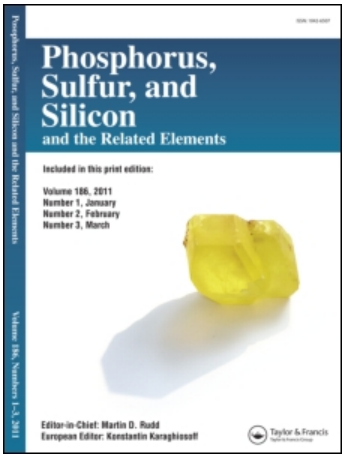

Phosphorus, Sulfur, and Silicon and the Related Elements

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Chemistry of 2,3-Dichloroquinoxalines

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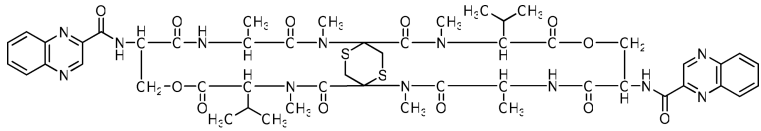
This review describes the synthesis, reactivity, and the utility of 2,3-dichloroquinoxalines as synthetic intermediates for the synthesis of condensed heterocycles with pharmacological interest.

Keywords 2,3-Dichloroquinoxalines condensed quinoxalines; quinoxalines

INTRODUCTION

Quinoxalines are in general comparatively easy to prepare. Numerous derivatives have been synthesized in order to produce biologically active materials. A number of polypeptide antibiotics, such as levomycin,[1] actinoleukin,[2] echinomycin,[3] quinomycin,[4] etc., containing the quinoxaline moiety have been reported. The structure of echinomycin, which was found to be identical to quinomycin A[5] (**1**), is composed of two quinoxaline rings linked by peptide chains.



(1)

In addition, many biologically active quinoxaline derivatives have been reported in the journal and patent literature. For example,

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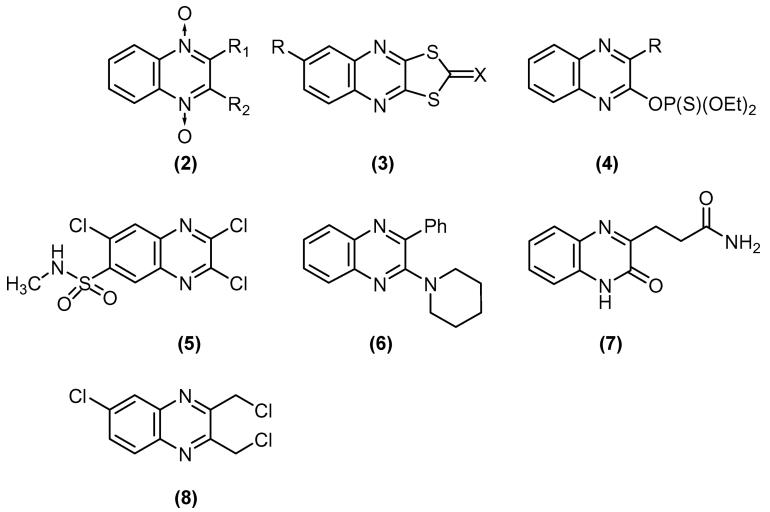
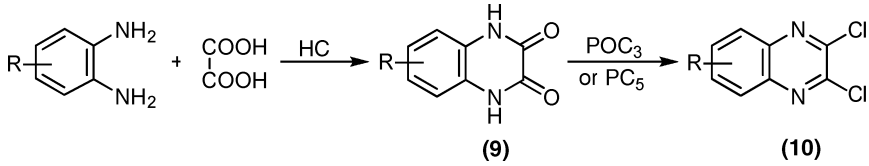
quinoxaline-1,4-dioxide (**2**)[6] has antibacterial activity, while quinoxaline-2,3-dione cyclic dithiocarbamate (**3**)[7] possesses fungicidal and insecticidal effects. The quinoxalinylphosphorothioates (**4**)[8] have been evaluated as insecticidal and anthelmintic agents. Also, 2,3,7-trichloro-6-methyl-sulfamoylquinoxaline (**5**)[9] has been patented as an anticancer agent. 2-Phenyl-3-piperidino-quinoxaline (**6**)[10] is a selective herbicide, while the quinoxalinones (**7**)[1–13] have been shown to possess anti-inflammatory, tranquilizing, and antidepressant properties. 6-Chloro-2,3-bis(chloromethyl)quino-xaline (**8**)[14] has been patented as a foliar fungicide.



There have been several reviews[15–19] dealing with the methods of preparation and chemical reactions for the quinoxaline derivatives, but this review handles the synthesis, reactivity, and the utility of 2,3-dichloroquinoxaline as building blocks for the synthesis of condensed heterocyclic compounds.

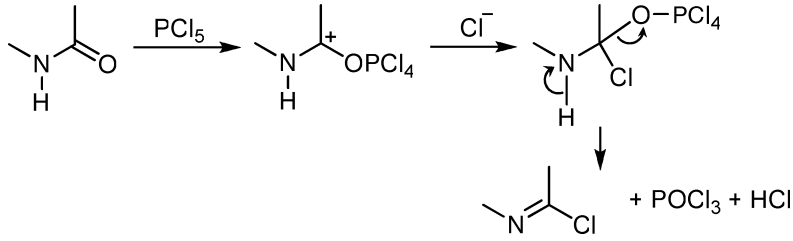
SYNTHESIS OF 2,3-DICHLOROQUINOXALINES

Condensation of *ortho*-phenylenediamines with oxalic acid in 2 *N*-hydrochloric acid produced the 1,2,3,4-tetrahydroquinoxaline-2,3-diones (**9**), which were subjected to chlorination with phosphoryl chloride or phosphorus pentachloride affording 2,3-dichloroquinoxalines (**10**) (Scheme 1).[20–24]

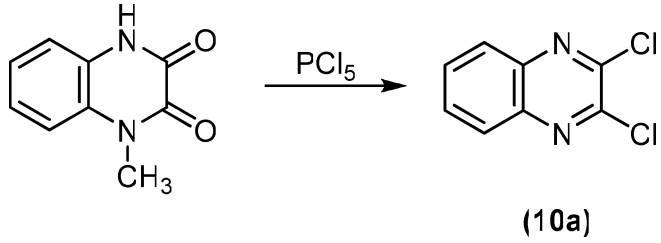


SCHEME 1

A general mechanism for this type of conversion[16] is as follows.



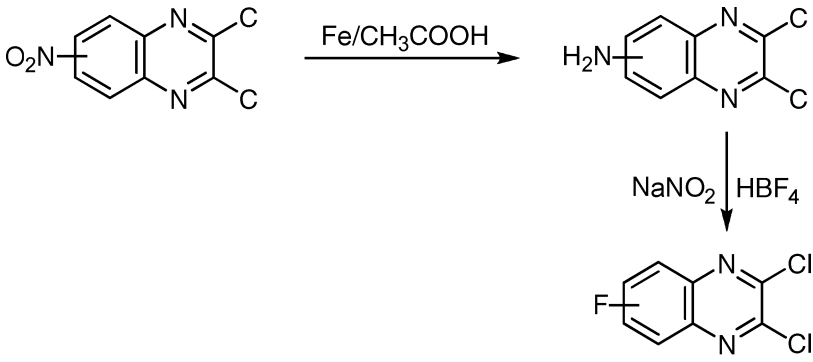
The conversion of CH_3-N-C=O → R–CCl=NR may also be effected in the same way with elimination of methyl chloride. Thus, treatment of 1-methylquinoxalin-2,3-diones with phosphorus pentachloride gives 2,3-dichloroquinoxalne (**10a**) (Scheme 2).[25]



SCHEME 2

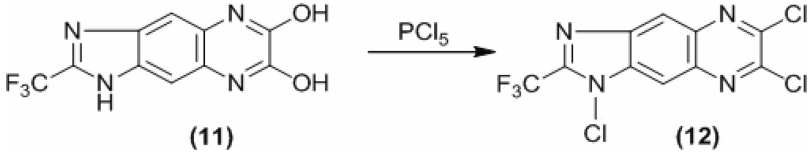
2,3-Dichloroquinoxaline and its 6-substituted derivative (**10**; R in position **6** = H, Cl, COPh, NO_2) were also prepared in high yields from 2,3-dihydroxyquinoxalines by using thionyl chloride in dioxane and dimethylformamide.[26]

Fluoro-2,3-dichloroquinoxalines were prepared from the corresponding amino derivatives. Thus, amino-2,3-dichloro-quinoxaline was prepared by reduction of its nitro derivative with iron powder in acetic acid followed by diazotization of the amino compound in the presence of HBF_4, a reaction that yielded the corresponding fluoro derivative (**10**) (Scheme 3).[27]



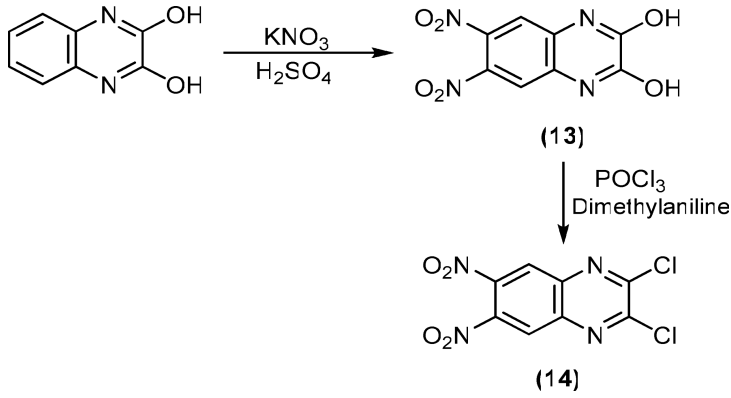
SCHEME 3

7-Trifluoromethyl-2,3,6-trichloroimidazo[4,5-g]quinoxaline (**12**) was prepared through chlorination of the corresponding dihydroxy derivative (**11**) with phosphorus pentachloride (Scheme 4).[27]



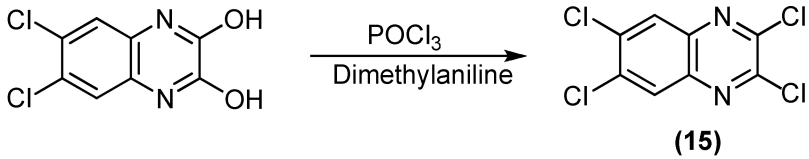
SCHEME 4

2,3-Dihydroxyquinoxaline was nitrated with potassium nitrate to give 6,7-dinitro-2,3-dihydroxyquinoxaline (**13**), which underwent chlorination with phosphoryl chloride and *N*, *N*-dimethylaniline to give 2,3-dichloro-6,7-dinitroquinoxaline (**14**) (Scheme 5).[22]



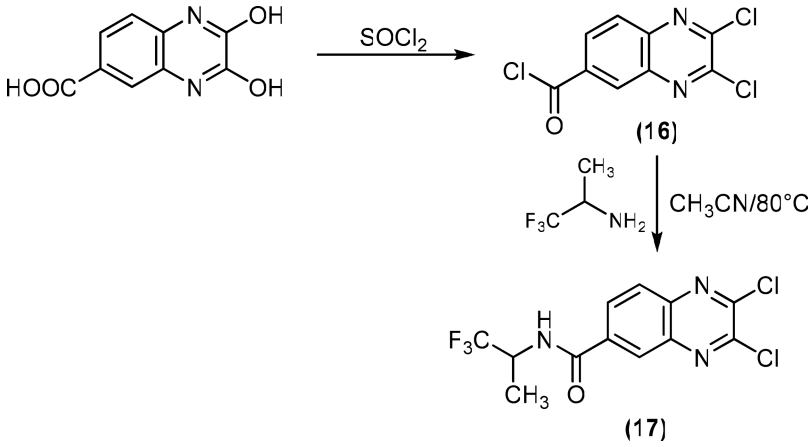
SCHEME 5

Also, 2,3,6,7-tetrachloroquinoxaline **15**was prepared via the interaction of 2,3-dihydroxy-6,7-dichloroquinoxaline with phosphoryl chloride and *N*, *N*-dimethylaniline (Scheme 6).[22]



SCHEME 6

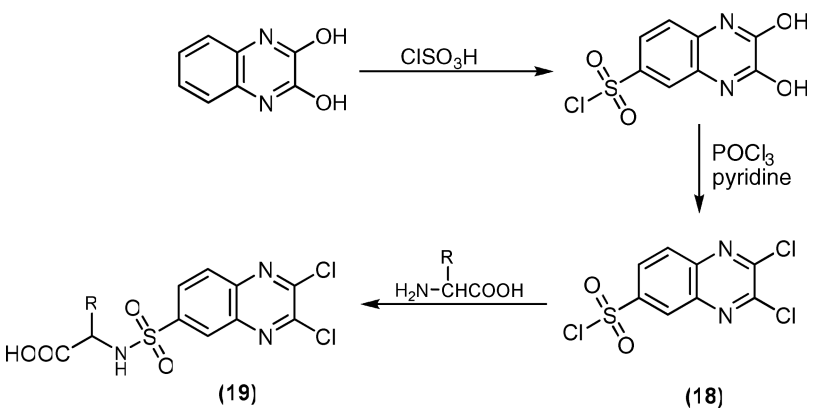
2,3-Dichloroquinoxaline-6-carbonyl chloride (**16**) was synthesized through interaction of 2,3-dihydroxy-6-carboxylic acid with thionyl chloride.[28,29] Treatment of the acid chloride (**16**) with $H_2NCH(CH_3)CF_3$ in acetonitrile at 80°C gave the amide derivative (**17**), which has been used as a growth enhancer for animals (Scheme 7).[29]



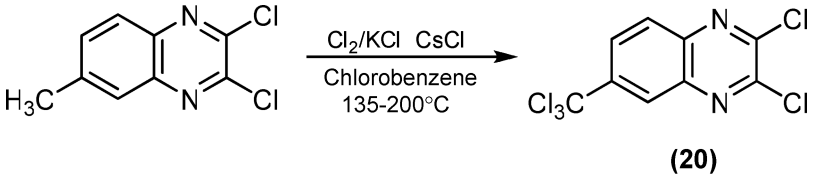
SCHEME 7

The 6-chlorosufonyl derivative (**18**) was prepared from chlorosulfonation of 2,3-dihydroxyquinoxaline, followed by chlorination with phosphoryl chloride in pyridine.[30] Condensation of chlorosulfonyl derivative (**18**) with amino acids furnished 2,3-dichloroquinoxaline-6-sulfonylamino acids (**19**) (Scheme 8).[30]

