Part-I

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General Introduction

Like all sciences organic chemistry has a unique place in our pattern of understanding of the universe. It is the sciences of molecules. But heterocyclic chemistry is something more. It literally creates itself as it grows. Of course, we need to study the molecules of nature both because they are interesting in their own right and because their functions are important to our lives.

Heterocyclic chemistry is the chemistry of cyclic compounds having hetero atoms like nitrogen, sulphur and oxygen along with carbon and other elements. Most probably two-thirds of organic compounds belongs to this class, and they number among them some of the most significant compounds for human beings. If we think only of drugs, we can define the history of medicine by heterocycles. Heterocyclic compounds plays an important role in medicinal and biochemical field. These compounds occur so widely in nature and are of such a importance that any discussion of organic chemistry will not get very far without mentioning them.

In present work, attempts have been made to explore the synthesis of five membered, six membered, bicyclic and fused ring heterocyclic compounds containing three hetero atoms viz. bis-1,3,4-thiadiazoloz (3,4-c)-1,2,4-triazoles, bis-1,3,4-thiadiazoles, bis-1,2,4-triazoles, bis-1,2,4,5-dithiadiazinanes, 2,3,5,7,8-pentaazabicyclo [4.2.1] nona-diens, 1,3,4-thiadiazoles and 1,2,4-dithiazolidines.
Literature Survey

The synthesis of these five and six membered and bicyclic heterocycles involved the use of N-aryl/alkyl-S-chloro isothiocarbamoyl chloride and aryl/alkyl isocyanodichlorides. These were first reported by Ottman and Hooks and Dyson and Harington, respectively.

**N-Aryl/Alkyl-S-chloro isothiocarbamoyl chloride (I):**

The N-aryl/alkyl-S-chloro isothiocarbamoyl chlorides (I) were prepared by Ottman and Hooks\(^1\) by the controlled reaction of molecular chlorine with aryl/alkyl isothiocyanates. (Chemically it is called as 1-(chlorothio)-formimidoyl chloride\(^2\) or arylimino-chloromethane sulphenyl chloride).

\[
\begin{align*}
\text{R - N = C = S} & \quad \xrightarrow{\text{Cl}_2 \text{ controlled}} \quad \text{R - N = C} \underbrace{\text{Cl}}_{\text{S - Cl}} \\
\text{Aryl/alkyl isothiocyanates} & \quad \text{N-aryl/alkyl-S-chloro isothiocarbamoyl chlorides}
\end{align*}
\]

**N-Aryl/Alkyl isocyanodichloride (II):**

The N-aryl/alkyl isocyanodichlorides (II) were prepared by Dyson and Haringston\(^3\) involving the exhaustive chlorination of aryl/alkyl isothiocyanates. (Chemically, these are aryl/alkylimino-dichloro methane)

\[
\begin{align*}
\text{R - N = C = S} & \quad \xrightarrow{\text{Cl}_2 \text{ Excess}} \quad \text{R - N = C} \underbrace{\text{Cl}}_{\text{Cl}} \\
\text{Aryl/alkyl isothiocyanates} & \quad \text{Aryl/alkyl isocyanodichlorides}
\end{align*}
\]

It will not be out of place here to review the synthetic methods explored so far for the synthesis of various heterocyclic compounds included in this thesis. The present review deals mainly with bis-1,3,4-thiadiazolo (3,4-c)-1,2,4-triazoles, bis-1,3,4-thiadiazoles, bis-1,2,4-triazoles, bis-1,2,4,5-dithiadiazinanes, 2,3,5,7,8-pentaazabicyclo [4.2.1] nona-diens, 1,3,4-thiadiazoles and 1,2,4-dithiazolidines.
Background of the earlier work on five and six membered, bicyclic and fused ring heterocycles and related compounds.

A] Brief review of bis-1,3,4-thiadiazolo (3,4-c)-1,2,4-triazoles:

Very few compounds of this class are on record Dejiang et al. synthesized 1,4-bis-[(3-aryl)-s-triazolo (3,4-b)-(1,3,4) thiadiazol-6-yl] benzenes (2) by the reaction of 3-aryl-4-amino-5-mercapto-1,2,4-triazoles (1) with terphthalic acid.

Jag Mohan and Sangeeta have achieved the synthesis of 7-aryl-3-ethyl imidazo [1,2-d]-s-triazolo [3,4-b] [1,3,4] thiadiazoles (5) by the interaction of 6-amino-3-ethyl-5-mercapto-s-triazole (4) with α-haloketones.

Nizamuddin and coworkers reported synthesis of 3-aryl-oxymethyl-6-(2-tolyloxymethyl)-1,2,4-triazolo [3,4-b] [1,3,4] thia diazoles (7) by the cyclocondensation of 4-amino-5-aryloxymethyl-3-mercapto-1,2,4-triazoles (6) and 2-tolyloxyacetic acid with DCC in CH₂Cl₂.
The reaction of 3-p-(t-butyl phenyl)-4-amino-5-mercapto-s-triazole (8) independently with various reagents like chloroacetic acid, α-haloketones, benzoin, 2,3-dichloroquinoxaline, aromatic carboxylic acids, carbon disulphide and aromatic carboxaldehydes furnished in one step the cyclic products.
Synthesis of new 3,9-di-p-(t-butylphenyl)-6,14-dioxo-bis-(s-triazolo [3,4-b] [1,3,4-thiadiazolo [3,2-b]-imidazo [4,5-b] cyclohexane]-5a, 6a-diene); 3-p-(t-butylphenyl)-s-triazolo [3,4-b] [1,3,4-thiadiazolo [3,2-b]-imidazo [4,5-b] quinoxaline and 7-aryl-3-p-(t-butylphenyl)-imidazo [2,1-b]-1,3,4-thiadiazolo [2,3-c]-s-triazoles, have been reported by the direct condensation of 6-amino-3-p-(t-butylphenyl)-s-triazolo [3,4-b] [1,3,4] thiadiazole with chloranil, 2,3-dichloroquinoxaline and α-haloketones, respectively by Jag Mohan and Anupama.

where, (i) CNBr, (ii) chloanil, anhydrous NaOAc, AcOH, (iii) 2,3-dichloroquinoxaline, anhydrous NaOAc, (iv) RCOCH₂Br and (v) Br₂, AcOH.
Rajive-Gupta and coworkers\(^9\) reported the synthesis of 2-substituted phenyl-3-(3-alkyl/aryl-5,6-dihydro-s-triazolo-[3,4-b] [1,3,4] thiadiazol-6-yl) indoles (23) by the condensation of 2-arylindole-3-aldehydes (22) with 3-substituted-4-amino-5-mercapto-1,2,4-triazoles (21) in DMF containing p-TSOH as catalyst.

![Chemical diagram](image)

Action of carbondisulphide on 3-(3'-arylpyrazol-5'-yl)-4-amino-5-mercapto-s-1,3,4-triazoles (24) afforded 3-(3'-arylpyrazol-5-yl)-s-triazolo [3,4-b] [1,3,4] thiadiazol-6(5H)-thione\(^10\) (25).

![Chemical diagram](image)

The reaction of 3-n-propyl-4-amino-5-mercapto-s-triazole\(^11\) (26) independently with various reagents like chloroacetic acid, \(\alpha\)-haloketone, benzoin, bromoacetaldehyde diethyl acetal, 2,3-dichloroquinoxaline, carbon disulphide, aromatic carboxylic acids and aromatic carboxaldehydes furnished in one-step the cyclic products.
where, \( R = \text{n-propyl} \)

(i) \( \text{CICH} = \text{COOH}, \text{NaOAc} \),
(ii) \( \text{ArCOCH} \_\text{Br}, \text{K}_2\text{CO}_3 \),
(iii) \( \text{PhCHOHCOPh}, \text{KOH} \),
(iv) \( \text{bromoacetaldehyde diethyl acetal} \),
(v) \( 2,3\text{-dichloroquinoxaline} \),
(vi) \( \text{CS}_2, \text{KOH} \),
(vii) \( \text{ArCOOH}, \text{POCl}_3 \),
(viii) \( \text{ArCHO} \)

Heng-Shan Dong and coworkers\(^{12}\) have synthesized 3-[5-methyl-1-(4-methyl phenyl)-1,2,3-triazol-4-yl]-6-substituted-s-triazolo [3,4-b]-1,3,4-thiadiazoles (36) by the condensation of 3-[5-methyl-1-(4-methyl phenyl)-1,2,3-triazol-4-yl]-4-amino-5-mercapto-s-triazole (35) with various aromatic carboxylic acids in presence of \( \text{POCl}_3 \).
Prasad and Reddy reported\textsuperscript{13} the synthesis of 2,6-diaryl-[1,2,4]-triazolo [5,1-b]-1,3,4-thiadiazoles (38) by oxidative cyclisation of N-2-(5-aryl-1,3,4-thiadiazolyl) arylamidines (37) with lead tetraacetate.

(Miss) Q Bano and coworkers\textsuperscript{14} have synthesized 3-aryloxymethyl-6-substituted-1,2,4-triazolo [3,4-b] [1,3,4]-thiadiazoles (41), (43), (44) and 3-aryloxymethyl-1,2,4-triazoles (40) and (42) from 3-aryloxymethyl-4-amino-5-mercapto-1,2,4-triazoles (39).
General Introduction

where, R = 2–CH₃
R = 3–CH₃
R = 4–CH₃
R = 2–Cl
R = 4–Cl
R = 2,4–Cl₂
R = 4–Cl, 3–CH₃
R = H
The 4-amino-3-(2'-benzofuranyl)-5-mercapto-1,2,4-triazole (45) undergoes ring closure with carbon disulphide, acid chlorides, aldehydes, isothiocyanates and chloroacetic acid to give the corresponding s-triazole-fused heterocycles.\(^\text{15}\)

\[\begin{align*}
&\text{(45)} \\
&\text{CS}_2 \quad \text{alc. KOH} \\
&\text{CH}_2\text{O} \\
&\text{CH}_2\text{OH} \\
&\text{(47)} \\
&\text{SOCl}_2 \\
&\text{CH}_2\text{Cl} \\
&\text{(48)} \\
&\text{CS}_2 \quad \text{alc. KOH} \\
&\text{RCOCl} \\
&\text{RCHO} \\
&\text{RNCx} \\
&\text{(49)} \\
&\text{(50)} \quad \text{where, } \text{Ar} = \text{Ph} \\
&\text{(51)} \\
&\text{(52)} \\
&\text{(53)}
\end{align*}\]
B] Brief review of 1,3,4-thiadiazoles/bis-1,3,4-thiadiazoles:

Thiadiazoles are of vital importance as drugs. These ring systems have been successfully incorporated in commercial drugs and pesticides in past and still offers chances to various new types to increase their activities.

