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Chemistry

SUB. CODE- BSCC2402

For B.Sc. 4th Semester

(Heterocycles)

Module-IV

Pyridine

By

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Assistant Professor,

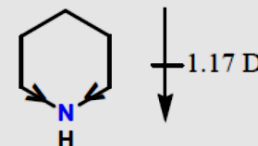
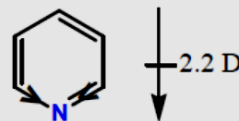
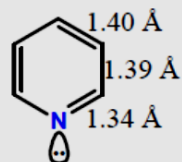
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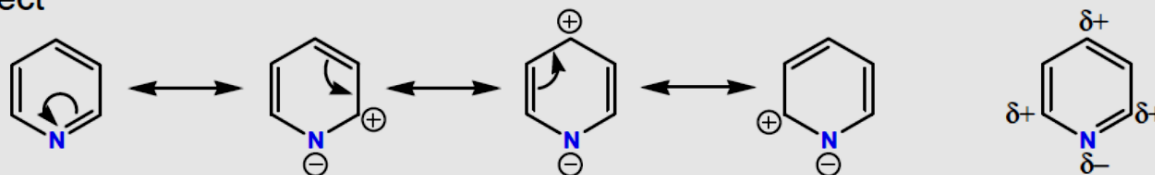
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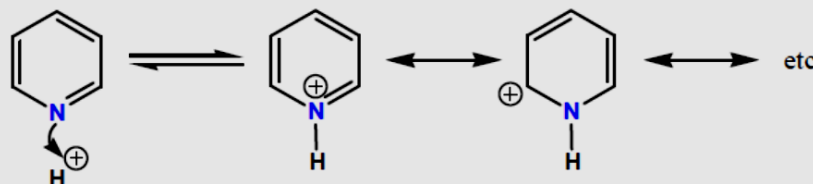
Pyridine



- Isoelectronic with and analogous to benzene
- Stable, not easily oxidised at C, undergoes substitution rather than addition
- -I Effect (inductive electron withdrawal)
- -M Effect



- Weakly basic – $pK_a \sim 5.2$ in H_2O (lone pair is **not** in aromatic sextet)
- Pyridinium salts are also aromatic – ring carbons are more δ^+ than in parent pyridine



