HETEROCYCLIC COMPOUNDS
(part 6)
(CONDENSED 6-MEMBERED HETEROCYCLES)

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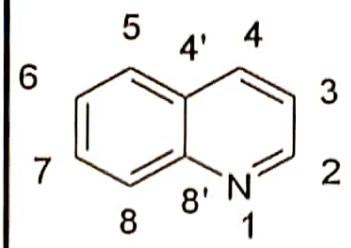
Topics to be Discussed:

1. Quinoline, Isoquinoline-Structure
2. Skraup Synthesis of Quinoline
3. Bischler-Napieralski Synthesis of Isoquinoline
4. Electrophilic Substitution of Quinoline
5. Electrophilic Substitution of Isoquinoline

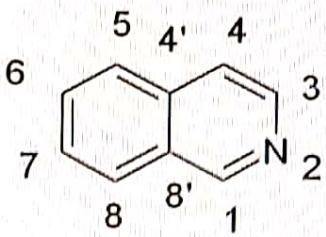
Structure

There are three ways in which pyridine may be fused with Benzene. Both Quinoline and Isoquinoline occur in coal tar.

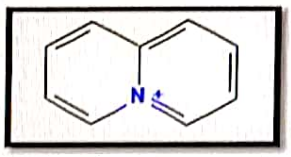
Quinoline and Isoquinoline



Quinoline

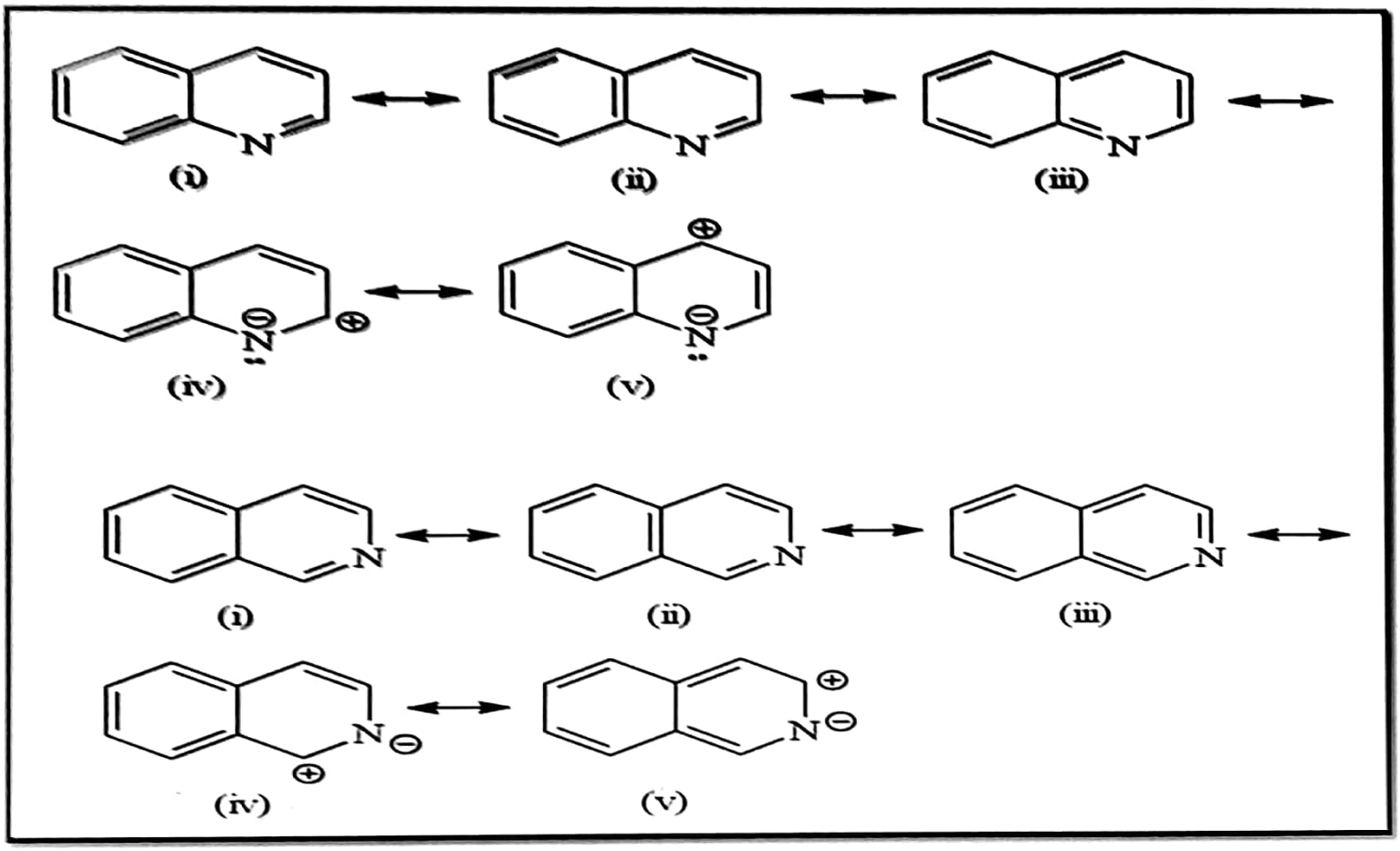


Isoquinoline



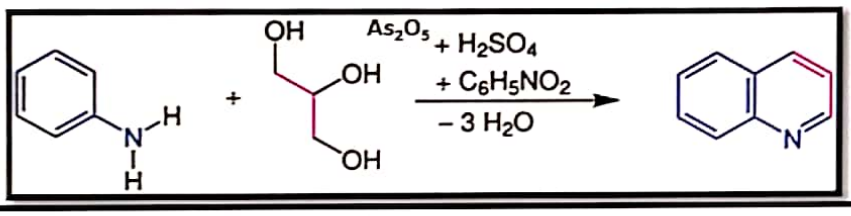
Quinolizinium salts

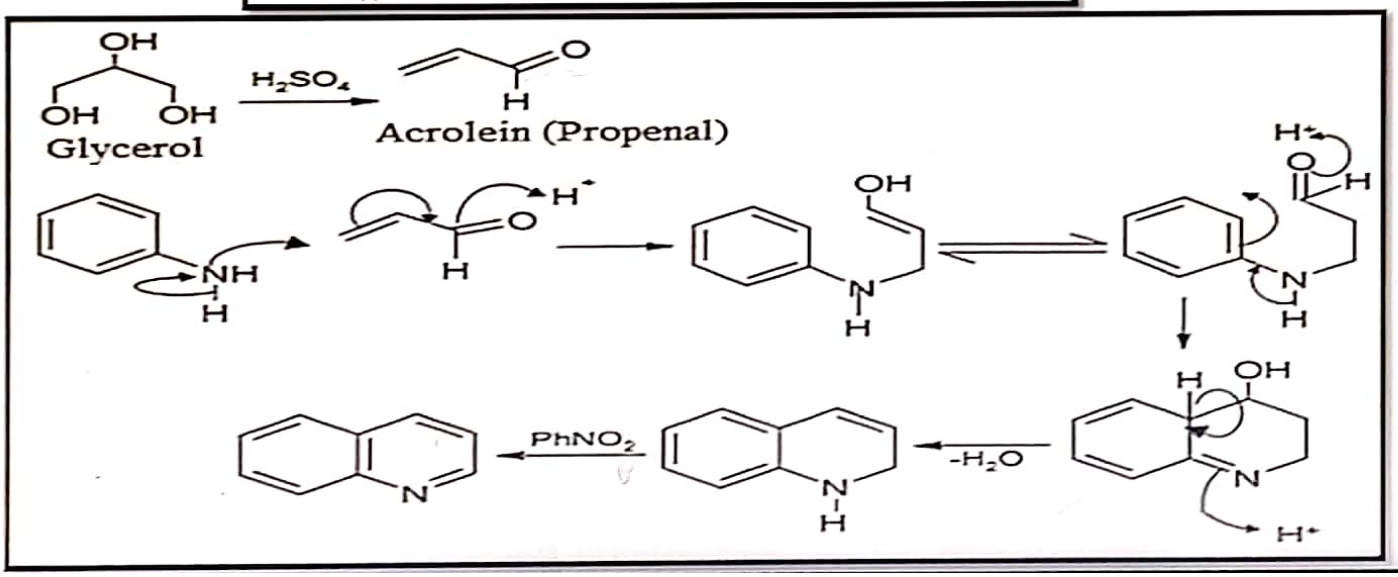
Resonance Structures of Quinoline and Isoquinoline



