In the part-I, we have incorporated two medicinally important heterocycles i.e. pyrazole and 2-oxo pyridine. It is our ongoing process to search for novel bio-active molecules.

**Introductory features of pyrazoles:**

Pyrazoles belong to the family of azoles, i.e. five-member ring containing only nitrogen and carbon atoms, ranging from pyrrole to pentazole. According to Albert’s classification, they are \( \pi \)-excessive, \( N \)-heteroaromatic derivatives and according to Kauffmann’s arenology principle, as a substituted carbon, they are analogues of amines and as substituted nitrogen they are analogues of halogens, i.e. pseudohalogenes. Synthesis of pyrazole and its \( N \)-aryl analogues have been a subject of consistent interest because of the wide applications of such heterocycles in pharmaceutical as well as in agrochemical industry.\(^1\)\(^-\)\(^3\) Numerous compounds containing pyrazole moiety have been shown to exhibit anti-inflammatory, analgesic, antihyperglycemic, antipyretic, antibacterial antiviral and sedative-hypnotic activities.\(^4\)\(^-\)\(^6\)

1-Phenylpyrazole moiety is present in several drug candidates for treatment of various diseases such as cyclooxygenase-2 (Cox-2) inhibitors, IL-1 synthesis inhibitors and protein kinase inhibitors etc.\(^7\)\(^-\)\(^10\) Similarly, few of the 1,5-diarylpyrazole derivatives have been shown to exhibit non-nucleoside HIV-1 reverse transcriptase inhibitor activity\(^11\) along with Cox-2 inhibitor.\(^9\),\(^10\) The corresponding 1,3,5-triaryl-4-alkylpyrazoles have been recently identified as efficient ligands for estrogen receptor displaying high binding affinities and selective transcriptional efficacy for ERI subtype.\(^12\)\(^-\)\(^16\)

In the last 20 years pyrazole ring has attracted much attention as it has become fairly accessible and shows diverse properties. Beside traditional interest in pyrazole derivatives, which has been the basis of numerous dyes and drugs, a number of pyrazole anesthetics have appeared.\(^17\)\(^-\)\(^18\) They are also studied as antioxidants, as interesting complexing agents for analysis and separation of cations. They are also reported for significant bacteriostatic, bacteriocidal and fungicidal action.\(^19\)
In this respect, sulfonamides based on pyrazole are of particular interest, e.g. Orisul (1) which has a prolonged bacteriostatic action in vivo.\textsuperscript{20}
Studies on potential antimicrobial agents

Steroidal compounds whose structure includes pyrazole ring are of interest as possible psychopharmacological agents.\textsuperscript{21} Synthesis of model system analogues of histamine led to the pharmacologically interesting aminoethylpyrazoles.\textsuperscript{22} Diethylcarbamates and dialkyl-phosphates of 5-hydroxypyrazoles have been used practically as choline esterase inhibitors.\textsuperscript{23} Some compounds such as isolan (2), pyrolan (3) and pyrazoxon (4) which are too toxic for pharmacology, are used as systemic insecticides. There is evidence that 3,5-dimethyl pyrazole has a stimulating action on plants.\textsuperscript{24}

Synthetic Study of Pyrazoles:

Most of the methods for the synthesis of pyrazoles involve approaches based on either

(i) Cyclocondensation of 1,3-dicarbonyl compounds and their equivalent 1,3-dienophilic synthons such as propargylic ketones, dialkylamino/alkoxy/chloro ketones with arylhydrazines.

(ii) Intermolecular [2+3] cycloadditions of 1,3-dipoles to alkynes.\textsuperscript{25-33}

However, the appealing generality of these methods are somewhat vitiated due to the frequent formation of regioisomeric mixtures of unsymmetrical pyrazoles in these reactions. Therefore, several elegant methods for the synthesis of unsymmetrical substituted pyrazoles have been reported in literature. Before presenting the results of our work, a brief literature survey on some of the recent synthesis of pyrazoles and its derivatives has been discussed. Among these methods, few selected recent examples have been highlighted in the following. Giacomelli G et al\textsuperscript{34} have developed
synthesis of 1,4,5-trisubstituted pyrazoles (9) from Meldrum acid (5) under microwave conditions. The Meldrum’s acid (5) was acylated with acid chlorides and the resulting products (6) were reacted with amines affording the substituted β-ketoamides (7) in good yields. Subsequent reaction of β-ketocarbonyl compounds (8) with N,N-dimethylformamide dimethylacetal (DMF-DMA) followed by cyclization with substituted monohydrazines furnished the corresponding 1,4,5-trisubstituted pyrazoles (9) in good yields.

