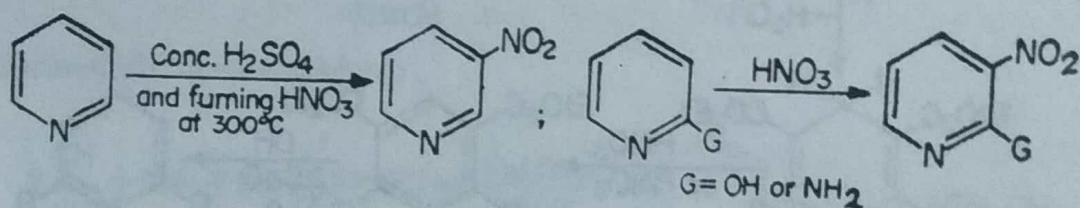


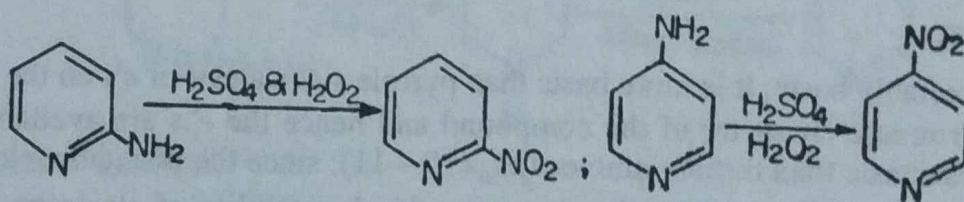
(ii) Electrophilic substitutions :

It has already been stated in the Problem 12.20 and in the sec. 17.4.4d that pyridine is less reactive than benzene in so far as electrophilic substitutions are concerned. The charge distribution in pyridine ring shows that 2, 4 and 6-positions are electron-deficient and hence  $\text{Ar.S}_\text{E}$  reactions occur at 3 and 5-positions. Since pyridine ring is a deactivated one. Strong conditions are required for the  $\text{Ar.S}_\text{E}$  reactions. Furthermore, in an acid-medium the N atom gets protonated and the protonated pyridine becomes more deactivated than the unprotonated one. The pyridine ring may be compared with the benzene ring of nitrobenzene. Therefore the presence of any + I-group in the ring will accelerate the  $\text{S}_\text{E}$  reactions. When such a group is present at 3-position, the electrophilic substitution occurs at 2- and 6-positions; but if the group occupies 2- or 4-position, the electrophilic attack occurs at 3- or 5-position.

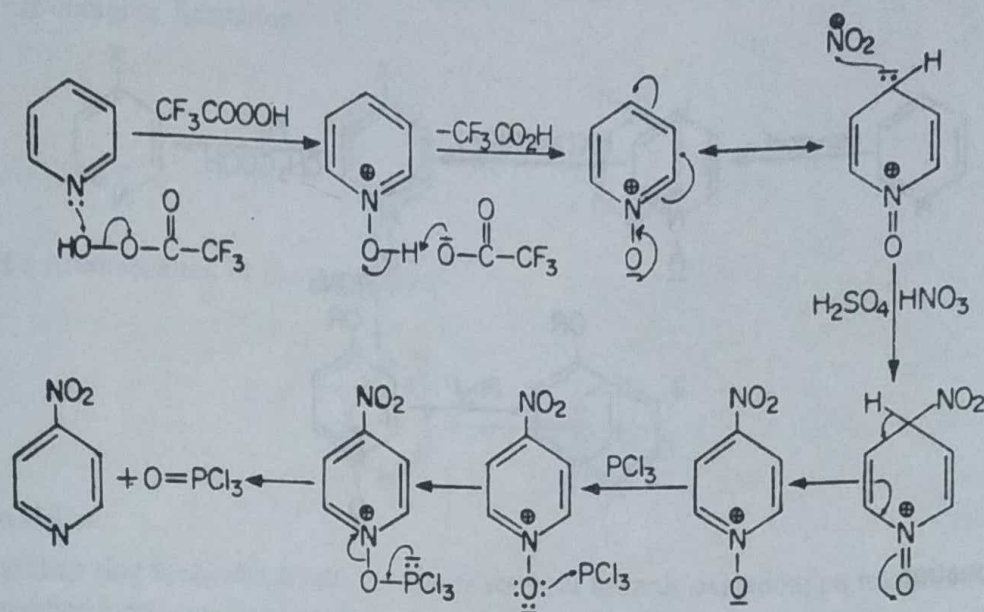
(a) Nitration :



