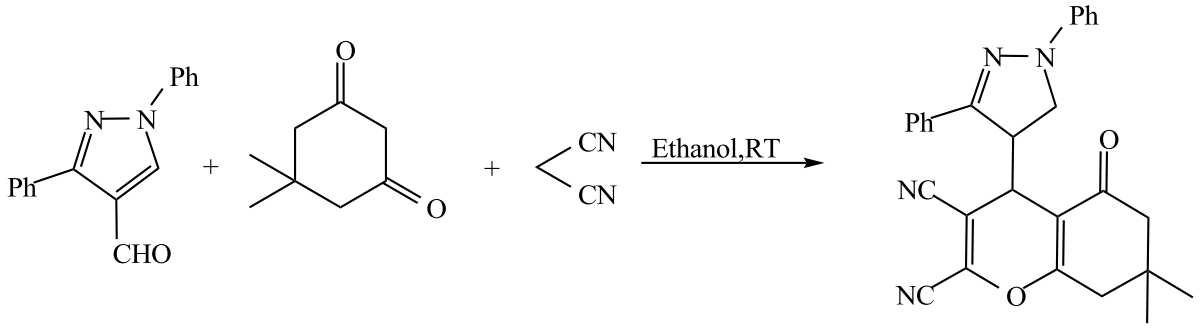
ISSN 2063-5346 *Section A-Research paper*



Synthesis of Pyrazole chalcone

Selvraj Jayanti et al,developed a catalyst-free synthetic strategy to chromone carbonitriles by MultiComponent reaction of pyrazole aldehydes, 5,5-dimethylcyclohexane-1,3-dione and malononitrile with ethanol, at room temperature is reported. Using methanol, water and ethanol, solvent screening was carried out. It was reported that, less yield was obtained in water; better results were obtained while using methanol and high yield were seen with ethanol.

Scheme 7:

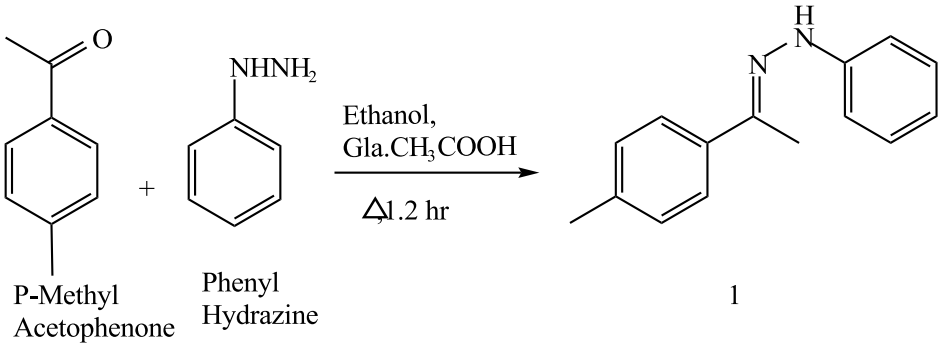


Scheme- Synthesis of Chromones

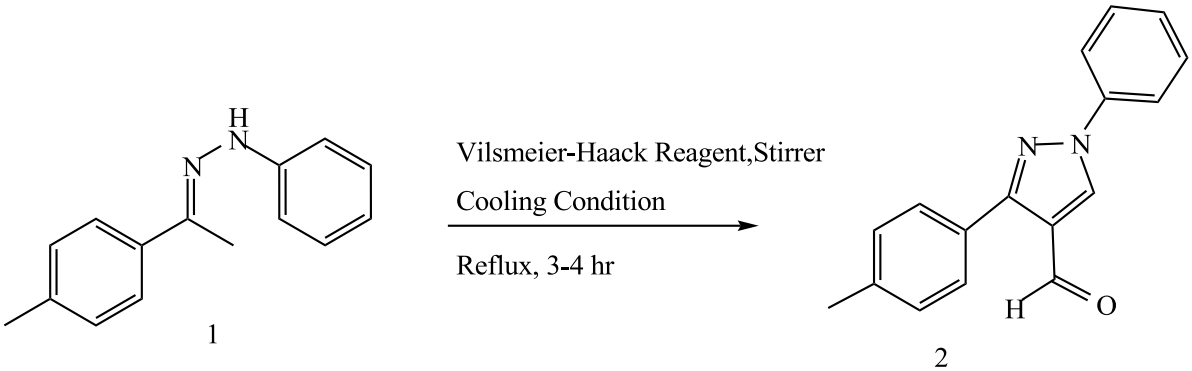
Pratap Odedra et al,performed the synthesis of some transition metal complexes such as Ni(II), Cu(II), Co(II), with a pyrazole heterocyclic compound as a ligand molecule was carried out in alcoholic medium.

Scheme 8:

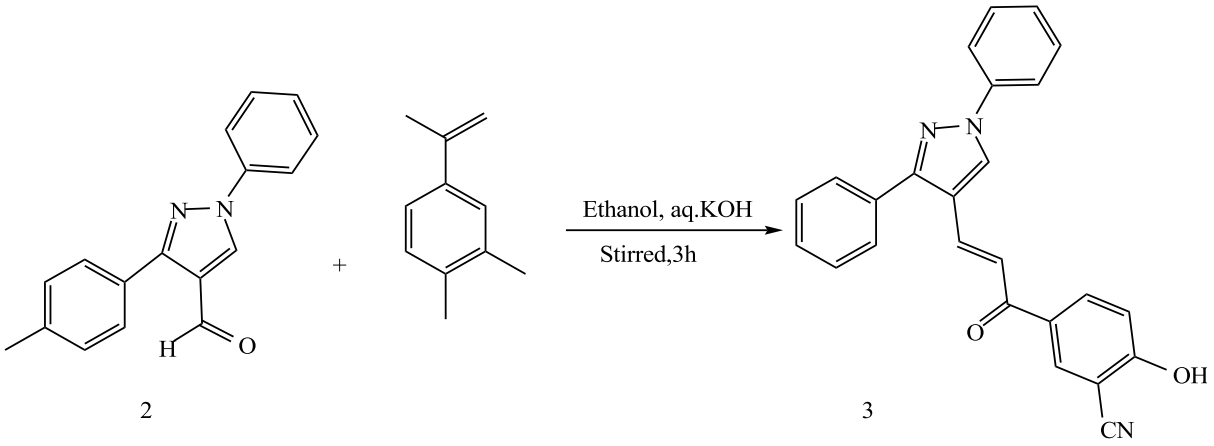
ISSN 2063-5346 *Section A-Research paper*



