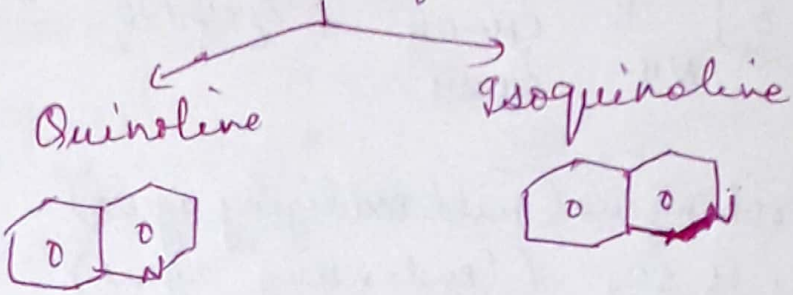
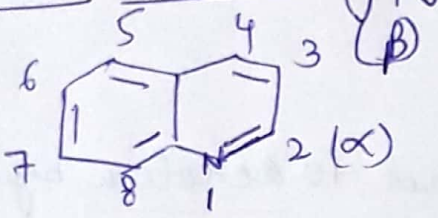
Condensed Six Membered Heterocyclic Compounds



Quinoline / 2,3-Benzopyridine



[Fusion of a benzene ring to the pyridine nucleus at α, β position]

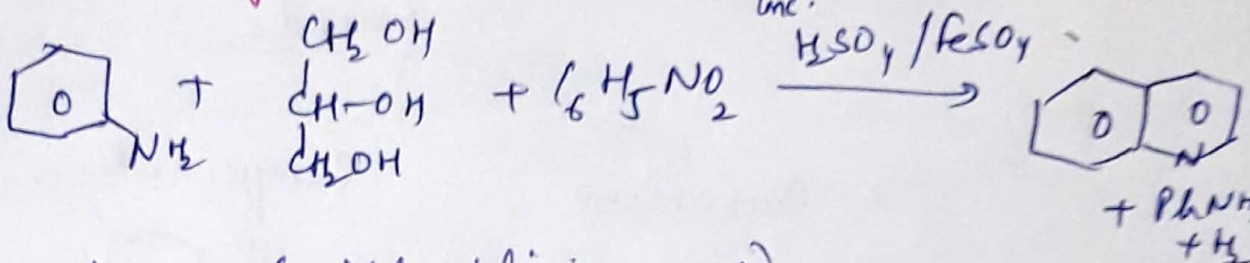
→ It occurs in coal tar, bone oil, Its name is derived from the fact that it was first obtained by heating famous alkaloid quinine with alkali.

→ This nucleus is found in several alkaloids such as quinine, cinchonine etc, antimalarial medicines like chloroquine, plasmoquine etc, antipyretics like cincophen and in laboratory reagent, 8-hydroxy quinoline.

Methods of Preparation:

Commercially, it is obtained from coal tar or bone oil or prepared synthetically.

1) Skraup Synthesis :-

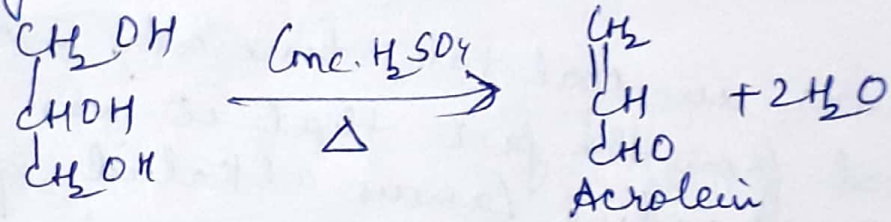


Nitrobenzene (mild oxidizing agent)
Conc. H_2SO_4 (Condensing agent)
~~$FeSO_4$~~
$FeSO_4$ → used to make the rx less violent