Mikulskiene G et al35 have synthesized some new 1-aryl-4-[(3,5–dimethylpyrazole-1-yl)carbonyl]-2-pyrrolidinones (12 a,b) by condensation of hydrazides (11 a,b) with 2,4-pentanedione in 2-propanol in the presence of a catalytic amount of hydrochloric acid.

Kira M A et al36 have reported 3-(aryl)-1-phenylpyrazol-4-carbaldehydes (14) prepared by Vilsmeier-Haack reaction of arylhydrazones (13) of acetophenones.
Recently Kim J N et al\textsuperscript{37} have reported the synthesis of 1,3,4,5-tetrasubstituted pyrazoles (16) involving the reaction of Baylis-Hillman adducts (15) and hydrazine hydrochloride in dichloroethane at 50-70°C.

Mori A et al\textsuperscript{38} have reported a novel one-pot synthesis of pyrazoles. In this method four component coupling of a terminal alkyne (17), hydrazine, carbon monoxide and an aryl iodide (18) furnishes pyrazole derivatives (19) in presence of palladium catalyst. The reaction proceeds at room temperature and an ambient pressure of carbon monoxide in an aqueous solvent system.

Tice M C et al\textsuperscript{39} have synthesized a 1-(2-thiazolyl)-5-(trifluoromethyl)pyrazole-4-carboxamides (25) using solution-phase synthesis. Thus, the reaction of ethyl-2-ethoxymethylene-3-oxo-4,4,4-trifluorobutanoate (20) with thiosemicarbazonide yielded ethyl 1-carbamothioyl-5-hydroxy-5-(trifluoromethyl)-4,5-dihydro-1H-pyrazole-4-carboxylate (21). The compound (21) reacts with a variety of α-bromoketones (22) affording ethyl-1-(2-thiazolyl)-5-(trifluoromethyl)pyrazole-4-
carboxylates (23) in good yield. The amides (25) were prepared by a series of reactions from compounds (24).

Meegalla S K et al have described the synthesis of 3,4-fused-cycloalkyl-1-arylpyrazoles (28) involving the reaction of aryl hydrazines with cyclic α-(dimethoxymethyl)ketones (27) followed by acid-assisted cyclization to give (28) in good yields. The cyclic α-(dimethoxymethyl)ketones (27) were obtained by BF₃-promoted alkylation of ketones (26) with trimethylorthoformate.
Pharmacological Significance of Pyrazoles:

Pyrazole derivative have a long history of application in agrochemicals and pharmaceutical industry as herbicides and active pharmaceutical ingredients. The recent success of COX-2 inhibitors has further highlighted the importance of this heterocyclic ring in medicinal chemistry. A systematic investigation of this class of heterocyclic lead revealed that pyrazole containing pharmacoactive agents play important role in medicinal chemistry.\textsuperscript{41} Rao M N A et al\textsuperscript{42} have synthesized some new 4-[5-(substituted aryl)-4,5-dihydro-1H-pyrazol-3-yl]-3-phenyl-sydrones (29) by treatment of 4-[1-oxo-3-(substitutedaryl)-2-propenyl]-3-phenylsydnones with hydrazine. These synthesized compounds have exhibited anti-inflammatory, antiarthritic and analgesic activities. Menozzi G et al\textsuperscript{43} have synthesized a number of 1,5-disubstituted 4-[1H-imidazol-1-yl(phenyl)methyl]-1H-pyrazoles (30) which showed antimycobacterial, antifungal and antibacterial activities.

![Diagram of compounds 29 and 30](image)

Palaska E et al\textsuperscript{44} have developed a synthesis of 1-phenyl-3-(4-methylphenyl)-5-(3,4-dimethoxyphenyl)-2-pyrazoline and 1-phenyl-3-(4-methylphenyl)-5-(2-chloro-3,4-di-methoxyphenyl)-2-pyrazolines (31). These compounds showed significant antidepressant activity. Ming LI et al\textsuperscript{45} have reported the formation of ethyl 5-amino-1-(5′-methyl-1′-t-butyl-4′-pyrazolyl)carbonyl-3-methylthio-1H-pyrazole-4-carboxylate (32) by treatment of ethyl 2-cyano-3,3-dimethylthioacrylate with 1-t-butyl-5-methyl-4-hydrazinocarbonylpyrazole. These compounds showed fungicidal and plant growth regulation activities. Daidone G et al\textsuperscript{46} have reported the formation of some new 4-diazapyrazole derivatives (33). These derivatives were prepared by the reaction of 3-methyl-5-(substituted benzamido)pyrazoles with an excess of nitrous acid in acetic acid. These compounds showed antineoplastic and antimicrobial activities.
Joshi H S et al have synthesized 1-acetyl-3-aryl-5-\{1-phenyl-3-[p-(methylthio)phenyl]pyrazol-4-yl\}-4,5-dihydro-\(1H\)-pyrazoles (34) by the reaction of 1-aryl-3-\{1-phenyl-3-[p-(methylthio)phenyl]pyrazol-4-yl\}-2-propen-1-ones with hydrazine hydrate in glacial acetic acid. These synthesized compounds were tested in vitro for their antitubercular, antibacterial and antifungal activities. Badawey EI-S A et al have reported novel 1-[6-amino-4-(substitutedphenyl)-5-cyanopyrimidin 2-yl]-4-(2-hydroxyethyl)-3-methylpyrazoline-5-ones (35) and 2-[6-amino-4-(substitutedphenyl)-5-cyanopyrimidin-2-yl]-1,2,4,5,6,7-hexahydro-\(3H\)-indazol-3-ones (36). These compounds were shown to possess anti-inflammatory, analgesic and antipyretic activities.

