Chapter – I

BRIEF REVIEW ON CHEMISTRY OF PYRAZOLINE AND ITS DERIVATIVES
Heterocyclic chemistry is the most challenging and a handsomely rewarding field of study, since it always attracts the attention of scientists working not only in the area of natural products but also in synthetic chemistry. Moreover, in tune with the present trend "scientists to the door steps of common man", there is always a challenging and rewarding task in search of more and more new scientific accomplishments. This is reflected by the voluminous data available in the literature on heterocyclic chemistry. Many useful drugs indeed have emerged from such investigations which strengthens the trend. Spectacular advanced has been made in this field to furtherance of the knowledge of relationship between chemical structure and biological activity. Thus, the successful application of this class of compounds in various fields ensures a limitless scope for the development of structurally novel compounds with a wide range of physico-chemical and biological properties.

Amongst different heterocyclic systems, the chemistry of five membered heterocycles with more than one heteroatom has gained importance as many of the them exhibit pronounced bioactive nature. One such type of compounds includes pyrazoles and pyrazolines. Hence, any attempt to study their detailed chemistry would add new dimensions to the existing knowledge. Pyrazolones, pyrazoles and related heterocycles possess various types of biological activities. A good deal of importance is given to pyrazolone derivatives. It is due to their wide use in medical chemistry and some of them possess antituberculosis antineoplastic, antidiabetic, anti fertility and antithyroid activity. In this perspective a study on synthesis, characterization, antimicrobial activity, electro-organic and bioactive studies on some pyrazolone derivatives have been taken up and incorporated in the thesis. Introduction is kept to minimum in order to draw more attention to the actual dissertation details. A brief
account on 2-pyrazolines and 2-isoxazolines, their impotence and various methods for their synthesis is discussed.

A five membered cyclic diene containing three carbons and two nitrogens is called a diazole. If two nitrogen atoms are adjacent, it is known as a pyrazole. If one double band is present, it is a pyrazoline. If two nitrogen atoms are separated by a carbon, it is known as an imidazole. Similarly, heterocyclic compounds composed of three carbons, one nitrogen and one oxygen atom is called an oxazole. If two heteroatoms are adjacent it is an isoxazole, whereas if one double bond is present, it is known as an isoxazole.

The biological properties of pyrazoles are reviewed extensively. Several pyrazolines (1) and annulated pyrazoles (2-4) posses antimicrobial activity\textsuperscript{1-5}.

Pyrazole and its N-substituted derivatives are potential inhibitors and deactivators of liver alcohol dehydrogenase. Difenamizole (5) posses analgesic activity greater than that of aspirin.
The trifluoro derivatives of pyrazoles (6 & 7) are about 0.5% as effective as an amebicide, comparable with emetin and metronindazole.

Several di- and trisubstituted pyrazole and pyrazoline derivatives and 4-pyrazolyl pyridinium salts (8) possess hypoglycemic activity. Muzolimine (9), 1-substituted 2-pyrazolin-5-one derivative is a highly active diuretic. It differs from other diuretics as it contains neither sulfonamide nor carboxyl group. Besides this, pyrazoline and indazole derivatives (10-12) are pharmacologically active and are useful as antinflammatory drugs.

![Chemical structures](image-url)
As well as 3,5-pyrazolidinedione derivatives such as phenylbutazone (13), oxyphenbutazone (14), sulfinpyrazone (15), etc., are some of the important class of anti-inflammatory agents which are most widely used.

The organophosphates (16) which contain pyrazole moiety find application in agrochemical field as insecticides and pesticides. Dimetilan (17), isolan (18) and 1-phenylcarbomoyl-2-pyrazolines (19) also possess useful insecticidal properties. It was reported that 3,4-diphenyl substitution in the heterocyclic ring increases the potency of insecticides when compared to 3-phenyl substitution by a factor of 3 to 100.

Apart from these, 5-pyrazoline derivatives have many applications as dye stuffs. Pyrazole, pyrazoline and pyrazolone derivatives are used in colour photography and as optical brighteners etc. polymers with a backbone of five-membered heterocyclic
rings were developed; a polypyrazole (20) and a polypyrazoline (21) belong to such a class.

\[
20
\]

2-Pyrazolines

A. Hydrazine based reactions

Pyrazoline was first synthesized in 1894 by Curtius and Wirising\textsuperscript{13} by the spontaneous reaction of acrolein with hydrazine in low yields (22). The principle of this method was adopted by many scientists over the years and found that it has been a facile one for the synthesis of a variety of 2-pyrazolines.

\[
\text{CH}_3\text{C}==\text{CH} + \text{NH}_2\text{NH}_2 \rightarrow \text{N}
\]

In fact the cyclocondensation of different \(\alpha,\beta\)-unsaturated ketones having alkyl, aromatic and heteroaromatic substituents with hydrazine and its alkyl and aryl derivatives was extensively utilized for the synthesis of 2-pyrazolines\textsuperscript{5,6,14-19}(23,24,25).
ArCOCH=CHR + R1NHNH₂ → [23]

