Shree H.N.Shukla College of Science Rajkot
B.Sc. (Sem- 5) (CBCS)
CHEMISTRY: [502]

Synthesis of Heterocyclic compound

❖ Contents:

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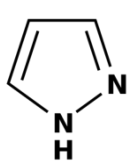
❖ Introduction:

Carbocyclic compound: A cyclic compound containing all carbon atoms in ring formation in referred to as carbocyclic compound.

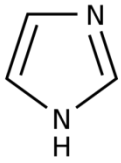
Heterocyclic compound: If a cyclic system, containing carbon and at least one other element is called Heterocyclic compound.

- Heterocyclic compound containing Nitrogen , Oxygen and Sulphur as a hetero atom in the cyclic system.
- Here, we are going to study the synthesis of heterocyclic compounds containing two heteroatom.

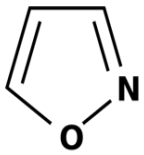
Some structures of heterocyclic compounds are as under.



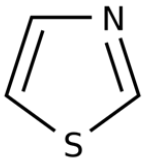
Pyrazole



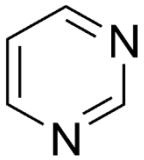
Imidazole



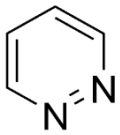
Isoxazole



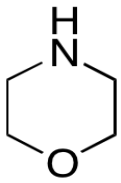
Thiazole



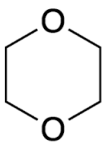
Pyrimidine



Pyridazine



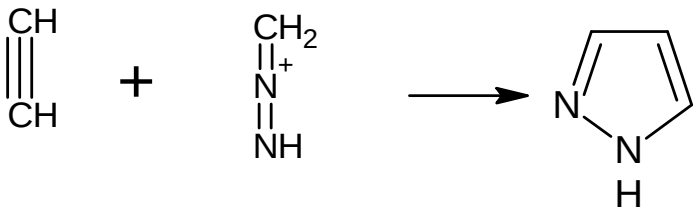
Oxazine



Dioxane

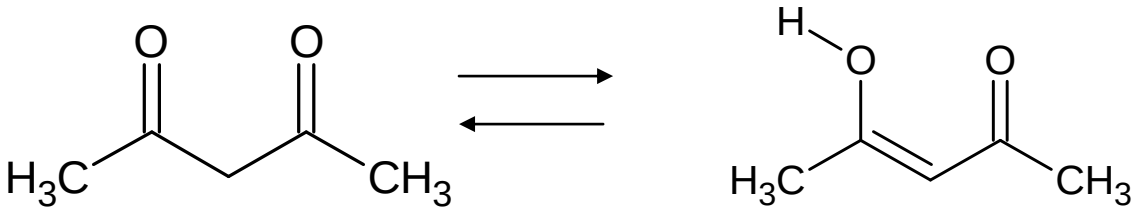
1. Synthesis of Pyrazole:

(a) Acetylene reacts with diazomethane to form pyrazole.



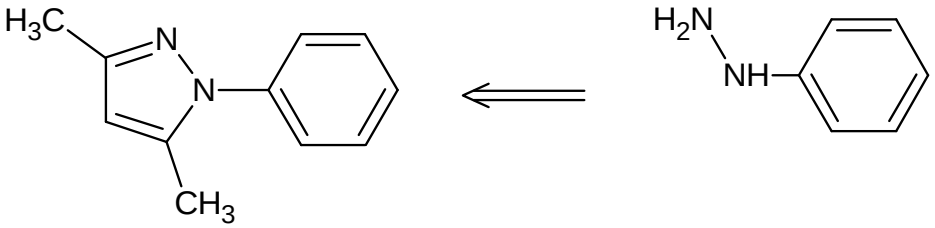
Acetylene Diazomethane Pyrazole

(b) 3,5-Dimethyl-1-phenylpyrazole is obtained by the reaction between acetyl acetone with phenyl hydrazine.



