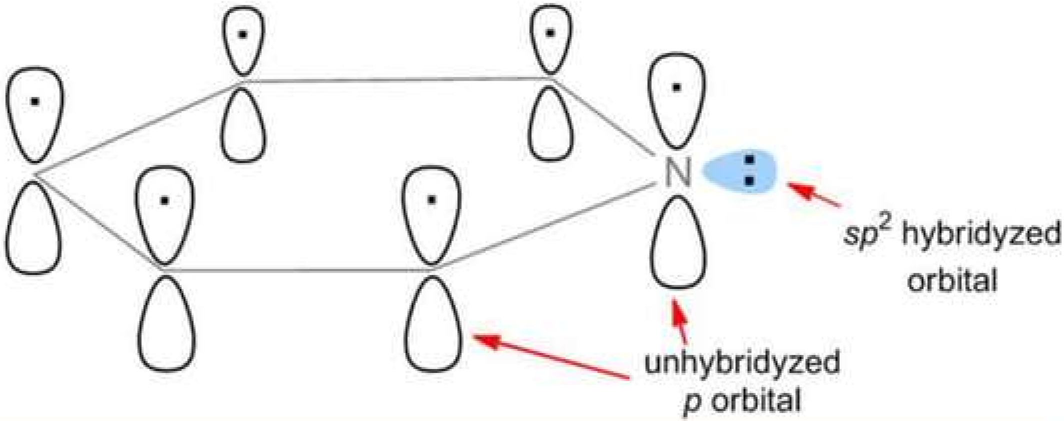
Properties

1. Aromaticity



Properties

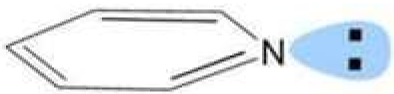
1. Aromaticity

- **Pyridine** have 5 C and 1 N , all are *sp^2* hybridized
- *sp^2* hybridization is planar, it makes a planar pyridine ring structure.
- Each ring atoms also contains unhybridized *p* orbital that is perpendicular to the plane of σ bonds (plane of ring).
- Here *p* orbitals are parallel to each other, so overlapping btwn *p* orbitals is possible.
- the total nu of non bonding e- are 6 (5 of five C, 1 from N)
- The resonance of 6 e- follows the Hückel's rule
- So ….