Thiadiazoles are the five membered ring system in which two nitrogen and one sulphur atom are present. They can also be called as diaza derivatives of thiophene, in which two –CH= groupings have been replaced by –N=. This heterocycle has four isomeric structures (54-57) as given below.

1,3,4-Thiadiazoles constitute a potentially useful class of organic compound for pharmaceutical applications as it possesses a diverse range of physiological activities.\(^\text{16-22}\) 2-Substituted amino-5-isonicotinyl-1,2,4-thiadiazole (58) is shown to exhibit plant growth promoting activity.\(^\text{23}\)

Budianu, Rusu and Nistor\(^\text{24}\) have synthesized 2-(benzilinidazoyl-2'-mercapto methyl)-5-arylamino-1,3,4-thiadiazoles (59). These compounds were found to be useful as antitumor agent.
Shvekhgeimer\textsuperscript{25} carried out acid catalysed cyclisation of thiosemicarbazide of benzimidazole (60) to get 2-amino-phenyl-5-benzimidazolyl-1,2,4-thiadiazole (61) in 76-90\% yield.

\[
\begin{align*}
\text{CONHNHCNHR} & \hspace{1cm} \text{Acid} \\
\begin{array}{c}
\text{(60)} \\
\end{array} & \hspace{1cm} \begin{array}{c}
\text{(61)} \\
\end{array}
\end{align*}
\]

Synthesis of 5-(2-mercaptobenzothiazolyl)-2-aminophenyl-1,3,4-thiadiazole (63)\textsuperscript{26} have also been reported from respective thiosemicarbazide (62) by cyclo-condensation with concentrated H\textsubscript{2}SO\textsubscript{4}.

\[
\begin{align*}
\text{SCHCNHNHCNHR} & \hspace{1cm} \text{Conc. H\textsubscript{2}SO\textsubscript{4}} \\
\begin{array}{c}
\text{(62)} \\
\end{array} & \hspace{1cm} \begin{array}{c}
\text{(63)} \\
\end{array}
\end{align*}
\]

where, R : (Ph, C\textsubscript{10}H\textsubscript{6})

Samuel and coworkers\textsuperscript{27} have synthesized 2-amino-1,3,4-thiadiazol-5-yl-methyl-1-benzimidazole (64), which was found to be active against \textit{S. aureus}, \textit{E. coli} and \textit{C. albicans}.

\[
\begin{align*}
\text{CH\textsubscript{2}CNHNHCNHR} & \hspace{1cm} \text{Conc. H\textsubscript{2}SO\textsubscript{4}} \\
\begin{array}{c}
\text{(64)} \\
\end{array}
\end{align*}
\]

Wei et al\textsuperscript{28} have reported the synthesis of benzotriazolyl derivative of thiadiazole (65) by reacting corresponding thiosemicarbazide with sulphuric acid.
A novel 1,3,4-thiadiazole derivatives of morpholinoquinoxaline (66) were prepared from ethyl-2-chloroquinoxaline-3-carboxylate in four steps and were tested for bacteriocidal activity.\textsuperscript{29}

Mcguinness, Minattele and coworkers\textsuperscript{30} have reported the synthesis of N,N'-dimethyl-N-[5-(2-pyridinylmethyl)-thio-1,3,4-thiadiazole] (67) as herbicide and desicants of cotton plant.

Preparation of 2,5-dipyridyl-1,3,4-thiadiazoles as pesticide\textsuperscript{31} have been reported from series of reactions. Nicotinic acid hydrazides (68) were reacted with pyridine-3-carboxaldehyde in ethanol containing acetic acid to give R–CO–NH–N=CH–R (69). This was then refluxed for 8 hrs in toluene containing sulphuryl chloride and the product (70) stirred for 30 minutes with Et\(_3\)N to give R–C(Cl)=N–N=CH–R. The latter was stirred for 2 hrs in H\(_2\)S saturated, aq. KOH to obtain in compound (71).
Abdel-Motti and coworkers\textsuperscript{32} have synthesized thio-pyridine derivative of 1,3,4-thiadiazole (72) as antibacterial agent.

Substituted thio-semicarbazones of aromatic aldehyde (73) were subjected to self cyclisation with \( \text{SO}_2\text{Cl}_2 \) at 40\(^\circ\)C to obtain the 2-substituted amino-1,3,4-thiadiazoles (74).\textsuperscript{33}
Thiosemicarbazide of the type (75) was cyclized by heating with concentrated sulphuric acid to obtain 2-aminophenyl-5-p-nitroaryl ethyl-1,3,4-thiadiazole (76).\(^{34}\)

Okawara\(^{35}\) intramolecularly cyclized 1-acyl bithiourea derivative (77) with 4-CH\(_3\)-C\(_6\)H\(_4\)-SO\(_2\)Cl in presence of triethylamine to afford the thiadiazole (78) while cyclization of (77) with methyl iodide in the absence of any base yielded 3-methylthio-1,3,4-triazole (79) and 2-amino-1,3,4-thiadiazoline (80).
Sridevi et al. have prepared series of 2-amino-5-aryl-1,3,4-thiadiazoles (82) by usual cyclization of substituted thiosemicarbazides (81) with sulphuric acid.

A new route for synthesising 1,3,4-thiadiazoles has been reported by Glotova and coworkers. They reacted 2-acyl-1-bromoacetylene (83) with thiobenzohydrazide (84) at 30°C to 10°C in diethylether, methylcyanide or methanol but preferably in triethylamine to get the thiadiazole (85).
Recently Dabhi et al\textsuperscript{38} reported to have synthesized 2-mercapto-5-(3-arylamino sulphophenyl)-1,3,4-thiadiazole (87) by condensation of 3-(arylamino sulfoo)-benzohydrazide (86) with CS\textsubscript{2}.

\[
\text{CONHNH}_2 \xrightarrow{\text{CS}_2} \text{S}\text{H}
\]

2-Substituted amino-5-(2,5-dihydroxyphenyl)-1,3,4-thiadiazoles (89) were prepared as potential antimicrobial agent by Chabban and El-Khawas\textsuperscript{39} by oxidising the hydroquinone derivative (88) to benzoquinone.

A novel aminothiadiazoles (91) useful antidibetics\textsuperscript{40} were prepared from thiosemicarbazides (90) by treating them with conc. H\textsubscript{2}SO\textsubscript{4}.

Fernandes et al\textsuperscript{41} reported to have synthesized 4-(3-methoxy pyrazo-5-yl)-thiosemicarbazide (92) which on cyclization gave respective thiadiazole (93).
2-[[1’-(3,5-disubstituted pyrazolyl)-methyl]-5-phenylamino-1,3,4-thiadiazoles (94) have been reported recently as potential therapeutic agent.\(^{42}\)

Action of phosphoric acid on 1-(3'-arylpyrazolyl)-thiosemicarbazide (95) afforded 2-(3'-arylpyrazol-5-yl)-5-amino-1,3,4-thiadiazole\(^{43}\) (96).

Action of carbondisulphide on 1-(3'-arylpyrazolyl)-thiosemicarbazides (97) gave 2-(3'-arylpyrazol-5-yl)-5-mercapto-1,3,4-thiadiazoles\(^{43}\) (98).
Shah and coworkers\cite{14} have synthesized 2-amino-1,3,4-thiadiazole (99) by self-cycloaddition of 1-aroyl thiosemicarbazide in presence of sulphuric acid.

\[
2 \text{ R'CONNHCSNHR} \xrightarrow{\text{H}_2\text{SO}_4} \text{RNH}_2 \text{S} \text{R'}
\]

Treatment of aldehyde with sulphur and hydrazine hydrate in the ratio 1:2:3 respectively under Willgerodt conditions afforded 2,5-disubstituted-1,3,4-thiadiazoles (100) by Mazzane et al.\cite{15}

\[
\text{R - C - H} + \text{S} + \text{N}_2\text{H}_4 \xrightarrow{} \text{R'S} \text{R}
\]

Umarov et al\cite{16} reported a simple synthesis of 1,3,4-thiadiazole (101) derivative from 2-amino-5-ethyl-1,3,4-thiadiazoles and salicylaldehyde and acetone in a 1:1:1 ratio in ethanol.
Yongiion et al\textsuperscript{41} synthesized 2,5-dimercapto-1,3,4-thiadiazole (102) by refluxing hydrazine hydrate sulfate with carbon disulphide and KOH.

\[
\text{CS}_2 + \text{H}_2\text{NNH}_2\text{H}_2\text{SO}_4 \xrightarrow{\text{KOH}} \begin{array}{c}
\text{N} \\
\text{S}
\end{array} \begin{array}{c}
\text{N} \\
\text{S}
\end{array} \begin{array}{c}
\text{S} \\
\text{H}
\end{array} \begin{array}{c}
\text{S} \\
\text{H}
\end{array}
\]

(102)

Oteleanu and Zuchi\textsuperscript{48} synthesized 2-aryl/alkyl-5-(4-ethoxy benzylidene)-amino-1,3,4-thiadiazoles (104) from 2-amino-4-aryl/alkyl-1,3,4-thiadiazoles (103) with p-ethoxy-benzaldehyde.