Chlorination of 2,3-dichloro-6-methylquinoxaline with chlorine in the presence of potassium or cesium chloride and chlorobenzene at 135–200°C afforded the 2,3-dichloro-6-trichloromethylquinoxaline (**20**) (Scheme 9).[31]

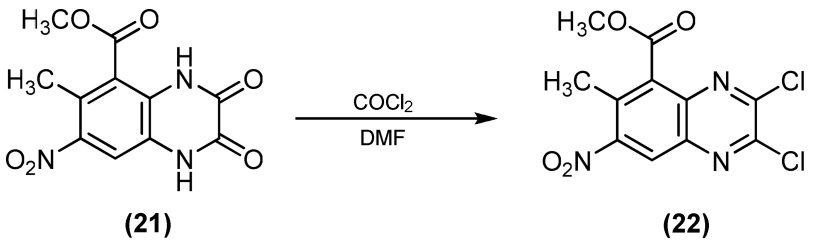


SCHEME 8



SCHEME 9

Methyl 2,3-dichloro-6-methyl-7-nitroquinoxaline-5-carboxylate (**22**) was prepared by dropwise addition of phosgene solution in toluene to a stirred solution of 5-methoxycarbonyl-6-methyl-7-nitroquinoxaline-2,3-dione (**21**) in dimethylformamide at room temperature with 90% yield, (Scheme 10 and Table I).[32]



SCHEME 10

REACTIVITY OF 2,3-DICHLOROQUINOXALINES

The two chlorine atoms in 2,3-dichloroquinoxalines are very reactive towards nucleophilic reagents. The reactivity of two chlorine atoms in

TABLE I Melting Points of Dichloroquinoxalines

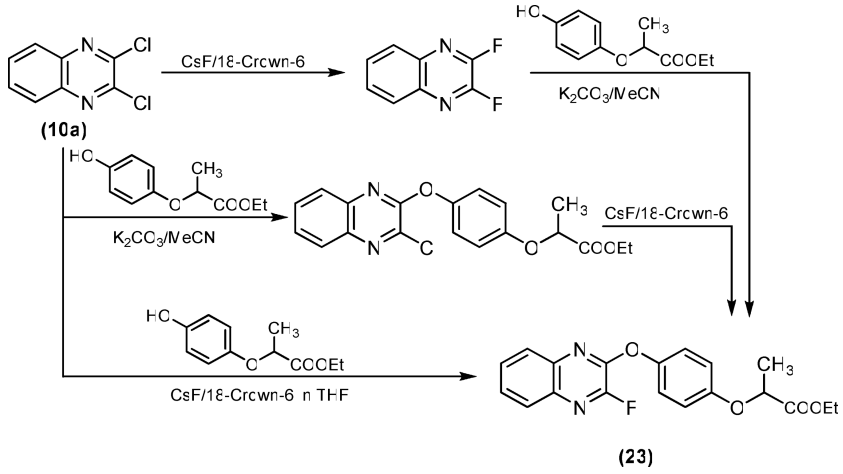
Compd. No.	R	mp[°C]	References
10a	H	146	[26]
10b	6-Cl	143	[26]
10c	6-COPh	160	[26]
10d	6-NO_2	147	[26]
10e	5-NH_2	123	[27]
10f	6-NH_2	200	[27]
10g	5-F	130	[27]
10h	6-F	145	[27]
14	6,7-$(NO_2)_2$-	218	[22]
15	6,7-$(Cl)_2$-	173	[22]
16	6-COCl	114	[28,29]

2- and 3-positions of quinoxaline depends on the nature of the group at position 6. Haworth and Robinson[33] have studied the reactivity of two chlorine atoms in the 2- and 3-positions. They found that the electron-withdrawing group at the 6-position activates the chlorine atom in the 2-position. Alternatively, the electron donating group in the 6-position activates the chlorine atom in the 3-position.

Reactions with Nucleophilic Reagents

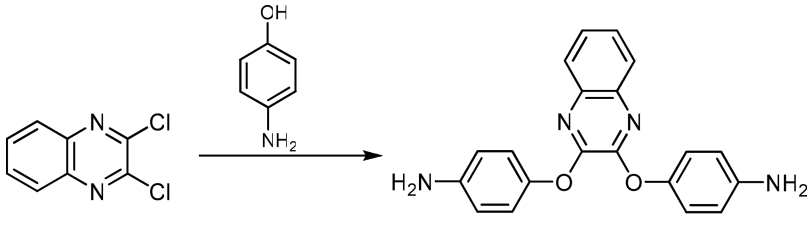
Reactions with Oxygen Nucleophiles

Ethyl 2-[4-(3-fluoro-2-quinoxalinoxy)phenoxy]propanoate (**23**) was prepared from 2,3-dichloroquinoxaline (**10a**) according to Scheme 11.[34,35]



SCHEME 11

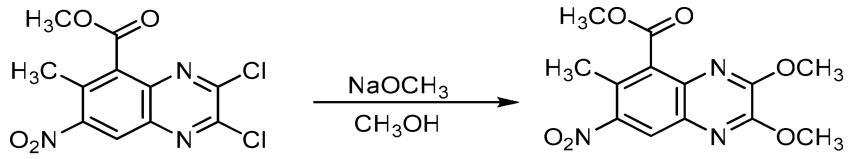
2,3-Bis(4′-aminophenyloxy)quinoxaline (**24**)was prepared from 2,3-dichloroquinoxaline (**10a**) and p-aminophenol. This type of compound could be used to prepare dyes or pigments (Scheme 12).[36]



(10a) (24)

SCHEME 12

The 2,3-dichloroquinoxaline derivative (**22**) was converted into the 2,3-dimethoxyquinoxaline (**25**) by reaction with sodium methoxide in methanol (Scheme 13).[32]

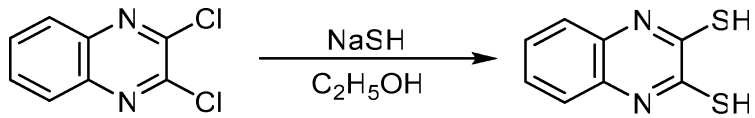


(22) (25)

SCHEME 13

Reactions with Sulfur Nucleophiles

2,3-Dimercaptoquinoxaline (**26**) was obtained by the reaction of 2,3-dichloroquinoxaline (**10a**) with sodium hydrogen sulfide in ethanol (Scheme 14).[37]

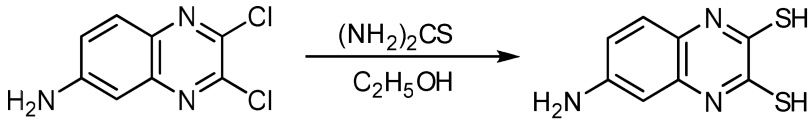


(10a) (26)

SCHEME 14

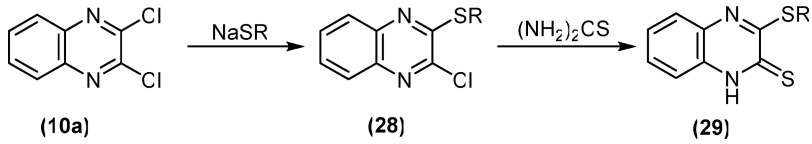
Treatment of 2,3-dichloroquinoxaline (**10f**) with thiourea in ethanol furnished dimercapto derivative (**27**), which has been used as

a neoplasm inhibitor, virucide, and agent for the control of SH metabolism disturbances(Scheme 15).[38]



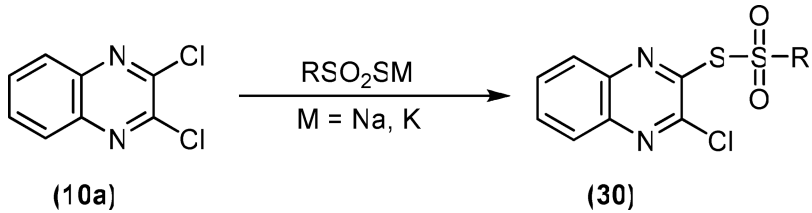
SCHEME 15

Interaction of 2,3-dichloroquinoxaline (**10a**) with sodium mercaptides gave the thioquinoxalines (**28**), which were condensed with thiourea to furnish the thione derivatives (**29**) (Scheme 16).[39]



SCHEME 16

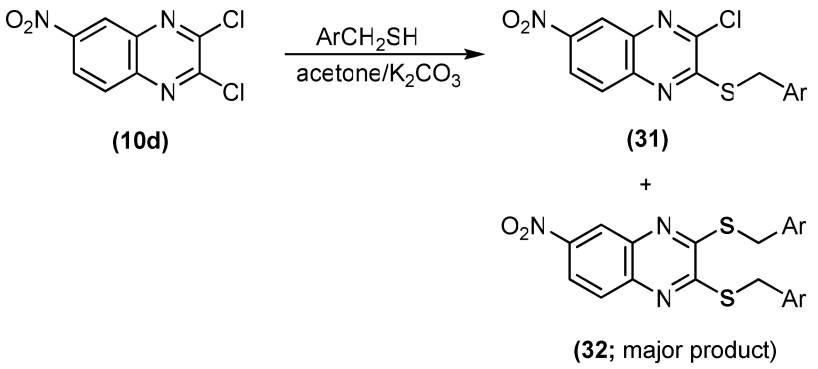
The reaction of 2,3-dichloroquinoxaline (**10a**) with salts of aliphatic and aromatic thiosulfonic acids in aprotic solvent (acetone, dioxane) at a temperature of 20–25°C furnished *S*-(3-chloroquinoxaline-2-yl) esters (**30**) of aliphatic and aromatic thiosulfonic acids with yields of 20–52% (Scheme 17).[40]



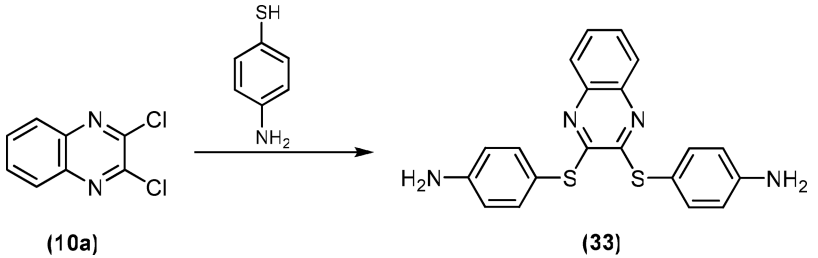
SCHEME 17

Treatment of compound (**10d**) with aromatic thiols in acetone in the presence of potassium carbonate led to a mixture in which the major component was the bis-thioether (**32**) along with the thioether substituted at C-2 (**31**) (Scheme 18).[41]

Condensation of (**10a**) with p-aminothiophenol produced 2,3-bis(4′-aminophenylthio)quinoxaline (**33**) (Scheme 19).[36]



SCHEME 18



SCHEME 19

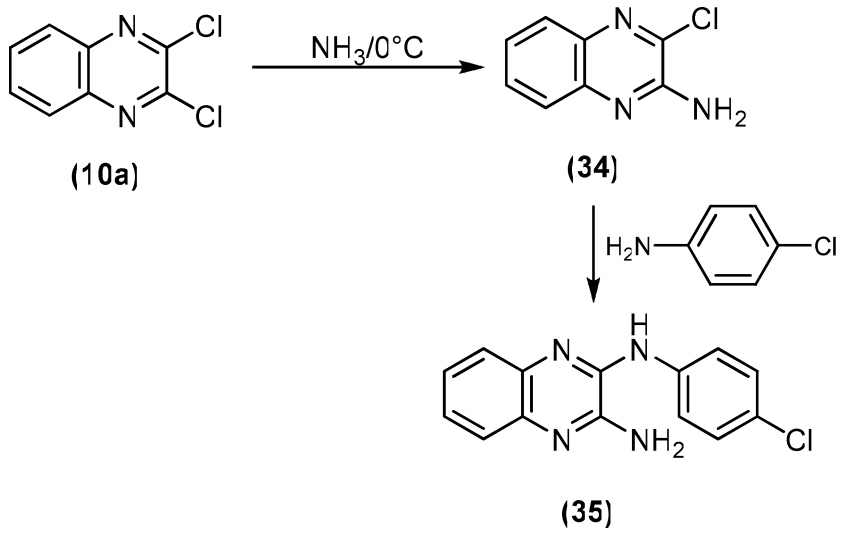
Reactions with Nitrogen Nucleophiles

Monoamination of 2,3-dichloroquinoxaline (**10a**) with ammonia gas at 0°C yielded 2-amino-3-chloroquinoxaline (**34**),[26,41] which upon treatment with parachloroaniline at 190°C gave 2-amino-3-(4-chloroanilino)quinoxaline (**35**) (Scheme 20).[33]

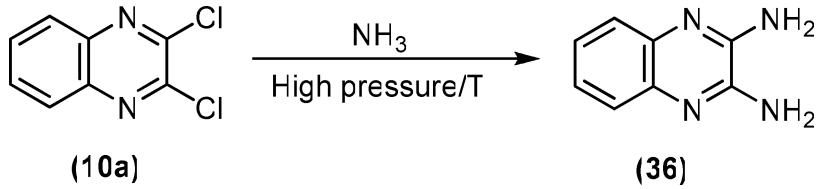
Under drastic conditions, ammonia was reacted with 2,3-dichloroquinoxaline (**10a**) to yield 2,3-diaminoquinoxaline (**36**) (Scheme 21).[43]

2,3-Dichloroquinoxaline (**10a**) was reacted with an excess of aniline under reflux conditions and yielded 2,3-dianilino-quinoxaline (**38**),[33] and 2-anilino-3-chloroquinoxaline (**37**) could not be prepared. On the other hand, condensation of compound (**10a**) with parachloroaniline in the presence of aqueous HCl under reflux produced 2-(4-chloroanilino)-3-chloroquinoxaline (**39**) (Scheme 22).[33]

2,3-Bis(4′-aminophenylamino)quinoxaline (**40**) was prepared from compound (**10a**) and para-phenylenediamine (Scheme 23).[36]



