

Heterocyclic Compds.

DATE

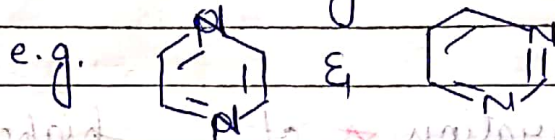
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Defination: It at least one atom other than carbon atom forms a part of the carbocyclic ring system, then it is designated as Heterocyclic compound.

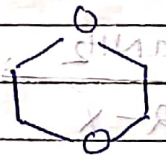
Heterocyclic compounds containing N, O & S are most common & useful in daily life.

Heterocyclic compounds are classified in two groups;

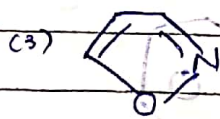
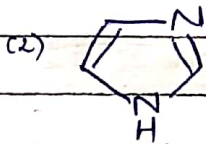
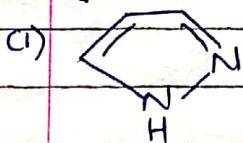
1) Aromatic heterocyclic compounds



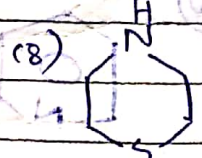
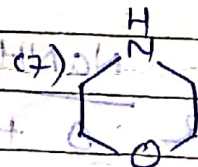
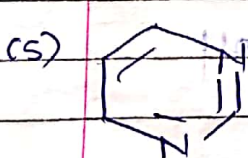
2) Non-aromatic heterocyclic compounds



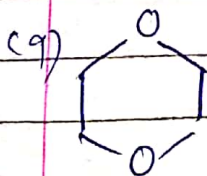
→ Some structures of heterocyclic compds are given below.



Pyrrole Imidazole Isoxazole



Pyrimidine Pyrazine Piperazine Oxazine Thiazine



dioxane

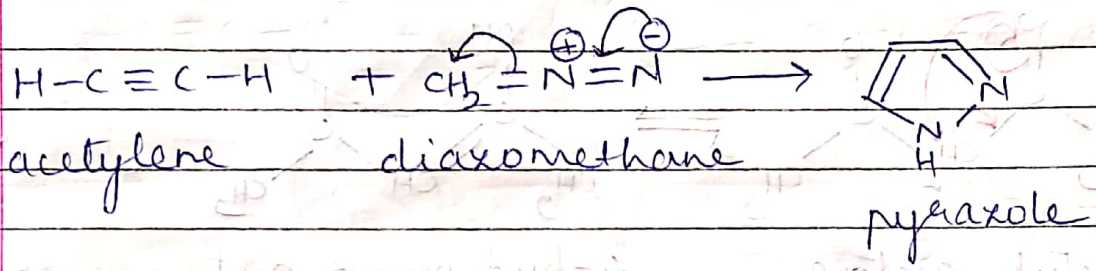
Concerted: Bond making & bond breaking takes place in a single step. Reactive intermediates are not involved

1) Synthesis of Pyrazole

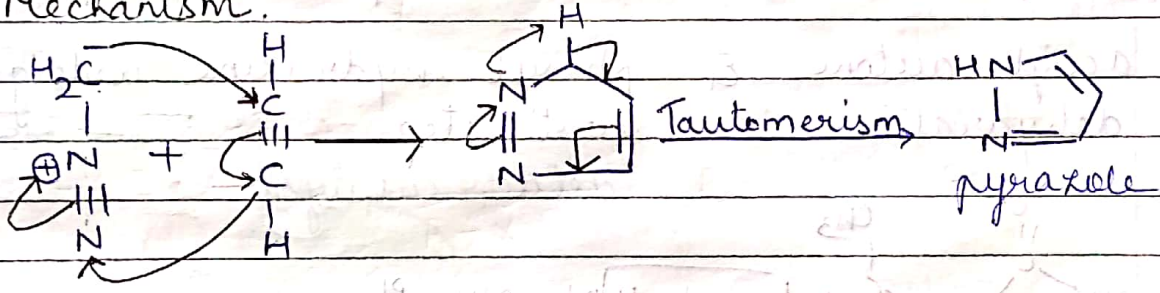
a) Pechmann Pyrazole synthesis

The 1,3-dipolar cycloaddition between diazoalkanes & alkynes resulting in pyrazole formation is known as the Pechmann pyrazole synthesis.

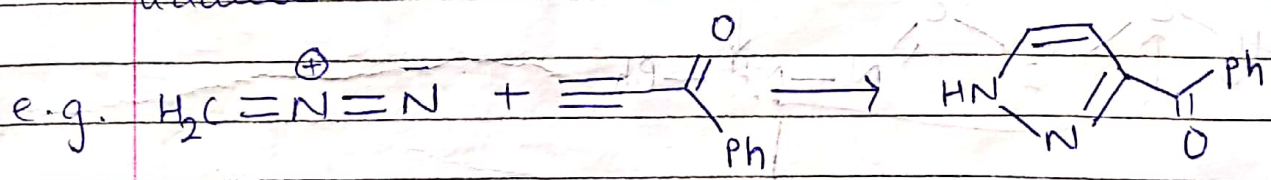
→ Reaction:



→ Mechanism:



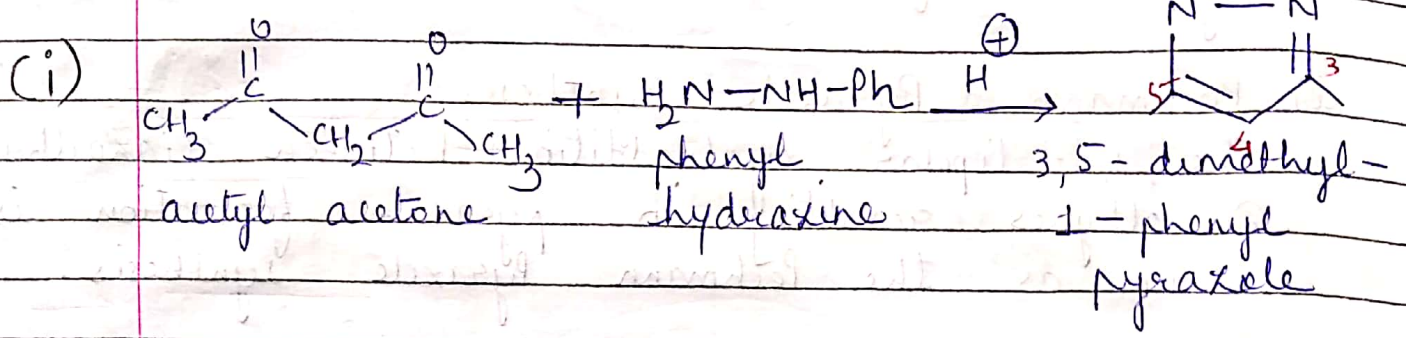
The Pechmann pyrazole synthesis features 1,3-dipolar cycloaddition between diazoalkane & an alkyne followed by tautomerization to give pyrazole. The reaction is an example of concerted addition.



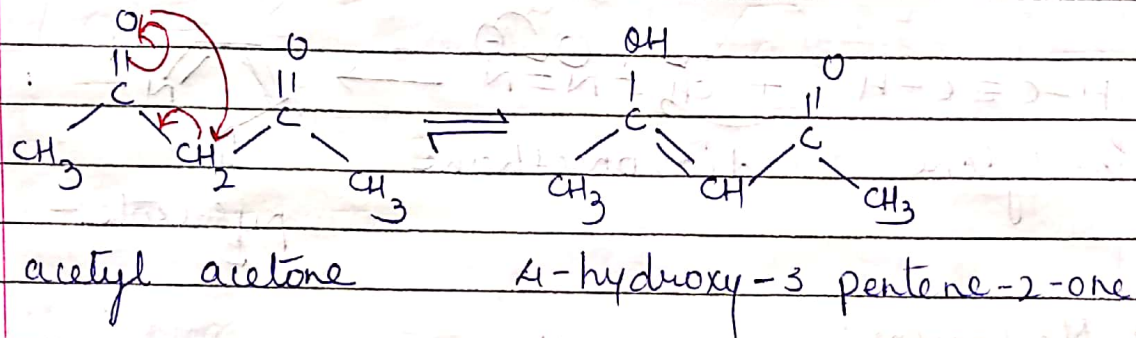
b) Knorr pyrazole synthesis

The Knorr pyrazole synthesis is an organic reaction used to convert a hydrazine or its derivatives & 1,3-dicarbonyl compd to a pyrazole using an acid catalyst.

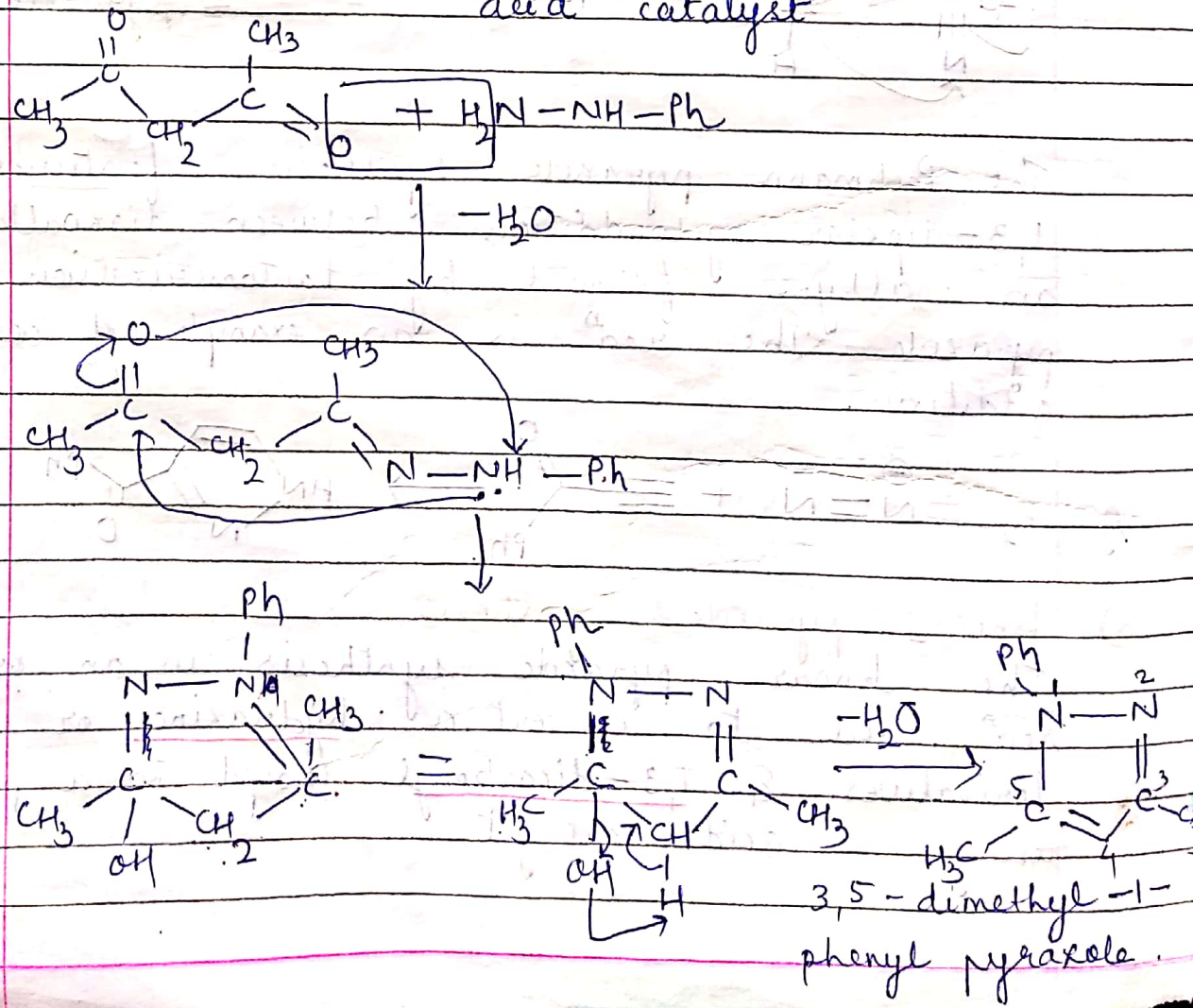
Reaction



Mechanism:

