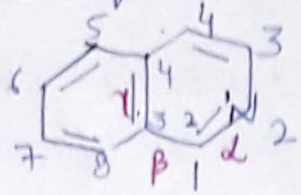
Isoquinoline



3,4-Benzopyridine

Benzene ring is fused to β, γ position of pyridine ring

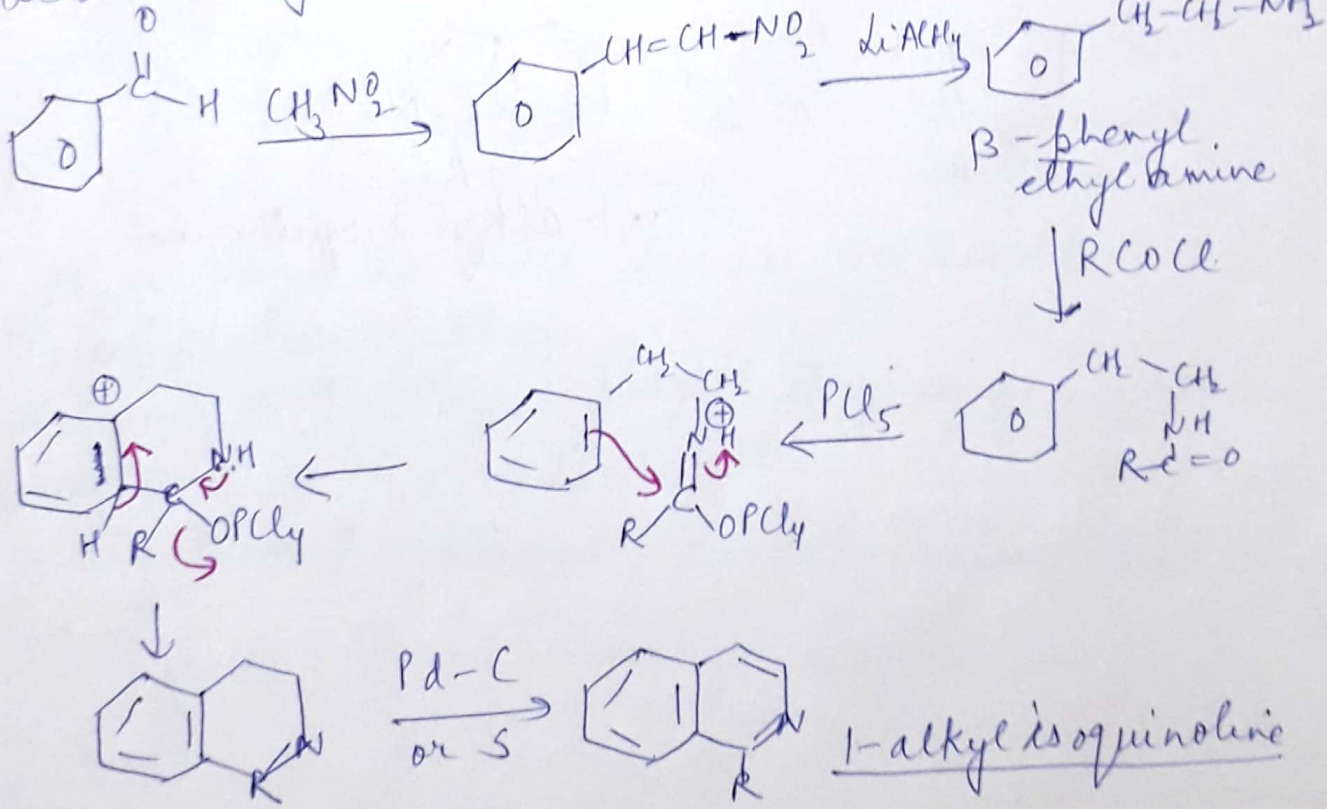
→ It is isomeric with quinoline ~~because~~ therefore, occurs with quinoline in coal-tar and bone oil.

→ It is present in various naturally occuring alkaloids like papaverin, narcotine, berberine etc.