SCHEME 20

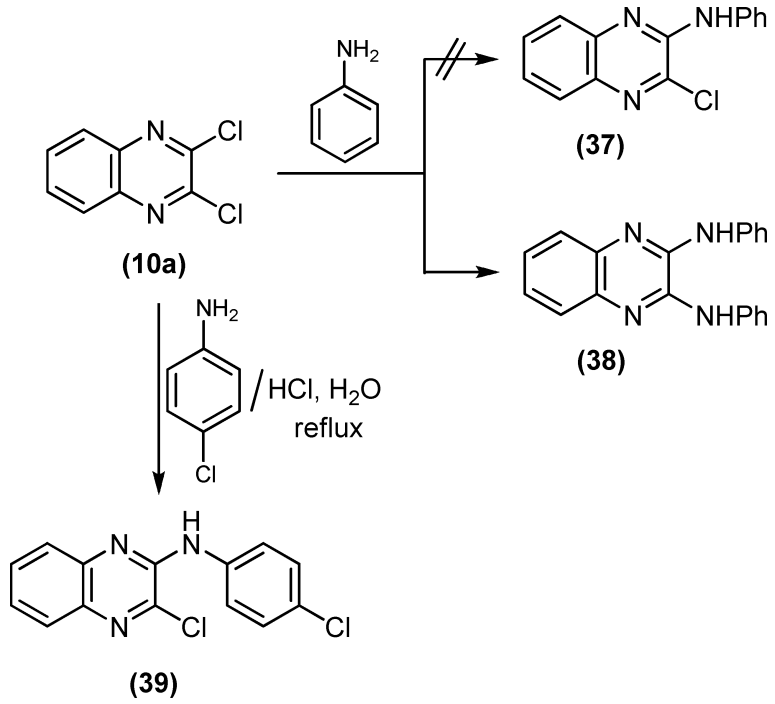


SCHEME 21

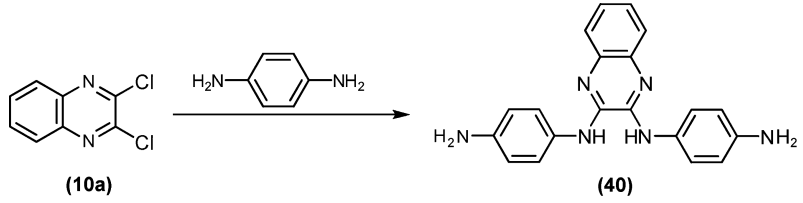
2-Chloro-3-(2-acetylanilino)quinoxaline (**41**) was obtained through the reaction of 2,3-dichloroquinoxaline (**10a**) with ortho-aminoacetophenone (Scheme 24).[44]

The reaction of 2,3,6-trichloroquinoxaline (**10b**) with 2-aminophenol in aqueous *N*, *N*-dimethylformamide and in the presence of nearly stoichiometric amounts of potassium hydroxide furnished compound (**44**). No product other than triazobenzo-phenoxazine (**42**) was obtained by reacting 2-aminophenol with 2,3-dichloroquinoxaline (**10b**) under similar conditions, showing that the (+R)-effect of the 6-chlorine atom in the structure (**10b**) is the responsible factor for the formation of a second product (**44**), and not (**43**) because the C-Cl bond C-2 is strengthened by the (+R)-effect of the 6-chlorine atom (Scheme 25).[45]

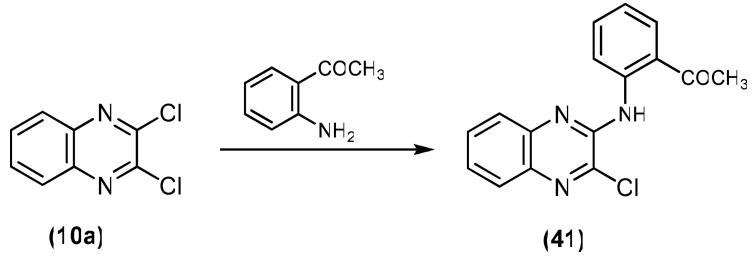
Under reflux conditions, *N*, *N*-dimethylformamide was hydrolyzed in an aqueous alkaline solution releasing dimethylamine. Thus the dimethylamine that was produced then attacks the more



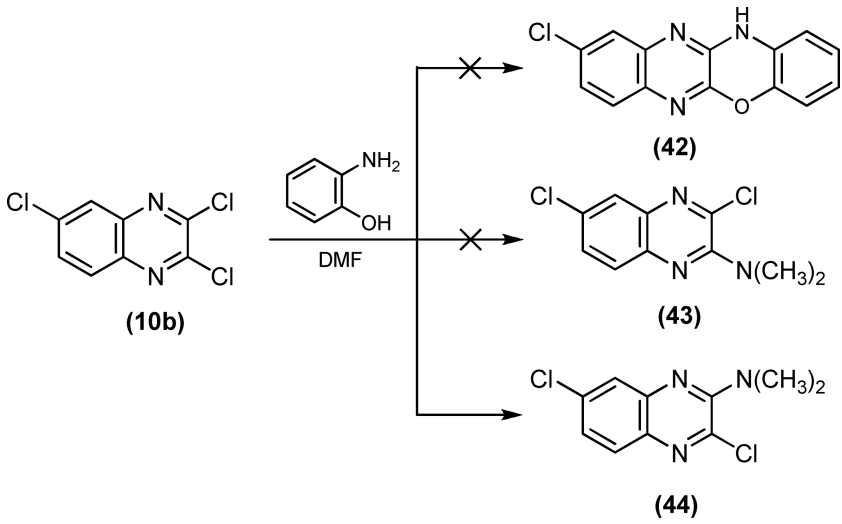
SCHEME 22



SCHEME 23

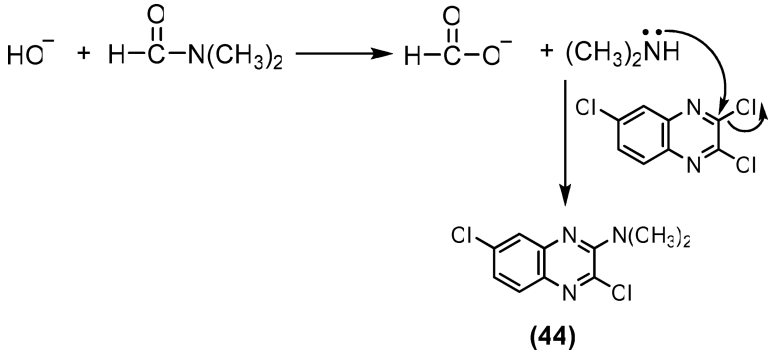


SCHEME 24



SCHEME 25

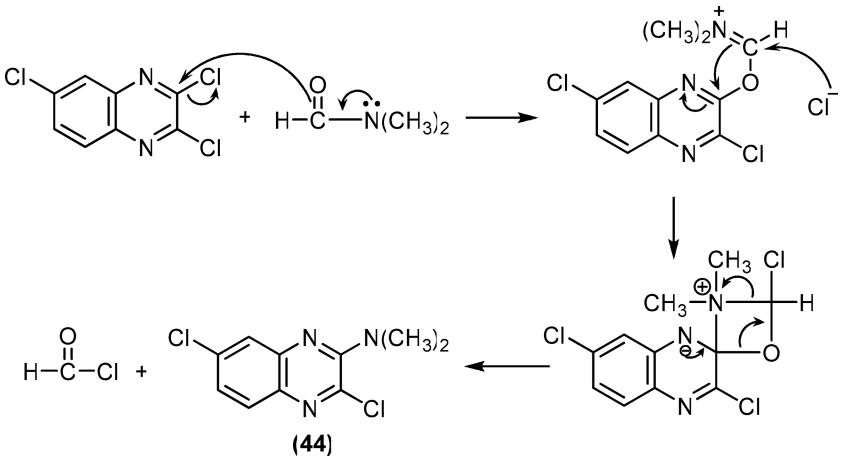
nucleophilic center C-3, leading to the formation of 2,6-dichloro-3-[*N*, *N*-dimethylamine]quinoxaline (**44**) (Scheme 26).[45]



SCHEME 26

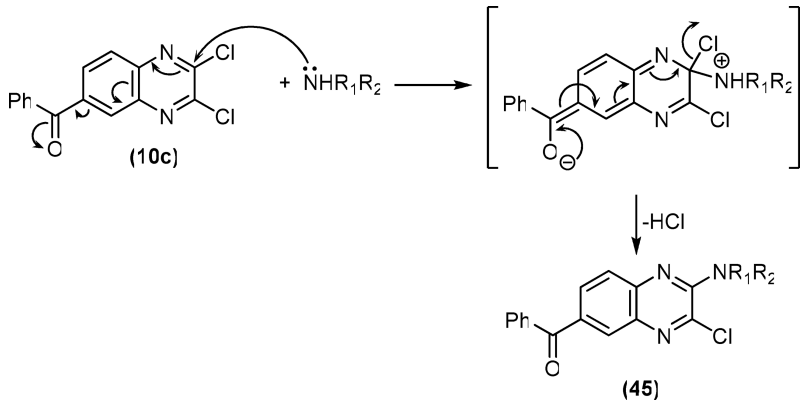
An alternative mechanism involving a nucleophilic attack at the 3-carbon center by the carbonyl oxygen of the *N*,*N*-dimethylformamide was also proposed (Scheme 27).[45]

Condensation of (**10c**) with primary and secondary amines in *N*, *N*-dimethylformamide under reflux conditions produces in each case a sole product that is identified as 2-substituted amino-3-chloro-6-benzoylquinoxaline (**45**).[46] The 2-carbon atom will be more susceptible to nucleophilic attack from the consideration of the (-R)-effect of the



SCHEME 27

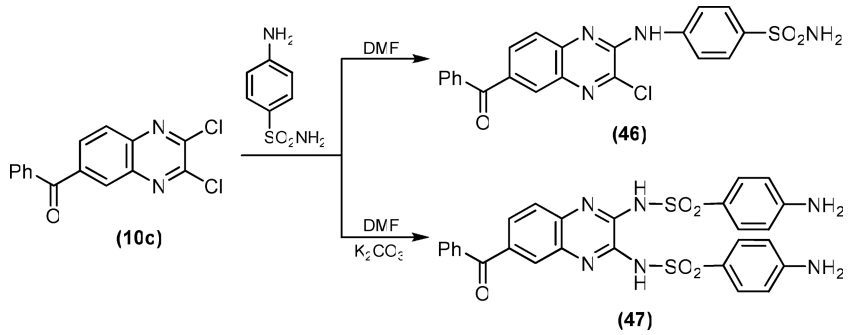
benzoyl group, which is the factor responsible for the formation of (**45**) (Scheme 28).[28]



SCHEME 28

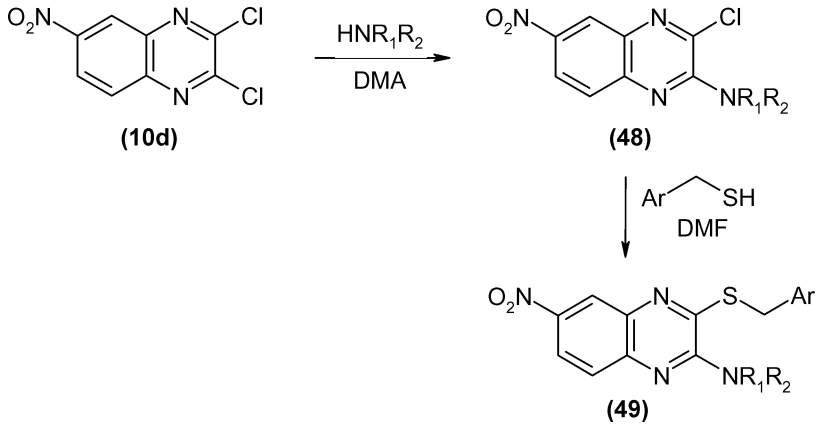
When compound (**10c**) was condensed with sulfanilamide in *N*,*N*-dimethylformamide, 1 mol of sulfanilamide was consumed to give 2-sulfanilamido-6-benzoyl-3-chloroquinoxaline (**46**).[45] Alternatively, the treatment of (**10c**) with sulfanilamide in the presence of potassium carbonate caused 2 mol of sulfanilamide to be consumed to furnish 6-benzoyl-2,3-bis-(4-aminosulfanilamido)quinoxaline (**47**).[46] The enhanced nucleophilicity of the potassium salt $KHNSO_2C_6H_4NH_2$-p,

which is used as the reagent, is responsible for the reaction even with the less-reactive chlorine in the 3-position (Scheme 29).[46]



SCHEME 29

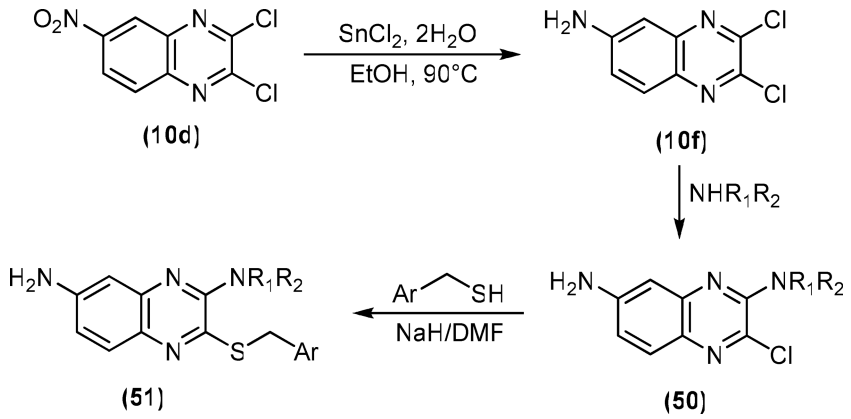
Condensation of compound (**10d**) with aromatic amines at room temperature yielded 2-aminoquinoxaline derivatives (**48**), which upon treatment with aromatic thiols in *N*,*N*-dimethyl-formamide, afforded thioethers (**49**) (Scheme 30).[47,48]



SCHEME 30

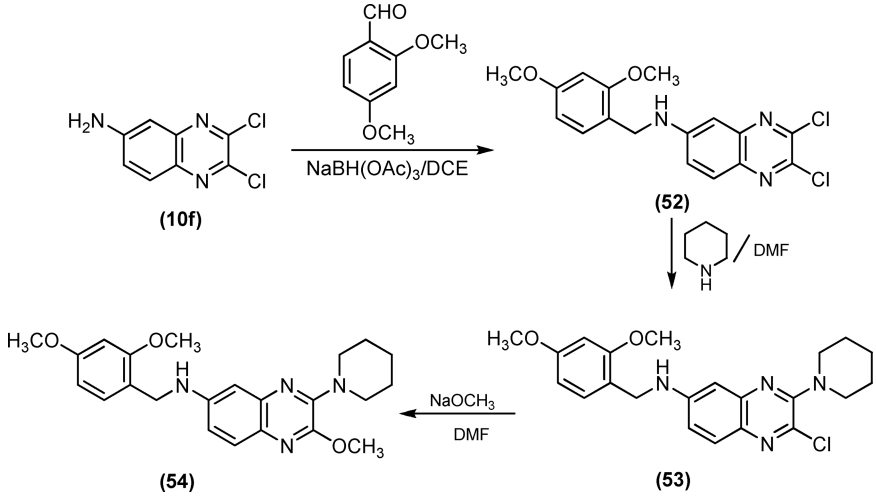
Reduction of compound (**10d**) to 6-amino-2,3-dichloro-quinoxaline (**10f**) was readily accomplished by use of tin(II) chloride dihydrate in ethyl acetate at reflux temperature. Addition of amines to (**10f**) followed by treatment with aromatic thiols furnished thioether derivatives (**51**) (Scheme 31).[41]