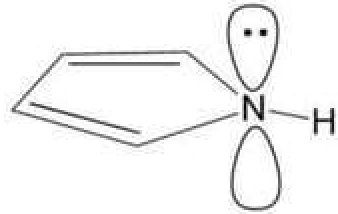
Properties

2. Basicity

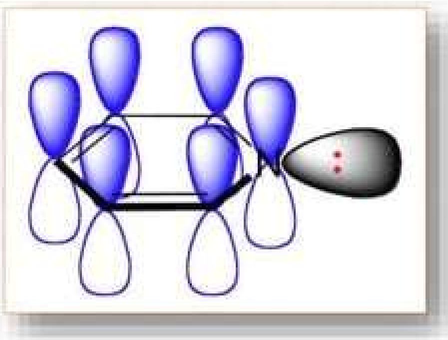
Pyridine is more basic than pyrrole

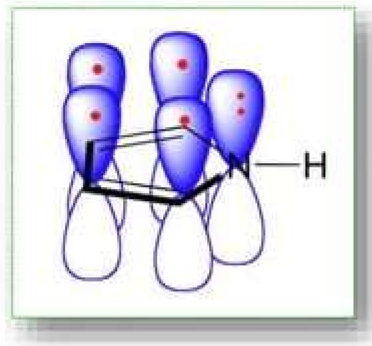


pyridine



pyrrole

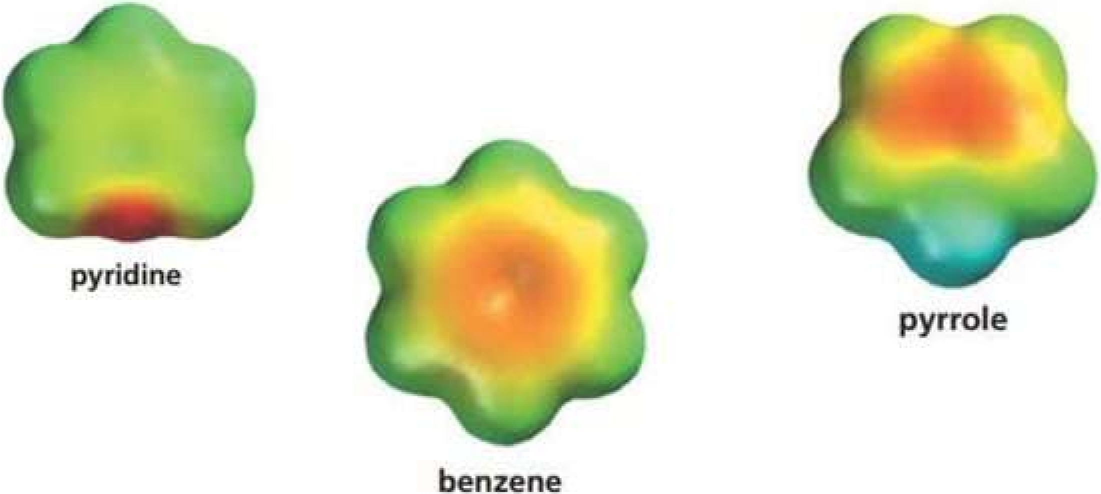




Properties

2. Basicity

Pyridine is more basic than pyrrole



Properties

2. Basicity

Pyridine is more basic than pyrrole

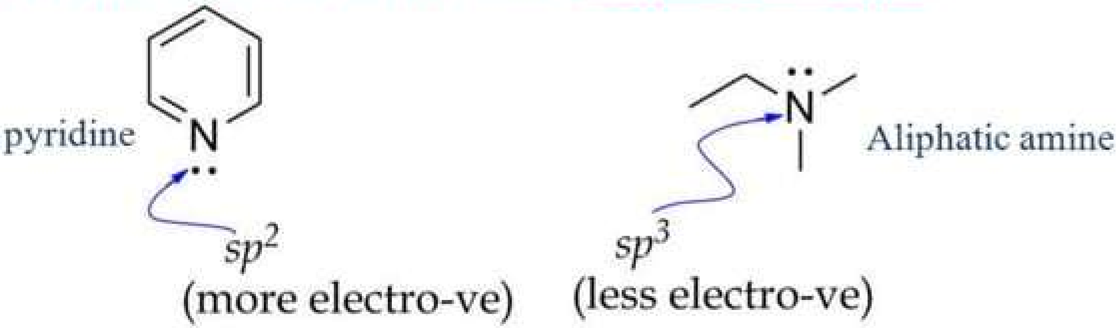
- Basicity depends on availability of lone pair.
- Pyridine N have lone pair of $\bar{e}$ in same plane of pyridine hybridized orbitals plane → So it is not participating to resonance phenomena → lone pair is readily available for acid-base reaction.
- Pyrrole N have lone pair of $\bar{e}$ perpendicular to plane of pyridine hybridized orbitals plane. → it participates in resonance (delocalization of lone pair) → not readily available for acid-base reaction.
- As lone pair of $\bar{e}$ of pyridine are readily available than pyrrole…

  … Pyridine is more basic than pyrrole

Properties

2. Basicity

Pyridine is less basic than aliphatic amines

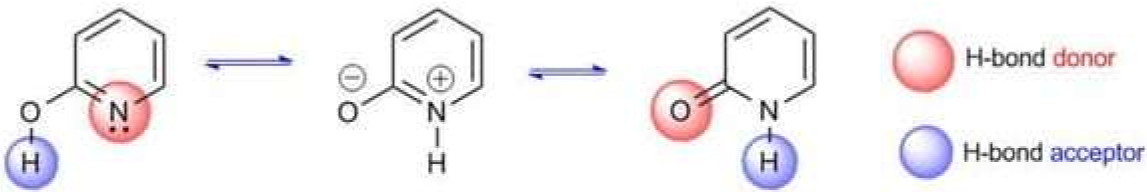


- Sp^2 hybridized N is more electro-ve (more *s* character) than Sp^3 → lone pair of $\bar{e}$ more closely held toward more electro-ve N → less available for acid-base reaction.
- As lone pair of $\bar{e}$ is not readily available in pyridine , it is less basic than aliphatic amines.

