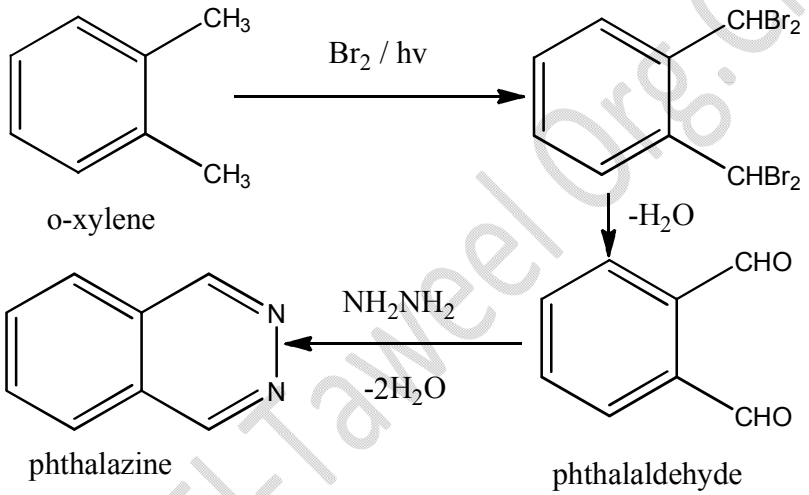
3)Phthalazine

A-Methods of preparation :

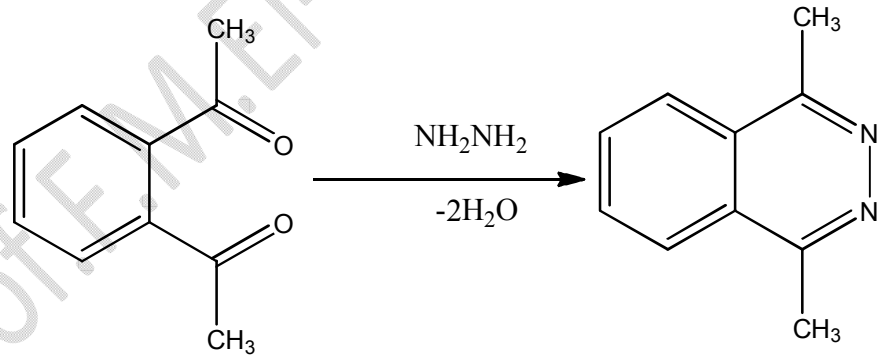
1-By ondensation of hydrazines with o-dialdehydes,o-diesters,o-diacylbenzenes (o-diformylbenzene,o-diacetylbenzene ,o-dibenzoylbenzene) and phthalimide derivatives.



o-xylene

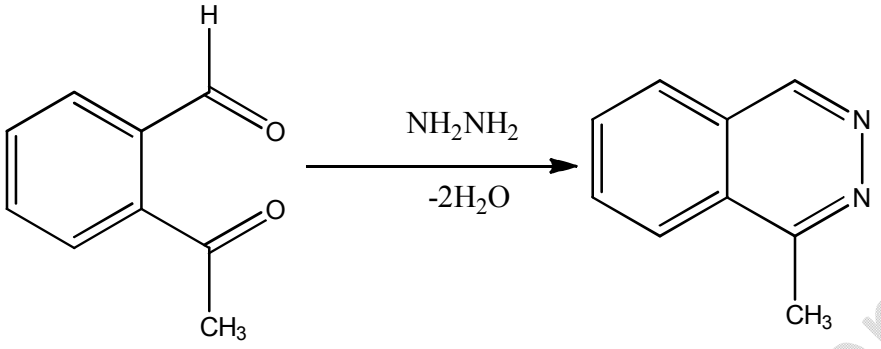
phthalazine

phthalaldehyde

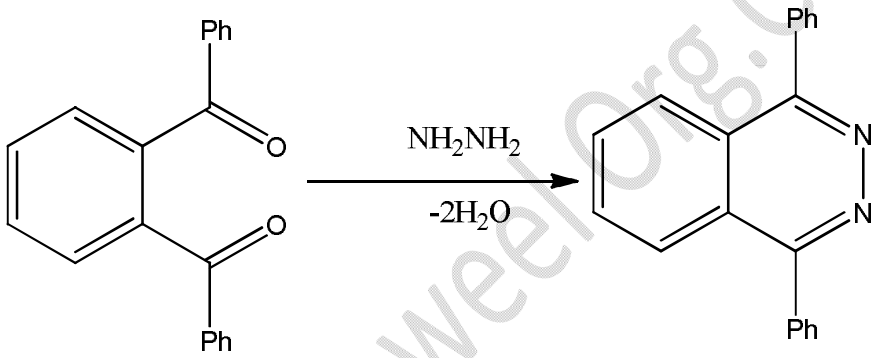


1,2-diacetylbenzene

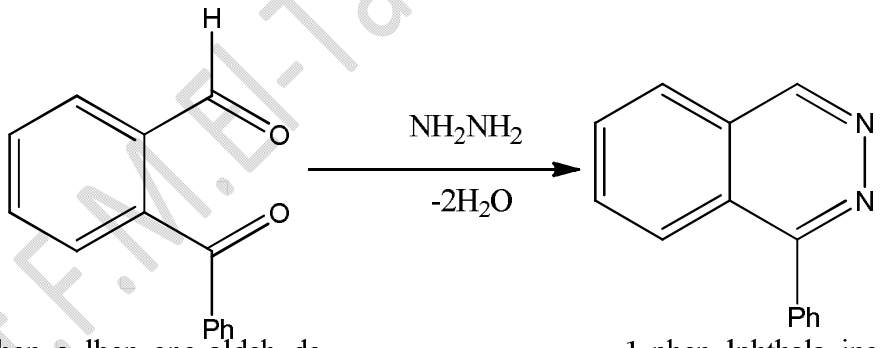
1,4-dimethylphthalazine



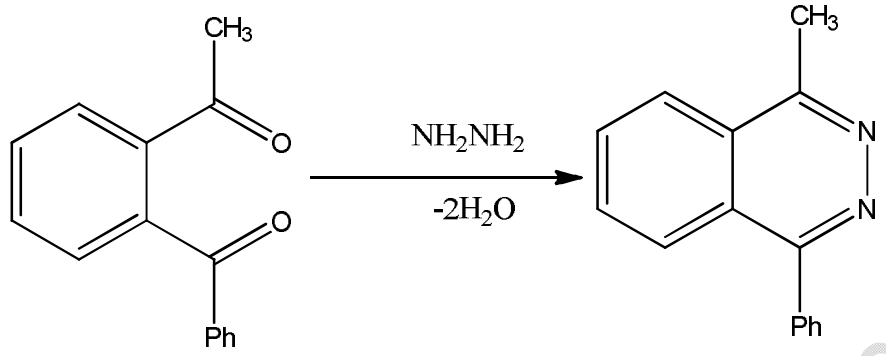
2-acetylbenzenezaldehyde 1-methylphthalazine



