

**B.Sc. Semester-IV
Core Course-IX (CC-IX)
Organic Chemistry-III**



III. Heterocyclic Compounds

**25. Oxy-Pyridines, Amino-Pyridines, Alkyl-Pyridines, Pyridinium Salts and
Pyridine *N*-Oxide**



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Heterocyclic Compounds

22 Lectures

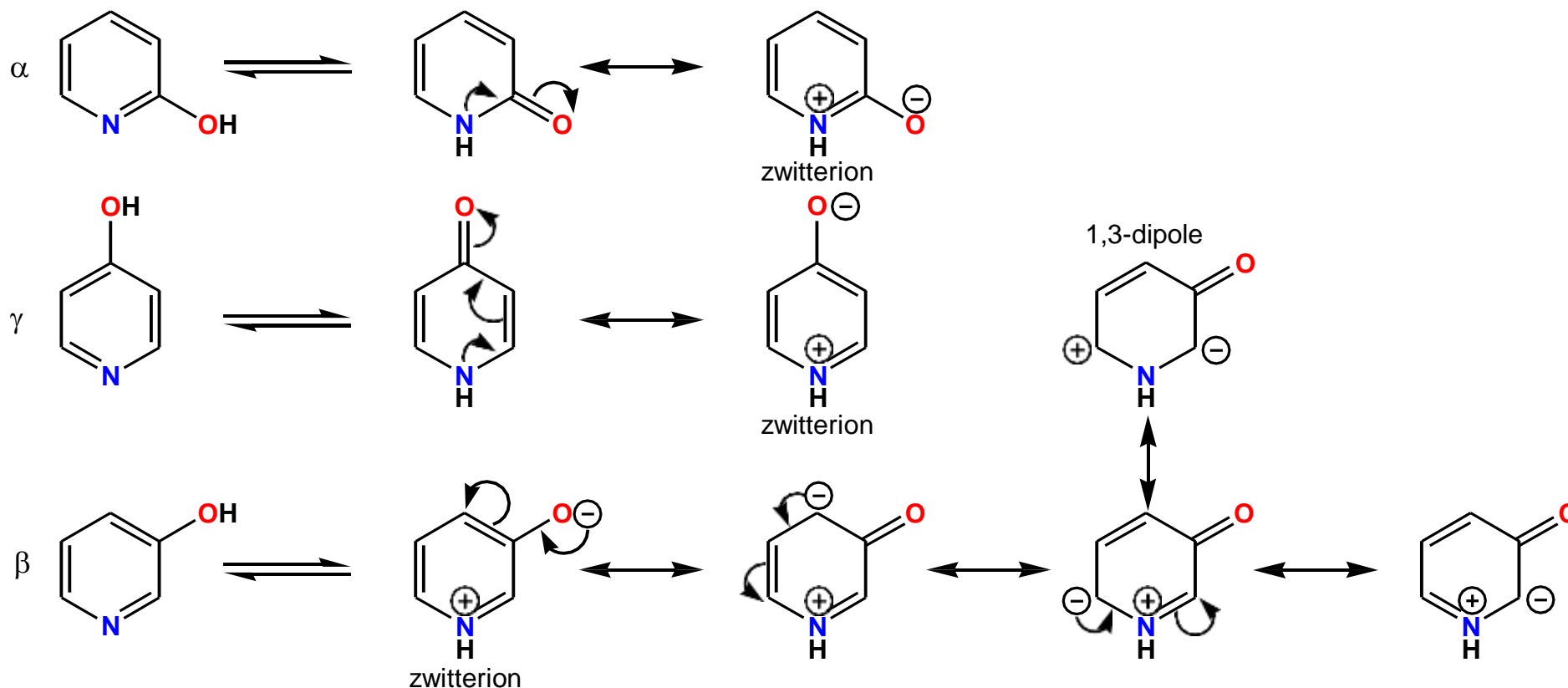
Classification and nomenclature, Structure, aromaticity in 5-numbered and 6-membered rings containing one heteroatom; Synthesis, reactions and mechanism of substitution reactions of: Furan, Pyrrole (Paal-Knorr synthesis, Knorr pyrrole synthesis, Hantzsch synthesis), Thiophene, Pyridine (Hantzsch synthesis), Pyrimidine, Structure elucidation of indole, Fischer indole synthesis and Madelung synthesis), Structure elucidation of quinoline and isoquinoline, Skraup synthesis, Friedlander's synthesis, Knorr quinoline synthesis, Doebner- Miller synthesis, Bischler-Napieralski reaction, Pictet-Spengler reaction, Pomeranz-Fritsch reaction
Derivatives of furan: Furfural and furoic acid.