ArCOCH=CRCOCH₂CH₂NHR₁ → [24]

(i) Equimolar PhNHNH₂  (ii) Equimolar PhNHNH₂, EtOH, AcOH, 40°C

ArOCH=HC—\ / N₀₂

ArOC—C=C—'

Br Br O N₀₂

(i) Br₂, AcOH  (ii) Et₃N, dry C₆H₆  (iii) Ar′OCH₂CONHNH₂  (iv) H₂SO₄, AcOH
In a much similar way, the reaction of mesityl oxide or its esters with hydrazine or arylhydrazines led to the formation of 3,4,5-trimethyl-2-pyrazolines\textsuperscript{20,21} (26).

\[
\text{Me} = \text{C} = \text{CHCOMe} + \text{RNHNH}_2 \rightarrow \text{Me} \quad \text{Me} \quad \quad \text{Me} \quad \text{N} \quad \text{Me} \quad \text{R}
\]

Some pyrazolidine-azomethine-2-pyrazolines were also reported by the reaction of 1-phenyl-3-methylpyrazolidine-azomethine-5-chalcones with hydrazine hydrate in the presence of gl.AcOH or with phenylhydrazine in dry alcohol in the presence of piperidine\textsuperscript{22} (27).

\[
\text{PhHC} = \text{HCOCN} \quad \text{Me} \quad \text{N} \quad \text{Ph} \\
\text{N} \quad \text{Me} \quad \text{i} \quad \text{N} \quad \text{Ph} \\
\text{Ph} \quad \text{Me} \quad \text{N} \quad \text{Ph}
\]

(i) N\textsubscript{2}H\textsubscript{4}, AcOH (ii) PhNHNH\textsubscript{2}, C\textsubscript{6}H\textsubscript{11}N

Different Michael acceptors were also condensed with substituted hydrazines viz., phenyl\textsuperscript{23,24}, benzyl\textsuperscript{25} acyl, phenyl\textsuperscript{26,27} and sulfonyl hydrazines\textsuperscript{28} to obtain the corresponding 2-pyrazolines (28). Under identical conditions the reaction of 2,6-diarylidene cyclohexanones with hydrazine hydrate was carried out to get some bicyclic 2-pyrazolines\textsuperscript{29} (29).
3,5-diaryl-4-arylsulfonyl-2-pyrazolines were reported by the cyclocondensation of α-arylsulfonyl chalcones with hydrazine hydrate in alcohol (30).

Adopting the same methodology, several bis (2-pyrazolines) were also obtained by the reaction of 1,1’-(1,4-phenylene)bis(3-aryl-2-propen-1-ones)\textsuperscript{31}, 3,3’-(1,4-phenylene)bis(1-aryl-2-propen-1-ones)\textsuperscript{32,33}, 2,4-bis(cinnamoyl)phenols\textsuperscript{34} and 1,1’-(1,3-phenylene)bis(3-aryl-2-propen-1-ones)\textsuperscript{35} with hydrazine hydrate and its alkyl derivatives (31&32).
Bifunctional olefins, 1-arylsulfonyl-2-aroylethenes, on reaction with hydrazine hydrate and phenyl hydrazine gave 4-arylsulfonyl-3-aryl-2-pyrazolines\textsuperscript{36} (33).

Akhiwala\textsuperscript{37} reported the synthesis and antimicrobial activity of 1H-3-(2"-hydroxy-3"-bromo-4"-n-butoxy-5"-nitrophen-1"-yl)-5-aryl-2-pyrazolines 35 by condensing 2'-hydroxy-3'-bromo-4'-butoxy-5'-nitrochalkones 34 with hydrazine hydrate in ethanol.

Jolly and psthak\textsuperscript{38} have reported the synthesis and antibacterial activity of 1-(anilinomalonyl)-3-(N-anilino-N-β-cyanoethylamino)-5-phenylpyrazolines 37.
4-aminoacetophenone was condensed with benzenesulphonyl chloride to get 4-benzenesulphonamidoacetophenone, which was then condensed with various aromatic aldehydes to get chlkones 38. The chlkones 38 on treatment with hydrazine hydrate/acetic acid and phenyl hydrazine separately gave the corresponding pyrazolines 39. The products have been screened for their antimicrobial activities.

\[ \text{4-aminoacetophenone} \xrightarrow{\text{condensation with benzenesulphonyl chloride}} \text{4-benzenesulphonamidoacetophenone} \xrightarrow{\text{condensation with various aromatic aldehydes}} \text{chlkones} \ 38 \]

\[ \text{NH}_2\text{NH}_2\cdot\text{H}_2\text{O} \]
\[ \text{CH}_3\text{COOH}/\text{PhNHNNH}_2 \]

\[ \text{pyrazolines} \ 39 \]

\[ X = \text{COCH}_3/\text{Ph} \]

The synthesis and antimicrobial activity some new pyrazolines 41a and N-phenyl pyrazolines 41b was reported by Subbawad and Vibhute. The results of inhibition were found to be significant. It was noted that the N-phenyl pyrazolines were found to be more inhibitory to both bacteria and fungi than the corresponding pyrazolines.
Andotra et al.\textsuperscript{41} have reported the synthesis and biocidal activity of 1-acetyl-3-(2,3-dialkoxyphenyl)-5-arylpyrazolines 43.

