Part – A

Synthesis
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 organic 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 include 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 medicinal 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 importance and various methods for their syntheses 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 bond is present, it is a pyrazoline. If two nitrogen atoms are separated by a carbon, it is known as an imidazole. Similarly, heterocyclic compound 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 isoxazoline.

The biological properties of pyrazoles are reviewed extensively. Several pyrazolines (1) and annelated pyrazoles (2-4) posses antimicrobial activity\(^1\)\(^-\)\(^5\).

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 metronidazole.

Several di- and trisubstituted pyrazole and pyrazoline derivatives\textsuperscript{6} 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\textsuperscript{7,8}. 

\begin{align*}
\text{Ph} & \quad \text{Me} \\
\text{N} & \quad \text{N} \\
\text{NHCOCHNMe}_2 & \quad \text{Ph} \\
\end{align*}

\begin{align*}
\text{CF}_3 & \\
\text{N} & \quad \text{H} \\
\end{align*}

\begin{align*}
\text{Me} & \quad \text{Me} \\
\text{CF}_3 & \\
\text{N} & \quad \text{H} \\
\end{align*}

\begin{align*}
\text{Me}_2\text{N} & \quad \text{R}^1 \\
\text{R}^2 & \quad \text{R}^3 \\
\end{align*}

\begin{align*}
\text{R}^1 & \quad \text{R}^2 \\
\text{R}^3 & \\
\end{align*}

\begin{align*}
\text{R}^1 & \quad \text{R}^2 \\
\text{Cl} & \\
\end{align*}

\begin{align*}
\text{R}^1 & \quad \text{R}^2 \\
\text{R}^3 & \\
\end{align*}

\begin{align*}
\text{Me} & \quad \text{Cl} \\
\text{Cl} & \\
\end{align*}

\begin{align*}
\text{R}^1 & \quad \text{R}^2 \\
\text{R}^3 & \\
\end{align*}

\begin{align*}
\text{R}^1 & \quad \text{R}^2 \\
\text{Cl} & \\
\end{align*}

\begin{align*}
\text{CO}_2\text{Et} & \\
\text{N} & \quad \text{N} \\
\end{align*}

\begin{align*}
\text{CO} & \quad \text{phenyl} \\
\text{Cl} & \\
\end{align*}
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-phenylcarbamoyl-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 or 3,5-diphenyl 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 back bone of five
memebered heterocyclic rings were developed; a polypyrrole (20) and a polypyrrololine (21) belongs to such a class.

\[ \text{2-Pyrazolines} \]

**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.

\[ \text{\textbf{C}} + \text{NH}_2\text{NH}_2 \rightarrow \text{N-N} \]

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).
(i) Equimolar PhNH₂H₂ (ii) Equimolar PhNH₂H₂, EtOH, AcOH, 40°C

(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 3,5,5-trimethyl-2-pyrazolines\textsuperscript{20,21} (26).

\[
\text{Me} \overset{\text{C=CHCOMe + }}{\longrightarrow} \text{Me}
\]

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

Different Michael acceptors were also condensed with substituted hydrazines viz., phenyl\textsuperscript{23,24}, benzyl\textsuperscript{25} acyl, phenacyl\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\textsuperscript{30} by the cyclocondensation of \(\alpha\)-arylsulfonyl chalcones with hydrazine hydrate in alcohol (30).

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

\[
\text{ArSO}_2\text{CH=CHCOAr'} + \text{RNHNH}_2 \rightarrow \text{ArO}_2\text{S} - \text{N} - \text{Ar'}
\]

Ankhiwala\(^{37}\) 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.

\[
\begin{align*}
\text{Br} & \quad \text{OH} \\
\text{O}_2\text{N} & \quad \text{C} = \text{C} = \text{CH} - \text{R} \\
\text{n-C}_4\text{H}_9\text{O} & \quad \text{Br} \\
\text{OH} & \quad \text{O}_2\text{N}
\end{align*}
\]

Jolly and Pathak\(^{38}\) have reported the synthesis and antibacterial activity of 1-(anilinomalonyl)-3-(N-anilino-\(N\)-\(\beta\)-cyanoethylamino)-5-phenylpyrazolines \(^{37}\).