The reductive amination of 6-amino-2,3-dichloro-quinoxaline (**10f**) with 2,4-dimethoxybenzaldehyde gave 2,3-dichloro-6-(2,4-



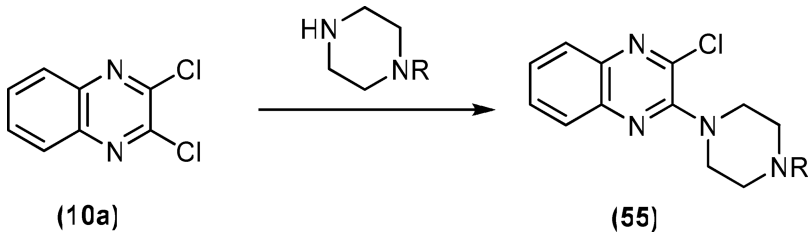
SCHEME 31

dimethoxybenzylamino)quinoxaline (**52**) with 75% yield. The reaction of (**52**) with excess piperidine in *N*,*N*-dimethylformamide at room temperature gave the 3-piperidino derivative (**53**) as a single regioisomer with 96% yield, and subsequent methoxylation of (**53**) with sodium methoxide proceeded successfully to form (**54**) (Scheme 32).[49]



SCHEME 32

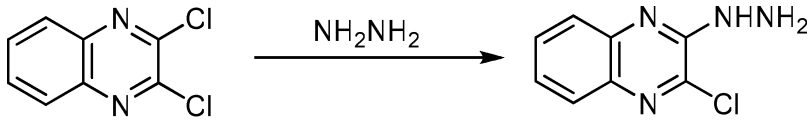
Piperazinylquinoxalines (**55**) were prepared from 2,3-dichloroquinoxaline (**10a**), and their 5-HT_3 receptor antagonist activity was evaluated (Scheme 33).[50]



(10a) (55)

SCHEME 33

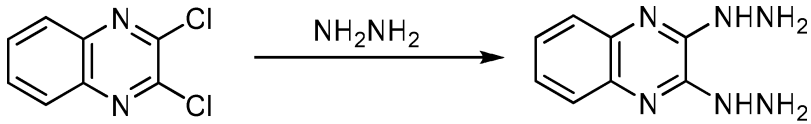
3-Chloro-2-hydrazinoquinoxaline (**56**) was obtained through interaction of (**10a**) with hydrazine hydrate (Scheme 34).[44]



(10a) (56)

SCHEME 34

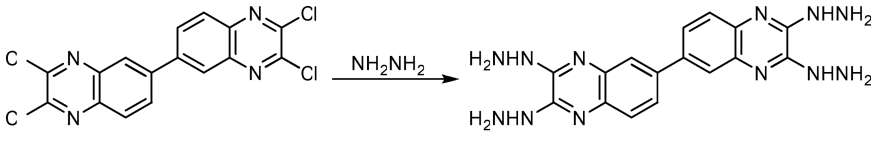
2,3-Dichloroquinoxaline (**10a**) was allowed to react with excess hydrazine hydrate to give (**57**),[51] which was reacted with several reagents to give many condensed heterocyclic products (Scheme 35).



(10a) (57)

SCHEME 35

Treatment of 2,2′,3,3′-tetrachloro-6,6′-biquinoxaline (**58**) with hydrazine hydrate produced the tetrahydrazino derivative (**59**) (Scheme 36).[52]



(58) (59)

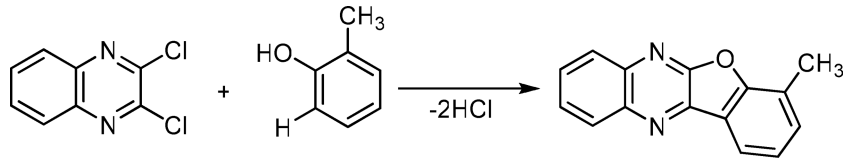
SCHEME 36

SYNTHESIS OF POLYCONDENSED SYSTEMS

In this part, the synthesis and biological activity of the compounds were arranged systematically according to the complexity of the heterocyclic ring directly fused to the quinoxaline nucleus, starting with those having one heteroatom in a five-membered ring in the order O, S, N and proceeding to the more complex ones.

Furo[2,3-b]quinoxalines

This class was prepared through interaction of 2,3-di-chloroquinoxaline (**10a**) with ortho-cresol as an oxygen nucleophile, and caused cyclization to furnish 1-methyl-benzofuro[2,3-b]-quinoxaline (**60**) (Scheme 37).[53]



(10a) (60)

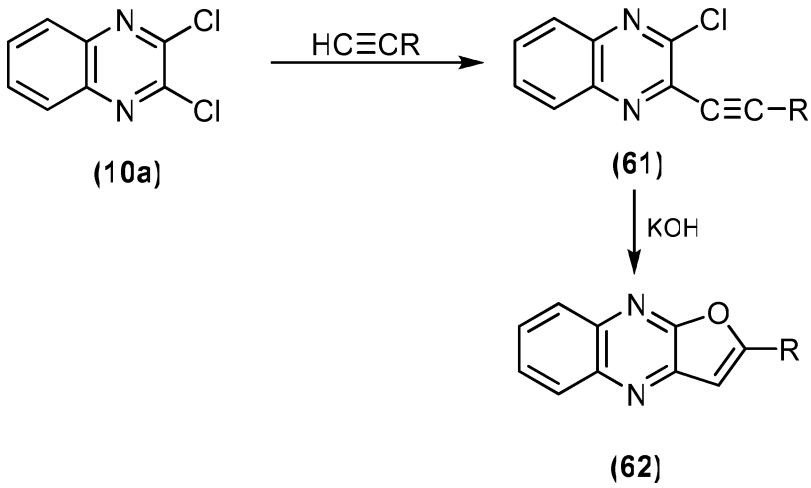
SCHEME 37

Treatment of 2,3-dichloroquinoxaline (**10a**) with terminal alkynes in the presence of Pd(II) or Cu(II) gave the corresponding 2-alkynyl-3-chloroquinoxaline (**61**), which underwent cyclization with potassium hydroxide in dioxane to give furo[2,3-b]quino-xalines (**62**) (Scheme 38).[54]

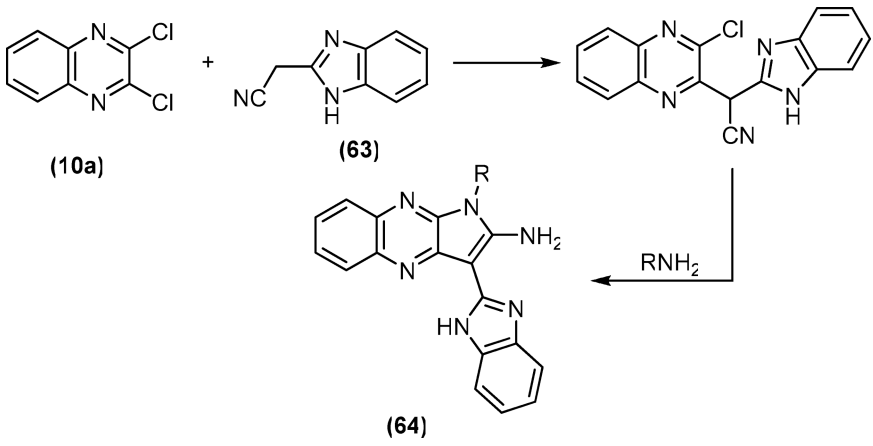
Pyrrolo[2,3-b]quinoxalines

Arylation of benzimidazol-2-ylacetonitrile (**63**) by 2,3-dichloroquinoxaline (**10a**) via the methylene group furnished 2-chloro-3[(α-cyano-α-benzimidazol-2-yl)methylene]quinoxaline, which upon treatment with primary amines led to 1-*R*-2-amino-3-(benzimidazol-2-yl)pyrrolo[2,3-b]quinoxalines (**64**) (Scheme 39).[55]

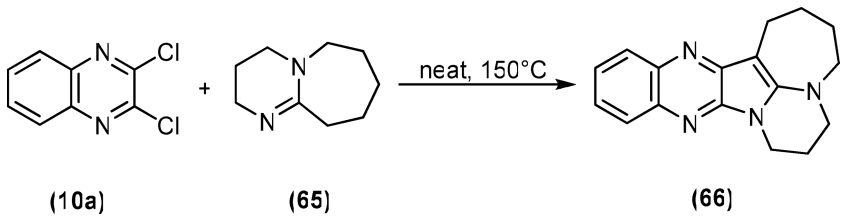
Cyclocondensation reaction of 1,8-diazabicyclic[5,4,0]undec-8-ene (DBU) (**65**) with 2,3-dichloroquinoxaline (**10a**) furnished a new pentacyclic derivative (**66**), which exhibits strong fluorescence both in solutions and in the solid state (Scheme 40).[56]



SCHEME 38



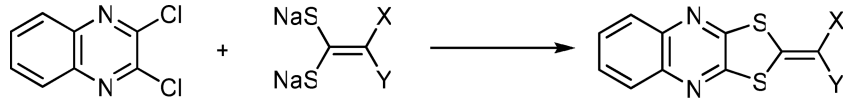
SCHEME 39



SCHEME 40

[1,3]Dithiolo[4,5-b]quinoxalines

The salts of enedithiols (**67**) reacted readily as binucleophiles with 2,3-dichloroquinoxaline (**10a**) in *N, N*-dimethylformamide to produce 2-substituted methylidene-1,3-dithiolo[4,5-b]quinoxalines (**68**) (Scheme 41).[46,57]

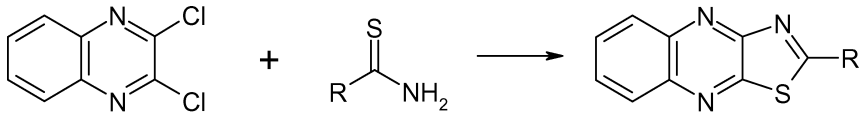


(10a) (67) (68)

SCHEME 41

Thiazolo[4,5-b]quinoxalines

Thioamides R–CS–NH_2 reacted with 2,3-dichloroquinoxaline (**10a**) in aqueous *N*,*N*-dimethylformamide to produce substituted thiazolo-[4,5-b]quinoxalines (**69**) (Scheme 42).[58]

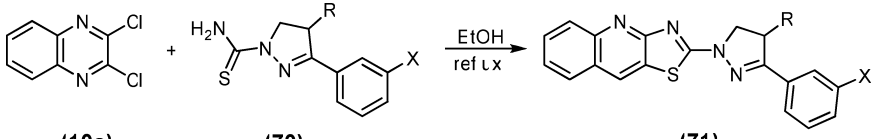


(10a) (69)

SCHEME 42

Some of the prepared compounds have been applied as fluorescent dyes on polyester fibers. These compounds appear to have fairly good dying properties.[58]

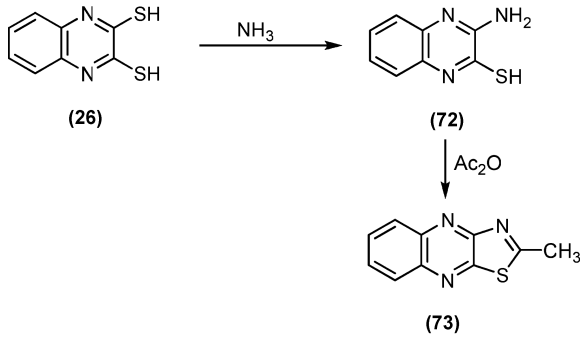
The refluxing of 1-*N*-thiocarboxamide-3-phenyl-2-pyrazolines (**70**) with 2,3-dichloroquinoxaline (**10a**) in absolute ethanol gave the corresponding fused 1-(thiazolo[4,5-b]quinoxaline-2-yl)-3-phenyl-2-pyrazolines (**71**), which were screened in vitro for anti-amoebic activity (Scheme 43).[59]



(10a) (70) (71)

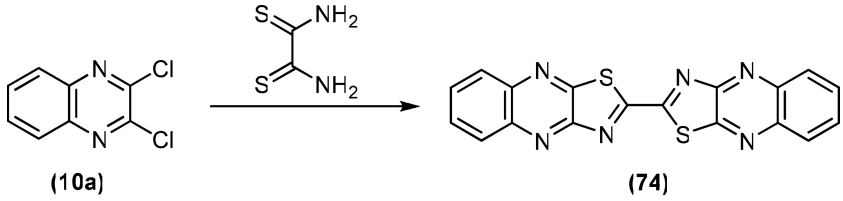
SCHEME 43

Thiazolo[4,5-b]quinoxaline (**73**)[58] was also prepared through cyclization of the dimercapto derivative (**26**) with ammonia to furnish 2-amino-3-mercaptoquinoxaline (**72**), followed by treatment with acetic anhydride (Scheme 44).



SCHEME 44

Cyclocondensation of dithiooxamide (rubeanic acid) with 1 mol of 2,3-dichloroquinoxaline (**10a**) afforded 2,2'-bi-thiazolo[4,5-b]quinoxaline (**74**)[58] (Scheme 45).