Banoglu E et al have synthesized some new amide derivatives of 3-[1-(3-pyridazinyl)-5-phenyl-1\(H\)-pyrazole-3-yl]propanoic acid (37). These compounds exhibited potent analgesic activity. Karthikeyan M S et al have reported the synthesis of 1-aryloxy-3-aryl-5-hydroxy-5-arylpurazolines (38) by the reaction of chalcone dibromides with aryloxy acid hydrazides in the presence of triethylamine and ethanol. These synthesized compounds showed very good antibacterial and antifungal activities.
Moreover, pyrazoles are reported to possess anticancer, germicidal, antidiuretic, antihistamine, antidiabetic, antirheumatic, antineoplastic, anti HIV and antifertility activities. Due to the interesting activities of variously substituted pyrazole as chemotherapeutic agents, considerable attention has been focused on this class. The pharmaceutical importance of these compounds lies in the fact that they can be effectively utilized as antibacterial, antifungal, antiviral, antiparasitic, and antitubercular agents. As evident from the literature, in recent years a significant research work in heterocyclic chemistry has been devoted to pyrazole containing different aryl groups as substituents.

**Brief introduction to 2-pyridone (2-oxopyridine):**

2-Pyridone is an organic colourless solid compound, used in peptide synthesis. It is known to form hydrogen bonded structures somewhat related to the base-pairing mechanism found in RNA and DNA. The most prominent feature of 2-pyridone is the amide group; a nitrogen with a hydrogen bound to it and a keto group next to it. In peptides, amino acids are linked by this pattern, a feature responsible for some remarkable physical and chemical properties. In this and similar molecules, the hydrogen bound to the nitrogen is suitable to form strong hydrogen bonds to other nitrogen and oxygen containing species.\(^5\)\(^1\)

Substituted 2-pyridones represent useful scaffolds for drug discovery and are also versatile synthetic building blocks. 2-Pyridones constitute important core units in a large number of pharmaceuticals, agrochemicals and functional materials. The development of their efficient synthesis is, therefore an important target in current organic synthesis.\(^5\)\(^2\) Some derivatives containing 2-oxopyridine ring system have
been shown to possess useful pharmacological activities, such as Milrinone (Primacor) is a phosphodiesterase III inhibitor, Olprinone is a cardiotonic agent, Camptothecin (CPT) is the DNA enzyme topoisomerase I (topo I) inhibitor. Two CPT analogues, Topotecan and Irinotecan have been approved and are used in cancer chemotherapy today. Then examples include phosphodiester inhibitor Amrinone, antifungal agent Ciclopirox, and an antitumor antibiotic Diazaquinomycin A.

**Commercially available pyridone based analogues**

**Methods for synthesis of 2-oxopyridine:**

*N*-substituted 4,6-dimethyl-3-cyano-2-pyridones (39) have been prepared by Mijin D et al from acetylacetone, *N*-substituted cyanoacetamide, and piperidine as catalyst under microwave irradiation without solvent. This rapid and simple method produced pure products in high yield.
Bogdanowicz-Szwed K et al\textsuperscript{60} have used another way of leading to the construction of the pyridine skeleton. The reaction of malononitrile with 3-morpholino-3-(2-thienyl)acrylic acid anilides (40) was carried out in acetonitrile solution in presence of a catalytic amount of triethylamine resulting in good yields of 6-amino-1-aryl-4-(2-thienyl)-1,2-dihydro-2-oxopyridine-5-carbonitriles (41).

Rong L et al\textsuperscript{61} have developed an efficient and facile synthesis of 4,6-diaryl-2-oxo-1,2-dihydropyridine-3-carbonitriles (42) via three-component cyclocondensation of aromatic aldehydes, aromatic ketones and 2-cyanoacetamide under solvent-free conditions. Mild reaction conditions, simple protocol and clean reaction make this protocol practical and economically attractive.

