International Journal of Allied Practice, Research and Review

Website: www.ijaprr.com (ISSN 2350-1294)

Approach for Synthesis of Some Novel Heterocyclic Analogues as Bioactive Agents

Mayursinh.J. Zala, Bonny.Y.Patel and Ramesh.D.Santa
B.V. Shah (Vadivihar) Science College,
Department of Chemistry, C. U. Shah University, Wadhwancity,
Surendranagar, Gujarat, India

Abstract - A series of (3'-(4-substituted phenyl)-5-(thiophene/naphthalen-2-yl)-1'-phenyl-3,4-dihydro1'H,2H-[3,4'-bipyrazol]-2-yl)(pyridin-3/4-yl)methanone [6(a-d)] have been synthesised by treatment with 1-phenyl-2-(1-(p-substituted phenyl)ethylidene)hydrazine hydrate in ethanol gave different 3-(4-substituted phenyl)-1-phenyl-1H-pyrazole-4-carbaldehyde by vilsmeier- hack reaction . All steps were synthesised by green procedure with excellent yield. Product obtained were characterised by means of the NMR, IR and Mass spectral analysis. The synthesized compounds were evaluated for their in-vitro antimicrobial activity against different bacterial and fungal strains using Mueller-Hinton Broth dilution method and also invitroantitubercular activity was performed.

Keywords: pyridin, pyrazole, vilsmeier hack reaction, Green synthesis

I. Introduction

The study of heterocyclic compounds is of great interest both from the theoretical as well as practical point of view. Organic chemistry is largely made up of heterocyclic chemistry. The heterocyclic compounds have a cyclic structure contain two or more heteroatoms in the rings. The number of possible heterocyclic systems is almost illimitable, a massive number of heterocyclic compounds are known and this number is increasing very fast. Heterocyclic rings bearing nitrogen atom are most copious in nature than those containing oxygen or sulphur.

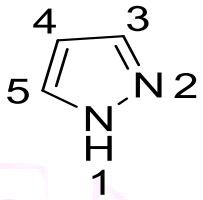
Heterocyclic compounds are very broad assigned in nature and are crucial to life in different ways, most of sugars and their derivatives including vitamins and some members of vitamin B group have heterocyclic rings with nitrogen atom. The countless plant alkaloids are aware example of complex nitrogenous ring compounds. They have been utilized for thousands of years in diverse religious, cultural and medicinal applications. Heterocyclic compounds are important components of side chain of the amino acid, histidine. It is found at the region active site of several enzymes, which involved in proton transfer reactions. The invention of penicillin

and its marvellous bactericidal properties and the urge to fulfill its synthesis, to promoted intensive research in the area of heterocyclic chemistry.

The occurrence of fungal and bacterial infections has increased dramatically since past few years. The infection has spread among human and also animals. The widely use of antifungal and antibacterial drugs and their resistance against fungal and bacterial infections has urge to chronic health issue. The resistance of broad spectrum antifungal and antibacterial agents has initiated discovery and modification of the modern antifungal and antibacterial drugs. Thus , these antifungal and antibacterial class of drugs is the vast contribution of the 20th century to Medicinal chemistry.

1.1 **PYRAZOLE:**

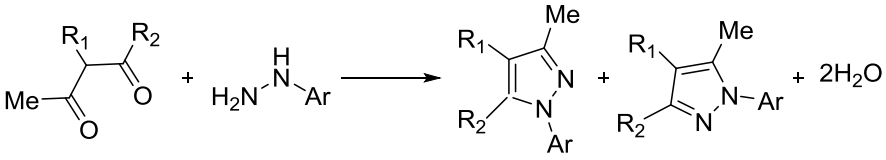
Pyrazole are well famous and important nitrogen containing five member heterocyclic atomic compounds. It has chemical compexicity in heterocyclic ring. Pyrazole which has two Nitrogen and aromatic character provides diverse functionality. They are Building blocks of life due to its wide range of biological activity like anti-bacterial, analgesic, anti-microbial, anti-inflammatory and Anti-cancer.



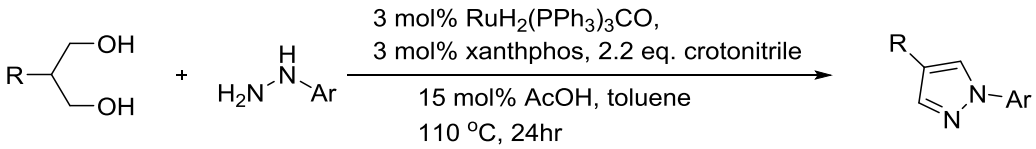
1.1.2 Synthetic Approach:

The five member hetrocyclic pyrazole ring system has been studied in detail because of its application in photography, dyes and as pharmaceutical agents. The five member ring system is a common for many pharmaceutical active molecules. polmacoxib, a newer drug with pyrazole five member ring system have been recently introduced in to the market. Although there are many ways to prepare the pyrazole ring, the condensation of the 1,3-dicarbonyl and its variation remains the most common and facile root to assemble this ring system.