Properties

3. Tautomerism

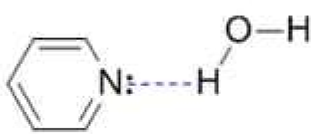
- Tautomeric structures involve when pyridine substituted at 2nd - / 4th - position with groups such as –XH (X = O,N or S)



2-hydroxypyridine 2-pyridone

4. Hydrogen bonding

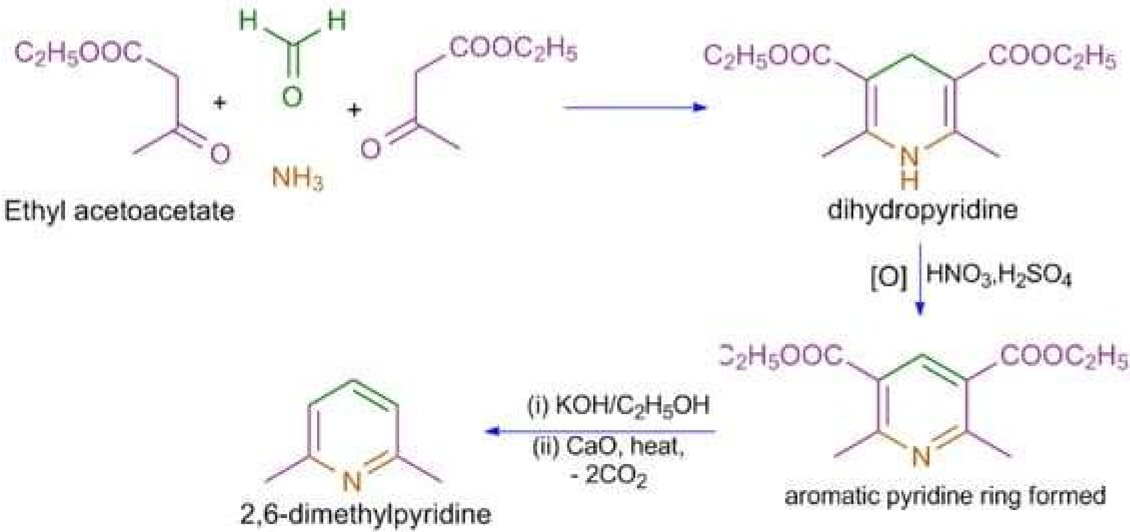
- Pyridine is water soluble



Synthesis

1. Hantzsch pyridine synthesis

- Condensation of an aldehyde with two moles of a β-dicarbonyl compound and ammonia.

