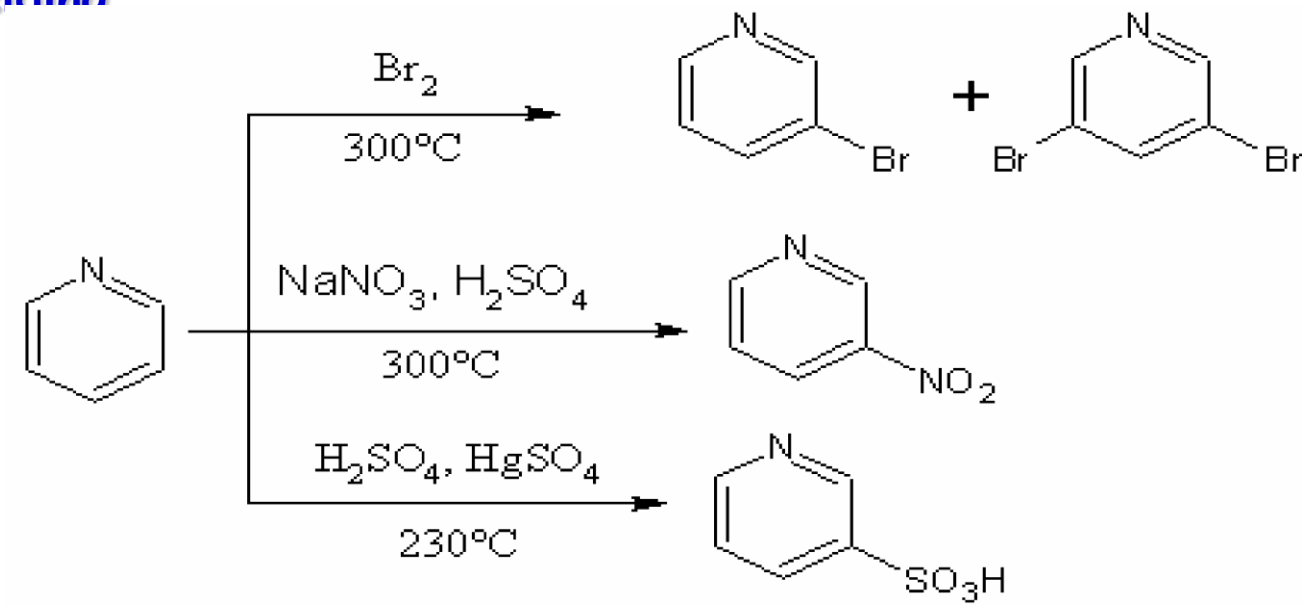
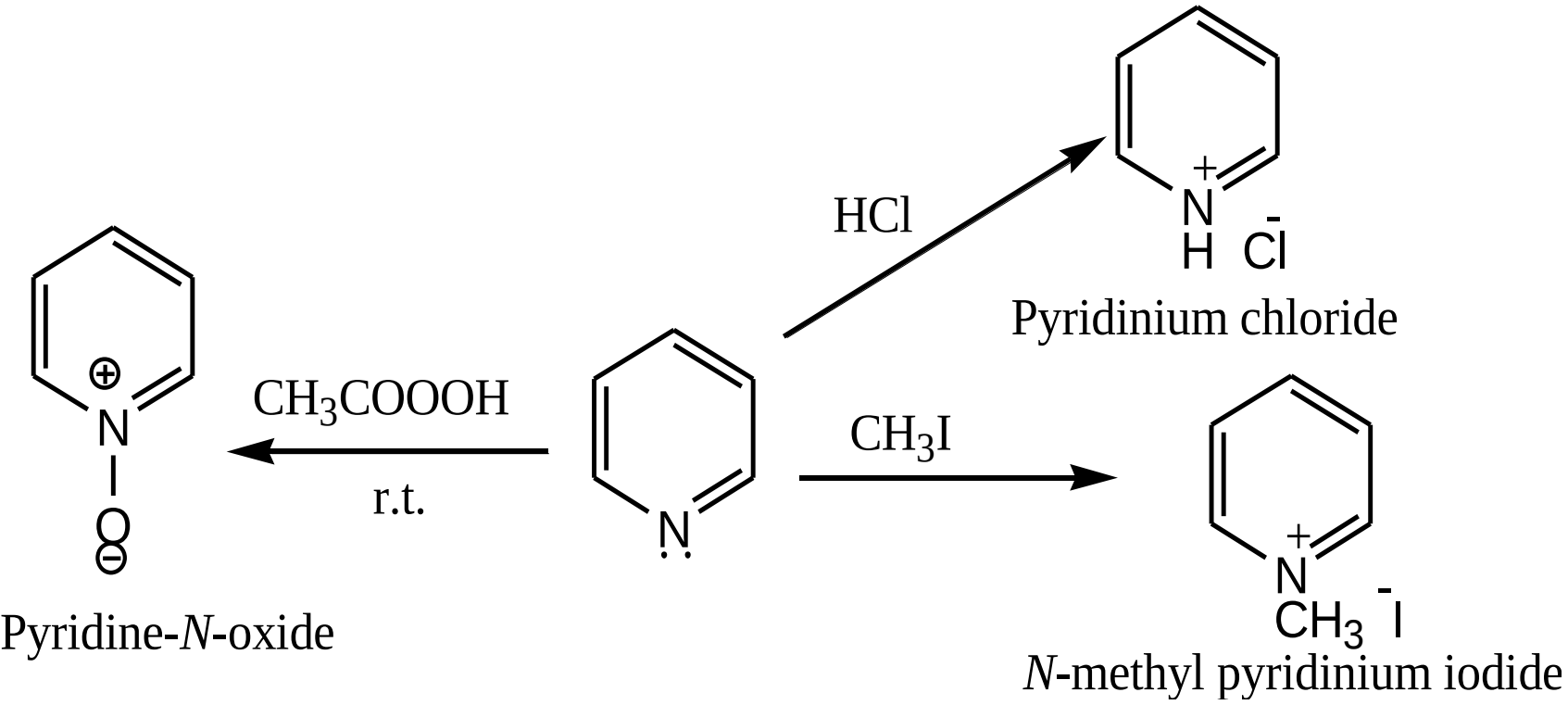
Chemical properties: 1-Electrophilic substitution