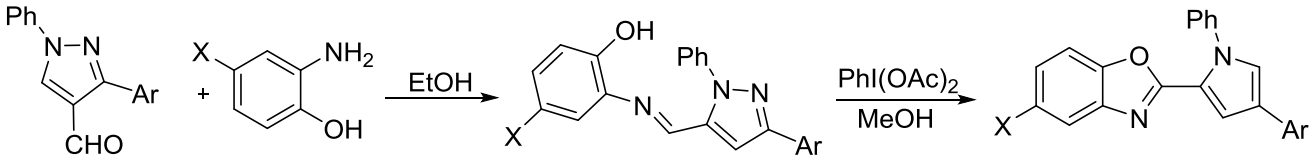
Knorr[1] reported the first pyrazole derivative in 1883. The reaction of ethylacetoacetate and phenyl hydrazine to obtain a novel structure identified as l-phenyl-3-methyl-5-pyrazolone.



Schmitt.[2]achieved a region selective synthesis of unsymmetrical pyrazoles from β-hydroxy ketones Ruthenium-catalyzed hydrogen transfer of 1,3-diols in the presence of alkyl hydrazines provides 1,4-disubstituted pyrazoles

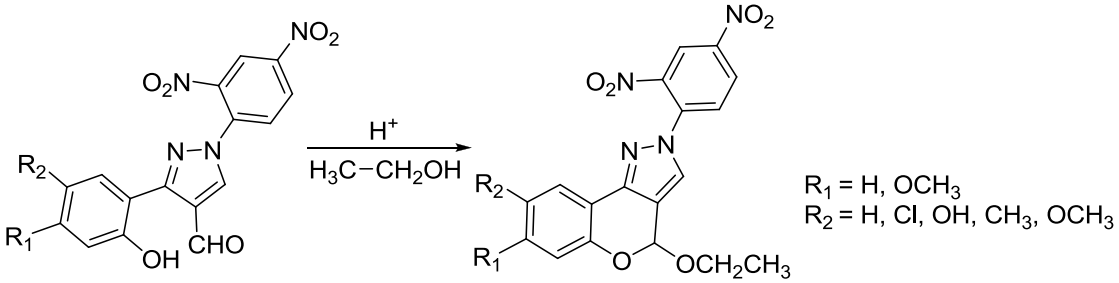


Prakash*et al*[3] synthesized 2-(3-aryl-1-phenyl-4-pyrazolyl) benzoxazoles by cyclization of the corresponding Schiff's bases using iodobenzenediacetate in methanol as an oxidant.



Ar = Ph, 4-Cl-C_6H_4, 4-CH_3-C_6H_4, 4-NO_2-C_6H_4, 4-OCH_3-C_6H_4 X = H, Cl

S. Selvi and P. T. Perumal[4] Synthesized of 4-ethoxy-4*H*-1-benzopyrano-[4,3-*c*] pyrazole.



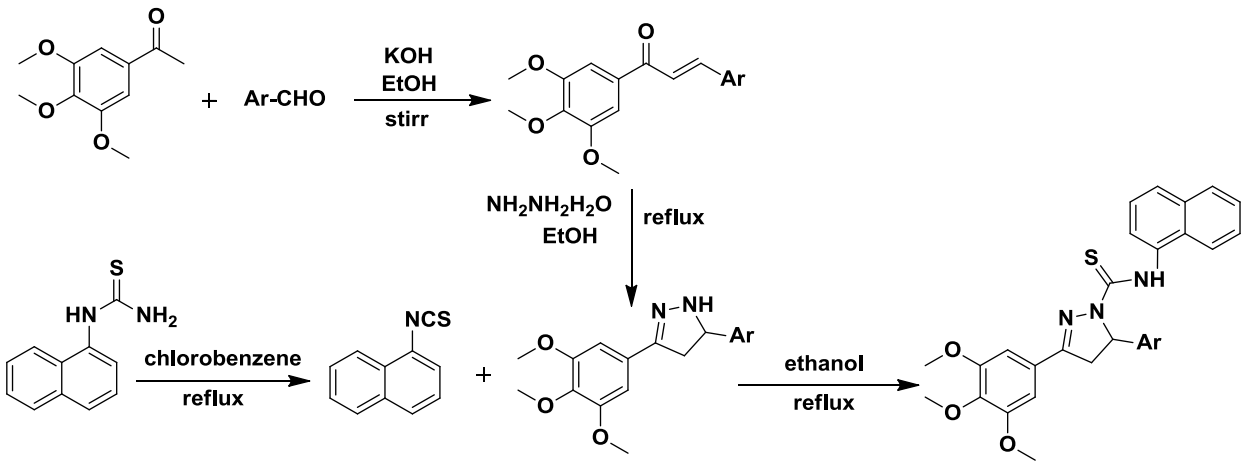
1.2. PYRAZOLINE

The synthesis of pyrazolylpyrazoline bearing, Pyridinederivatives and investigation of their potent biological activities. This study involves one-pot condensation reaction of more reactive pyrazole-chalconewith pyridine nucleus compound in presence of NaOH in EtOH at room temperature to gives pyrazolylpyrazoline bearing pyridine derivatives. So, it is valuable to describe brief introduction regarding synthetic and biological consequence of the pyrazolylpyrazoline derivatives.