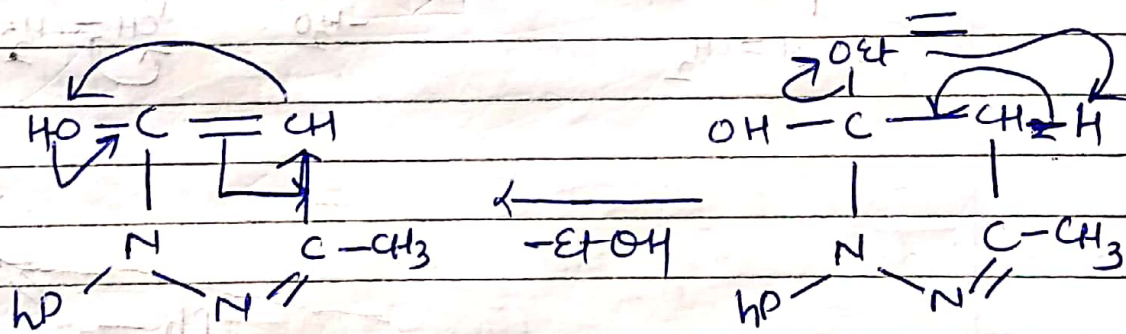
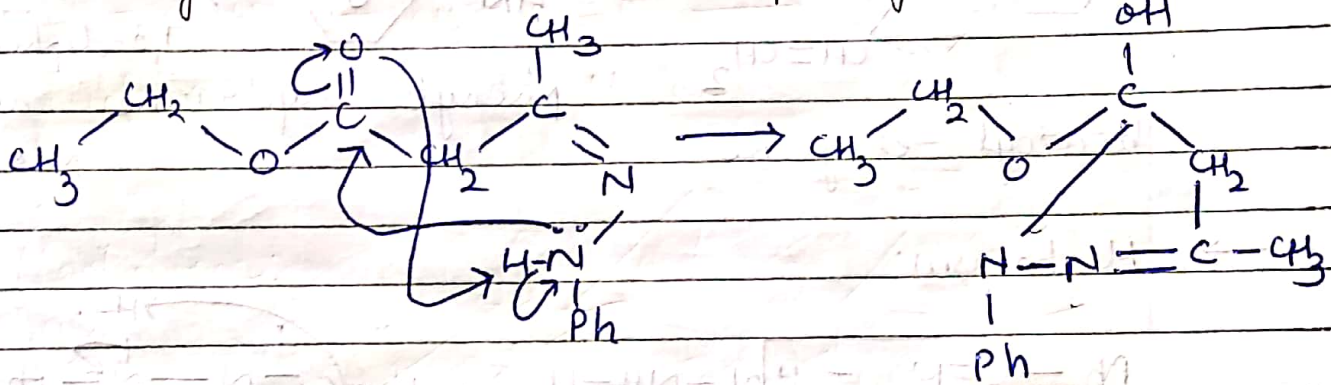
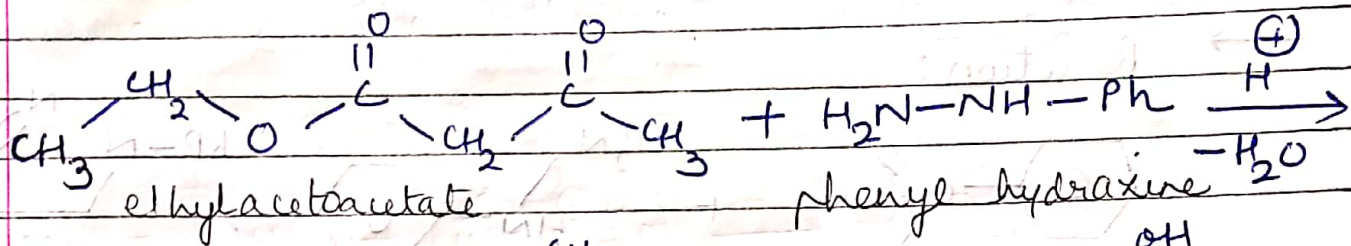


acetyl acetone & phenyl hydrazine undergoes dehydration in first step in presence of acid catalyst

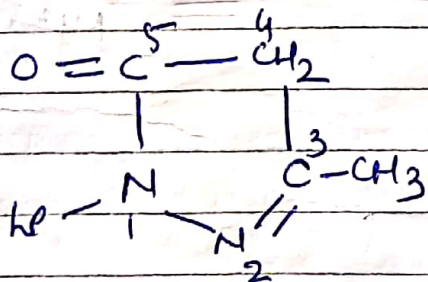


(ii) ~~Synthesis of 3-methyl-1-phenyl-5-pyrazolone~~
 → 3-methyl-1-phenyl-5-pyrazolone can be also synthesized by applying above mechanism to ethyl acetoacetate & phenyl hydrazine.

Reaction:



keto-enol tautomerism

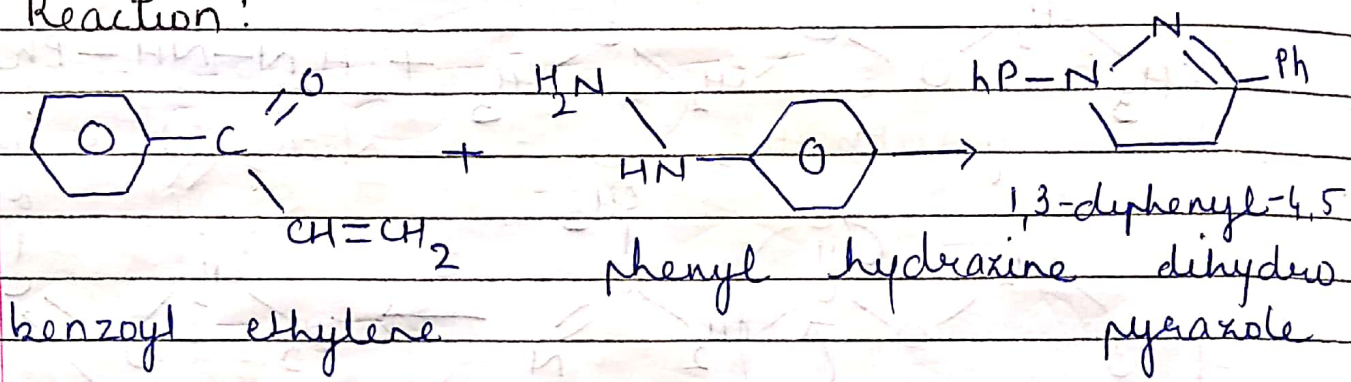


3-methyl-1-phenyl-5-pyrazolone

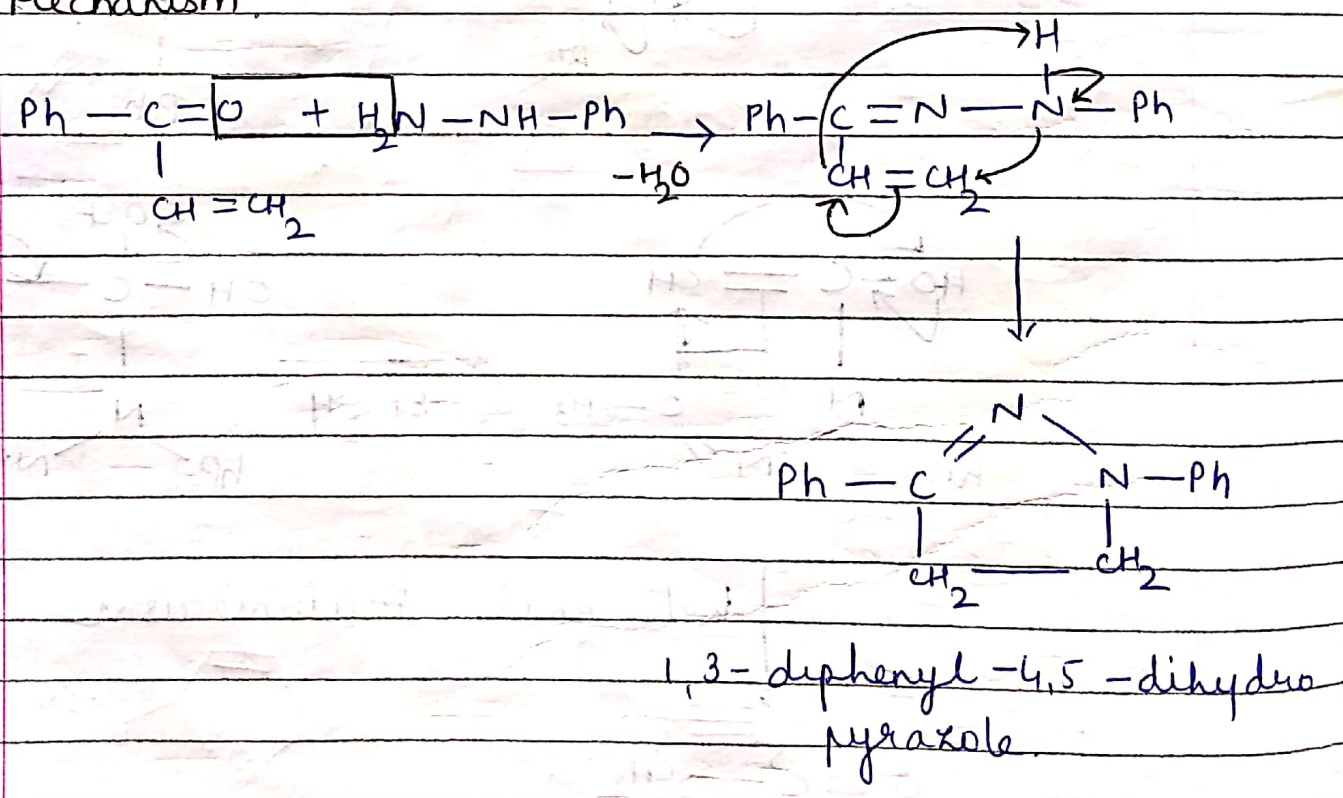
(iii) Synthesis of 1,3-diphenyl-4,5-dihydro pyrazole

α, β -unsaturated carbonyl compounds react with hydrazine derivatives to yield pyrazole derivatives.