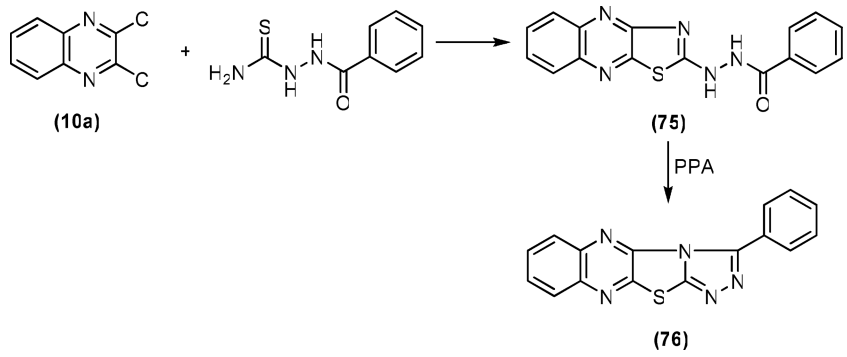


SCHEME 45

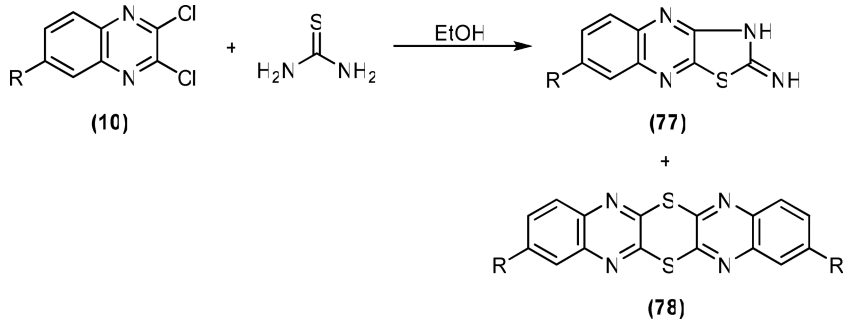
Cyclization of 2,3-dichloroquinoxaline (**10a**) with benzoylthiosemicarbazide in the presence of fused sodium acetate afforded 2-benzoylhydrazinothiazolo[4,5-b]quinoxaline (**75**), which upon treatment with polyphosphoric acid (PPA) yielded 3-phenyltriazolo-[3′,4′:2,3]thiazolo[4,5-b]quinoxaline (**76**)[60] (Scheme 46).

When 2,3-dichloroquinoxalines (**10**) were reacted with thiourea in ethanol, a mixture of 2-imino-2,3-dihydrothiazolo[4,5-b]quinoxalines (**77**) and dithiolo derivatives (**78**) was obtained[61–63] (Scheme 47).

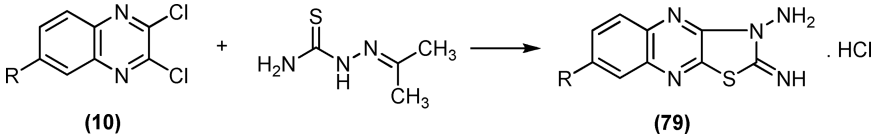
Condensation of (**10**) with acetonethiosemicarbazone in ethanol yielded 3-amino-2-imino-2,3-dihydrothiazolo[4,5-b]quinoxaline hydrochlorides (**79**)[61–64] (Scheme 48).



SCHEME 46



SCHEME 47

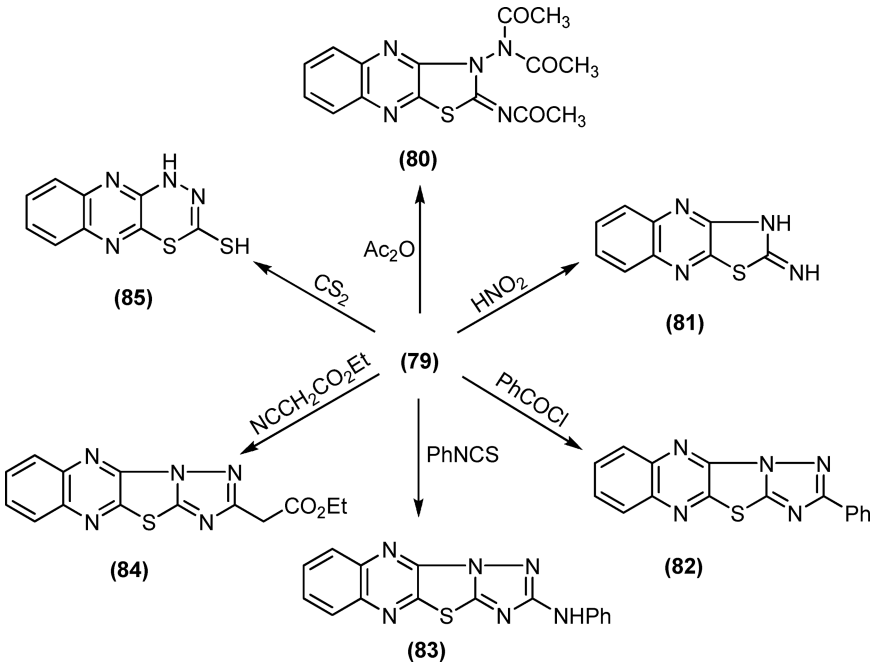


SCHEME 48

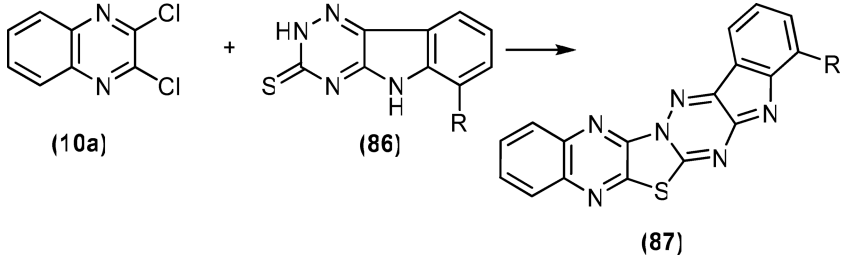
The free amino derivative of (**79**; R = H) was used as starting material in the synthesis of many heterocyclic compounds (**80**–**85**)[65,66] (Scheme 49).

Condensation of 5*H*-2,3-dihydro-1,2,4-triazino[5,6-b]indol-3-thiones (**86**) with 2,3-dichloroquinoxaline (**10a**) gave linear thiazoloquinoxalines (**87**)[67] (Scheme 50).

In addition, condensation of 2,3-dichloroquinoxaline (**10a**) with 2-mercaptopyridines (**88**) afforded the corresponding salts of azino[2′,1′:2,3]thiazolo[4,5-b]quinoxaline (**89**), which have been used for the synthesis of cyanine dyes[68] (Scheme 51).

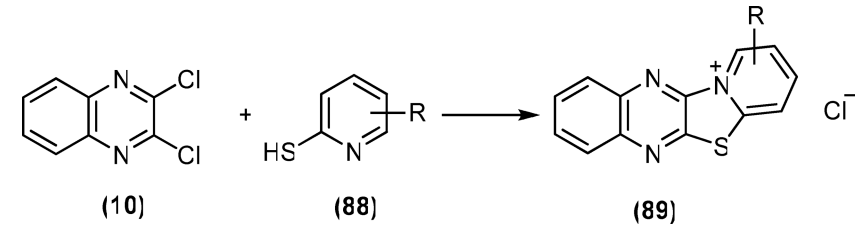


SCHEME 49



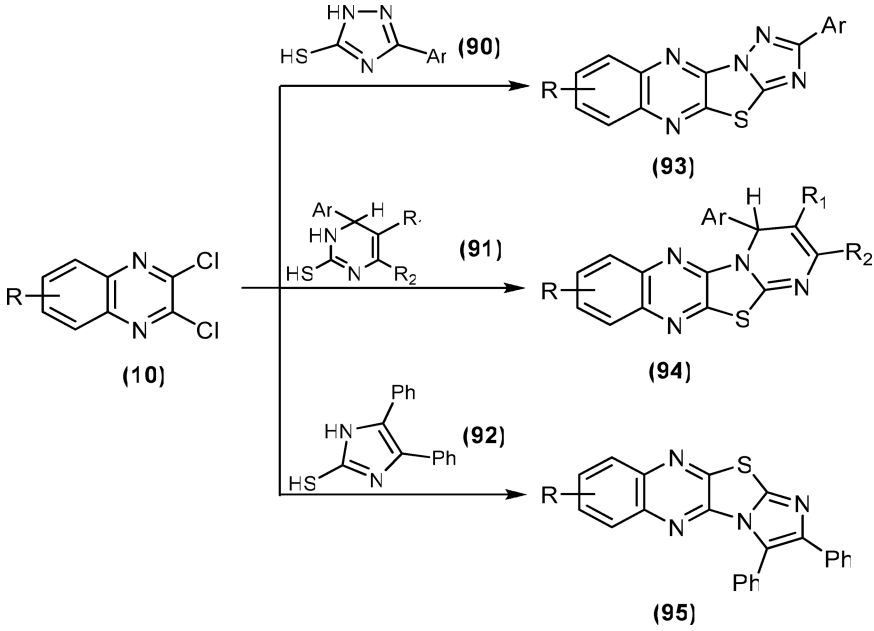
SCHEME 50

Furthermore, condensation of 2,3-dichloroquinoxalines (**10**) with 3-aryl-5-mercaptotriazoles (**90**), 2-mercaptopyrimidines (**91**), and 4,5-diphenylimidazolin-2-thione (**92**) caused cyclization to furnish triazolo[3′,2′:2,3-]thiazolo[4,5-b]quinoxaline (**93**),[69] pyrimido[2′,1′:2,3] thiazolo[4,5-b]quinoxaline (**94**),[70] and imidazo[2′, 1′:2,3]thiazolo[4,5-b]quinoxalines (**95**),[71] respectively (Scheme 52).



(10) **(88)** **(89)**

SCHEME 51



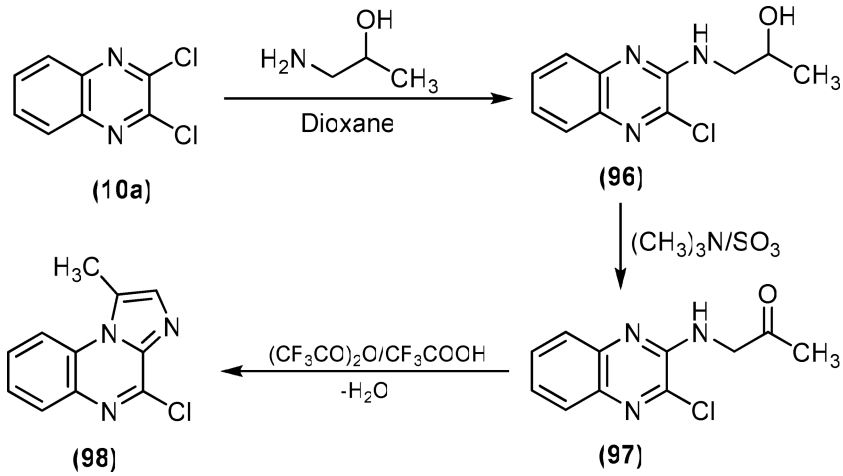
(10) **(90)** **(91)** **(92)** **(93)** **(94)** **(95)**

SCHEME 52

Imidazo[1,2-a]quinoxalines

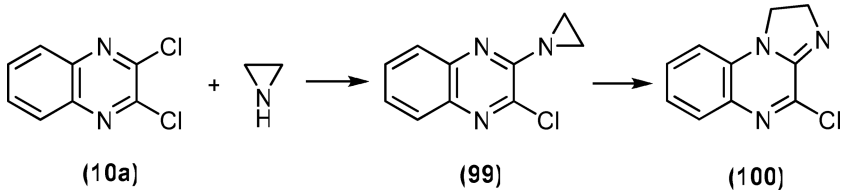
The condensation of 2,3-dichloroquinoxaline (**10a**) with 1-amino-propan-2-ol was followed by oxidation of the hydroxyl function of the intermediate alcohol (**96**) using the sulfur trioxide trimethylamine complex as the oxidizing agent to give the ketone derivative (**97**). The carbonyl compound (**97**) was then cyclized in trifluoroacetic anhydride and trifluoroacetic acid to yield 4-chloro-1-methylimidazo[1,2-a]quinoxaline (**98**)[72] (Scheme 53).

Reaction of 2,3-dichloroquinoxaline (**10a**) with aziridine furnished 2-(1-aziridinyl)-3-chloroquinoxaline (**99**), which upon



SCHEME 53

rearrangement gave 1,2-dihydro-4-chloroimidazo[1,2-a]quinoxaline (**100**)[73] (Scheme 54).

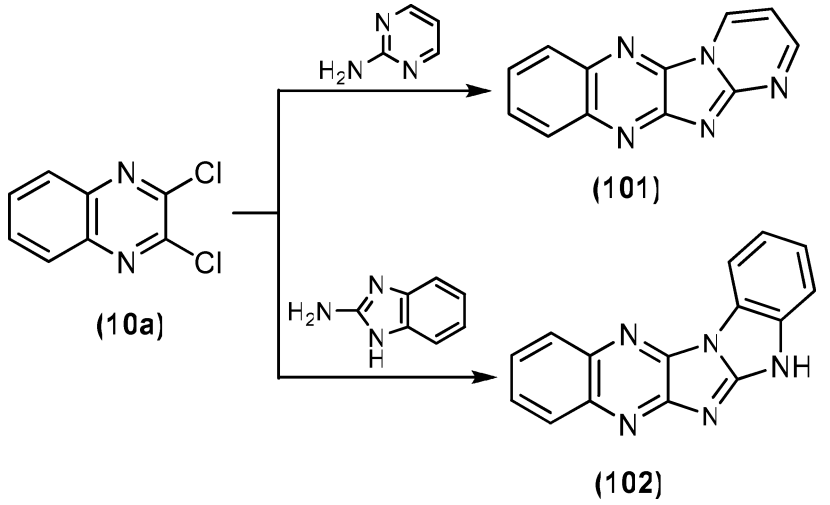


SCHEME 54

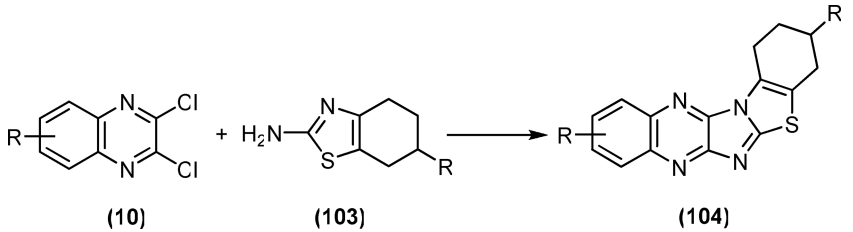
Imidazo[4,5-b]quinoxalines

2-Aminopyrimidine and 2-aminobenzimidazole were also used as binucleophiles. Fusion with 2,3-dichloro-quinoxaline (**10a**) in the presence of sodium acetate produced imidazo[4,5-b]quinoxalines (**101**) and (**102**),[74] respectively (Scheme 55). The fluorescent properties of these compounds have been studied.

2-Amino-6-R-4,5,6,7-tetrahydrobenzothiazoles (**103**) underwent cyclocondensation with 2,3-dichloroquinoxalines (**10**) in hot ethanol to yield quinoxalino[2,3:4′,5′]imidazo[2′,1′-b]benzo-thiazoles (**104**).[75] The anthelimintic, antibacterial, and antifungal properties of these compounds have been evaluated (Scheme 56).