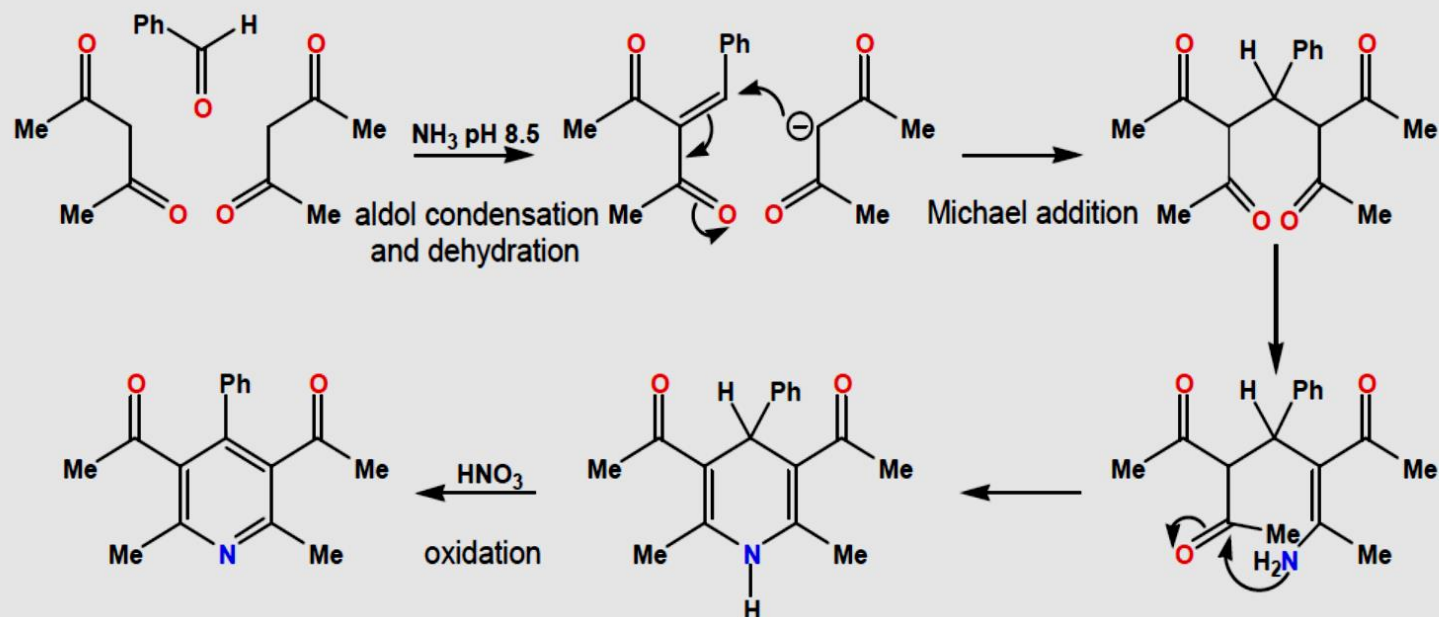


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Synthesis

Hantzsch Method



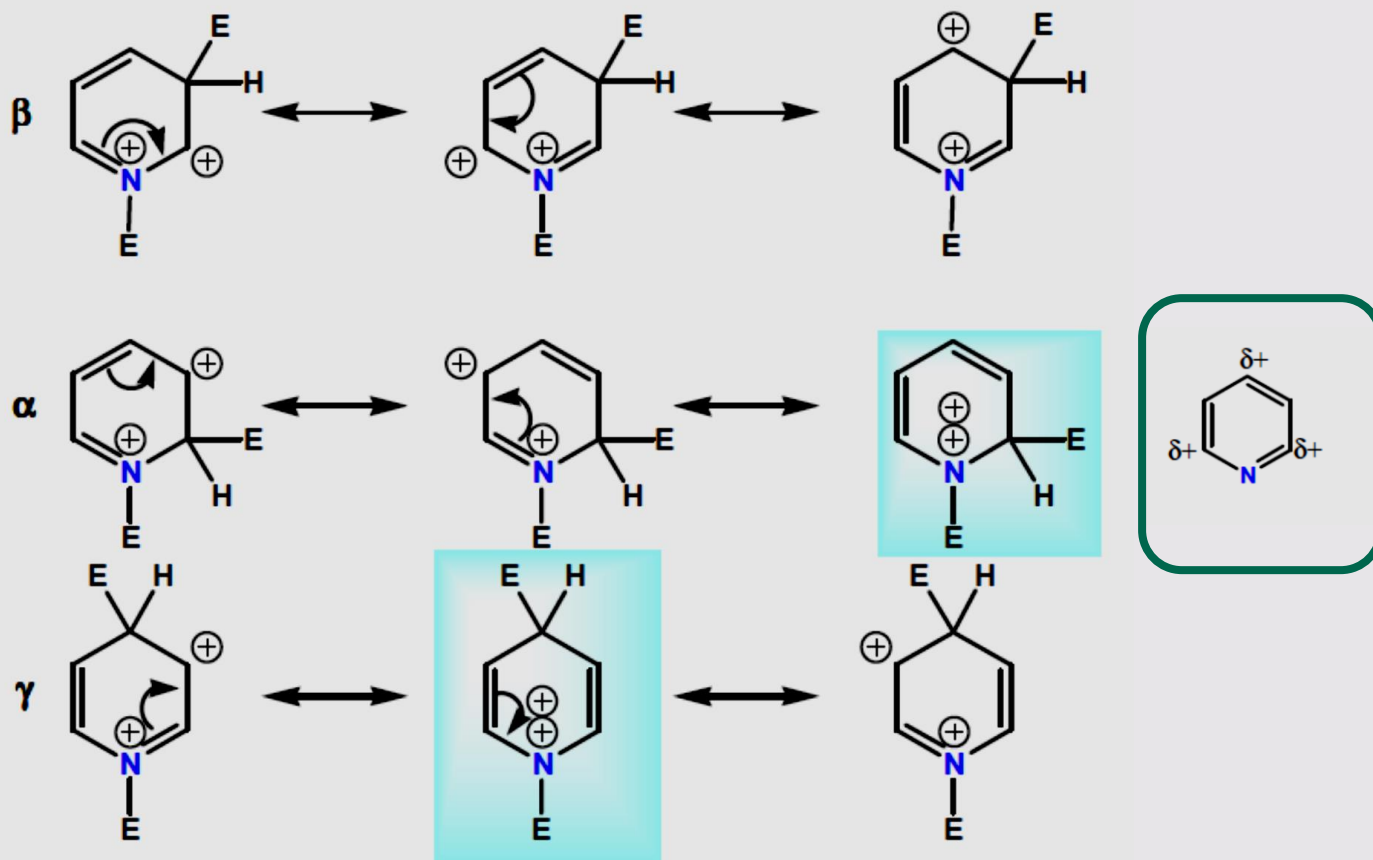
- The reaction is useful for the synthesis of symmetrical pyridines
- The 1,5-diketone intermediate can be isolated in certain circumstances
- A separate oxidation reaction is required to aromatize the dihydropyridine