→ Reaction:



→ Mechanism:





DATE

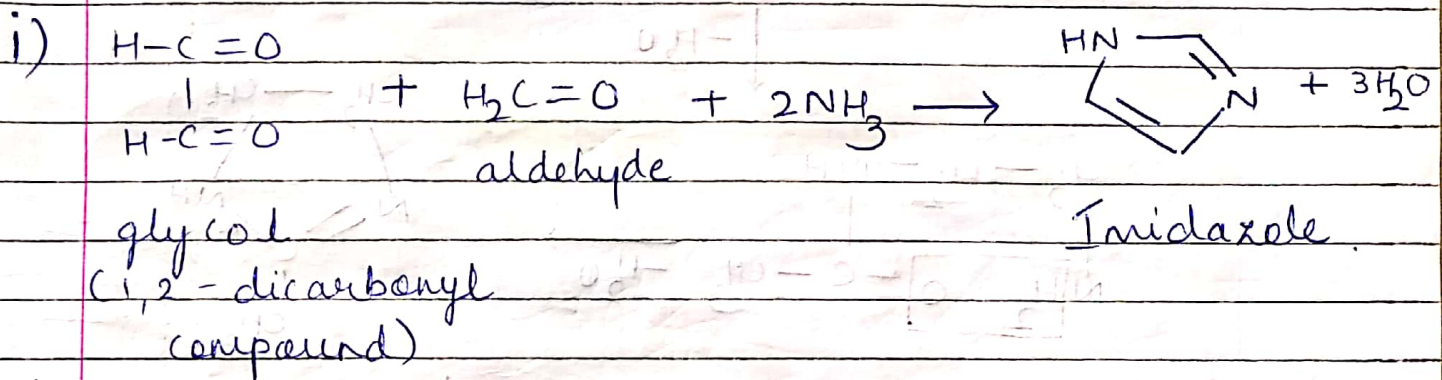
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Synthesis of Imidazole

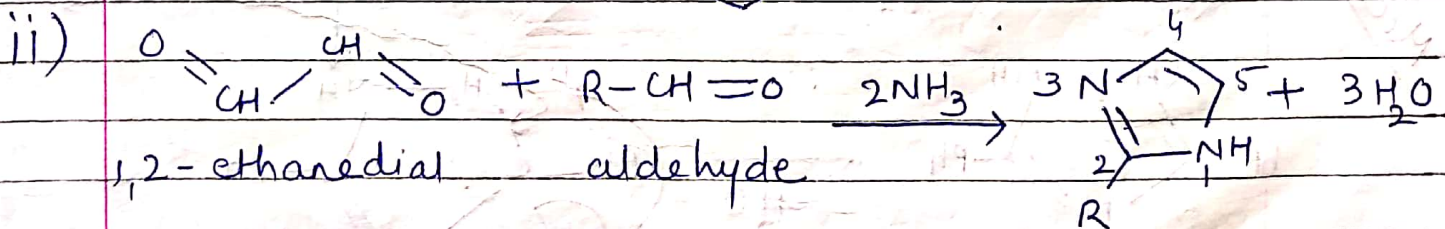
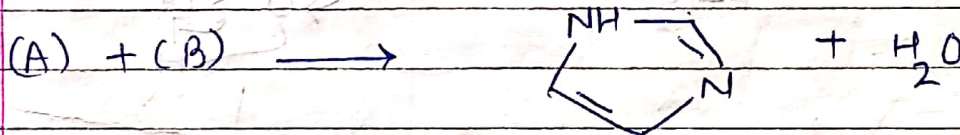
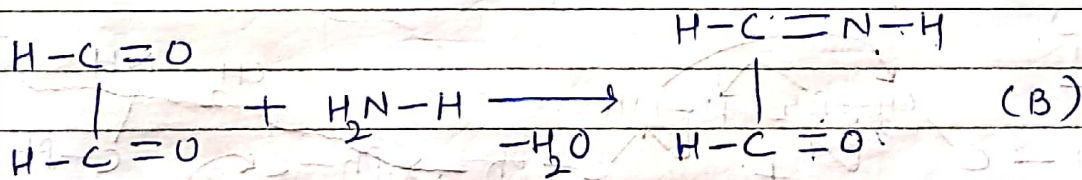
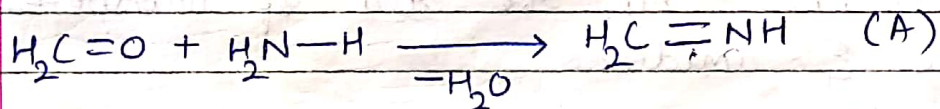
1) Redziszewski Synthesis

In this method Imidazole was synthesized by condensation of a dicarbonyl compound with an aldehyde & ammonia.

Reaⁿ:



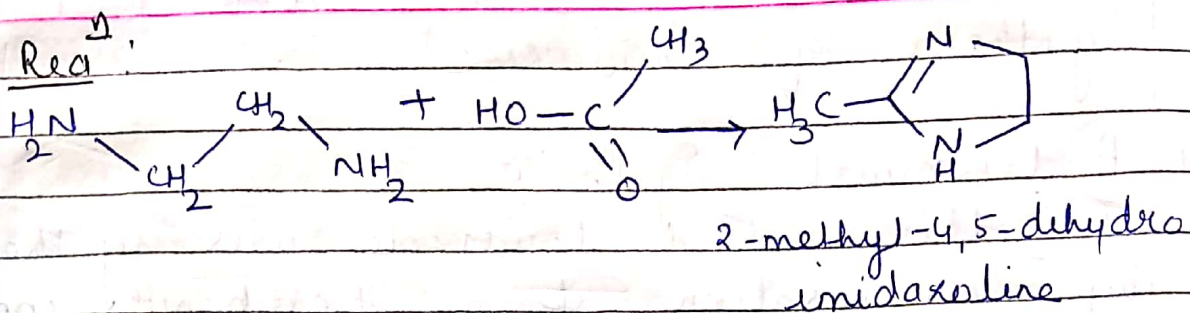
→ Mechanism:



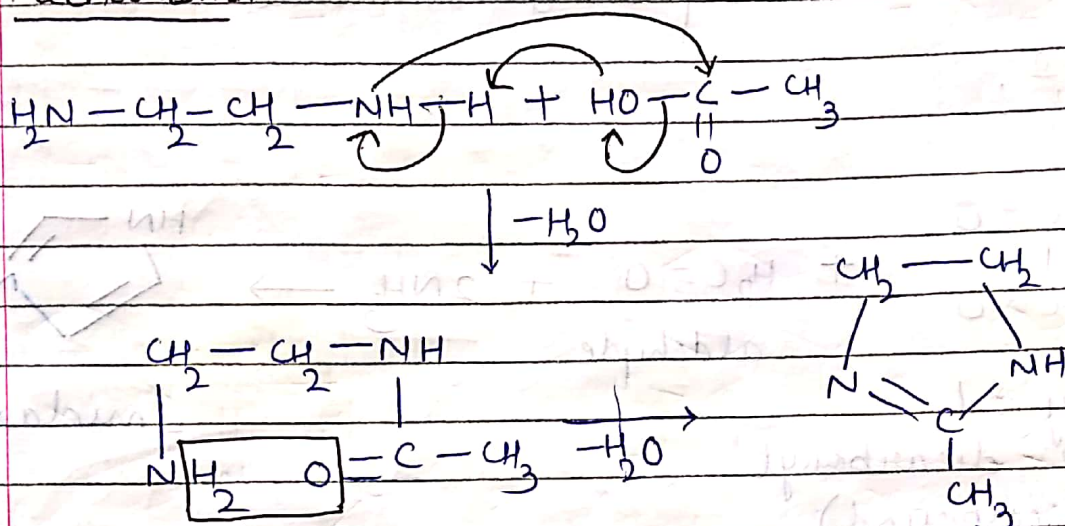
Mechanism is same as above 2-alkyl/aryl Imidazole

2) Synthesis of 2-methyl-4,5-dihydroimidazolone

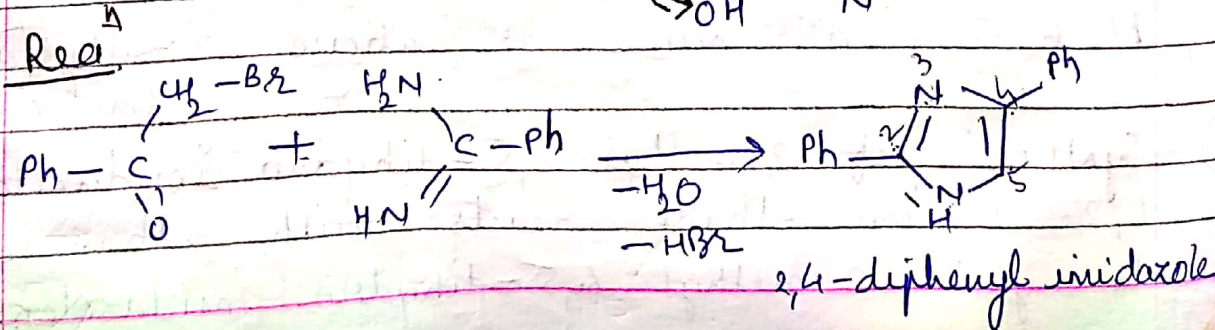
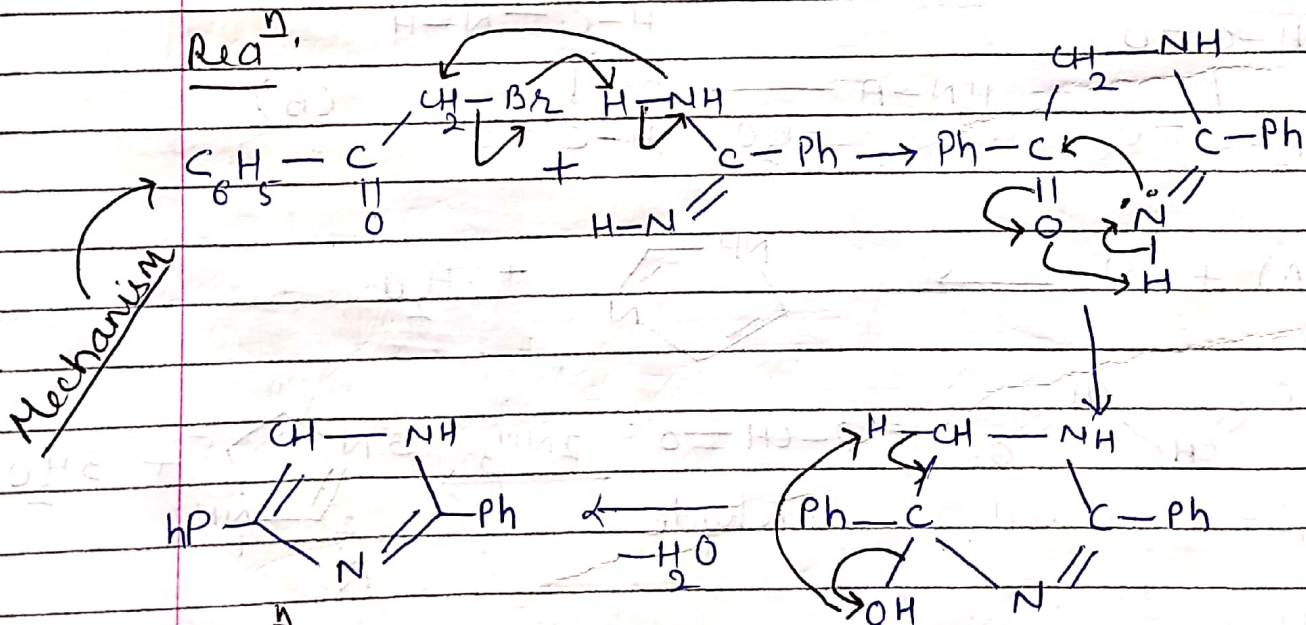
1,2-diamino ethane reacts with ethanoic acid to yield 2-methyl-4,5-dihydroimidazolone



Mechanism:



3) Synthesis of 2,4-diphenyl imidazole
 It is obtained by the reaⁿ of bromoethyl acetophenone & amidine.



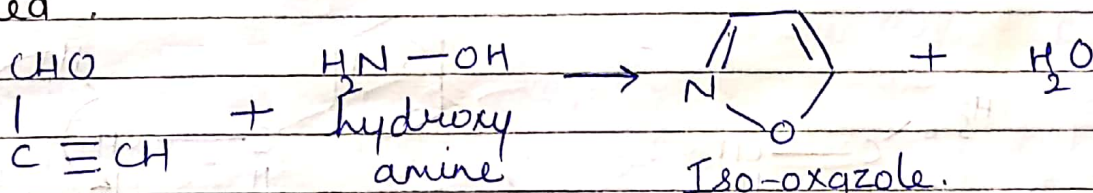
Synthesis of Iso-oxazole

Iso-oxazole is five membered heterocycle containing two heteroatoms i.e. O & N.