1,2-dibenzoylbenzene 1,4-diphenylphthalazine

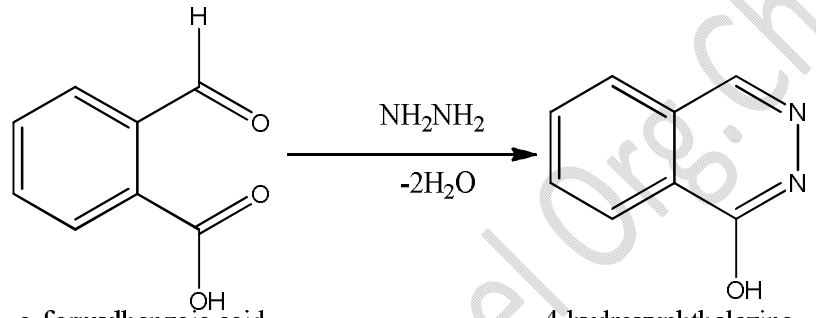


1-benzoylbenzenezaldehyde 1-phenylphthalazine



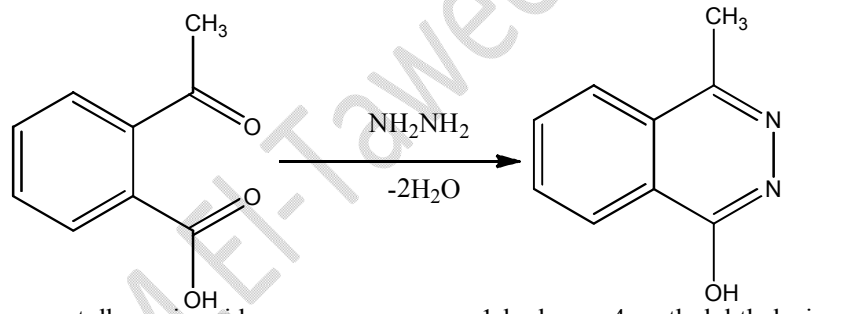
1-acetyl-2-benzoylbenzene

1-methyl-4-phenylphthalazine



o-formylbenzoic acid

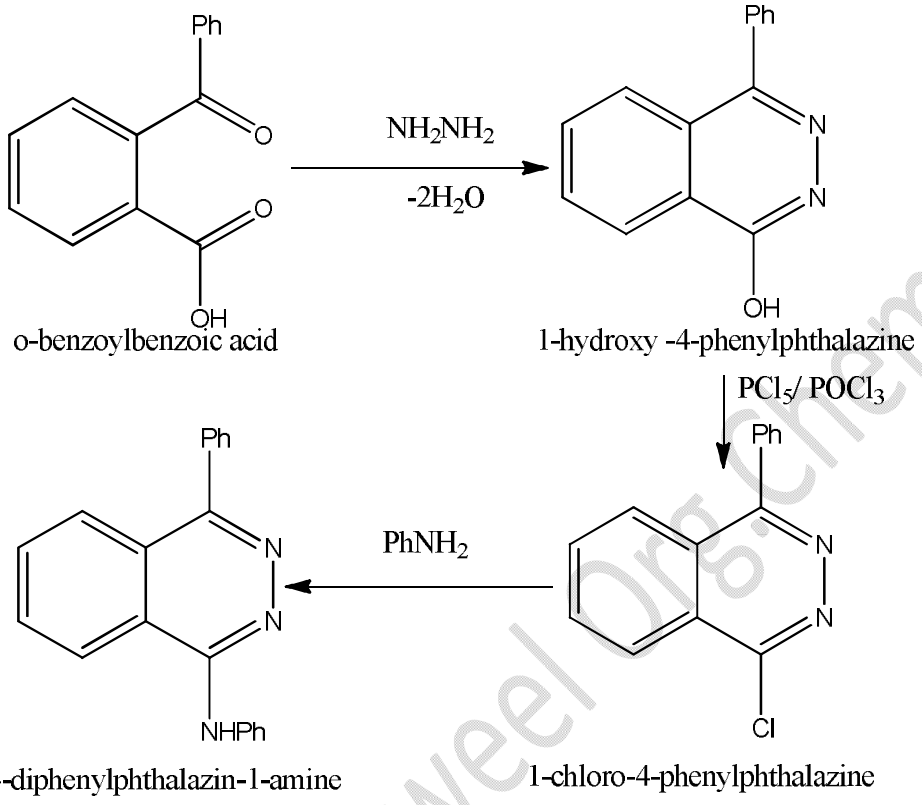
4-hydroxyphthalazine



o-acetylbenzoic acid

1-hydroxy- 4-methylphthalazine

(4-methylphthalazin-1-ol)

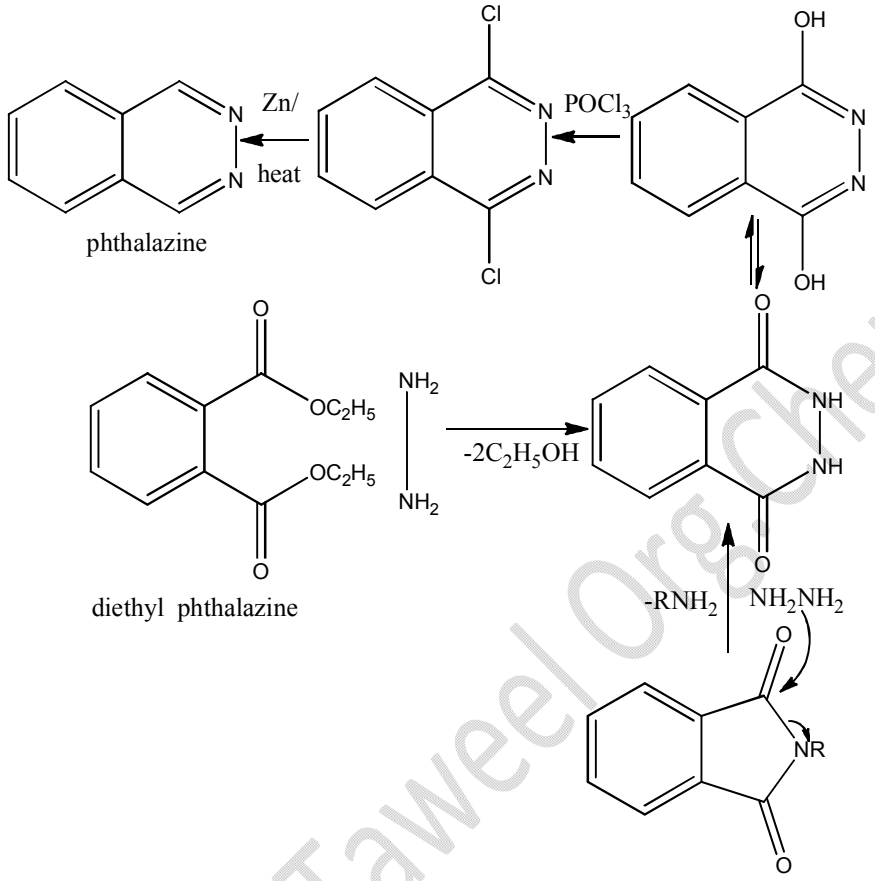


o-benzoylbenzoic acid

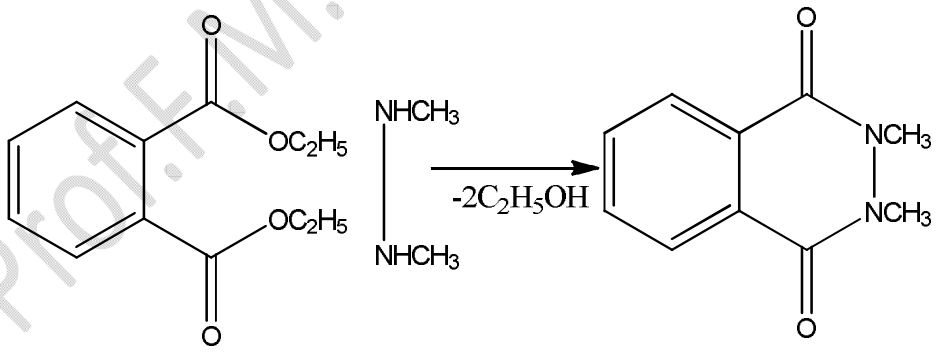
1-hydroxy -4-phenylphthalazine

1-chloro-4-phenylphthalazine

N,4-diphenylphthalazin-1-amine

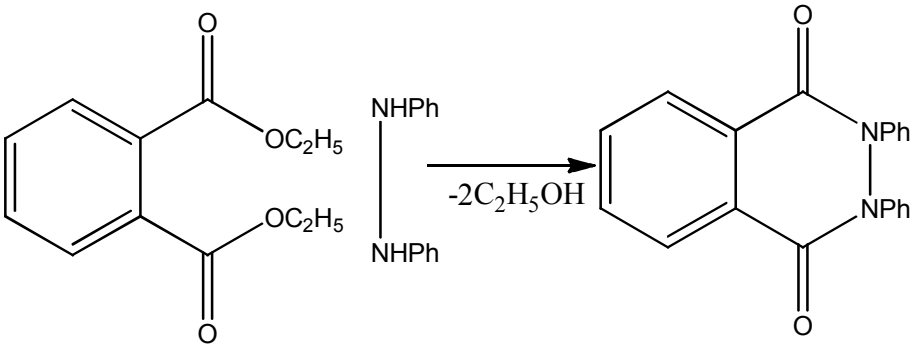


By condensation of 1,2-dimethylhydrazine or 1,2-diphenylhydrazine with diethyl phthalate