\[
\text{N} \\
\text{N}
\]

(103)

\[
\text{OHC} \longrightarrow \begin{array}{c}
\text{N} \\
\text{S}
\end{array} \begin{array}{c}
\text{N} \\
\text{S}
\end{array} \begin{array}{c}
\text{R} \\
\text{EtO}
\end{array}
\]

(104)

Reaction of N-phenylthioformohydrazide (Ph.NHNHC\textsubscript{2}H\textsubscript{4}) with carbonyl compounds such as aliphatic, aromatic and heterocyclic aldehydes and a ketone in presence of trimethyl silyl chloride proceeded easily to afford the corresponding 1,3,4-thiadiazole\textsuperscript{49} (105).

\[
\begin{array}{c}
\text{R}^1 \\
\text{S}
\end{array} \begin{array}{c}
\text{N} \\
\text{N}
\end{array} \begin{array}{c}
\text{Ph} \\
\text{R}^2
\end{array}
\]

(105)

Xicun Wang and coworkers\textsuperscript{50} reported the synthesis of 2-(4-bromo benzoylamino)-5-aryloxymethyl-1,3,4-thiadiazoles (107) by intramolecular dehydrative cyclization of 1-aryloxyacetyl-4-(4-bromobenzoyl)-thiosemicarbazides (106) with excess glacial acetic acid.
Brief review of bis-1,2,4-triazoles/1,2,4-triazoles:

1,2,4-Triazoles (108a, 108b) may be looked on as cyclic amidrazones. Indeed amidrazones and in particular, their acyl derivatives have been convenient starting points for the synthesis of 1,2,4-triazoles and much of the earlier work is discussed in reviews by Potts and Boyer.

The main application of amidrazones to the synthesis of triazoles is to give triazoles with varying substitution patterns.

Monosubstituted triazoles have been synthesized in the following way. A series of 3-alkyl-1,2,4-1H-triazoles (109) have also been prepared by
the cyclization of other N-formylamidrazones or by the reaction of the amidrazones with N'-acylamidrazones,

\[
R - C\equiv \text{NNHCHO} \xrightarrow{\Delta} R - C\equiv \text{NNH}_2
\]

(109)

Disubstituted triazoles (111) formed spontaneously or under mild conditions of heating from N'-acylamidrazones.

\[
R - C\equiv \text{NNH}_2\text{Cl} + \text{HCOC}_2\text{H}_5 \rightarrow R - C\equiv \text{NNHCOR}'
\]

(109)

Trisubstituted triazoles: Amidrazones of the type (R" = CONH$_2$, COOC$_2$H$_5$ or COR") have also formed feasible pathway to 3,4,5-trisubstituted triazoles.

\[
R - C\equiv \text{NNHR}'' R - C\equiv \text{NNHCOOC}_2\text{H}_5 \rightarrow R - C\equiv \text{NNHCOOC}_2\text{H}_5
\]

(112) (113) (114)

Bladin obtained two products from the action of excess benzaldehyde with an alcoholic solution of N'-phenylcyanoformamidrazones, namely a Schiff base (115) and a triazole (116). Later he showed that the Schiff base was readily oxidized to the triazole, e.g. by ferric chloride.
Newlands also found that N'-arylmandelamidrazones condensed with a series of aldehydes (aromatic or heterocyclic) to give 1,2,4-triazoles directly. The corresponding benzoylformamidrazone, however, gave a stable Schiff base (117) which required ferric chloride to convert it into the triazole. Newlands suggested that the isolation of the Schiff bases (115) and (117) could be accounted for by the enhanced stability arising through conjugation of the NC or \( C_6H_5CO \) group with the amidrazone grouping.

N3-Substituted arylamidrazones also reacted with aryl aldehydes to give Schiff bases, readily oxidizable by yellow mercury oxide to the corresponding 1,2,4-4H-triazoles.

\[
\begin{align*}
\text{NCC} & \overset{\text{NNHC}_6\text{H}_5}{\text{NH}_2} + \text{C}_6\text{H}_5\text{CHO} \rightarrow \text{NCC} \overset{\text{NNHC}_6\text{H}_5}{N = \text{CHC}_6\text{H}_5} + \text{NC} \overset{\text{N} = \text{CHC}_6\text{H}_5}{\text{C}_6\text{H}_5} \\
(118) & \quad (119)
\end{align*}
\]

\[
\begin{align*}
\text{C}_6\text{H}_5\text{CH(OH)}\overset{\text{NNHC}_6\text{H}_5}{\text{NH}_2} + \text{ArCHO} & \rightarrow \text{C}_6\text{H}_5\text{CH(OH)} \overset{\text{N} = \text{C}_6\text{H}_5}{\text{Ar}} \\
(120)
\end{align*}
\]

\[
\begin{align*}
\text{C}_6\text{H}_5(\text{C}=\text{O})\overset{\text{NNHC}_6\text{H}_5}{\text{NH}_2} + \text{ArCHO} & \rightarrow \text{C}_6\text{H}_5(\text{C}=\text{O}) \overset{\text{NNHC}_6\text{H}_5}{N=\text{CHAr}} \\
(121)
\end{align*}
\]

Kudari and Lagati obtained the acylhydrazones (123) from the treatment of sebacic acid dihydrazide (122) with various aromatic aldehydes, on oxidative cyclization with ferric chloride yields 1,8-bis-(1,3,4-oxadiazol-2-yl) octanes (124) which are converted into 1,8-bis-(4-amino-1,2,4-triazol-3-yl) octanes (125) with hydrazine hydrate.
Kudari and Badigar\textsuperscript{70} synthesized bis-1,2,4-triazole, 1,8-bis-(5-aroloxysubstituted-1,3,4-oxadiazol-2-yl)-octane (126) by the reaction with sebacic acid dihydrazide and various substituted aroloxysubstituted 4-amino-1,2,4-triazol-3-yl)-octanes (127a) and their derivatives (127b) have been obtained by the reaction of 1,8-bis-(5-aroloxysubstituted-1,3,4-oxadiazol-2-yl)-octane (126) and hydrazine hydrate/phenyl hydrazine.
\[
\begin{align*}
H_2C_2OOC-(CH_2)_8 COOC_2H_5 \\
\quad \xrightarrow{H_2N-\text{NH}_2} \\
H_2N-\text{NH}-OC-(CH_2)_7 CO - \text{NH} - \text{NH}_2 \\
\quad \xrightarrow{\text{R-OCH}_2\text{COOH/POCl}_3} \\
\quad \xrightarrow{\text{PhNHNH}_2} \\
\text{ROH}_2C-\overset{\text{O-CH}_2\text{OR}}{\text{O}}-(CH_2)_7 \overset{\text{CH}_2\text{OR}}{\text{CH}_2\text{OR}} \text{(126)}
\end{align*}
\]

\[
\begin{align*}
\text{(127a)} \\
\text{(127b)}
\end{align*}
\]

\(\alpha,\omega, \text{Bis (1,2,4-triazolyl-3)-alkanes}^{71} \text{(128)}\) have been prepared via the following reaction sequence.

\[
2 \text{ArC} \overset{\text{NNH}_2}{\xrightarrow{\text{NHBr}}} + \overset{\text{O}}{\text{Cl}} \overset{\text{O}}{\text{C-(CH}_2)_n \text{C-Cl}} \xrightarrow{\text{Ar}} \text{Ar}
\]

where, \(n = 0-8\)

Fused heterocyclic systems based on triazoles \(\text{(129)}\) have also been reported.\(^{72}\)
Katritzky and coworkers\textsuperscript{73} synthesized 1,2,3-triazoles (133a) and (133b) from benzyl azide (130a) with carbamoyl substituted propiolates (131a) or (131b). Thus, microwave reaction of benzyl azide (130a) with bis-carbamoyl propiolates (132a-d) gave the corresponding bis-triazoles (134a'), (134a''), 134b), (134c), (134d).
Katritzky and coworkers$^{73}$ have reported 1,2,3-triazoles (136a,b) and bis-triazoles (137a,b) from 3-(azidomethyl)-3-methyloxctane carbamoyl propiolates (131a) or (131b) and bis-carbamoyl propiolates (132a) or (132d).

Microwave reaction of diazide (130b) with carbamoylpropiolates (131a) or (131b) resulted into the formation of azido-triazoles$^{73}$ (138a) and (138a') or (138b) and (138b'). Similarly bis-triazoles (139a) and (139b) were obtained from the reaction of diazide (130b) with 2 equiv of ethyl 4-amino-4-oxo-2-butynoate (131a) in toluene or ethyl 4-oxo-4-(4-toluidino)-2-butynoate (131b) in toluene.
Benzyl azide (130a) with N-propioloylbenzo triazole in acetone gave benzotriazolylcarbamoyl substituted 1,2,3-triazole (140) further treatment of (140) with amines such as morpholine, p-chloroaniline, phenethyl amine or benzylamine in dichloromethane give the corresponding C-carbamoyl 1,2,3-triazoles\textsuperscript{73} (141a-d).
**General Introduction**

(i) acetone, reflux  
(ii) toluene, microwave  
(iii) amine, CH$_2$Cl$_2$

Adamantylation of the 3,4-diaryl-substituted-1,2,4-triazoles (144a-d) and benzimidazolium salt (145a-c) and (146).