→ Synthesis of Iso-oxazole

1) It can be obtained by the reaction of hydroxy amine & propylaldehyde.

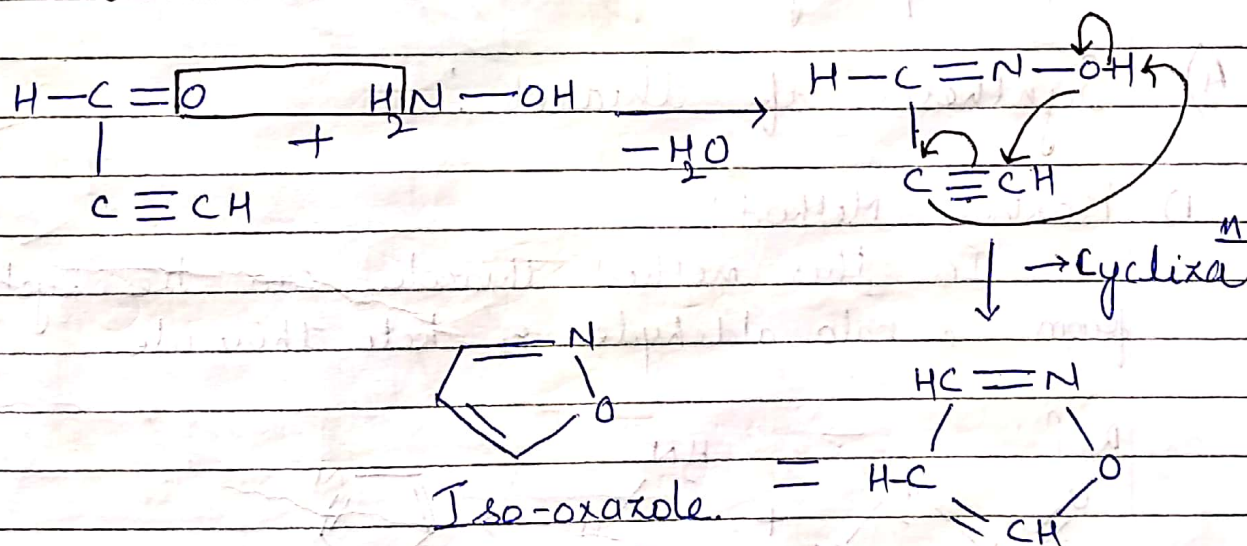
Reaⁿ:



propylaldehyde

Mechanism

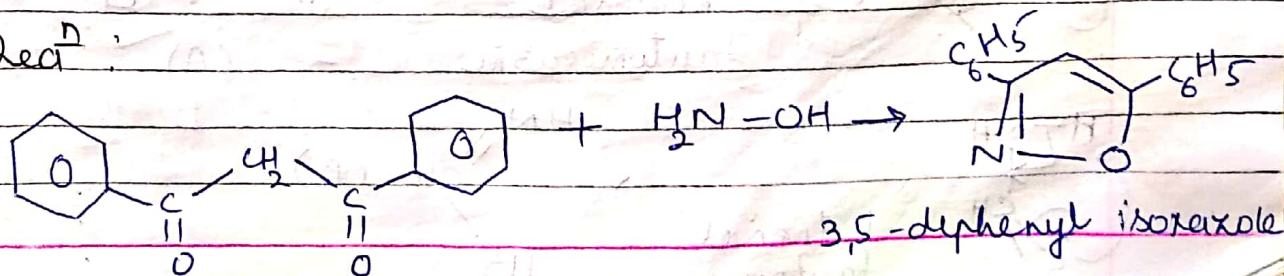
aldoxime



2) Synthesis of 3,5-diphenyl isoxazole

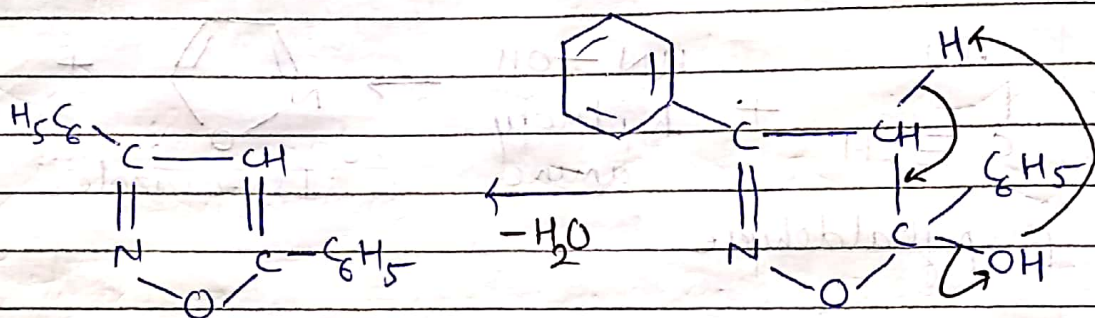
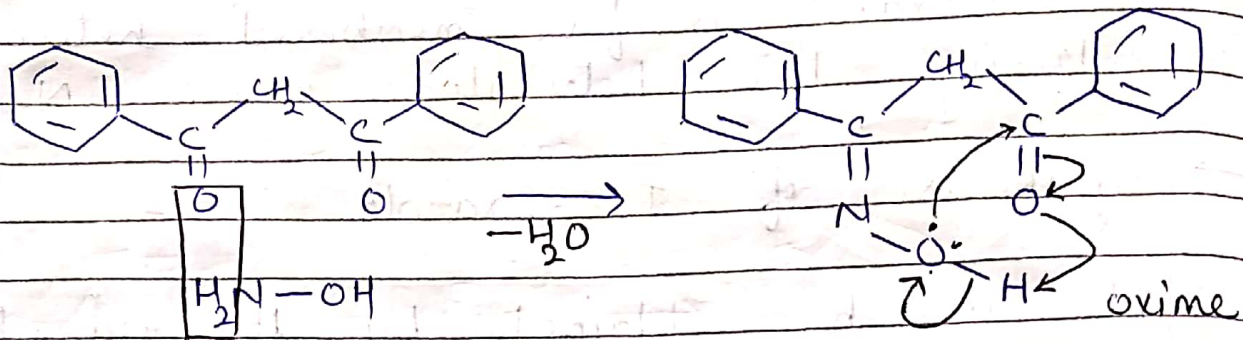
It can be obtained by the reaction of 1,3-diketone comp. with hydroxy amine

Reaⁿ:



Mechanism:

Ketoxime

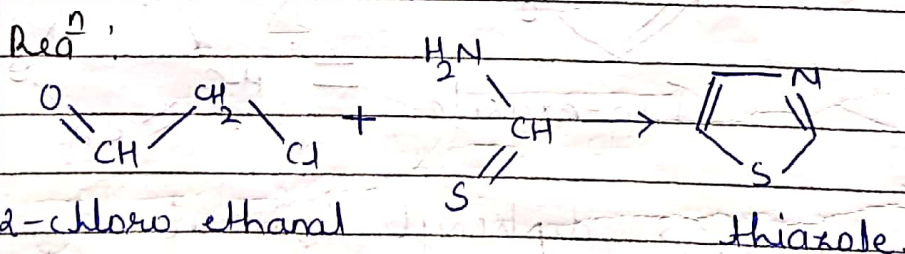


3,5-diphenyl isoxazole

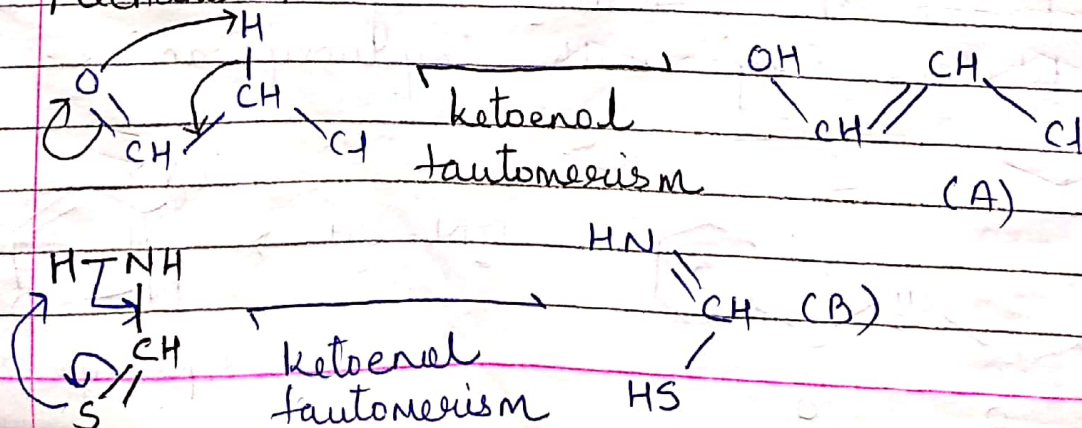
A) Synthesis of thiazole:

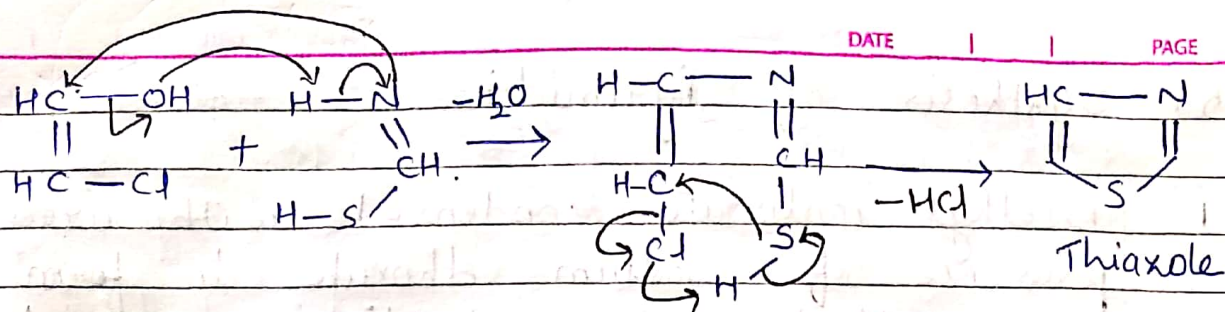
i) Hantzsch Method:

In this method thiazole can be synthesized from α -halo aldehyde & keto thiamide



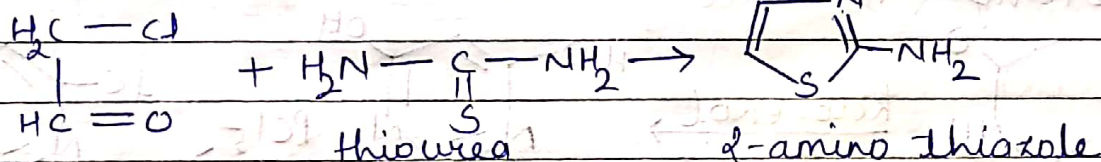
Mechanism:



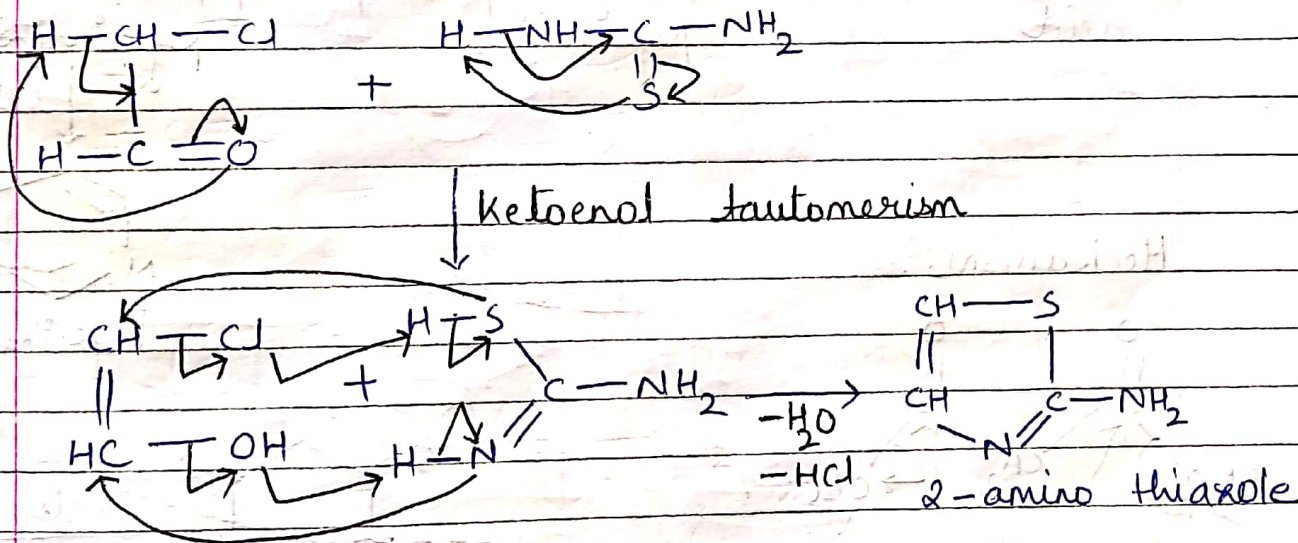


→ Synthesis of 2-amino thiazole
 α -halo aldehyde on treatment with thiourea gives 2-amino thiazole.

Reaⁿ:

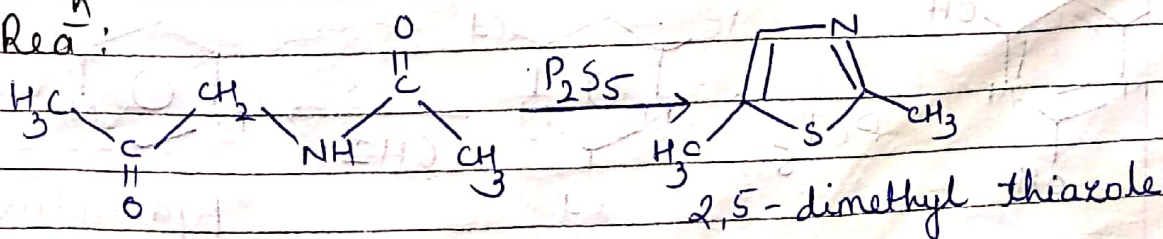


Mechanism:



ii) Acetyl amino carbonyl compounds react with P_2S_5 to yield substituted thiazole derivatives.

Reaⁿ:

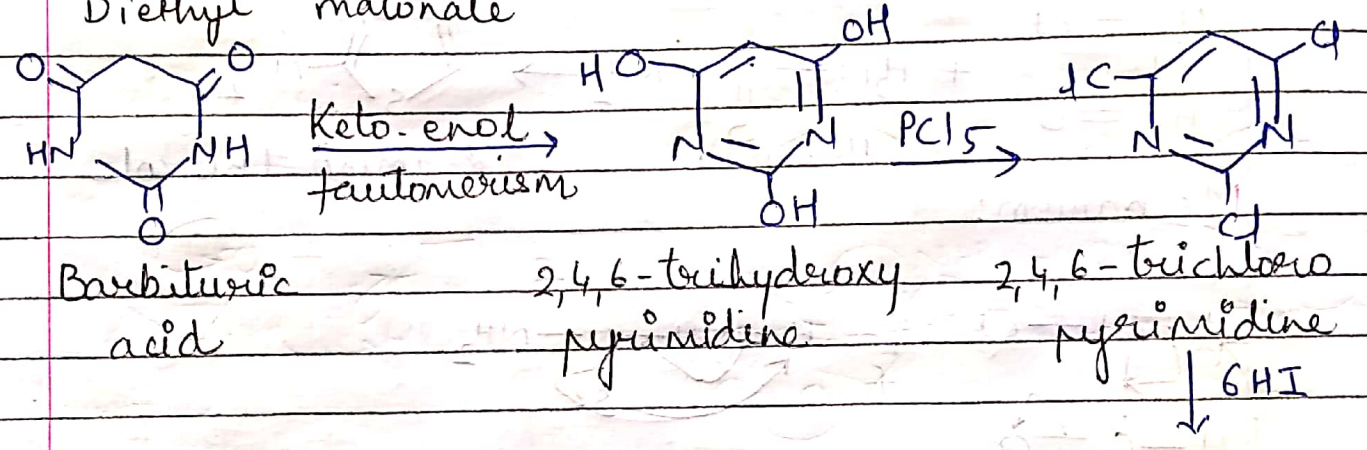
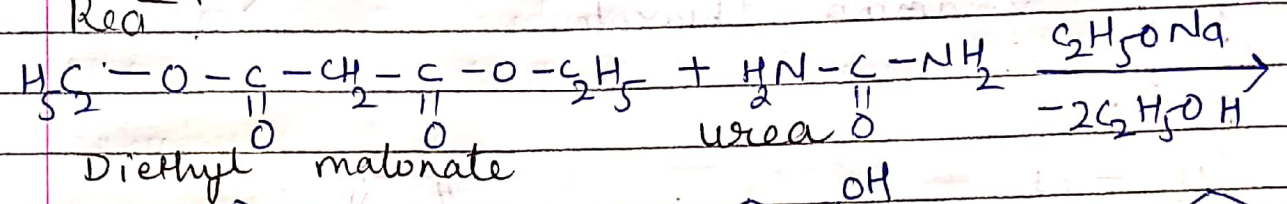


acetyl amino carbonyl compound.

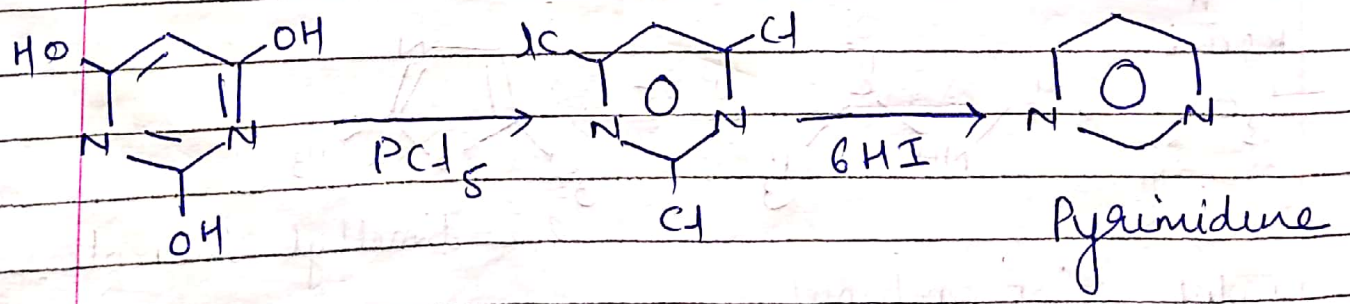
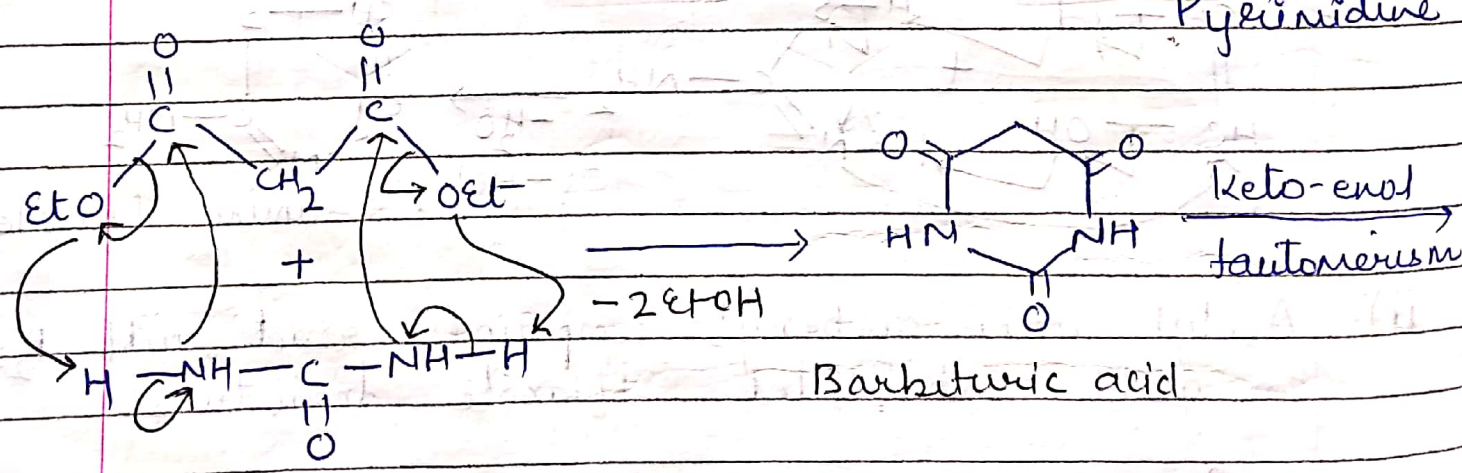
5) Synthesis of Pyrimidine

i) Diethyl malonate condensed with urea in presence of sodium ethoxide to form 2,4,6-trihydroxy pyrimidine, which further reacts with PCl_5 & HI to give pyrimidine.

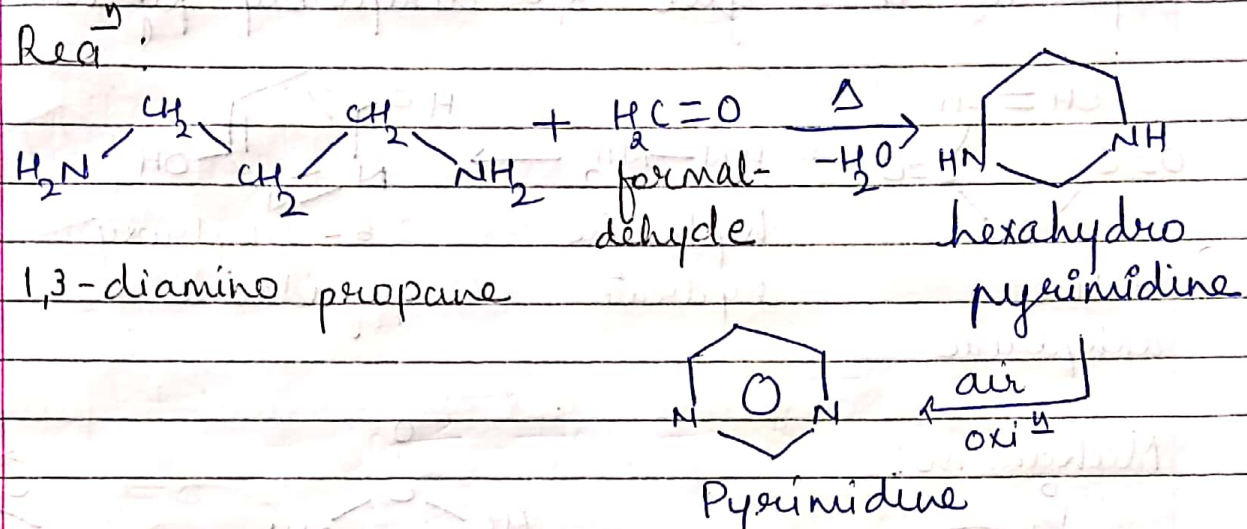
Reaⁿ:



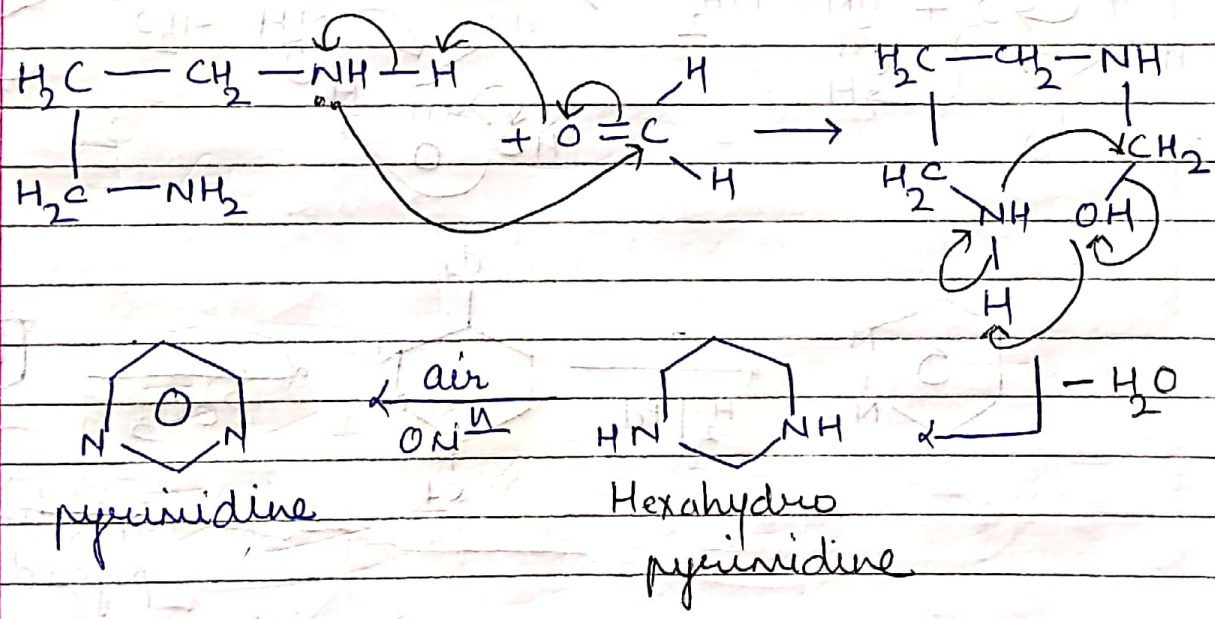
Mechanism:



ii) 1,3-diamino propane reacts with formaldehyde to form hexahydro pyrimidine, which gives pyrimidine in presence of air.

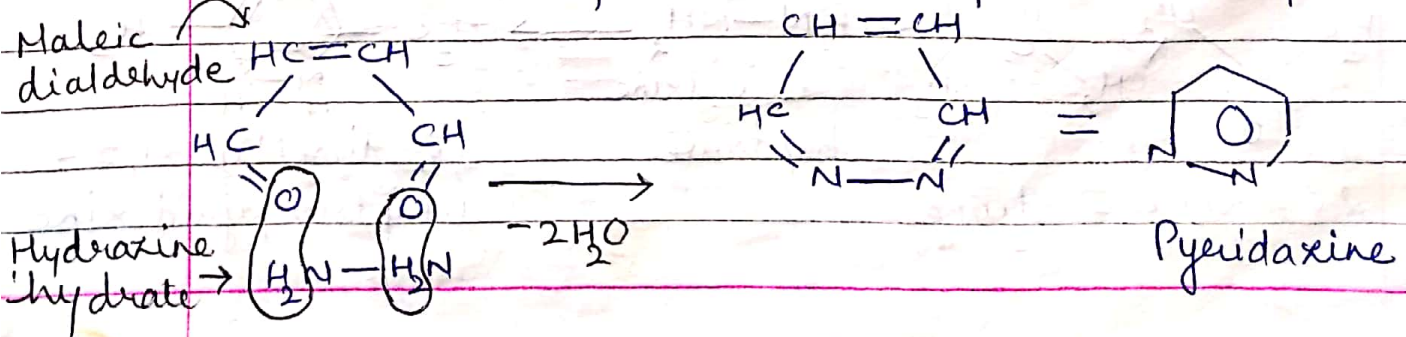


Mechanism:



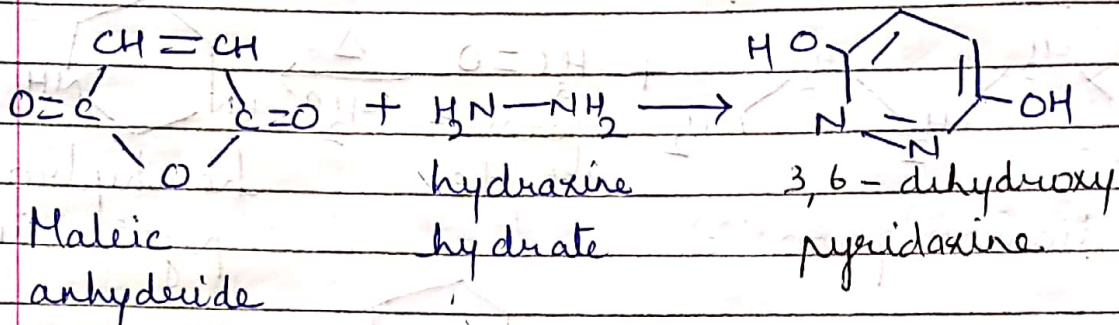
(6) Synthesis of pyridazine

i) It can be prepared by condensation of maleic dialdehyde with hydrazine hydrate.

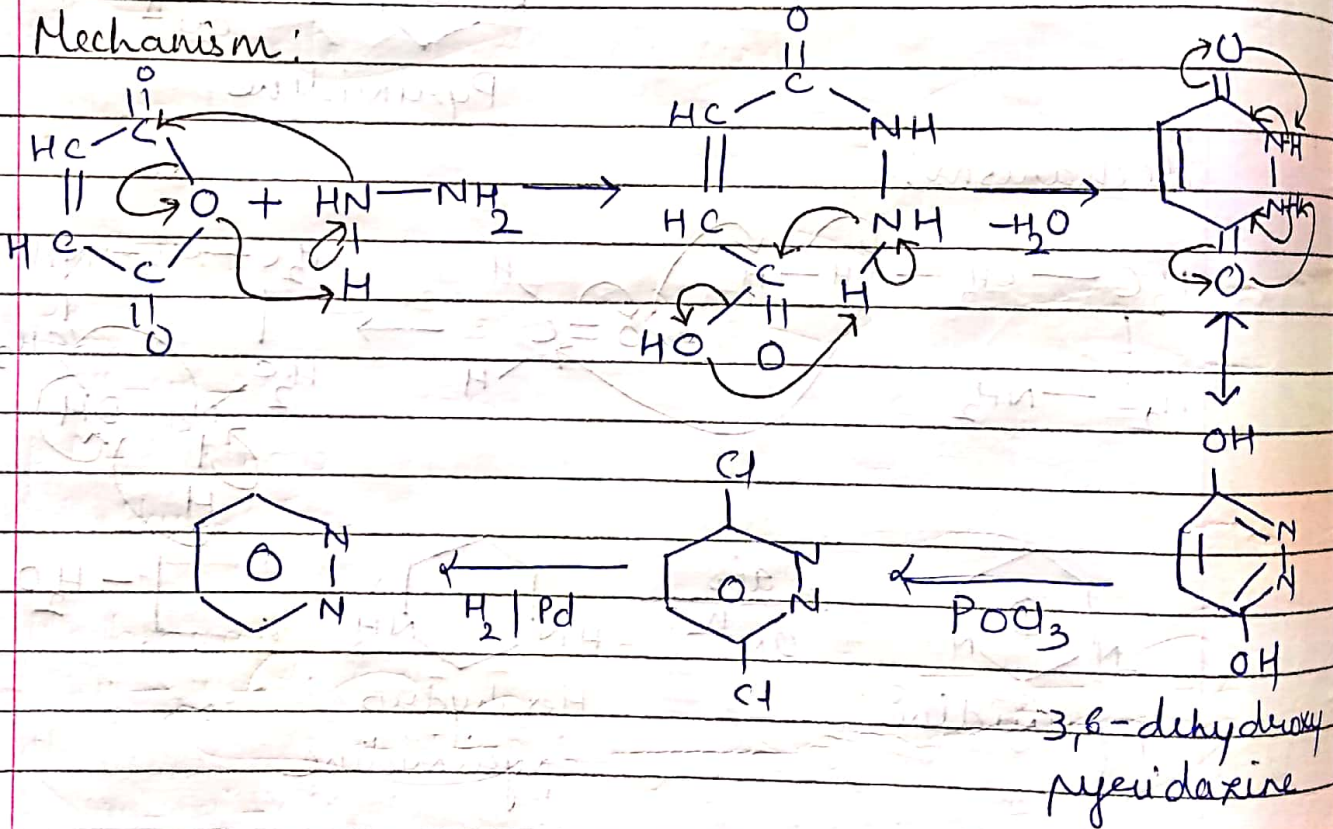


ii) Synthesis of 3,6-dihydroxy pyridazine
~~pyridazine~~
 Pyridazine

Maleic anhydride reacts with hydrazine hydrate to give 3,6-dihydroxy pyridazine

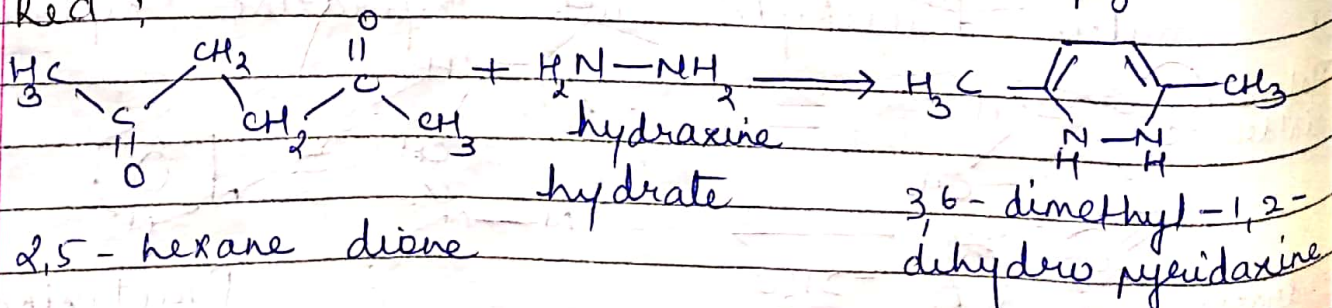


Mechanism:

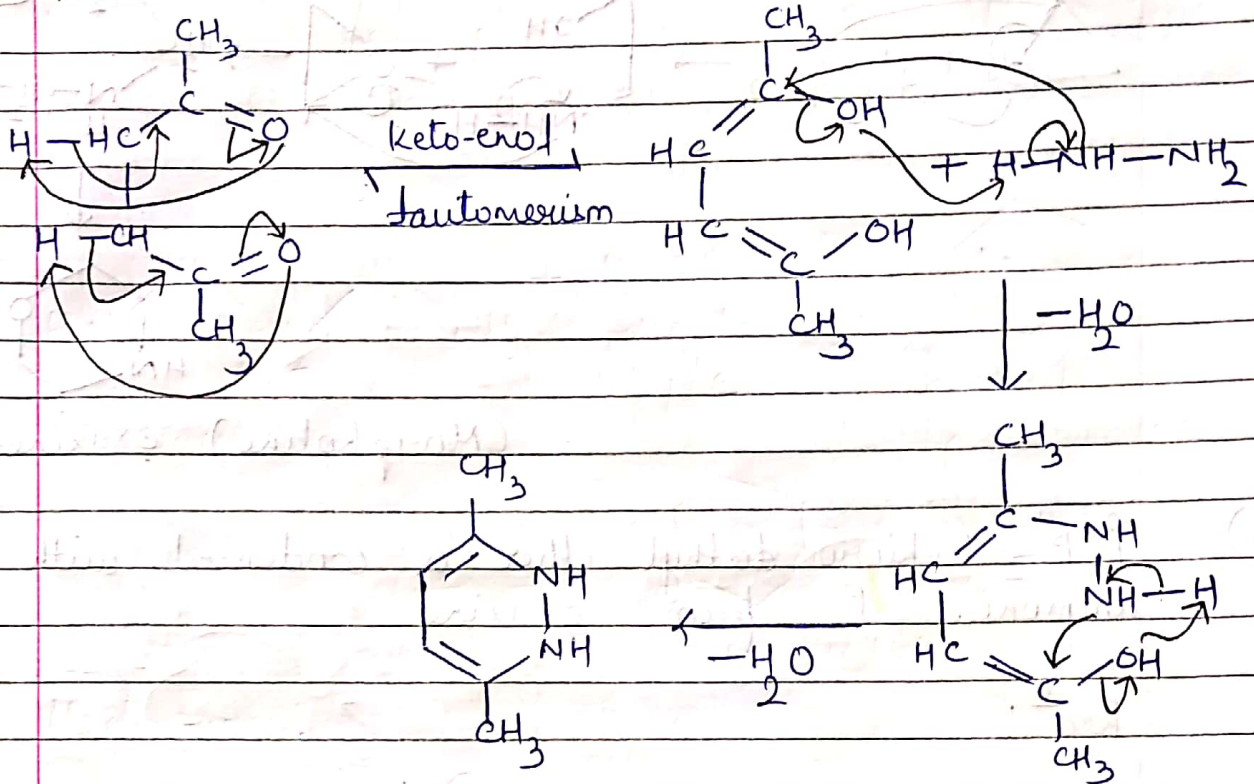


iii) Synthesis of 3,6-dimethyl-1,2-dihydro pyridazine
 2,5-diketone derivatives react with hydrazine hydrate to yield 3,6-disubstituted pyridazine

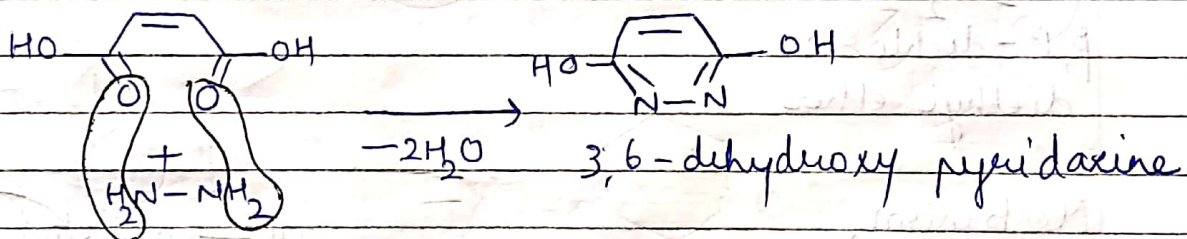
Reactⁿ:



Mechanism:

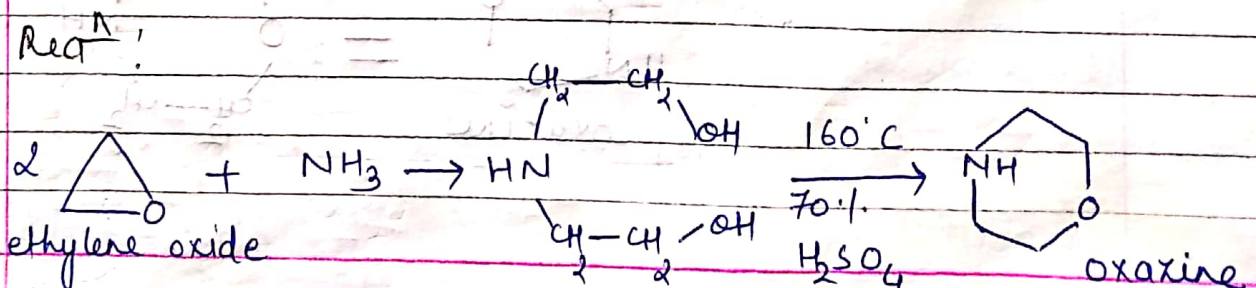


iv) Maleic acid condensed with hydrazine hydrate to form 3,6-dihydroxy pyridazine.

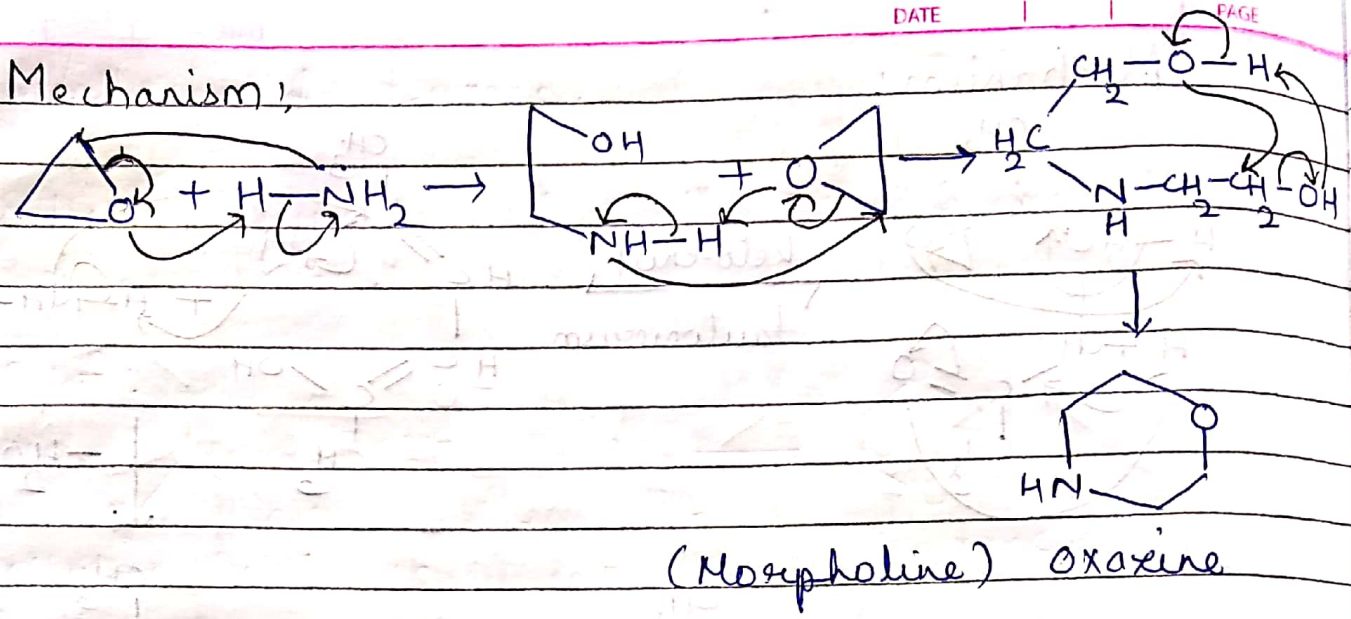


7) Synthesis of oxazine (Morpholine)

i) Two moles of ethylene oxide reacts with one mole of ammonia to yield dihydroxyl diethyl amine which is heated with 70% H_2SO_4 at 160°C temp. to obtain oxazine.

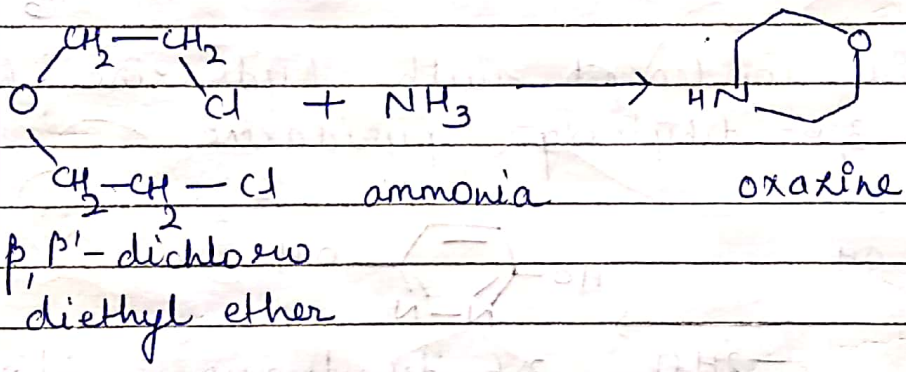


Mechanism,

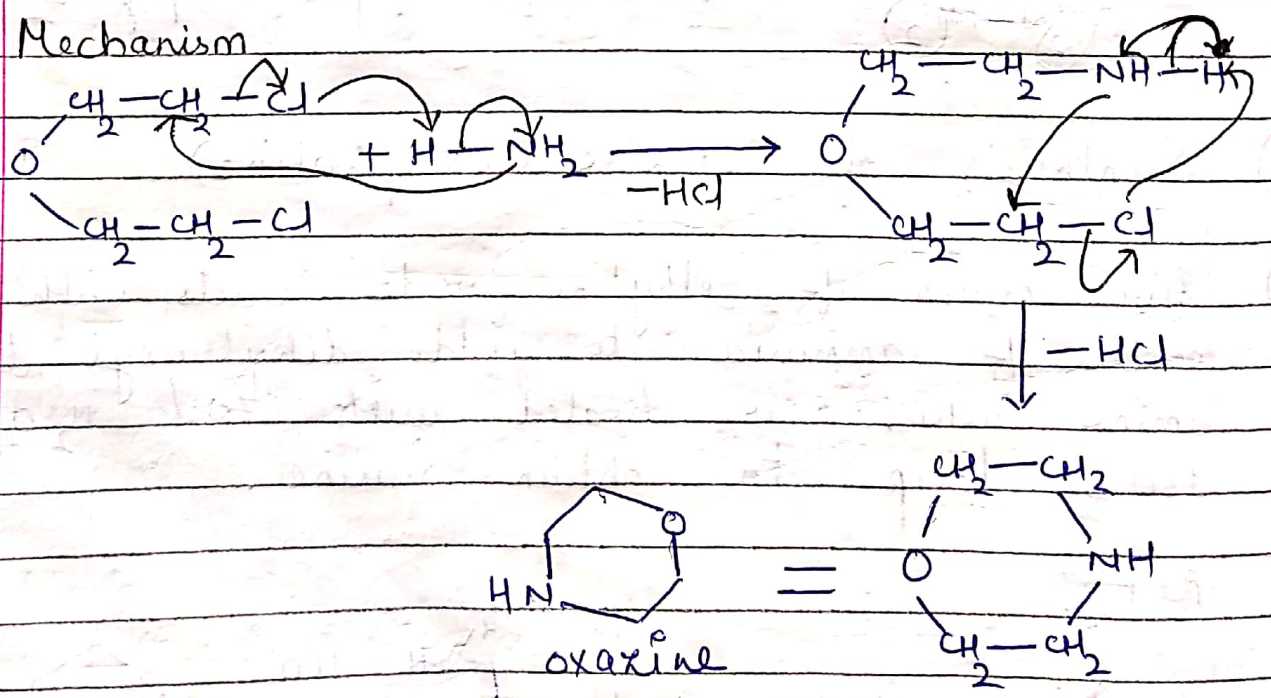


ii) β, β' -dichloro diethyl ether is condensed with ammonia to form oxazine

Reaⁿ:

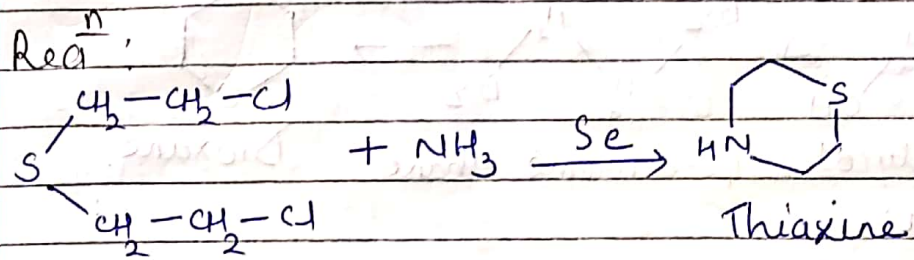


Mechanism

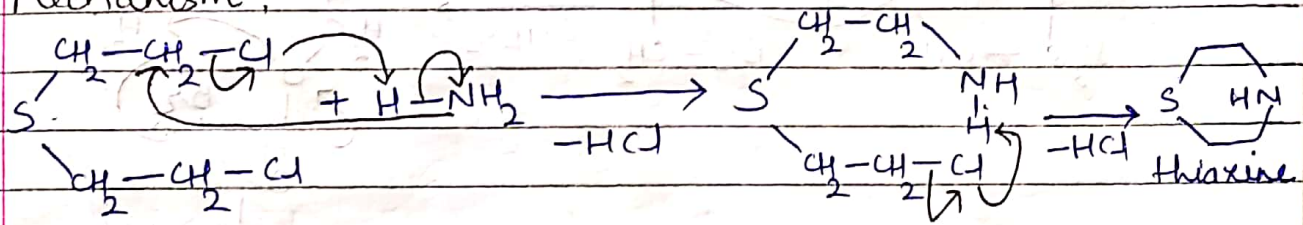


8) Synthesis of Thiazine (Thiomorpholine)

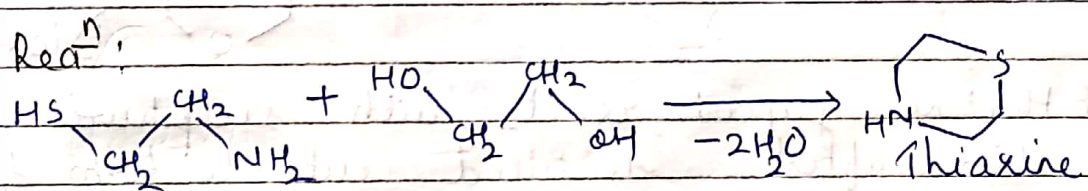
i) β, β' -dichloro diethyl sulphide condensed with ammonia in the presence of Se to obtain thiazine



Mechanism:

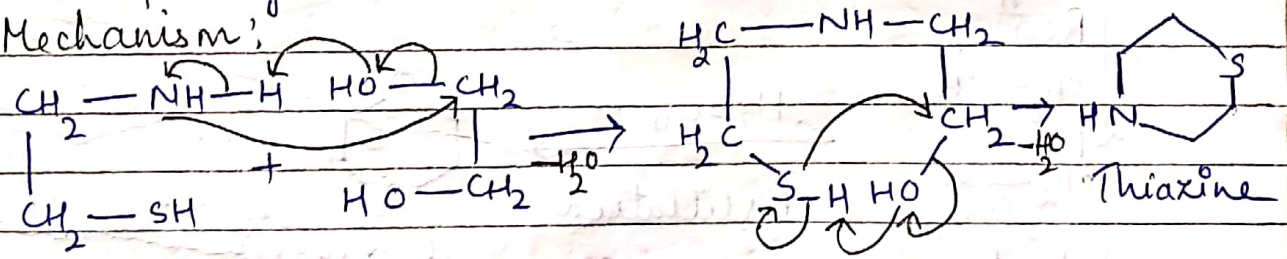


ii) Thiazine can be also obtained by the reaction of α -mercapto ethylamine with 1,2-ethanedithiol



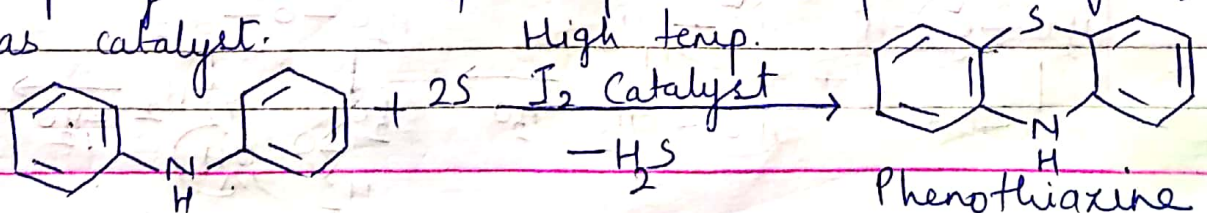
α -mercapto ethylamine 1,2-ethanedithiol

Mechanism:



iii) Synthesis of Phenothiazine

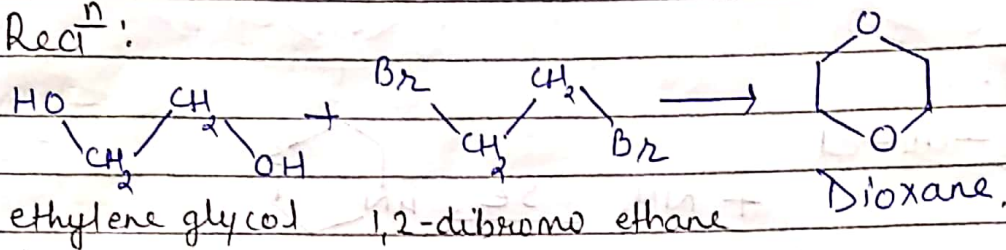
It can be obtained by the condensation of diphenyl amine & sulphur in presence of I_2 as catalyst.



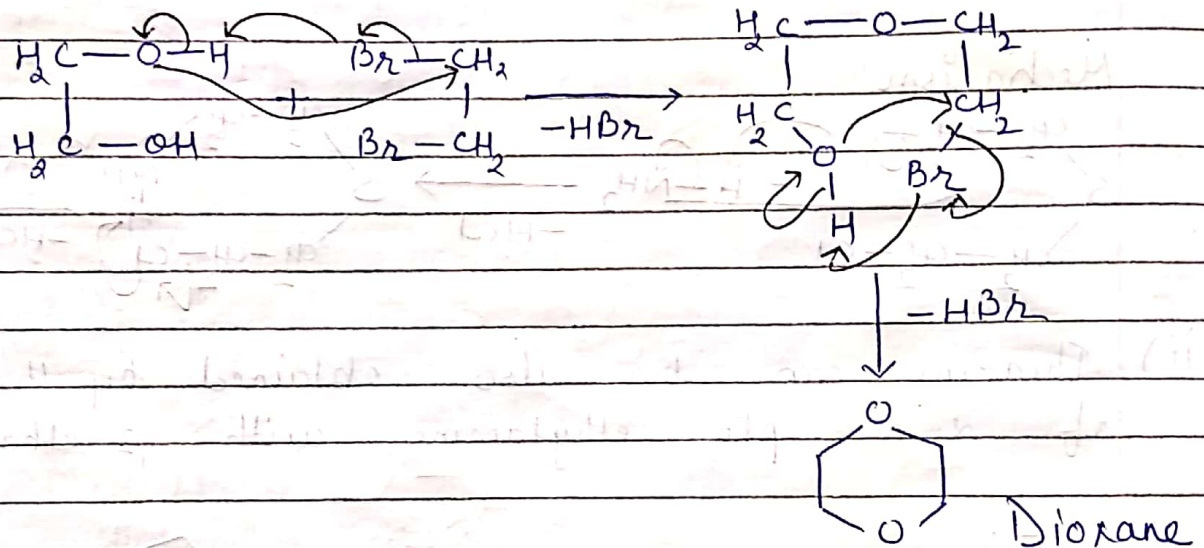
9) Synthesis of Dioxane.

i) Ethylene glycol react with 1,2-dibromo ethane to yield dioxane.

Reactⁿ:

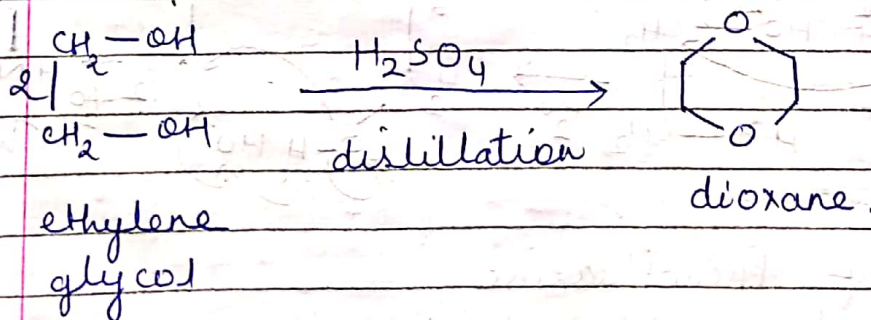


Mechanism:

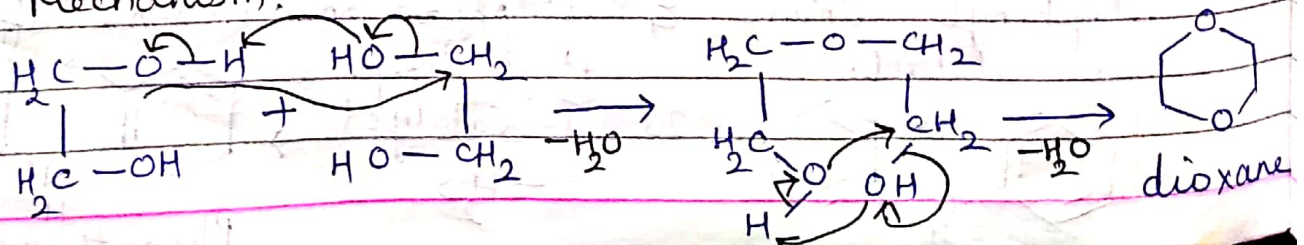


ii) Ethylene glycol react with sulphuric acid, then after distilled out to form dioxane.

Reactⁿ:

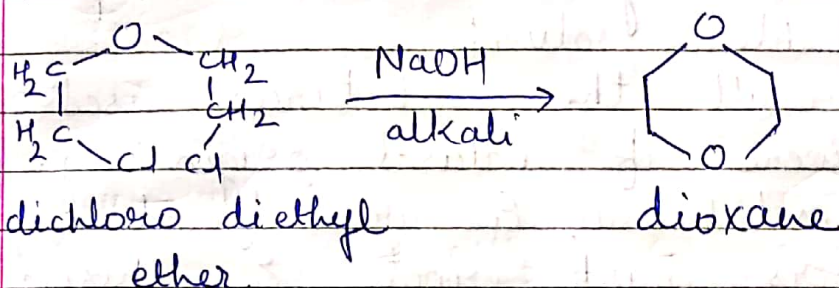


Mechanism:



iii) β, β' -dichloro diethyl ether condensed with alkali to form dioxane.

Reaⁿ:



Mechanism