\[
\begin{align*}
\text{R} & \quad \text{N} - \text{C} = \text{N} \\
\text{H} & \quad \text{C} = \text{C} = \text{CH} - \text{Ph} \\
\text{H}_2\text{H} & \quad \text{O} - \text{NHNHNH}_2 \\
\text{R}_1 & \quad \text{N} - \text{C} = \text{N} \\
\text{O} & \quad \text{NH} - \text{Ph} \\
\end{align*}
\]
4-aminoacetophenone was condensed with benzenesulphonyl chloride to get 4-benzenesulphonamidoacetophenone, which was then condensed with various aromatic aldehydes to get chalkones 38. The chalkones 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\textsuperscript{39}.

\[
\text{HN} \quad \text{SO}_2 \quad \text{Ph} \quad \text{C} \quad \text{CH}_3 \quad + \quad \text{Ar} \quad \text{CHO} \quad \text{CH} = \text{Ar} \quad \text{HN} \quad \text{SO}_2 \quad \text{Ph} \quad \text{C} \quad \text{CH} \quad \text{Ar} \quad 38
\]

\[
\text{NH}_2\text{NH}_2\text{H}_2\text{O}; \text{CH}_3\text{COOH} \quad \text{PhNHNH}_2 \quad \downarrow \quad \text{HN} \quad \text{SO}_2 \quad \text{Ph} \quad \text{C} \quad \text{N} \quad \text{N} \quad \text{Ar} \quad 39 \quad X = \text{COCH}_3/\text{Ph}
\]

The synthesis and antimicrobial activity some new pyrazolines 41\textsuperscript{a} and \textit{N}-phenyl pyrazolines 41\textsuperscript{b} was reported by Subbanwad and Vibhute\textsuperscript{40}. The results of inhibition were found to be significant. It was noted that the \textit{N}-phenyl pyrazolines were found to be more inhibitory to both bacteria and fungi than the corresponding pyrazolines.
Andotra et al., have reported the synthesis and biocidal activity of 1-acetyl-3-(2,3-dialkoxyphenyl)-5-arylpyrazolines 43.

Andotra et al., 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 \textit{44} by condensing \textit{p}-sulphamylphenylhydrazine with chalcones.

\begin{center}
\includegraphics[width=0.5\textwidth]{reaction1.png}
\end{center}

Ankhiwala and Hathi\textsuperscript{43} have reported the synthesis and antibacterial activity of 1-phenyl-3,5-diaryl-2-pyrazolines \textit{46}.

\begin{center}
\includegraphics[width=0.5\textwidth]{reaction2.png}
\end{center}

Sorathiya et al.,\textsuperscript{44} have reported the synthesis and antimicrobial activity of some pyrazoline derivatives \textit{48a–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.

\begin{align*}
\text{R-CHO} & \xrightarrow{\text{40\%NaOH/EtOH}} \text{N} \rightarrow \text{COCH}_3 \\
\text{N}_2\text{H}_4\cdot\text{H}_2\text{O} & \xrightarrow{\text{PhNHNH}_2/\text{CH}_3\text{COOH}} \\
\end{align*}
Malik and co-workers\textsuperscript{47} have described the synthesis and bioefficacy of 2-[4-(5-aryI-4,5-dihydro-1\textit{H}-pyrazol-3-yl)phenoxy] acetic acid hydrazides 52.

New 1-(phenylsulphonyl)-3,5-diarylpyrazolines 54 and 1-(3-chlorophenyl)-3,5-diarylpyrazolines 55 have been synthesized by the action of benzenesulphonyl hydrazine and 3-chlorophenylhydrazine with 1,3-diaryl-prop-2-ene-1-ones 53 in DMF\textsuperscript{48}. 