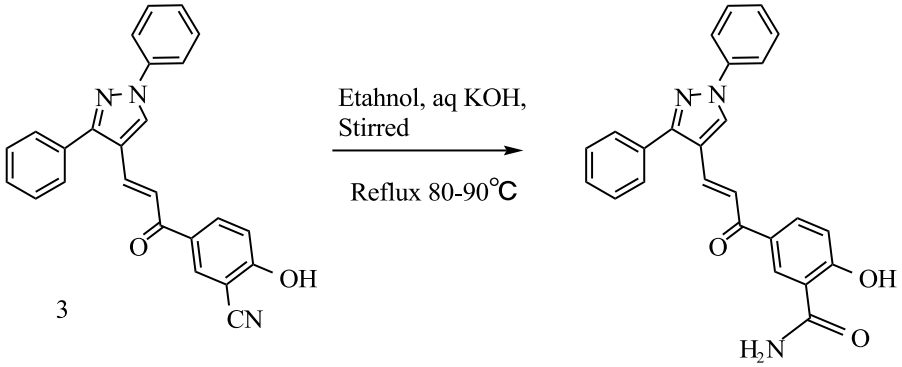
Scheme 1- Synthesis of (E)-1-Phenyl 2-(1(P-P-tolyl) ethylidene)hydrazine



Scheme 2- Synthesis of 1- Phenyl -3-(P-tolyl)-1H-Pyrazole-4-carbaldehyde

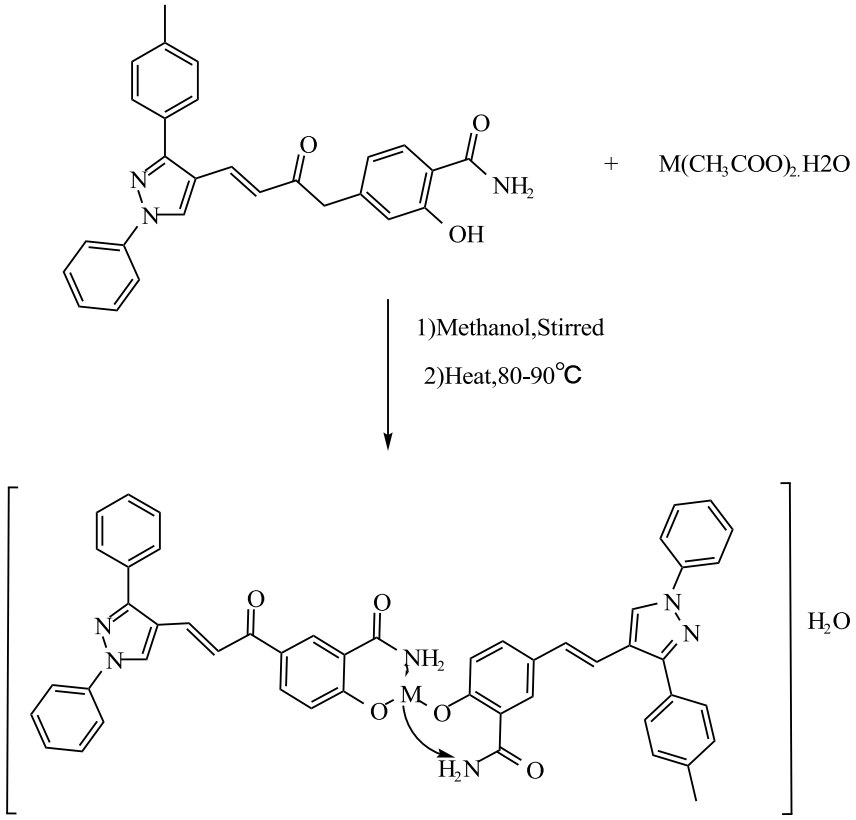


Scheme 3- synthesis of (E)-2 hydroxy -5-(3-(1-phenyl-3-(p-tolyl)-1H-pyrazole-4-yl)acryloyl)benzamide ligand.



Scheme 4- Synthesis of (E)-2- hydroxy-5-(3-1- phenyl-3-(p-tolyl)-1H-pyrazol-4-yl-acrylolyl)benzamide(OPD-1)Ligand

ISSN 2063-5346 *Section A-Research paper*



Scheme 5- Synthesis for synthesis of metal complex

M=Cu, Co, Ni

X= No.of Water molecules in metal complexes

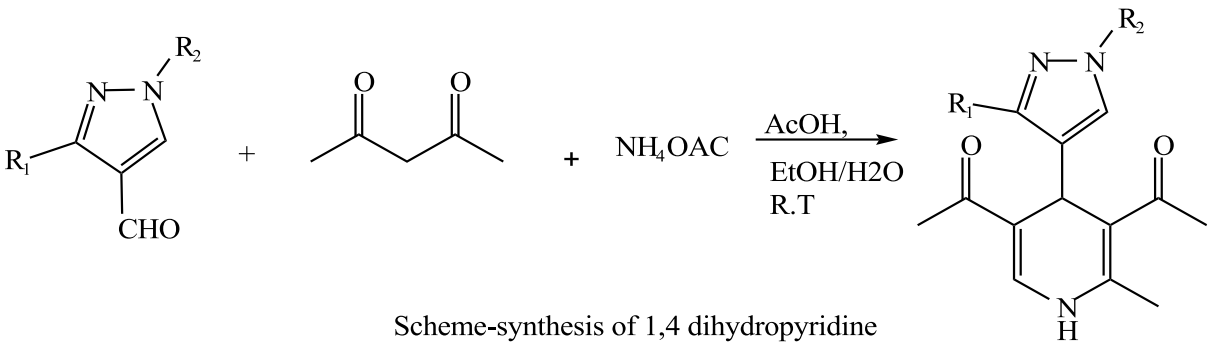
For Cu=2, Co=4, Ni=4.