Preparation :-

i) Bischler Napieralski Synthesis :-

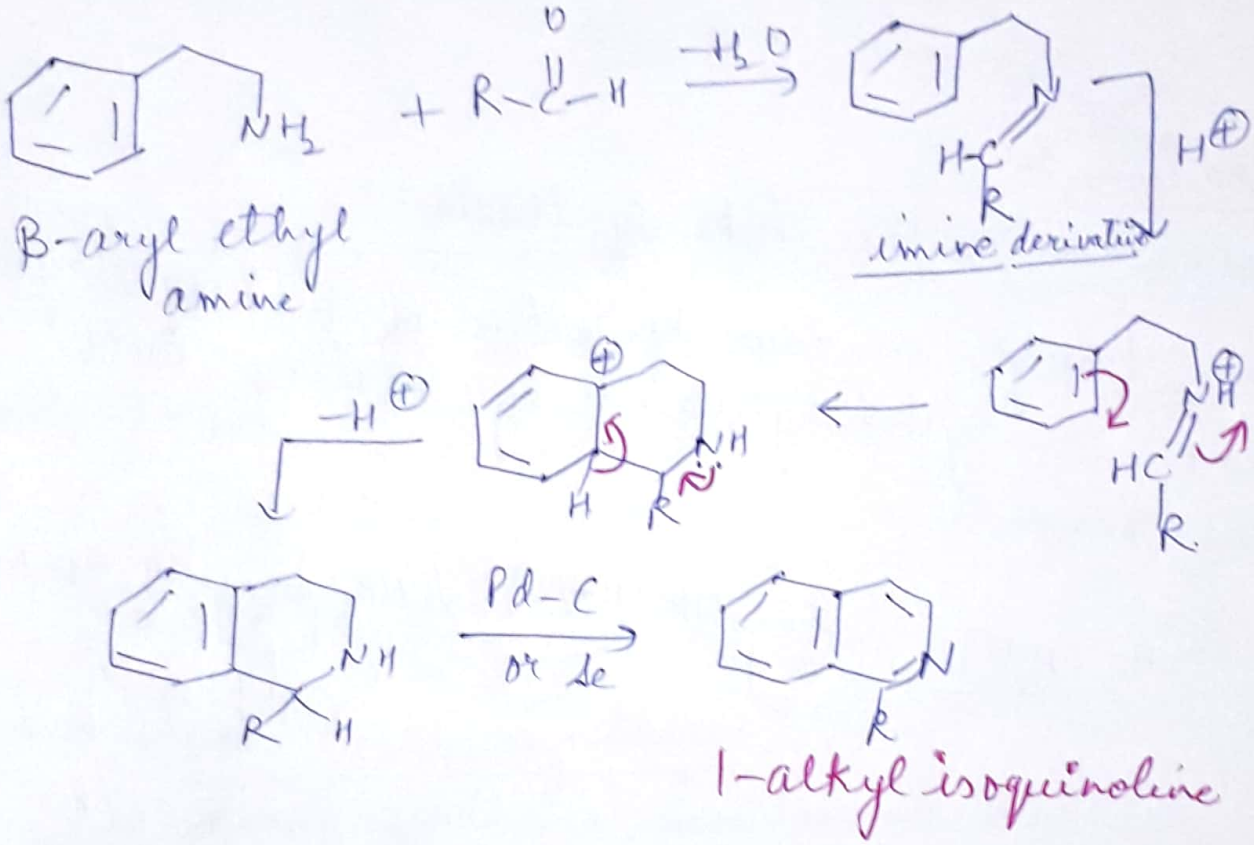
→ Here, formyl or acyl derivative of β-phenylethyl amine is cyclodehydrated by heating with acidic reagents.