Teruyuki K et al\textsuperscript{62} synthesized polysubstituted 2-pyridones (43) by controlling the ratio of alkynes and isocyanate in the presence of rhodium (I) as a catalyst.
Studies on potential antimicrobial agents

Condensation of ethyl benzylidencyanoacetate with thiocarbamoylacetamide in the presence of an equimolar amount of piperidine yielded a new method for the synthesis of 6-alkylthiosubstituted-5-carbamoyl-3-cyano-4-phenyl-3,4-dihydropyridin-2(1H)-ones (44), which was reported by Krauze A et al.\textsuperscript{63}

\[ \text{Et}_2\text{C}==\text{Et} + \text{Ph}-\text{N}==\text{C}=\text{O} \xrightarrow{[\text{RhCl(C}_2\text{H}_4\text{I})_2]_2} \text{Mesitylene, 120 }^\circ\text{C, 12 h} \]

\[ \text{Et}_2\text{NPhCO} \]

\[ \text{(43)} \]

\(\alpha,\beta\)- Unsaturated acid chlorides (46) can react with enaminonitriles (45) in presence of triethylamine to produce polysubstituted 3,4-dihydro-2(1H)-pyridones (47) in presence of regiospecifically under mild conditions.\textsuperscript{64}

\[ \text{CN} \text{NH}_2 + \text{R}_3 \text{C}==\text{Cl} \xrightarrow{\text{Et}_3\text{N, Et}_2\text{O}} \]

\[ \text{R}_1, \text{R}_2, \text{R}_3 = \text{Different substituents} \]

Krivokolysko S G et al\textsuperscript{65} have used Meldrum’s acid to synthesize sulfur-containing partially hydrogenated pyridones. They have prepared non-hydrogenated pyridones by the reaction of di(methylthio)methylene-substituted Meldrum’s acid (48) with
Studies on potential antimicrobial agents

cyanothioacetamide by boiling in ethanol in presence of sodium ethoxide. The synthesized sodium pyridine-2-thiolate (49) was converted into corresponding sulfide (50) by alkylation with methyl iodide.

Collins I et al\textsuperscript{66} have developed a novel series of 3,6-bis(heteroaryl)-5-aryl-1-methyl-2-pyridones (51) with high affinity for the benzodiazepine (BZ) binding site of human \( \gamma \)-aminobutyric acid (GABA\( \text{\textsubscript{A}} \)) receptor ion channels, low binding selectivity for \( \alpha2- \) and/or \( \alpha3- \) over \( \alpha1- \) containing GABA\( \text{\textsubscript{A}} \) receptor subtypes and high binding selectivity over \( \alpha5 \) subtypes. Kim K S et al\textsuperscript{67} have discovered some conformationally constrained 2-pyridone (52) analogues as potent met kinase inhibitor. Many of these analogues showed potent antiproliferative activity against met dependent GTL-16 gastric carcinoma cell line. It possesses a favorable pharmacokinetic profile in mice and demonstrates significant \textit{in vivo} antitumor activity in the GTL-16 human gastric carcinoma xenograft model.

By using molecular modeling and the information derived from X-ray crystal structures of human neutrophil elastase (HNE) and porcine pancreatic elastase (PPE) complexed to peptidic ligands, Edwards P D et al\textsuperscript{68} have developed a new series of nonpeptidic inhibitors of HNE, the pyridopyrimidine trifluoromethyl ketones (TFMKS) (53) which afforded potent inhibitors of elastase. Proudfoot J R et al\textsuperscript{69} have
synthesized 3-[2'-(S)-(dimethyl)-naphthylacetylamino-3'[4''-(1'''-carboxy-1'''-methyl)-ethyl]benzene]propanoylamino-1-[4-methoxybenzyl]-4-methyl-2-pyridone (54). This molecule displays good binding affinity for the p56lck SH2 domain ($K_d = 1 \mu M$) and good cell permeations and this combination of properties allowed demonstrating clear-cut inhibitory effects on a very early event in T cell activation, namely calcium mobilization.

Ammar Y A et al\textsuperscript{70} have synthesized a new series of polysubstituted 1-aryl-2-oxo-1,2-dihydropyridine-3-carbonitriles (55) as novel Pirfenidone analogues, which have shown very high antifibrotic activity. Rollas S et al\textsuperscript{71} have reported 6-amino-4-aryl-2-oxo-1-(1-pyrid-3-yl)-1,2-dihydropyridine-3,5-dicarbonitriles series (56), which exhibited a high percentage of tumor growth inhibition at concentrations of $10^{-5}$ to $10^{-7}$ M in cancer cell lines.