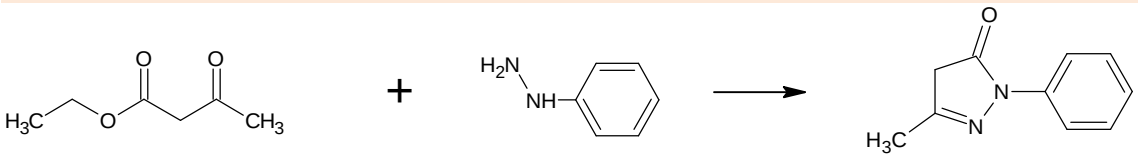
Acetyl acetone — 4-hydroxy-3-pentene-2-one

+



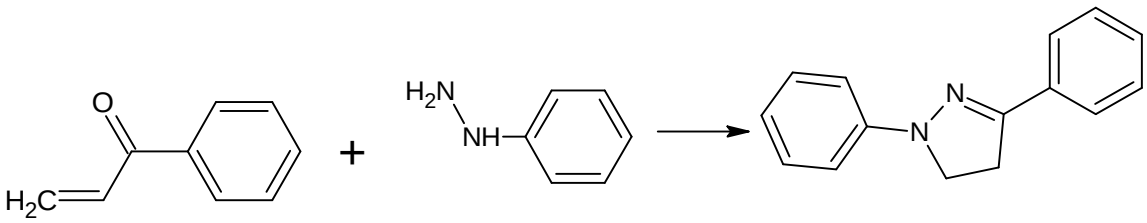
3,5-dimethyl-1-phenyl pyrazole — phenyl hydrazine

(C) 3-methyl-1-phenyl-5-pyrazolone is obtained by the reaction between ethyl aceto acetate with phenyl hydrazine.



Ethyl aceto acetate — Phenyl hydrazine — 3-methyl-1-phenyl-5-pyrazolone

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



Benzoyl ethylene — Phenyl hydrazine — 1,3-diphenyl-4,5-dihydro pyrazole

❖ Synthesis of Imidazole:

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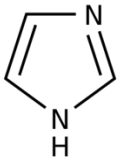
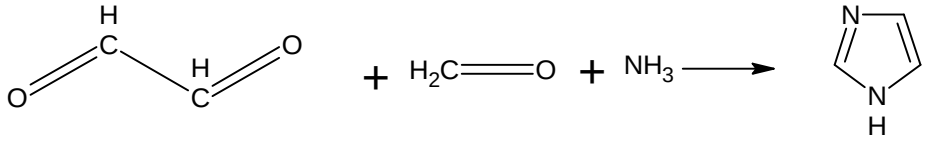
Structure:

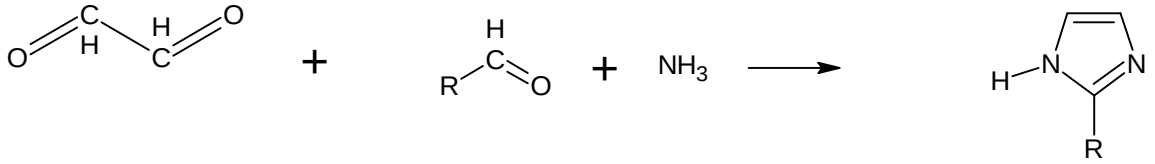


(1) Imidazole is obtained by the reaction among glycol, aldehyde and two moles of ammonia.



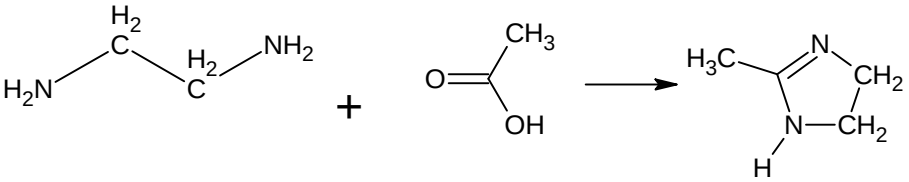
1,2-diamino dial or glycol Methanal Ammonia Imidazole

(2) Imidazole derivatives is obtained by the reaction of one mole glycol, two moles of ammonia and one mole of alkyl or aryl aldehyde.