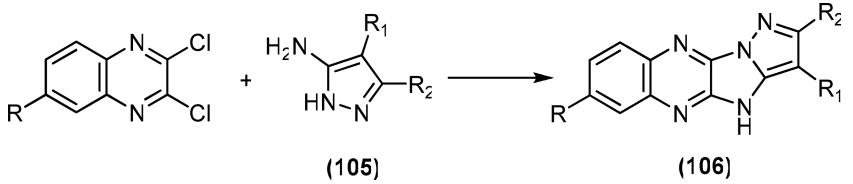


SCHEME 55



SCHEME 56

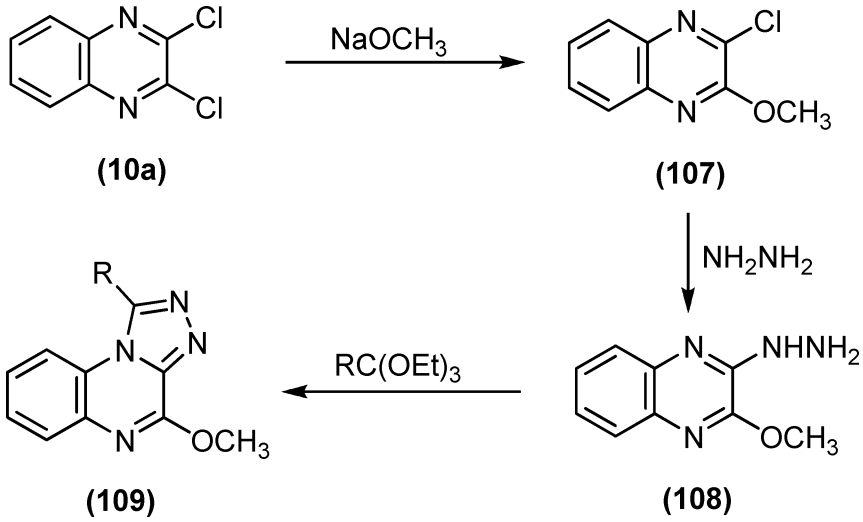
Members of these ring systems also were synthesized by the condensation of 2,3-dichloroquinoxalines (**10**) with 5-aminopyrazoles (**105**) via the elimination of 2 mol of hydrogen chloride to give pyrazolo[1',5':1,2]imidazo[4,5-b]quinoxalines (**106**)[76] (Scheme 57).



SCHEME 57

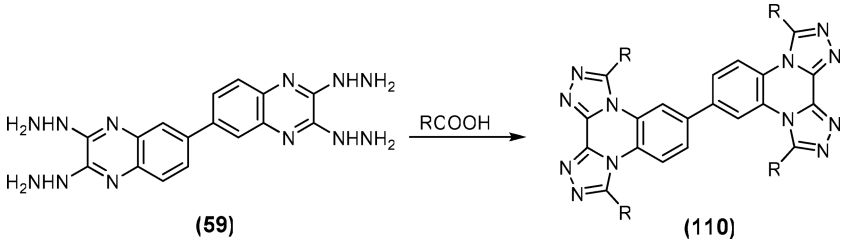
Triazolo[4,3-b]quinoxalines

2,3-Dichloroquinoxaline (**10a**) was treated with sodium methoxide to give 3-methoxy derivative (**107**). The subsequent reaction of (**107**) with hydrazine produced the hydrazino derivative (**108**), which upon treatment with orthoesters gave 4-methoxy-[1,2,4]triazolo[4,3-a]-quinoxalines (**109**)[77] (Scheme 58).



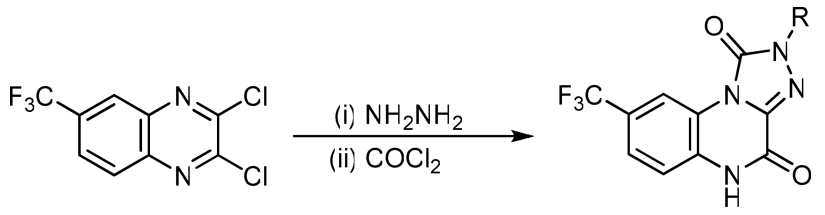
SCHEME 58

Treatment of tetrahydrazino derivative (**59**) with carboxylic acids afforded the condensed [1,2,4]triazolo[4,3-a]quinoxalines (**110**)[52] (Scheme 59).



SCHEME 59

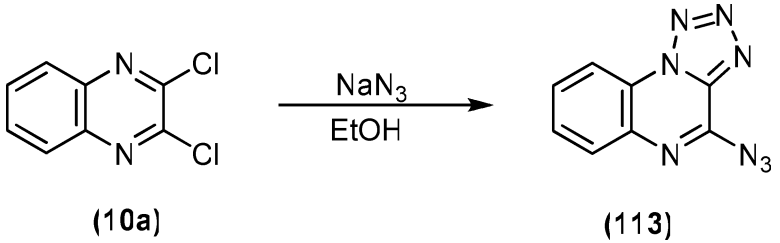
7-(Trifluoromethyl)-[1,2,4]triazolo[4,3-b]quinoxaline-1,4-[2*H*,5*H*]-diones (**112**) were prepared from 6-(trifluoromethyl)-2,3-dichloroquinoxaline (**111**), subsequent to hydrazinolysis and phosgenation [78] (Scheme 60).



SCHEME 60

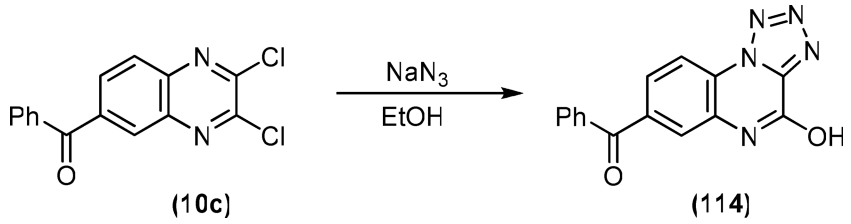
[1,2,3,4]Tetrazolo[1,5-a]quinoxalines

Treatment of 2,3-dichloroquinoxaline (**10a**) with sodium azide in ethanol gave [1,2,3,4]-tetrazolo-3-azidoquinoxaline(**113**)[79] (Scheme 61).



SCHEME 61

Alternatively, 6-benzoyl-2,3-dichloroquinoxaline (**10c**) was reacted with sodium azide to furnish 3-hydroxy[1,2,3,4]tetrazolo[1,5-a]quinoxaline (**114**)[46] (Scheme 62).

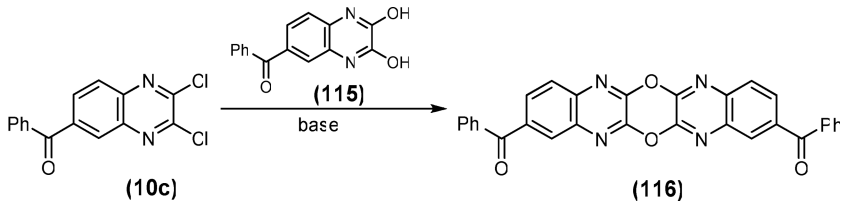


SCHEME 62

[1,4]Dioxino[2,3-b]quinoxalines

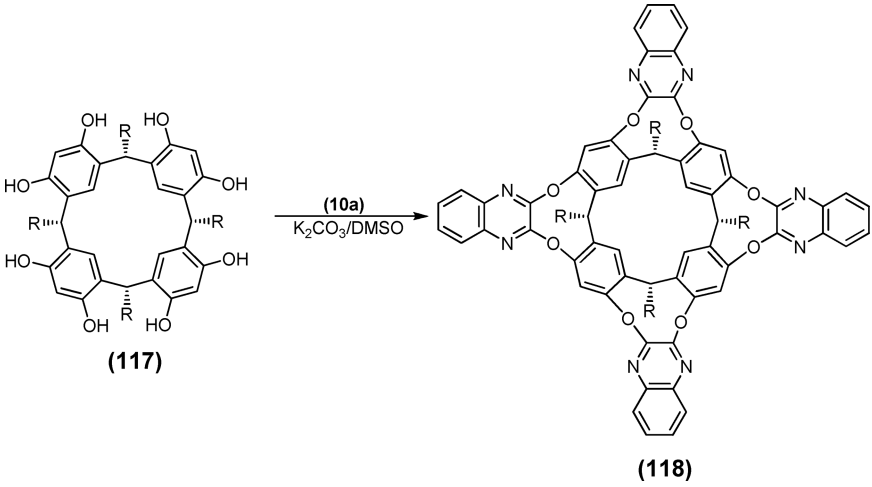
Treatment of 6-benzoyl-2,3-dichloroquinoxaline (**10c**) with 6-benzoyl-2,3-dihydroxyquinoxaline (**115**) as binucleophile in a basic environment

caused cyclocondensation to form quinoxalino-[2',3':5,6]dioxino[2,3-b]quinoxaline (**116**)[46] (Scheme 63).



SCHEME 63

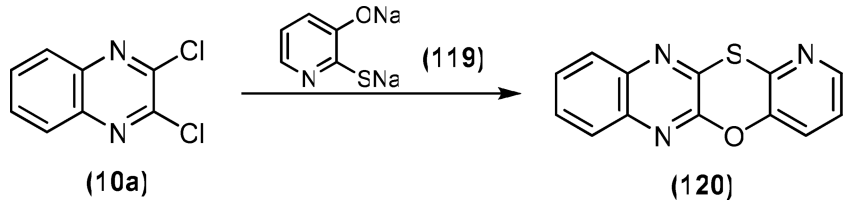
A resorcin[4]arene (**117**) was treated with 4–6 equiv. of 2,3-dichloroquinoxaline (**10a**) under basic conditions in dimethylsulfoxide to afford the tetraquinoxaline-spanned cavitand (**118**)[80] with yields ranging from 60% to 93%, (Scheme 64).



SCHEME 64

[1,4]Oxathino[2,3-b]quinoxaline

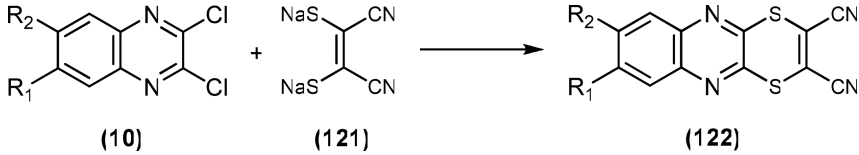
Condensation of 2,3-dichloroquinoxaline (**10a**) with 2-mercapto-3-pyridinol disodium salt (**119**) gave the pyridoxathinoquinoxaline derivative (**120**)[81] (Scheme 65).



SCHEME 65

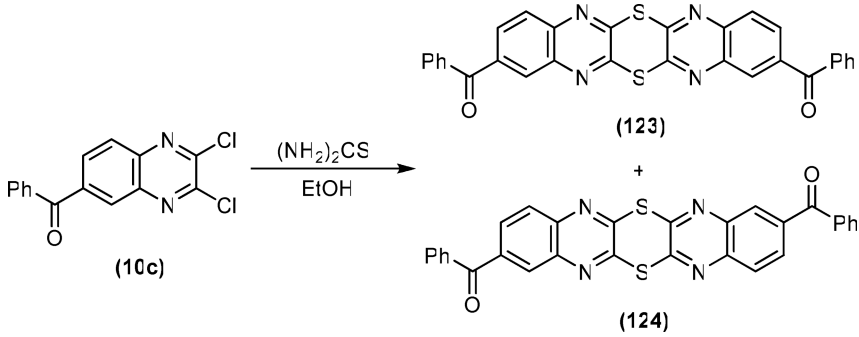
[1,4]Dithiino[2,3-b]quinoxalines

A series of 1,4-dithiino[2,3-b]quinoxaline-2,3-dicarbonitriles (**122**)[82] was prepared by the reaction of 2,3-dichloroquinoxalines (**10**) with disodium (*Z*)-2,3-dimercapto-2-butenedinitrile (**121**) in dimethylformamide (Scheme 66). These products were tested for in vitro fungicidal activity by an MIC method.



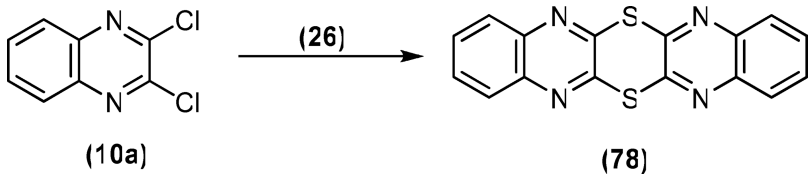
SCHEME 66

Refluxing of 6-benzoyl-2,3-dichloroquinoxaline (**10c**) with thiourea in ethanol gave two products, which can be analyzed as two isomers of dithiino derivatives (**123**) and (**124**)[46] (Scheme 67).



SCHEME 67

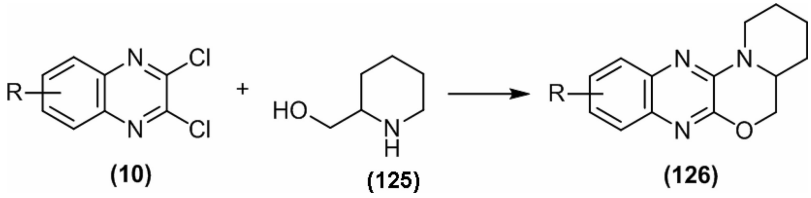
It has been reported that compound (**78**) was formed by the reaction of 2,3-dichloroquinoxaline (**10a**) with 2,3-dimercaptoquinoxaline (**26**)[83] (Scheme 68).



SCHEME 68

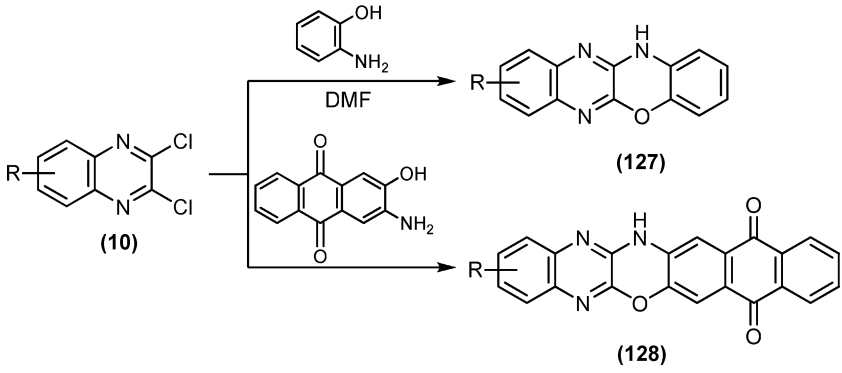
[1,4]Oxazino[2,3-b]quinoxalines

Substituted 2,3-dichloroquinoxaline (**10**) was reacted with 2-hydroxymethylpiperidine (**125**) in the presence of triethylamine and *N*, *N*-dimethylformamide as the solvent to give pyrido[1′,2′:4,5]-oxazino[2,3-b]quinoxalines (**126**)[84] (Scheme 69).