1.2.1. SYNTHETIC AND BIOLOGICAL ASPECT OF PYRAZOLINE DERIVATIVES:

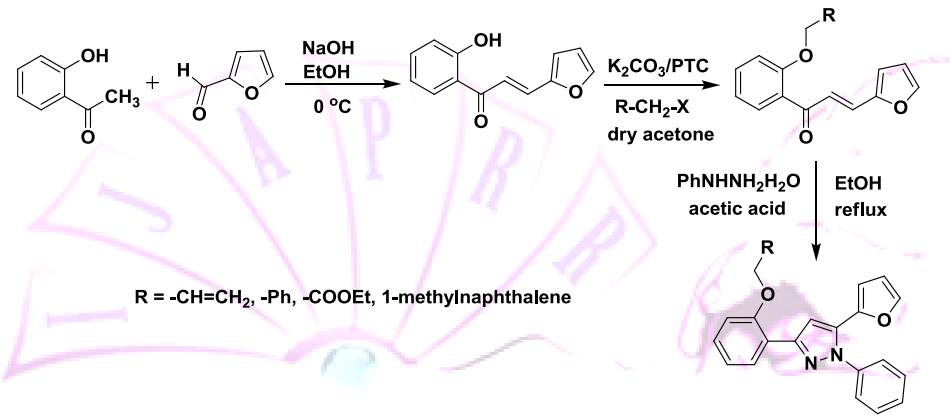
Recently, there has been a lots off the investigation of novel pyrazoline scaffold which are able to inhibit the biologicalactivities. However, a various changes have been made on the pyrazoline derivatives to obtain its biological activity, because pyrazoline derivatives are five members nitrogen containing rings reach of electrons which play an important role in the various medicinalfield. From the literature survey, many report for the synthesis of pyrazoline was found. Some of them cited below.

Lu *et al*[5]have reported the synthesis of newer 3,5-disubstituted pyrazoline analogues from the reaction of pyrazoline and α-naphthylisothiocyanate in presence of ethanol and their evaluated for their *in vitro* anticancer efficacies against human non-small-cell lung cancer cell line A549.



Ar = 1-naphthaldehyde, 4-pyridine carbaldehyde, 4-CH_3, 4-SCH_3, 4-F, 4-Br, 4-Cl, 4-OCH_3

Rani and co-workers[6] have synthesized a series of *N*-substituted 5-(furan-2-yl)-phenyl pyrazoline derivatives from the cyclization of various 1-[2-(alkoxy) phenyl]-3-(furan-2-yl)prop-2-en-1-one with *N*-substituted phenyl hydrazine in the presence of CH_3COOH in ethanol and studies of their*in vitro* antibacterial activity.



II. EXPERIMENTAL

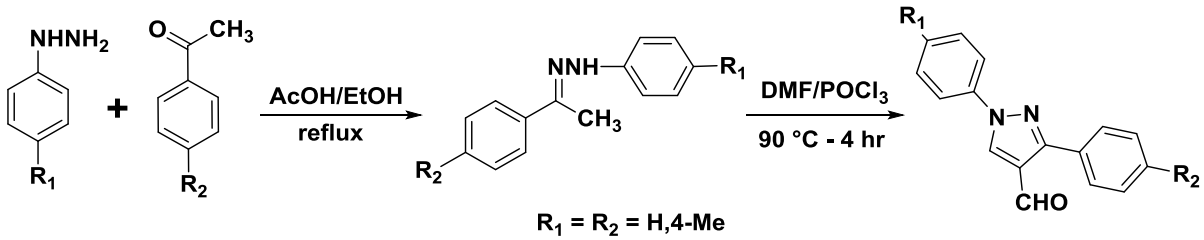
All reactions were performed with commercially available reagents. The solvents were used of analytical grade. They were used without further decontamination. All reactions were monitered by thin-layer chromatography (TLC) on aluminium plates coated with silica gel, 0.25 mm thickness (Merck). Mass spectra were recorded on Shimadzu LCMS 2010 spectrometer (Shimadzu, Tokyo, Japan).The IR spectra were confirmed by FTIR MB 3000 spectrophotometer (ABB Bomem Inc., Canada/Agaram Industries, Chennai) using Zn-Se Optics (490-8500 cm^{-1}).^1H and ^{13}C Nuclear Magnetic Resonance spectra were checked in DMSO-d_6 on a BrukerAvance 400F (MHz) spectrometer (Bruker Scientific Corporation Ltd., Switzerland) using residual solvent signal as an internal standard at 400 MHz and 100 MHz respectively. Splitting patterns were designated as follows: s for singlet; d for doublet; dd for doublet of doublet; t for triplet and m for multiplet. Chemical shifts are reported in parts per million (ppm).The elemental analysis was done by using Perkin-Elmer 2400 series-II elemental analyzer (Perkin-Elmer, USA).