Skraup Synthesis of Quinoline

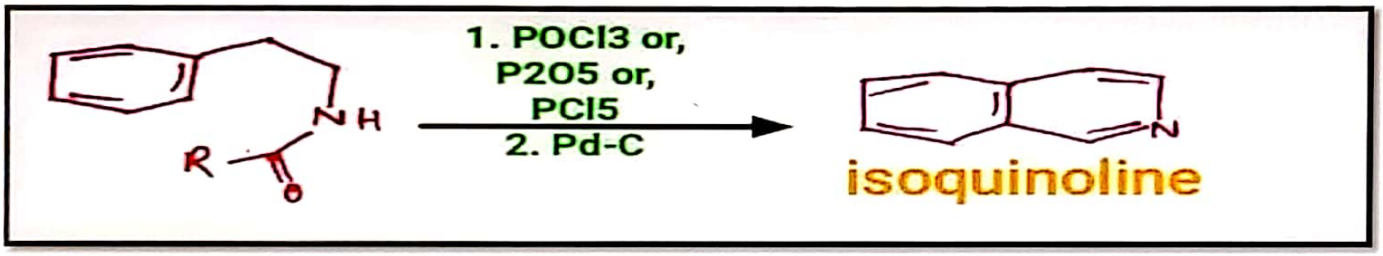
Aniline or substituted Aniline is treated with glycerol, sulphuric acid and an oxidising agent such as As_2O_5 or ferric salt or nitrobenzene. The mechanism involves initial dehydration of the glycerol to give Acrolein which undergoes 1,4-Michael Addition with Aniline. The resulting β-anilinopropionaldehyde is then cyclised to a dihydroquinoline, which is finally oxidised to give Quinoline

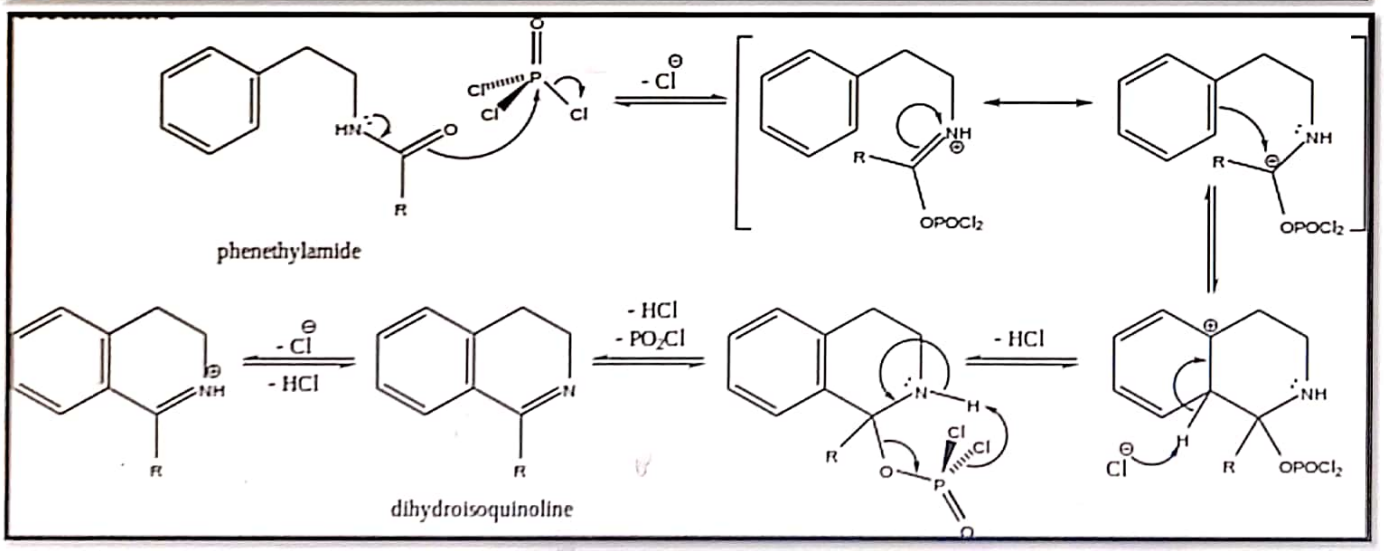




Bischler Napieralski Synthesis of Isoquinline

An acyl derivative of β-phenylethylamine is treated with a dehydrating agent($POCl_3$ or P_2O_5) give dihydroisoquinoline which is dehydrogenated to Isoquinoline.