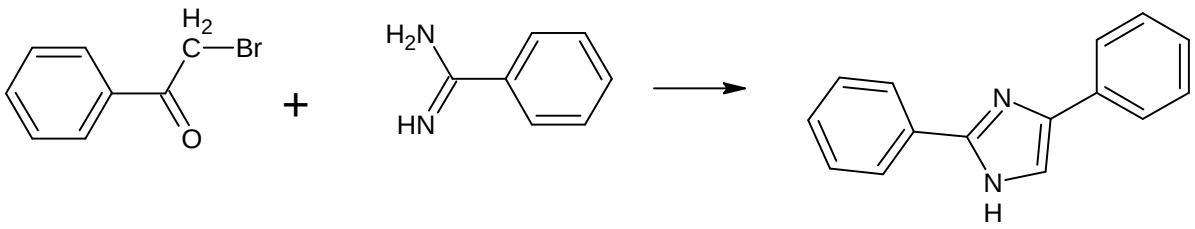
1,2-ethae dial or glycol Alkyl/aryl aldehyde Ammonia 2-alkyl/aryl imidazole

(3) 1,2-diamino ethane reacts with ethanoic acid to yield 2-methyl-4,5-dihydro-2-imidazoline.



1,2-diamino ethane Ethanoic acid 2-methyl-4,5-dihydro imidazole

(4) 2,4-diphenyl imidazole is obtained by the reaction of bromomethyl acetophenone and amidine.



Bromo methyl acetophenone amidine 2,4-diphenyl imidazole

❖ Synthesis of Isoxazole:

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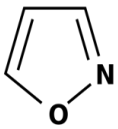
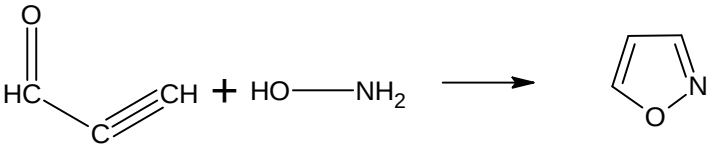
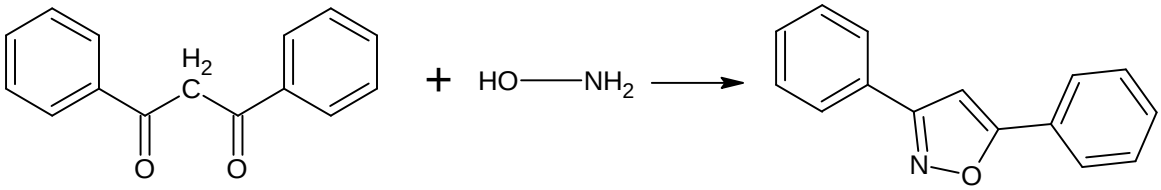
Structure:

1. Isoxazole is obtained by  the reaction between propylnaldehyde and hydroxylamine.



Propylnaldehyde Hydroxylamine Isoxazole

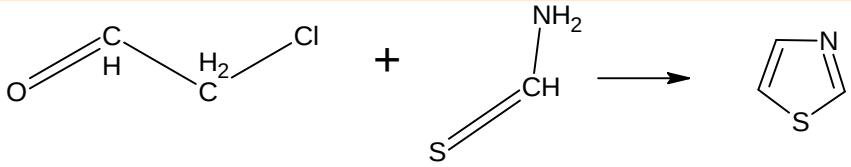
2. 3,5-dipheyl Isoxazole is obtained by the reaction of 1,3 diketone and hydroxyl amine.



1,3 diketone Hydroxylamine 3,5-dipheyl Isoxazole

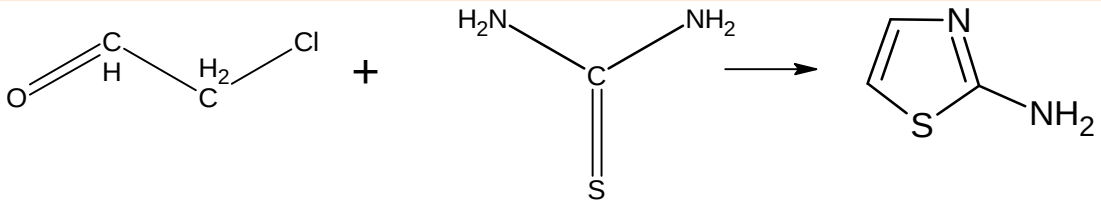
❖ Synthesis of Thiazole:

1. **Haunt's method**: α-halo aldehyde is reacted with keto thiamine to yield thiazole.