New 1-(phenylsulphonyl)-3,5-diarylpyrazolines 54 and 1-(3-chlorophenyl)-3,5-diarylpyrazolines 55 have been synthesized by the action of benzenesulphonyl hydrazine and 3-chlorophenylhydrazine with 1,3-diaryl-prop-2-ene-1-ones 53 in DMF\textsuperscript{48}.
Hiremath et al.\textsuperscript{49} have reported the synthesis, antimicrobial, analgesic and anti-inflammatory activities of 1-(10-substituted-7\textit{H}-indolo[2,3-\textit{c}]-isoquinolino-5-yl)-3,5-disubstituted pyrazolines 57.
Nimavat et al.\textsuperscript{50} have described the synthesis, anticancer, antitubercular and antimicrobial activities of 1-substituted 3-aryl-5-(3'-bromophenyl)-pyrazolines 59.

\[ \text{CHO} + \text{CH}_3\text{C}=\text{C}-\text{R} \xrightarrow{\text{aq. alkali}} \text{Br} \]

\[ \text{R'NHNH}_2/\text{CH}_3\text{COOH} \]

\[ \text{R = aryl; R' = H,COCH}_3 \]

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

\[ \text{SO}_2\text{NH} - \text{O} - \text{C}-\text{CH}_3 + \text{HOC} - \text{C}-\text{R} \xrightarrow{40\%\text{NaOH/EtOH}} \text{R}^2 \]

\[ \text{O}_2\text{N} \]

\[ \text{R = aryl; R' = H,COCH}_3 \]

\[ \text{NH}_2\text{HNCONH}_2\text{HCl} \]

\[ \text{Pyridine} \]

\[ \text{SO}_2\text{NH} - \text{N} - \text{C}=\text{N} - \text{R}^1 \]

\[ \text{CO} \]

\[ \text{NH}_2\text{HNCONH}_2\text{HCl} \]

\[ \text{Pyridine} \]
Kumar and coworkers\textsuperscript{52} have reported the synthesis and anti-inflammatory, analgesic, ulcerogenic and cyclooxygenase activity of novel quinazolinyl-Δ²-pyrazolines 65.

Azo pyrazoline heterocycles

Pyrazoline-5-one 66 were prepared in 67 – 94% by cyclo condensing E-3-oxo-3-furyl proportionate with PhNHNNH₂ and coupling the resulting 3-furyl-1-phenyl-2-pyrazoline-5-one with diazotized p-RC₆H₄NH₂. Several of these compounds showed antifungal inflammatory and antibacterial activity (Usher et al.,\textsuperscript{53}).

\[ R = \text{Cl, NO₂, CO₂H, SO₂H.} \]
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 antimicrobial activity (Niwa et al., 54).

\[
\begin{align*}
\text{X} & = \text{Phenoxyethyl, benzyl; } R = \text{alkenyl.}
\end{align*}
\]

67

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

68

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

\[
\begin{align*}
R & = \text{alkyl, alkenyl; } R^1 = R^2 = \text{H, Cl, Br;}
R^3 & = \text{C}_{5-8} \text{ alkyl, aralkyl.}
\end{align*}
\]

69
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}).

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}).

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 \textit{et al.},\textsuperscript{59}, Ridyard and Renfren\textsuperscript{60}).
The azopyrazoline compound 74 is prepared by diazotized 2-butoxyethyl-p-aminobenzoate and coupling it with 2,4-dihydroxy quinoline, are used antifungal and antimicrobial agent (Boulton et al., 60).

Pyrazoline monoazo compound 75 were prepared by condensation of cyanuric chloride with \( p\-\text{MeNH C}_6\text{H}_4\text{SO}_2\text{CH}_2\text{OSO}_3\text{H} \) and then with 1-(4-aminophenyl)-3-methyl-5-pyrazolone. These compounds show anti inflammatory and anti fungal activity (Sumitomo chemical co, Ltd. 61).

Pyrazolone monoazo reactive compound 76 are prepared from neutral solution of the sodium salts of 4-(\( \beta\)-sulfatoethyl sulfonyl)aniline was diazotized and the diazonium salt cyclocondensed and coupled with diacetyl succinate (Schlaefer et al., 62).
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.,\textsuperscript{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-disulfo-2-napthyl)-3-methyl-5-pyrazolone. The coupling product was then condensed with m-EtNHC\textsubscript{6}H\textsubscript{4}SO\textsubscript{2}CH\textsubscript{2}CH\textsubscript{2}SO\textsubscript{3}H and salted out to give the corresponding compound (Sumitomo chemical co.Ltd.,\textsuperscript{64}).