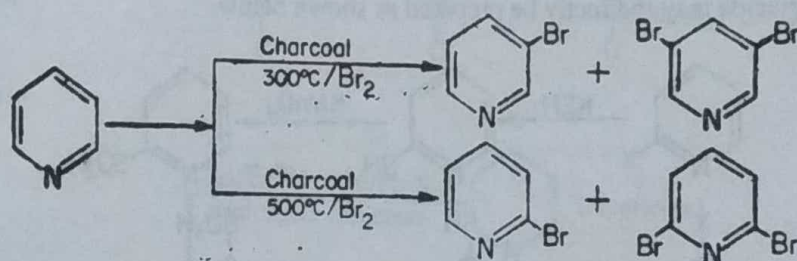
Pyridine is indirectly nitrated by oxidising 2- and 4-aminopyridines with hydrogen peroxide and sulphuric acid.



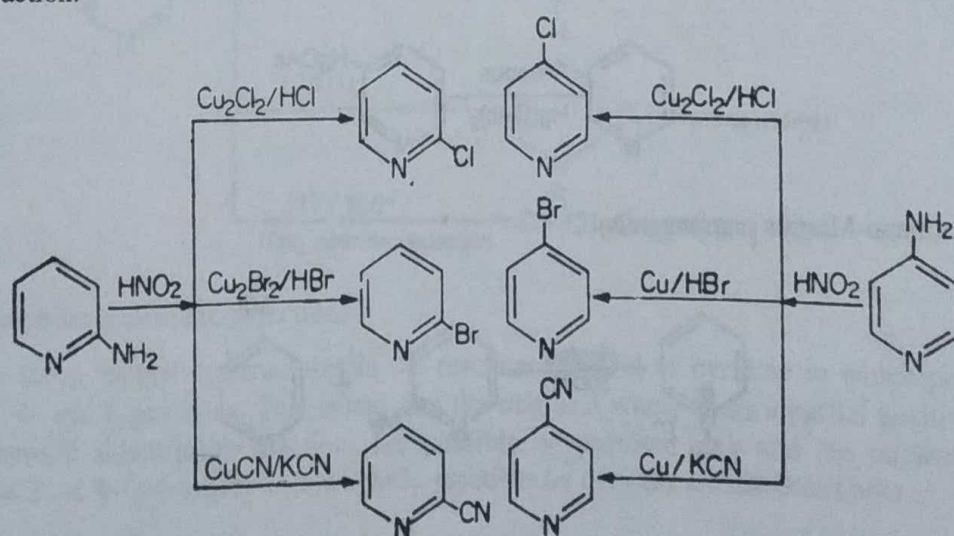
Nitration at 4-position may be done via pyridine-l-oxide.



(b) Halogenation :

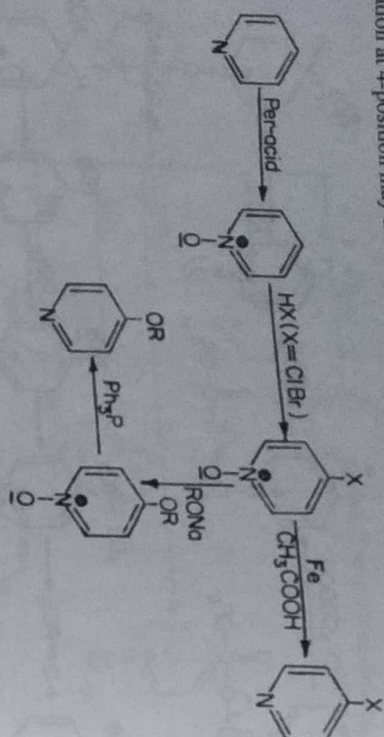


2-and 4-halopyridines are prepared by indirect methods from 2-and 4-amino-pyridines through the Sandmeyer reaction.

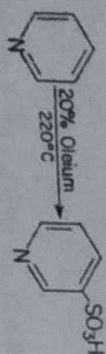




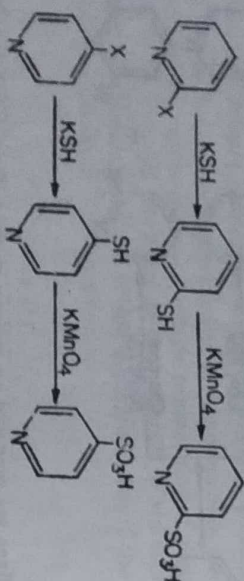
Halogenation at 4-position may also be carried out via pyridine-1-oxide.