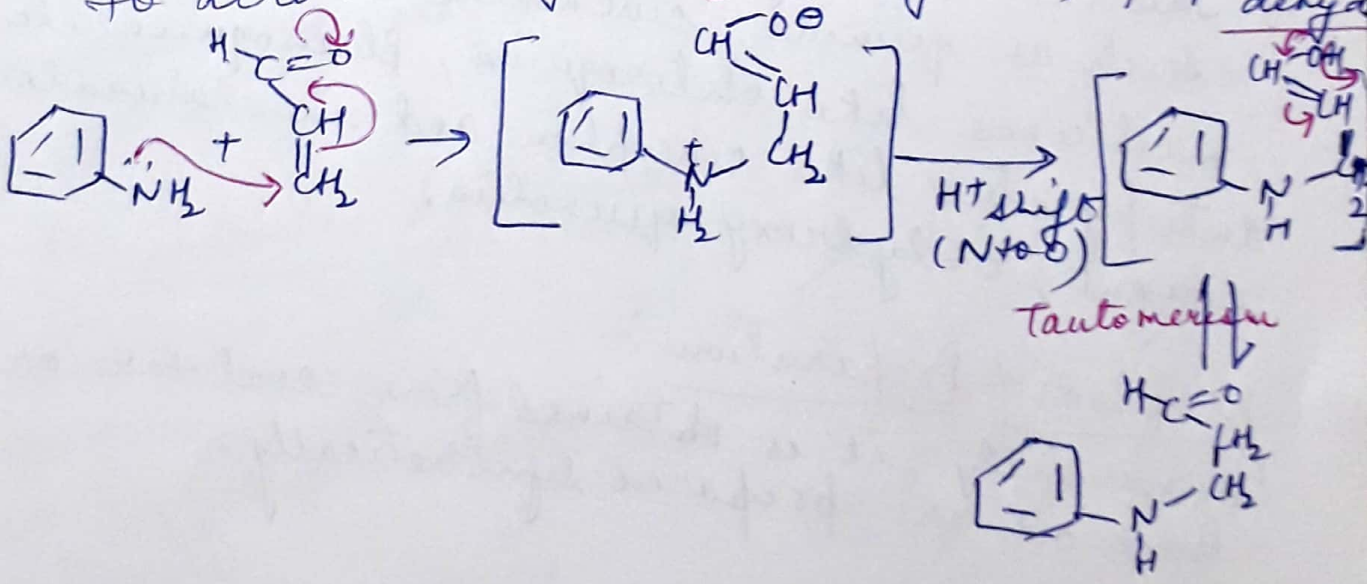
Mechanism :-

→ involve 4 steps :-

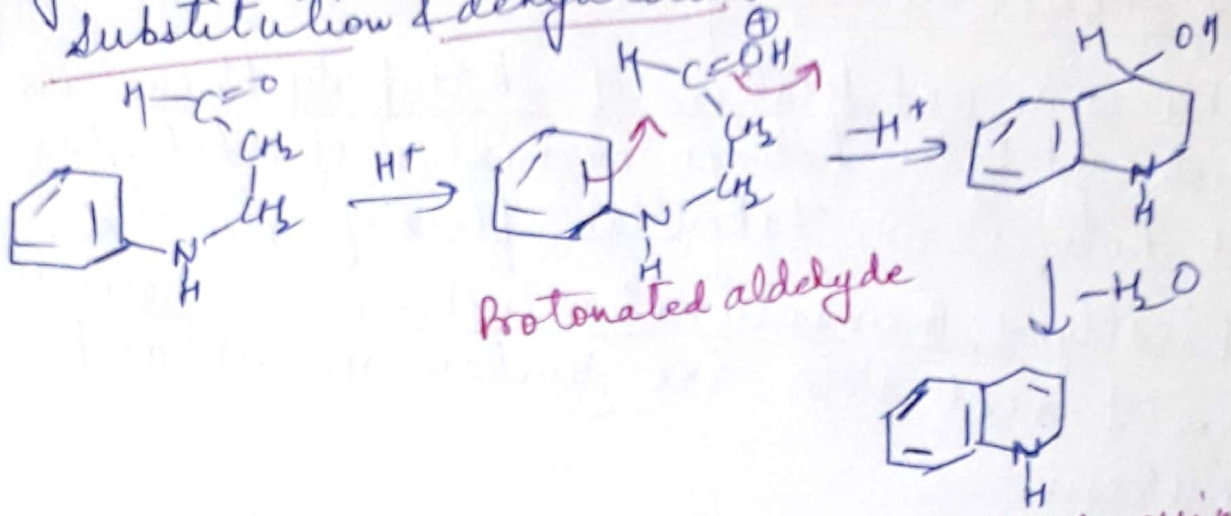
a) Dehydration of glycerol to acrolein by conc. H_2SO_4. (heat)



b) Nucleophilic (1,4 addition) (Michael type) of aniline to acrolein to yield β-(phenylamino) propional dehyd

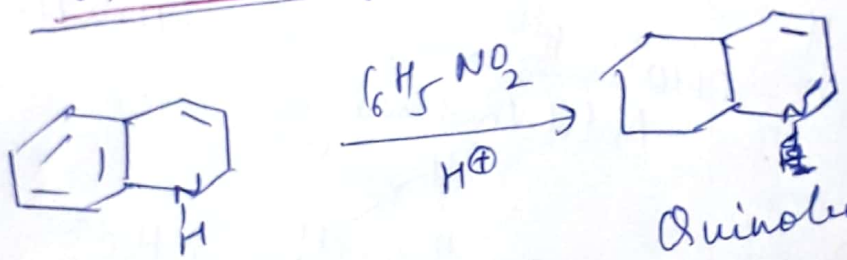


c) Cyclization by protonation of aldehydic group followed by intramolecular electrophilic substitution & dehydration ③



1,2-dihydroquinoline

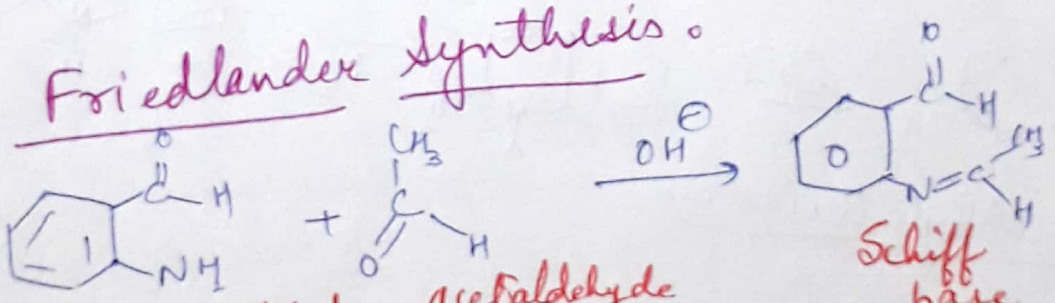
d) Oxidation of 1,2-dihydroquinoline :



Quinoline

* Arsenic acid (H_3AsO_4) may be used in place of nitrobenzene.