The antimicrobial activity of these synthesized metal complexes are also tested against some selected bacterial and fungal strains and good to moderate biological activity of the metal complexes against selected bacterial and fungal strains are found in DMF and DMSO solvents.

Paramasivam. T et al, demonstrateda one-pot multicomponent reaction through Hantszch pyridine synthesis which providesa facile method for the synthesis of highly substituted 1, 4-dihydropyridines from pyrazole aldehyde, acetylacetone and ammonium acetate. They also tried to make the reaction eco-friendly using various solvents and catalyst. The better result was obtained using ethanol-water mixture and acetic acid as a catalyst. The synthesized compounds were well characterized by various spectroscopic techniques. It was expected that the calcium channel activity of 1,4-dihydropyridines may be enhanced by addition of pyrazole unit.

ISSN 2063-5346 *Section A-Research paper*

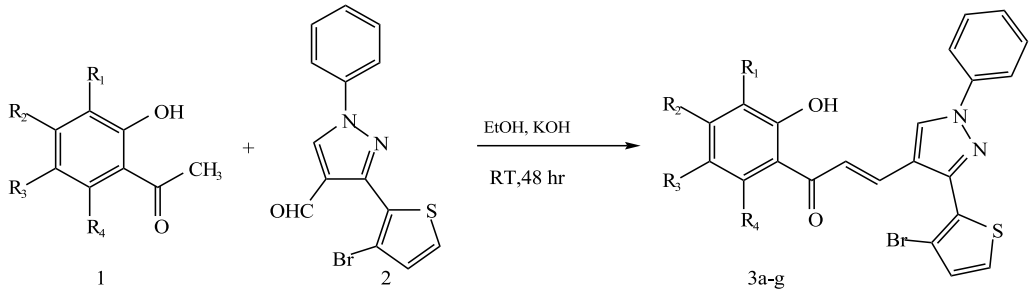
Scheme 9:



Scheme-synthesis of 1,4 dihydropyridine

Amol J Shirsat et al,developed a green, efficient and rapid method to synthesize novel chalcone derivatives containing pyrazole moiety has been developed by the condensation of various pyrazole aldehyde and ketone, in the presence of Potassium Hydroxide (KOH) in Ethanol (EtOH). This method has the advantages of operational simplicity, and high yield of products via a simple experimental and work-up procedure.

Scheme 10:



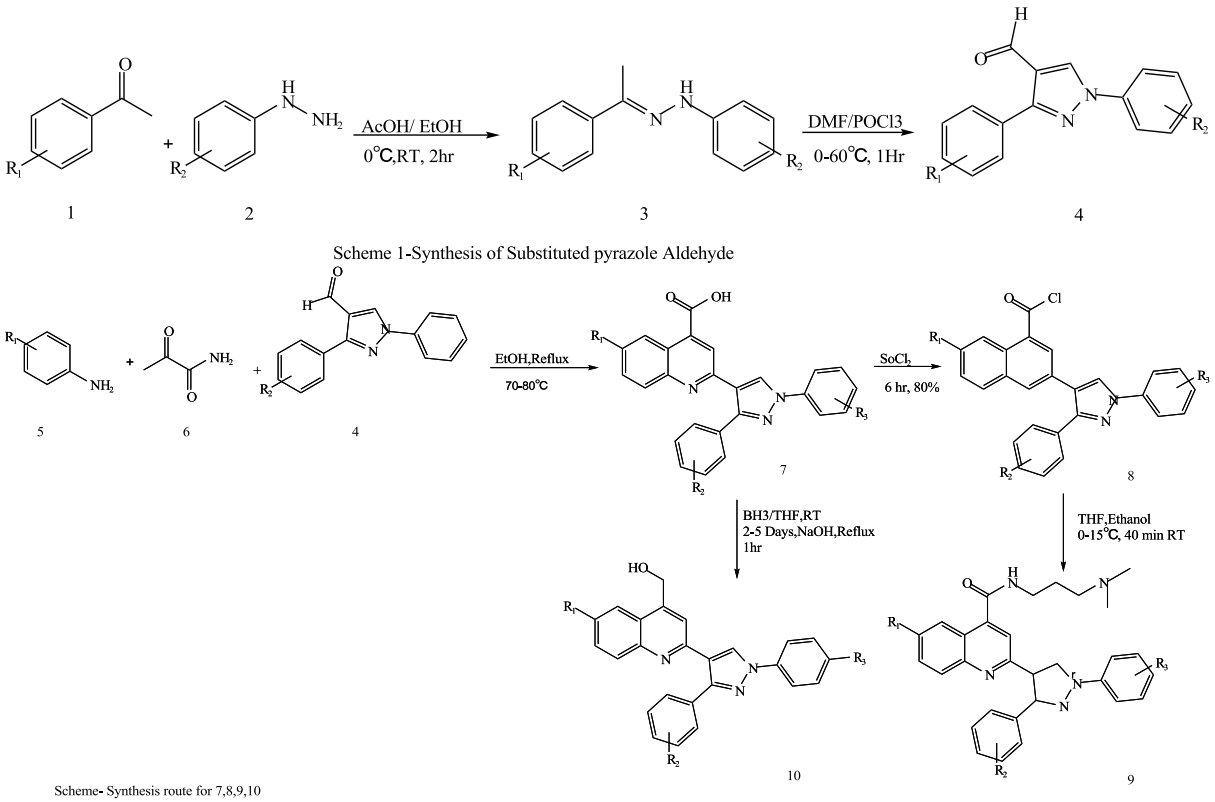
Scheme- Synthesis of series of various (E)-3-(3-3-bromothiopene -2-yl)1-phenyl)1H-Pyrazol-4-yl)-1-(2-hydroxyphenyl)prop-2-en-1-one

Compound	R_1	R_2	R_3
3a	H	H	H
3b	H	H	CH_3
3c	H	H	Cl
3d	Cl	H	Cl
3e	H	H	F
3f	H	CH_3	Cl
3g	H	H	Br

Using disc diffusion method,the newly synthesized compounds were screened for antimicrobial activity.