Basaif and coworkers\textsuperscript{42} have reported the synthesis of some pyrazolines 44 by condensing $p$-sulphamylphenylhydrazine with chalkones.
Ankhiwala and Hathi\textsuperscript{43} have reported the synthesis and antibacterial activity of 1-phenyl-3,5-diaryl-2-pyrazolines 46.

Sorathiya et al.,\textsuperscript{44} have reported the synthesis and antimicrobial activity of some pyrazoline derivatives 48\textsubscript{a-c}. 
Synthesis of 2-pyrazolines 49 under microwave irradiation in open borasil vessels using unmodified domestic microwave oven is described by Paul and Gupta\textsuperscript{45}.

Shingare et al\textsuperscript{46} have reported the synthesis and antimicrobial activities of dihydropyrazoles (pyrazolines) 50.
Malik and co-workers\textsuperscript{47} have described the synthesis and bioefficacy of 2-[4-(5-aryl-4,5-dihydro-1H-pyrazol-3-yl) phenoxy] acetic acid hydrazides \textsuperscript{52}.

New 1-(phenylsulphonyl)-3,5-diarylpyrazolines \textsuperscript{54} and 1-(3-chlorophenyl)-3,5-diarylpyrazolines \textsuperscript{55} have been synthesized by the action of benzenesulphonyl hydrazine and 3-chlorophenylhydrazine with 1,3-diaryl-prop-2-ene-1-ones \textsuperscript{53} in DMF\textsuperscript{48}.
Hiremeth et al.\textsuperscript{49} have reported the synthesis, antimicrobrial, analgesic and anti-inflammatory activities of 1-(10-substituted-7H-indolo [2,3-c]isoquinolino-5-yl)-3,5-disubstituted pyrazolines 57.

\[ 
\begin{align*}
\text{R} & \quad \text{H} & \quad \text{O} & \quad \text{R} \\
\text{S} & \quad \text{O} & \quad \text{R} & \quad \text{R'} \\
\text{N} & \quad \text{S} & \quad \text{R'} & \quad \text{R''} \\
\end{align*}
\]

\[ 
\begin{align*}
\text{S} & \quad \text{SO}_2 & \quad \text{N} & \quad \text{R'} & \quad \text{R''} \\
\text{N} & \quad \text{N} & \quad \text{S} & \quad \text{R'} & \quad \text{R''} \\
\end{align*}
\]

Hiremeth et al.\textsuperscript{49} have reported the synthesis, antimicrobrial, analgesic and anti-inflammatory activities of 1-(10-substituted-7H-indolo [2,3-c]isoquinolino-5-yl)-3,5-disubstituted pyrazolines 57.
Nimavat et al.,\textsuperscript{50} have reported described the synthesis, anticancer, antitubercular and antimicrobial activities of 1-substituted 3-aryl-5-(3'-bromophenyl)-pyrazolines 59.

\[
\begin{array}{c}
\text{Br} & \text{CHO} \quad \overset{\text{aq. alkali}}{\longrightarrow} \quad \text{Br} \quad \text{C} \quad \text{R} \\
\end{array}
\]

Jamode et al.,\textsuperscript{51} have described the synthesis and antimicrobial activity of some 1-isonicotinyl/carboxamido-2-pyrazolines 61 and 62.

\[
\begin{array}{c}
\text{SO}_2\text{NH} & \text{CH}_3 \\
\end{array}
\]

\[
\begin{array}{c}
\text{R} = \text{aryl}, \text{R'} = \text{H}, \text{COOCH}_3 \\
\end{array}
\]

16
Kumar and co-workers\textsuperscript{52} have reported the synthesis and anti-inflammatory, analgesic, ulcerogenic and cyclooxygenase activity of novel quinazolinyl-\(\Delta^2\)-pyrazolines 65.

\[ \text{Azo pyrazoline hererocycles} \]

Pyrazoline-one 66 were prepared in 67-94\% by cyclo condensing E-3-oxo-3-furyl proportionate with \(\text{PhNHNH}_2\) and coupling resulting 3-furyl-1-phenyl-2-pyrazoline-one with diazotized \(p-\text{RC}_6\text{H}_4\text{NH}_2\). Several of these compounds showed antifungal inflammatory and activity (Usher et al.,\textsuperscript{53}).
Pyrazolone mono azo compound 67 are prepared by diazotization of 4-(2-phenoxyethyl-oxycarbonyl) aniline and coupled with 1-phenyl-3-allyoxy-carbonyl-5-pyrazolone. The compound showed significant antibacterial activity (Niwa et al.,54).

\[
\begin{align*}
&\text{XOOC} \quad \text{Ph} \\
&\text{\quad N=N} \\
&\text{\quad COOR} \\
&\text{\quad Ph}
\end{align*}
\]

\[\text{X = Phenoxyethyl, benzyl; R = alkenyl, 67}\]