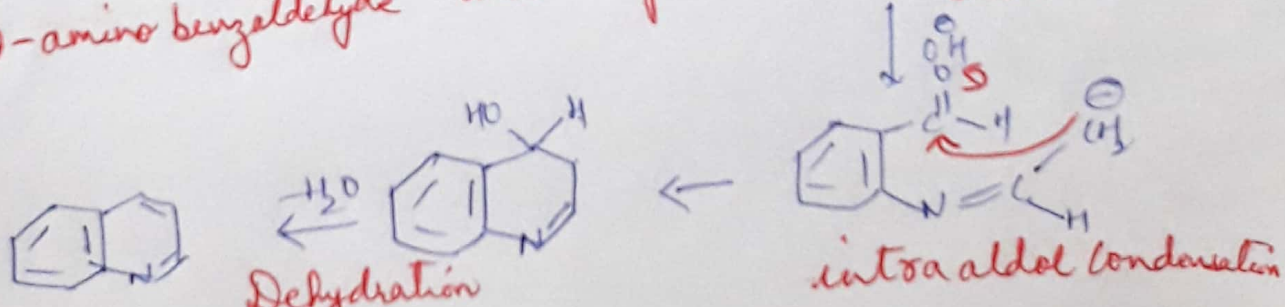
2) Friedlander Synthesis :



o-amino benzaldehyde

acetaldehyde

Schiff base



Quinoline

Dehydration

intra aldol condensation

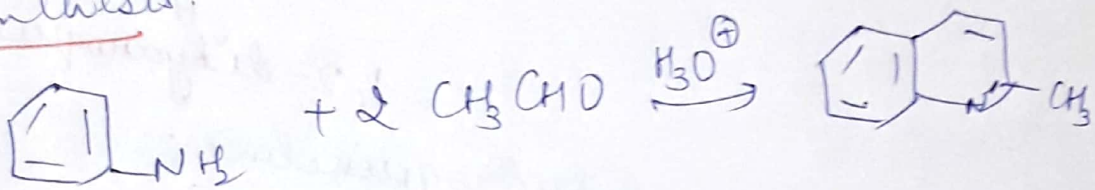
* The carbonyl compound should contain $-CH_2CO$ gp.

(4)

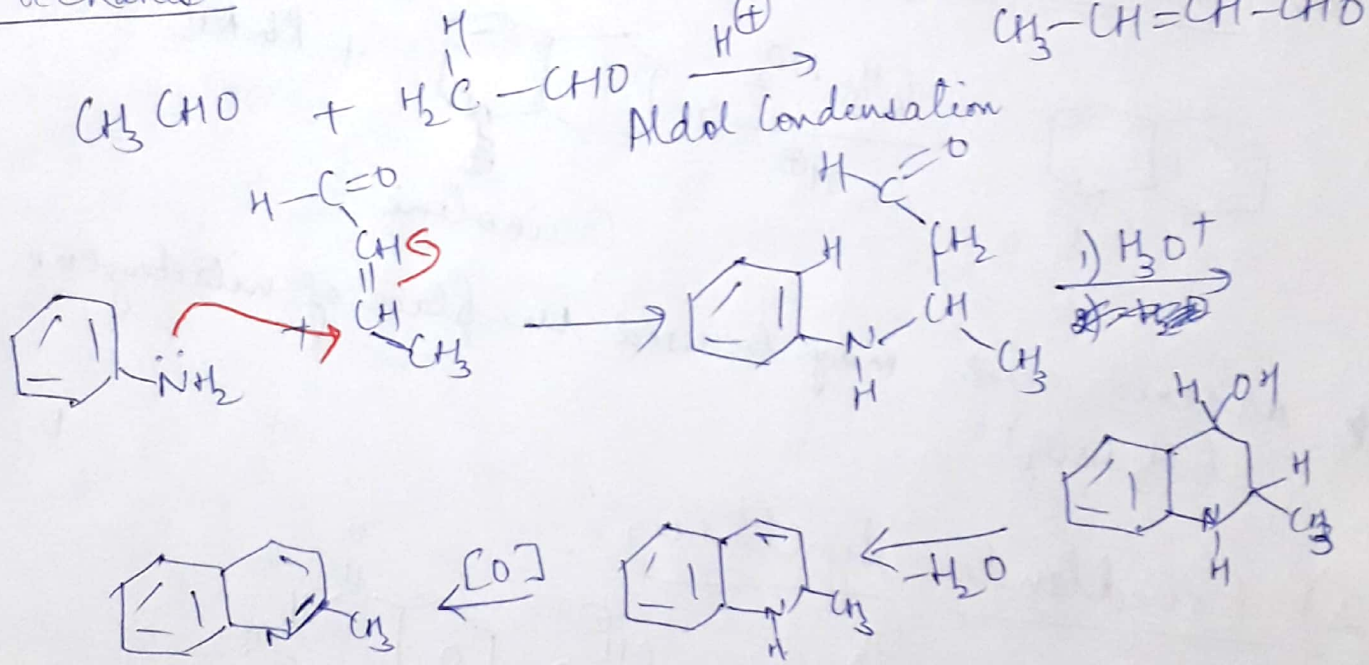
3) Doebner Miller Synthesis

→ This is a modification of Skraup Synthesis in which aldehydes, Ketones or mixture of aldehydes and Ketones are taken in place of glycerol.

→ Firstly, α, β-unsaturated carbonyl compound form & rest steps are similar to skraup Synthesis.