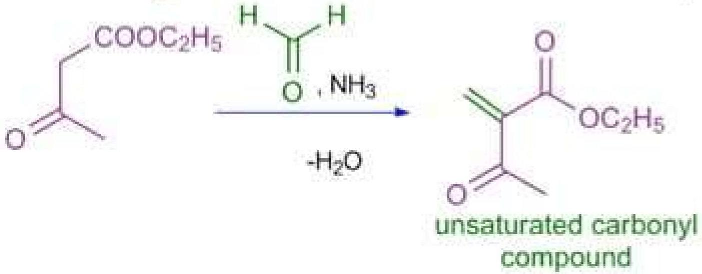


Synthesis

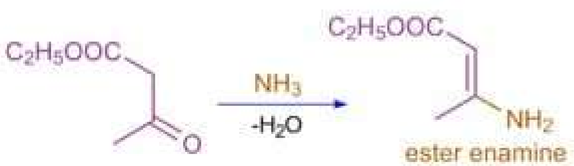
1. Hantzsch pyridine synthesis

Mechanism

Step 1: Knoevenagel Condensation between the β-ketoester and aldehyde



Step 2: Formation of the ester enamine



Synthesis

1. Hantzsch pyridine synthesis

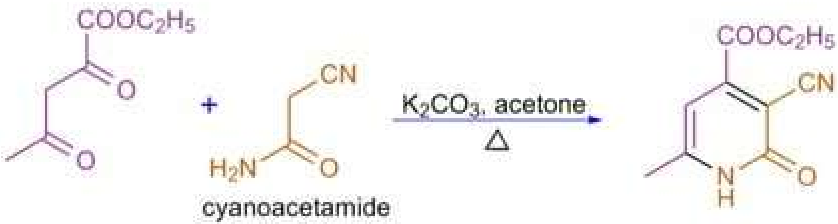
Mechanism

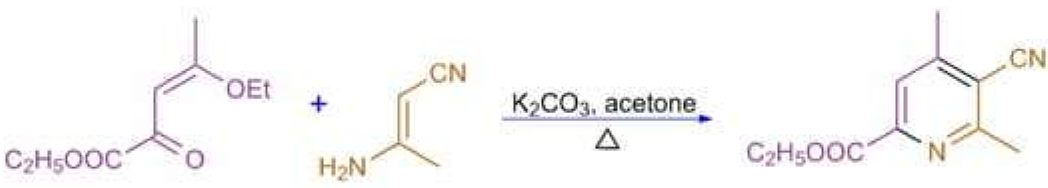
Step 3: Formation of the dihydropyridine

Synthesis

2. The Guareschi Synthesis

- Modification of Hantzsch synthesis, use of cyanoacetamide as the nitrogen - containing component.





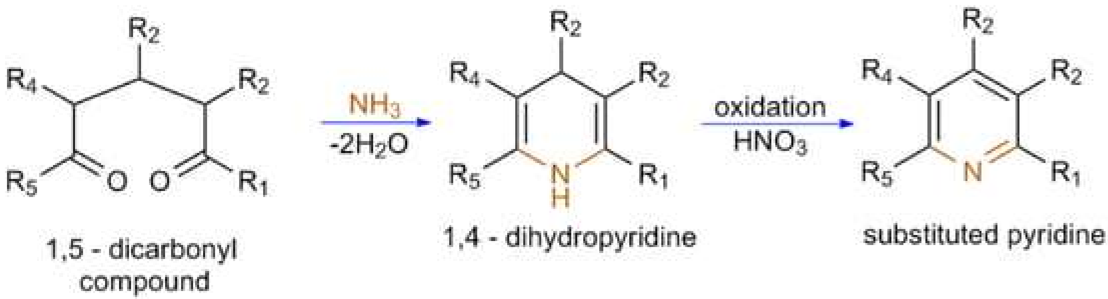
3 - alkoxy - enones

enenitrile

Synthesis

3. From 1,5 - Dicarbonyl Compounds

- Ammonia reacts with 1,5 - dicarbonyl compounds to give 1,4 - dihydropyridines, which are easily dehydrogenated to pyridines.



Synthesis

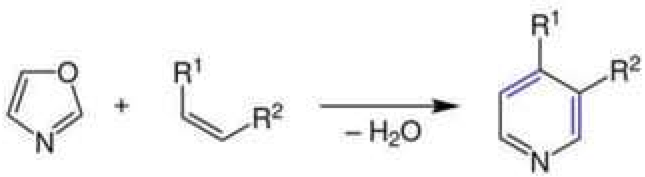
4. From Oxazoles Kondrat'eva pyridine synthesis

Reactions

3. Diels-Alder Reaction

(2) Kondrat'eva pyridine synthesis

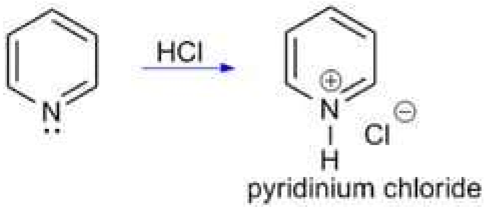
- synthesizing pyridine derivatives by Diels–Alder cycloaddition between an azadiene and a dienophile followed by an extrusion of the resulting bridge of the bicyclic intermediate.