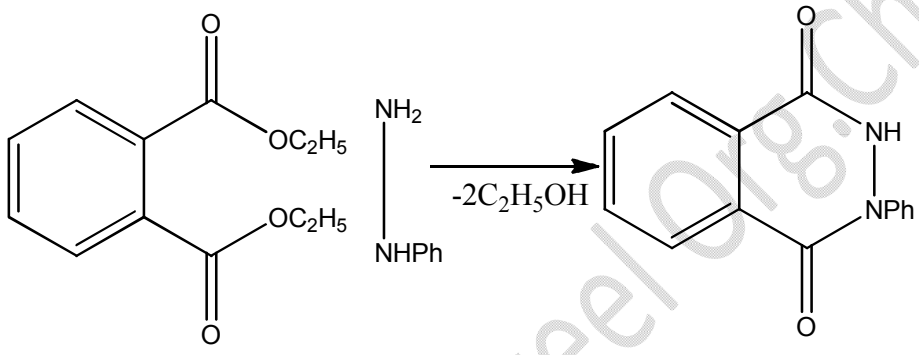


diethyl phthalate

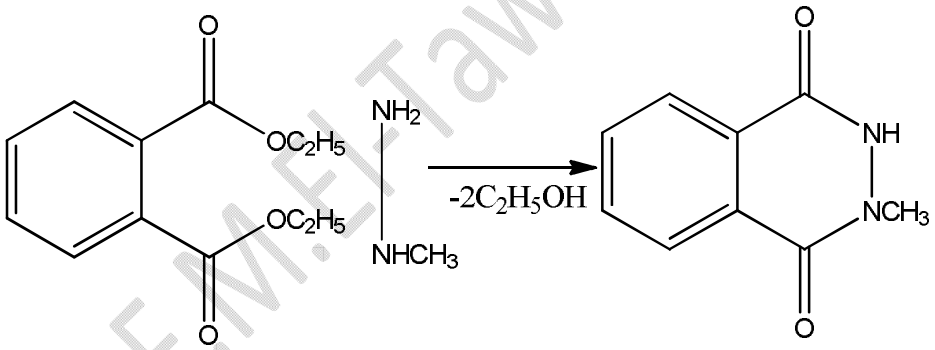
2,3-dimethyl-2,3-dihydrophthalazine-1,4-dione



diethyl phthalate 2,3-diphenyl-2,3-dihydrophthalazine-1,4-dione



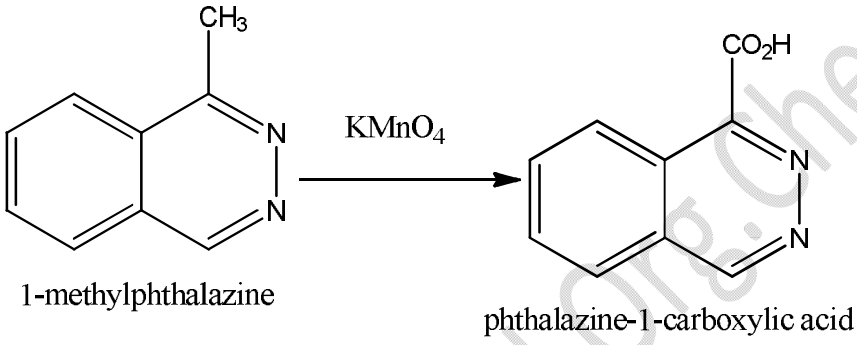
diethyl phthalate 2-phenyl-2,3-dihydrophthalazine-1,4-dione



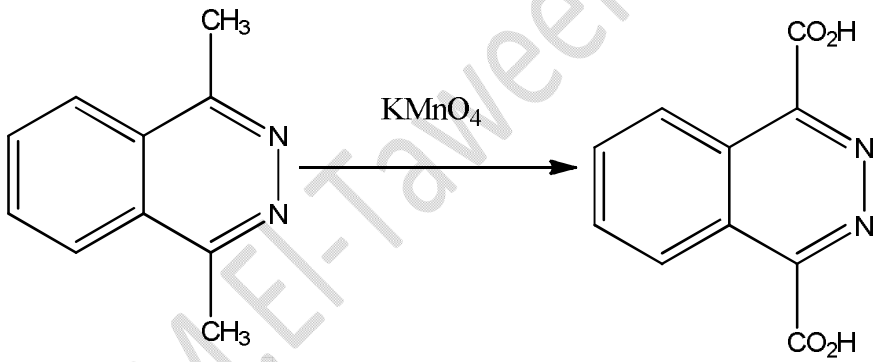
diethyl phthalate 2-methyl-2,3-dihydrophthalazine-1,4-dione

Reactivity of the methyl groups at C-1 and C-4 positions :

Methyl groups in the 1-and 4-positions are readily condense with aromatic aldehydes and other carbonyl compounds .They can also oxidized with oxidizing agents such as $KMnO_4$ and SeO_2.



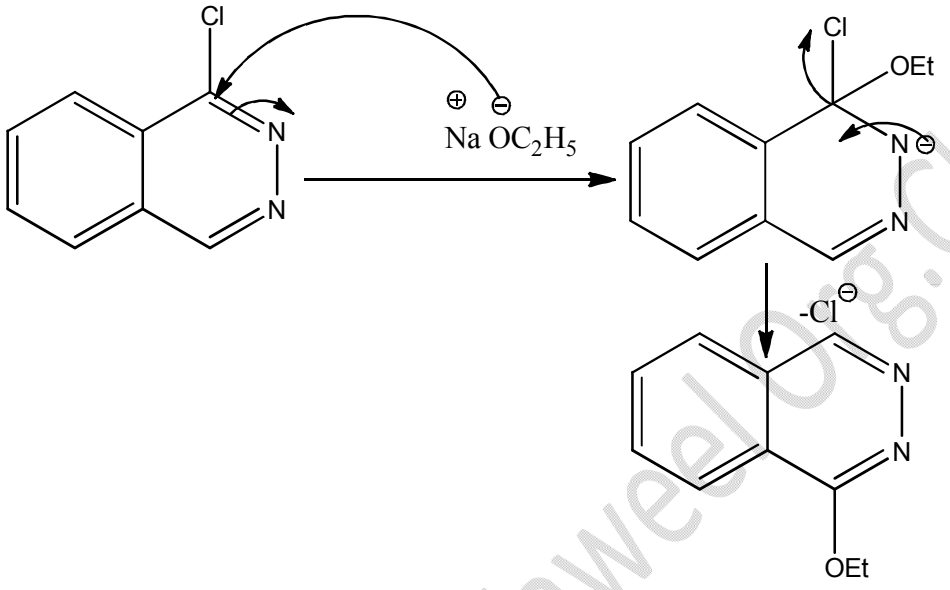
1-methylphthalazine phthalazine-1-carboxylic acid