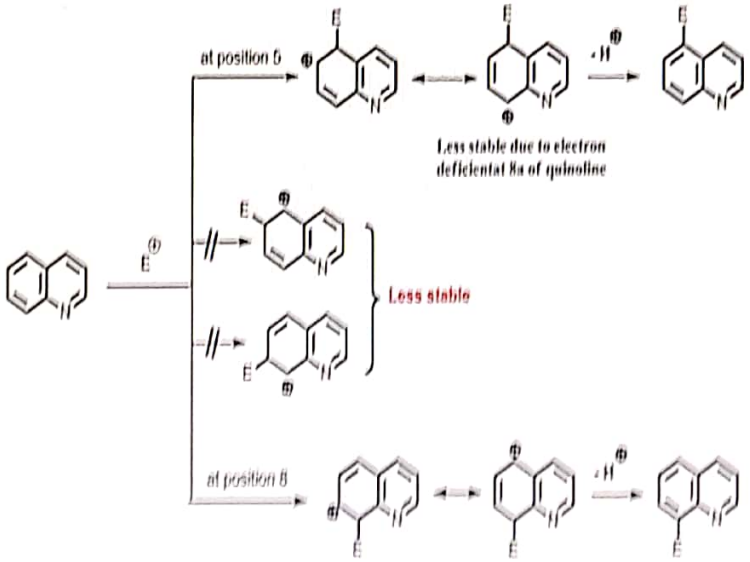




Electrophilic Substitution Reaction-Quinoline

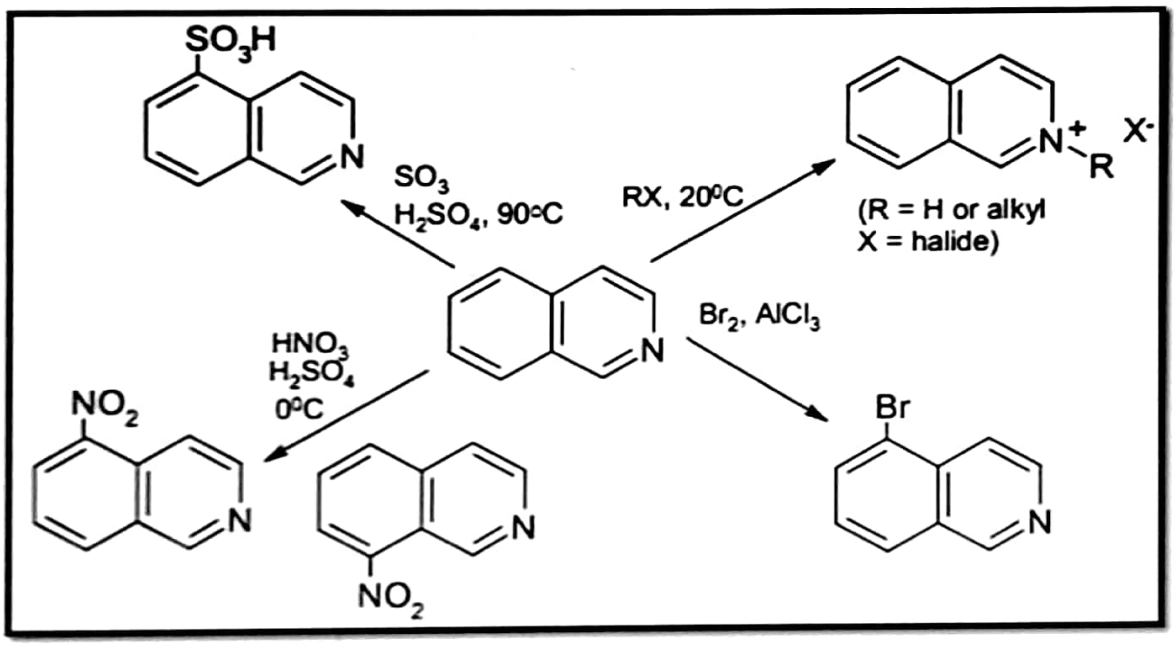
- Electrophilic substitution reactions do not occur in π-deficient pyridine ring of quinoline.
- It becomes even more electron deficient by protonation (in acidic medium).
- In acidic medium preferentially E.S occurs in the Benzene ring of Quinoline at position 5- and 8.
- At low acidic strength E.S. may occur in the 3-position of pyridine ring also.

Quinoline undergoes electrophilic substitution, e.g., nitration, sulphonation and halogenation. As the nitrogen atom deactivates the pyridine, electrophilic substitution occurs in the benzene ring (at position -5 and -8). Postion-8 is more preferred.