SCHEME 69

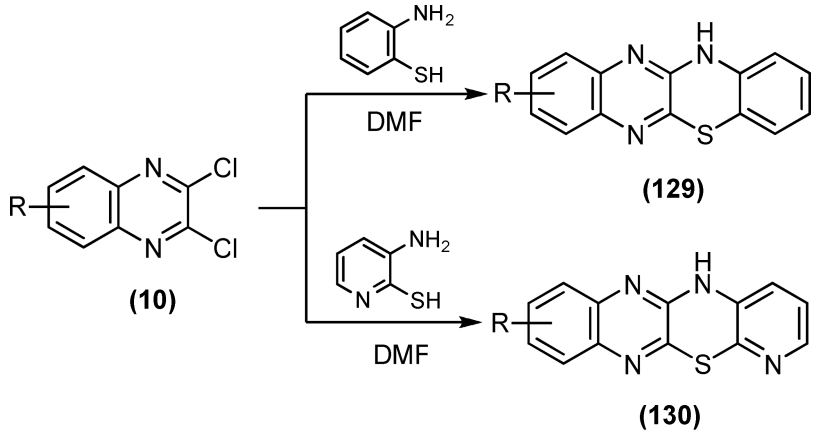
Cyclocondensation of 2,3-dichloroquinoxalines (**10**) with 2-aminophenol and 2-hydroxy-3-aminoanthraquinone in the presence of alkaline *N*, *N*-dimethylformamide afforded the corresponding benzoxazinoquinoxaline derivatives (**127**)[45,85] and (**128**)[84] respectively (Scheme 70).



SCHEME 70

[1,4]Thiazino[2,3-b]quinoxaline

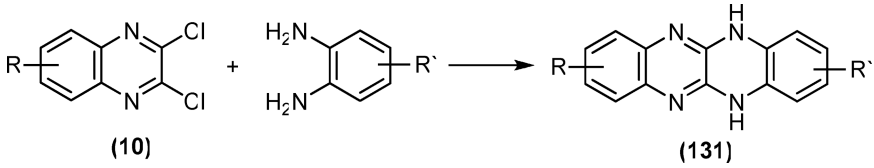
Cyclization of 2,3-dichloroquinoxalines (**10**) with 2-amino-thiophenol and 3-amino-2-mercaptopyridine in refluxing *N*, *N*-dimethylformamide furnished [1,4]thiazino[2,3-b]quinoxaline derivatives (**129**)[86–88] and (**130**)[81] (Scheme 71). These types of compounds have been used as pigment dyes.



SCHEME 71

Pyrazino[2,3-b]quinoxalines

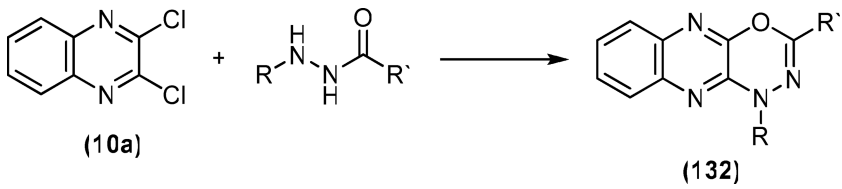
5,12-Dihydroquinoxalino[2,3-b]quinoxaline derivatives (**131**)[85] were synthesized by reacting the appropriate substituted 1,2-phenylenediamines with 2,3-dichloroquinoxalines (**10**) under reflux conditions in dimethylformamide/potassium carbonate (Scheme 72).



SCHEME 72

[1,3,4]Oxadiazino[5,6-b]quinoxalines

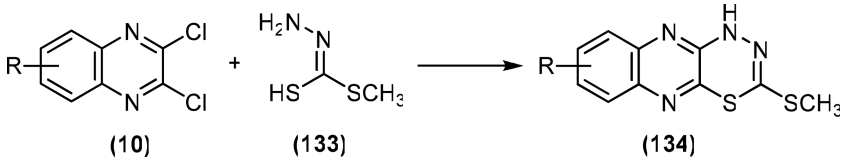
The [1,3,4]-oxadiazino[5,6-b]quinoxalines (**132**) have generally been synthesized from the reaction of 2,3-dichloroquinoxaline (**10a**) with acylhydrazides (Scheme 73).[89]



SCHEME 73

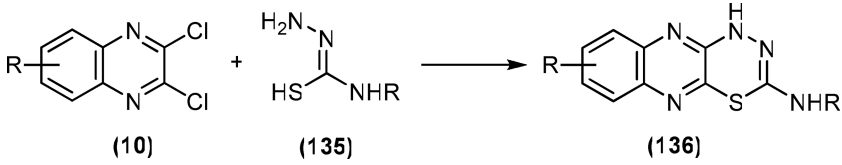
[1,3,4]Thiadiazino[5,6-b]quinoxalines

[1,3,4]-Thiadiazino[5,6-b]quinoxalines (**134**)[65] were obtained via cyclocondensation of 2,3-dichloroquinoxalines (**10**) with methyldithiocarbazate (**133**) (Scheme 74).



SCHEME 74

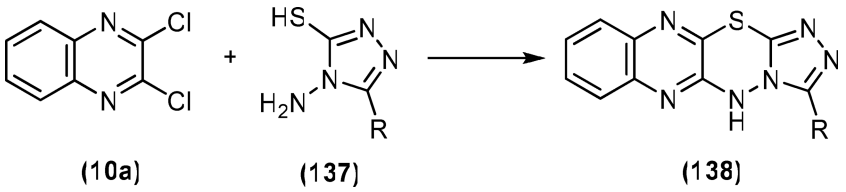
Treatment of 2,3-dichloroquinoxalines (**10**) with thiocarbohydrazides (**135**) yielded the corresponding [1,3,4]thiadizino[5,6-b]quinoxaline derivatives (**136**)[65] (Scheme 75).



SCHEME 75

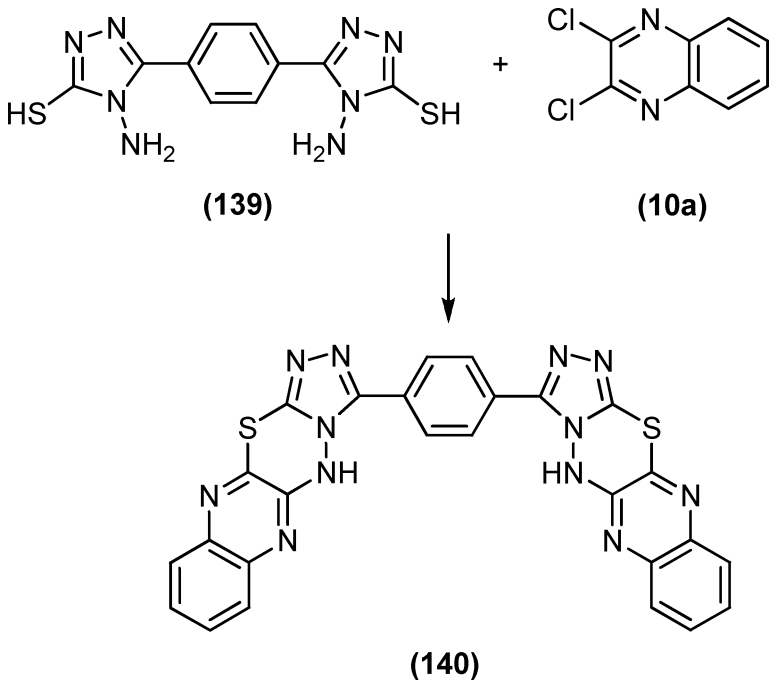
Condensation of 3-substituted 4-amino-5-mercapto-*S*-triazoles (**137**) with 2,3-dichloroquinoxaline (**10a**) in one step furnished the cyclic products 5H-*S*-triazolo[3′,4′:1,2][1,3,4]thiadiazino[5,6-b]quinoxalines (**138**)[90–93] (Scheme 76).

Also, cyclization of para-bis(5-mercapto-4-amino-*S*-triazolo-3-yl)benzene with 2,3-dichloroquinoxaline (**10a**) afforded p-bis(*S*-triazolo[3′,4′:2,3][1,3,4]thiadiazino[5,6-b]quinoxalin-2-yl)benzene (**140**)[94] (Scheme 77).



(10a) (137) (138)

SCHEME 76



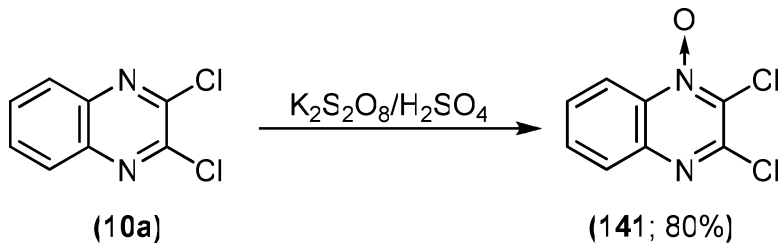
(139) (10a) (140)

SCHEME 77

OXIDATION OF 2,3-DICHLOROQUINOXALINES

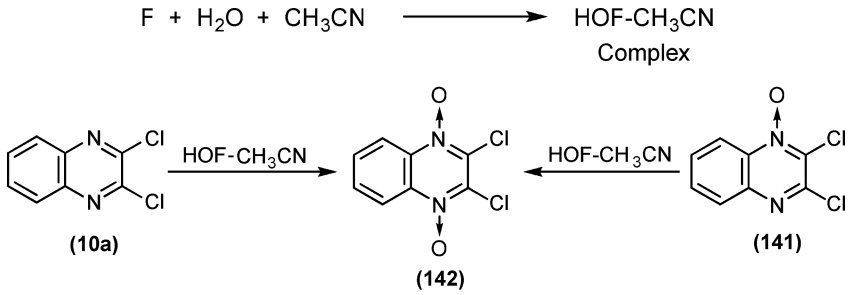
Dihalogenated quinoxalines are notoriously difficult to oxidize by direct oxidation, and the yields in the few successful cases are usually lower than 50%.[95] Oxidation of 2,3-dichloroquinoxaline (**10a**) with potassium persulfate in the presence of sulfuric acid afforded 2,3-dichloroquinoxaline mono-oxide (**141**)[96] with 80% yield (Scheme 78).

Treatment of 2,3-dichloroquinoxaline (**10a**) with HOF-CH_3CN complex furnished 2,3-dichloroquinoxaline *N*, *N*-dioxide (**142**) with 45% yield.[97] In addition, compound (**142**) was obtained with 65% yield by



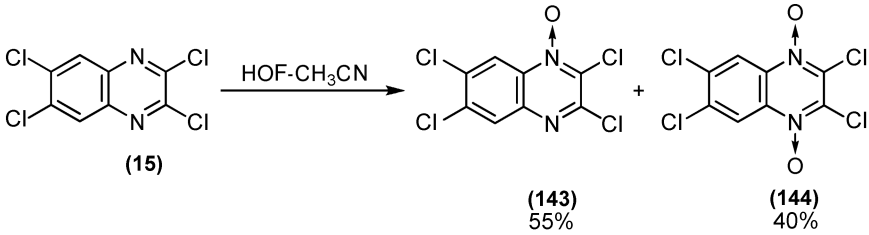
SCHEME 78

the oxidation of mono-oxide (**141**) with the HOF-CH_3CN complex after a short reaction time[97] (Scheme 79).



SCHEME 79

Oxidation of 2,3,6,7-tetrachloroquinoxaline (**15**) with a large excess of the HOF-CH_3CN complex produced the two unknown derivatives 2,3,6,7-tetrachloroquinoxaline *N*-oxide (**143**) with 55% yield and 2,3,6,7-tetrachloroquinoxaline *N*,*N*′-dioxide (**144**) with 40% yield[97] (Scheme 80).



SCHEME 80

CONCLUSIONS

This review article includes various methods for the preparation of dichloroquinoxalines, which are formed by the condensation of

orthophenylenediamines with oxalic acid, followed by the chlorination of dihydroxyquinoxalines with phosphorus oxychloride, phosphorus pentachloride, or thionyl chloride. It also includes the displacement of the two chlorine substituents by oxygen, nitrogen, and sulfur nucleophiles in the presence of electron-withdrawing and electron-donating groups in the 6-position of the quinoxaline ring. Moreover, the article highlights the use of dichloroquinoxalines in the synthesis of polycondensed heterocyclic compounds, which are of great biological benefit.