Coverage:

Pyridines : Oxy-Pyridines, Amino-Pyridines, Alkyl-Pyridines, Pyridinium Salts and Pyridine *N*-Oxide

Oxy-Pyridines – Structure

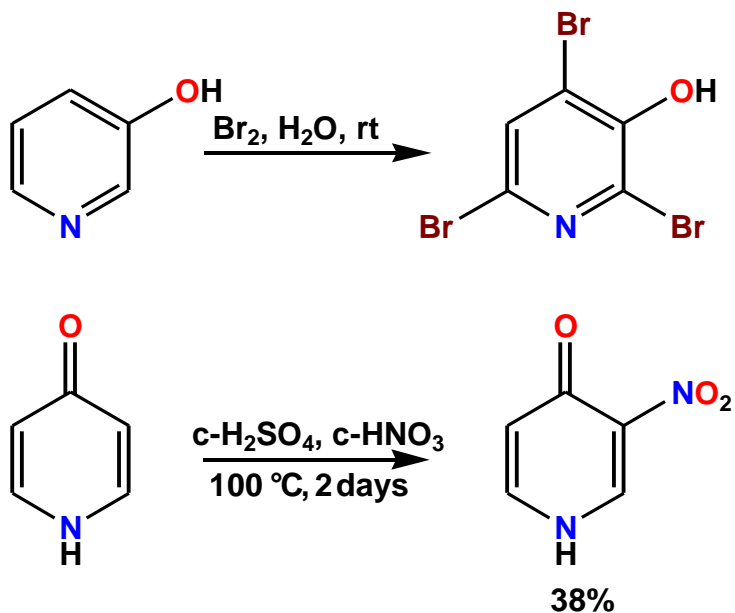
Oxy-Pyridines/Pyridones



- Subject to tautomerism
- The α , γ systems differ from the β systems in terms of reactivity and structure
- In the α case, the equilibrium is highly solvent dependent, but the keto form is favoured in polar solvents