Bis oxadiazoles (147a,b) with amines (a) gave 3,3-bridged bis-1,2,4-triazoles (148a,b). Further quaternization of bis-triazoles (148) by alkyl halogenides in acetic acid afforded 3,3-bridged triazolium salts (149a-d).
Reagents: a, R NH₂/ trifluoroacetic acid, o-dichlorobenzene, b, R,W / AcOH
Where,
147a : x = p-C₆H₄; 147b : x = m-C₆H₄; 147c : x = (CH₂)₄
148a : R = Ph, x = p-C₆H₄; 148b : R = Ph, x = m-C₆H₄; 148c : R = p-BrC₆H₄, x = (CH₂)₄
149a : R = Ph, R₁ = 1-Ad, x = m-C₆H₄; 149b : R = Ph, R₁ = 1-Ad, x = m-C₆H₄; 149c : R = Ph, R₁ = t-Bu, x = p-C₆H₄; 149d : R = p-BrC₆H₄, R₁ = 1-Ad, x = (CH₂)₄

Bis-triazoles (150a,b) were obtained by the ring transformation of 2-phenyl-1,3,4-oxadiazole (143) with p-phenylene diamine hydrochloride in presence of trifluoroacetic acid in o-dichlorobenzene, in turn 9a,b were quaternized with 1-bromo-adamatane to afford the 4,4-bridged-bis-triazolium salts⁷⁴ (151a,b).

![Chemical Structures]

Reagents: a, H₂N x NH₂, H⁺, o-dichlorobenzene, b, R Hal, AcOH
Where,
150a : x = p-C₆H₄; 150b : x = m-C₆H₄; 151a : R = 1-Ad, x = p-C₆H₄; 151b : R = 1-Ad, x = m-C₆H₄; 151c : R = t-Bu, x = p-C₆H₄; 151a-c : w = Br, ClO₄⁻.

Alkylation of triazole (143a) with 2,2-dichlorodiethyl ether or 1-bromo-4-chlorobutane produced the monohalogenalkyl-triazolium salts (153a,b) which further alkylated second molecules of triazoles (143a) to form bis-salts⁷⁴ (153a-b).

Where,
152a, 153a : R = C₆H₅, R₁ = p-BrC₆H₄, x = (CH₂)₄; 152b = R = R₁ = C₆H₅, x = (CH₂)₂O(CH₂)₂; 153a, 153b : w = ClO₄⁻; 152b, R = R₁ = C₆H₅, R₂ = (CH₂)₂O(CH₂)₂Cl.
The synthesis of one such precursor was carried out in two stages\textsuperscript{74}. First, 3-phenyl-4-(2-hydroxyphenyl)-1,2,4-triazole (154) was prepared by the ring transformation of 2-phenyl-1,3,4-oxadiazole (143a) with o-amino-phenole in o-dichlorobenzene solution and second, 1-(1-adamantyl)-3-phenyl-4-(2-hydroxyphenyl)-1,2,4-triazolium bromide (155) ($x = \text{Br, ClO}_4^-$) was prepared by the quaternization of triazole (154) with 1-bromoadamantane in acetic acid.

\[
\begin{align*}
\text{Ph} & \quad \text{N} \quad \text{O} \quad \text{N} \\
\text{H} & \quad \text{N} \quad \text{O} \\
\text{H} & \quad \text{N} \quad \text{O} \\
\end{align*}
\]

Iqal et al\textsuperscript{75} gave new route for 1,2,4-triazole by intramolecular cyclization of the three isomeric 1,4-disubstituted thiosemicarbazides in aqueous NaOH which afforded 2,4-dihydro-4-(benzyl)-5-(isomeric pyridyl)-3H-1,2,4-triazole-3-thiones (156).

\[
\begin{align*}
\text{Ph} & \quad \text{CH}_2 - \text{NCS} \\
\text{N} & \quad \text{C} - \text{NHNH}_2 \\
\text{N} & \quad \text{C} - \text{NH} - \text{NH} - \text{C} - \text{NH} - \text{CH}_2 - \text{Ph} \\
\end{align*}
\]
Sing synthesized and studied the activity of certain 1,2,4-triazoles (157).

Cyclocondensation reaction of 1-(3-aryl-1H-5-pyrazol-5-yl)-4-substituted thiosemicarbazides with 2N KOH solution yielded s-triazoles while with hot anhydrous ortho-phosphoric acid gave 2-(3-aryl-1H-pyrazol-5-yl)-5-amino-1,3,4-thiadiazoles. Oxidative cyclization of same thiosemicarbazides with
L₂/KI in alkaline condition afforded 1,3,4-oxadiazoles. Some of the thiosemicarbazides on reaction with CS₂/DMF under reflux resulted in the formation of 5-(3-aryl-1H-pyrazol-5-yl)-2-mercapto-1,3,4-thiadiazoles. Similarly, triazoles with α-chloroacetic acid in presence of fused sodium acetate yielded thiazolo-s-triazolones.⁷⁷

\[
\text{HET-CO-NHNH₂} \xrightarrow{\text{KNCS or R₂NCS}} \text{HET-CO-NHNH-CS-NH-R₄}
\]

\[
\begin{align*}
\text{HET-} & \begin{array}{c}
\text{N} \\
\text{N} \\
\text{SH} \\
\text{R₄}
\end{array} \\
\text{HET} & \begin{array}{c}
\text{N} \\
\text{S} \\
\text{NHR₄} \\
\text{N}
\end{array} \\
\text{HET} & \begin{array}{c}
\text{O} \\
\text{NHR₄} \\
\text{N}
\end{array} \\
\text{HET} & \begin{array}{c}
\text{S} \\
\text{SH}
\end{array}
\end{align*}
\]

(160) (161) (162) (163)

The reactions of 3-(3-aryl-1H-pyrazol-5-yl)-4-amino-5-mercapto-s-triazoles with various reagents like monochloroacetic acid, benzoin, carbon...
disulphide and phenacyl bromide have yielded various fused heterocyclic compounds.  

\[
\text{HET-CO-NHNH}_2
\]  

(166)

\[
\text{i) CS}_2/\text{KOH}
\]

\[
\text{ii) NH}_2\text{-NH}_2\text{H}_2\text{O}
\]

\[
\text{CICH}_2\text{COOH}
\]

(168)

\[
\text{K}_2\text{CO}_3
\]

(167)

\[
\text{PhCOCH}_2\text{Br}
\]

(169)

\[
\text{Benzoin KOH}
\]

(170)

\[
\text{K}_2\text{CO}_3/\text{Br}_2/\text{AcOH}/\text{AcONa}
\]

(171)

Chang-Huchu and coworkers have synthesized several \(\text{w-c-5-aryl-1,2,4-triazol-3-thio)}-\text{w-(1H-1,2,4-triazol-1-yl) acetophenones. These compounds exhibited some antifungal and plant growth regulatory activities.}

\[
\text{Ar-CNHNH}_2
\]

(172)

(173)

(174)
Pengfei et al. have synthesized 1,2,4-triazole and 1,3,4-thiadiazole derivatives of 6-nitrobenzimidazole.
Kido et al. have found out a new route for synthesis of 1,2,4-triazoles (184).

\[(\text{Me})_2N-C-\overset{\text{O}}{\text{OEt}} \xrightarrow{\text{NH}_2\text{NH}_2\text{H}_2\text{O, EtOH}} (\text{Me})_2N-C-\text{NHNH}_2\]
D] Brief review of 1,2,4,5-Dithiadiazines:

Smiths and coworkers\(^8\) reported the synthesis of 3,6-bis-(4-methoxyphenyl)-1,4,2,5-dithiadiazine (185) from aminosulfines (thiosamide-5-oxides) and triethyloxonium tetrafluoroborate.

\[
\text{OCH}_3
\]

\[\text{Nielsen and Alexander}^{83}\] gave the synthesis of 2,3-bis-(4-methylphenyl)-5,5,6,6-tetrachloro-2,3,5,6-tetrahydro-1,4,2,3-dithiadiazine (187) by mixing N-(4-methyl phenyl)-trichloromethane sulfenamide (186) with base.

\[\text{2,3-bis-(4-methylphenyl)-5,5,6,6-tetrachloro-2,3,5,6-tetrahydro-1,4,2,3-dithiadiazine}\]

Barton et al\(^84\) oxidised thiocarbohydrazides to gave corresponding disulphides (188). Oxidation of disulphide with potassium ferrocyanide produced the dithiadiazine (189).
Yonemoto and Shibuya\textsuperscript{85} studied the ring expansion of heterocyclic cations by interaction of nitrogen atom.

\begin{center}
\begin{tikzpicture}
\node [align=center] at (0,0) {\begin{tabular}{c}
\begin{minipage}{0.4\textwidth}
\begin{equation}
\text{Ar} \quad \text{S-S} \quad \text{S-S} \quad \text{Ar}
\end{equation}
\end{minipage}
\begin{minipage}{0.4\textwidth}
\end{minipage}
\end{tabular}\end{tikzpicture}
\end{center}

\begin{equation}
\text{PhN=N} \quad \text{N—N} \quad \text{Ph}
\end{equation}

\begin{equation}
\text{3,4-dihydro-3,4,6-triphenyl-3-phenylazo-1,2,4,5-dithiadiazine}
\end{equation}

\begin{center}
\begin{tikzpicture}
\node [align=center] at (0,0) {\begin{tabular}{c}
\begin{minipage}{0.5\textwidth}
\begin{equation}
\text{N,S} + \text{PhC} \equiv \text{CPh}
\end{equation}
\end{minipage}
\end{tabular}\end{tikzpicture}
\end{center}

\begin{equation}
\text{3,5-diphenyl-1,4,2,6-dithiadiazine}
\end{equation}

Stephen and coworkers\textsuperscript{86} gave new route for the formation of 3,5-diphenyl-1,4,2,6-dithiadiazine (191) by the interaction of tetrasulphur tetranitride with phenylacetylene in boiling toluene.

\begin{equation}
\text{N}_2\text{S}_4 + \text{PhC} \equiv \text{CPh}
\end{equation}

Yonemoto et al\textsuperscript{87} synthesized 3-diethylamino-6-phenyl-1,2,4,5-dithiadiazine (193) by the reaction of 5-diethylamino-3-phenyl-1,4,2-dithiazolium perchlorate (192), iodine and aqueous ammonia in MeCN. This is an oxidation process.