- Also as a consequence of electron deficiency on pyridine ring , pyridine is less reactive towards electrophiles than pyrrole and benzene (it resembles highly deactivated benzene derivatives), where it does not undergo Friedel-Craft's alkylation or acylation or coupling with diazonium salts.
- Moreover, electrophilic substitution reactions of pyridine require very harsh conditions (e.g. v. high temp.) to take place and are low yielding



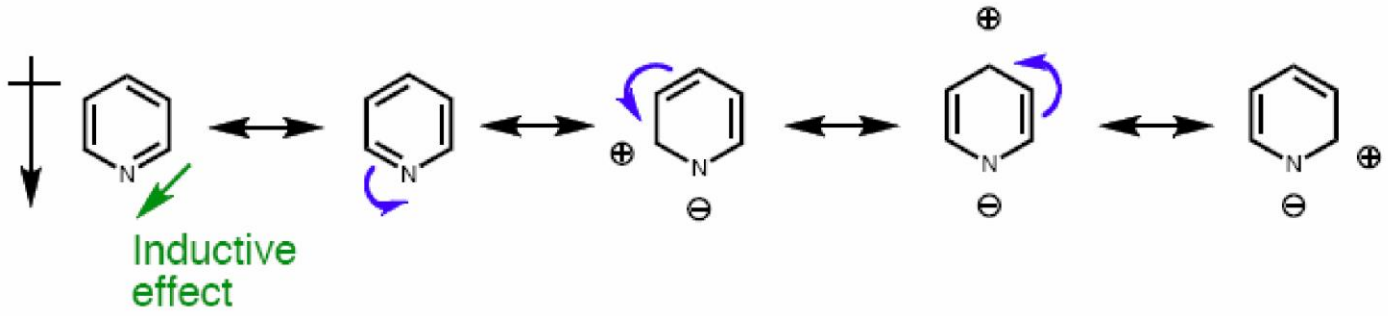
2-Pyridine as a nucleophile (reactions on N atom)