The azo pyrazolone 68 were prepared by coupling 3-aminophenyl-β-chlorovinyl sulfone with 3-methyl-1-phenyl-5-pyrazolone. They were found to be active antimicrobial activity (Stefaniak et al.,55).

\[
\begin{align*}
&\text{Me} \\
&\text{\quad N=N} \\
&\text{\quad Ph} \\
&\text{\quad OH} \\
&\text{\quad SO_2Me}
\end{align*}
\]

\[\text{68}\]

Pyrazolone mono azo compound 69 has good antimicrobial and antifungal activity. Derivatives of these compounds prepared by diazotizing p-carbotetra flurfurloxy aniline and coupling with substituted pyrazolones (Nippon Kayakyu et al.,56).

\[
\begin{align*}
&\text{ROOC} \quad \text{Ph} \\
&\text{\quad N=N} \\
&\text{\quad COOR^3} \\
&\text{\quad R^1} \\
&\text{\quad R^2} \\
&\text{\quad R^3}
\end{align*}
\]

\[\text{R = alkyl, alkenyl; R^1 = R^2 = H, Cl, Br, R^3 = C_5-alkyl, aralkyl.}\]
3-(arylazo)-5-cyano-4-methyl-1H-pyrazolo [3,4-6]pyridines 70 and 71 were prepared by diazotization and coupling reactions. These compounds showed antimicrobial activity (Hahamand Maszynski\textsuperscript{57}).

![Chemical structures of 70 and 71]

Diazotization of 3-amino-6-anilino-5-cyano-4-methyl-1H-pyrazolo [3,4-6]pyridine and coupling with 1-N-methyl-5-cyano-2-hydroxy-6-pyridone producing compound 72 (Walter and Rigassi\textsuperscript{58}).

![Chemical structure of 72]

Water soluble azocompounds 73 prepared by diazotized sodium salt of 2,5-dichloro sulfonilate and coupling with 2,5-dimethyl-7-amino pyrazolo [1,5a]1, pyrimidine are having anti microbial activity (Elgemeie et al.,\textsuperscript{59}, Ridyard and renfren\textsuperscript{60}).

![Chemical structure of 73]
The azo pyrazoline compound 74 is prepared by diazotized 2-butoxyethyl-p-aminobenzenoate and coupling it with 2,4-dihydroxy quinoline, are used antifungal and antimicrobial agent (Boulton et al.,60).

![Diagram of 74]

Pyrazoline monoazo compound 75 were prepared by condensation of cyanuric chloride with \( p\)-MeNH \( C_6H_4SO_2CH_2SO_3H \) and then with 1-(4-aminophenyl)-3-methyl-5-pyrazolone. These compounds show anti inflammatory and anti fungal activity (Sumitomo chemical co, Ltd.61).

![Diagram of 75]

Pyrazolone mono azo reactive compound 76 prepared from neutral solution of the sodium salts of 4-(\( \beta\)-sulfatoethyl sulfonyl) amine was diazotized and the diazoniam salt cyclocondensed and coupled with diacetyl succinate (Schlaefer et al.,62).

![Diagram of 76]

Reactive chloro or fluortriazine derivatives dis azo compounds 77 were prepared by condensing cyanuric chloride with 4,4-diamino-2,2'-stilbenediamine,
diazotizing the product and coupled with 3-methyl-1[4-(2-sulfactoethyl)sulfonyl]phenyl-pyrazolone (Schlaefer et al.,63).

Pyrazole reactive azo compound 78 are prepared by condensation of 2,4-diamino benzenesulfonic acid and cyanuric chloride then coupled with 1-(4,8-disulfo2-napthyl)-3-methyl-5-pyrazolone. The coupling product was then condensed with m-EtNHC6H4SO2CH2CH2SO3H and salted out to give the corresponding compound (Sumitomo chemical co. Ltd.,64).

Pyrazole mono azo reactive compound 79 was prepared by condensation of cunuric chloride with 1-(4-aminophenyl)-3-methyl-5-pyrazolone. The condensate coupled with diazotized 1,2,5 NH2CHO2SO3H and the coupling product condensed with p- EtNHCH6H4SO2CH2CH2SO3H and then m- EtNHCH6H4SO2CH2CH2SO3H (Yoshikawa and Omura65).
Naphthylazo pyrazolone reactive compound 80 were prepared where 4-(β-
sulfatoethylsulfonyl) aniline was diazotized with acetyl succinic acid die-ester at pH =
4 and the pyrazolone intermediate was coupled with diazotized (6- β-sulfatoethyl
sulfonyl)-1-sulfo-2-napthalamine (Tappe et al.,66).

Benzo triazol group containing reactive azodye 81 are prepared by 2-amino-
4-[2-amino-4-(β-hydroxyethyl-sulfonyl)phenylamino]benensulfonic acid was
diazotized and coupled with 3-methyl-1-( β-hydroxyethyl-sulfonylphenyl)-5-
pyrazolone and the intermediate sulfonated with oleum (Berger Lohr et al.,67).