General procedure for the preparation of 6(a-h)

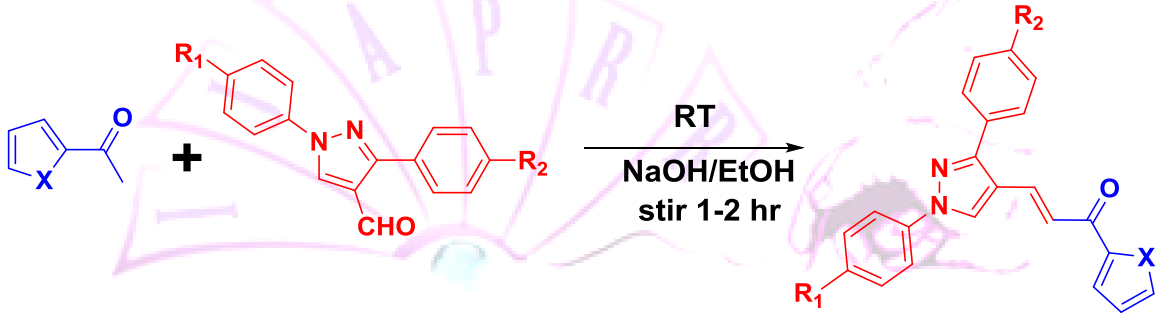
Take an equivalent mixture of 3-(4-sub. phenyl)-1-phenyl-1*H*-pyrazole-4-carbaldehyde (1 mol) and 2-acetyl thiophene/Napthelene (1.2 mol) were placed in a three-necked round bottom flask equipped with a mechanical stirrer at room temperature for 1-2 hr and adding 5

mol% of NaOH is dissolved in water/ethanol (1:2) (30 mL) solution.the reaction was monitored by TLC. After completion of reaction, the solid crystalized precipited separate out and recrystallized from methanol to obtain pure compounds**(*E*)-3-(1-phenyl-3-(*p*-sub. phenyl)-1*H*-pyrazol-4-yl)-1-(thiophen/nepthelene-2-yl)prop-2-en-1-one5[a-d].**now take a Mixture of the compound 5(a-d) and Nicotinic hydrazide/isoniazide was charged in 100ml round bottom flask,in this flask NaOH (0.125 mmol) in ethanol (10 mL) under simple conventional method stir for 8-9 min. at room temperature, completion of the reaction was confirmed by TLC. The solid mass separated was collected by filtration and easy isolation of the product obtain were purified by recrystallization with methanol and dried. The products 6(a-h) were received quantitatively (85-94% yield) with good purity.

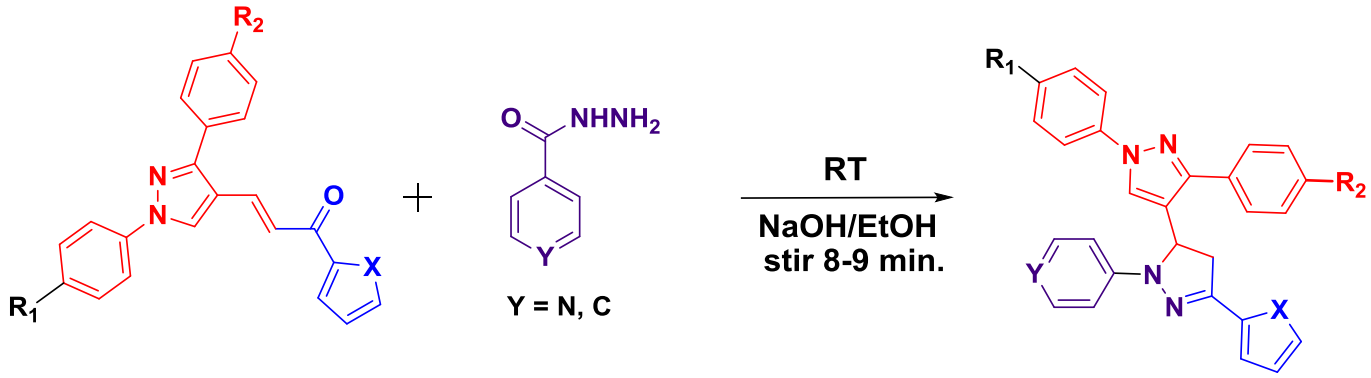
Step-1:



Step-2:



Step-3:



[6a](1',3'-diphenyl-5-(thiophen-2-yl)-3,4-dihydro-1'H,2H-[3,4'-bipyrazol]-2-yl)(pyridin-3-yl)methanone.