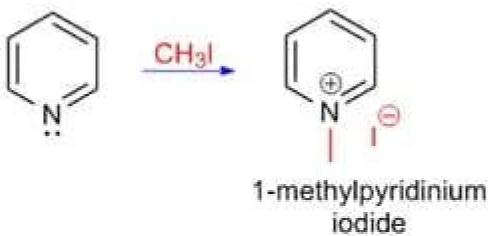
Reactions

1. Electrophilic addition to N

a. Protonation (basic property)



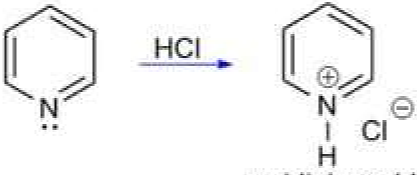
b. *N*-alkylation



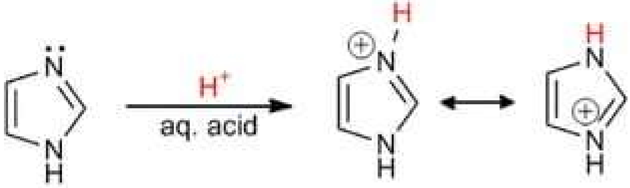
Reactions

Imidazole is approximately 100 times more basic than pyridine.

- Protonation of imidazole yields an ion that is stabilized by the electron delocalization



pyridinium chloride

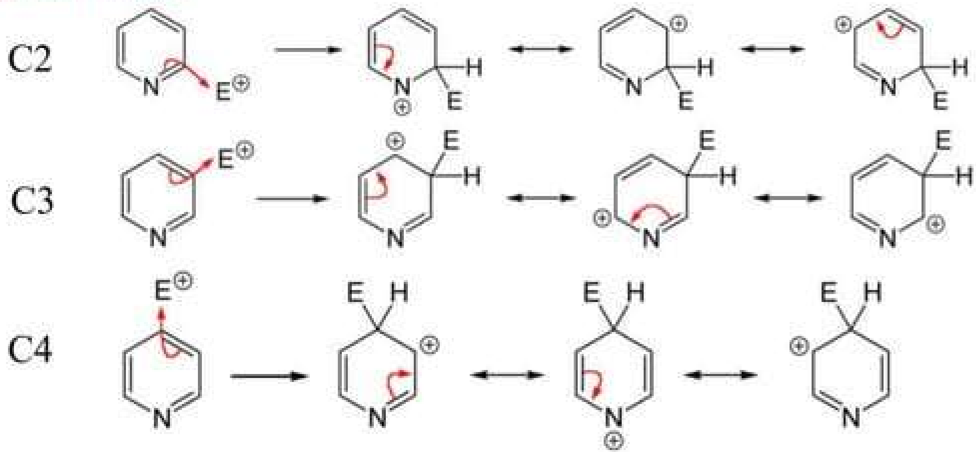


imidazolium cation

Reactions

2. Electrophilic substitution to C

Pyridine gives electrophilic substitution reaction at 3rd position.

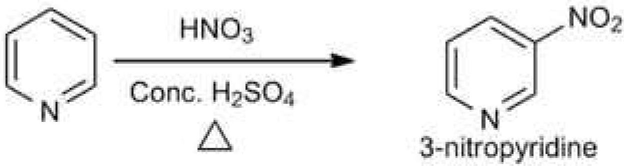


- N is electro-ve , so +ve *charge on N destabilize structure* → here attack at C2 , C4 generates N+ intermediates→ less favourable → only C3 is favourable as it can not generate N+ intermediate.

Reactions

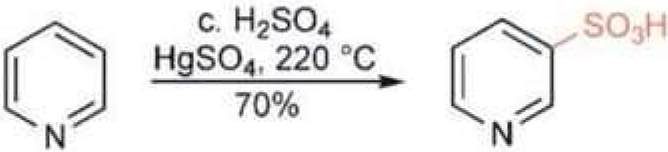
2. Electrophilic substitution to C

a. Nitration



b. sulphonation

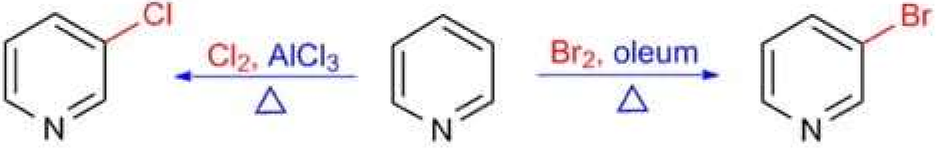
- Pyridine is very resistant to sulfonation using concentrated sulfuric acid *or* oleum, addition of mercuric sulfate in catalytic quantities allows smooth sulfonation.