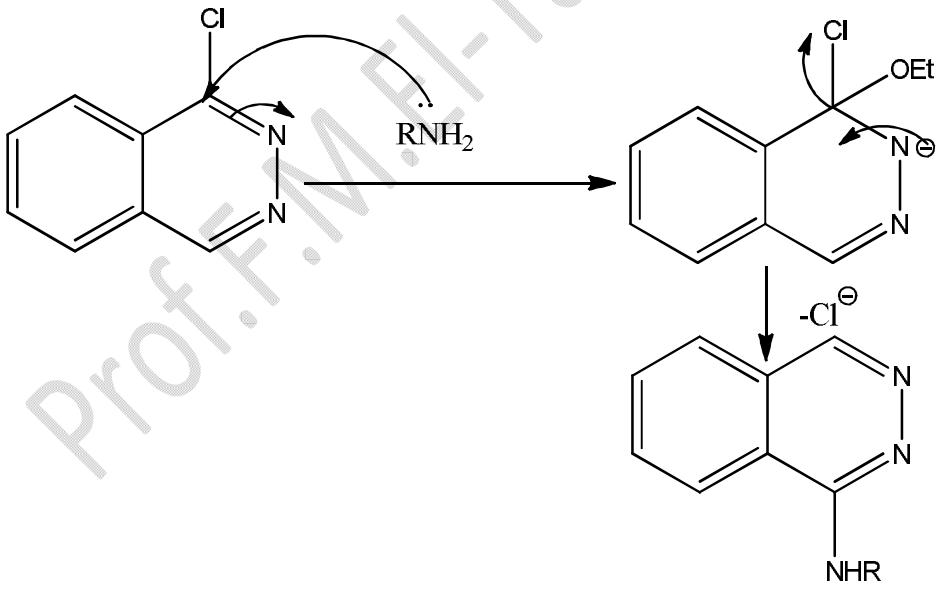
1,4-dimethylphthalazine phthalazine-1,4-dicarboxylic acid

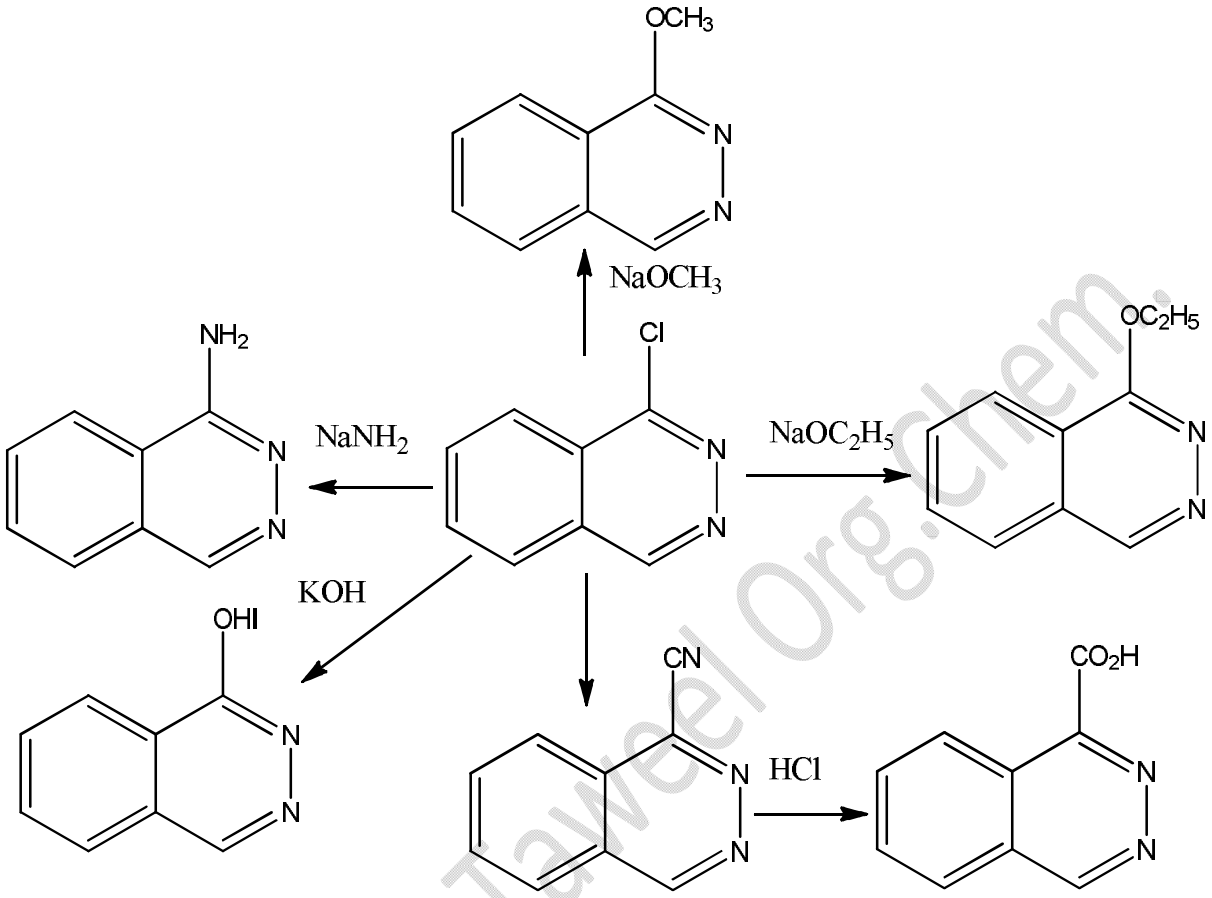
Nucleophilic substitution reactions:

The effect of the second ring nitrogen atom is demonstrated by a comparison of the rates of reaction of 1-chlorophthalazine and 1-chlorouinoline with ethoxide ions at 20^{o}C,the rates are about 3000 to isoquinoline.



1-ethoxyphthalazine



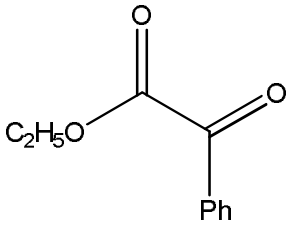


4)Quinoxaline

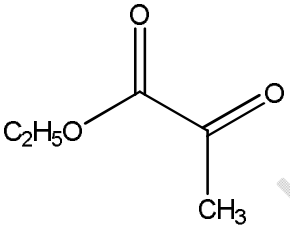
The standard method of quinoxaline is the interaction of o-phenylenediamine with an α-diketones, α-ketoesters or diethyl oxalate ,a 2,3-disubstituted quinoxalines are formed *via* two consecutive Schiff base formations.

A simple extension of the method using α-ketoesters gives the quinoxalin-2(1*H*)-ones.