$C_{28}H_{21}N_5OS$;M.W.-475.15g/mole; C,70.72;H,4.45;N,14.73;O,3.36;S,6.74;(ν_{max}, cm^{-1})= Ar-CH (3017); 1599 (C=N); 1567 (C=C);^{1}H NMR (400 MHz, DMSO) ppm:2.50,3.35,7.43,7.52,7.54,7.57,7.59,7.61,7.63,7.69,7.70,7.70,7.72,7.74,7.74,7.78,7.97, 8.03,8.06,8.10,8.15,8.17,8.79,9.49;^{13}C:124.4,125.8,155.6,149.9,123.6,61.1,117.2,127.4,127.2,40.6,139.7,148.7,149.9, 125.1,129.3,126.3,167.2(100 MHz,DMSO)ppm; m/z: 475.15 (100.0%), 476.15 (30.3%), 477.14 (4.5%), 477.15 (2.7%), 476.14 (1.8%), 477.15 (1.7%), 478.15 (1.4%).

[6b] (1'-phenyl-5-(thiophen-2-yl)-3'-(p-tolyl)-3,4-dihydro-1'H,2H-[3,4'-bipyrazol]-2-yl)(pyridin-3-yl)methanone.

$C_{29}H_{23}N_5OS$;M.W.-489.60g/mole;C,71.14;H, 4.74;N,14.30;O,3.27;S, 6.55;(ν_{max}, cm^{-1})= Ar-CH(3017);1599(C=N);1567(C=C);^{1}H NMR (400 MHz, DMSO) ppm:2.50,2.67,3.33,3.39,7.20,7.297.30,7.35,7.36,7.41,7.42,7.44,7.47,7.50,7.52,7.56,7.58,7.60,7.62,7.65,7.68,7.73,7.81,7.84,7.86,7.94,7.96,8.001;^{13}C:124.4,125.8,155.6,149.9,123.0,61.1,117.2,127.4,127.2,40.6,139.7,148.7, 130,130.7,131.7,119.9,125.7,129.5,129.3,167.2,21.3(100 MHz,DMSO)ppm; m/z: 489.16 (100.0%), 490.17 (31.4%), 491.16 (4.5%), 491.17 (2.7%), 491.17 (2.0%), 490.16 (1.8%), 492.16 (1.4%).

[6c] 1',3'-diphenyl-5-(thiophen-2-yl)-3,4-dihydro-1'H,2H-[3,4'-bipyrazol]-2-yl)(pyridin-4-yl)methanone.

$C_{28}H_{21}N_5OS$;M.W.-475.57g/mole;C,70.72;H,4.45;N,14.73;O,3.36;S, 6.74;(ν_{max}, cm^{-1})= Ar-CH(3017);1599(C=N);1567(C=C);^{1}H NMR (400 MHz, DMSO) ppm:2.50,3.35,7.43,7.44,7.52,7.53,7.54,7.59,7.61,7.63,7.70,7.74,7.78,7.97,7.99,8.01,8.02,8.03,8.05,8.10,8.14,8.16;^{13}C:124.4,125.8,155.6,149.9,123.0,61.5,117.2,127.4,127.2,40.6,139.7,149.7,133.2,140.8,128.7,119.9,121.7,129.2,119.9,127.5,129.2,129.3,126.3,167.2;(100 MHz,DMSO)ppm; m/z: 475.15 (100.0%), 476.15 (30.3%), 477.14 (4.5%), 477.15 (2.7%), 476.14 (1.8%), 477.15 (1.7%), 478.15 (1.4%).

[6d] (1'-phenyl-5-(thiophen-2-yl)-3'-(p-tolyl)-3,4-dihydro-1'H,2H-[3,4'-bipyrazol]-2-yl)(pyridin-4-yl)methanone.

$C_{29}H_{23}N_5OS$;M.W.-489.60g/mole;C,71.14;H,4.74;N,14.30;O,3.27;S, 6.55;(ν_{max}, cm^{-1})= Ar-CH(3017);1599(C=N);1567(C=C);^{1}H NMR (400 MHz, DMSO) ppm:2.28,3.39,4.10,4.12,6.69,7.12,7.19,7.39,7.41,7.42,7.51,7.52,7.55,7.57,7.59,7.66,7.69,7.78,7.82,7.95,8.27,8.76,8.70,9.27;^{13}C:39.34,40.60,53.12,118.11,121.86,12.7,128.28,1291,129.25,129.31,129.37,130.01,32.38,133.72,139.72,144.35,144.97,153.44;(100 MHz,DMSO)ppm; m/z: 489.16 (100.0%), 490.17 (31.4%), 491.16 (4.5%), 491.17 (2.7%), 491.17 (2.0%), 490.16 (1.8%), 492.16 (1.4%)

[6e] (5-(naphthalen-2-yl)-1',3'-diphenyl-3,4-dihydro-1'H,2H-[3,4'-bipyrazol]-2-yl)(pyridin-3-yl)methanone.