Buckle D R et al\textsuperscript{72} have synthesized a novel series of smooth muscle relaxants which have been shown to act via the opening or activation of potassium channels. One compound in particular, 1,1-dimethyl-5-nitro-3-(2-pyridin-1-yl)indan-2-ol (57) was identified as a potent relaxant of airways smooth muscle in vitro with $IC_{50} = 0.15 \mu M$.
Studies on potential antimicrobial agents

and was found to significantly inhibit histamine-induced dyspnoea in conscious guinea pigs when given orally 30-45 min prior to challenges. Matsui T et al\textsuperscript{73} have carried out synthesis and pharmacological evaluation of a series of 1,2-dihydro-1-[(5-methyl-1-imidazol-4-yl)methyl]-2-oxopyridine as 5-HT\textsubscript{3} antagonists. Among the synthesized compounds, (58) showed the most potent activity in the inhibition of Bezold-Jarisch reflex in rats. Compounds (59) and (60) were orally active in protection against cisplatin-induced emesis in dogs or ferrets.

![Images of chemical structures](57, 58, 59, 60)

Dragovich P S et al\textsuperscript{74,75} have synthesized and optimized orally bioavailable 2-pyridone containing peptidomimetics (61, 62) which have shown very good activity as human rhinovirus 3C protease inhibitors.

![Images of chemical structures](61, 62)

Ke Li et al\textsuperscript{76} designed and synthesized four novel 5-substituted pyridine-2(1H)-one derivatives (63a,b and 64a,b) using addition–elimination reactions, all four compounds were found to be highly efficient against hepatitis B virus (HBV) in
cultured HepG2 2.2.15 cell, making them promising drug candidates for potential bioactive molecule against hepatitis B. Jinyou Xu et al.\textsuperscript{77} discovered a novel series of potent and selective dipeptidyl peptidase-4 (DPP-4) inhibitors. The optimized compound (65b) exhibited good pharmacokinetic profiles in three preclinical species. \textit{In vitro} and \textit{in vivo} metabolism studies revealed that \textit{N}-demethylation occurred in compound (65a), leading to the formation of the initial lead compound (65b), which had unacceptable hERG binding. Replacement of the \textit{N}-methyl pyridone with a less metabolically labile group and improving the potency of (65b) will be the focus of future work in this series.

Prevalence of pyrazole and 2-pyridone cores in biologically active molecules have stimulated the need for elegant and efficient way to make these heterocyclic lead. In continuation to this, we have synthesized the following compounds in Part - I.

**Part – I**  
This part is divided into following four sections.

**Section 1:** 1-\{1-Aza-2-{1,3-diphenylpyrazol-4-yl}vinyl\}-2-amino-4-(aryl)-6-oxohydropyridine-3,5-dicarbonitriles.

**Section 2:** 1-\{1-Aza-2-{3-(4-methylphenyl)-1-phenylpyrazol-4-yl}vinyl\}-2-amino-4-(aryl)-6-oxohydropyridine-3,5-dicarbonitriles.

**Section 3:** 1-\{1-Aza-2-{3-(4-methoxyphenyl)-1-phenylpyrazol-4-yl}vinyl\}-2-amino-4-(aryl)-6-oxohydropyridine-3,5-dicarbonitriles.

**Section 4:** 1-\{1-Aza-2-{3-(4-fluorophenyl)-1-phenylpyrazol-4-yl}vinyl\}-2-amino-4-(aryl)-6-oxohydropyridine-3,5-dicarbonitriles.
EXPERIMENTAL PROCEDURE

PREPARATION OF 3-(ARYL)-1-PHENYL PYRAZOLE-4-CARBALDEHYDES (II) BY VILSMEIER-HAACK REACTION

**Preparation of (1-aza-2-phenylprop-1-enyl)phenylamine (I)**

Glacial acetic acid (1 mL) and phenylhydrazine (0.01 mol) were added to a solution of acetophenone (0.01 mol) in 30 mL of ethanol (95%). Then, reaction mixture was warmed for 1 h. The precipitates were filtered and washed with ethanol (95%). Then it was dried in vacuum over P₂O₅, recrystallized from methanol. Yield: 92%; m.p.: 104 °C; Anal. calcd. for C₁₄H₁₄N₂: C-79.97, H-6.71, N-13.32; Found: C-79.90, H-6.66, N-13.39%.