- **As a tertiary amine pyridine has nucleophilic properties thus it reacts with electrophiles:**

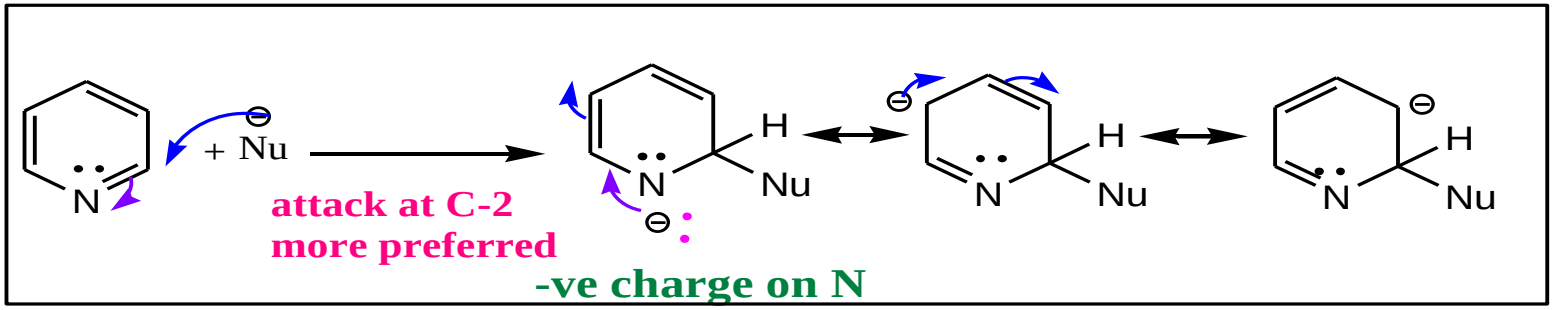


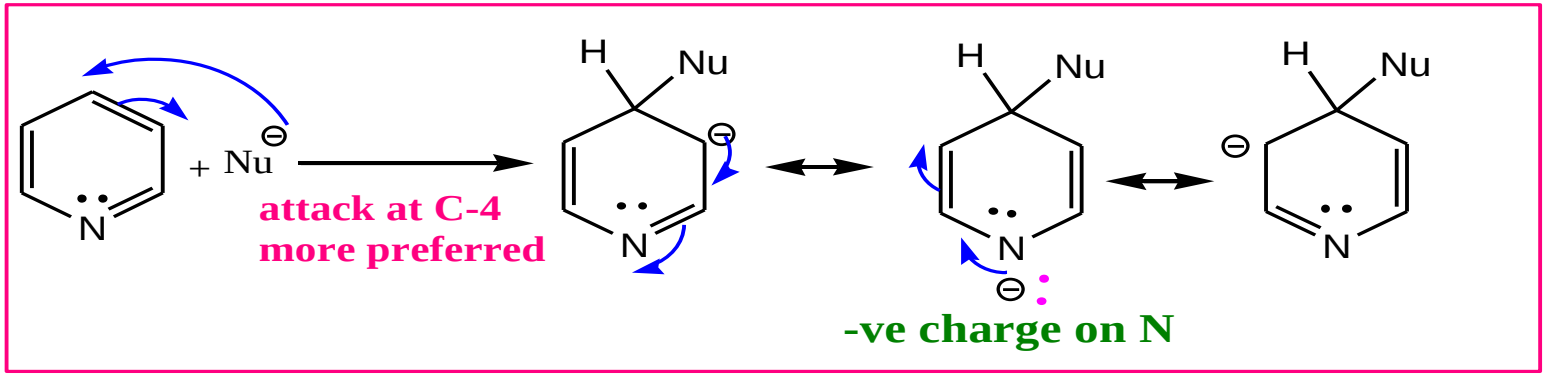
3-Nucleophilic substitution on carbon

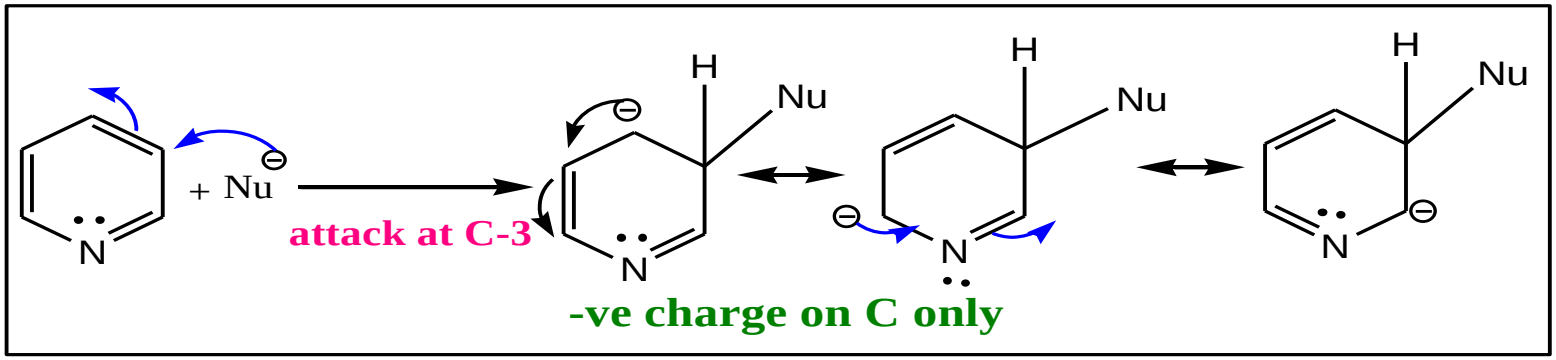
- **Pyridine is very reactive towards nucleophiles than benzene it resembles benzene having strong E.W.G due to the withdrawing effect of the electronegative N atom .**
- **AS appeared from the canonical structures of pyridine positions 2, 4 and 6 carry partial positive charges thus ncleophilic substitution proceeds readily at the 2-position followed by 4-position but not at the 3-position.**
- **Additionally, attack at positions 2, 4 or 6 results in resonance structure in which the negative charge is delocalized at N thus it is more preferred while attack at position 3 or 5 results in resonance structures in which the negative charge is delocalized over carbons only.**