2-chloro ethanol keto thiamine Thiazole

2. α- halo aldehyde is reacted with thiourea to form 2-amino thiazole.



2-chloro ethanol Thiouea 2-amino thiazole

3. Aceyl amino carbonyl compounds react with P_2S_5 to yield substituted thiazole derivatives.

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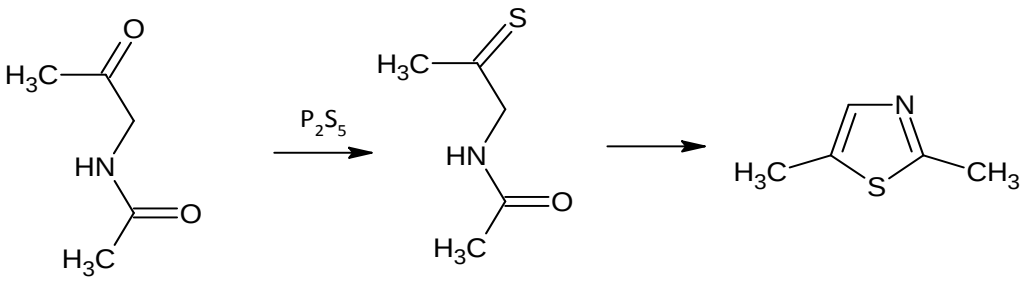
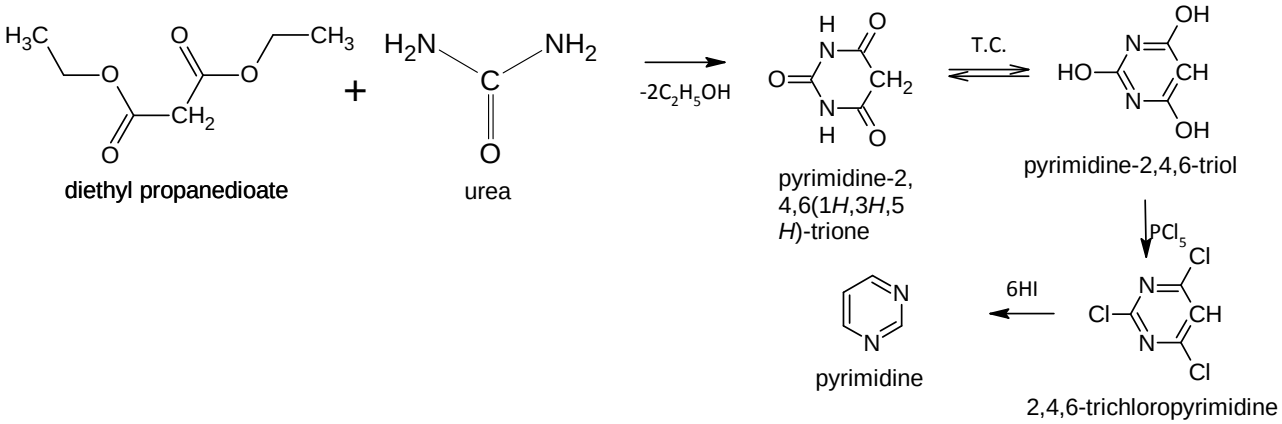


Aceyl amino carbonyl Compound

2,5-dimethyl thiazole

❖ Synthesis of Pyrimidine:

1. Diethyl malonate is condensed with urea in presence of sodium ethoxide to form 2,4,6 trihydroxy Pyrimidine, which further reacts with PCl_5 and HI to yield pyrimidine.