Oxy-Pyridines – Reactions

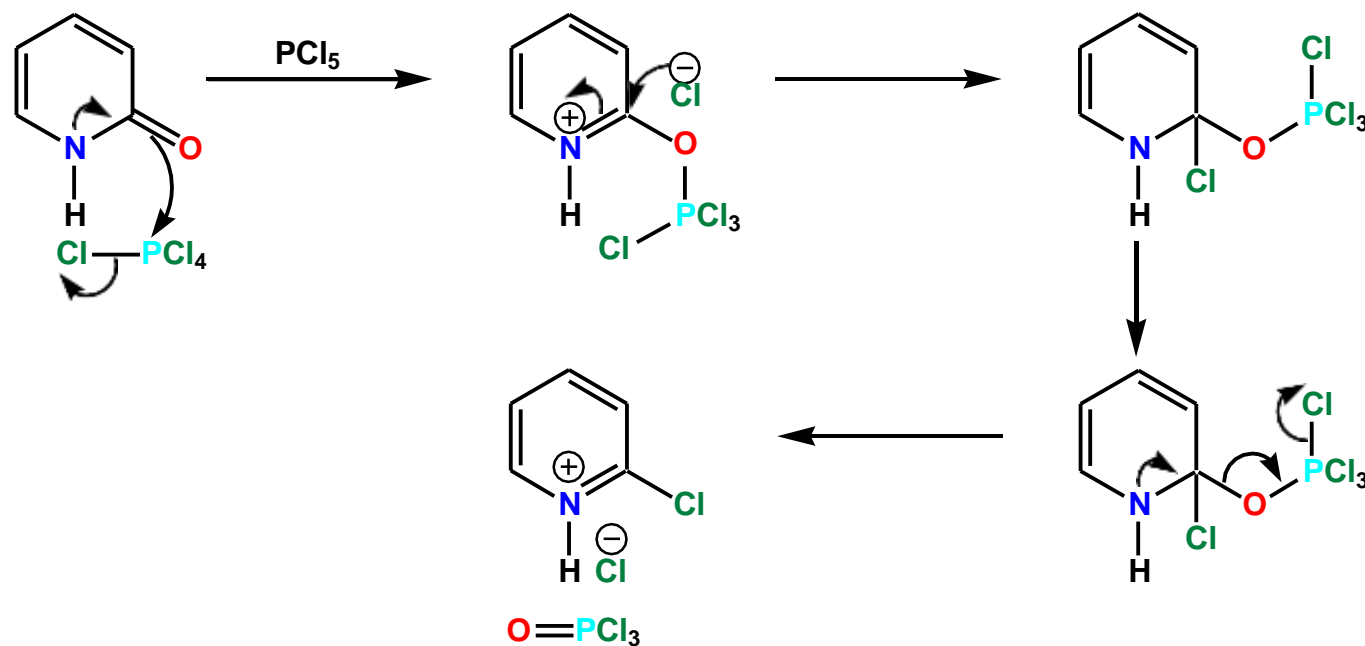
Electrophilic Substitution



- Reactions such as halogenation, nitration, sulfonation etc. are possible
- *N* is much less basic than that in a simple pyridine
- Substitution occurs ortho or para to the oxygen substituent (cf. phenols)

Oxy-Pyridines – Reactions

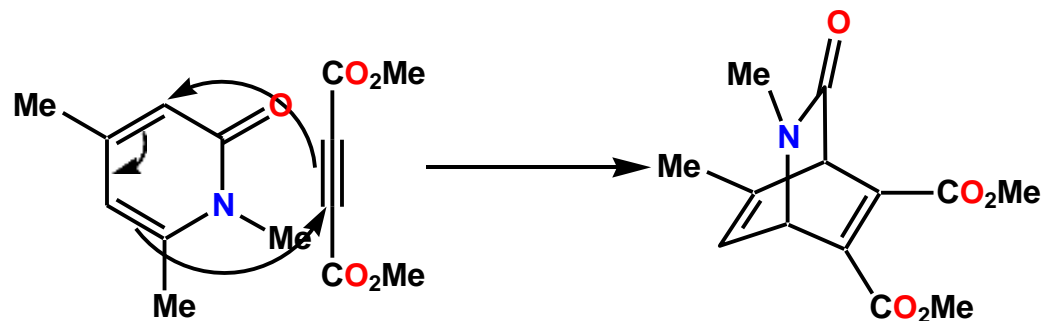
Nucleophilic Substitution



- Replacement of the oxygen substituent is possible
- In this case, the reaction is driven by the formation of the very strong $\text{P}=\text{O}$ bond

Oxy-Pyridines – Reactions

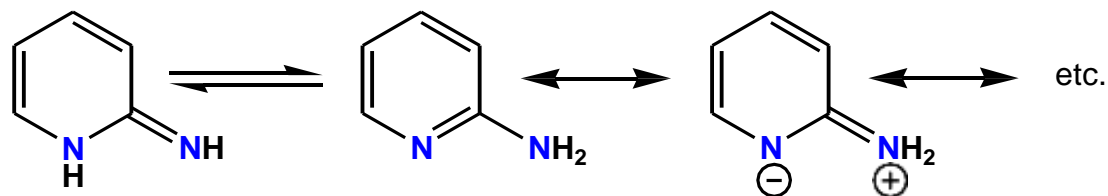
Cycloaddition



- Oxy-pyridines have sufficiently low aromatic character that they are able to participate as dienes in **Diels-Alder reactions** with highly reactive dienophiles