Reactions

2. Electrophilic substitution to C

c. Halogenation

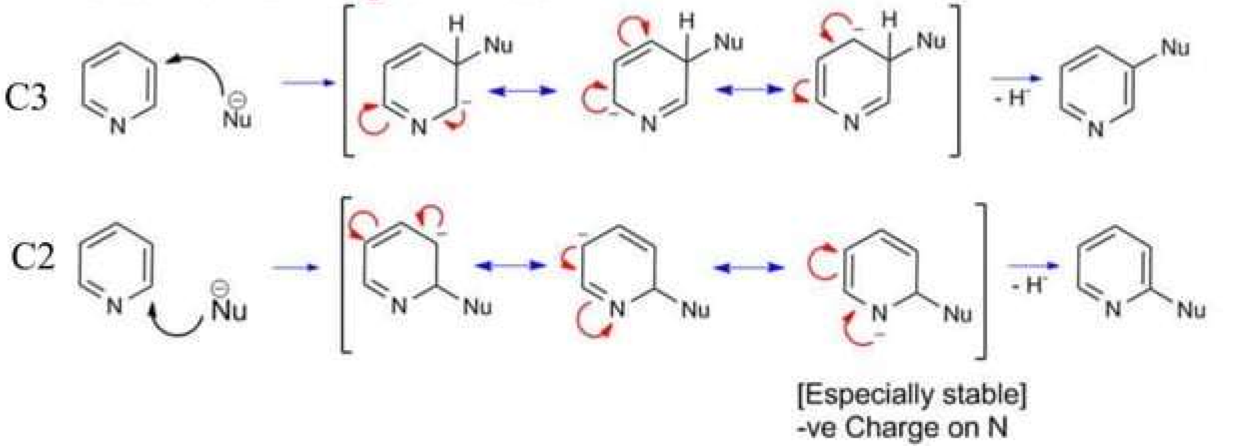


- 3-Bromopyridine is produced in good yield by the action of bromine in oleum.
- 3-Chloropyridine can be produced by chlorination in the presence of aluminium chloride.

Reactions

3. Nucleophilic substitution

Why pyridine undergoes nucleophilic substitution reaction at 2-position.



- Attack on 2nd position gives more stable intermediate containing –ve charge on N. thus…

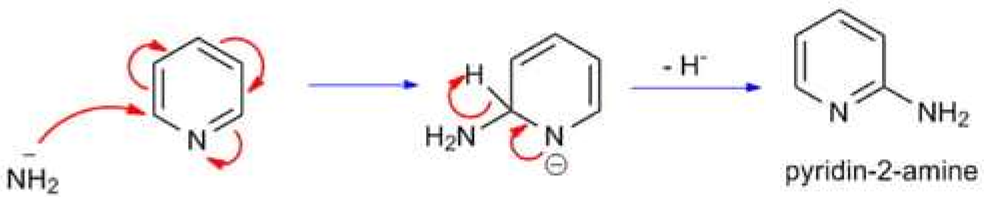
Reactions

3. Nucleophilic substitution

Chichibabin rxn

- Rxn of pyridine with sodamide at high temp.