diethyl propanedioate

urea

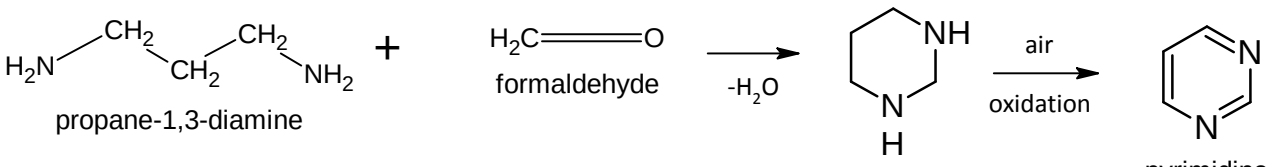
pyrimidine-2, 4,6(1*H*,3*H*,5 *H*)-trione

pyrimidine-2,4,6-triol

pyrimidine

2,4,6-trichloropyrimidine

2. 1,3-diamino propane reacts with formaldehyde to form hexahydro Pyrimidine, further in the presence of air, it yields Pyrimidine.



propane-1,3-diamine

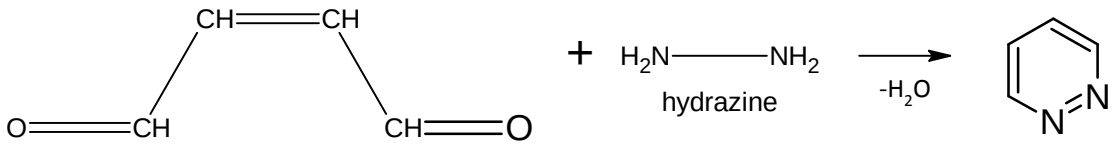
formaldehyde

hexahydropyrimidine

pyrimidine

❖ Synthesis of Pyridazine:

1. Pyridazine is prepared by the condensation of maleic anhydride with hydrazine.

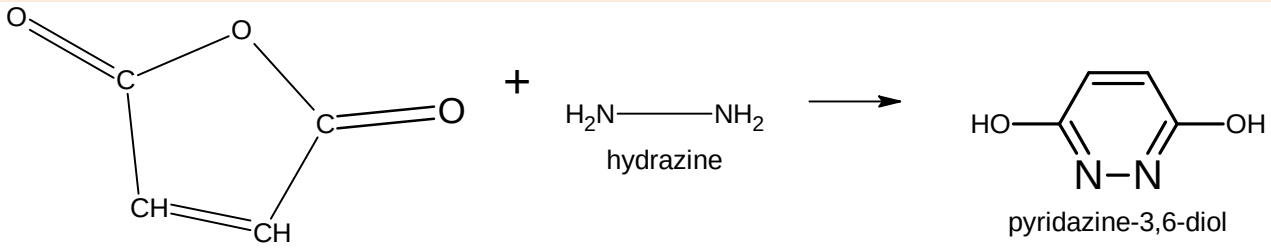


(2*Z*)-but-2-enedial

Maleic dialdehyde

pyridazine

2. Maleic anhydride reacts with hydrazine to form 3,6-dihydroxy Pyridazine.

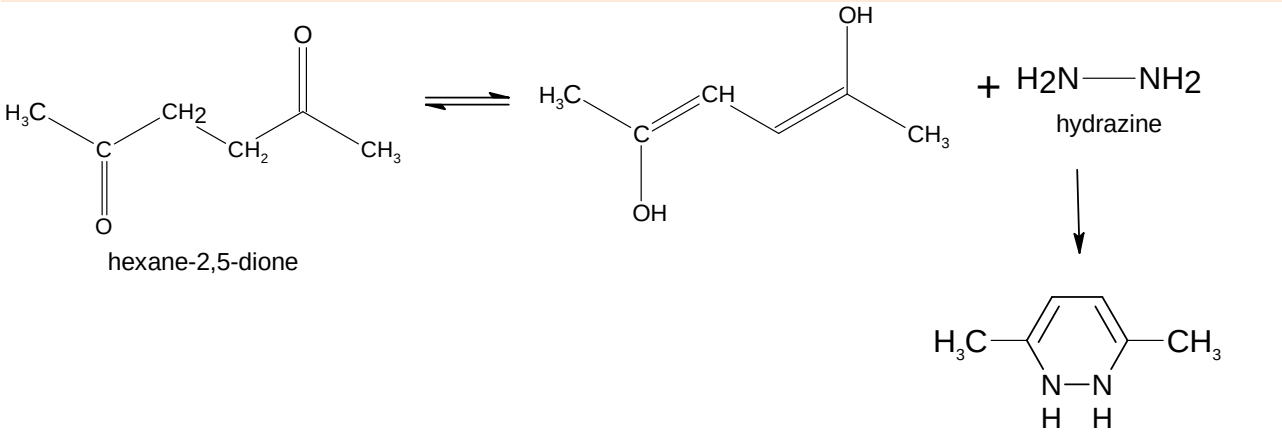


furan-2,5-dione

(Maleic anhydride)