2) Pictet - Spengler Synthesis :-

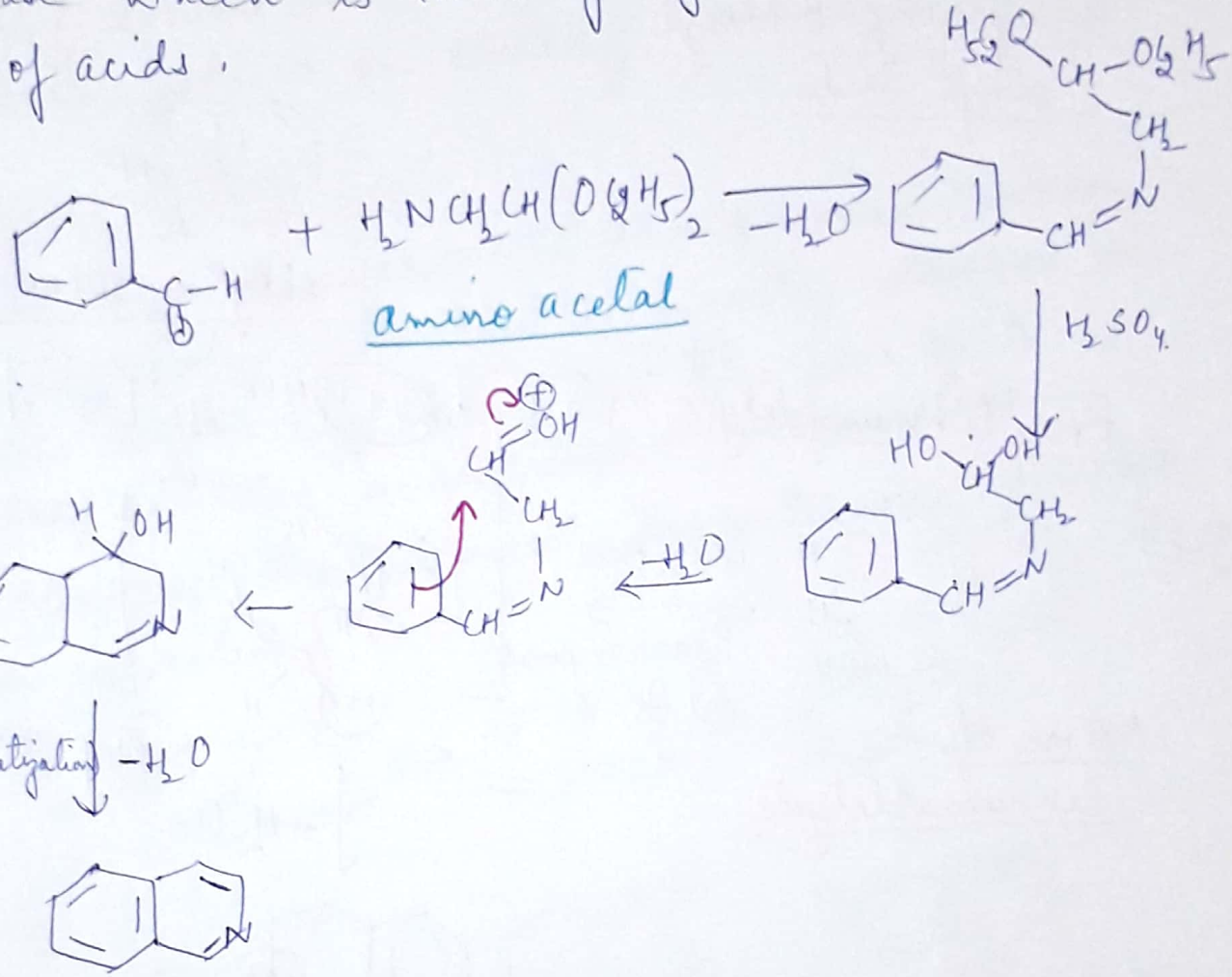
→ It involves condensation of a β-arylethyl amine with an aldehyde in the presence of excess of acids.

→ Initially, an imine is formed which is protonated and subsequently affects intramolecular electrophilic substitution similar to Bischer-Napieralski synthesis



3) Pomeranz-Fritsch Synthesis :

→ It involves condensation of an aromatic aldehyde with an aminoacetal to yield schiff base which is then cyclized in the presence of acids.

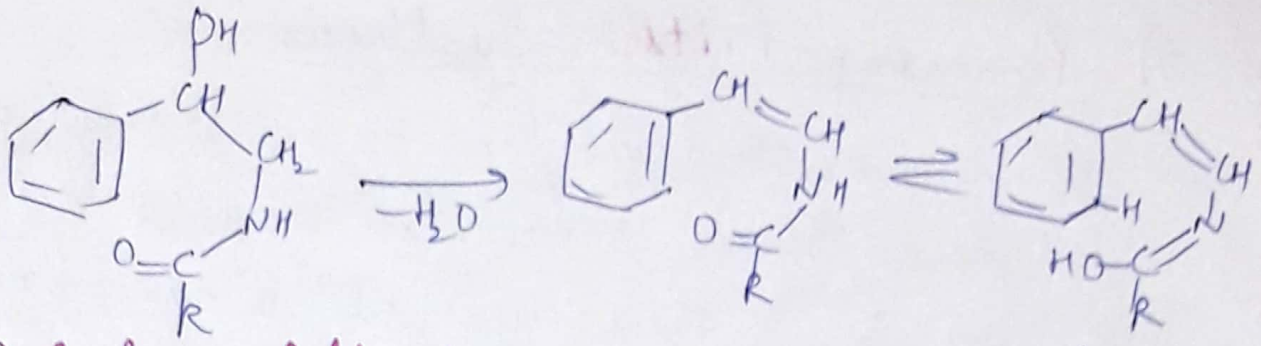


4) Pictet Gams Synthesis :