\begin{equation}
\text{ClO}_4 + \text{Et}_2\text{N-S-S-N-S-S-Et}_2\text{N}
\end{equation}

\begin{equation}
\text{+ I}_2 + \text{NH}_3 \quad \text{MeCN}
\end{equation}

\begin{equation}
\text{3-diethylamino-6-phenyl-1,2,4,5-dithiadiazine}
\end{equation}
Tashiro and Mataka\textsuperscript{88} reported the synthesis of 1,3,2,4-dithiadiazine (195) from benzoin hydrazide (194) and tetrasulphur tetranitride.

\[
\begin{align*}
\text{Ph} - 
\text{C} = 
\text{NNH}_2 + \text{N}_4\text{S}_4 & \rightarrow \text{Ph} \quad \text{Ph} \quad \text{Ph} \\
\text{Ph} - 
\text{C} = 
\text{NNH}_2
\end{align*}
\]

(194)  
5,6-diphenyl-1,3,2,4-dithiadiazine

Bhaskar and coworkers\textsuperscript{89} have synthesized some \(\gamma\)-picolinoyl-1,2,4,5-dithiadiazines (197) by the reaction of phenylimino chloromethane sulphenyl chloride and 4-aryl/alkyl-1-\(\gamma\)-picolinoyl thiosemicarbazides (196) in boiling chloroform medium.

\[
\begin{align*}
\text{O} & \quad \text{C} - 
\text{NH} - 
\text{NH} - 
\text{C} \quad \text{C} - \text{NHR} + \text{Ph} - \text{N} = \text{C} - \text{Cl} \\
\text{SH} & \quad \text{S} \quad \text{Cl} \\
\quad \text{CHCl}_3 & \rightarrow \ \\
\quad \text{H} & \quad \text{O} \quad \text{N} \quad \text{C} = \text{NR} \\
\quad \text{C} \quad \text{N} & \quad \text{S} \\
\quad \text{C} \quad \text{S} & \quad \text{NPh}
\end{align*}
\]

(196)  

\[
\begin{align*}
\text{O} & \quad \text{N} \quad \text{C} = \text{NR} \\
\text{C} \quad \text{N} & \quad \text{S} \\
\text{C} \quad \text{S} & \quad \text{NPh}
\end{align*}
\]

(197)

where, \( R \) : Phenyl, \( o\)-tolyl, \( m\)-tolyl, \( p\)-tolyl, \( o\)-chlorophenyl, \( p\)-chlorophenyl and \( t\)-butyl.

Deshmukh et al\textsuperscript{90} have reported the synthesis of 3-aryl/alkylimino-6-phenylimino-3,4,5,6-tetrahydro-1,2,4,5-dithiadiazines (199) by the interaction of 4-aryl/alkyl-3-thio semicarbazide (198) and N-phenyl-S-chloro isothiocarbamoyl chloride.
General Introduction

\[
\text{Ph} - \text{N} = \text{C} < \text{Cl} + \text{NHNH}_2 \quad \rightarrow \quad \text{R-N} = \text{C} \quad \left\{ \begin{array}{l}
\text{N} \\ 
\text{C} = \text{S} \\ 
\text{NH} - \text{R}
\end{array} \right.
\]

(198) (199)

where, R : Phenyl, o-tolyl, m-tolyl, p-tolyl, o-chlorophenyl, p-chlorophenyl and t-butyl.

Synthesis of 3,6-diaryl/dialkylimino-3,4,5,6-tetrahydro-1,2,4,5-dithiadiazines (201) by oxidation of 1,6-diaryl/dialkyl-2,5-dithiobiurea (200) with I\(_2\) in ethanol have been reported by Deshmukh\(^9\).

\[
\text{RNH} - \begin{array}{c}
\text{C} - \text{NH} \\
\text{S}
\end{array} + \text{NH} - \begin{array}{c}
\text{C} - \text{NHR} \\
\text{S}
\end{array} \quad \rightarrow \quad \text{I}_2 \quad \text{in ethanol}
\]

(200) (201)

where, R : Phenyl, o-tolyl, m-tolyl, p-tolyl, o-chlorophenyl, p-chlorophenyl and t-butyl.

Formation of 3-ary/alkylimino-6-hydrazino-1,2,4,5-dithiadiazines (203) have also reported by Deshmukh\(^9\) from thiocarbohydrazide (202) and N-aryl/alkyl-S-chloro isothiocarbamoyl chloride.

\[
\text{H}_2\text{N} - \text{HN} - \begin{array}{c}
\text{C} - \text{NH} \\
\text{S}
\end{array} + \text{R} - \text{N} = \text{C} < \text{Cl} \quad \rightarrow \quad \text{H}_2\text{N} - \text{N} = \text{C} \quad \left\{ \begin{array}{l}
\text{N} \\ 
\text{C} = \text{NR}
\end{array} \right.
\]

(202) (203)

where, R : Phenyl, o-tolyl, m-tolyl, p-tolyl, o-chlorophenyl, p-chlorophenyl and t-butyl.

Choudhari\(^9\) has synthesized 3-phenylimino-4-ary/acyl-6-ary/acyl hydrazino-1,2,4,5-dithiadiazines (205) by one step condensation reaction of bis-1,5-ary/acyl-3-thiocarbohydrazides (204) and N-phenyl-S-chloro isothiocarbamoyl chloride.
E] 2,3,5,7,8-Pentaazabicyclo [4.2.1] nona-diens:

Crystal and molecular structure of the monothioketal of 2,4-diphenyl-3-azabicyclo [3.3.1] nonan-9-one have been reported by P. Laavanya et al.92

1H-NMR spectral study of some 4-hydroxy-2,6-diphenyl piperidines and a systematic analysis of 1H chemical shift in some piperidines and 3,7-diazabicyclo [3.3.1] nonane derivatives have been recorded by Pandiarajan and coworkers.93
F] Brief review of 1,2,4-dithiazolidines:

Paranjpe and co-workers\textsuperscript{94} have synthesized 4-aryl-5-phenylimino-3-thio-1,2,4-dithiazolidines (209) by the interaction of N-phenyl-S-chloro isothiocarbamoyl chloride with ammonium salt of aryl dithiocarbamic acid (208).

\[
\text{Ph} - N = \begin{array}{c}
\text{Cl} \\
\text{S} - \text{Cl}
\end{array}
\quad + \quad \begin{array}{c}
\text{HN} - R \\
\text{C} = \text{S}
\end{array}
\xrightarrow{\text{Cold benzene}}
\begin{array}{c}
\text{Ph} - N = \begin{array}{c}
\text{N} \\
\text{C} = \text{S}
\end{array}
\end{array}
\]

(208)  
(209)

Where, \( R \): phenyl, \( p \)-tolyl, \( p \)-chlorophenyl, \( p \)-anisyl, \( o \)-tolyl, \( m \)-tolyl, cyclohexyl, methyl and benzyl

5-Arylimino-3-thio-1,2,4-dithiazolidines (211) and their mercaptobenzyl derivatives 1,2,4-dithiazolidines\textsuperscript{95} (213) were synthesized by reaction of N-aryl-S-chloro isothiocarbamoyl chlorides with ammonium dithiocarbamate (210) and benzyl dithiocarbamate (212) respectively.

\[
\text{R} - N = \begin{array}{c}
\text{Cl} \\
\text{S} - \text{Cl}
\end{array}
\quad + \quad \begin{array}{c}
\text{HN} - \text{H} \\
\text{C} = \text{S}
\end{array}
\xrightarrow{\text{SNH}_4}
\begin{array}{c}
\text{R} - N = \begin{array}{c}
\text{N} \\
\text{C} = \text{S}
\end{array}
\end{array}
\]

(210)  
(211)

\[
\text{R} - N = \begin{array}{c}
\text{Cl} \\
\text{S} - \text{Cl}
\end{array}
\quad + \quad \begin{array}{c}
\text{N} - \text{H} \\
\text{C} - \text{S} - \text{Bz}
\end{array}
\xrightarrow{\text{S} - \text{H}}
\begin{array}{c}
\text{R} - N = \begin{array}{c}
\text{N} \\
\text{C} = \text{S} - \text{Bz}
\end{array}
\end{array}
\]

(212)  
(213)

Where, \( R \): phenyl, \( p \)-chlorophenyl, \( p \)-tolyl
4-Aryl-5-oxo-2-phenylimino-1,3,4-dithiazolidines (215) and 4-aryl-2-phenylimino-5-thio-1,3,4-dithiazolidines (217) have also been synthesized by the reaction of triethylamine salt of aryl thiocarbamic acids (214) and triethylamine salt of aryl dithiocarbamic acids (216) respectively with N-phenyl-S-chloro isothiocarbamoyl chloride.

\[
\begin{align*}
\text{HN} - R & \quad C = O \\
\text{Ph} - N & = C \quad S - C \quad + \quad - \text{SNH} \left( \text{C}_2\text{H}_5 \right)_3
\end{align*}
\]

(214)

\[
\begin{align*}
\text{HN} - R & \quad C = S \\
\text{Ph} - N & = C \quad S - N - R
\end{align*}
\]

(215)

\[
\begin{align*}
\text{HN} - R & \quad C = S \\
\text{Ph} - N & = C \quad S - C \quad + \quad - \text{SNH} \left( \text{C}_2\text{H}_5 \right)_3
\end{align*}
\]

(216)

\[
\begin{align*}
\text{HN} - R & \quad C = S \\
\text{Ph} - N & = C \quad S - N - R
\end{align*}
\]

(217)

Where, R : aryl

Nimdeokar and co-workers have synthesized 4-aryl-5-arylimino-3-phenylimino-1,2,4-dithiazolidines (219) from N-phenyl-S-chloro isothiocarbamoyl chloride and 1,3-diaryl thiocarbamides (218).

\[
\begin{align*}
\text{HN} - R & \quad C = N - R' \\
\text{Ph} - N & = C \quad S - H \quad + \quad - \text{SNH} \left( \text{C}_2\text{H}_5 \right)_3
\end{align*}
\]

(218)

\[
\begin{align*}
\text{R} - N & \quad C = N - R' \\
\text{Ph} - N & = C \quad S - H
\end{align*}
\]