Amino-Pyridines – Structure

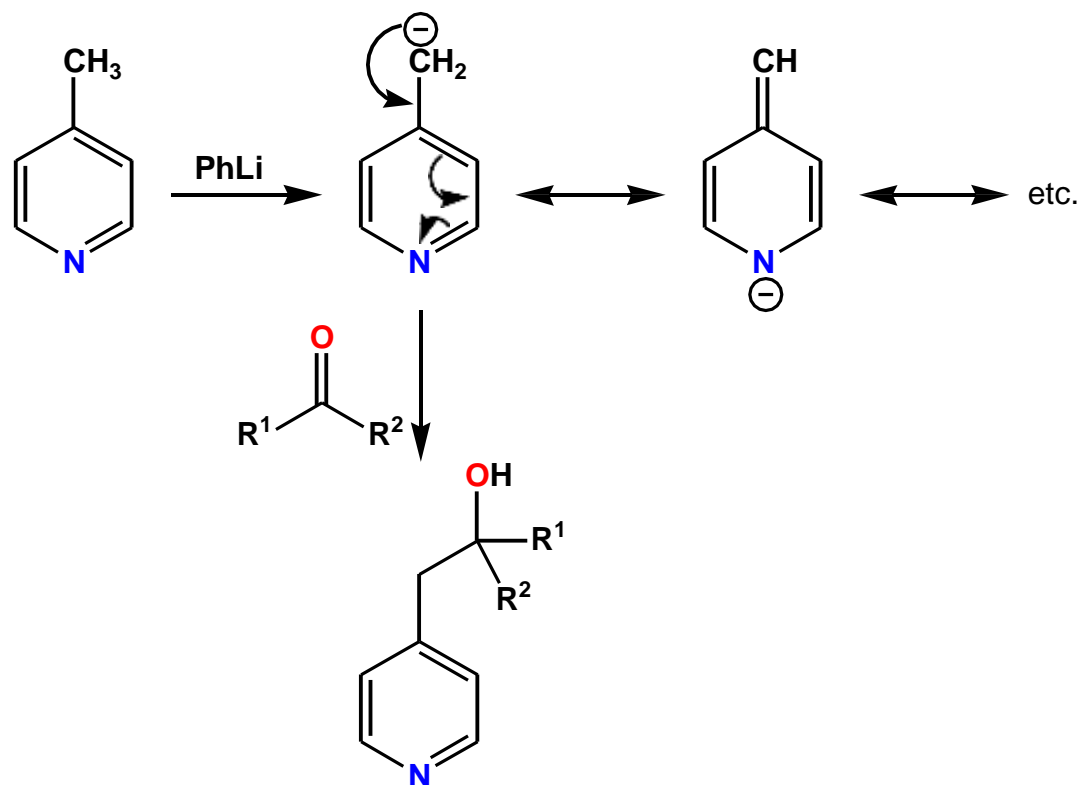
Amino Pyridine Systems



- Contrast with oxy-pyridines
- Amino pyridines are polarised in the opposite direction to oxy-pyridines