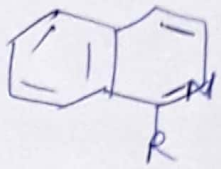
It involves synthesis similar to Bischler Napieralski synthesis.

→ Here, β-hydroxy-β-phenyl ethyl amide is heated with P_2O_5 or acid catalyst.

→ The product obtained, on dehydration and cyclization form 1-alkyl isoquinoline.



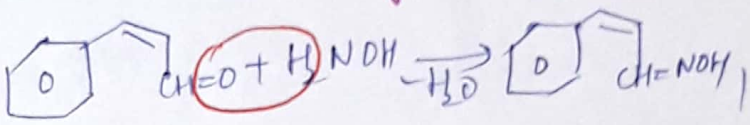
β-hydroxy-β-phenyl ethyl amide



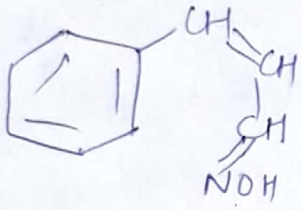
1-alkyl isoquinoline

5) From Cinnamaldehyde

Step I :-

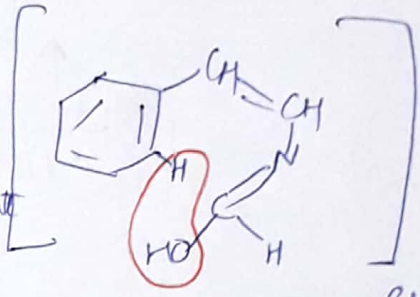


Step II

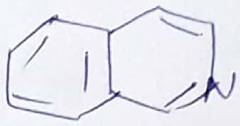


Oxime of cinnamaldehyde

Beckman Rearrangement ΔP_2O_5



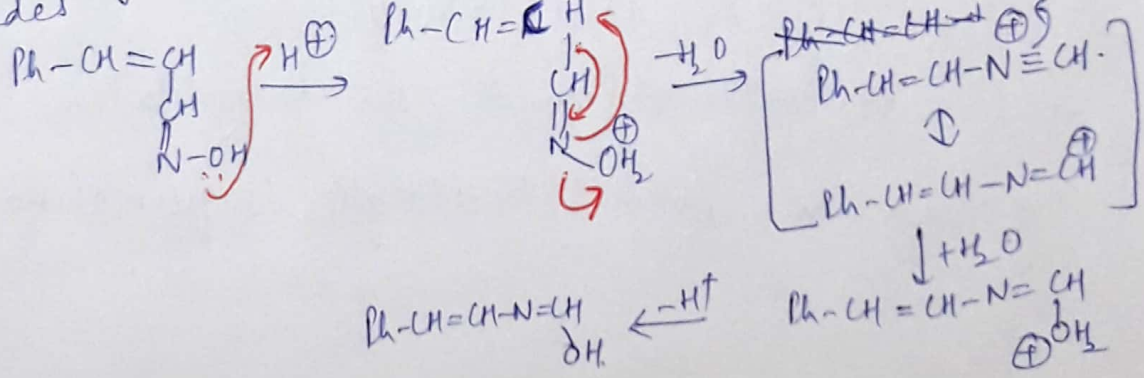
Step III



Isoquinoline

* Beckman Rearrangement :-

Rearrangement of oxime functional gp to substituted amides

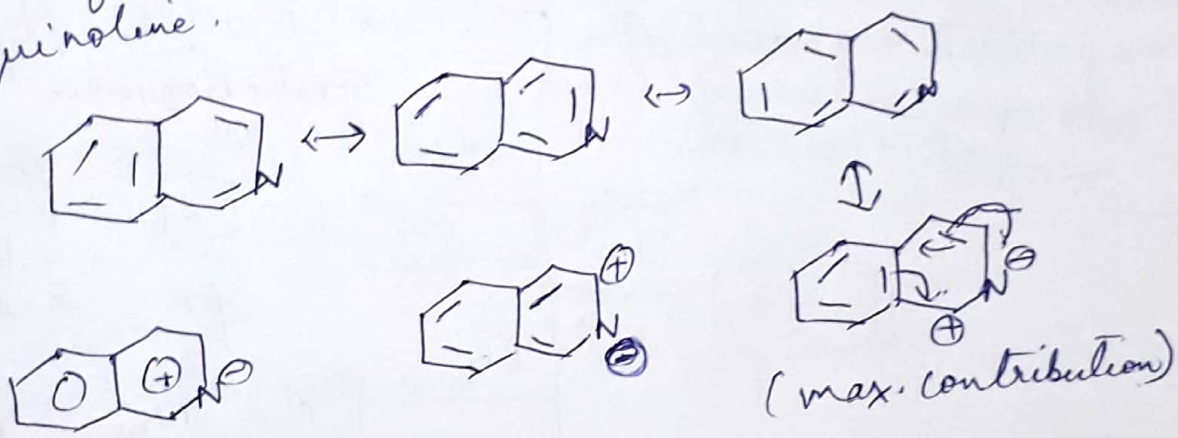


Physical Properties :-

⇒ Colourless solid (m.p. 26°C, b.p. 243°C)
→ Smell like that of benzaldehyde.