**Preparation of 1,3-diphenylpyrazole-4-carbaldehyde (II)**

Dimethylformamide (0.35 mol) and phosphorus oxychloride (0.35 mol) were separately cooled at 0 °C before being stirred at same temperature. A solution of compound I (0.11 mol) in dimethylformamide was added dropwise to the reaction mixture which was then allowed to attain room temperature and refluxed at
Studies on potential antimicrobial agents

70–80 °C for 5 h. After cooling at room temperature, the mixture was treated with a cold saturated K$_2$CO$_3$ solution. The precipitate was filtered, strongly washed with water and recrystallized from ethanol (95%). Yield: 82%; m.p.: 164 °C; Anal. calcd. for C$_{16}$H$_{12}$N$_2$O: C-77.40, H-4.87, N-11.28; Found: C-77.33, H-4.94, N-11.22%.

The progress of reaction and purity of compounds I and II were checked on TLC [Aluminium sheet silica gel 60 F$_{245}$ (E. Merck)] plates using n-hexane:ethyl acetate (7:3) as an irrigator and plates were visualized with ultraviolet (UV) light, or iodine vapour. All compounds were prepared by using the same method and their physical constants are recorded in TABLE A.

**TABLE A**

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**SECTION 1**

**PREPARATION OF 1-[1-AZA-2-(1,3-DIPHENYL-PYRAZOL-4-YL)VINYL]-2 AMINO-4-(ARYL)-6-OXOHYDROPYRIDINE-3,5-DICARBONITRILES**

**SYNTHETIC SCHEME 1**

R = -H, -2-OH, -4-OH, -2-Cl, -3-Cl, -4-Cl, -2-F, -3-F, -4-F, 4-CH₃, -4-OCH₃, -3,4,5-(OCH₃)₃, -2-NO₂, -3-NO₂, -4-NO₂
PHYSICAL CONSTANTS OF 1-[1-AZA-2-(1,3-DIPHENYLPYRAZOL-4-YL)VINYL]-2-AMINO-4-(ARYL)-6-OXOHYDROPYRIDINE-3,5-DICARBONITRILES

R = Different substituents

![Chemical Structure](image)

### TABLE 1

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<th>Sr. No.</th>
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<th>Molecular Formula</th>
<th>% Yield</th>
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EXPERIMENTAL PROCEDURE

Preparation of \( N\- [1\- aza\- 2\- (1,3\- diphenylpyrazol\- 4\- yl)vinyl]\- 2\- cyanoacetamide \( \text{III} \)

A mixture containing 1,3-diphenylpyrazole-4-carbaldehyde \( \text{IIa} \) (0.01 mol) and 2-cyanoacetohydrazide (0.01 mol) in 1,4-dioxan (30 mL) was refluxed for 1 h and then cooled down to room temperature. After cooling, crystals formed were filtered, washed with water and recrystallized from ethanol (95%) to give compound \( \text{III} \). Yield: 79%; m.p.: 162 °C; Anal. calcd. for C\(_{19}\)H\(_{15}\)N\(_{5}\)O: C-69.28, H-4.59, N-21.26; Found: C-69.21, H-4.53, N-21.30%.

Preparation of \( 1\- [1\- aza\- 2\- (1,3\- diphenylpyrazol\- 4\- yl)vinyl]\- 2\- amino\- 6\- oxo\- 4\- phenylhydropyridine\- 3,5\- dicarbonitrile \( \text{IV} \) KR\(_{1}\) -1

A mixture containing \( N\- [1\- aza\- 2\- (1,3\- diphenylpyrazol\- 4\- yl)vinyl]\- 2\- cyanoacetamide \( \text{III} \) (0.01 mol), (phenylmethylene)methane-1,1-dicarbonitrile (0.01 mol) and catalytic amount of piperidine in ethanol (95%) (30 mL) was refluxed for 3 h. After cooling, the crystals formed were filtered, washed with water and recrystallized from aqueous DMF to give compound \( \text{IV} \). Yield: 63%; m.p.: 194 °C; Anal. calcd. for C\(_{29}\)H\(_{19}\)N\(_{7}\)O: C-72.34, H-3.98, N-20.36; Found: C-72.40, H-3.92, N-20.40%.