Pyrazole mono azo reactive compound 79 was prepared by condensation of cyanuric chloride with 1-(4-aminophenyl)-3-methyl-5-pyrazolone. The condensate coupled with diazotized 1,2,5-H\textsubscript{2}NC\textsubscript{10}H\textsubscript{5}(SO\textsubscript{3}H) and the coupling product condensed with p- EtNHC\textsubscript{6}H\textsubscript{4}SO\textsubscript{2}CH\textsubscript{2}CH\textsubscript{2}SO\textsubscript{3}H and then m-H\textsubscript{2}NC\textsubscript{6}H\textsubscript{4}SO\textsubscript{2}CH\textsubscript{2}CH\textsubscript{2}SO\textsubscript{3}H (Yoshikawa and Omura\textsuperscript{65}).
Naphtylazo pyrazolone reactive compound 80 were prepared where 4-(β-sulfatoethylsulfonyl)aniline was diazotized and cyclized with acetylsuccinic acid diester 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]benzensulfonic 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 H₂N(CH₂)₃SO₂CH₂CH₂SO₃H, the product was coupled with diazotized 2,2,5-H₃NCOH₃SO₃H and the resulting chlorotriazine azo compound was condensed with 3-H₂NC₆H₄SO₃H to give 82 (J.P. Appl., 68).
The reaction of 4,3,5Me(H₂N)₂C₆H₂SC≡3Na with 2-(fluorodichloromethyl)-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 monoazo compound 84 were prepared by diazotization 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 monoazo 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, filtrated 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 (Stefaniak\textsuperscript{72}).

Derivatives of triazine azo compound 87 are prepared by diazotization and coupling of substituted pyrazolone (Podder\textsuperscript{73}).

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 \textit{et al.}\textsuperscript{74}).
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 benzyolated to give 3-(4-benzamidophenyl)-7-hydroxy-3-quinolinyl)-3-phenyl-2-enzisonalzole and by azo coupling (Krishnan and Seshadri\textsuperscript{75}).

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 Me\textsubscript{2} SO\textsubscript{4} (Stingelin and Moser\textsuperscript{76}).

Pyrazole azo compound 91 is obtained where the cationic 1,3,4-thiadiazole treated with methandic malononitrile (Hemming\textsuperscript{77}).
Mordant 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 azo compound 94 is manufactured by mixing 3-methyl-5-pyrazolone with the corresponding diazotized aniline derivatives at 10 – 30°C in water containing an 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 Tyagi 82 have reported the synthesis of 3-arylazo-3-bromopantane 2,4dione 96 and its derivatives.

Y. Missa and Beelanadouli 83 have reported the synthesis of 5-(arylazo)-8-quinolinol 97 and its derivatives.

R.N. Goyal Rajeev Jain and Sudha Tyagi 84 described the synthesis of antineoplastic 5-arylazo pyrimidines 98.
Wahid U Malik and P.N. Dua have reported the synthesis of Benzene sulphonamide, \( p-[(8\text{-hydroxy quinolyl})\text{azo}] \)).

\[ \text{HO-SO}_2\text{COR} \]

Wahid U Malik, V.K. Mahesh and R.N. Goyal have reported the synthesis of 1-thiocarbonyl-4-substituted arylazopyrazoles.

\[ \text{N} \equiv \text{N} - \text{R} \]

M.A. Mossi and A.M.A. Helly have reported the synthesis of 2-phenyl azo 1,3-indandione.

\[ \text{NH}_2 \]

M. U. Malik (Miss) S. Agarwal and Rajeev Jain have reported the synthesis of 5,5-dimethyl cyclohexane-2-benzothiazolyl hydrazono-1,3-diones and its derivatives.
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 104.