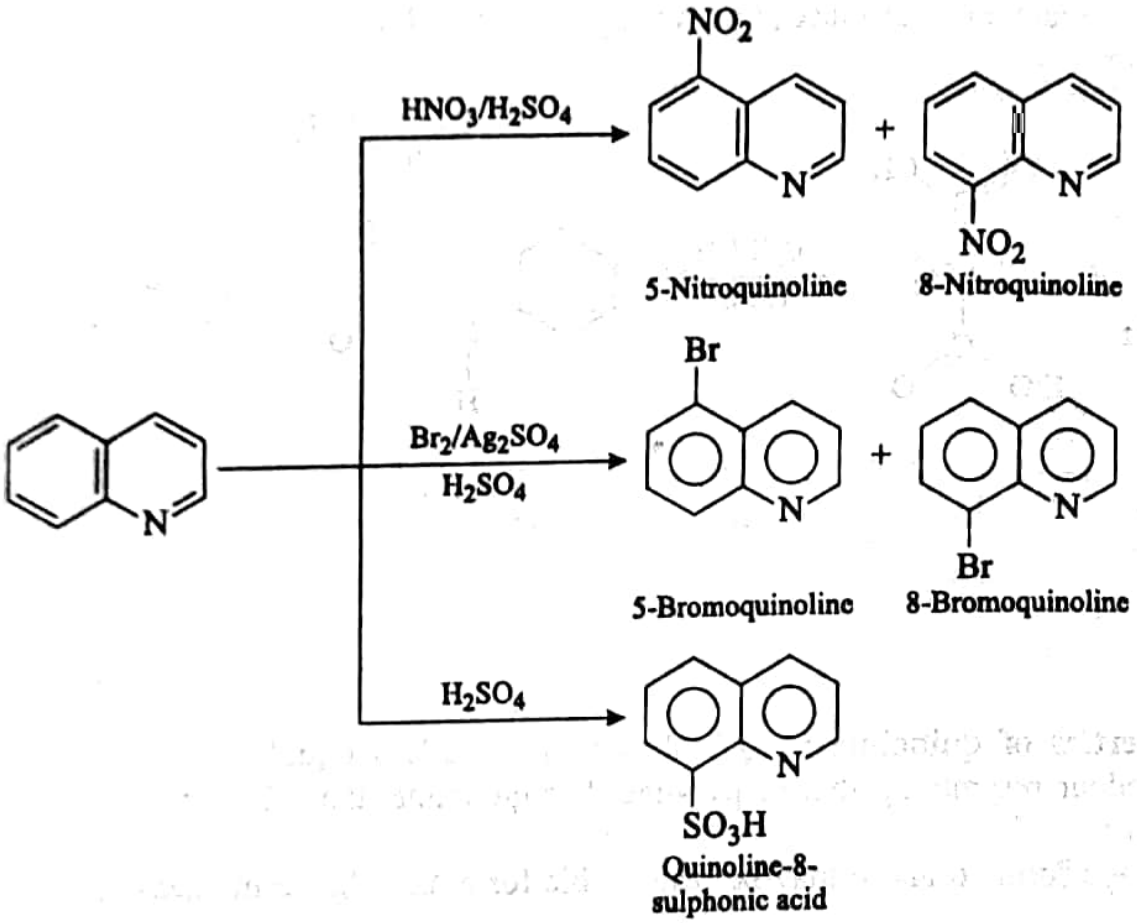
Electrophilic Substitution Reaction-Isoquinoline

Chemically Isoquinoline resembles quinoline in most of the reactions. It undergoes electrophilic substitutions e.g.-sulphonation, nitration occurs at the 5- and 8- positions

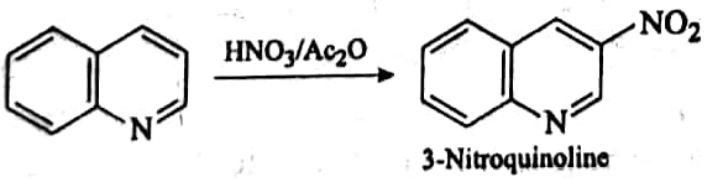


THANK YOU

(2) Electrophilic aromatic substitution reactions : Since pyridine ring of quinoline is π-deficient and can be made even more electron deficient by protonation (in acidic condition) or quaternisation, electrophilic reagents will show a preference for attack on the benzene ring of quinoline specially if acidic conditions are used. Positions 5 and 8 are most reactive for electrophilic substitution reactions. Some of the electrophilic substitutions reactions are given below :



At low acidic strength substitution may be observed in the pyridine ring at position 3.



Formation of N-oxide of quinoline activates pyridine ring (at position 4) towards electrophilic reagents as in case of pyridine. Quinoline-N-oxide may therefore be substituted by electrophilic reagents in pyridine ring.