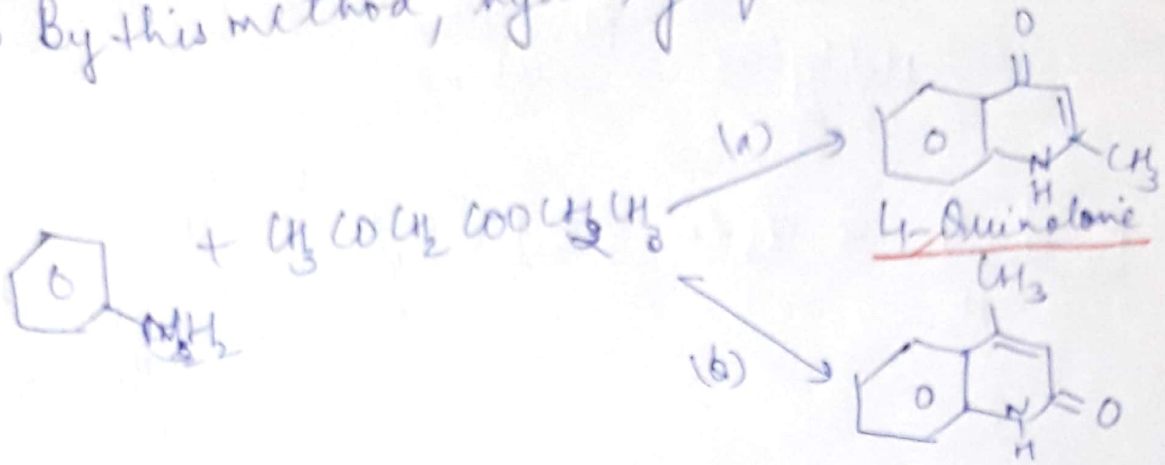
Mechanism



2-Methyl Quinoline

4) Conrad-Limpach and Knorr Synthesis

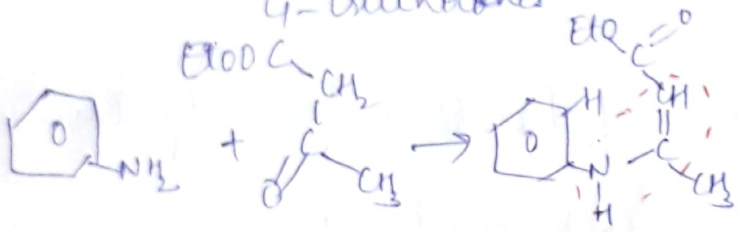
→ By this method, hydroxy quinoline is obtained.



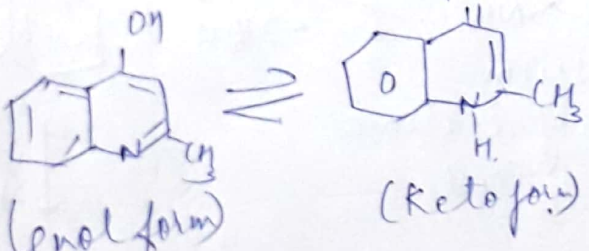
Conrad Limpac Synthesis

↓ 250°C

4-Quinolines



↓ 250°C



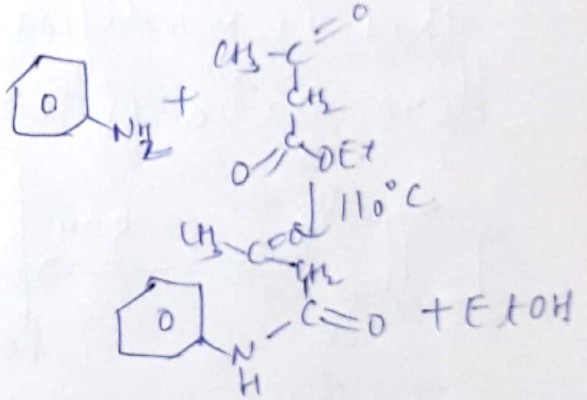
(enol form) ⇌ (Keto form)

Here, examines form

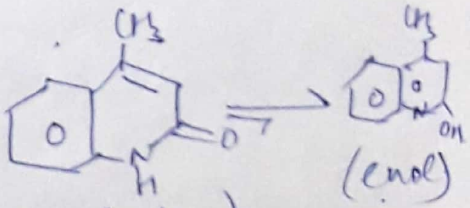
Knorr-Quinoline Synthesis

↓ 100°C

2-Quinolone



100°g H_2SO_4



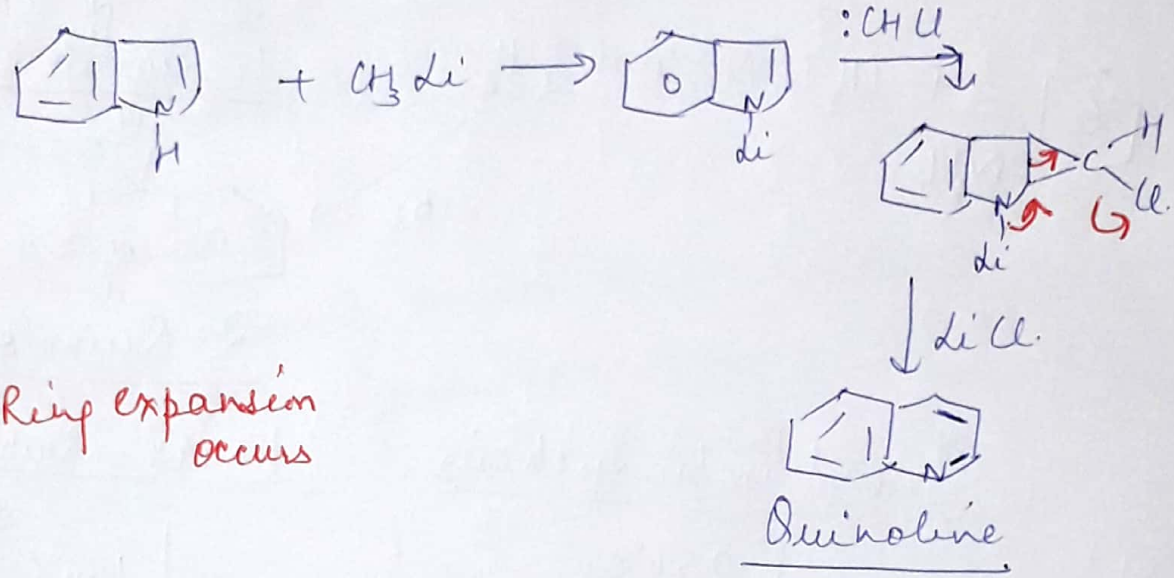
4-Methyl-2-hydroxy Quinoline

Here, anilide form

5) Closs Reaction :-

$CH_2Cl_2 \rightarrow :CHCl + HCl$

Methylene chloride — Mono chloro carbene.