Arpan patel et al,In an effort for the development of novel antimicrobial, antimalarial and antitubercular agents, aseries of quinoline carboxylic acid derivatives containing substituted pyrazole moiety were synthesized from derivatives of substituted pyrazole aldehydes.

Scheme 11:



Scheme- Synthetic route for 7, 8, 9, 10

Compound	R_1	R2	R_3	Compound	R_1	R_2	R_3
7a	H	H	H	8f	H	H	P-NO_2
7b	H	H	H	8g	H	H	P--2,4 DiCl
7c	H	H	H	9a	H	H	H
7d	H	H	P-F	9b	H	P-Br	H
7e	H	H	P-NO_2	9c	H	P-CH_3	H
7f	H	H	P-Cl	9d	H	H	P-F
7g	H	H	P-2,4 DiCl	9e	H	H	P-NO_2
7h	CH_3	H	H	9f	H	H	P-Br

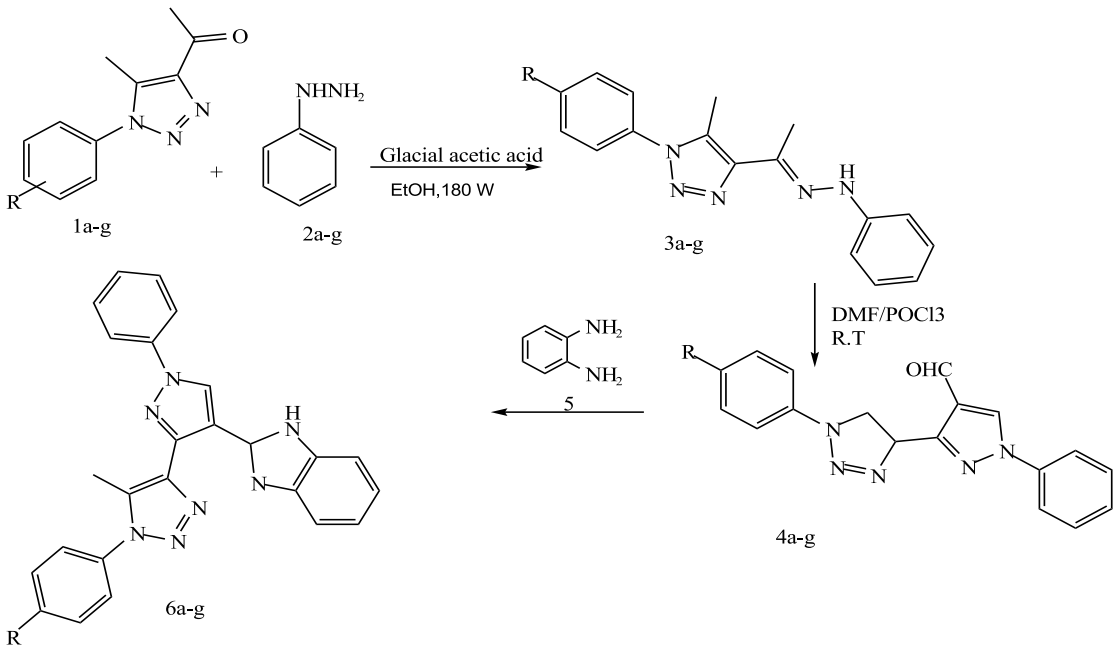
7i	CH_3	P-Br	H	9g	H	H	P-2,4 DiCl
7j	CH_3	P-CH_3	H	10a	CH_3	H	H
7k	CH_3	H	P-F	10b	CH_3	P-Br	H
7l	CH_3	H	P-NO_2	10c	CH_3	P-CH_3	H
7m	CH_3	H	P-Br	10d	CH_3	H	P-F
7n	CH_3	H	P-2,4, DiCl	10e	CH_3	H	P-NO_2
8a	H	H	H	10f	CH_3	H	P-Br
8b	H	P	H	10g	CH_3	H	P-2,4 DiCl
8c	H	P	H				
8d	H	H	P-F				
8e	H	H	P-Br				

The antibacterial activity of all synthesized compounds were examined against three Gram-positive bacteria (Bacillus subtilis, Clostridium tetani, Streptococcus pneumonia) and three Gram-negative bacteria (Escherichia coli, Salmonella typhi, Vibrio cholerae) by using ampicillin, norfloxacin and ciprofloxacin as the conventional antibacterial drugs. Antifungal activity was examined against two fungal species (Candida albicans and Aspergillus fumigatus) where nystatin and griseofulvin were used as the conventional antifungal drugs.

P. Shravani et al, A series of new 3-(5-methyl-1-aryl-1H-1,2,3-triazol-4-yl)-1-phenyl-1H-pyrazole-4-carbaldehydes and their benzimidazole derivatives were synthesized under both conventional and microwave irradiation methods. However, we successfully obtained good yields in shorter reaction times under microwave irradiation. All the synthesized compounds were characterized by ^{1}H NMR, ^{13}C NMR, IR and mass spectral analyses. The synthesized compounds have been screened as potential antiproliferative agents. The antiproliferative activity of the synthesized compounds was studied against two cancer cell lines C6 (nerve cells) and MCF-7 (human breast adenocarcinoma cells) and among them, compounds and exhibited highly potent activity against C6 cell line and exhibited highly potent activity against MCF-7 cell line.

