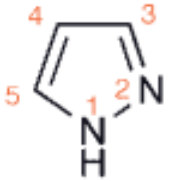
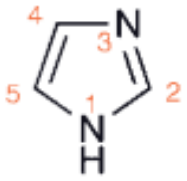
CH-2-III

Imidazole and Pyrazole

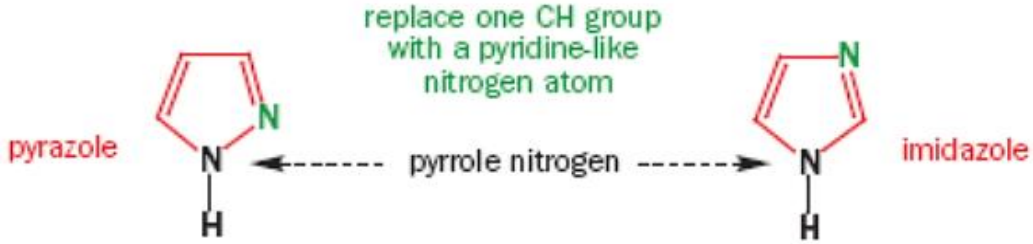
Introduction



pyrazole



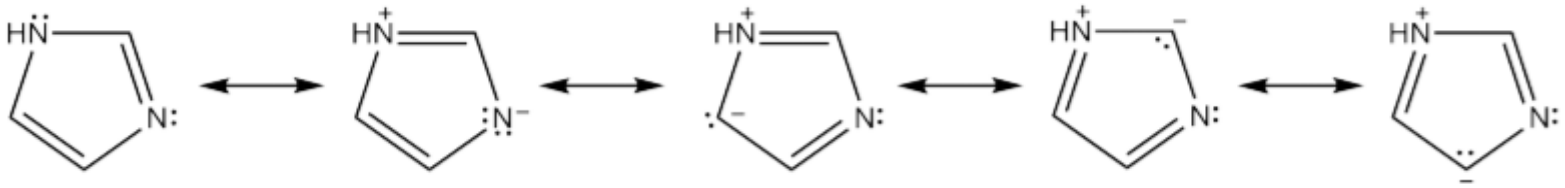
imidazole



Only one nitrogen atom can contribute two electrons to the aromatic sextet. It is the nitrogen with the hydrogen (red) and it is described as pyrrole-like nitrogen. While the second nitrogen which has no hydrogen (blue) is described as pyridine-like.

Resonance structures of imidazole

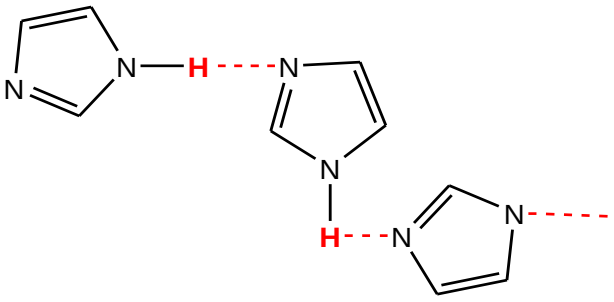
- The lone pair on pyrrole-like nitrogen is delocalized round the ring while that on the pyridine-like nitrogen is localized in sp^2 orbital on nitrogen. Thus these compounds have properties intermediate between those of pyrrole and pyridine.



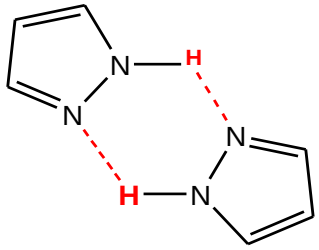
Physical Properties of Imidazole and Pyrazole

- Imidazole and pyrazole are water soluble solids and insoluble in aprotic solvent.
- They have very much higher boiling points than pyridine: 256 and 187 °C respectively, this difference is due to imidazole has an extensive hydrogen bonding than pyrazole thus imidazole molecules can exist as oligomers, consequently more energy is required to break these bonds to bring the molecules from one phase to another.
- On the other hand pyrazole molecules can form dimers only thus lesser energy is required to break these molecules.

imidazole molecules as a polymer



pyrazole molecules as a dimer



- N-subsituted imidazole and pyrazole have lower boiling and melting points than the unsubstituted compounds due to inability to form H-bonds.