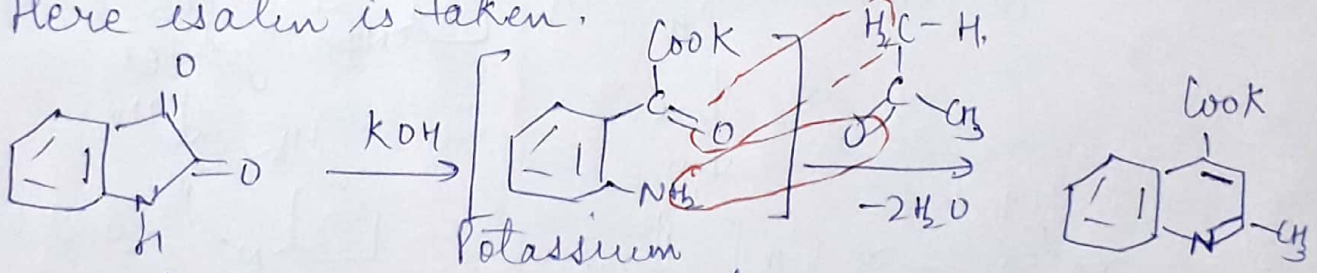


Quinoline

* Ring expansion occurs

6) Pfitzinger Reaction :-

This is modification of Friedlander's synthesis.
Here isatin is taken.



Isatin

Potassium salt of isatinic acid

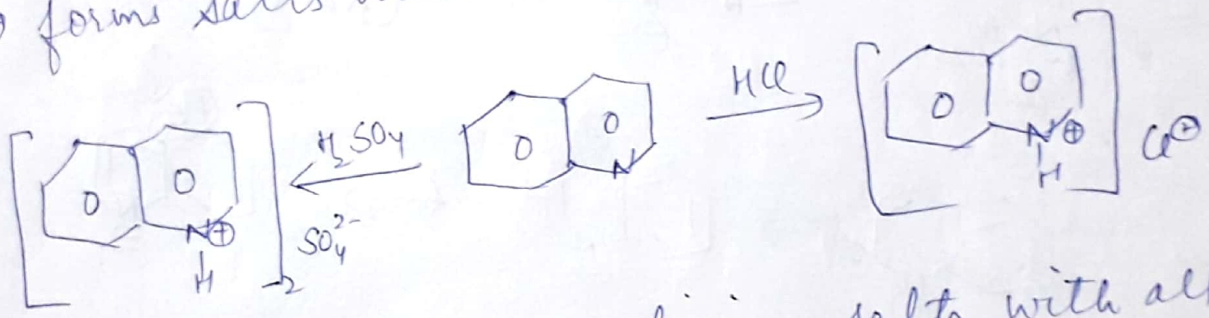
2-Methyl Quinoline

Physical Properties :-

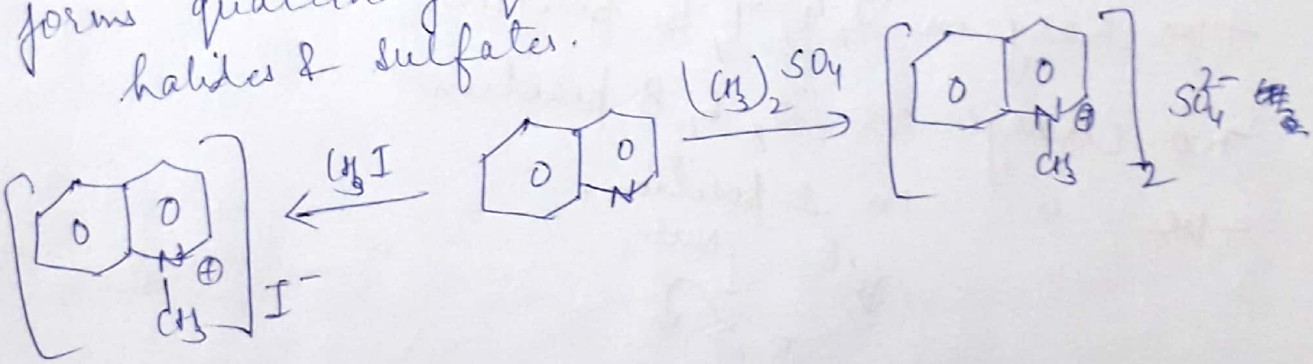
→ Colourless liquid (b.p. 237°C)
→ characteristic odour similar to pyridine.
→ Sparingly soluble in H_2O but completely soluble in most of the organic solvents.
→ turns yellow on standing.

Chemical Properties :-

→ 3° base (pKa = 9.1) basicity is similar to aniline.
→ Less basic than pyridine (pKa = 8.7)
→ forms salts with mineral acids.



