CHAPTER

2

HETEROCYCLIC CHEMISTRY

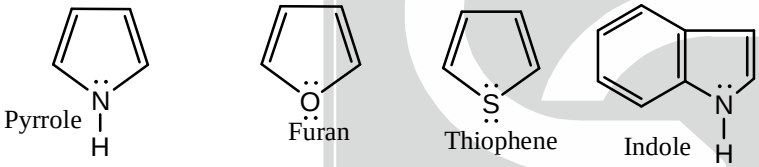
2.1. INTRODUCTION :

The atoms other than carbon and hydrogen are known as hetero atom. The cyclic compound containing hetero atom[such as N, S, O etc], is known as heterocyclic compound.

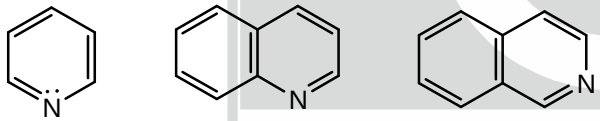
Monocyclic compounds with one hetero atom:

Some of the important heterocyclic compounds containing one hetero atom are:

(i) 5-membered heterocyclic compounds:



(ii) 6-membered heterocyclic compounds:



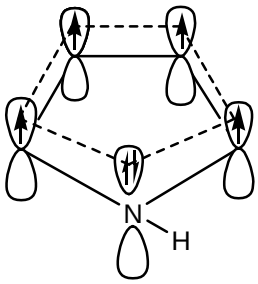
2.2. PYRROLE

(A) General characteristics:

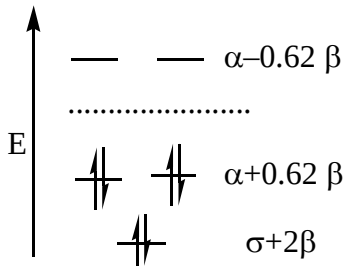
(1) Molecular formula C_4H_5N. Resonance Energy is 21 Kcal/mole, pKa = 16.5

(2) The pyrrole ring system is important as it is found in many natural products including hemoglobin, chlorophyll and alkaloids.

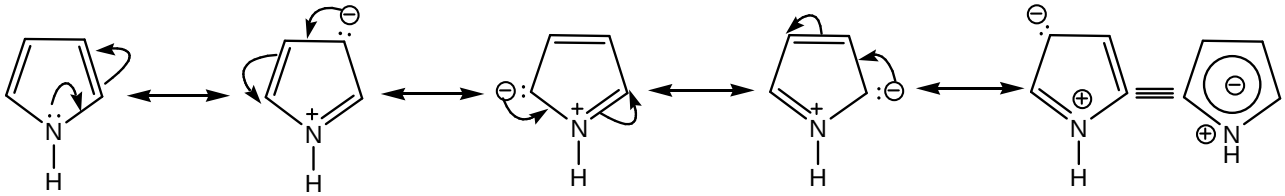
(3) Molecular orbital picture:



The ring has five 'p' orbitals that can overlap to create five new orbitals, three bonding and two antibonding molecular orbitals, there are six electrons for these orbitals. The four 'p' orbitals of the double bonds each contribute one and the filled orbital contribute the other two electrons. The six electrons occupy the bonding orbitals and constitute an aromatic sextet.

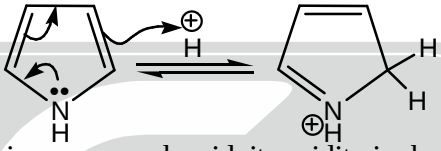


(4) Resonance structure:

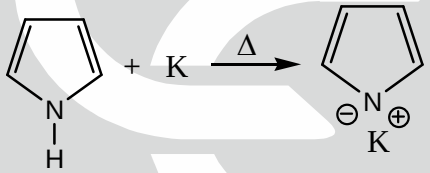


(5) Pyrrole is a weak base:

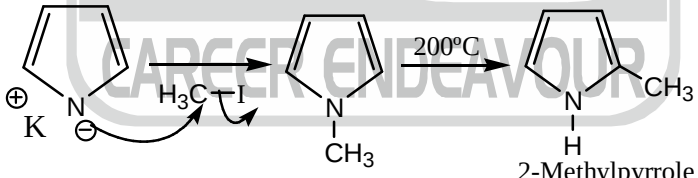
Pyrrole is an extremely weak base because the pair of electrons shown as non bonding electrons is part of the p cloud. When pyrrole is protonated its aromaticity is destroyed. Therefore the conjugate acid of pyrrole is a very strong acid pKa = –3.8.