→ Volatile in steam, sparingly soluble in water but soluble in many organic solvents.
→ turns yellow on standing in normal conditions.

Chemical Properties :-

→ Stronger base ($pK_b = 8.58$) than quinoline because in quinoline, N-atom is directly attached to the benzene ring hence the lone pair of N is less available as compared to isoquinoline.
→ Most of the chemical properties are similar to quinoline.



Resonance hybrid

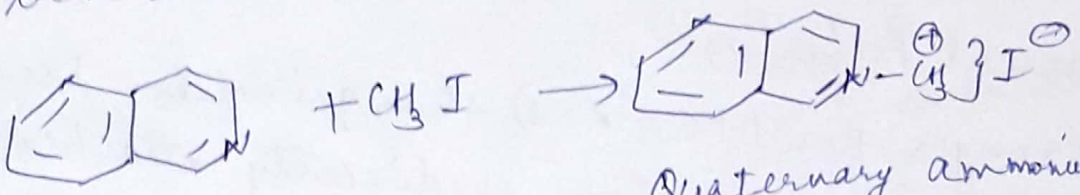
(max. contribution)

Just like quinoline, in isoquinoline, due to presence of N, pyridine ring is deactivated for electrophilic attack and it occurs predominantly at 5 and 8 positions.
Because at these positions, carbocation obtained by electrophile attack is more stable.

→ For Nucleophilic substitution, it occurs predominantly at 1st position because the transitory σ-complex at 1 position is more stable.

① Basic Character:-

→ behaves like 3° amine.