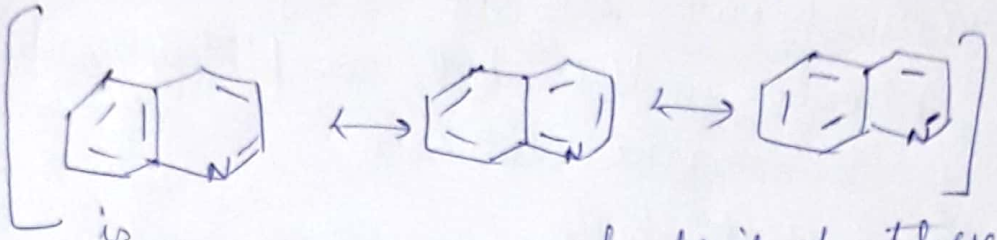
→ forms quaternary quinolinium salts with alkyl halides & sulfates.



Aromaticity :-

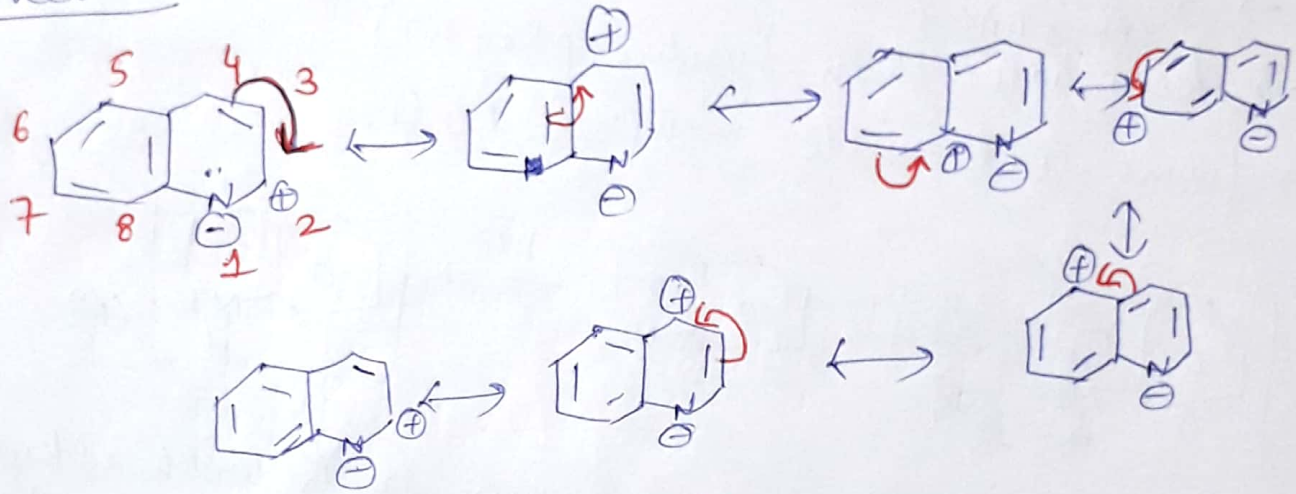
Due to 10 e^- system, show aromaticity and easily show electrophilic substitution reactions.
→ Like pyridine, the e^- withdrawing properties of nitrogen atom deactivates the pyridine ring of quinoline towards electrophilic reagents but nucleophiles attack quinoline at 2,4 position preferentially.

Electrophilic sub. occurs in benzene ring at (8) 5, 6 & 8 position.

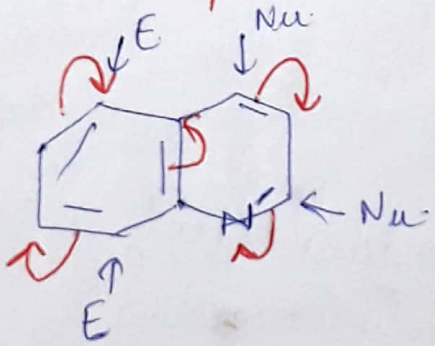


Quinoline is mainly resonance hybrid of these three resonating st. R.E = 264.9 KJ/mol.

Other st:-

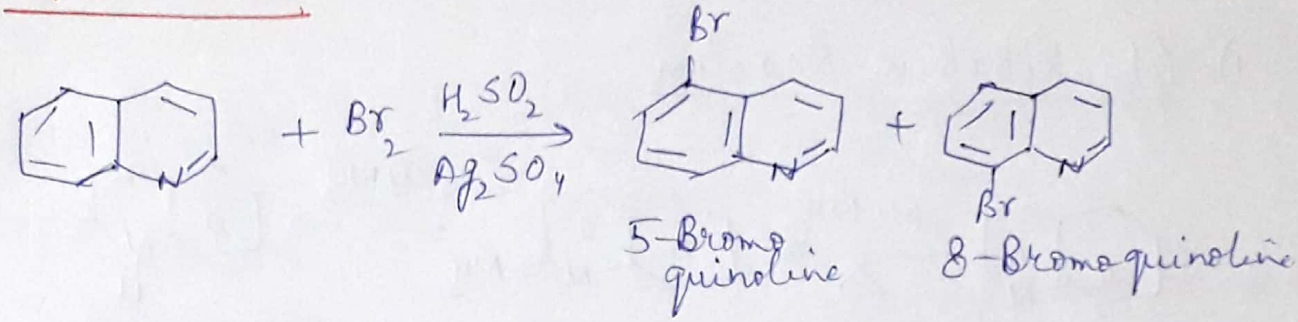


+ve charge on 2, 4, 7, 5 position
no charge on 3, 6, 8 position
-ve " on 1 position.