The progress of reaction and purity of the compounds \( \text{III} \) and \( \text{IV} \) were checked on TLC [Aluminium sheet silica gel 60 F\(_{254}\) (E. Merck)] plates using chloroform:methanol (9.5:0.5) as an irrigator and plates were visualized with ultraviolet (UV) light, or iodine vapour. All compounds of this series were prepared by using the same method and their physical constants are recorded in TABLE 1.
SECTION 2

PREPARATION OF 1-{1-AZA-2-[3-(4-METHYLPHENYL)-1-PHENYL-PYRAZOL-4-YL]VINYL}-2-AMINO-4-(ARYL)-6-OXOHYDROPYRIDINE-3,5-DICARBONITRILES

SYNTHETIC SCHEME 2
PHYSICAL CONSTANTS OF 1-{1-AZA-2-[3-(4-METHYLPHENYL)-1-PHENYL-PYRAZOL-4-YL]VINYL}-2-AMINO-4-(ARYL)-6-OXOHYDROPYRIDINE-3,5-DICARBONITRILES

R = Different substituents

TABLE 2

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**EXPERIMENTAL PROCEDURE**

**Preparation of N-{1-aza-2-[3-(4-methylphenyl)-1-phenylpyrazol-4-yl]vinyl}-2-cyanoacetamide (III)**

A mixture containing 3-(4-methylphenyl)-1-phenylpyrazole-4-carbaldehyde IIb (0.01 mol) and 2-cyanoacetoxyhydrazide (0.01 mol) in 1,4-dioxan (30 mL) was refluxed for 1 h and then cooled down to room temperature. After cooling, crystals formed were filtered, washed with water and recrystallized from ethanol (95%) to give compound III. Yield: 78%; m.p.: 180 °C; Anal. calcd. for C_{20}H_{17}N_{5}O: C-69.95, H-4.99, N-20.39; Found: C-69.90, H-4.94, N-20.33%.

**Preparation of 1-{1-aza-2-[3-(4-methylphenyl)-1-phenylpyrazol-4-yl]vinyl}-2-amino-6-oxo-4-phenylhydropyridine-3,5-dicarbonitrile (IV) KR_{2}-1**

A mixture containing N-{1-aza-2-[3-(4-methylphenyl)-1-phenylpyrazol-4-yl]vinyl}-2-cyanoacetamide III (0.01 mol), (phenylmethylene)methane-1,1-dicarbonitrile (0.01 mol) and catalytic amount of piperidine in ethanol (95%) (30 mL) was refluxed for 3 h. After cooling, the crystals formed were filtered, washed with water and recrystallized from aqueous DMF to give compound IV. Yield: 53%; m.p.: 189 °C; Anal. calcd. for C_{30}H_{21}N_{7}O: C-72.71, H-4.27, N-19.78; Found: C-72.64, H-4.24, N-19.82%.

The progress of reaction and purity of compounds III and IV were checked on TLC [Aluminium sheet silica gel 60 F_{245} (E. Merck)] plates using chloroform:methanol (9.5:0.5) as an irrigator and plates were visualized with ultraviolet (UV) light, or iodine vapour. All compounds of this series were prepared by using the same method and their physical constants are recorded in **TABLE 2**.
SECTION 3

PREPARATION OF 1-{1-aza-2-[3-(4-methoxyphenyl)-1-phenylpyrazol-4-yl]vinyl}-2-amino-4-(aryl)-6-oxohydropyridine-3,5-dicarbonitriles

SYNTHETIC SCHEME 3
PHYSICAL CONSTANTS OF 1-{1-aza-2-[3-(4-Methoxyphenyl)-1-phenylpyrazol-4-yl]vinyl}-2-amino-4-(aryl)-6-oxohydropyridine-3,5-dicarbonitriles

R = Different substituents

TABLE 3

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EXPERIMENTAL PROCEDURE

**Preparation of** $\text{N-\{1-aza-2-[3-(4-methoxyphenyl)-1-phenylpyrazol-4-yl]vinyl\}-2-cyanoacetamide (III)}$

A mixture containing 3-(4-methoxyphenyl)-1-phenylpyrazole-4-carbaldehyde $\text{IIc}$ (0.01 mol) and 2-cyanoacetohydrazide (0.01 mol) in 1,4-dioxan (30 mL) was refluxed for 1 h and then cooled down to room temperature. After cooling, crystals formed were filtered, washed with water and recrystallized from ethanol (95%) to give compound $\text{III}$. Yield: 77%; m.p.: 192 °C; Anal. calcd. for $\text{C}_{20}\text{H}_{17}\text{N}_{5}\text{O}_{2}$: C-66.84, H-4.77, N-19.49; Found: C-66.90, H-4.81, N-19.43%.

**Preparation of** $\text{1-\{1-aza-2-[3-(4-methoxyphenyl)-1-phenylpyrazol-4-yl]vinyl\}-2-amino-6-oxo-4-phenylhydropyridine-3,5-dicarbonitrile (IV) KR_{3-1}}$

A mixture containing $\text{N-\{1-aza-2-[3-(4-methoxyphenyl)-1-phenylpyrazol-4-yl]vinyl\}-2-cyanoacetamide III}$ (0.01 mol), (phenylmethylene)methane-1,1-dicarbonitrile (0.01 mol) and catalytic amount of piperidine in ethanol (95%) (30 mL) was refluxed for 3 h. After cooling, the crystals formed were filtered, washed with water and recrystallized from aqueous DMF to give compound $\text{IV}$. Yield: 62%; m.p.: 201 °C; Anal. calcd. for $\text{C}_{30}\text{H}_{21}\text{N}_{7}\text{O}_{2}$: C-70.44, H-4.14, N-19.17; Found: C-70.37, H-4.19, N-19.13%.