Physical Properties of Imidazole and Pyrazole

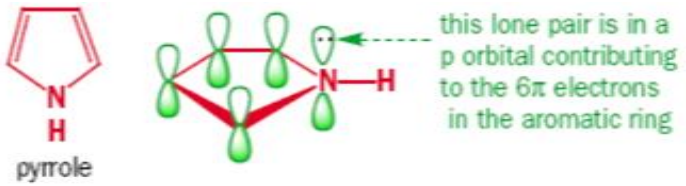
Basicity

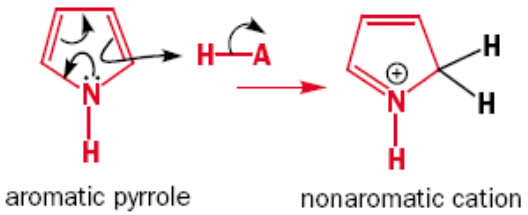
- Imidazole is a stronger base than pyrazole or pyridine and of course pyrrole. Thus imidazole and pyrazole are more stabilized than pyrrole in acidic medium.

Basicity order: Imidazole > Pyridine > Pyrazole > Pyrrole

This can be explained as follows:

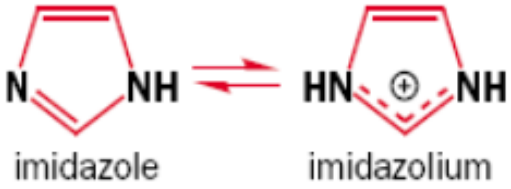
i) Pyrrole is not basic because the lone pair on the only nitrogen is needed to complete the aromatic π system and protonation if occurs at all occurs at carbon rather than on nitrogen and the resulting cation is not aromatic.

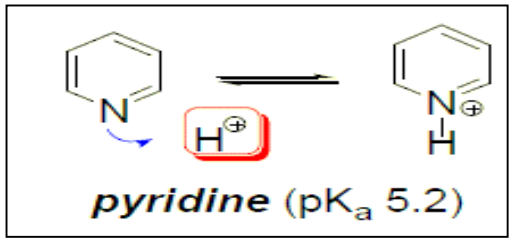




Physical Properties of Imidazole and Pyrazole

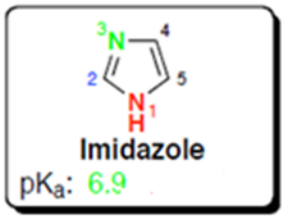
ii) Imidazole has two nitrogen atoms and on protonation the positive charge can be delocalized over them but although in pyridine its l.p. is available for protonation as it is not involved in maintaining aromaticity, it has only has one nitrogen on which to stabilize the positive charge thus it is less basic than imidazole.

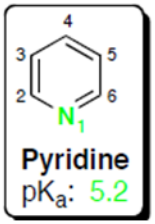


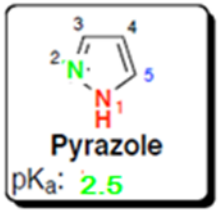


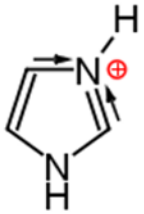
Physical Properties of Imidazole and Pyrazole

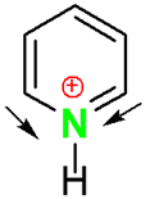
iii) Pyrazole is much weaker base than imidazole and pyridine although it also have two nitrogen atoms as in case of imidazole. This difference is due to the fact that the positive charge in pyarzolium ion is less stabilized than in the imidazolium ion and pyridinium ion.