The pyrazolo monoazo compound 82 were prepared by condensation of
cyanuric chloride with 1-(4-aminophenyl)-3-methyl-5-pyrazolone and
NH₂(CH₂)₅SO₂CH₂CH₂SO₃H, the product was coupled with diazotized 2,2,5-
NH₂C₆H₅SO₃H and the resulting chlorotriazine azo compound was condensed with 3-
NH₂C₆H₄SO₃H to give 82 (J.P. Appl.,68).
The reaction of 3,4,5-Me(NH₂)₂CH₆H₂SO₃Na with 2-(fluorochloromethyl)4,6-difluoro-5-chlorophyrimidine, diazotization of the product and coupling with carboxy-1-(2-methyl-4-sulfophenyl)-5-pyrazolene 83 (Schuendehuete and Klauke69).

Pyrazolone mono azo compound 84 were prepare by diazodization of 4-(2-sulfatoethyl sulfonyl)-3-(2-sulfatoethyl sulfonyl methyl) aniline and coupling with 1-(4-sulfophenyl)-3-carboxy-5-pyrazolone (Muszynski and halm70).

Pyrazolone mono azo compound 85 are prepared by coupling diazotized amino pterephthalic acid with 1-(4-sulfophenyl-3-methyl-5-pyrazolone in aqueous Na₂CO₃ and the product salted out with NaCl, filtered and dried (Kuthan et al., 71).
Water soluble pyrazoline 86 were prepared by coupling diazotized 3-aminophenylmethylsulfone with 3-carboxy-1(4-sulfophenyl)-5-pyrazolone and hydrolysis in alkali medium (Stefaniak72).

![Diagram of 86]

Derivatives of triazine azo compound 87 are prepared by diazotization and coupling of substituted pyrazolone (Podder73).

![Diagram of 87]

Mono and diazo pyrazolo[3,4-b]pyridine acid compound 88 are prepared by diazotizing 3-amino-5-cyano-4-methyl-6(3-sulfophenylamino)-1H-pyrazolo[3,4-b]pyridine and coupled with N-methyl-4-methyl-5-cyano-2-hydroxy-6-pyridone (Hahn et al.,74).

![Diagram of 88]

Some azoic compounds 89 derived from 7-hydroxy-3-phenylquinoline was evaluated as azoic coupler. For an example 7-hydroxy-3-(4-nitrophenyl) quinoline is reduced and benzoylated to give 3-(4-benzamidophenyl)-7hydroxy-3-quinolinyl)-3-phenyl-2benzisonalzole and by azo coupling (Krishnan and Seshadri75).
The cationic pyrazole mono azo compound 90 are prepared by diazotization of 5-amino-3-methyl-1-phenylpyrazole and coupled with N,N-dipropylaniline and then alkylated with Me2so4 (Stingelin and Moser76).

Pyrazole azo compound 91 is obtained where the cationic 1,3,4-thiadiazole treated with methandic malononitrile (Hemming77).

Mardant hydroxyl pyrazole diazo compound 92 and their Cu complexes are suited for application to natural or synthetic substrates (Kaack et al.,78).
Phenylpyrazolone based azo compound 93 is prepared as salts with Na, Ca, NH₄⁺ and/or primary aromatic amine compounds are prepared by coupling diazotized 2-amino-4,5-dichlorobenzenesulfonic acid with 3-methyl-1-(3-sulfophenyl)pyrazolone at pH 5-6 gave an azo compound (Chlost and Lusting⁷⁹).

Pyrazolone group containing mono compound 94 is manufactured by mixing 3-methyl-5-pyrazolone with the corresponding diazotized aniline derivatives at 10-30°C in water containing acetate butter solution (Boruszczak and Kraska⁸⁰).

Pyrazoloquinazolone compounds 95 are prepared by coupling the pyrazolo[5,1-b]quinazolone with diazotized 2-nitro-4-chloroaniline or 1-amino anthraquinone (Imakomi et al.,⁸¹).

R.N.Goyal and Sudha Tyagi⁸² have reported the synthesis of 3-arylazo-3-bromopantane 2,4-dione 96 and its derivatives.
Y. Missa and Beelanadouli\textsuperscript{83} have reported the synthesis of 5-(arylazo)-8-quinolinol 97 and its derivatives.

R.N. Goyal Rajeev and Sudha Tyagi\textsuperscript{84} described the synthesis of antineoplastic 5-arylazo pyrimidines 98.

Wahid U Malik and P.N. Dua\textsuperscript{85} have reported the synthesis of Benzene sulphonamide, p-[(8-hydroxy quinolyl) azo] 99.

Wahid U Malik, V.K. Mahesh and R.N. Goyal\textsuperscript{86} have reported the synthesis of 1-thiocarbonyl-4-substituted arylazopyrazoles 100.
M.A. Mossi and A.M.A. Helly\textsuperscript{87} have reported the synthesis of 2-phenyl azo 1,3-indandione 101.

Watud U. Malik (Miss) S. Agrawal and Rajeev Jain\textsuperscript{88} have reported the synthesis of 5,5-dimethyl cyclohexane-2-benzothiazolyl hydrazono-1,3-diones and its derivatives 102.