(219)

Where, R and R' : phenyl, p-tolyl, p-chlorophenyl

\[
\begin{align*}
\text{HN} - R & \quad C = N - R' \\
\text{Ph} - N & = C \quad S - H
\end{align*}
\]

(220)
Intermolecular reactions of N-phenyl-S-chloro isothiocarbamoyl chloride have been shown to result in the formation of 1,2,4-dithiazolidines (221) and 1,3,4-dithiazolidines (222).\(^9\)

\[
\begin{array}{c}
\text{aq. EtOH} \\
\text{Ph - N = C \overset{\text{S-Cl}}{\longrightarrow} Ph - N = C = O} \\
\text{1,2,4-dithiazolidine} \\
\text{(221)}
\end{array}
\]

\[
\begin{array}{c}
\text{aq. EtOH} \\
\text{Chloroform} \\
\text{(1:1 v/v)} \\
\text{O = C \overset{\text{S}}{\longrightarrow} C = N - Ph} \quad \text{+} \quad \text{Ph - N = C = O} \\
\text{1,3,4-dithiazolidine} \quad \text{1,2,4-dithiazolidine} \\
\text{(222) (221)}
\end{array}
\]

\[
\begin{array}{c}
\text{aq. EtOH} \\
\text{Chloroform} \\
\text{(1:2 v/v)} \\
\text{O = C \overset{\text{S}}{\longrightarrow} C = N - Ph} \\
\text{1,3,4-dithiazolidine} \\
\text{(222)}
\end{array}
\]

\[
\begin{array}{c}
\text{aq. EtOH} \\
\text{Chloroform} \\
\text{(1:3 v/v)} \\
\text{Ph - N = C = O} \quad \text{Ph - N = C = O} \\
\text{1,2,4-dithiazolidine} \\
\text{(221)}
\end{array}
\]

Intramolecular reaction of N-phenyl-S-chloro isothiocarbamoyl chloride afforded 2-chlorobenzothiazole (223).\(^9\)

\[
\begin{array}{c}
\text{Ph - N = C \overset{\text{S-Cl}}{\longrightarrow} AlCl}_3 \\
\text{Ph - N = C = C - Cl} \\
\text{(223)}
\end{array}
\]
Khandelwal have introduced the new route for the synthesis of 4-aryl-3-\(\alpha\)-butylimino-5-imino-1,2,4-dithiazolidines (225) or 5-\(\alpha\)-imino-3-\(\alpha\)-butyl-1,2,4-dithiazolidines (226) from aryl thiocarbamides (224) and N-\(\alpha\)-butyl-S-chloro isothiocarbamoyl chloride.

\[
\text{TB} - N = C < \text{Cl} S - \text{Cl} + HN - R \quad \xrightarrow{\text{C} = N - H} \quad R \quad N = C = N - \text{TB} \\
(224)
\]

Where, \(R\) : phenyl, \(o\)-tolyl, \(p\)-tolyl, \(o\)-chlorophenyl, \(p\)-chlorophenyl and \(t\)-butyl

\[
\text{OR}
\]

\[
H - N \quad C = N - \text{TB} \\
R - N = C S - S
(226)
\]

Synthesis of 4-aryl-5-\(\alpha\)-arylimino-3-\(\alpha\)-butylimino-1,2,4-dithiazolidines (227) from N-\(\alpha\)-butyl-S-chloro isothiocarbamoyl chloride and 1,3-diaryl thiocarbamides (226) have been reported by Khandelwal.

\[
\text{TB} - N = C < \text{Cl} S - \text{Cl} + HN - R \quad \xrightarrow{\text{C} = N - R} \quad R \quad N = C = N - \text{TB} \\
(226)
\]

Where, \(R\) : phenyl, \(o\)-tolyl, \(p\)-tolyl, \(o\)-chlorophenyl, \(p\)-chlorophenyl and \(t\)-butyl

Berad has reported the formation of 3-tetra-O-acetyl-\(\beta\)-D-glucopyranosylimino-4-aryl-5-phenylimino-1,2,4-dithiazolidines (229) by the reaction of glucosylated thiocarbamides (228) and N-phenyl-S-chloro isothiocarbamoyl chloride.
General Introduction

3-Aryl/alkylimino-4-(4-phenylthiazol-2-yl)-5-phenylimino-1,2,4-dithiazolidines (231) have been prepared by Bhaskar from 1-(4-phenylthiazol-2-yl)-3-aryl/alkyl thiocarbamides (230) and N-phenyl-S-chloro isothiocarbamoyl chloride.

Singh and Verma have synthesized 1,2,4-dithiazolidines (233) by oxidation of 1-aryl-4-S-allyl-2,4-isodithiobiurets (232) with I₂. The 5-aryl-imino-3-imino-1,2,4-dithiazolidine hydroiodides have been isolated.
Singh and co-workers\textsuperscript{103} have synthesized 3,5-diarylimino-1,2,4-dithiazolidines (233) by oxidation of 1,5-diaryl-2-S-allyl-isodithiobiurets (233) with iodine in boiling chloroform as well as by oxidation of 1,5-diaryl-2,4-dithiobiurets (237) with iodine in ethanol.

\[
\begin{align*}
R - N &= C - NH_2 \\
S &+ R' - NCS \\
\text{CH}_2 - \text{CH} &= \text{CH}_2
\end{align*}
\]

\( (234) \)

\[
\begin{align*}
R - N &= C - NH - C - NH - R' \\
S &+ R' - NCS \\
\text{CH}_2 - \text{CH} &= \text{CH}_2
\end{align*}
\]

\( (235) \)

Where, \( R \) and \( R' \): aryl

The 1,5-diaryl-2-S-benzyl-2,4-isodithiobiurets (241) and their oxidation to 3,5-diarylimino-1,2,4-dithiazolidines (242) have been reported by Dixit.\textsuperscript{104}

\[
\begin{align*}
R - NH &= C - NH_2 \\
S &\xrightarrow{\text{BzCl}} R - NH - C - NH . \text{HCl} \\
S &\xrightarrow{\text{R'-NCS}} R - NH - C - NH - R' \\
\text{S} &- \text{Bz}
\end{align*}
\]

\( (238) \)

\[
\begin{align*}
R - NH &= C - NH_2 \\
S &\xrightarrow{\text{BzCl}} R - NH - C - NH . \text{HCl} \\
S &\xrightarrow{\text{R'-NCS}} R - NH - C - NH - R' \\
\text{S} &- \text{Bz}
\end{align*}
\]

\( (239) \)

\[
\begin{align*}
R - NH &= C - NH_2 \\
S &\xrightarrow{\text{BzCl}} R - NH - C - NH . \text{HCl} \\
S &\xrightarrow{\text{R'-NCS}} R - NH - C - NH - R' \\
\text{S} &- \text{Bz}
\end{align*}
\]

\( (240) \)

\[
\begin{align*}
R - N &= C - C = N - R' . \text{HX} \\
\text{S} &\xrightarrow{\text{I}_2 \text{ or Br}_2 \text{C}_2\text{H}_5\text{OH}} R - NH - C - NH - C - NH - R' \\
\text{S} &\xrightarrow{\text{Na}_2\text{S in EtOH}} R - NH - C - NH - C - NH - R'
\end{align*}
\]

\( (242) \)

\( (241) \)

Where, \( R \): aryl
Synthesis of 3,5-diarylimino-1,2,4-dithiazolidines (244) have been achieved by Verma\textsuperscript{105} by oxidation with bromine and iodine.

\[
\begin{align*}
R - NH - C = NH + R' - NCS & \rightarrow R - NH - C = N - C - NH - R' \\
\text{where, } R : \text{aryl} & \\
\end{align*}
\]

\[
\begin{align*}
(242) & \\
(243) & \\
(244) & \\
(245) & \\
(246) & \\
\end{align*}
\]

Joshua\textsuperscript{106} gave one step synthesis of 1,5-disubstituted-2,4-dithiobiurets and their oxidation to 3,5-disubstituted imino-1,2,4-dithiazolidines.

\[
\begin{align*}
R - NH - C - NH_2 + R' - NCS & \rightarrow R - NH - C - NH - C - NH - R' \\
\end{align*}
\]

\[
\begin{align*}
(245) & \\
(246) & \\
\end{align*}
\]
Rai and coworkers\textsuperscript{107} synthesized 3-arylimino-5-(\(\alpha\)-methyl benzylidene hydrazino)-1,2,4-dithiazolidines (247) by the oxidation of 1-aryl-5-(\(\alpha\)-methyl benzylidene hydrazino dithiobiuret (248).

\[ \text{CH}_3\text{C}_6\text{H}_5\overset{\text{C}=\text{N}}{\text{N} \rightarrow \text{C} \rightarrow \text{N} \rightarrow \text{C} \rightarrow \text{NH}_2} \overset{1)}{\text{NaOEt}} \rightarrow \text{CH}_3\text{C}_6\text{H}_5\overset{\text{C}=\text{N}}{\text{N} \rightarrow \text{C} \rightarrow \text{NH}_2} \overset{2)}{\text{C}_6\text{H}_5\text{CH}_2\text{Cl}} \]

(247)

(248)

5-Phenylamino-3-phenylimino-1,2,4-dithiazolidine (249) and 5-aryl/alkylamino-3-imino-1,2,4-dithiazolidines\textsuperscript{108} (250) have been synthesized from 1,5-diphenyl-2,5-benzyliso-2,4-dithiobiuret by oxidation with bromine.

\[ \text{Ph} \rightarrow \text{NH} \rightarrow \text{C} \rightarrow \text{NH} \rightarrow \text{Ph} \overset{\text{Br}_2}{\rightarrow} \text{Ph} \rightarrow \text{NH} \rightarrow \text{C} \rightarrow \text{NH} \rightarrow \text{Ph} + \text{BzBr} + \text{HBr} \]