$C_{34}H_{25}N_5O$;M.W.-519.20g/mole;C,78.59;H,4.85;N,13.48;O,3.08(ν_{max}, cm^{-1})= Ar-CH(3017);1599(C=N);1567(C=C);^{1}H NMR (400 MHz, DMSO) ppm:3.35,7.42,7.43,7.58,7.60,7.67,7.70,7.78,7.84,7.96,8.01,8.03,8.16,8.78;^{13}C:39.97,78.1,118.31, 119.1,124.58,127.4,127.57,128.23,123.84,128.95,129.24,129.60,130.66,13.73,135.48, 135.53,139.47,153.52,189.03;(100 MHz,DMSO)ppm; m/z: 519.21 (100.0%), 520.21 (36.8%), 521.21 (3.9%), 521.21 (2.7%), 520.20 (1.8%)

[6f] (5-(naphthalen-2-yl)-1'-phenyl-3'-(p-tolyl)-3,4-dihydro-1'H,2H-[3,4'-bipyrazol]-2-yl)(pyridin-3-yl)methanone.

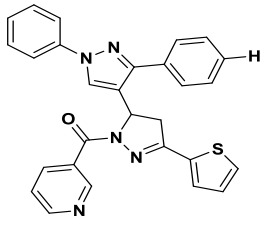
$C_{35}H_{27}N_5O$;M.W.-533.33g/mole;C,78.78;H,5.10;N,13.12;O,3.00(ν_{max}, cm^{-1})= Ar-CH(3017);1599(C=N);1567(C=C);^{1}H NMR (400 MHz, DMSO) ppm:2.35,3.35,7.31,7.36,7.41,7.43,7.55,7.59,7.61,7.64,7.67,7.80,7.89,7.94,7.98,8.06,8.07; ^{13}C:31.37,39.67,39.97,118.04,119.18,1217,127.66,128.8,129.20,129.3,129.50,129.9,130.22, 133.8,135.84,139.84,145.97,153.50(100MHz,DMSO)ppm,m/z: 533.22 (100.0%), 534.22 (37.9%), 535.23 (4.3%), 535.23 (2.7%), 534.22 (1.8%)

[6g] (5-(naphthalen-2-yl)-1',3'-diphenyl-3,4-dihydro-1'H,2H-[3,4'-bipyrazol]-2-yl)(pyridin-4-yl)methanone.

$C_{34}H_{25}N_5O$;M.W.-519.60g/mole;C,78.59;H,4.85;N,13.48;O,3.08(ν_{max}, cm^{-1})= Ar-CH(3017);1599(C=N);1567(C=C);^{1}H NMR (400 MHz, DMSO) ppm:3.45,7.34,7.36,739,7.41,7.48,7.56,7.58,7.61,7.74,7.78,7.95,7.97,8.04,8.09,8.11,8.13,8.15,8.22,8.31,8.53,8.58;^{13}C(100MHz,DMSO)ppm:39.93,60.8,118.2,119.1,121.8,127.5,127.58,128.1,128.83,129.31,129.3,129.91,130.16,130.31,135.51,139.46,146.88,153.52,171.04;m/z: 519.21 (100.0%), 520.21 (36.8%), 521.21 (3.9%), 521.21 (2.7%), 520.20 (1.8%).

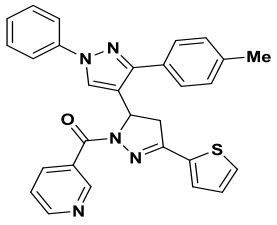
[6h] (5-(naphthalen-2-yl)-1'-phenyl-3'-(p-tolyl)-3,4-dihydro-1'H,2H-[3,4'-bipyrazol]-2-yl)(pyridin-4-yl)methanone.

$C_{34}H_{27}N_5O$;M.W.-533.64g/mole;C,78.78;H,5.10;N,13.12;O,3.00(ν_{max}, cm^{-1})= Ar-CH(3017);1599(C=N);1567(C=C);^{1}H NMR (400 MHz, DMSO) ppm:3.35,4.57,7.24,7.25,7.34,7.35,7.36,7.38,7.41,7.56,7.57,7.59,7.64,7.67,7.76,7.80,7.93,8.01,8.23,8.70,8.97;^{13}C(100MHz,DMSO)ppm:21.37,3934,39.55,40.38,40.59,118.04,119.17,121.7,127.65,128.81,129.2,129.32,129.40,129.5,129.9,130.2,130.89,133.8,135.77,139.44,145.99,153.50;m/z: 533.22 (100.0%), 534.22 (37.9%), 535.23 (4.3%), 535.23 (2.7%), 534.22 (1.8%).