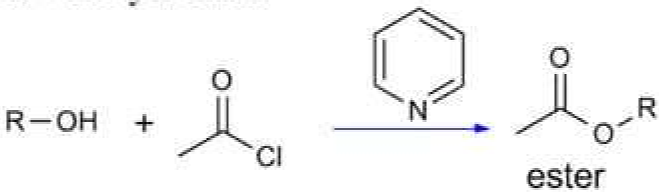
Mechanism



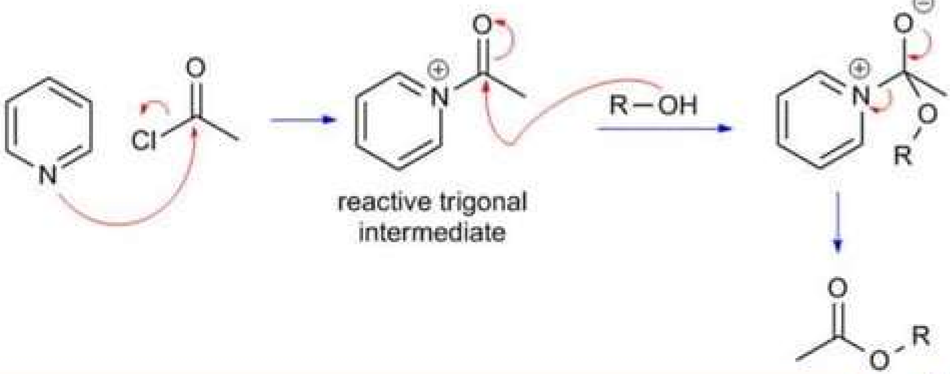
Reactions

4. Pyridine as Nucleophilic catalyst

- Used as catalyst for *acylating* phenols, alcohols and amines using acyl chlorides / anhydrides.

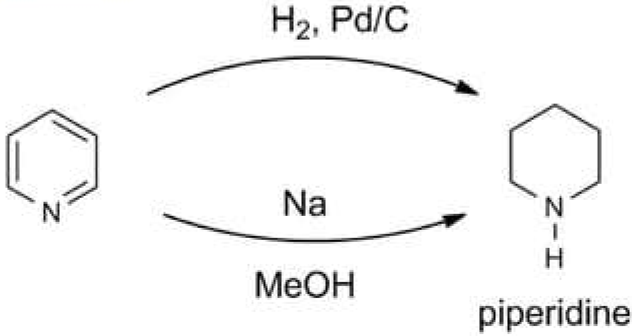


Mechanism



Reactions

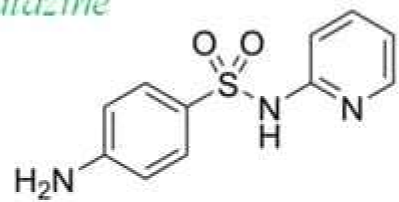
5. Reduction



Medicinal uses

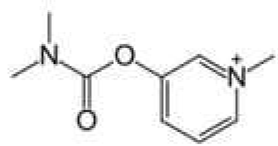
(1) Antitubercular Agent : *Isoniazid*

(2) Antibacterial agent: *Sulfapyridine, Sulfasalazine*



(3) Anticholinesterase agent : *pyridostigmine*

- used in myasthenia gravis



Medicinal uses

(4) Proton Pump Inhibitors : *Omeprazole, Lansoprazole, Pantoprazole, Rabeprazole* - used in peptic ulcer

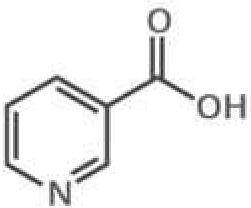
PPI

PPI	X	Y	Z	R
Omeprazole	CH_3	CH_3O	CH_3	CH_3O
Lansoprazole	CH_3	CF_3CH_2O	H	H
Pantoprazole	CH_3O	CH_3O	H	CHF_2O
Rabeprazole	CH_3	$CH_3OCH_2CH_2CH_2O$	H	H

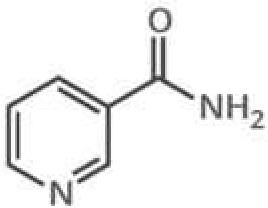
PYRIDINE

Medicinal uses

VITAMIN B3



NICOTINIC ACID

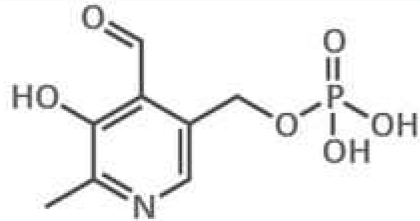


NICOTINEAMIDE

niacin is collective name for these compounds

Helps with digestion and digestive system health. Also helps with the processing of carbohydrates.

VITAMIN B6



PYRIDOXAL PHOSPHATE

active form in mammalian tissues

Helps make some brain chemicals; needed for normal brain function. Also helps make red blood cells and immune system cells.