pyridazine-3,6-diol

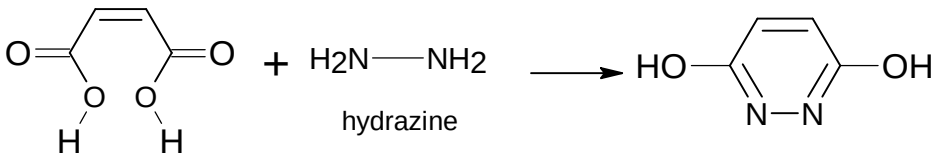
3. 2,5-diketone derivatives react with hydrazine hydrate to yield 3,6-di-substituted Pyridazine.



hexane-2,5-dione

3,6-dimethyl-1,2-dihydropyridazine

4. Maleic acid is condensed with hydrazine hydrate to form 3,6-dihydroxy Pyridazine.



pyridazine-3,6-diol

❖ Synthesis of oxazine (morpholine)

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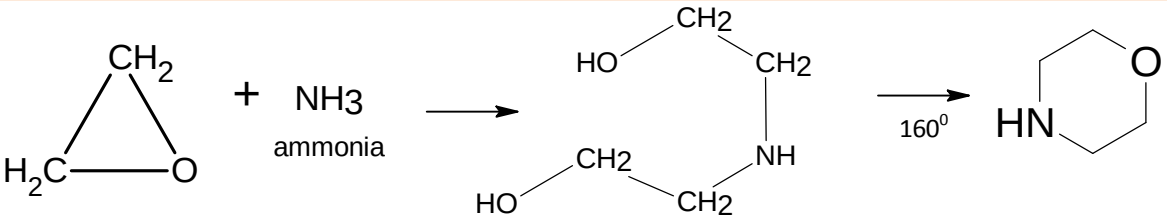
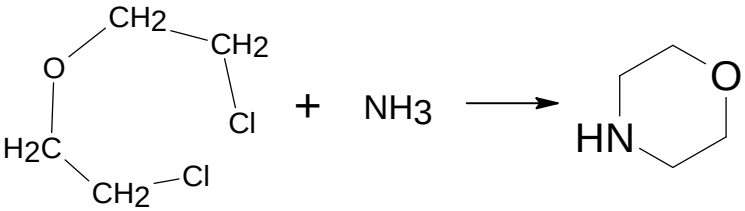
1. Two moles of ethylene oxide reacts with one mole of ammonia to form dihydrxy diethyl amine which is heated with 70 % H_2SO_4 at 160° C temperature to obtain oxazine (morpholine).



Ethylene oxide — Dihydroxy diethyl amine — Oxazine

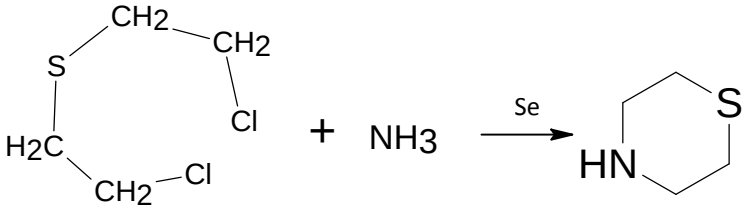
2. β, β'-dichloro diethyl ether is condensed with ammonia to form oxazine.



β, β'- dichloro diethyl ether — Oxazine

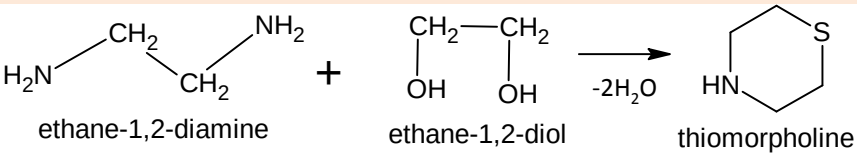
❖ Synthesis of Thiazine (Thio morpholine)

1. β, β'- Dichloro diethyl sulphide is condensed with ammonia in the presence of Se to obtain Thiazine.