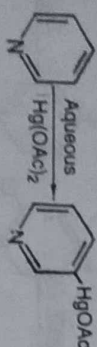
(c) Sulphonation :



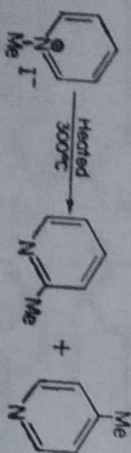
2- and 4-sulphonic acids may indirectly be prepared as shown below.



(d) Mercuriation :



(e) The Hofmann-Martius rearrangement :

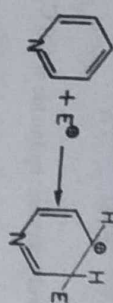


(f) Alkylation and acylation :

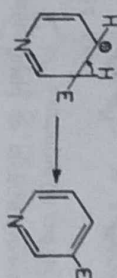
Since pyridine forms salts with acids, Lewis and protonic, it cannot be alkylated by the Friedel-Crafts method. However, it can be indirectly alkylated by the Hofmann-Martius rearrangement.

### Mechanism of the $S_E$ reactions :

Step I :  $\sigma$ -complex formation.

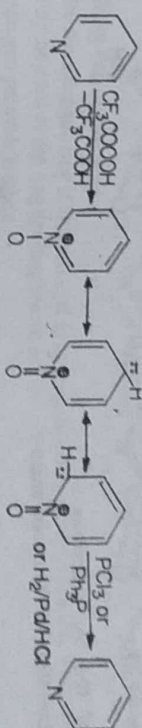


Step II : Aromatisation of the  $\sigma$ -complex

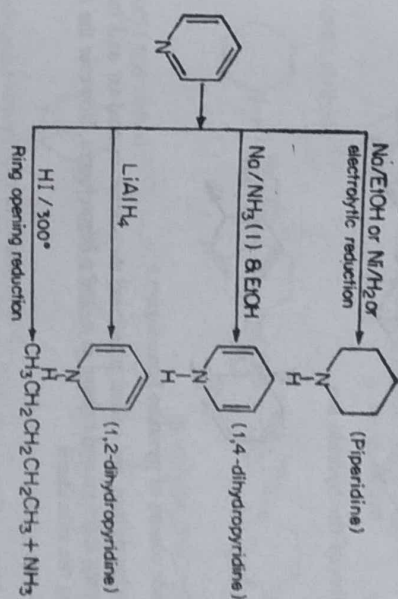


(iii) Oxidation :

The pyridine ring being deactivated, it is very resistant towards oxidation; on treatment with peracids, however, pyridine forms pyridine-1-oxide.



(iv) Reduction :



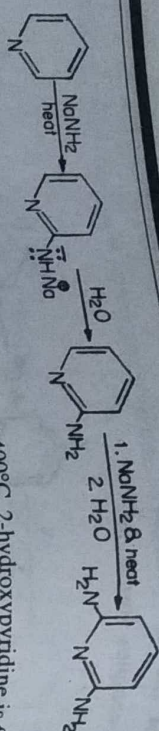
(v) Nucleophilic substitution reactions :

There are three resonating structures in the resonance hybrid of pyridine in which positive charge appears at 2-, 4- and 6-positions. This means that the ring as a whole bears a partial positive charge and hence nucleophilic substitution reactions are possible on pyridine ring and the nucleophile will be incorporated at 2- or 4- or 6-position. A few  $ArS_N$  reactions on pyridine are discussed here :

(a) Tischitschabin reaction :

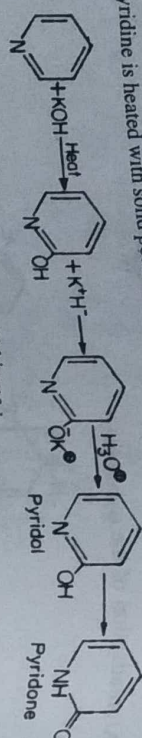
When pyridine is heated with sodamide in toluene sodio salt of 2-aminopyridine is formed which on hydrolysis gives the amine; when excess of sodamide is used 2, 6-diaminopyridine is obtained.