Scheme 12:

ISSN 2063-5346 *Section A-Research paper*



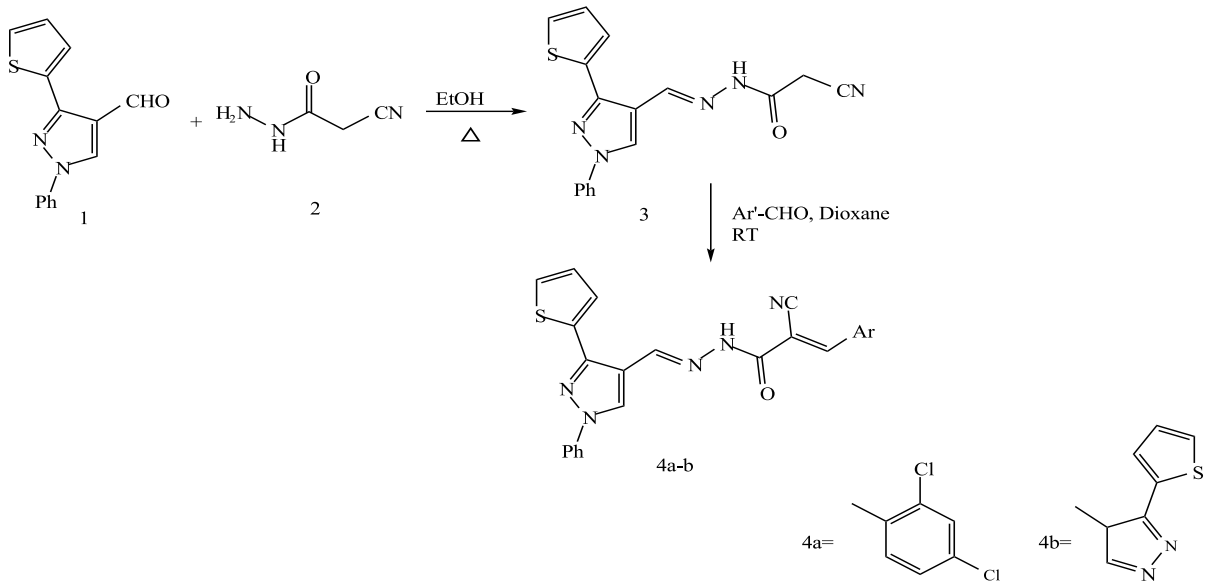
a=R: H, b=R:OMe, c=R: F, d=R:Cl,

e=R:Br, f=R:Me,g=R: NO_2

Eman A et al, performed condensation of pyrazole aldehyde with 2 acetohydrazide in refluxing ethanol for 2 hours afforded N condensation products in better yield. Knovengel condensation of active methylene compound with aldehyde, dioxane containingpiperdine at base at ambient temp. gives α, β unsaturated carbonyl compound.

Scheme 13:

ISSN 2063-5346 *Section A-Research paper*



Scheme- Synthesis of hydrazide hydrazone and knovengel codensation products

Some of the synthesized compounds were screened for their in vitro antitumor activities against two different human tumor cell lines including hepatocellular liver carcinoma (HepG2) and breast adenocarcinoma (MCF7) activities. Compound 3 was the most potent against the two tumor.

In the present work, in our laboratory, we have prepared chalcone from o-hydroxy acetophenone by the simple condensation reaction. A simple, efficient and fast procedure for the synthesis of novel chalcone derivatives having pyrazole moiety has been developed by the condensation of pyrazole aldehyde, in the presence of Ethanol (EtOH) and Potassium Hydroxide (KOH). The given method has the advantages of simplicity of work, and better yield of products through a simple experimental as well as work-up procedure. all the synthesized compound were characterized by spectral data like Mass, IR, ^{1}H NMR, ^{13}C NMR.

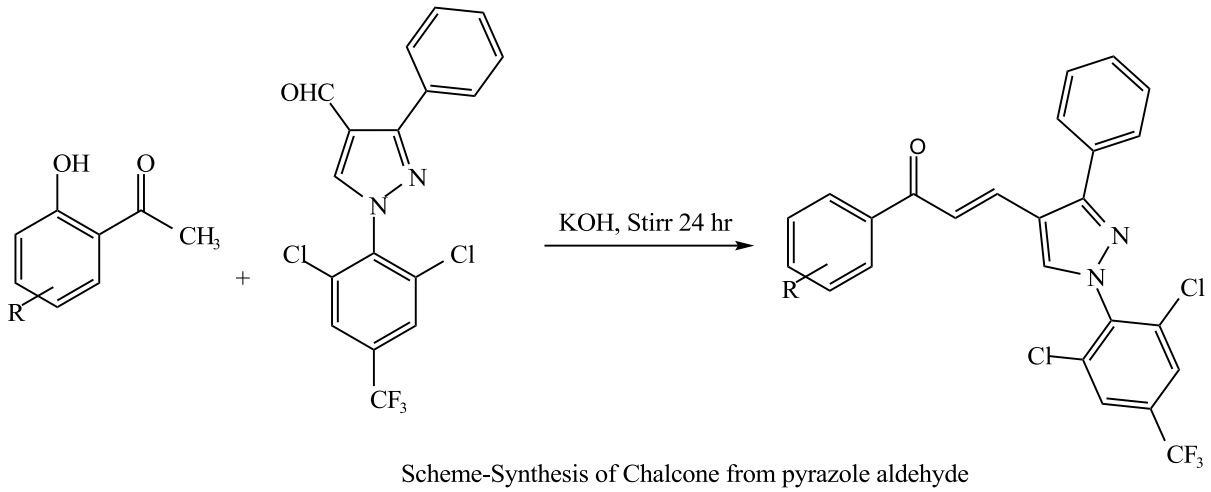
A. Experimental Section:

(i) General procedure for synthesis of Chalcone

Acetophenone (10 mmol) was dissolved in suitable solvent and aromatic aldehyde (10 mmol) was added with constant stirring at room temperature. Then KOH solution was added to reaction mixture which was stirred for 24 hrs at room temperature.The progress of the reaction was monitored by thin layeredchromatography. Finally the reaction mixture was poured into crushed ice and neutralized with HCl. The product separated out, was filtered, washed with water, dried and recrystallized from alcohol to give chalcone.