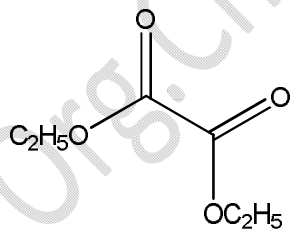
Some reagents:



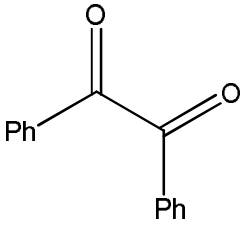
ethyl 2-oxo-2-phenylacetate



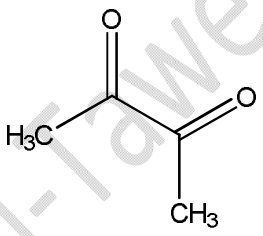
ethyl 2-oxopropanoate



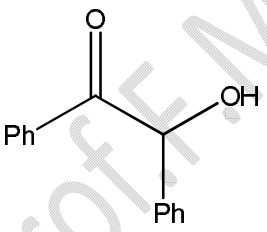
diethyl oxalate



benzil

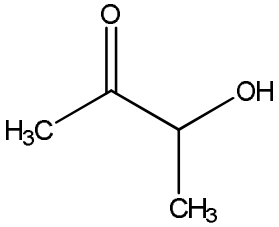


biacetyl



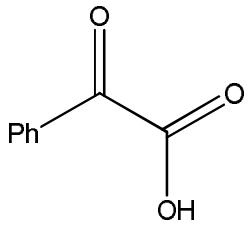
2-hydroxy-1,2-diphenylethanone

benzoin

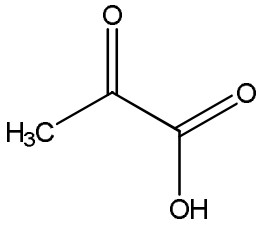


3-hydroxybutan-2-one

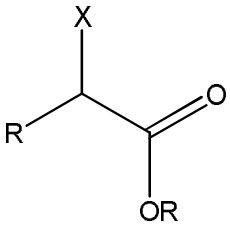
acetoin

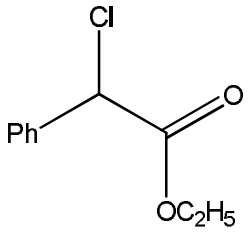


2-oxo-2-phenylacetic acid

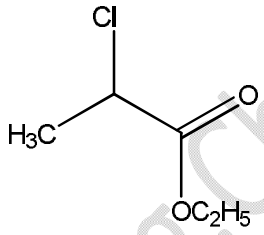


2-oxopropanoic acid

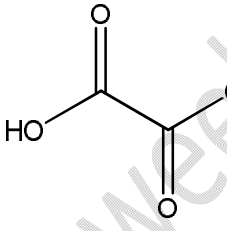




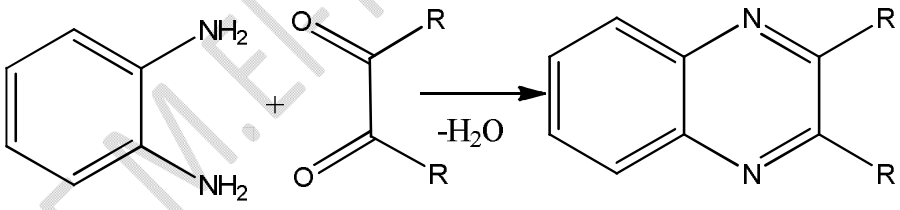
ethyl 2-chloro-2-phenylacetate



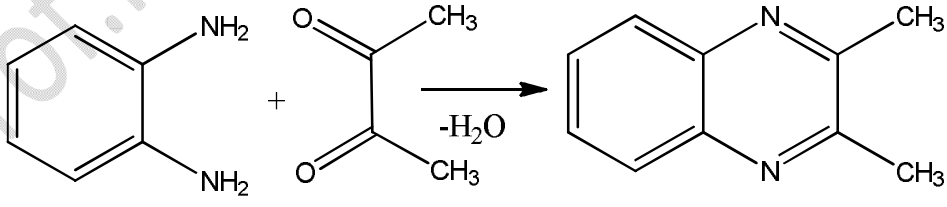
ethyl 2-chloropropanoate



oxalic acid

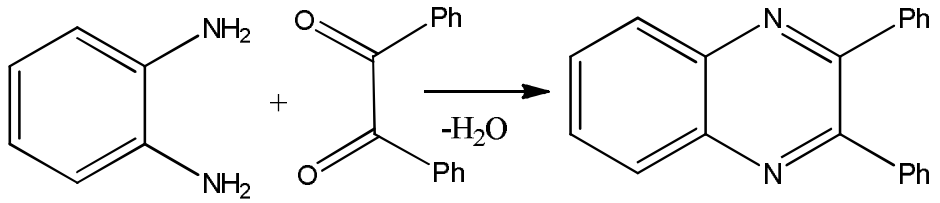


diacyl



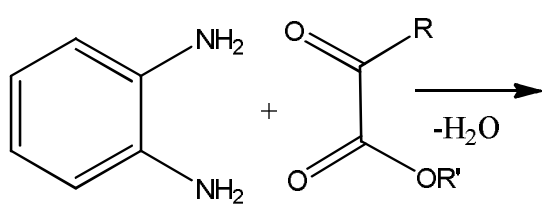
diacetyl

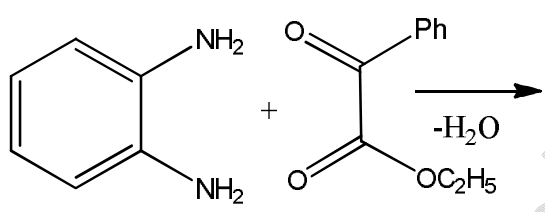
2,3-dimethylquinoxaline



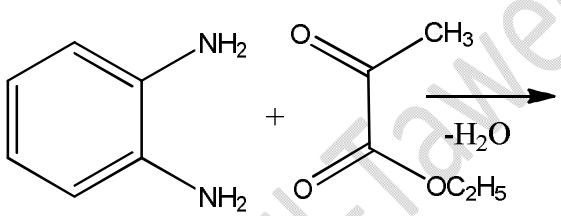