Alkyl Pyridines – Deprotonation

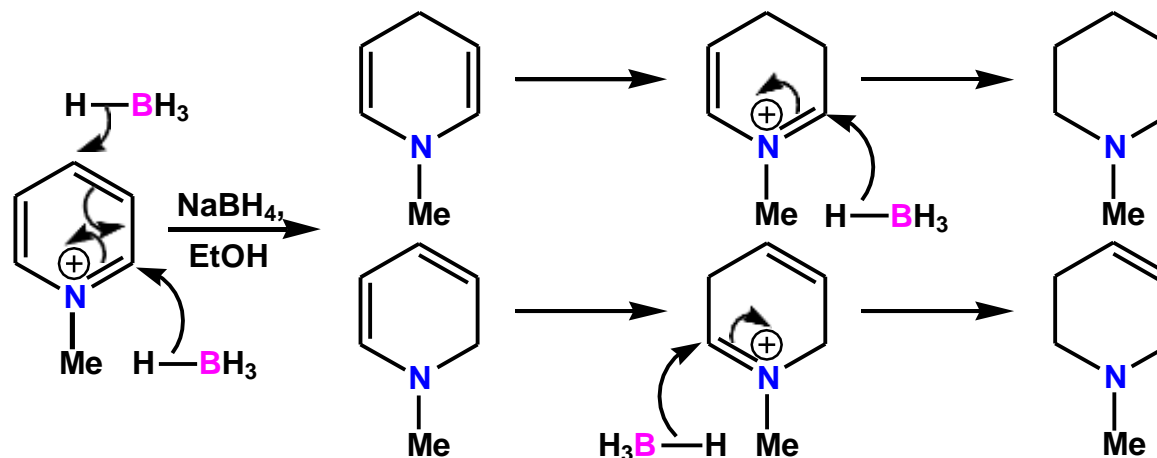
Deprotonation with a Strong Base



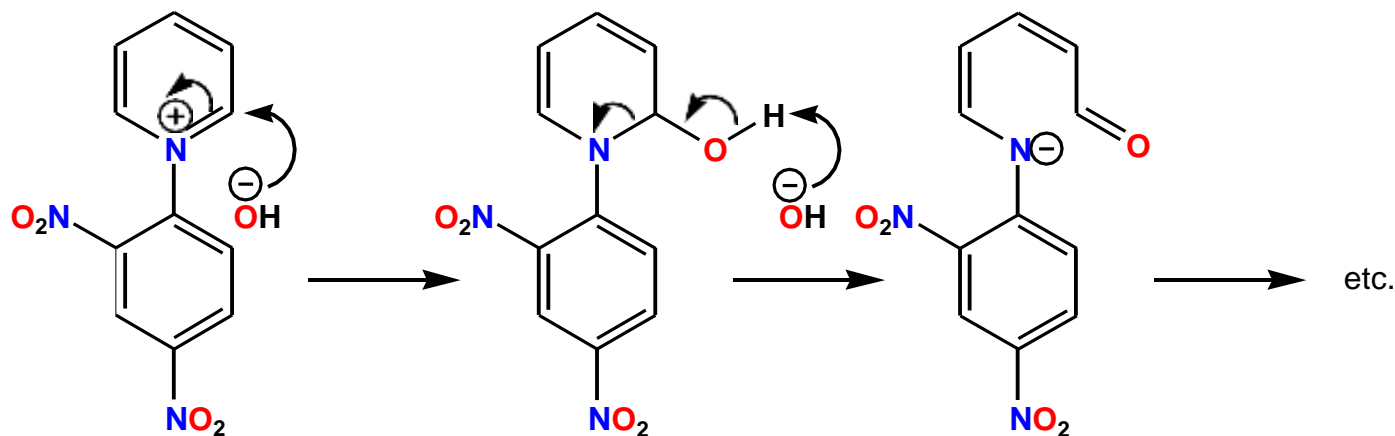
- Deprotonation of α and γ alkyl groups proceeds at a similar rate, but β alkyl groups are much more difficult to deprotonate
- Bases are also potential nucleophiles for attack of the ring