Wahid U Malik and Rajeev Jain\textsuperscript{89} have reported the synthesis of N-phenylthiocarbonyl-3,5-dimethyl-4-arylazopyrazoles 103.
L.K. Ravindranath, S.R. Ramadas and S. Brahmaji Rao\textsuperscript{90} have reported the synthesis of 1-phenyl-3-amino-4-arylazo pyrazole-5-one \textit{104}.

\begin{center}
\includegraphics[width=0.2\textwidth]{image104}
\end{center}

H.G. Grag et al.,\textsuperscript{91} described the synthesis of 3,5-substituted phenyl 4-benzeneazo-isoxazoles \textit{105}.

\begin{center}
\includegraphics[width=0.2\textwidth]{image105}
\end{center}

Wahid U Malik, R.N. Goyal and Rajeev Jain\textsuperscript{92} reported the synthesis of N-carbamyl-3,5-dimethyl-4-arylazo pyrazoles \textit{106}.

\begin{center}
\includegraphics[width=0.2\textwidth]{image106}
\end{center}

Rajeev Jain, Sudha Rani and R.N. Goyal\textsuperscript{93} described the synthesis of N-benzyl sulphonyl 3-methyl/phenyl/5-methyl/phenyl 4-arylazo-pyrazoles \textit{107}.

\begin{center}
\includegraphics[width=0.2\textwidth]{image107}
\end{center}
R.N. Goyal and Rajeev Jain\textsuperscript{94} described the synthesis of arylazo pyrimidinyl pyrazoles 108.

\[
\begin{array}{c}
\text{R} = \text{Ar} \\
\text{N}=\text{N} \\
\text{R}_1 \\
\text{N} \\
\text{H}_3\text{C} \\
\text{CH}_3
\end{array}
\]

108

Chandra Mohan, G.S. Saharia and H.R. Sharma\textsuperscript{95} have reported the synthesis of 3-methyl-5-aryl-4-(substituted sulphanamido benzene azo)pyrazoles 109.

\[
\begin{array}{c}
\text{R} = \text{Ar} \\
\text{N}=\text{N} \\
\text{R}_1 \\
\text{R}_2 \\
\text{N} \\
\text{CH}_3
\end{array}
\]

109

3,5-diaryl-4-(substituted sulphonamido-benzene azo) pyrazole 110 is synthesized by (Mrs) Ajaya, G.S.Saharia and H.R. Sharma\textsuperscript{96}.

\[
\begin{array}{c}
\text{R} = \text{Ar} \\
\text{N}=\text{N} \\
\text{R}_1 \\
\text{N} \\
\text{Ar} \\
\text{N} \\
\text{X}
\end{array}
\]

110

1-phenyl carboxamido-3,5-diaryl-4-(substituted sulphanamido benzene azo) pyrazoles 111 obtained from 1,3-diaryl-2(substituted sulphanmido benzene azo)
propone 1,3-dione, in ethanol is added with 4-phenyl semicarbazide and reflux on water bath\textsuperscript{96}.

\begin{center}
\includegraphics[width=0.3\textwidth]{111.png}
\end{center}

3-methyl-5-(4-chloro-3-methyl phenyl)-4-(N-substituted \textit{p}-sulphamyl benzene azo) pyrazole \textbf{112} were synthesized by C. Mohan, G.S. Sharia and H.R. Sharma\textsuperscript{98}.

\begin{center}
\includegraphics[width=0.3\textwidth]{112.png}
\end{center}

K. Bag, T.K. Misra and C. Simha\textsuperscript{99} reported the synthesis of dichloroN (I)-alkyl-2-(arylazo) imidazole mercury (II) complexes \textbf{113}.

\begin{center}
\includegraphics[width=0.3\textwidth]{113.png}
\end{center}

Mahmoud, A.S. Munshi\textsuperscript{100} have reported the synthesis of 5-[4'--(nitro phenyl) azo] salcylaldehyde-3-thiosemicarbazone \textbf{114}.
Y.I. Moharram and M.M. Ghaneum have reported the synthesis of N-benzylsulfonyl-3,5-dimethyl-4-aryl azo pyrazole 115.

RAJEEV Jain, Sudha Tyagi Sharad Agarwal have reported the synthesis of 3,5-dimethyl-4-phenyl azo-N-thiocarbonyl pyrazoles 116.

l-anilinomalonyl-3-methyl-4-p-substituted phenyl azo-5-pyrazolines 117 were synthesized by V.S. Jolly, A.K. Shrivastava, S.P. Singh and K.S. Tiwari.
2,4-diamino-5-aryl-6-(substituted amino)pyramidines 118 are prepared by D.Sen, Smriti Rekha Bhaumiks, Pumedu Sengupta.  

\[ \text{Hydrazonopyrazoline heterocycles} \]

Wahid U. Malik, R.N. Goyal and Rajeev Jain have reported the synthesis of 4-arylhydrazono-1-guanylnitrate-3-methyl-2-pyrazoline-5-one 119.