Electrophilic Sub. Rxs

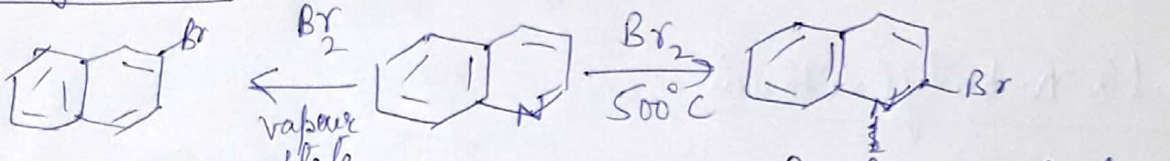
1) Bromination



5-Bromo quinoline

8-Bromoquinoline

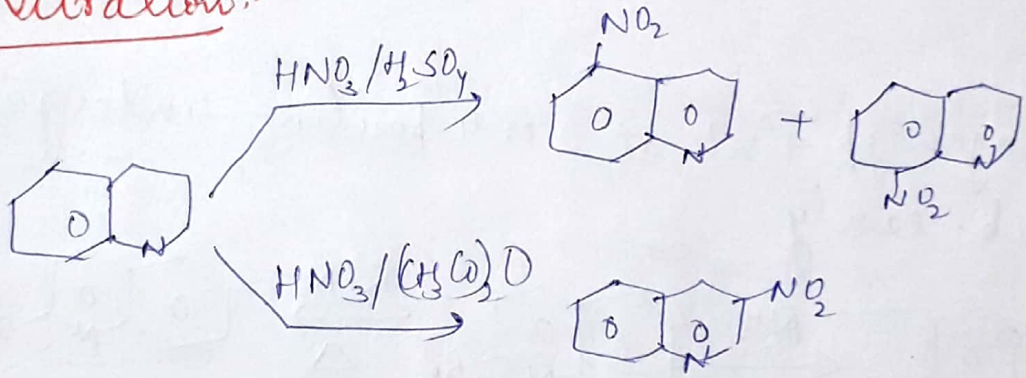
At high temp.