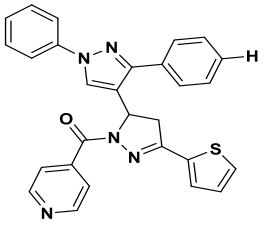
6a

(1',3'-diphenyl-5-(thiophen-2-yl)-3,4-dihydro-1'*H*,2*H*-[3,4'-bipyrazol]-2-yl)(pyridin-3-yl)methanone



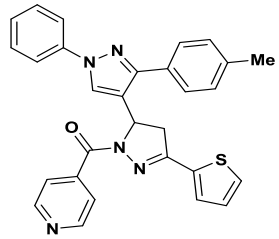
6b

(1'-phenyl-5-(thiophen-2-yl)-3'-(*p*-tolyl)-3,4-dihydro-1'*H*,2*H*-[3,4'-bipyrazol]-2-yl)(pyridin-3-yl)methanone



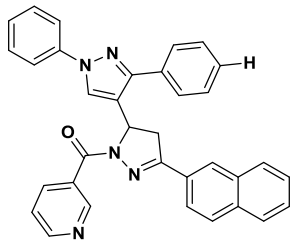
6c

(1',3'-diphenyl-5-(thiophen-2-yl)-3,4-dihydro-1'*H*,2*H*-[3,4'-bipyrazol]-2-yl)(pyridin-4-yl)methanone



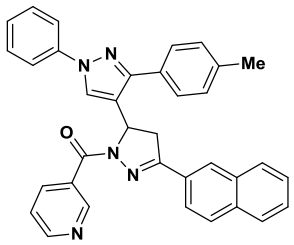
6d

(1'-phenyl-5-(thiophen-2-yl)-3'-(*p*-tolyl)-3,4-dihydro-1'*H*,2*H*-[3,4'-bipyrazol]-2-yl)(pyridin-4-yl)methanone



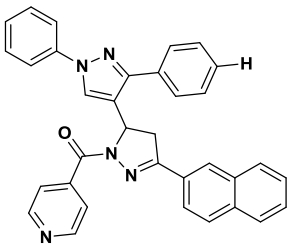
6e

(5-(naphthalen-2-yl)-1',3'-diphenyl-3,4-dihydro-1'*H*,2*H*-[3,4'-bipyrazol]-2-yl)(pyridin-3-yl)methanone



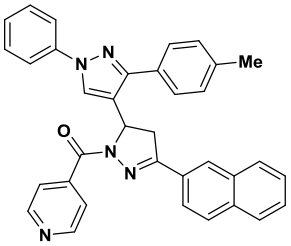
6f

(5-(naphthalen-2-yl)-1'-phenyl-3'-(*p*-tolyl)-3,4-dihydro-1'*H*,2*H*-[3,4'-bipyrazol]-2-yl)(pyridin-3-yl)methanone



6g

(5-(naphthalen-2-yl)-1',3'-diphenyl-3,4-dihydro-1'*H*,2*H*-[3,4'-bipyrazol]-2-yl)(pyridin-4-yl)methanone



6h

(5-(naphthalen-2-yl)-1'-phenyl-3'-(*p*-tolyl)-3,4-dihydro-1'*H*,2*H*-[3,4'-bipyrazol]-2-yl)(pyridin-4-yl)methanone

III. Resut and Discussion

The synthetic results for the products 6**(a-h)**

Compound	R_1	X	Time (min.)	Yield(%)	m. p. (˚C)
6a	H	S	8.2	86	222-226
6b	4-Me	S	8.3	87	236-239
6c	H	S	9	89	189-191
6d	4-Me	S	8.6	92	197-199
6e	H	-	8.7	93	211-214
6f	4-Me	-	9.1	94	232-235
6g	H	-	9.6	86	236-238
6h	4-Me	-	8.2	84	225-227

Antibacterial Activity

The investigation of antimicrobial activity data **table 3.6**, we conclude that some compounds showed good to tremendous antibacterial and antifungal activity against the illustrative specie compared to standard drugs. Against Gram-positive bacteria *B. subtilis*, compound **6a** (MIC=100 µg/mL) were shown potenetas compare to ampicillin (MIC=100 µg/mL). Against *C. tetani*, compound **6b** (MIC=50 µg/mL) prompted outstanding activity as compare to ampicillin (MIC=250 µg/mL), ciprofloxacin (MIC=100 µg/mL) and comparable activity to that norfloxacin. Compounds **6c** and **6d** (MIC=100 µg/mL) were elicited similar potency as compare to ciprofloxacin (MIC=100 µg/mL). Against *S. aureus*, compound **6e**

(MIC=100 µg/mL) and **6f**(MIC=62.5 µg/mL) have shown supplementary potent as compare to ampicillin (MIC=100 µg/mL). Against Gram-negative bacteria *E. coli*, compound **6d** (MIC=100 µg/mL) have shown equal activity and **6h** (MIC=62.5 µg/mL) have shown excellent activity as compare to ampicillin (MIC=100 µg/mL). Against *S. typhi*, compounds **6g**, **6h**, **8d**, **8e** (MIC=100 µg/mL) were found equipotent to ampicillin (MIC=100 µg/mL).