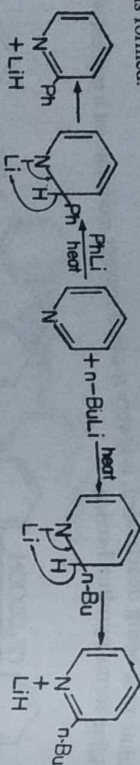
(b) Hydroxylation :

When pyridine is heated with solid potassium hydroxide at 400°C, 2-hydroxypyridine is formed.



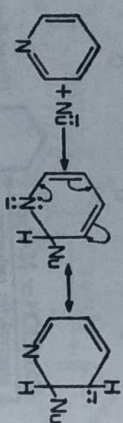
(c) Alkylation and arylation by alkyl- and aryllithiums :

When pyridine is heated with *n*-butyllithium or phenyllithium, 2-butyl- or 2-phenylpyridine respectively is formed.

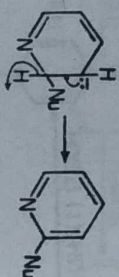


**Mechanism of the  $S_N$  reactions :**

**Step I : Formation of the cyclic anion :**



**Step II : Abstraction of the hydride ion.**

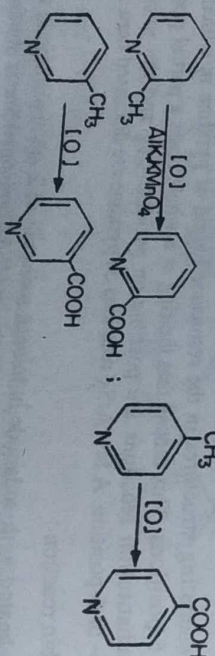


(vi) Reactions on side chains of pyridine homologues :

2-, 3- and 4-methylpyridines are called picolines; they occur in coal-tar and in bone oil; 2- and 4-methylpyridines are very reactive and behave as *o*- and *p*-nitrotoluenes. However the following are the main reactions involving the side chain.

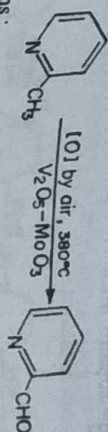
(a) Oxidation :

Chromic acid or acid permanganate or alkaline permanganate oxidises picolines to the corresponding pyridinecarboxylic acids.

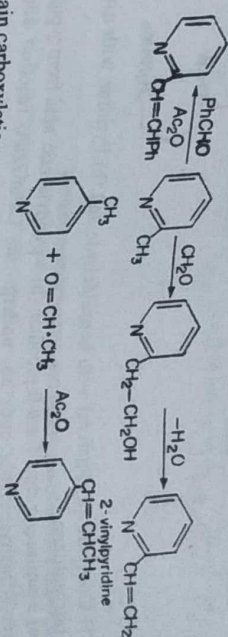


#### CH. 19 : A FEW HETEROCYCLIC COMPOUNDS

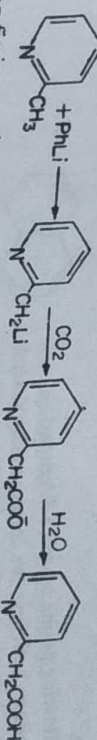
When gaseous picolines are oxidised by air at 380°C over vanadium-molybdenum oxides, formylpyridines are formed.



(b) Condensation reactions :



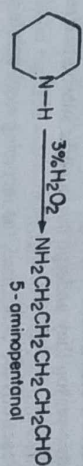
(c) Side-chain carboxylation :



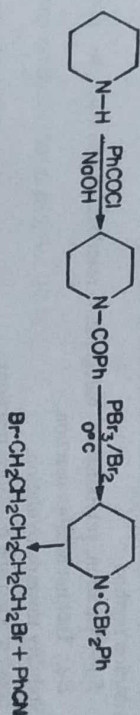
(vii) Ring-fission reactions :

Usually the aromatic ring is first reduced to hydrogenated ring before fission. Then any of the following methods may be used as the ring opening reaction.

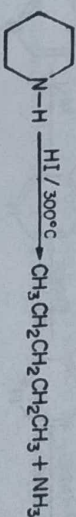
(a) Hydrogen peroxide method :



(b) Von Brown's method :



(c) Hydroiodic acid method :



(d) The Hofmann exhaustive methylation method :