Regiochemical Outcome of Electrophilic Substitution of Pyridinium Ions



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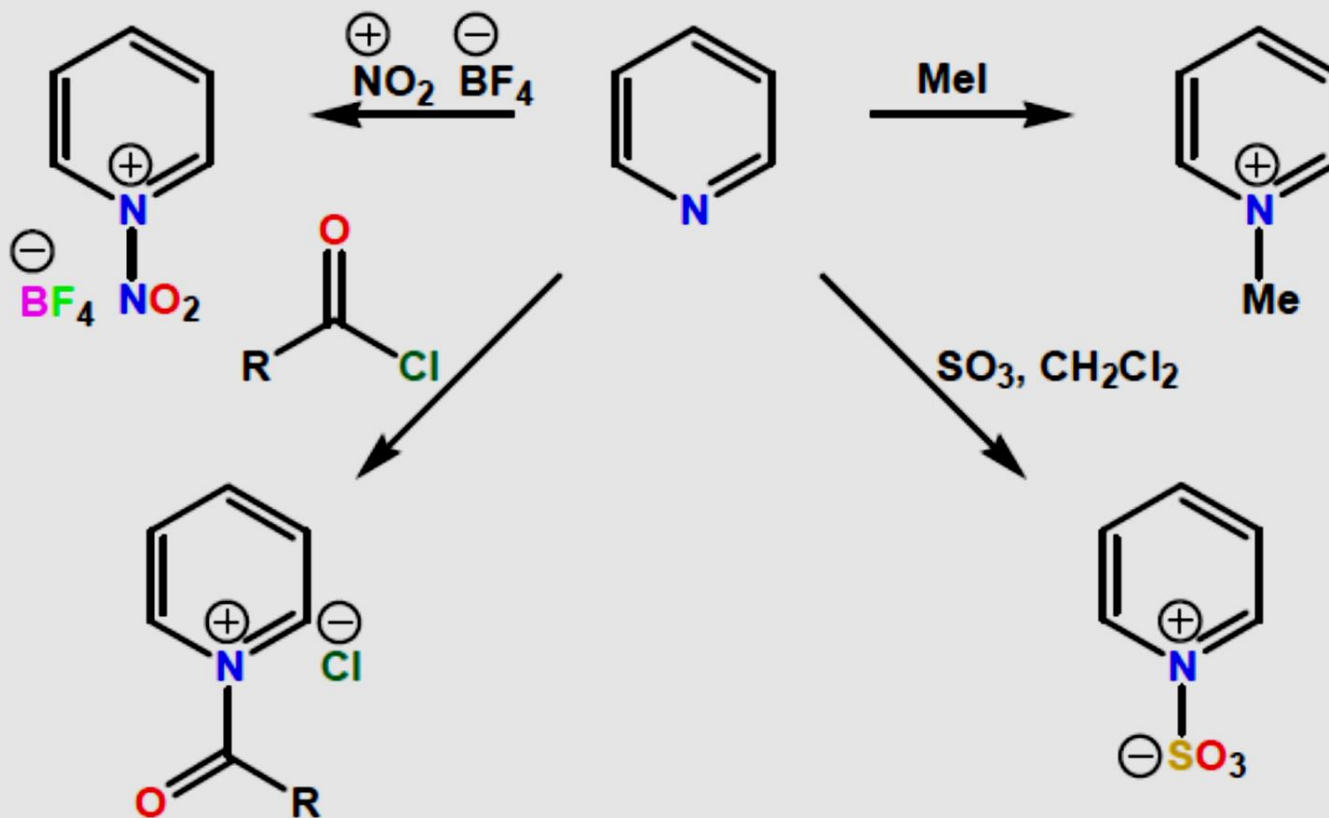
- Regiochemical control is even more pronounced in the case of pyridinium ions
- In both pyridine and pyridinium systems, β substitution is favoured but the reaction is slower than that of benzene