\[
\text{CH, N-N=W} \quad \text{COCH} \quad \text{NHCOC}_6\text{H}_5
\]

P. Venkata Ramana and L.K. Ravindranath have reported the synthesis of N'-{(2-hydroxy benzoyl)-3-methyl-4-substituted phenyl hydrazobe-2-pyrazoline-5-one 121.

\[
\text{OH} \quad \text{C=O}
\]

Rajeev Jain, P. Pandmaja, Jyothi Bhaduria and Sandeep Tomar have reported the synthesis of 1-guanyl-3-methyl-4-[4'-(4,6-dimethyl pyramidyl)sulfonamoyl] hydrazono-2-pyrazolin-5-one nitrate 122.
1-benzenesulfonyl-3-benzenesulfanaminido-4-(4'-substituted aryl hydrazono)-2-pyrazoline-5-ones 123 are prepared by D.N. Satyanarayana L.K. Ravindranath, T. Ravisankar and Venkata Ramana\(^\text{109}\).

4-aryl hydrazono-N'-benzoyl-3-methyl-2-pyrazoline-5-one 124 were prepared by H.G. Grag and Chandra prakash\(^\text{110}\).

C.P. Singh et al.,\(^\text{111}\) reported the synthesis of N’-(2-pyridine carbonyl)-3-methyl-(substituted hydrazono)-2-pyrazoline-5-one 125.
S. Guniz kucukguzel et al., have reported the synthesis of 3-methyl-4-\{4-[(1,3,4-oxadiazole-2-(3H)-thione-5yl) phenyl] hydrazono\}-2-pyrazoline-5-one 126.

S. Guniz kucukguzel reported the synthesis and antimicrobial activity of 4-arylhydrazono-2-pyrazoline-5-one 127.

S. Guniz kucukguzel\textsuperscript{113} reported the synthesis and antimicrobial activity of 4-arylhydrazono-2-pyrazoline-5-one 127.
REFERENCES

1. S.A.M. Osman, M. Hammad, R.H. Swellm and K.A.M. El Bayouki,

2. V.S. Jolly, Pathak and Manish,

3. M.D. Ankhiwala and M.V. Hathi,

4. G.R. Subbanwad and Y.B. Vibhute,

5. B. Oza Haresh, G. Darti Joshi and H. Parekh Hansa,

6. S.L. Makki Mohammad and M. Fuidallah Hassan,

7. A. Newberry Robert,

8. J. Talley Jhon, Jr. J. Rogier Donald, D. Penning Thomas and S. Yu Stella,


11. K.L. Mc Laren, M.B. Hortlein, J.T. Pechacek, Y.C. Tong and L.Laura,

12. A.R. Katritzky and C.W. Rees,
    "*Comprehensive Heterocyclic Chemistry*", Vol. 5 Pergamon Press, New York

13. Th Curtius and F. W. Res,

14. G.H. Syed,

15. L. F. Fieser and M.A. Peters,

16. A.A. Raval and N.M. Shah,
17. B.S. Holla and Shridhara,

18. M.A. El-Hashash, F.M.A. Soliman L.M. Souka and A.S.S. Salamn,

19. A.B. Salem, A.A. Hassan and M.F. Hassan,

20. M.S. Venkatesh and V.V. Nadkarny,

21. N.M. Frank and M.Miesh,


23. K.V. Komarov, N.D. Chkanikov, S.V. Sereda M. Yu Antipin, T. Yu Struchkor,

24. E.G. Parbinyan, M.S. Matsoyan, A.A. Saakyan,


26. P.B. Terentev and A.G. Kalandarishvili,

27. M.Yu Malor, K.N. Zelenin and S.I. Yakimovich,

28. H.K.V. Patel and P.S. Fernandes,

29. M.A. Elkasaby and N.A.A. Noureldin,

30. D. Bhaskar Reddy, K. Radha Krishna Murthy, T. Seshamma, B. Seenaiah and A. Padmaja,

31. G.P. Tokmakora, M. Udachinl Yu and N.S. Patalakha,
32. S.V. Tsukerman, V.M. Nikitchenko, V.P. Maslennikova and V.F. Larvushin, 
33. El R. Nizar, AL Johary and A.A. Jabbar, 
34. N.K. Sangawan, B.S. Verma and K.S. Dhindsa, 
   Reddy, 
36. M.S. Shingare and H.B. Siddiqui, 
37. M.D. Anchiwala, 
38. V.S. Jolly & M. Pathak, 
39. J. Upadhyay, U. Dave & H. Parekh, 
40. G.R. Subbanwad & Y.B. Vibhute, 
41. C.S. Andotra, J. Khajuria, G.B. Singh & S.Singh, 
42. S.A. Basaif, H.A. Albar & H.M. Faidallah, 
43. M.D. Ankhiwala & M.V. Hathi, 
44. S.D. Sorathiya, V.B.Patel & A.R. Parikh, 
45. S. Paul & R. Gupta, 
46. M.S. Gaikawad, A.S. Mane, V.P. Chavan, R.V. Hangarage & M.S. Shingage, 
47. H. Malik, A. Dahiya, R. Kumar, M.S.Sanwan N. Mehta & N.K. Sangwan, 
48. D.V. Thakare & V.S. Jamode,  