(6) Acidic character pyrrole: Pyrrole is a very weak acid, its acidity is about the same as that of acetylene.
Example: If pyrrole is heated with metallic potassium in n-heptane as solvents, stable potassium pyrrolide is formed.



Potassium pyrollidine reacts with alkyl halides at 60°C to give N-alkyl pyrroles. On heating to 200°C these readily rearrange to C-alkyl pyrroles



(7) Physical properties:

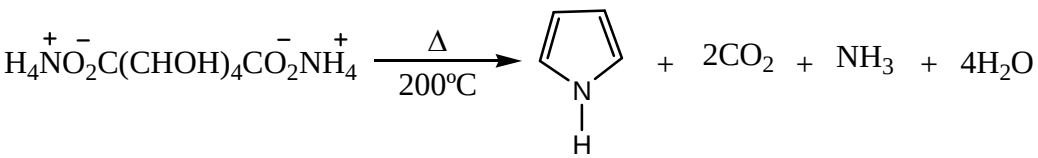
- Pyrrole is a colourless liquid.
- Boiling point 131°C.
- It turns brown in the air and gradually resinifies.
- It is only slightly soluble in water but totally miscible with ether or ethanol.

(B) Synthesis of Pyrrole:

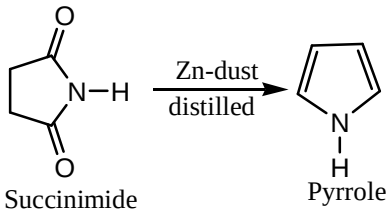
(I) By passing a mixture of acetylene and ammonia through red hot tube.

$$2C_2H_2 + NH_3 \longrightarrow C_4H_5N + H_2$$

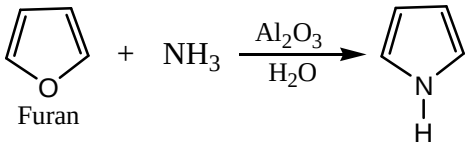
(II) By distilling a mixture of ammonium mucate and glycerol at 200°C.



(III) From Succinamide

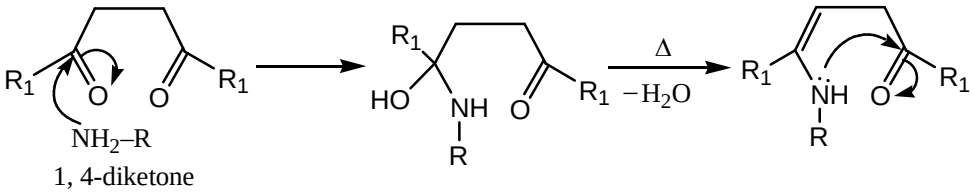


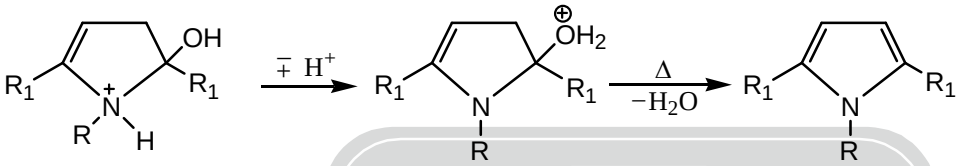
(IV) From Furan



(V) Paal-Knorr synthesis:

By treating 1, 4-diketone with ammonia, primary amine or hydrazine etc.