3-Bromo quinoline

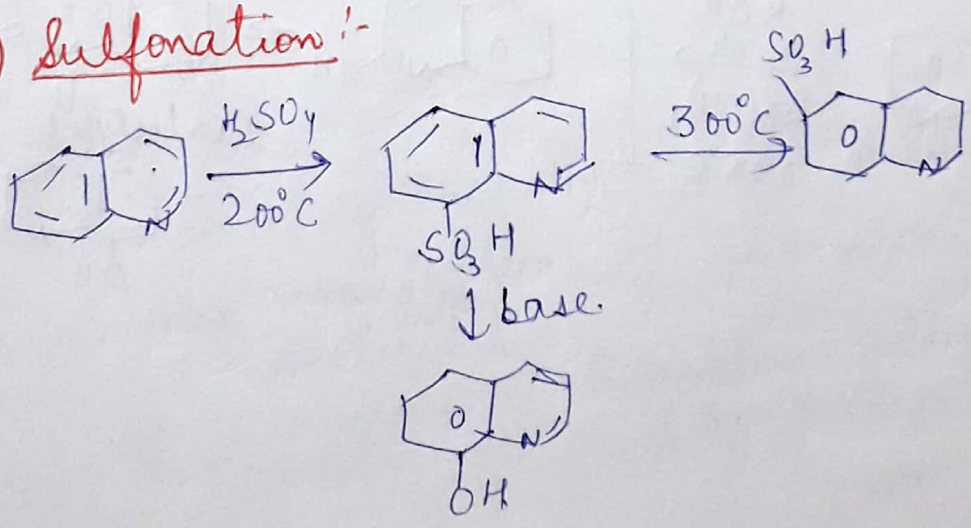
2-Bromoquinoline

2) Nitration:-



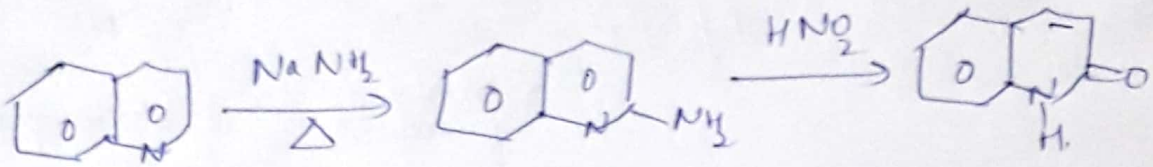
3-nitroquinoline

3) Sulfonation:-



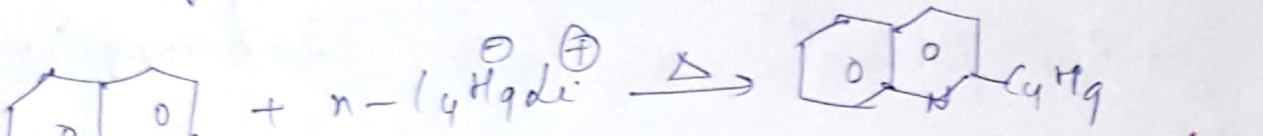
Nucleophilic Substitution Reactions

1) Chichibabin Reaction :-



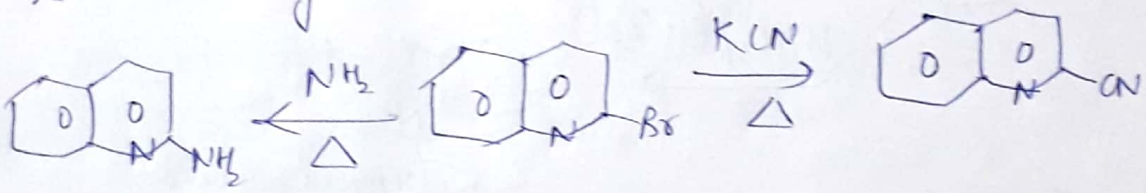
2-Amino quinoline — Carbostyril

With n-butyl lithium

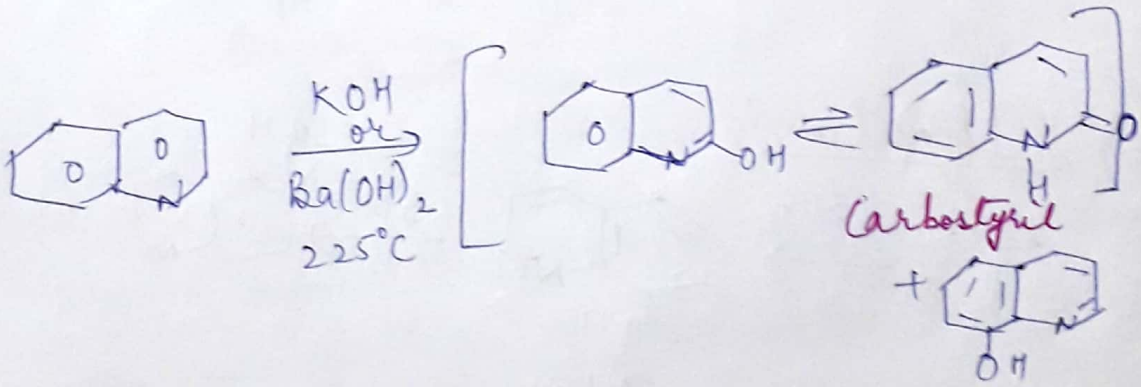


2-(n butyl)-quinoline

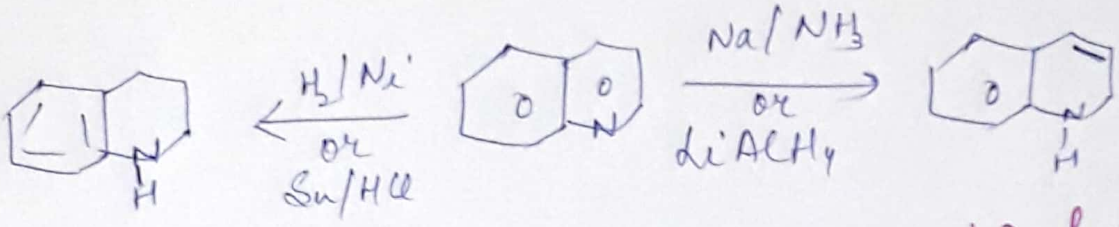
2) Halogen gp + nt at 2 or 4 position undergo $Nu^{\ominus}$ sub. easily.



3)

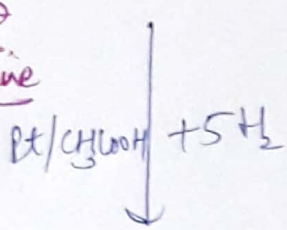


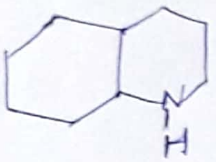
4) Reduction :-



1,2,3,4-Tetrahydro quinoline

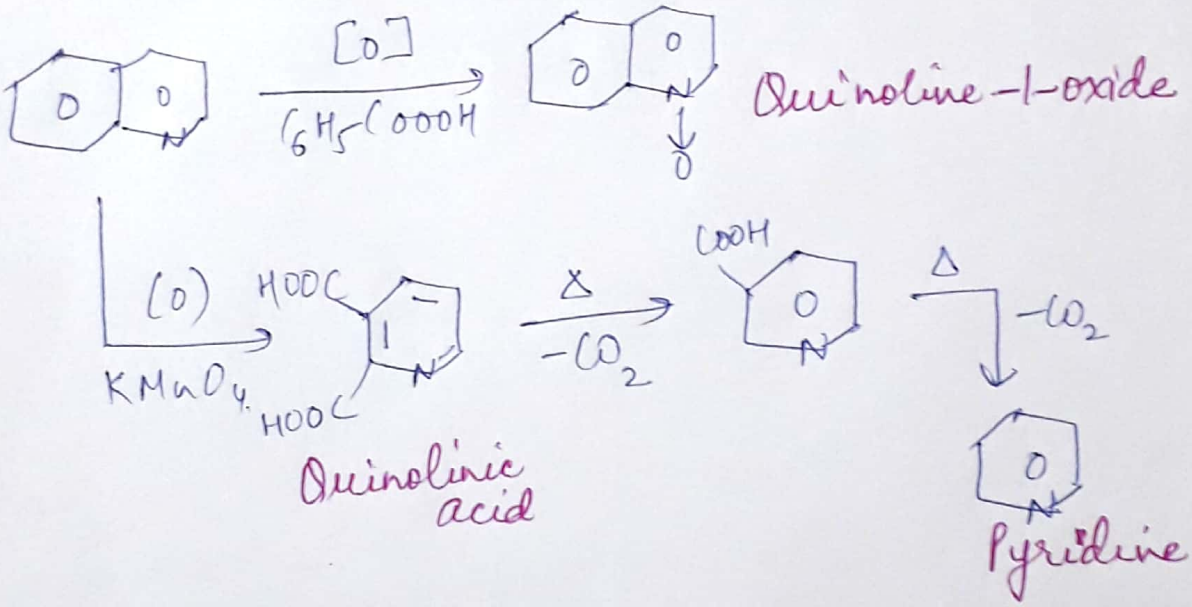
1,2-hydroquinoline





Decahydroquinoline

5) Oxidation :-



Quinoline-1-oxide

Quinolinic acid

Pyridine

~~6) Root~~ Uses :-

→ in organic synthesis as a high boiling basic solvent.

→ in the manufacture of pharmaceuticals, dyes and insecticides.

eg. Chloroquin (antimalarial)

Quinoline yellow (dye for textile)