Pyridinium Salts – Reactions

Nucleophilic Attack with Reducing Agents

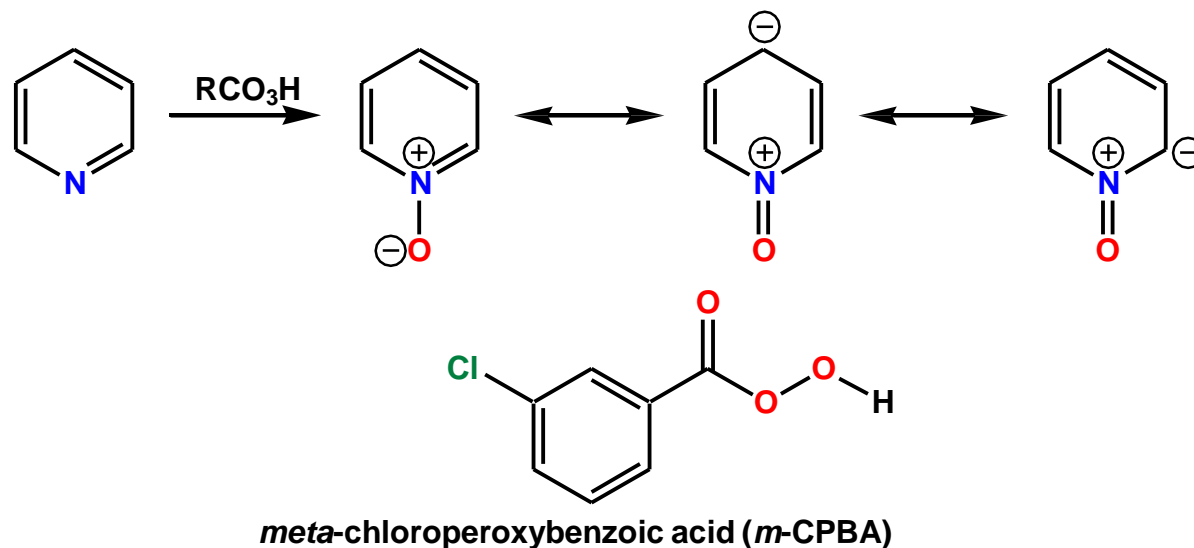


- Nucleophilic attack is much easier (already seen this)
- Deprotonation of alkyl substituents is easier (weak bases are suitable)
- Ring opening is possible by attack of hydroxide



Pyridine *N*-Oxides

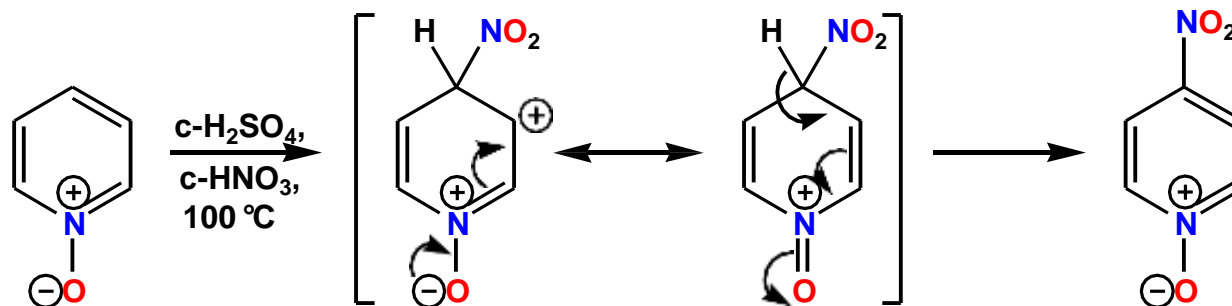
N-Oxide Formation



- 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

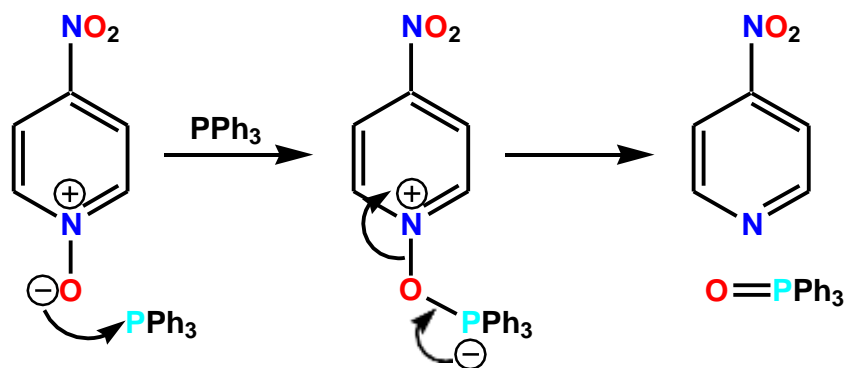
Pyridine *N*-Oxides

Electrophilic Substitution



- The *N*-oxide is activated to attack by electrophiles at both the α and γ positions
- Nitration of an *N*-oxide is easier than nitration of the parent pyridine
- Reactivity is similar to that of a pyridinium salt in many cases e.g. nucleophilic attack, deprotonation of alkyl groups etc.

Removal of O



- Deoxygenation is driven by the formation of the very strong $\text{P}=\text{O}$ bond