REFERENCES

[1] H. F. Carter, C. P. Schaffner, and D. Gottlieb, *Arch. Biochem. Biophys.*, **53,** 282 (1954).
[2] M. Ueda, Y. Taniawa, Y. Ueda, and J. Okami, *Antibiotics*, **7,** 152 (1954).
[3] W. Keller, L. Mihaliovic, and V. Prelog, *Helv. Chem. Acta*, **40,** 199 (1957).
[4] T. Yoshida, K. Katagiri, and S. Yokozawa, *J. Antibiotics*, **14A,** 330 (1961).
[5] A. Dell, D. H. Williams, H. R. Morris, G. A. Simth, J. Feeney, and G. C. K. Roberts, *J. Am. Chem. Soc.*, **97,** 2497 (1975).
[6] M. I. Edwards, R. E. Bambury, and H. W. Ritter, *J. Med. Chem.*, **18,** 637 (1975).
[7] K. Sasse, R. Wegler, G. Unterstenhoefer, and F. Grewe, *Angew. Chem.*, **72,** 973 (1960).
[8] R. J. Magee, *US Pat.*, 3634425 (1972); *Chem. Abstr.*, **76,** 99709 (1972).
[9] T. Miyagi and H. Yamamoto, *Jap. Pat.*, 17747 (1967); *Chem. Abstr.*, **69,** 10475 (1968).
[10] Q. S. Soper, *US Pat.*, 36467793 (1972); *Chem. Abstr.*, **77,** 303392 (1972).
[11] H. Yamamoto, *Jap. Pat.*, 6917136 (1969); *Chem. Abstr.*, **71,** 124505 (1969).
[12] T. O. Yellin, *US Pat.*, 3635971 (1972); *Chem. Abstr.*, **76,** 99708 (1972).
[13] C. W. Huffman, J. J. Krajewski, P. J. Kotz, J. T. Traxler, and S. S. Ristich, *J. Agr. Food Chem.*, **1,** 298 (1971).
[14] R. R. Schaffer, *US Pat.*, 3560616 (1971); *Chem. Abstr.*, **75,** 47839 (1971).
[15] G. W. H. Cheeseman and R. F. Cookson, In *The Chemistry of Heterocyclic Compounds, Condensed Pyrazines*, A. Weissberger and E. C. Taylor, Eds. (John Wiley and Sons, New York, 1979) Chapter 35.
[16] G. W. H. Cheeseman, *Adv. Heterocycl Chem.*, **2,** 203 (1963).
[17] G. W. H. Cheeseman and E. S. G. Werstiuk, *Adv. Heterocycl. Chem.*, **22,** 267 (1978).
[18] Y. Kurasawa and A. Takada, *Heterocycles*, **23,** 2083 (1985).
[19] Y. Kurasawa and A. Takada, *Heterocycles*, **24,** 2321 (1986).
[20] K. Winterfeld and M. Wilderson, *Arch. Pharm.*, **303,** 1002 (1970).
[21] K. Zauer, M. T. Gzygaran, and E. A. Markarayan, *Khim. Geterotsikl, Soedin*, **9,** 43 (1972).
[22] G. W. H. Cheeseman, *J. Chem. Soc.*, 1170 (1962).
[23] J. K. Landquist, *J. Chem. Soc.*, 2816 (1953).
[24] J. Liu, A. Wu, M. Huang, C. Wu, and W. Chung, *J. Org. Chem.*, **65,** 3395 (2000).
[25] E. H. Usherwood and M. A. Whiteley, *J. Chem. Soc.*, 1084 (1923).
[26] K. Tanaka, H. Takahashi, K. Takimoto, M. Sugita, and K. Mitsuhasi, *J. Heterocyl. Chem.*, **29,** 771 (1992).
[27] F. M. E. Abdel-Megeid, M. A. F. El-Kaschef, and A. A. G. Ghattas, *Egypt. J. Chem.*, **20**(5), 427 (1977); *Chem. Abstr.*, **94,** 30703 (1981).
[28] J. Pirkl and C. Fisar, *Czech. Patent*, **116,** 695 (1965); *Chem. Abstr.*, **65,** 13737 (1966).

[29] A. De Jong and R. Fuchs, *Eur. Pat. Appl.* EP456, 067 (Cl.C07D241/44), 13 Nov. 1991, DE Appl. 4, 014, 937, 10 May 1990; *Chem. Abstr.*, **116,** 59404 (1992).
[30] F. A. Kora, M. E. Hussein, R. A. El-Said, and A. M. El-Naggar, *Pol. J. Chem.*, **62,** 749 (1988).
[31] G. Steffan, *Ger. Offen.* DE 4, 133, 676 (Cl. C07B39/00) 15 Apr. 1993, Appl. 11 Oct. 1991; *Chem. Abstr.*, **119,** 138845 (1993).
[32] B. E. Kornberg, S. S. Nikam, and M. F. Rafferty, *J. Heterocycl Chem.*, **36,** 1271 (1999).
[33] R. D. Haworth and S. Robinson, *J. Chem. Soc.*, 777 (1948).
[34] K. Makino and H. Yoshioka, *J. Fluor. Chem.*, **37,** 119 (1987).
[35] K. Makino and H. Yoshioka, *Heterocycles*, **26,** 1215 (1987).
[36] A. Gerlicz and J. Kraska, *Rocz. Chem.*, **51**(6), 1087 (1977); *Chem. Abstr.*, **88,** 22832 (1978).
[37] N. Sai Kachi and S. Tagami, *Chem. Pharm. Bull.*, **9,** 941 (1961).
[38] N. Muresan and V. E. Muresan, *Rom.* RO 88, 072 (Cl. C07D 241/40), 30 Oct. 1985, Appl. 122, 849, 14 Dec. 1983; *Chem. Abstr.*, **105,** 115095 (1986).
[39] E. Campaigne and A. R. Mclaughlin, *J. Heterocycl. Chem.*, **20,** 623 (1983).
[40] V. I. Lubenets, S. V. Vasylyuk, and V. P. Novikov, *Chem. Heterocycl. Compd.*, **41,** 1547 (2005).
[41] E. Ford, A. Brewster, G. Jones, J. Bailey, and N. Sumner, *Tetrahedron Lett.*, **41,** 3197 (2000).
[42] M. A. Zahran, M. M. Ali, and A. M. Abdel-Salam, *Al-Azhar Bull. Sci.*, **5,** 821 (1994).
[43] J. R. Stevens, K. Delester, and F. J. Wolf, *J. Am. Chem. Soc.*, **68,** 1036 (1946).
[44] M. G. Lila, *Mansoura J. Pharm. Sci.*, **10,** 237 (1994); *Chem. Abstr.*, **123,** 9412 (1995).
[45] C. O. Okafor, *J. Heterocycl. Chem.*, **18,** 1445 (1981).
[46] M. S. A. El-Gaby, A. M. Sh. El-Sharief, Y. A. Ammar, Y. A. Mohamed, and A. A. Abd El-Salam, *Indian J. Chem. Sect. B.*, **40B,** 195 (2001).
[47] K. Tanaka, H. Takahashi, K. Takimoto, M. Sugita, and K. Mitsuhashi, *J. Heterocycl. Chem.*, **29,** 771 (1992).
[48] A. Katoh, S. Ueda, J. Ohkando, M. Hirota, K. Komine, and K. Mitsuhashi, *Heterocycles*, **34,** 1965 (1992).
[49] M. Jeon, D. Kim, H. La, and Y. Gong, *Tetrahedron Lett.*, **46,** 4979 (2005).
[50] M. Antonio, P. Juan, D. Juan, R. Gonzalo, L. Berta, D. Joaquin, C. Jose, B. Ana, and R. Juan, *Acad. Farm.*, **60,** 91 (1994); *Chem. Abstr.*, **123,** 55808 (1995).
[51] S. E. Zayed, M. M. Taha, and A. E. Mohamed, *Mansoura J. Pharm. Sci.*, **11,** 266 (1995); *Chem. Abstr.*, **123**, 339992 (1995).
[52] V. V. Titov and L. F. Kozhokina, *Khim. Geterotsikl. Soedin*, **3,** 414 (1977); *Chem. Abstr.*, **87,** 39419 (1977).
[53] R. K. Anderson and G. W. H. Cheeseman, *J. Chem. Soc., Perkin Trans.* 1, 129 (1974).
[54] D. E. Ames, T. C. Mitchell, and C. C. Takundwa, *J. Chem. Res. Synop.*, 144 (1985).
[55] A. P. Kozynhenko, Y. H. Voloenko, V. K. Promonenkov, A. V. Turor, and F. S. Babichev, *Chem. Heterocycl. Compd.*, **24,** 923 (1988).
[56] D. T. Gryko, J. Piechowska, M. Tasior, J. Waluk, and G. Orzanowsk, *Org. Lett.*, **8,** 4747 (2006).
[57] R. R. Duane, B. S. Ravi, and P. Crath, *U.S*, US 5, 200, 409 (CI. 514-250; CO7D 49/404), 06 Apr 1993, US Appl. 814, 527, 30 Dec. 1991; *Chem. Abstr.*, **119,** 139271 (1993).
[58] A. R. Katritzky and Q. Fan, *J. Heterocycl. Chem.*, **25,** 901 (1988).
[59] M. Abid and A. Azam, *Bioorg. Med. Chem. Lett.*, **16,** 2812 (2006).
[60] K. S. Dhaka, J. Mohan, V. K. Chadha, and H. K. Pugari, *Indian J. Chem.*, **12,** 966 (1974).

[61] Y. A. Ammar, I. M. Ismail, A. M. Sh. El-Sharief, Y. A. Mohamed, and R. A. Mer, *J. Ind. Chem. Soc.*, **66,** 124 (1989).
[62] A. M. Sh. El-Sharief, Y. A. Ammar, Y. A. Moahmed, and R. M. Amer, *J. Prakt. Chem.*, **330,** 421 (1988).
[63] I. M. Ismail and W. Sauer, *Indian J. Chem.*, *Sect. B.*, **16B,** 683 (1978).
[64] A. M. Sh. El-Sharief, M. M. Ali, Y. A. Ammar, and A. A. Abd El-Salam, *Pak. J. Sci. Ind. Res.*, **39,** 5 (1996); *Chem. Abstr.*, **127,** 358836 (1997).
[65] (a) Y. A. Ammar, M. S. A. El-Gaby, M. A. Zahran, and A. A. Abdel-Salam, *Phosphorus, Sulfur, and Silicon*, **175,** 87 (2000); (b) M. Bakavoli, M. Nikpour, and M. Rahimzadeh, *Phosphorus, Sulfur, and Silicon*, **180,** 2265 (2005).
[66] S. Singh and C. Singh, *J. Indian Chem. Soc.*, **48,** 925 (1971).
[67] (a) J. Mohan and P. Verma, *J. Indian Chem. Soc.*, **67,** 438 (1990); (b) J. Mohan and V. Singh, *J. Indian Heterocycl. Chem.*, **4,** 147 (1994); *Chem. Abstr.*, **122,** 290822 (1995).
[68] Y. U. A. Nesternko and N. N. Romanou, *Chem. Heterocycl. Compd.*, **23,** 460 (1987).
[69] K. S. Dhaka, J. Mohan, V. K. Chadha, and H. K. Pujari, *Indian J. Chem.*, **12,** 287 (1974).
[70] (a) M. M. Ghorab, M. A. Zahran, Y. A. Mohamed, S. A. Mohamed, and Y. A. Ammar, *Phosphorus*, *Sulfur, and Silicon*, **108,** 249 (1996); (b): M. S. A. El-Gaby, S. G. Abd El-Hamide, M. M. Ghorab, and S. M. El-Sayed, *Acta Pharm.*, **49,** 149 (1999).
[71] J. Mohan, V. K. Chadha, and H. K. Pujari, *Indian J. Chem. Soc.*, **47,** 1150 (1970).
[72] S. Parra, F. Laurent, G. Subra, C. Deleuze-Masquefa, V. Benezech, J. Fabreguttes, J. Vidal, T. Pocock, K. Elliott, R. Small, R. Escale, A. Michel, J. Chapat, and P. Bonnet, *Eur. J. Med. Chem.*, **36,** 255 (2001).
[73] H. W. Heine and A. C. Brooker, *J. Org. Chem.*, **27,** 2943 (1962).
[74] P. V. Tagdiwala and D. W. Ranynekar, *Indian J. Chem. Sec. B*, **25,** 1057 (1986).
[75] S. Amrik, J. Mohan, and H. K. Pujari, *Indian J. Chem. Sec. B*, **14B,** 997 (1976).
[76] M. A. Zahran, A. A. H. Hassanin, H. A. Emam, M. Z. El-Said, and Y. A. Ammar, *Croatica Chim. Acta*, **70,** 1039 (1997).
[77] R. Sarges, H. R. Howard, R. G. Browne, L. A. Lebel, P. A. Seymour, and B. K. Koe, *J. Med. Chem.*, **33,** 2240 (1990).
[78] J. Poul and N. Flemming, *PCT Int.* Appl. WO 9306, 103 (Cl C0 7D 487/04), 01 Apr 1993, DK Appl. 91/1, 624, 20 Sep. 1991; *Chem. Abstr.*, **119,** 117278 (1993).
[79] R. Stolle and F. Hanuch, *J. Prakt. Chem.*, **136,** 9 (1933); *Chem. Abstr.*, **27,** 1632 (1933).
[80] (a) J. R. Moran, J. L. Ericson, E. Dalcanale, J. A. Bryant, C. B. Knobier, and D. J. Cram, *J. Am. Chem Soc.*,**113,** 5707 (1991); (b) E. Dalcanale, P. Soncini, G. Bacchilega, and F. J. Ugozzoli, *Chem. Commun.*, 500 (1989); (c) P. P. Castro, G. Zhao, G. A. Masangkay, C. Hemandez, and L. M. Gutierrez-Tunstad, *Org. Lett.*, **6,** 33 (2004).
[81] C. O. Okafor, *J. Heterocycl. Chem.*, **17,** 149 (1980).
[82] D. R. Romer, B. L. Aldrich, R. C. Pews, and R. W. Walter, *Pestic. Sci.*, **43,** 263 (1995); *Chem. Abstr.*, **122,** 284524 (1995).
[83] L. Wajciechowski, *Rozz. Chem.*, **43,** 1205 (1969); *Chem. Abstr.*, **71,** 124373 (1969).
[84] W. B. Wright, J. G. O. Morton, and A. S. Tomcuficik, *J. Heterocycl. Chem.*, **16,** 1345 (1979).
[85] G. Riedel and W. Deuschel, *Brit.*, 971, 048 (Cl. C09b), Sept. 30, 1964; *Ger. Appl.* Dec. 19, 1959; *Chem. Abstr.*, **62,** 1774 (1965).
[86] A. K. El-Shafei, G. Vernin, and J. Metzger, *Gazz. Chim. Ital.*, **111,** 413 (1981).
[87] C. O. Okafor, *J. Heterocycl. Chem.*, **18,** 405 (1981).
[88] S. D. Carter and G. H. W. Cheeseman, *Tetrahedron*, **33,** 827 (1977).
[89] C. V. R. Sastry, V. H. S. Krishnam, G. K. A. Narayan, K. Vemana, and M. Vairamani, *Indian J. Chem.* Sec. B, **30B,** 936 (1991).

[90] J. Mohan, *Indian J. Chem.*, Sect. B., **22B,** 270 (1983).
[91] T. R. Ovsepyan, A. Kh. Avetisyan, S. M. Terdzhanyan, E. V. Kazaryan, Y. Z. Ter-Zakharyan, G. M. Paronikyan, and L. G. Akopyan, *Arm. Khim. Zh.*, **43,** 399 (1990); *Chem. Abstr.*, **114,** 122190 (1991).
[92] J. Mohan, G. S. R. Anjaneyulu, and K. V. S. Yamini, *J. Ind. Chem. Soc.*, **68,** 474 (1991).
[93] J. Mohan and P. Verma, *Indian J. Heterocycl. Chem.*, **1,** 211 (1992); *Chem. Abstr.*, **117,** 171395 (1992).
[94] R. P. Gupta, M. L. Sachdeva, and H. K. Pujari, *Indian J. Chem.*, *Sect. B*, **15,** 746 (1977).
[95] G. Palamidessi and L. Bernardi, *Il Farmaco*, **21,** 805 (1966).
[96] C. E. Mixan and R. G. Pew, *J. Org. Chem.*, **42,** 1869 (1977).
[97] M. Carmeli and S. Rozen, *J. Org. Chem.*, **71,** 5761 (2006).