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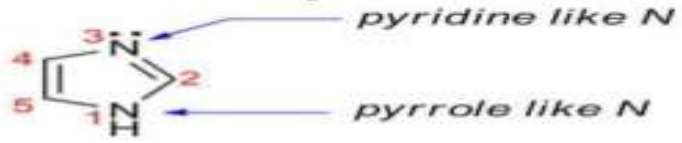
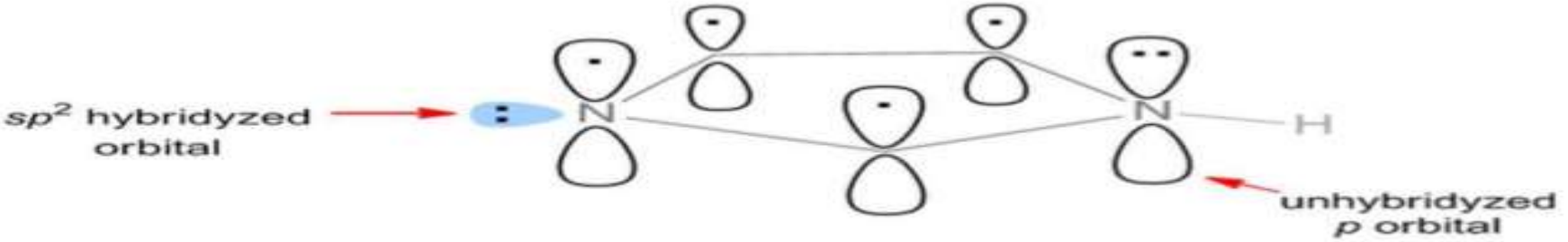
Designation: Professor
Department: Pharmacy
Subject: Pharma. Organic Chemistry (BP 401T)
Unit: IV
Topic: Imidazole Synthesis

IMIDAZOLE

Properties

1. Aromaticity





IMIDAZOLE

Properties

1. Aromaticity

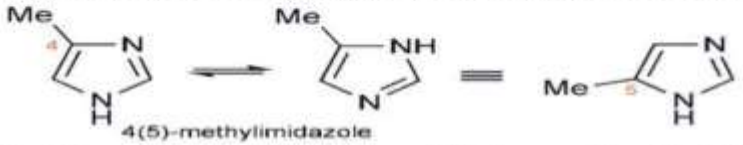
- **Imidazole** have 3 C and 2 N , all are sp^2 hybridized
- sp^2 hybridization is planar, it makes a planar imidazole ring structure.
- Each ring atoms also contains unhybridized p orbital that is perpendicular to the plane of σ bonds (plane of ring).
- Here p orbitals are parallel to each other, so overlapping btwn p orbitals is possible.
- the total nu of non bonding e- are 6 (3 of three C, 1 from one N and 2 of other N)
- The resonance of 6 e- follows the Hückel's rule
- So ....

IMIDAZOLE

Properties

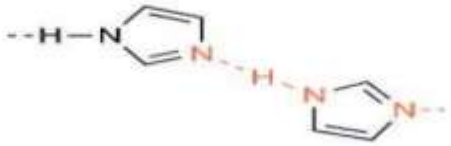
2. Tautomerism

- Imidazole with a ring N- hydrogen are subject to tautomerism.



- 4 –methylimidazole equilibrium with 5 – methylimidazole

3. Hydrogen bonding



IMIDAZOLE

Synthesis

3. From Dehydrogenation of Imidazoline

- Condensation of 1,2-diamines with nitriles gives imidazoline.
- Imidazoline reaction with barium manganate yiels 2-substituted imidazole.

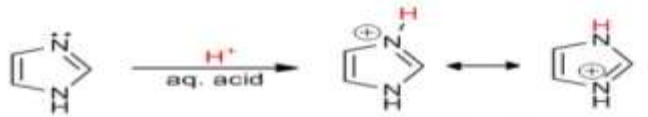
IMIDAZOLE

Reactions

1. Electrophilic addition to N

a. Protonation (basic property)

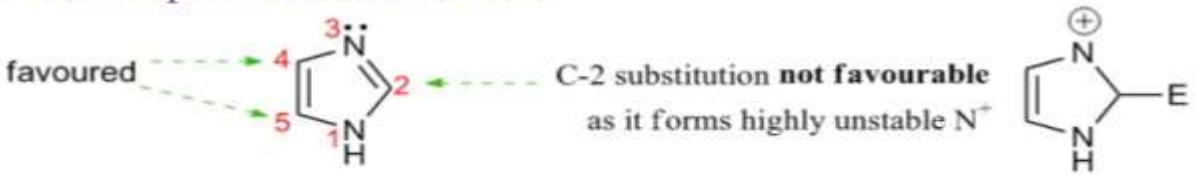
- **imidazole accept proton, act as base.**



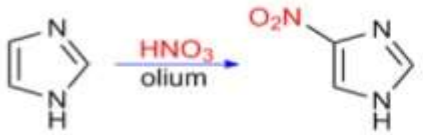
IMIDAZOLE

Reactions

2. Electrophilic substitution to C

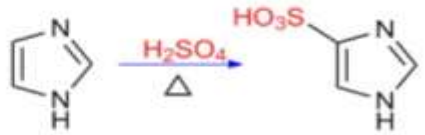


a. Nitration



4(5)-nitroimidazole

b. sulphonation



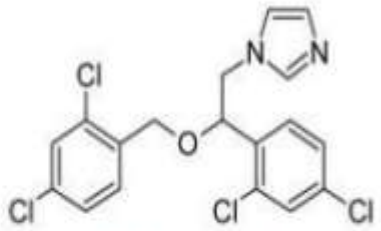
imidazole-4(5)-sulfonic acid

IMIDAZOLE

Medicinal uses

(1) Azole Antifungal Agents:

Ketoconazole
Miconazole
Clotrimazole



Miconazole

(2) Antihistaminic drug: *Cimetidine*

- used to treat and prevent peptic ulcer, gastro esophageal reflux disease (GERD) and heartburn.

(3) Antiprotozoal agents: *Metronidazole*

- used in amoebic dysentery