Orientation of nucleophilic substitution in pyridine

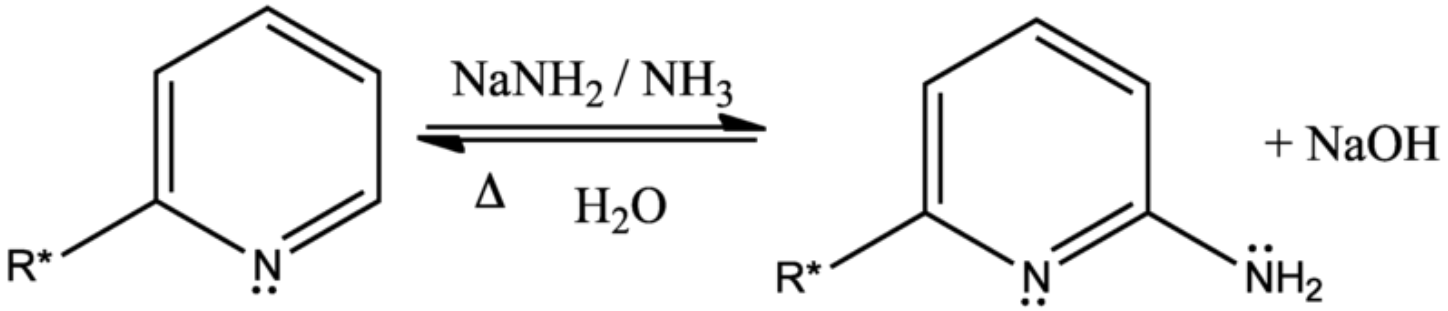






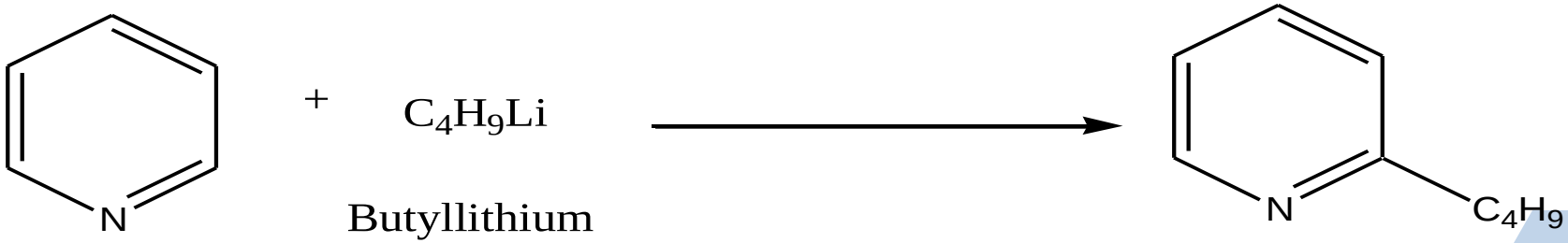
3- Nucleophilic Substitution reactions

i) The Chichibabin reaction



R can be *o-, m-, or p-* substituent

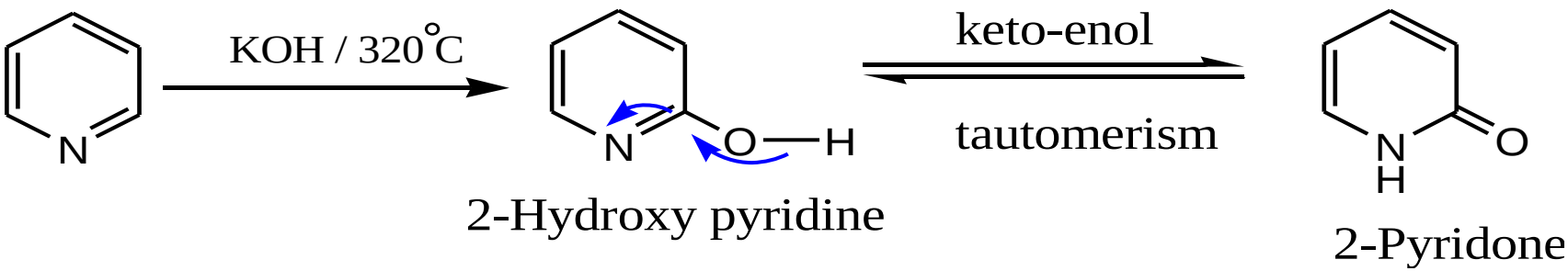
ii) Reaction with organometallic compounds lithium reagents