ISSN 2063-5346 *Section A-Research paper*

Scheme 15:



Scheme-Synthesis of Chalcone from pyrazole aldehyde

Table- Data of Synthesized Compounds-

Compound	R_1	R_2
1a	H	CH_3
1b	H	Cl
1c	Cl	Cl
1d	H	Br
1e	Br	Br
1f	CH_3	Cl

Synthesis of chalcone derivatives:

1a-3-(1-(2,6-dichloro-4-(trifluoromethyl)phenyl)-3-phenyl-1H-pyrazol-4-yl)-1-(2-hydroxy-5-methylphenyl)prop-2-en-1-one.

Yield:62 %

M.P:132C

m/e=516.06.

^{1}H NMR-(300 MHz, DMSO,ɗ, ppm): 16.47(s,1H, OH), 8.44 (s,1H,Ar-H), 8.06 (d,2H,J=15.1Hz,Vinyl C-H), 7.67((d,2H,J=7.5Hz, 1H ,Ar-H), 7.60(d, 2H, J=15.1 Hz, Vinyl C-H), 7.54(d, 2H, J=7.5Hz, 2H), 7.42(s,1H, J=7.5Hz, Ar-H) 6.95(s, 1H, J=7.5Hz, Ar-H).

^{13} C NMR- 192.1,160.6, 145.1, 150.4, 139.3, 136.2, 130.3,130.0, 131.5, 131.3, 129,2, 128,7, 127.5, 123.6, 123.1, 117.2, 21.3.

1b-1-(5-chloro-2-hydroxyphenyl)-3-(1-(2,6-dichloro-4-(trifluoromethyl)phenyl)-3-phenyl-1H-pyrazol-4-yl)prop-2-en-1-one.

Yield:67%

M.P:162

m/e=536.01

^{1}H NMR-(300 MHz, DMSO, ɗ, ppm):16.47(s, 1H, OH),8.44 (s,1H,Ar-H), 8.06 (d,2H,J=15.1Hz,Vinyl C-H), 7.67((d, 2H, J=7.5Hz, 1,Ar-H), 7.60(d, 2H, J=15.1 Hz, Vinyl C-H), 7.54(d, 2H, J=7.5Hz, 2H), 7.42(s,1H, J=7.5Hz, Ar-H) 6.95(s, 1H, J=7.5Hz, Ar-H).

^{13}C NMR-192.8,148.1, 161.7,150.4,139.3,137.1,135.2,133.5,131,5, 131.1,130.3, 129.2,128,7, 128.7, 127.9, 127.3, 124.0.

1c:1-(3,5-dichloro-2-hydroxyphenyl)-3-(1-(2,6-dichloro-4-(trifluoromethyl)phenyl)-3-phenyl-1H-pyrazol-4-yl)prop-2-en-1-one.

Yield: 71%

M.P:181

m/e=569.97.

^{1}H NMR-(300 MHz, DMSO, ɗ, ppm):15.78(s, H, OH), 8.44 (s,1H,Ar-H), 8.06 (d,2H,J=15.1Hz,Vinyl C-H), 7.67((d, 2H, J=7.5Hz,Ar-H), 7.60(d, 2H, J=15.1Hz, Vinyl C-H), 7.54(d, 2H, J=7.5Hz, 2H), 7.42(s,1H, J=7.5Hz, Ar-H), 6.95(s, 1H, J=7.5Hz, Ar-H).

^{13}C NMR-192.8, 160.9,150.4, 145.1, 141.9,139.3, 135.2, 133.8, 131.3, 130.3, 129.2, 128.7, 128.3, 127.5, 127.3, 127.0, 123.5, 116.5, 113.9, 113.0.

1d: 1-(5-bromo-2-hydroxyphenyl)-3-(1-(2,6-dichloro-4-(trifluoromethyl)phenyl)-3-phenyl-1H-pyrazol-4-yl)prop-2-en-1-one.

Yield:69%

M.P:142

m/e=501.04

^{1}H NMR-(300 MHz, DMSO, ɗ, ppm):16.47(s, 1H, OH),8.44 (s, 1H, Ar-H), 8.06 (d, 2H, J=15.1Hz,Vinyl C-H), 7.67(d, 2H, J=7.5Hz, 1,Ar-H), 7.60(d, 2H, J=15.1 Hz, Vinyl C-H), 7.54(d, 2H, J=7.5Hz, 2H), 7.42(s,1H, J=7.5Hz, Ar-H) 6.95(s, 1H, J=7.5Hz, Ar-H).

^{13}C NMR-190.8, 148.1, 162.8, 152.4,140.3, 137.1, 136.2, 134.5, 131,5, 131.0, 130.3, 129.2, 128,8, 128.7, 127.6, 127.3, 123.0.

1e:1-(3,5-dibromo-2-hydroxyphenyl)-3-(1-(2,6-dichloro-4-(trifluoromethyl)phenyl)-3-phenyl-1H-pyrazol-4-yl)prop-2-en-1-one.