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N Substitution





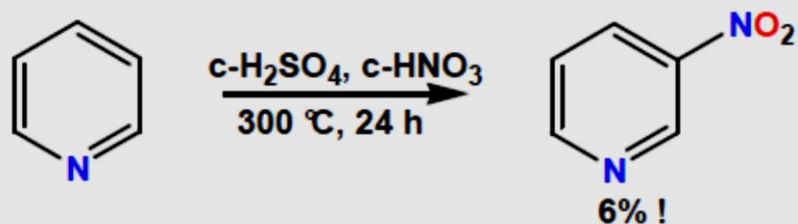
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C Substitution

- Reaction at C is usually difficult and slow, requiring forcing conditions
- **Friedel-Crafts reactions** are not usually possible on free pyridines

1. Nitration

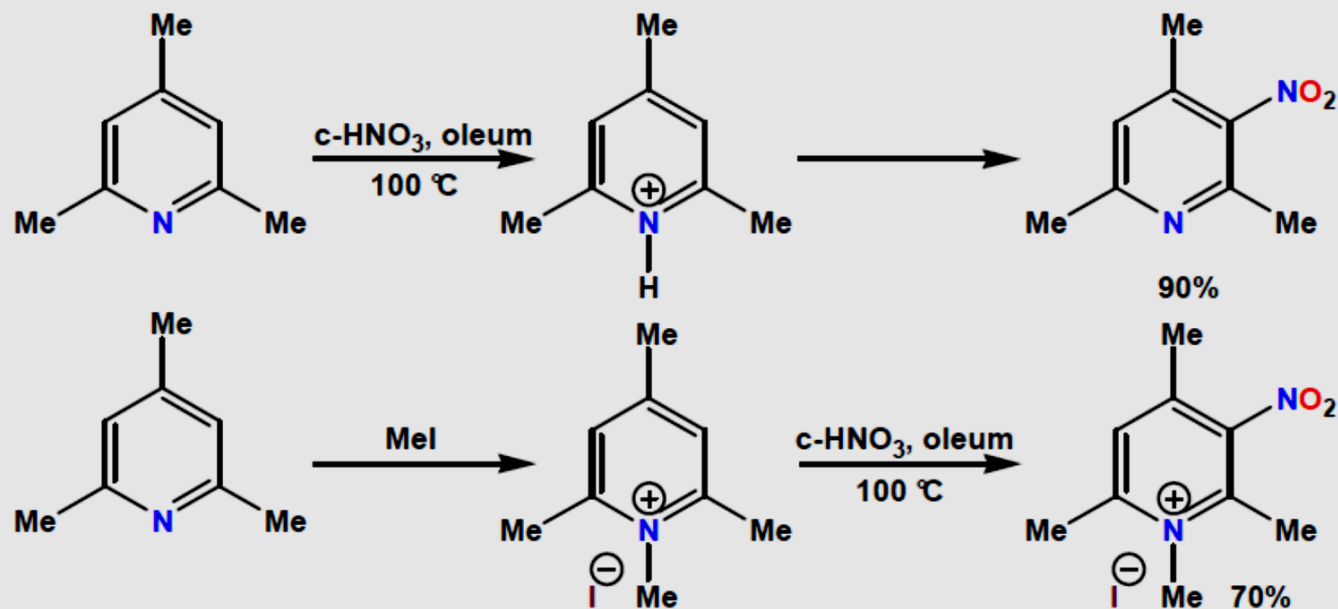




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- Multiple electron-donating groups accelerate the reaction
- Both reactions proceed at similar rates which indicates that the protonation at *N* occurs prior to nitration in the first case



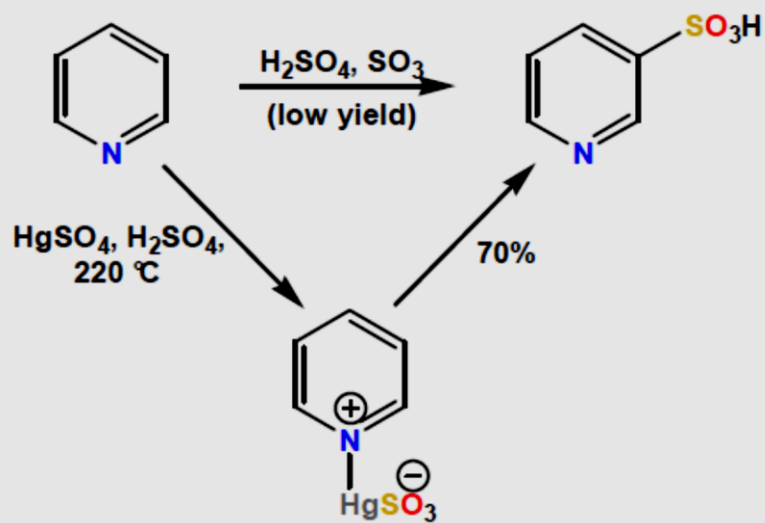


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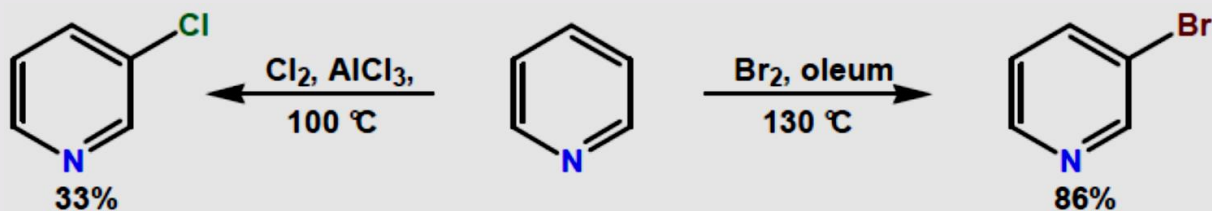
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2. Sulfonation of Pyridine