(249)

\[ \text{Ar} \rightarrow \text{NH} \rightarrow \text{C} \rightarrow \text{NH} \rightarrow \text{C} \rightarrow \text{NH} \overset{\text{Br}_2}{\rightarrow} \text{Ar} \rightarrow \text{NH} \rightarrow \text{C} \rightarrow \text{NH} \rightarrow \text{C} \rightarrow \text{NH} + \text{HBr} + \text{BzBr} \]

(250)

George and coworkers\textsuperscript{109} have concentrated on the preparation of 1,2,4-dithiazolidine. Thus 3-ethyl-1,2,4-dithiazoline-5-one (251) and 1,2,4-dithiazolidine-3,5-dione (252) were prepared and used as sulfuration agent in preparation of thiophosphopetides and phosphorothioate linked DNA and RNA.
Briel and coworkers\textsuperscript{110} synthesized 6,6'-(1,2,4-dithiazolidin-3,5-ylidene)-bis-2,4-cyclohexadien-1-ones as below. The title compounds (253) have been obtained high yield by treating 2-hydroxy-4-alkylthioamide with bromine hydrochloric acid.

\[
\begin{align*}
\text{R} & \quad \text{OH} \\
\text{R} & \quad \text{CSNH} \\
\text{Br}_2 \text{in HCl} & \quad \text{R} \quad \text{O} \\
\text{R} & \quad \text{N} \\
\end{align*}
\]

(253)

Fukami and coworkers\textsuperscript{111} have synthesized 1,2,4-dithiazolidines (254) and used as blank mold controlling agents, useful for walls of bathrooms, coating. Treatment of EtN-(m-tolyl) carbamothioate with chlorocarbonylsulphenyl chloride in MePh at room temperature for 5 hrs gave (254).

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

(254)

Deohate\textsuperscript{112} have introduced the synthesis of 3-(2'-amino) phenylimino-4-aryl/alkyl-5-phenyl-imino-1,2,4-dithiazolidines (256) from aryl/alkyl thiocarbamides (265) and N-phenyl-S-chloro iothiocarbamoyl chloride.
Synthesis of 3-naphthylimino-4-aryl/alkyl-5-phenylimino-1,2,4-dithiazolidines (258) from N-phenyl-S-chloroisothiocarbamoyl chloride and 1-naphthyl-3-aryl/alkyl thiocarbamides (257) have been reported by Deohate.\textsuperscript{112}

Choudhari\textsuperscript{113} have synthesized 3-phenylimino-4-arylidene/alkylidene amino-5-arylidene/alkylidene hydrazino-1,2,4-dithiazolidines (259) by the interaction of N-phenyl-S-chloroisothiocarbamoyl chloride and bis-1,5-arylidene/alkylidene-3-thiocarbohydrazides (260).
Manna et al. have synthesized 5-substituted arylimino-3-(2,4-diethoxyarylício)-1,2,4-dithiazolidines (262) by oxidative debenzylation and cyclization with bromine in chloroform from the corresponding 1-substituted aril-5-(2,4-diethoxyaryl)-2-S-benzyl-iso-2,4-dithiobiurets (261) or by the oxidation of 1-substituted aryl-5-(2,4-dithoxy aryl)-2,4-dithiobiurets (263) obtained from (261) by reductive debenzylation with \( \text{H}_2\text{S/} \text{C}_5\text{H}_5\text{N(Et)}_3\text{N} \).
References


64. J.A. Bladin, Ibid, 125, 183 (1892).


74. Nikolai I. Karotkikh, Oles P. Shvaika, Gennady F., Rayenko, Artyom V. Kiselyov, Arthur V. Knishevisky, Alan H. Cowley, Jamie N. Jones and Charles L.B. Maedon; ARKAT USA, 08 (2005) - Ukraine/1234/1234 abs.


Object of the Present Work

The synthesis and structural chemistry of heterocyclic compounds with special reference to the synthesis of five and six and bicyclic heterocycles containing three heteroatoms is being investigated in the laboratory. It appeared quite interesting to prepare sulphur and nitrogen containing five and six membered and bicyclic compounds by using sebacic acid dihydrazide and thiocarbohydrazide as a starting compounds. It was also appeared interesting to use N-aryl isocyanodichloride for the synthesis of these heterocyclic compounds.

The synthesis of following compounds have been proposed to be carried out by using sebacic acid dihydrazide or thiocarbohydrazide.

1] Bis-1,3,4-thiadiazolo (3,4-c)-1,2,4-triazoles
2] Bis-1,3,4-thiadiazoles
3] Bis-1,2,4-triazoles
4] Bis-1,2,4,5-dithiadiazines
5] 2,3,5,7,8-pentaazabicyclo [4.2.1] nona-dienes
6] 1,3,4-thiadiazoles
7] 1,2,4-dithiazolidines.
Present Work

Part - I : Introduction

It comprises of general introduction, literature survey of the related work carried out earlier on synthesis of bis-1,3,4-thiadiazolo (3,4-c)-1,2,4-triazoles, bis-1,3,4-thiadiazoles, bis-1,2,4-triazoles, bis-1,2,4,5-dithiadiazinanes, 2,3,5,7,8-pentaazabicyclo [4.2.1] nona-dienes, 1,3,4-thiadiazoles and 1,2,4-dithiazolidines.

Part - II :

This part deals with the synthesis and structural studies of five membered bis-heterocyclic compounds viz., 1,3,4-thiadiazolo (3,4-c)-1,2,4-triazoles, 1,3,4-thiadiazoles and 1,2,4-triazoles.

The part has been subdivided into following three chapters.

Chapter - 1 : Synthesis of 1,8-bis-[4-amino/phenylamino-5-aryl/alkyl imino-1,3,4-thiadiazolo (3,4-c)-1,2,4-triazol-5-yl]-octanes.

Chapter - 2 : Synthesis of 1,8-bis-(2-aryl/alkylamino-1,3,4-thiadiazol-5-yl)-octanes.

Chapter - 3 : Synthesis of 1,8-bis-(3-mercapto-4-aryl/alkyl-1,2,4-triazol-5-yl)-octanes.

Part - III :

This part deals with the synthesis and structural studies of six membered and bicyclic heterocyclic compounds viz.; 1,2,4,5-dithiadiazinanes and 2,3,5,7,8-pentaazabicyclo [4.2.1] nona-dienes.

The part has been subdivided into following two chapters.
Chapter - 4 : Synthesis of 1,10-bis-(3-phenylimino-6-aryl/alkylimino-[1,2,4,5]-dithiadiazinan-4-yl)-decane-1,10-diones.

Chapter - 5 : Synthesis of N-(4-phenylimino)-N-(5-aryl-9-thia-2,3,5,7,8-penta-azabicyclo [4.2.1]nona-1(8),6-dien-4-yldiene) amines.

Part - IV :

This part deals with the synthesis and structural studies of five membered heterocyclic compounds viz.; 1,3,4-thiadiazoles and 1,2,4-dithiazolidines.

The part has been subdivided into following two chapters.

Chapter - 6 : Synthesis of 2-(substituted) benzylidene hydrazino-5-arylarnino-1,3,4-thiadiazoles.

Chapter - 7 : Synthesis of 3-phenylimino-4-[2'-(substituted) alkyl/benzylidene amino] phenyl-5-arylimino-1,2,4-dithiazolidines.

Part - V :

This part deals with the antimicrobial activity of the newly synthesized compounds.

The part comprises one chapter.

Chapter - 8 : Antimicrobial activity.

Each chapter is complete within itself and comprises of the sections; Abstract, Introduction, Results and discussion, Experimental and References.
Chapterwise summary of the thesis is as follows.

Chapter - 1 : Synthesis of 1,8-bis-[4-aminophenylamino-5-aryl/alkyl imino-1,3,4-thiadiazolo (3,4-c)-1,2,4-triazol-5-yl]-octanes.

This chapter is related with the synthesis of bis-1,3,4-thiadiazolo (3,4-C)-1,2,4-triazoles (IV) from sebacic acid dihydrazide (I).

The parent compound sebacic acid dihydrazide (I) was prepared by refluxing the mixture of sebacic acid and thionyl chloride for 20 min, followed by addition of hydrazine hydrate. It was transformed into 1,8-bis-(3-mercapto-4-amino/phenyl amino-1,2,4-triazol-5-yl)-octanes (II) by stirring with hydrazine hydrate/phenyl hydrazine and CS₂/KOH. The compound (II) were then reacted with N-aryl/alkyl isocyanodichlorides in boiling chloroform for 3 hr. The evolution of hydrogen chloride gas was clearly noticed. On cooling the reaction mixtures and distilling off chloroform afforded a solid mass, which on trituration with petroleum ether gave granular solids. These were acidic to litmus and on determination of equivalent weights, found to be monohydrochlorides of 1,8-bis-[4-aminophenylamino-5-aryl/alkyl imino-1,3,4-thiadiazolo (3,4-c)-1,2,4-triazol-5-yl]-octanes (III). These on basification with dilute ammonium hydroxide solution afforded free bases (IV).

The compounds (IV) were acylated in 1:2 ratio using acetic anhydride and glacial acetic acid to give 1,8-bis-[4-acetyl-5-aryl/alkyl imino-1,3,4-thiadiazolo (3,4-c)-1,2,4-triazol-5-yl]-octanes (V).

The structures of all these synthesized compounds were assigned on the basis of chemical transformation, elemental analysis, equivalent weight determination and IR, ¹H-NMR and mass spectral data.
Chapter - 2 : Synthesis of 1,8-bis-(2-aryl/alkylamino-1,3,4-thiadiazol-5-yl)-octanes.