benzil

2,3-diphenylquinoxaline

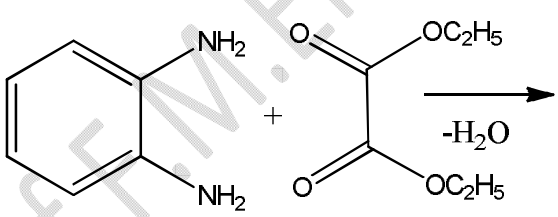




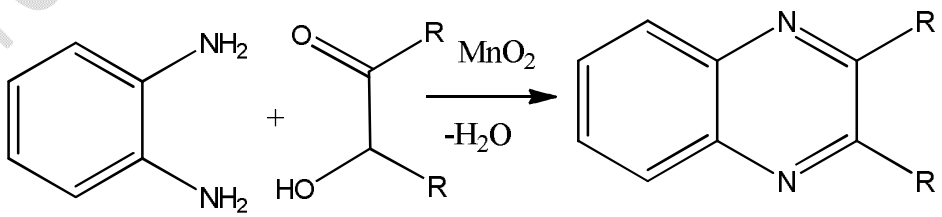
3-phenylquinoxalin-2-ol



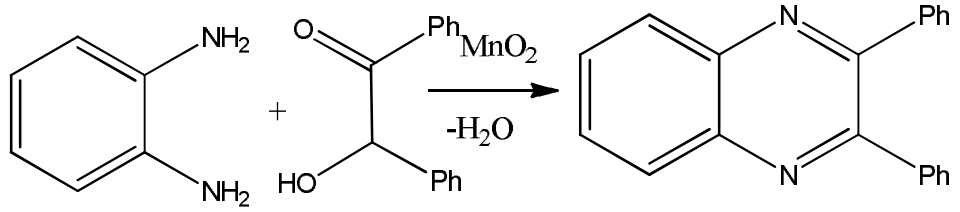
3-methylquinoxalin-2-ol



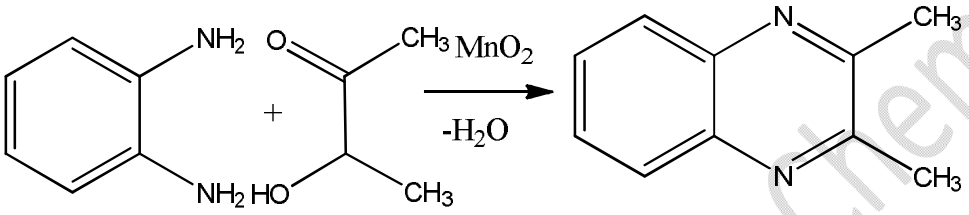
quinoxaline-2,3-diol



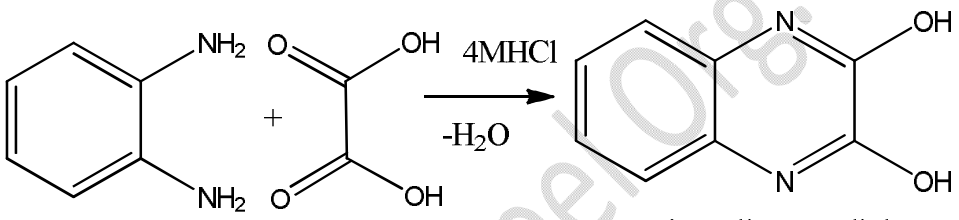
acyloin



benzoin 2,3-diphenylquinoxaline



acetoin 2,3-dimethylquinoxaline

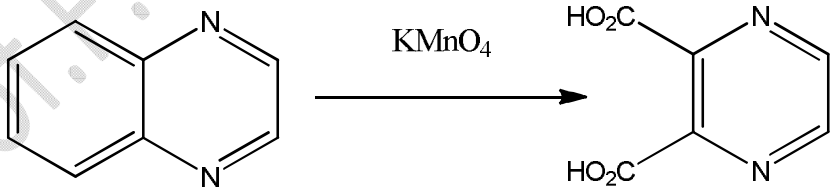


oxalic acid quinoxaline-2,3-diol

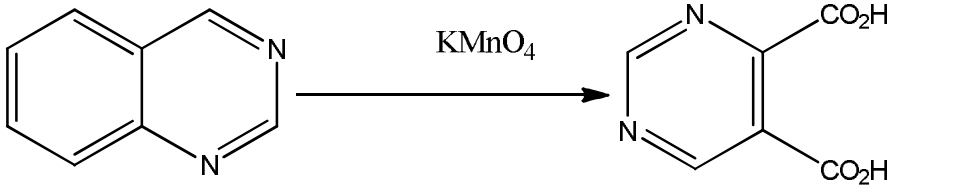
Oxidation of benzodiazenes:

1-With $KMnO_4$:

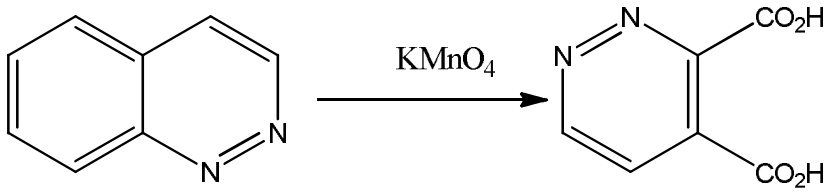
In general,oxidation of benzodiazenes ,with alkaline $KMnO_4$,normally leads to destruction of the carbocyclic ring and formation of the corresponding diazene dicarboxylic acids.



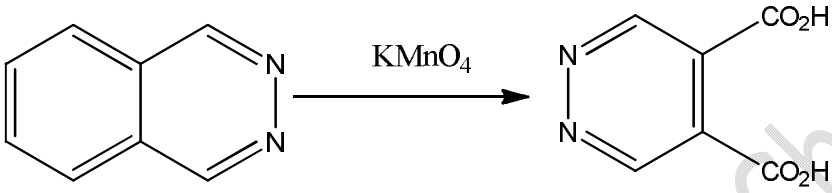
quinoxaline pyrazine-2,3-dicarboxylic acid



quinazoline pyrimidine-4,5-dicarboxylic acid

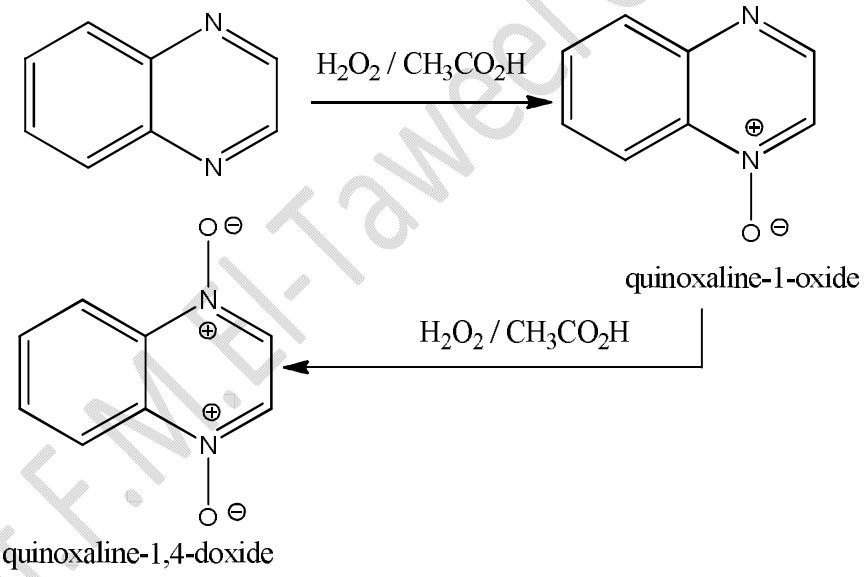


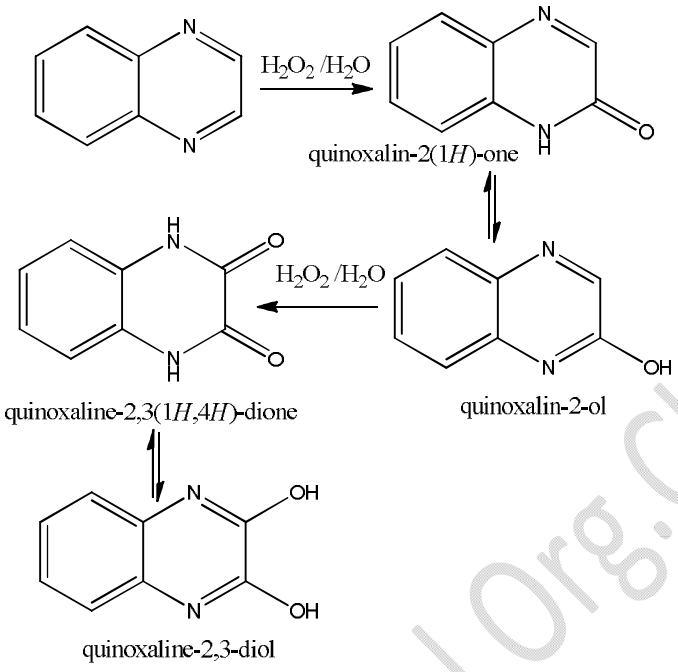
cinnoline pyridazine-3,4-dicarboxylic acid