3. Halogenation

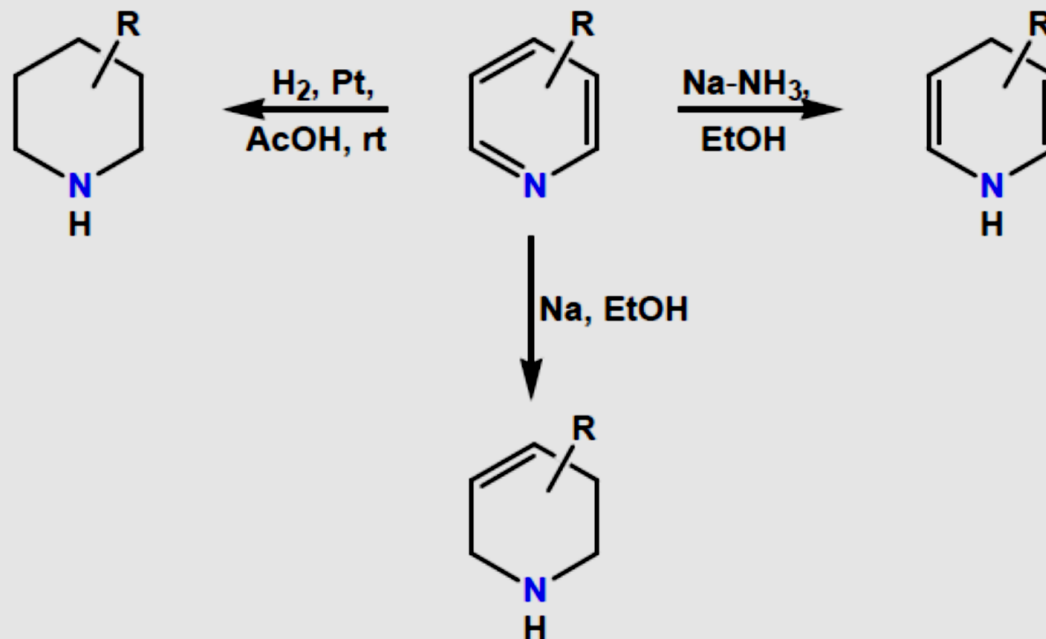




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4. Reduction



Pyridines generally resist oxidation at ring carbon atoms and will often undergo side-chain oxidation in preference to oxidation of the ring.

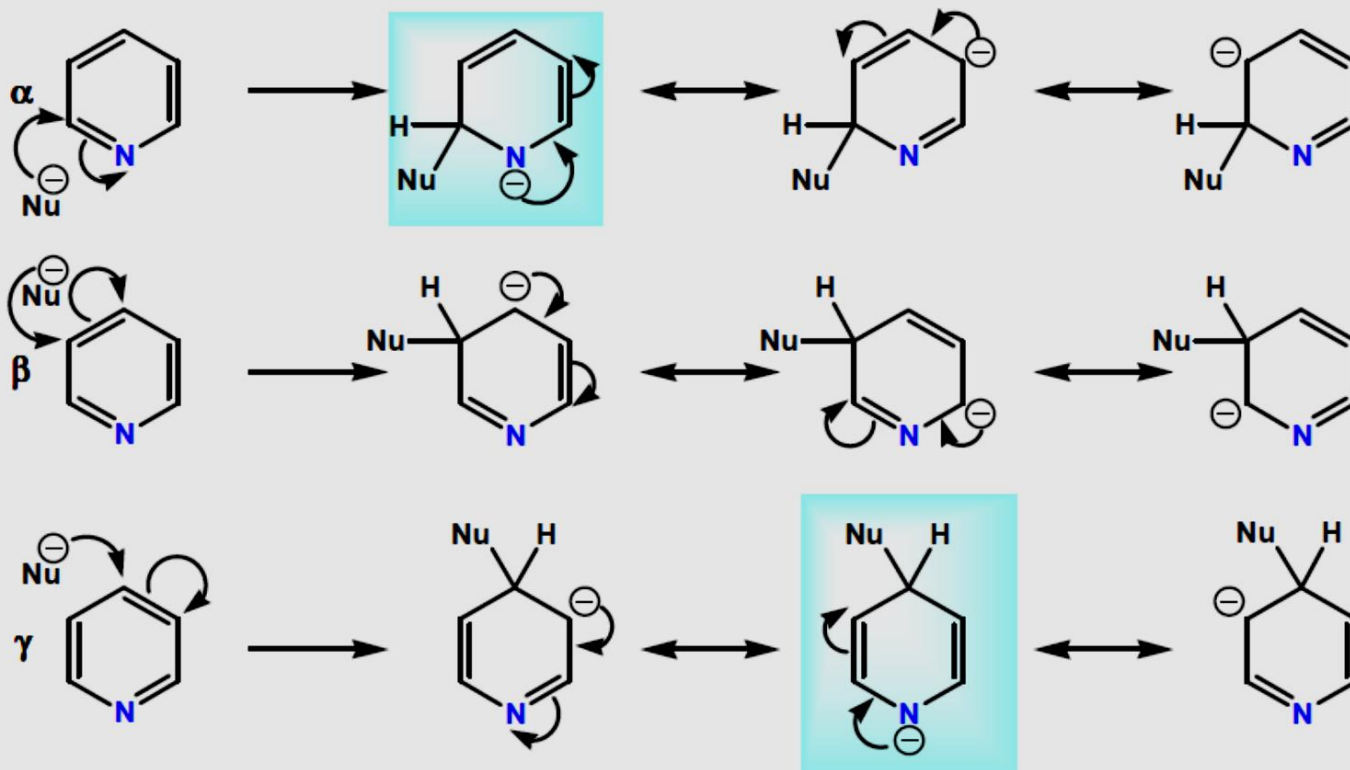
Full or partial reduction of the ring is usually easier than in the case of benzene