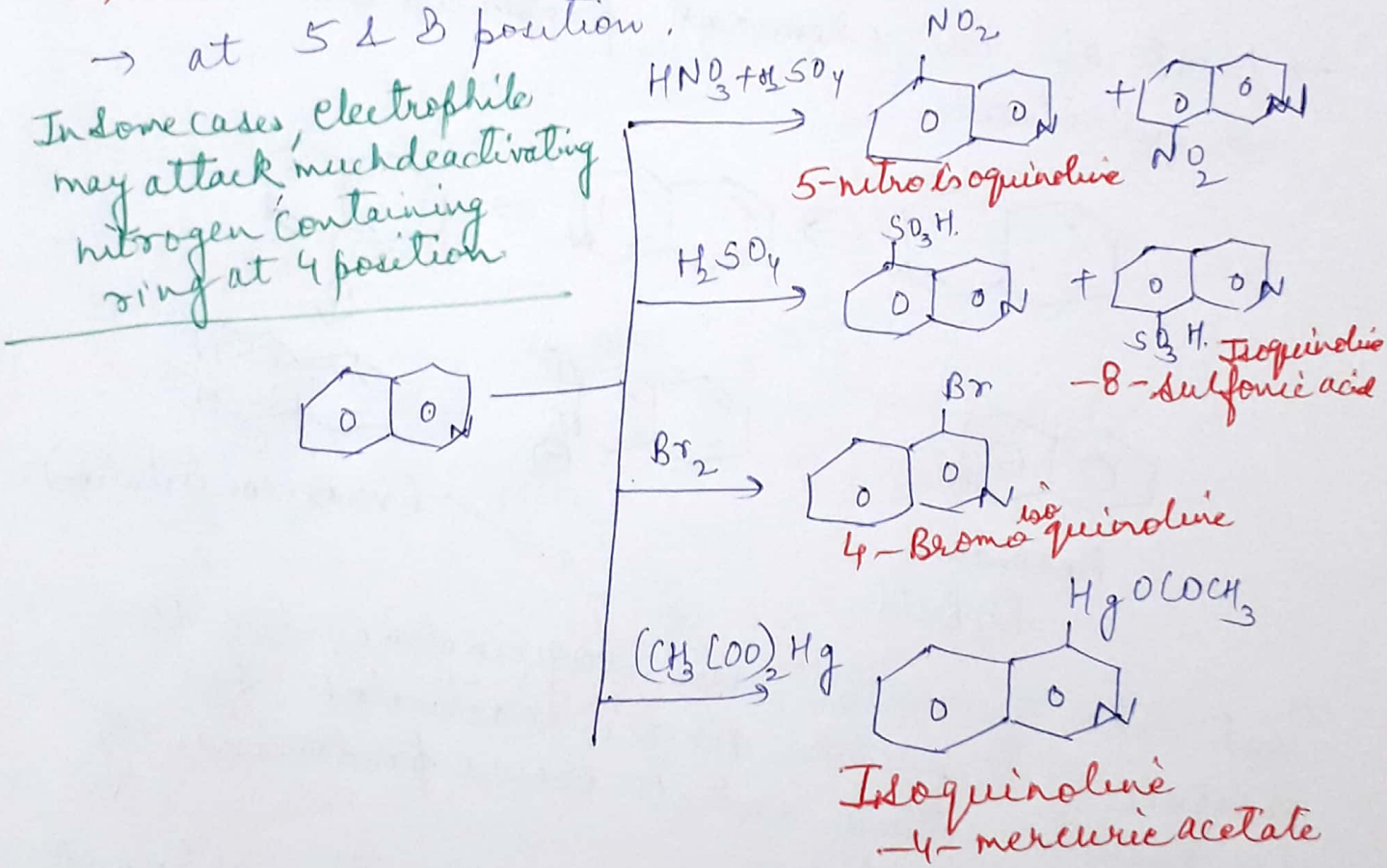


Quaternary ammonium salt

2) Electrophilic substitution:-

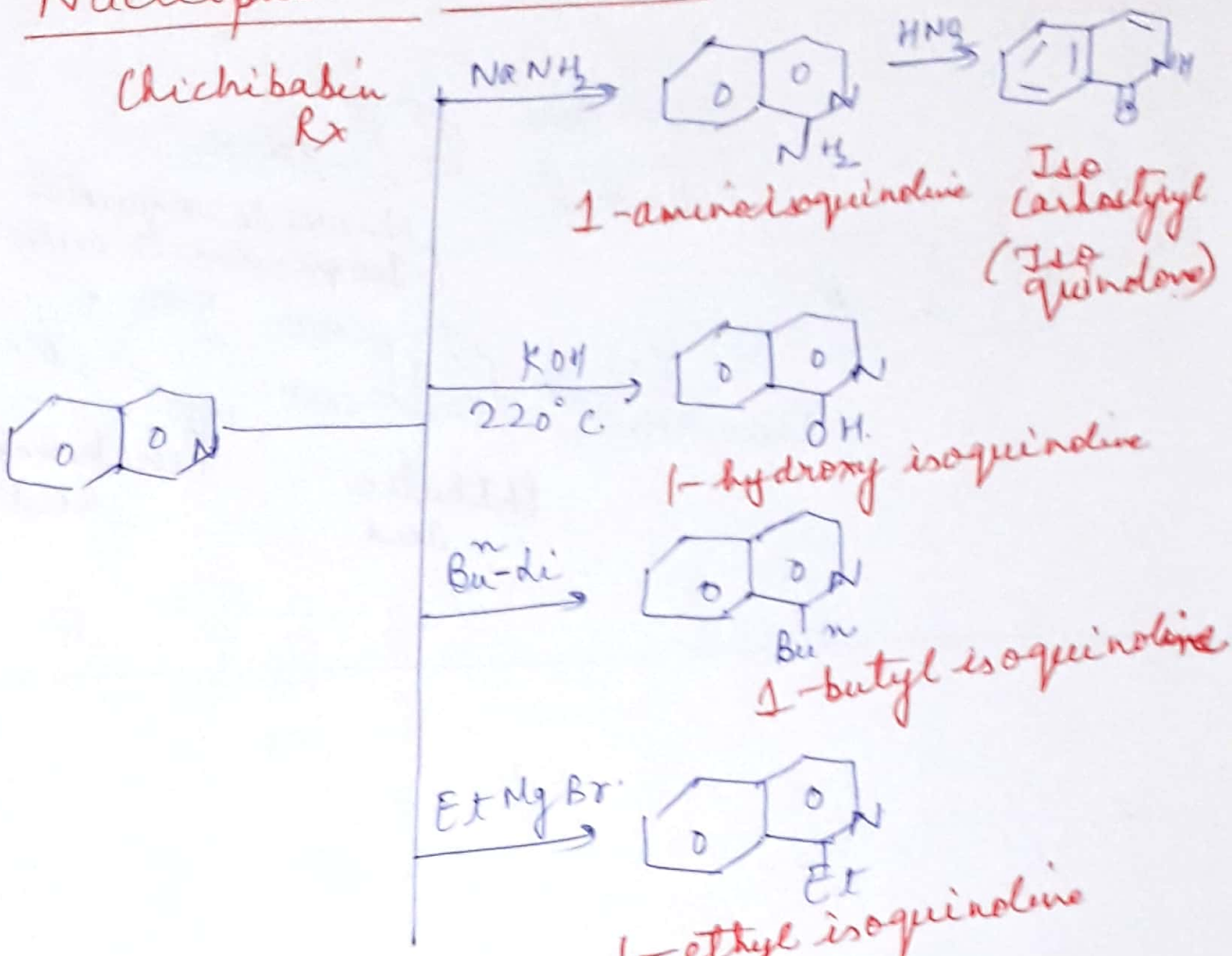
→ at 5 & 8 position.