Yield:63%

M.P:173

m/e=613.92

^{1}H NMR-(300 MHz, DMSO, ɗ, ppm): 21.78(s, H, OH), 8.44 (s,1H,Ar-H), 8.06 (d,2H,J=15.1Hz,Vinyl C-H), 7.67((d, 2H, J=7.5Hz, 1,Ar-H), 7.60(d, 2H, J=15.1 Hz, Vinyl C-H), 7.54(d, 2H, J=7.5Hz, 2H), 7.42(s,1H, J=7.5Hz, Ar-H) 6.95(s, 1H, J=7.5Hz, Ar-H).

^{13}C NMR-192.8, 160.9,150.4, 145.1, 141.9,139.3, 135.2, 133.8, 131.3, 130.3, 129.2, 128.7, 128.3, 127.5, 127.3, 127.0, 123.5, 116.5, 113.9, 113.0.

1f: 1-(5-Chloro-2 hydroxy -4-methylphenyl-3-(1-(2,6 dichloro-4-(trifluromethyl)phenyl-3-phenyl-1H-pyrazol-4 yl)prop-2-ene-1-one.

Yield:64%

M.P:170

m/e=550.02

^{1}H NMR-(300 MHz, DMSO, ɗ, ppm): 12.4(s,1H,Ar), 8.44(s,1H,Ar), 8.08(s,J=15.1Hz, 1H,Ar), 7.67(d, J=7.5Hz, 1H, Ar), 7.54(dd,J=7.5Hz,1H,Ar),7.53(s,J=1.5Hz,1H,Ar),7.52(d,J=7.5Hz,1H,Ar), 7.12(dd,1H,Ar),2.33(s,1H,Ar).

^{13}C NMR-192.8, 162.9, 150.4,145.1, 141.5, 139.3, 135.6, 135.2, 131.3, 130.4, 129.2, 128.9, 127.5, 127.3, 123.6, 123.5, 121.8, 113.5.

(ii) Biological activity:

All the synthesized compounds were screened for their antibacterial activity by using the Cup plate method, against selected Gram positive and Gram-negative bacteria. Dimethyl sulfoxide (DMSO) was used as a solvent while Amoxycillin and Streptomycin were used as the standard drugs. The results of antibacterial activity of all the synthesized compounds by cup plate method are presented in table. All synthesized compounds were screened for their antibacterial activity by using the Cup-plate method.

The following bacterial cultures were used for antibacterial studies

1) Bacillus subtilis

2) Staphylococcus aureus

3) Escherichia coli

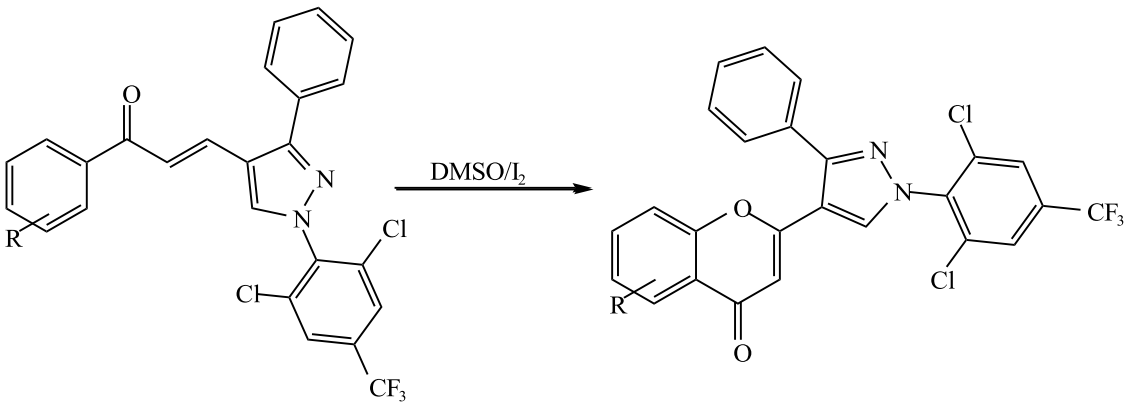
4) Pseudomonas aeruginosa

In addition, we also prepared derivatives of chromone from the chalcone through cyclization method. It is a simple, efficient method and fast procedure gives better yield.

(iii) General procedure for Synthesis of Chromone:

Chalcone (0.001 mol) was dissolved in 10 mL of DMSO containing catalytic amount of iodine. The reaction contents were heated at 145oC for 2 h and left overnight. The reaction mixture was poured over crushed ice and separated solid product 4 was filtered, washed with cold water followed by 10% Sodium thiosulphate solution and again with cold water. Product was recrystallized from ethanol. Data of synthesized compounds are given below.

Scheme 16:



Scheme 2- Synthesis of Chromones from Chalcone

Data of synthesized compounds:

Compound	R_1	R_2
2a	CH_3	H
2b	Cl	Cl
2c	H	Cl
2d	Br	Br
2e	H	Br
2f	CH_3	Cl

2a- 2-(1-(2,6-dichloro-4-trifluromethyl) phenyl)-3-phenyl-1H-Pyrazole-4-yl)5-methyl-4H-chromen-4-one.

Yield:62%

M.P:162

m/e-568.99

^{1}H NMR-(300 MHz, DMSO, ɗ, ppm): 8.47 (s, 1H, Ar), 7.68 (d, 1H, J=7.5Hz, Ar), 7.67 (d, J=7.5Hz, 1H, Ar), 7.53 (dd, J=1.5Hz, 1H, Ar), 7.53(s, J=7.5Hz, 1H, Ar), 7.28(s, 1H, Ar), 7.22(s, 1H, Ar), 6.71(s, 1H, Ar).

^{13}C NMR- 177.5, 163.6, 153.2, 150.4, 139.3, 135.2, 133.1, 133.0, 131.3, 130.3, 129.2, 128.9, 127.5, 124.6, 125.1, 123.6, 123.1, 120.8, 113.0, 110.5, 21.3.