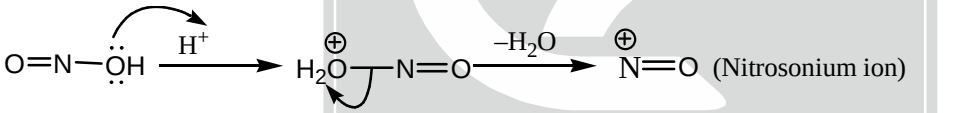


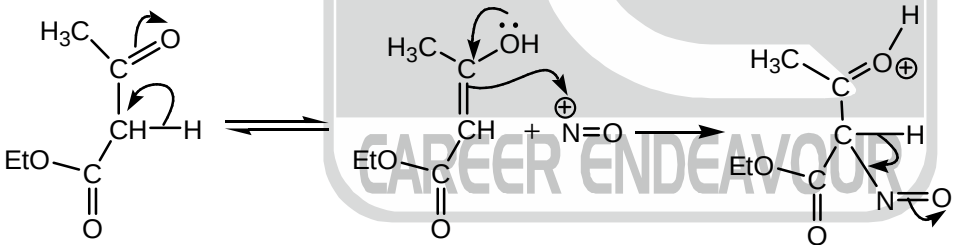


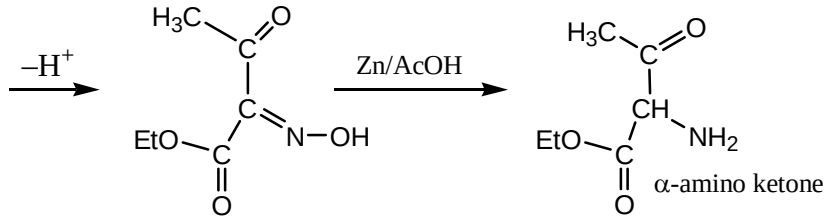
(VI) Knorr Pyrrole synthesis:

It involves the condensation between an α – amino ketone and a β – diketone or β – ketoester which produces derivative of pyrrole.

Mechanism:







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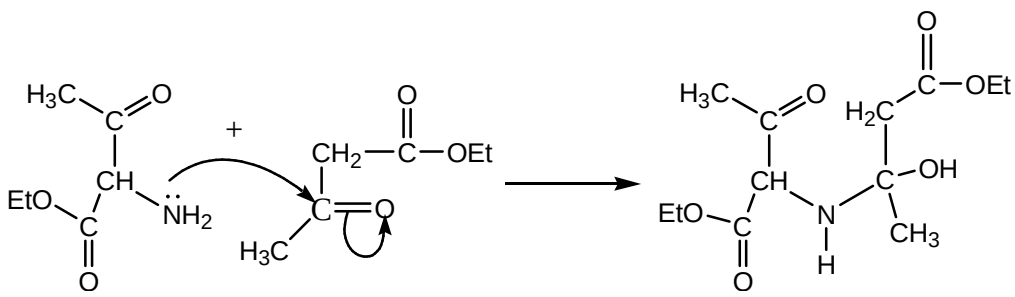
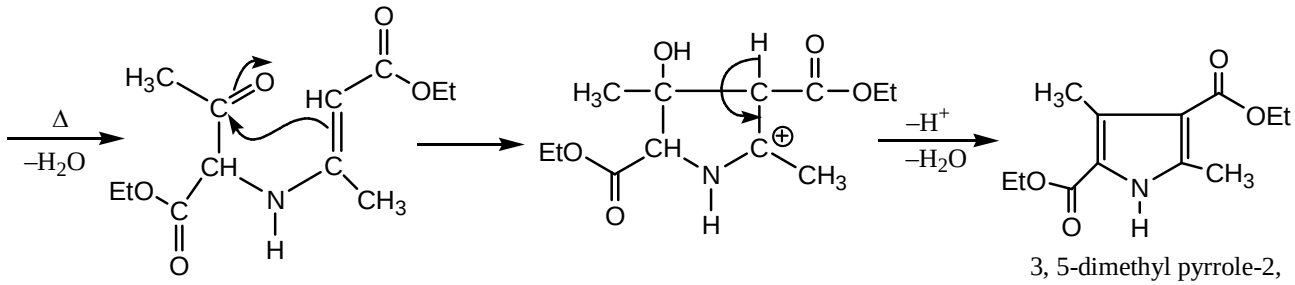
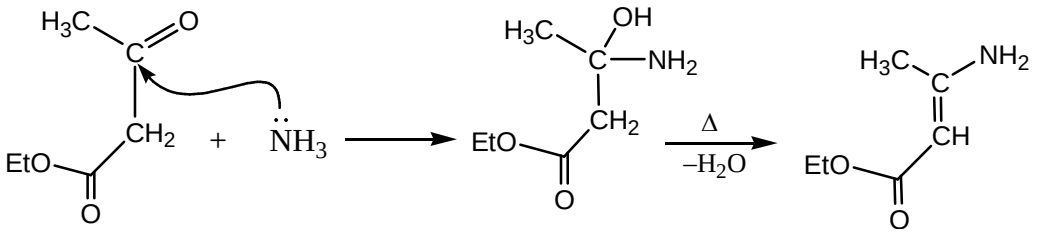
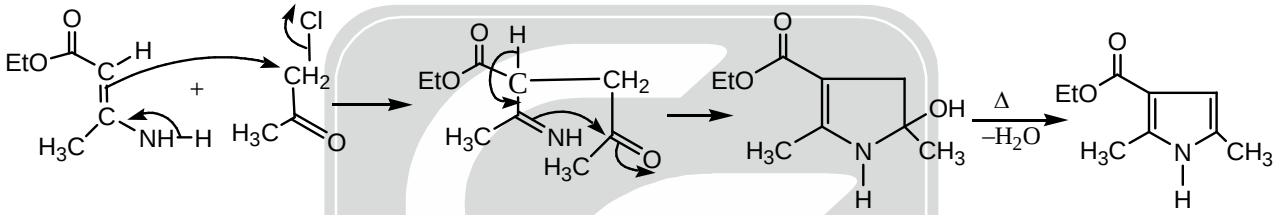