This chapter describes the synthesis of some bis-1,2,4-thiadiazoles (IV) from sebacic acid dihydrazide (I).
The parent compound sebacic acid dihydrazide (I) was prepared as described in Chapter-1. It was transformed into bis-(N-aryl/alkyl thiocarbamido) sebacic acid diamides (III) by condensing with different aryl/alkyl isothiocyanates (II) in boiling chloroform medium. To the sebacic acid diamides (III) was placed in ortho-phosphoric acid with constant stirring. The stirring was continued for 30 minutes. On cooling the reaction mixture and pouring in water, when a whitish coloured solids were precipitated. The compounds were found to be non-desulphurisable on boiling with alkaline plumbite solution indicating absence of >C=S group, and identified as 1,8-bis-(2-aryl/alkylamino-1,3,4-thiadiazol-5-yl)-octanes (IV).

The compounds (IV) were benzoylated using benzoyl chloride and 10% NaOH solution to yield benzoyl derivatives (V).

\[ \text{C}_8\text{H}_7\text{COCl} + 10\% \text{NaOH} \]

(1:2)

Where,

\[ R = p\text{-tolyl}, m\text{-tolyl}, o\text{-tolyl}, \text{Phenyl}, m\text{-chloro phenyl}, p\text{-chloro phenyl}, t\text{-Butyl} \]
General Introduction

The structures of all these synthesized compounds were assigned on the basis of chemical transformation, elemental analysis, equivalent weight determination and IR, $^1$H-NMR and mass spectral studies.

Chapter - 3 : Synthesis of 1,8-bis-(3-mercapto-4-aryl/alkyl-1,2,4-triazol-5-yl)-octanes.

This chapter deals with the synthesis of some bis-1,2,4-triazoles (IV) from sebacic acid dihydrazide (I).

The parent compound sebacic acid dihydrazide (I) was prepared as described in Chapter-1. It was transformed into bis-(N-aryl/alkyl thiocarbamido) sebacic acid diamides (III) by condensing with different aryl/alkyl isothiocyanates (II) in boiling chloroform medium. To the sebacic acid diamides (III) were added dropwise 5% aq. KOH with constant stirring. The stirring was continued for 30 minutes. On cooling the reaction mixture and pouring in water, when a whitish coloured solids were precipitated. The compounds were found to be non-desulphurisable on boiling with alkaline plumbite solution indicating absence of >C=S group, and identified as 1,8-bis-(3-mercapto-4-aryl/alkyl-1,2,4-triazol-5-yl)-octanes (IV).

The compounds (IV) were ethylated using ethyl iodide to yield ethyl derivatives (VI).

The structures of all these synthesized compounds were established on the basis of chemical transformation, elemental analysis, equivalent weight determination and IR, $^1$H-NMR and mass spectral studies.
Chapter - 4 : Synthesis of 1,10-bis-(3-phenylimino-6-aryl/alkylimino-[1,2,4,5]-dithiadiazinan-4-yl)-decane-1,10-diones.

This chapter consists of the synthesis of some bis-1,2,4,5-dithiadiazinanes (V) from sebacic acid dihydrazide (I).

The parent compound sebacic acid dihydrazide (I) was prepared by the method described in Chapter-1. It was transformed into bis-(N-aryl/alkyl thiocarbamido) sebacic acid diamides (III) by condensing with different aryl/alkyl isothiocyanates (II) in chloroform medium. The compounds (III) were then reacted with N-phenyl-S-chloro isothiocarbamoyl chloride in boiling chloroform for 3 hr. The evolution of hydrogen chloride gas was clearly noticed. On cooling the reaction mixtures and distilling off chloroform afforded a solid mass, which on
trituration with petroleum ether gave granular solids. These were acidic to litmus and on determination of equivalent weights, found to be monohydrochlorides of 1,10-bis-(3-phenylimino-6-aryl/alkylimino-[1,2,4,5]-dithiadiazinan-4-yl)-decane-1,10-diones (IV). These on basification with dilute ammonium hydroxide solution afforded free bases (V). The compounds (V) were acylated with acetic anhydride in 1:2 ratio using glacial acetic acid as a solvent to afford acetyl derivatives (VI).

The structures of all these synthesized compounds were assigned on the basis of chemical transformation, elemental analysis, equivalent weight determination and IR, $^1$H-NMR and mass spectral data.
Chapter - 5 : Synthesis of N-(4-phenylimino)-N-(5-aryl-9-thia-2,3,5,7,8-pentaazabicyclo [4.2.1] nona-1(8),6-dien-4-yldene) amines.

This chapter is concerned with the synthesis of some pentaazabicyclo [4.2.1] nona-dienes (V) from thiocarbohydrazide (I).

The parent compound thiocarbohydrazide (I) was prepared by refluxing the mixture of carbon disulphide and hydrazine hydrate in H₂O for 1 hr. It was transformed into 1-(N-aryl thioamido)-3-thiocarbohydrazides (II) by condensing with different aryl isothiocyanates in refluxing benzene medium. The 3-thiocarbohydrazides (II) on refluxing alone in ethanolic medium got intramolecularly cyclized into 2-hydrazino-5-arylamino-1,3,4-thiadiazoles (III) with evolution of hydrogen sulphide gas (tested with lead acetate paper). The compounds (III) were also obtained directly by following the interaction of thiocarbohydrazide (I) and aryl isothiocyanates in refluxing ethanol medium. The compounds (III) were then reacted with N-phenyl isocyanodichloride in boiling chloroform for 3.0 hr. The evolution of hydrogen chloride gas was clearly noticed. On cooling the reaction mixtures and distilling off chloroform afforded sticky masses, which on trituration with petroleum ether gave granular solids. These were acidic to litmus and on determination of equivalent weights, found to be monohydrochlorides of N-(4-phenylimino)-N-(5-aryl-9-thia-2,3,5,7,8-pentaazabicyclo [4.2.1] nona-1(8),6-dien-4-yldene) amines (IV). These on basification with dilute ammonium hydroxide solution afforded free bases (V).

The compounds (V) on acylation with acetic anhydride in 1:2 ratio using glacial acetic acid as a solvent afforded 2,3-diacetyl derivatives (VI), on reaction with sodium nitrite in 1:2 ratio in acidic medium afforded 2,3-dinitroso derivatives (VII).

The structures of all these synthesized compounds were established on the basis of chemical transformation, elemental analysis, equivalent weight determination and IR, ¹H-NMR and mass spectral data.
Where, \( R = m\)-tolyl, \( o\)-tolyl, \( p\)-tolyl, Phenyl, \( m\)-chlorophenyl, \( p\)-chlorophenyl

**Chapter - 6 : Synthesis of 2-(substituted) benzylidene hydrazino-5-arylamino-1,3,4-thiadiazoles.**

This chapter is the record of the synthesis of some 1,3,4-thiadiazoles (IV) from thiocarbohydrazide (I)

The parent compound thiocarbohydrazide (I) was preapred by method described in Chapter-5. It was transofrmed into 1-(N-aryl thioamido)-3-thiocarbohydrazides (II) by condensing with different aryl isothiocyanates in refluxing benzene medium. The 3-thiocarbohydrazides (II) were reacted with...
different aromatic aldehydes in benzene medium, followed by intramolecular cyclization of compounds (III) with the evolution of hydrogen sulphide (tested with lead acetate paper) in refluxing ethanol for 4.0 hr. On cooling the reaction mixtures and pouring in water, a granular solids were obtained. These were found to be non-desulphurizable on boiling with alkaline plumbite solution indicating absence of >C=S group and identified as 2-(substituted) benzylidene hydrazino-5-arylamino-1,3,4-thiadiazoles (IV).

The compounds (IV) on bromination with bromine in glacial acetic acid yielded dibromo derivatives (V).

The structures of all these synthesized compounds were established on the basis of chemical transformation, elemental analysis, equivalent weight determination and IR, $^1$H-NMR and mass spectral data.

![Chemical Structures](image)

Where,

- $R = p$-tolyl, $m$-tolyl, $o$-tolyl, Phenyl, $m$-chlorophenyl, $p$-chlorophenyl
- $R' = o$-hydroxyphenyl, Phenyl, $p$-methoxyphenyl
Chapter - 7 : Synthesis of 3-phenylimino-4-[2'--(substituted) alkyl/benzyl-idene amino] phenyl-5-arylimino-1,2,4-dithiazolidines.

This chapter is an account of the synthesis of some 1,2,4-dithiazolidines (IV) from 1-phenyl-3-(2'-'amino) phenyl thiocarbamide (I).

The parent compound 1-phenyl-3-(2'-amino) phenyl thiocarbamide (I) was prepared by refluxing the mixture of o-phenylene diamine and phenyl isothiocyanate in chloroform medium for 2 hr. It was transformed into 1-phenyl-3-[(2'-'(substituted) alkyl/benzyl-idene amino) phenyl thiocarbamides (II) by condensing with different aliphatic and aromatic aldehydes in refluxing chloroform medium. The compounds (II) were then reacted with N-aryl-S-chloro isothiocarbamoyl chloride in boiling chloroform for 3.0 hr. The evolution of hydrogen chloride gas was clearly noticed. On cooling the reaction mixtures and distilling off chloroform afforded sticky masses, which on washing with petroleum ether several times gave granular solids. These were acidic to litmus and on titrimetric analysis identified as monohydrochlorides of 3-phenylimino-4-[2'-(substituted) alkyl/benzyl-idene amino] phenyl-5-arylimino-1,2,4-dithiazolidines (III). These on basification with dilute ammonium hydroxide solution afforded free bases (IV).

The compounds (IV) on bromination with bromine in glacial acetic acid yielded dibromo derivatives (V).

The structures of all these synthesized compounds were established on the basis of chemical transformation, elemental analysis, equivalent weight determination and IR, $^1$H-NMR and mass spectral data.
Chapter - 8 : Antimicrobial activity.

This chapter is an account of the antimicrobial activity of the newly synthesized compounds in Chapter 1 to 7.

These compounds were screened for their antibacterial activity using cup plate diffusion method and their MIC was determined using broth microdilution method. The bacterial organisms used included both gram-positive as well as gram-negative strains like *E. coli*, *S. aureus*, *B. subtilis*, *P. vulgaris* and *Shigella flexneri* and antifungal activity was performed against the fungus *A. niger* using paper-disc diffusion method.