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Nucleophilic Addition to Pyridines



- β Substitution is less favoured because there are no stable resonance forms with the negative charge on *N*
- Aromaticity will be regained by loss of hydride or a leaving group, or by oxidation

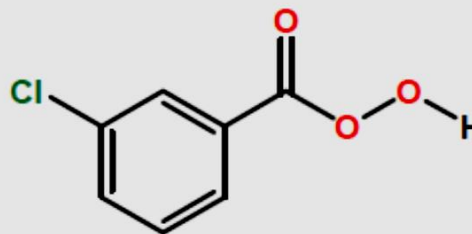
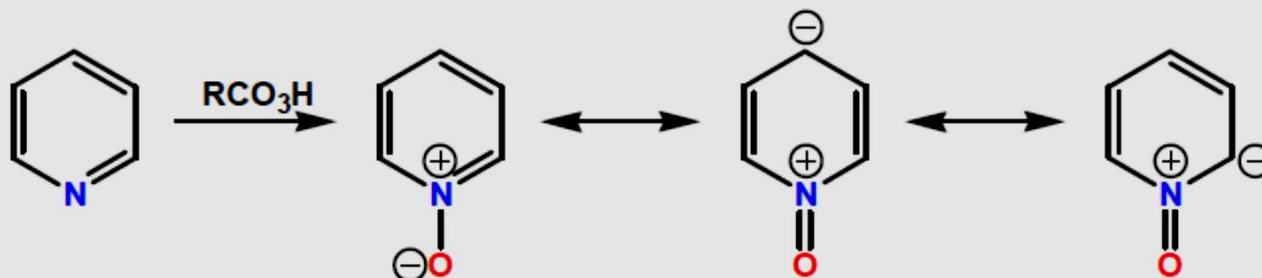


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Pyridine *N*-Oxides

N-Oxide Formation



meta-chloroperoxybenzoic acid (*m*-CPBA)

The reactivity *N*-oxides differs considerably from that of pyridines or pyridinium salts

- A variety of peracids can be used to oxidise *N* but *m*-CPBA is used most commonly
- *N*-Oxide formation can be used to temporarily activate the pyridine ring to both nucleophilic and electrophilic attack



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References

1. **K.D Sharma and Y. R. Sharma, Kalyani Publishers, Unit III**
2. **University Chemistry, Vol-IV, Dr. U. N. Dash, Dr. K. K. Ojha, Himalaya Publishing house, Unit IV**