ANTIFUNGAL ACTIVITY:-It has been observed that against *C. albicans*, compounds **6g**, **6h**, **6d**, **6e**(MIC=250 µg/mL) were found excellent activity as compare to griseofulvin (MIC=500 µg/mL). Against *T. rubrum*, Compound **6h** (MIC=100 µg/mL) were found equipotent as compare to nystatin and griseofulvin (MIC=100 µg/mL).

In vitro antimicrobial activity of **6(a-h)** MICs (µg/mL).

	Gram-positive bacteria			Gram-negative bacteria			Fungi	
Compd	BS MTCC 441	CT MTCC 449	SA MTCC 96	EC MTCC 443	ST MTCC 98	VC MTCC 3906	CA MTCC 227	TR MTCC 296
6a	250	250	500	200	200	250	>1000	>1000
6b	**100**	**50**	500	500	500	**100**	500	500
6c	250	500	500	250	200	250	1000	1000
6d	250	500	250	**100**	125	250	1000	250
6e	200	**200**	500	200	250	**200**	500	1000
6f	250	**100**	250	500	500	250	1000	>1000
6g	200	250	**100**	125	**100**	250	**250**	1000
6h	200	250	**62.5**	250	250	**200**	1000	1000
A	100	250	100	100	100	250	-	-
B	50	50	50	50	50	50	-	-
C	50	100	25	25	25	50	-	-
D	10	50	10	10	10	100	-	-
E	-	-	-	-	-	-	100	100
F	-	-	-	-	-	-	500	100

BS: *Bacillus subtilis*; CT: *Clostridium tetani*; SA: *Staphylococcus aureus*; EC: *Escherichia coli*; ST: *Salmonella typhi*; VC: *Vibrio cholerae*; CA: *Candida albicans*; TR: *Trichophytonrubrum*. MTCC: Microbial Type Culture Collection. A: Ampicillin, B: Chloramphenicol, C: Ciprofloxacin, D: Norfloxacin, E: Nystatin, F: Griseofulvin

IV. Conclusion

To develop a simple, eco-friendly and efficient method for synthesis of (1', 3'-diphenyl-5-(thiophen-2-yl)-3, 4-dihydro-1'H, 2H-[3, 4'-bipyrazol]-2-yl) (pyridin-3-yl) methan one novel derivatives **6(a-h)**. This synthetic approach allows the integration of three auspicious bioactive nuclei in single scaffold through an easy way, for aiming their potent antimicrobial activities.

V. Acknowledgements

I am grateful for the research chemistry department of C.U.SHAH.University for providing a fininacial and technical supprort for this work.

VI. Referances

1. **ssKnorr,L.Ber,org.chem.1883,16,2597.**
2. **D.c.schmitt,A,,P taylor J chrm 42B (2003) .**
3. **6.O Prakash, K Pannu, A Kumar *Molecules*11 (2006) 43.**
4. **S Selvi, P T Perumal*Indian J Chem*41B (2002) 1887.**
5. **Z-HLu, X Gu, K Shi, X Li, D Chen, L Chen, *Arabian J Chem,* 2014, http://dx.doi.org/10.1016/j.arabjc.2014.11.002.**
6. **M Rani, M Yusuf, S A Khan, P PSahota, G Pandove, *Arabian J Chem,* 2015, 8, 174.**
7. **G GMandawad, B S Dawane, S D Beedkar, C N Khobragade, O S Yemul, *Bioorg Med Chem,*2013, 21, 365.**
8. **J Rangaswamy, H V Kumar, S T Harini, N Naik, *Arabian J Chem,* 2013, http://dx.doi.org/10.1016/j.arabjc.2013.10.012.**
9. **N B Patel, F M Shaikh, H R Patel, D Rajani, *J Saudi ChemSoc,* 2016, 20, S451.**
10. **N S Gonjare, S SAwati, S R Kumbhoje, Pramod B Patil, S SPatil, Manish S Kondawar, *Der PharmaChemica,* 2013, 5, 86.**
11. **C Xie, Z Lu, W Zhou, J Han, Y Pan, *Tetrahedron Lett,* 2012, 53, 6650.**
12. **P R Krishna, Y L Prapurna, *Tetrahedron Lett,* 2010, 51, 6507.**
13. **C Rajashree, N More Harinath, *Der Pharmacia Lettre*, 2012, 4 1236.**
14. **S Dadiboyena, A T Hamme II, *Tetrahedron Lett,* 2011, 52, 2536.**
15. **S Samshuddin, B Narayana, B K Sarojini, M T H Khan, H S Yathirajan, C G D Raj, R Raghavendra, *Med Chem Res,* 2012, 21, 2012.**
16. **N Harikrishna, A M Isloor, K Ananda, A O H Fun, *New J Chem*, 2016, 40, 73.**
17. **P Ahmad, H Woo, K Jun, AAKadi, H A Abdel-Aziz, Y Kwon, A F M MRahman, *Bioorg Med Chem,* 2016, 24, 1898.**