In some cases, electrophile may attack much deactivating nitrogen containing ring at 4 position

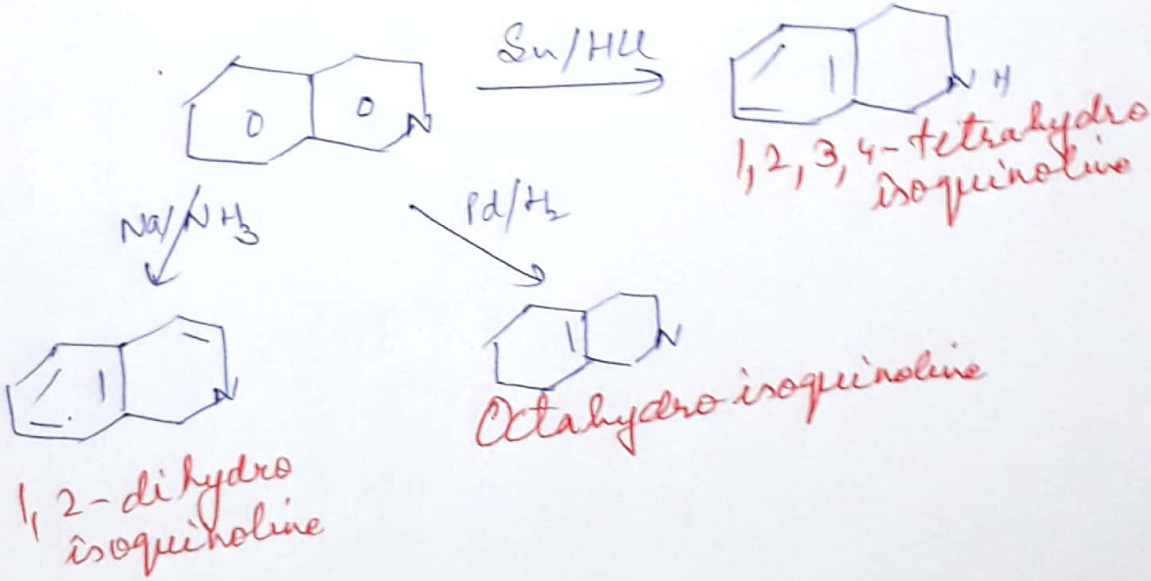


Nucleophilic substitution:-

Chichibabin Rx



Reductions:-



Oxidation :-