phthalazine pyridazine-4,5-dicarboxylic acid

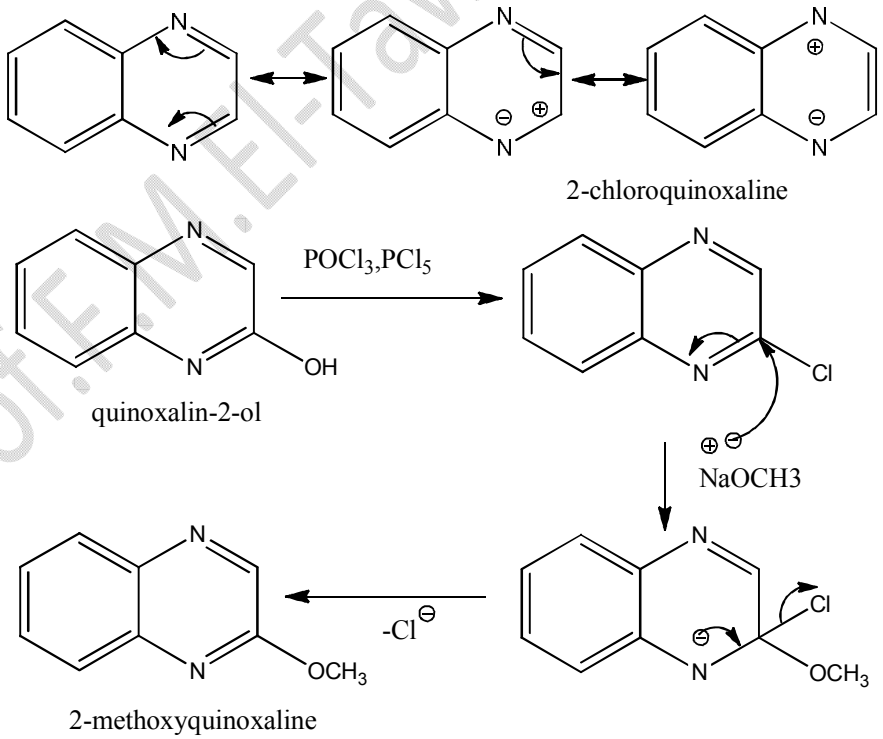
2-Oxidation of quinoxaline with preacetic acid(H_2O_2/CH_3CO_2H):

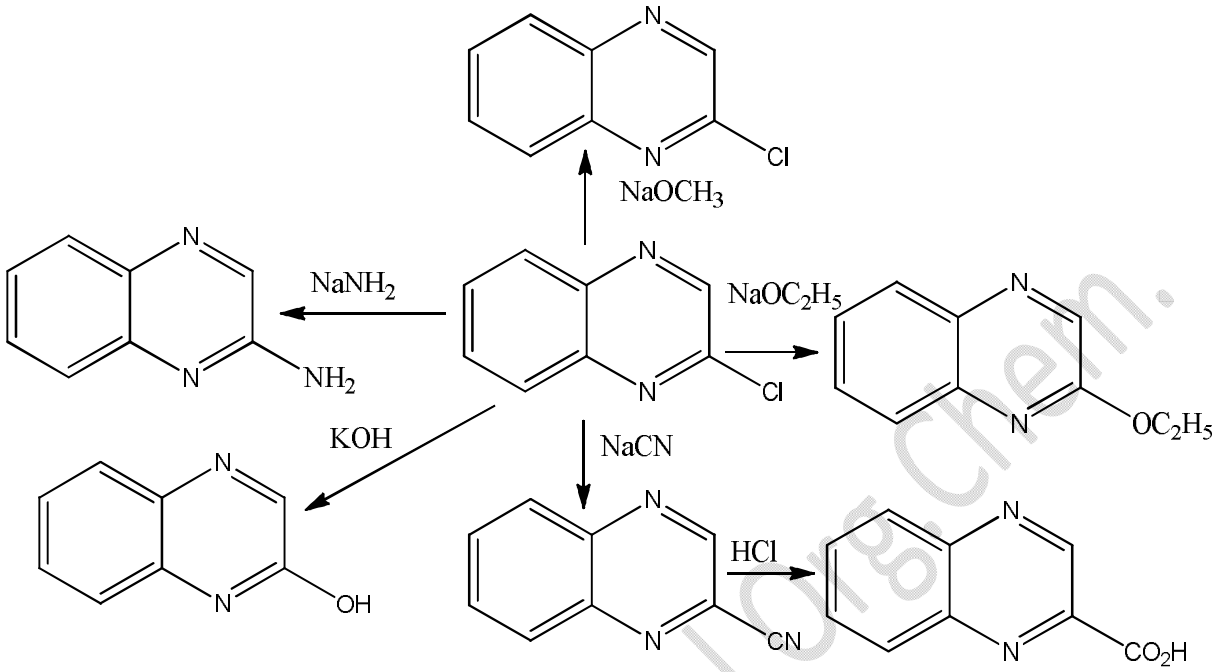




Nucleophilic substitution in quinoxaline:

This is expected to take place at C-2 or C-3 ;they are equivalent in this case.

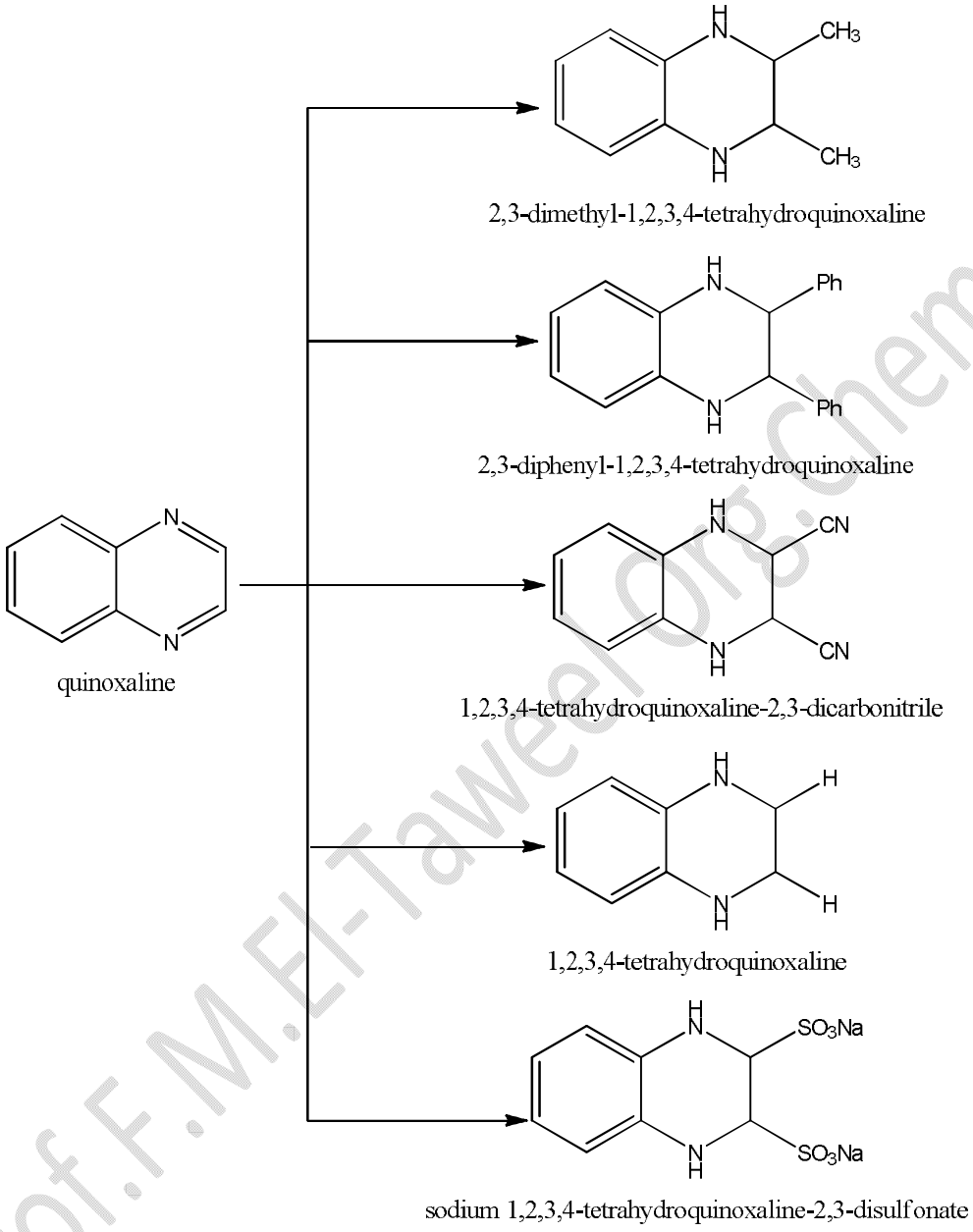




Nucleophilic addition in quinoxaline:

The addition of strongly nucleophilic reagents to the 1,2-bonds is general for quinoxaline without substituents in the 2,3-positions.