The progress of reaction and purity of compounds $\text{III}$ and $\text{IV}$ were checked on TLC [Aluminium sheet silica gel 60 F$_{245}$ (E. Merck)] plates using chloroform:methanol (9.5:0.5) as an irrigator and plates were visualized with ultraviolet (UV) light, or iodine vapour. All compounds of this series were prepared by using the same method and their physical constants are recorded in TABLE 3.
SECTION 4

PREPARATION OF 1-{1-aza-2-[3-(4-fluorophenyl)-1-phenylpyrazol-4-yl]vinyl}-2-amino-4-(aryl)-6-oxohydropyridine-3,5-dicarbonitriles

SYNTHETIC SCHEME 4
Studies on potential antimicrobial agents

PHYSICAL CONSTANTS OF 1-{1-ÁZÀ-2-[3-(4-FLUOROPHENYL)-1-PHENYL-PYRAZOL-4-YL]-VINYL}-2-AMINO-4-(ARYL)-6-OXOHYDROPYRIDINE-3,5-DICARBONITRILES

![Structure of the compound]

R = Different substituents

**TABLE 4**

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<td>-3,4,5-(OCH_{3})</td>
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<td>59</td>
<td>217</td>
<td>65.19</td>
</tr>
<tr>
<td>KR-13</td>
<td>-2-NO_{2}</td>
<td>C_{29}H_{17}F_{2}N_{7}O_{3}</td>
<td>61</td>
<td>184</td>
<td>63.97</td>
</tr>
<tr>
<td>KR-14</td>
<td>-3-NO_{2}</td>
<td>C_{29}H_{17}F_{2}N_{7}O_{3}</td>
<td>64</td>
<td>204</td>
<td>63.97</td>
</tr>
<tr>
<td>KR-15</td>
<td>-4-NO_{2}</td>
<td>C_{29}H_{17}F_{2}N_{7}O_{3}</td>
<td>59</td>
<td>194</td>
<td>63.97</td>
</tr>
</tbody>
</table>
EXPERIMENTAL PROCEDURE

Preparation of $N$-[1-aza-2-[3-(4-fluorophenyl)-1-phenylpyrazol-4-yl]vinyl]-2-cyanoacetamide (III)

A mixture containing 3-(4-fluorophenyl)-1-phenylpyrazole-4-carbaldehyde IId (0.01 mol) and 2-cyanoacetohydrazide (0.01 mol) in 1,4-dioxan (30 mL) was refluxed for 1 h and then cooled down to room temperature. After cooling, crystals formed were filtered, washed with water and recrystallized from ethanol (95%) to give compound III. Yield: 75%; m.p.: 167 °C; Anal. calcd. for C$_{19}$H$_{14}$ClN$_{5}$O: C-62.73, H-3.88, N-19.25; Found: C-62.80, H-3.92, N-19.31%.

Preparation of 1-{1-aza-2-[3-(4-fluorophenyl)-1-phenylpyrazol-4-yl]vinyl}-2-amino-6-oxo-4-phenylhydropyridine-3,5-dicarbonitrile (IV) KR4-1

A mixture containing $N$-[1-aza-2-[3-(4-fluorophenyl)-1-phenylpyrazol-4-yl]vinyl]-2-cyanoacetamide III (0.01 mol), (phenylmethylene)methane-1,1-dicarbonitrile (0.01 mol) and catalytic amount of piperidine in ethanol (95%) (30 mL) was refluxed for 3 h. After cooling, the crystals formed were filtered, washed with water and recrystallized from aqueous DMF to give compound IV. Yield: 56%; m.p.: 201 °C; Anal. calcd. for C$_{29}$H$_{18}$ClN$_{7}$O: C-67.51, H-3.52, N-19.00; Found: C-67.46, H-3.48, N-19.04%.

The progress of reaction and purity of compounds III and IV were checked similarly on TLC [Aluminium sheet silica gel 60 F$_{245}$ (E. Merck)] plates using chloroform:methanol (9.5:0.5) as an irrigator and plates were visualized with ultraviolet (UV) light, or iodine vapour. All compounds of this series were prepared by using the same method and their physical constants are recorded in TABLE 4.
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