(7) Hantzsch synthesis: Condensation between chloroacetone, a β – ketoester and primary amine or amonia.



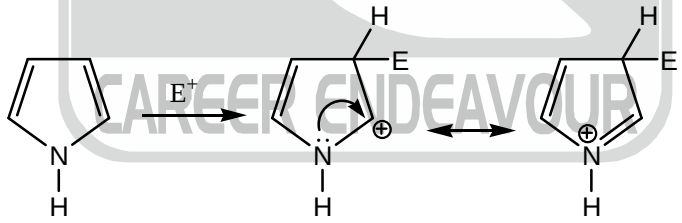


(C) Chemical Properties:

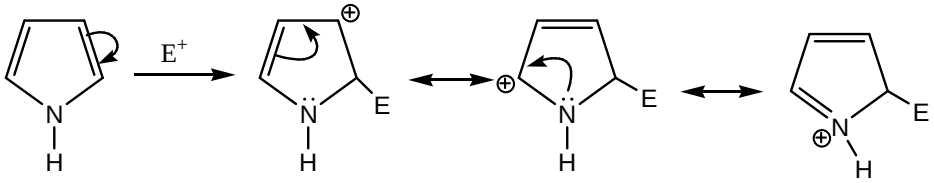
- Pyrrole is aromatic and more reactive than benzene.
- It gives electrophilic substitution reaction.

Preferential position for the attack of E^+:

Case 1: Electrophilic attack at 3-position.



Case 2: Electrophilic attack at 2-position.



Since intermediate formed after the attack of E^+ at 2-position is more stable (due to more resonating structure) than that of intermediate formed after electrophilic attack at 3-position so, electrophilic substitution are favorably occured at 2-position rather than three. If the 2-position is occupied then next substitution will be at 5-carbon if both position 2 and 5 are occupied then substitution can be possible at 3-position.

(1) Reaction with Br_2: Reaction with bromine requires no Lewis acid and leads to substitution at all four free positions.