49. S.P. Hiremath, K. Rudresh & A.R. Saundane,  

50. K.S. Nimavat, K.H. Popat & H.S. Joshi,  

51. V.S. Jamode, H.S. Chandak, P.R. Bhagar & D.H. Tambekar,  

52. A. Kumar, S. Sharma, K. Balaji, D. Bansal, S. Sharma, K.K. Saxena, S. Lata,  
B. Gupta & V.K. Srivastava,  

53. Uhar, M., Diaz de Arce, C., Lopez, R., Santacruz, G., Guerra, M., Rodriguez, V., Pantoja, G. and Matheu, G.,  

54. Niwa, T., Himeno, K., Hibara, T. and Shimizu, Y.,  
*Jpn. Kokai Tokkyo Koho JP.*, **6136**, 366 (C1. C09B29/36);  

55. Stefaniak, S., Klimaszewski, R., Straka, K. and Graczyk, B.,  
*Pol. Pl.*, **108**, 746 (C1. C09B29/00);  

56. Nippon Kayaku Co. Ltd.,  
*Jpn. Kokai Tokkyo Koho JP.*, **5953**, 553 (C1. C09B29/52);  

57. Hahn, W.E. and Muszynski, M.,  

58. Walter, H. and Rigassi, T.,  

59. Ridyard, D.R.A. and Renfrea, A.H.M.,  
*Chem Abst.*, **93**, 196228 m (1980).

61. Sumitomo Chemical Co. Ltd.,

62. Schlaefer, L., Schwaiger, G. and Russ, W.H.,

63. Schlaefer, L., Springer, H. and Kunze, M.,

64. Sumitomo Chemical Co. Ltd.,

65. Yoshikawa, S. and Omura, T.,

66. Tappe, H., Oehme, D., Schlaefer, L. and Russ, W.H.,

67. Berer-Lohr, B., Leverenz, K. and Meier, H.


69. Schuendehuette, K.H. and Stoehr, F.M.,

70. Muszynski, M. and Hahn, W.,

71. Kuthan, P., Pavlikova, J. and Marhan, J.,
_Czech. Cs.,_ 269, 615, (C1, C09B29/03); _Chem Abst.,_ 116, 237352 t (1992).

72. Stefaniak, S.,
_Przem. Chem.,_ 63, 114 (19840.

73. Podder, N.G.,
74. Hahn, W.E., Strzyewski, W., Jatczak, M. and Turala, L.,

75. Krishnan, R. and Seshadri, S.,

76. Stingelin, W. and Moser, P.,

77. Henning, G.,

78. Kaack, H., Prakash, A.A. and Ganapathy, R.,

79. Chlost, M. and Lusting, J.,

80. Boruszczak, Z., and Kraska, J.,


82. R.N. Goyal and Sudha Tyagi.,

83. Y. Missa and Beelanandouli,

84. R.N. Goyal, Rajeev Jain and Sudha Tyagi.

85. Wahid U. Malik and P.N. Goyal.

86. Wahid U. Malik, V.K. Mahesh and R.N. Goyal

87. M.A. Mosi and A.M.A. Helly,

88. Wahid U. Malik, S. Agarwal and Rajbbu Jain,
89. Wahid U. Malik and Rajeev Jain,
90. L.K. Ravindranath, S.R. Ramadasu and S. Brahmaji Rao,
91. H.G. Grag,
92. Wahid U. Malik, R.N. Goyal and Rajeev Jain,
93. Rajeev Jain, Sudha Rani and R.N. Goyal,
94. R.N. Goyal and Rajeev Jain,
95. Chandra Mohan, G.S. Saharia and H.R. Sharma,
96. (Mrs) Ajaya Kabra, G.S. Saharia and H.R. Sharma,
97. G.C. Chadra Prakash, Saharaia and H.R. Sharma,
98. C. Mohan, G.S.Saharia and H.R. Sharma,
99. K. Bag, T.K. Misra and C. Sinda,
100. A.S. Mohamoud, Monshi,
101. Y.I. Moharram and M.M. Ghoneim,
102. Rajeev Jain, Sudha Tyagi and Sharad Agarwal,
103. V.S. Jolly, A.K. Shrivastava, S.P. Singh and K.S. Tiwari,
104. D. Sen, Smriti REkha Boumik & Pumendu Senguptha,
105. Wahid U. Malik, R.N. Goyal and Rajeev Jain,
106. Rajeev Jain et al.,

107. P. Venkata Ramana and L.K. Ravindranath,

108. Rajeev Jain, P. Padmaja, Jyothi Bhaduria,

109. D.N. Satyanarayana, L.K. Ravindranath, T. Ravi Sankar and P. Venkata Ramana,

110. H.G. Grag and C. Prakash,

111. C.P. Singh et al.,

112. S. Guniz Kucukguzel et al.,

113. S.G. Kucukguzel, S. Rollas,