2b- 5,7-dichloro-2-(1-(2,6-dichloro-4-trifluromethyl) phenyl)-3-phenyl-1H-Pyrazole-4-yl)-4H-chromen-4-one.

Yield:67%

M.P: 204

m/e-569.95

^{1}H NMR- (300 MHz, DMSO, ɗ, ppm): 8.44(s,1H,Ar), 7.67(d,J=7.5Hz, 1H,Ar), 7.54(dd,J=1.5Hz, 1H,Ar), 7.53(s,1H,7.5Hz, Ar), 7.28(s,1H, Ar), 7.22(s,1H,Ar), 6.71(s,1H,Ar).

^{13}C NMR-182.3, 155.5, 145.4, 139.3, 133.5, 133.1, 129.3, 128.3, 126.5, 126.2, 124.6, 124.1, 113.5, 62.7, 50.1, 38.3, 33.9, 32.6.

2c- 5 chloro-2-(1-(2,6 dichloro-4-trifluromethyl) phenyl)-3-phenyl-1H-Pyrazole-4-yl)-4H-chromen-4-one.

Yield: 72%

M.P:188

m/e-533.99

^{1}H NMR-(300 MHz, DMSO, ɗ, ppm): 8.45 (s, 1H, Ar), 7.67(d, J=7.5Hz, 1H, Ar), 7.54(dd, J=1.5Hz, 1H,Ar), 7.53(s,1H,1.5Hz, Ar), 6.70(s, 1H, Ar), 5.90(s, 1H, Ar), 5.80 (dd, 1H, Ar), 2.52(d, 1H, Ar).

13C NMR- 200, 154.5, 150.4, 139.3, 133.3, 133.0, 129.2,128.7, 127.5, 126.0, 123.6, 123.1, 113.0, 61.7, 49.1, 37.3, 33.9, 32.8

2d- 5,7dibromo-2-(1-(2,6-dichloro-4-trifluromethyl) phenyl)-3-phenyl-1H-Pyrazole-4-yl)-4H-chromen-4-one.

Yield:62%

M.P:197

m/e-657.85

^{1}H NMR-(300 MHz, DMSO, ɗ, ppm): 8.45 (s, 1H, Ar), 7.73(s, 1H, Ar), 7.67(d, J=7.5Hz, 1H, Ar), 7.54(dd, J=1.5Hz, 1H,Ar), 7.53(s,1H,1.5Hz, Ar), 6.70(s, 1H, Ar), 5.90(s, 1H, Ar), 5.80 (dd, 1H, Ar), 2.52(d, 1H, Ar).

^{13} C NMR-182.1, 163.6, 150,4, 139.3, 135.2, 133.0, 131.3, 130.3, 129.3, 129.4, 128.4, 127.5, 125.2, 123.6, 123.1, 115.0, 113.0, 110.5.

2e-5bromo-2-(1-(2,6-dichloro-4-trifluromethyl)phenyl)-3-phenyl-1H-Pyrazole-4-yl)-4H-chromen-4-one.

Yield: 69%

M.P:169

m/e-577.95

^{1}H NMR-(300 MHz, DMSO, ɗ, ppm): 8.45 (s, 1H, Ar), 7.73(s, 1H, Ar), 7.67(d, J=7.5Hz, 1H, Ar), 7.54(dd, J=1.5Hz, 1H,Ar), 7.53(s,1H,1.5Hz, Ar), 6.70(s, 1H, Ar), 5.90(s, 1H, Ar), 5.80 (dd, 1H, Ar), 2.52(d, 1H, Ar).

^{13} C NMR- 182.4, 163.6, 159.4, 150.4, 139.3, 136.4, 135.2, 133.0, 131.3, 130.3, 129.2, 128.7, 128.5, 127.5,127.4, 123.6,123.1, 123.0, 115.1, 113.0, 110.5.

2f- 6-Chloro-2-(1-(2,6 dichloro-4- trifluromethyl)phenyl)-3-phenyl-1H-pyrazole-4-yl)7methyl-4H-chromen-4-one.

Yield:67%

M.P:204

m/e- 548.48.

^{1}H NMR-(300 MHz, DMSO, ɗ, ppm): 8.46 (s, 1H, Ar), 7.73(s, 1H, Ar), 7.67(d, J=7.5Hz, 1H, Ar), 7.58(dd, J=1.5Hz, 1H, Ar), 7.53(s,1H,1.5Hz, Ar), 6.70(s, 1H, Ar), 5.90(s, 1H, Ar), 5.80 (dd, 1H, Ar), 2.52(d, 1H, Ar), 2.35(s, 3H, CH).

^{13} C NMR- 177.5, 163.6, 155.2, 150.4, 139.3, 135.2, 133.0, 131.3, 130.5, 130.3, 129.2, 128.7, 127.5, 126.5, 123.6, 123.1,122.3, 117.9, 110.5, 113.0, 20.2.

(iv) Biological activity:

The ability of the compounds to inhibit growth of clinical bacteria was determined using the agar disc diffusion method. Sterile filter paper discs, 11 mm in diameter were impregnated with each compound concentration and dried at 30°C in the static incubator. They were then carefully placed aseptically with a forceps on the surface of the Nutrient Agar (NA) plates that were preinoculated with the 24hr culture of bacteria and 0.1 ml spore suspension (1 × 105 spores/ml). The control antibiotics disc containing gentamicin (40 µg/ml) was placed on each of the inoculated plates of nutrient agar. The plates were left on the bench undisturbed for few minutes, after which the bacterial culture plates were incubated at 37°C for 24 h. The external diameters of visible zones of growth inhibition were measured after incubation.

Conclusion-

We report and discussed different synthetic methods of pyrazole aldehyde and their biological activity.Here, we developed asimple, efficient and fast procedure for the synthesis of novel chalcone derivatives having pyrazole moiety as well as series of chromone. The

given method has the advantages of simplicity of work, and better yield of products through a simple experimental as well as work-up procedure.

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