Organometallic reagents,cyanide ions and bisulphate ions .All add to these positions giving 1,2,3,4-tetrahydro quinoxalines.

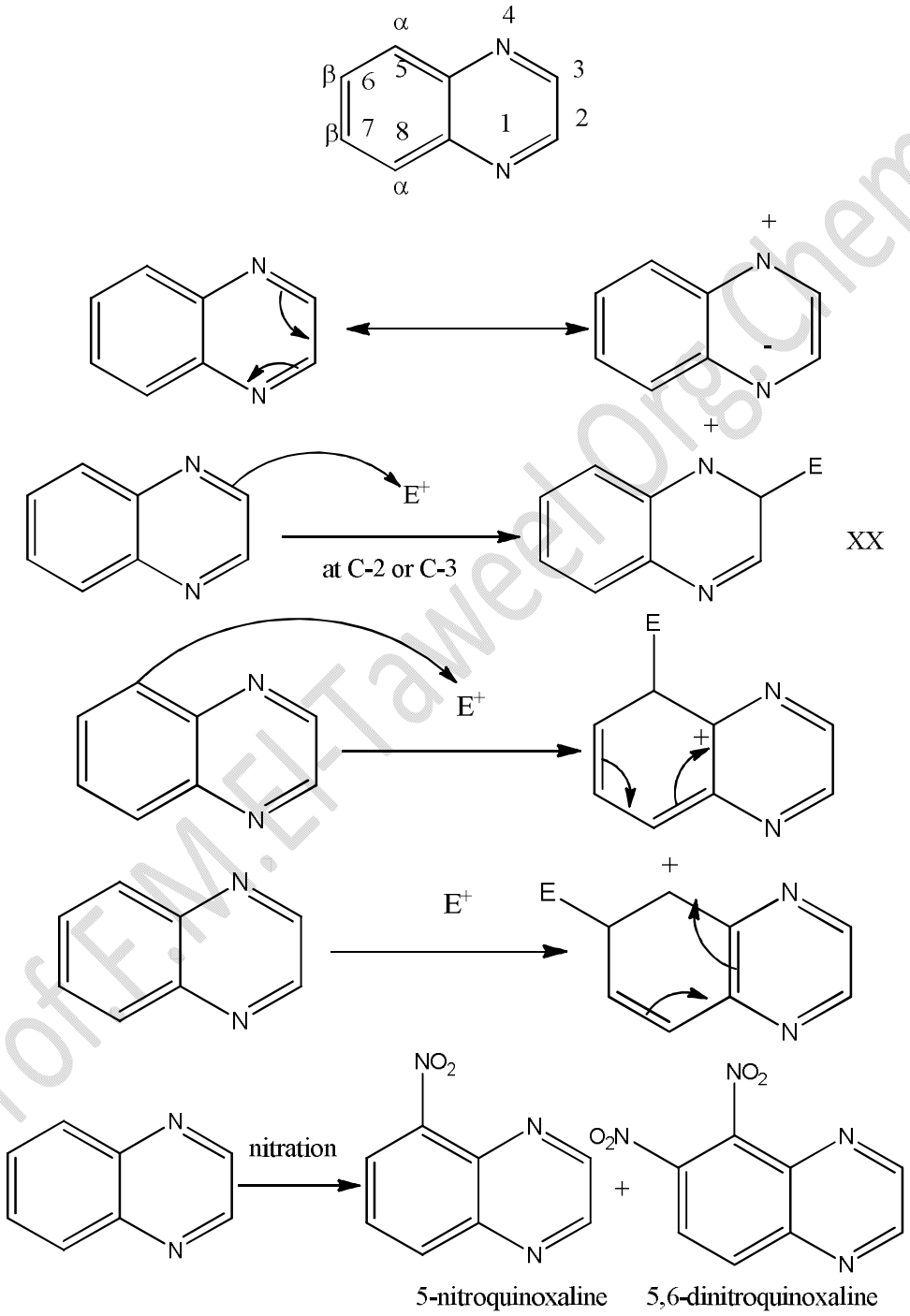


Electrophilic substitution in quinoxaline:

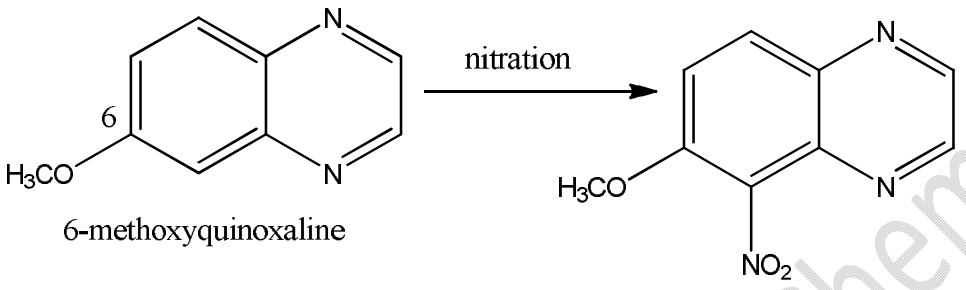
Electrophilic substitution occurs under forcing conditions in quinoxaline itself,a small amount of 5-nitroquinoxaline being formed.

In fact,the major product from the nitration of quinoxaline is the 5,6-dinitro quinoxaline .

This is curious since the predicted major product is 5,7-dinitroquinoxaline by analogy with 5- or 8-nitroquinoxalines.

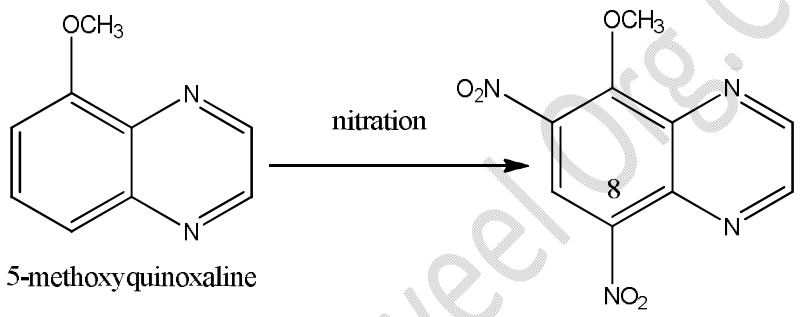


Nitration of quinoxalines having electron donating substituents proceeds as expected ,the (5-,8-)positions being more reactive than the (6-,7-) positions.



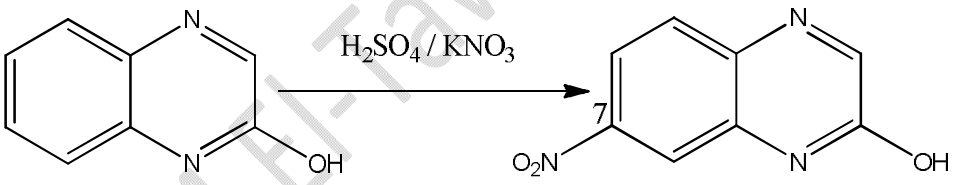
6-methoxyquinoxaline

6-methoxy-5-nitroquinoxaline



5-methoxyquinoxaline

5-methoxy-6,8-dinitroquinoxaline



quinoxalin-2-ol

7-nitroquinoxalin-2-ol

Reactivity of methyl groups at C-2 and C-3:

The methyl groups show high reactivity normally associated with a methyl group adjacent to the ring nitrogen ,since they are readily halogenated and undergo a variety of condensation reactions with aromatic aldehydes.