2-Butylpyridine

3-Nucleophilic substitution Reactions

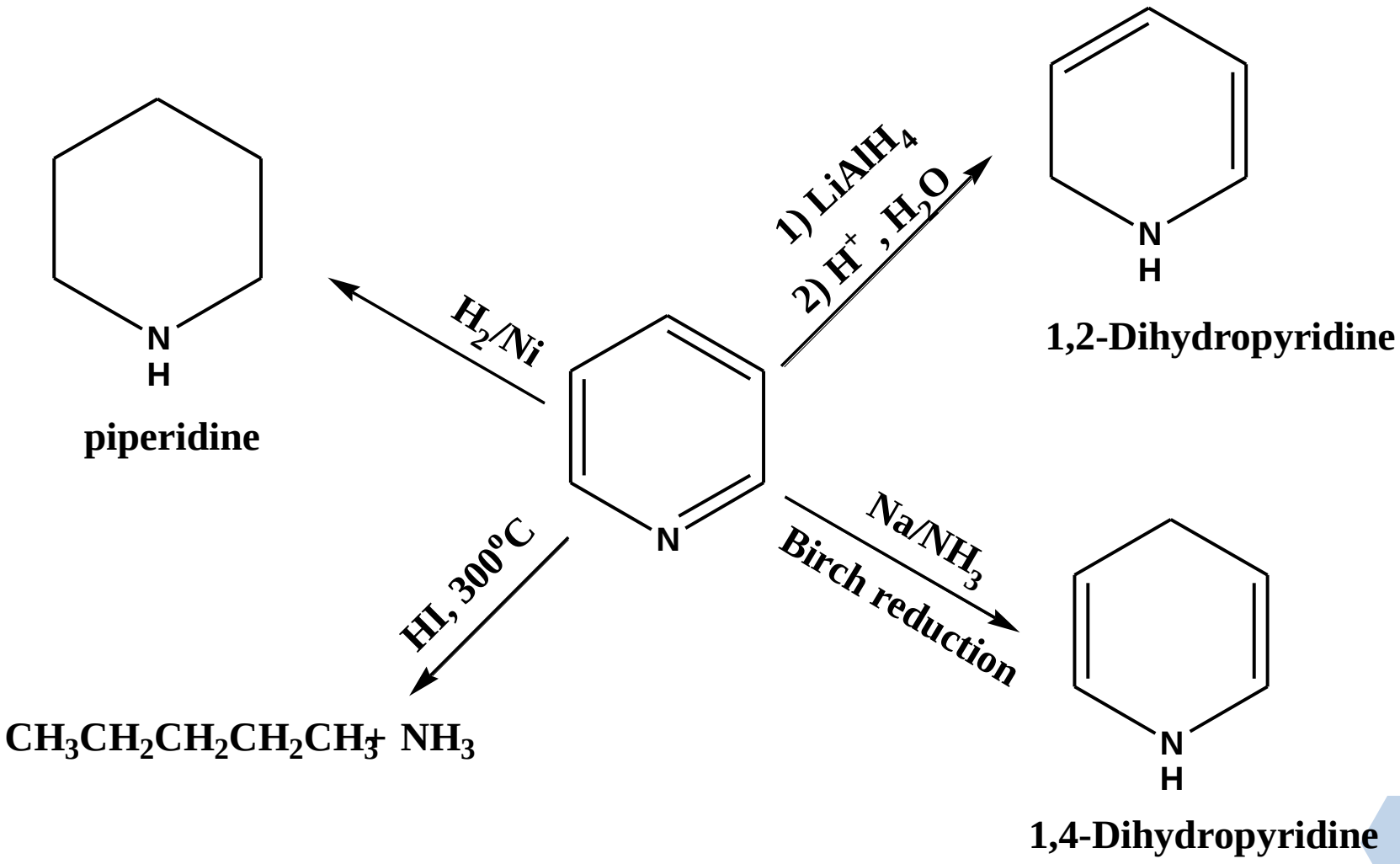
iii) Reaction with potassium hydroxide



2-Hydroxy pyridine

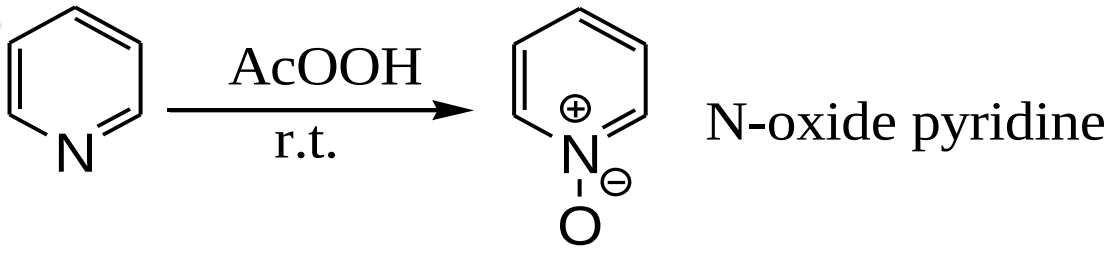
2-Pyridone

4-Reduction Reactions



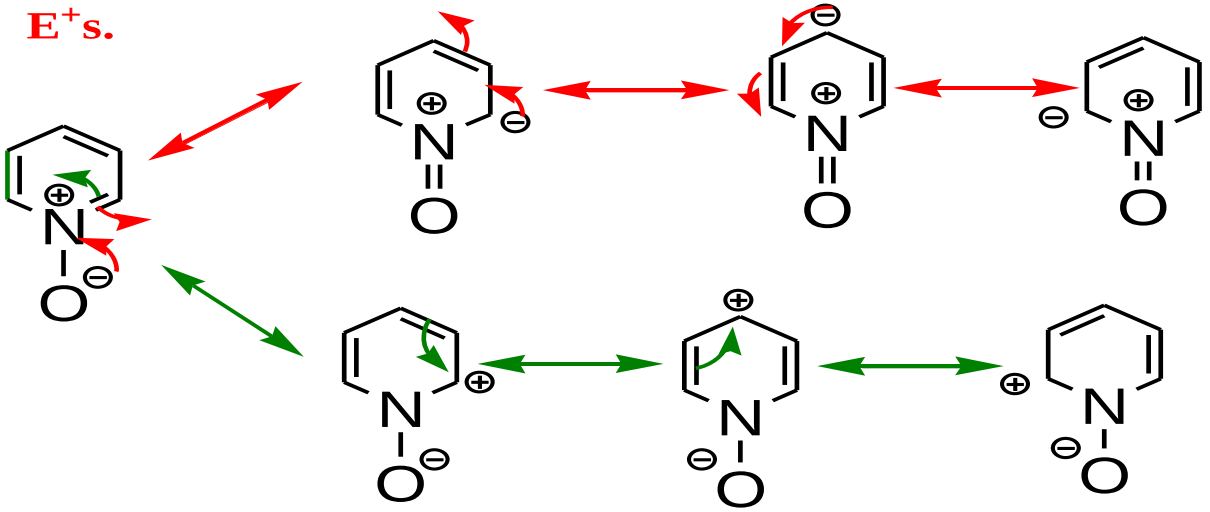
Derivative of pyridine: N-oxide pyridine

- Pyridine can be oxidized easily to N-oxide pyridine by peracids.



- On the basis of dipole moment studies, N-oxide pyridine is considered as a resonance hybrid of the following structures

The -ve. charges appear at positions 2, 4 thus active towards E^+s.



The +ve. charges appear at positions 2, 4 thus active towards nucleophiles

N-oxide pyridine

- As appears from the previous canonical forms , there are positive and negative charges at positions 2 and 4 thus N-oxide pyridine is more activated for electrophilic and nucleophilic attack at these positions than pyridine itself.

- N-oxide pyridines are very important intermediates for preparing pyridine derivatives that are difficult to prepare due to the easiness of removal of oxygen atom by reduction.

- For instance, nitration of pyridine is very difficult and low yielding reaction and it occurs at position 3, however using N-oxide pyridine will direct the nitration to position 4 and then the oxygen can be easily removed by reduction as shown in the following scheme.

Reactions of N-oxide pyridine