β, β'- Dichloro diethyl sulphide — Thiazine

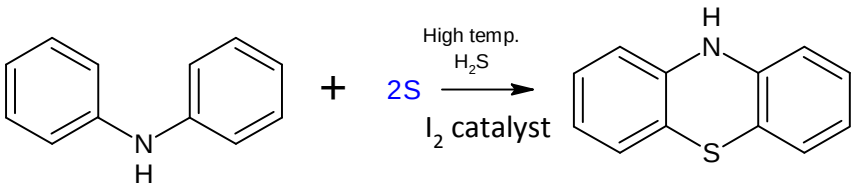
2. Thiazine is obtained by the condensation of 2-mercapto ethyl amine with 1,2-ethane diol.



ethane-1,2-diamine — ethane-1,2-diol — thiomorpholine

3. Phenothiazine is obtained by the condensation of diphenylamine with sulphur in the presence of I_2 catalyst.

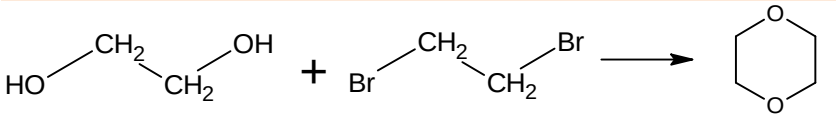
CH_4



Diphenyl amine — Phenothiazine

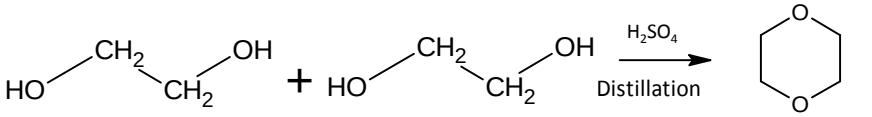
❖ **Synthesis of Dioxane**:

1. Ethylene glycol reacts with 1,2-dibromo ethane to yield Dioxane.



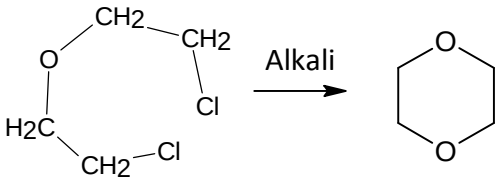
ethane-1,2-diol + 1,2-dibromoethane → 1,4-dioxane

2. Ethylene glycol reacts with sulphuric acid then after distilled out to form Dioxane.



ethane-1,2-diol + ethane-1,2-diol → 1,4-dioxane

3. β, β'-dichloro diethyl ether is condensed with alkali to form Dioxane.



Dichloro diethyl ether → Dioxane

Question	Answer
1. Which heteroatom is present in imidazole?	N

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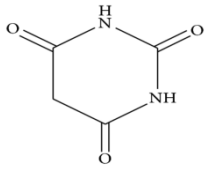
2. Which heteroatom is present in Isoxazole?	N and O
3. Which heteroatom is present in Thiazole?	S and N
4. Which heteroatom is present in Oxazine?	O and N
5. Which heteroatom is present in Dioxane?	O and O
6. Write the structure of barbitaric acid	
7. Give the molecular formula of imidazole.	$C_3H_4N_2$
8. Give only method of preparation of Dioxane.	Ethylene glycol reacts with 1,2-dibromo ethane to yield Dioxane.
9. Give only method preparation of Phenothia-zine.	Phenothiazine is obtained by the condensation of diphenylamine with sulphur in the presence of I_2 catalyst.
10. Give only method preparation of oxazine.	Two moles of ethylene oxide reacts with one mole of ammonia to form dihydrxy diethyl amine which is heated with 70 % H_2SO_4 at 160° C temperature to obtain oxazine (morpholine).
11. Which heteroatoms are present in hetero cyclic compound?	O, N and S
12. Define : Heterocyclic compound	If a cyclic system, containing carbon and at least one other element is called Heterocyclic compound.
13. Write the structure of Thiazole and Thiazine.	 Thiazole  Thiazine

:: **Thank You** ::

Prepared by Oza Vinit B.