H.G. Garg \textit{et al.},\textsuperscript{91} described the synthesis of 3,5-substituted phenyl 4-benzeneazo-isoxazoles 105.
Wahid U Malik, R.N. Goyal and Rajeev Jain\textsuperscript{92} reported the synthesis of N-carbamyl-3,5-dimethyl-4-arylazo pyrazoles 106.

\[
\text{R} \quad \begin{array}{c}
\text{N=N} \\
\text{C=O} \\
\text{NH}_2 \\
\text{106}
\end{array}
\]

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 107.

\[
\text{R} \quad \begin{array}{c}
\text{N=N} \\
\text{R}_2 \\
\text{SO}_2\text{CH}_2 \\
\text{107}
\end{array}
\]

R.N. Goyal and Rajeev Jain\textsuperscript{94} described the synthesis of arylazo pyrimidinyl pyrazoles 108.

\[
\text{R} \quad \begin{array}{c}
\text{N=N} \\
\text{R}_2 \\
\text{H}_3\text{C} \\
\text{108}
\end{array}
\]

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

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

3-methyl-5-(4-chloro-3-methyl phenyl)-4-(N-substituted p-sulphamyl benzene azo)pyrazole 112 were synthesized by C. Mohan, G.S. Sharia and H.R. Sharma.
Mahmoud, A.S. Munshi\textsuperscript{100} have reported the synthesis of 5-[4'- (nitropheynyl)azo]salicylaldehyde 3-thiosemicarbazone 114.

Y.I. Moharram and M.M. Ghaneum\textsuperscript{101} have reported the synthesis of N-benzylsulfonyl-3,5-dimethyl 4-aryl azo pyrazole 115.
Rajeev Jain, Sudha Tyagi and Sharad Agarwal\textsuperscript{102} have reported the synthesis of 3,5-dimethyl-4-phenyl azo-N-thiocarbonyl pyrazoles 116.

\[ \text{116} \]

1-anilinomalonyl-3-methyl-4-p-substituted phenyl azo-5-pyrazolines 117 were synthesize by V.S. Jolly, A.K. Shrivastava, S.P. Singh and K.S. Tiwari\textsuperscript{103}.

\[ \text{117} \]

2,4-diamino-5-arylazo-6-(substituted amino)pyrimidines 118 are prepared by D. Sen, Smriti Rekha Bhaumiks, Purnendu Sengupta\textsuperscript{104}.

\[ \text{118} \]

Hydrazonopyrazoline heterocycles

Wahid U. Malik, R.N.Goyal and Rajeev Jain\textsuperscript{105} have reported the synthesis of 4-arylhydrazono-1-guanynitrato-3-methyl-2-pyrazoline-5-one 119.
4-aryl hydrazono-N'-Hippyryl-3-methyl-2-pyrazoline-5-one 120 are prepared by Rajeev Jain et al.106.

P. Venkata Ramana and L.K. Ravindranath107 have reported the synthesis of N'-(2-hydroxy benzoyl)-3-methyl-4-substituted phenyl hydrazone-2-pyrazoline-5-one 121.

Rajeev Jain, P. Pandmaja, Jyothi Bhaduria and Sandeep Tomar108 have reported the synthesis of 1-guanyl- 3- methyl- 4-[4'- (4,6- dimethyl pyrimidyl) sulfonamoyl] hydrazono-2-pyrazolin-5-one nitrate 122.
1-benzenesulfonyl-3-benzenesulfanamino-4-(4'-substituted aryl hydrazono)-2-pyrazoline-5-ones 123 are prepared by D.N. Satyanarayana L.X. Ravindranath, T. Ravisankar and P. Venkata Ramana\textsuperscript{109}.

4-aryl hydrazono-N'-benzoyl-3-methyl-2-pyrazoline-5-one 124 were prepared by H.G. Garg and Chandra Prakash\textsuperscript{110}.

C.P. Singh \textit{et al.}\textsuperscript{111} reported the synthesis of N’-(2-pyridine carbonyl)-3-methyl, 4-(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-5-yl)phenyl]hydrazono]-2-pyrazoline-5-one 126.

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