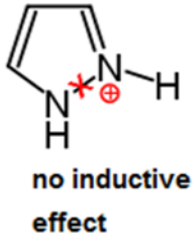












In imidazole the cation is stabilized for **inductive effect** and also less influenced by the E W behavior of nitrogen

The "**pyrrole**-like" nitrogen exerts EW effect

Thus destabilize the +ve charge

Physical Properties of Imidazole and Pyrazole

Effect of substitution on basicity

- Generally E.D.G groups on the ring increase the basicity while E.W.G. decrease it.
- N-methyl imidazole is more basic than imidazole itself.
- However, N-methylpyrazole is less basic than pyrazole which can be attributed to steric hindrance effect which cause difficulty in accessing the lone pair of electron by the proton.

Basicity

Acidity

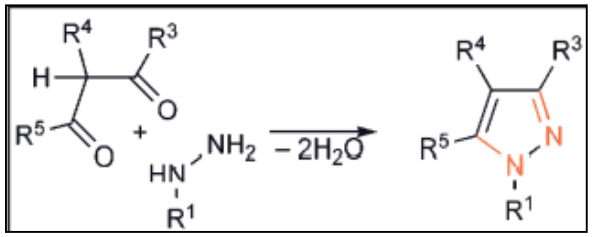
- Imidazoles unsubstituted in the 1-position are weak acids. Its acidity is greater than that of pyrrole and equals that of pyrazole.
- Thus imidazole and pyrazole are amphoteric substances.

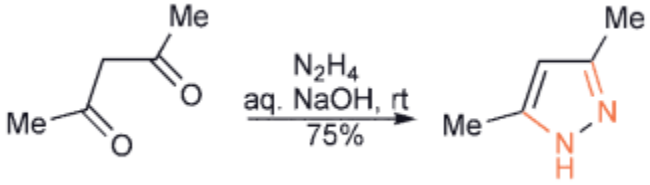
Acidity

Synthesis of imidazole and pyrazole

Pyrazole

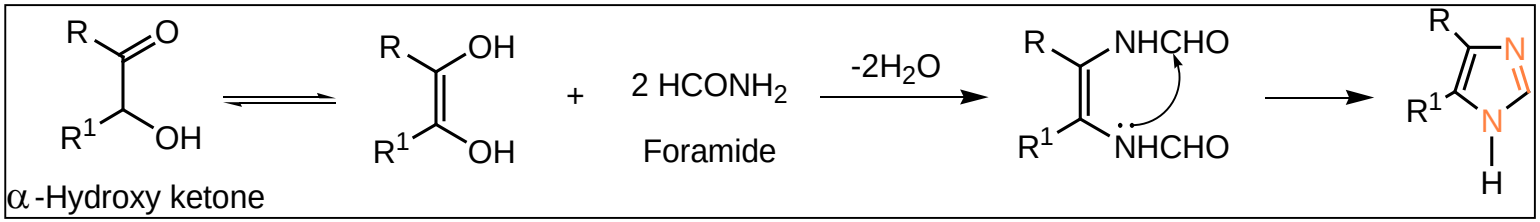
- From 1,3 - Dicarbonyl Compounds and Hydrazines.





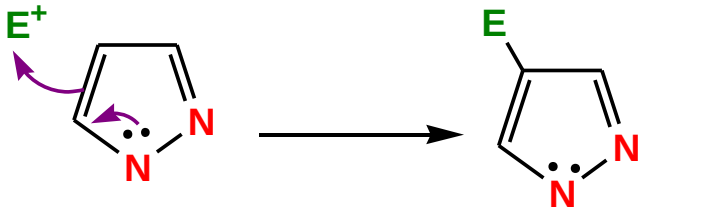
Imidazole

- From α-Hydroxy ketone and Foramide.



Electrophilic Substitution

- Diazoles are less reactive than 5-membered heterocycles with one heteroatom (pyrrole and its analogs) in electrophilic aromatic substitution due to the inductive electron-withdrawing effect of the second heteroatom.
- However, they are more reactive than pyridine due to delocalization of the lone pair of electrons on the N-atom make the C- atoms bear negative charges while in pyridine the N- atom exerts inductive electron withdrawing effect only.
- The orientation in pyrazole, is at the 4-position due to the deactivation effect of the pyridine-like nitrogen.



Pyrazole 4-substituted

- The orientation in imidazole, is at 4 or 5-position.

Electrophilic Substitution

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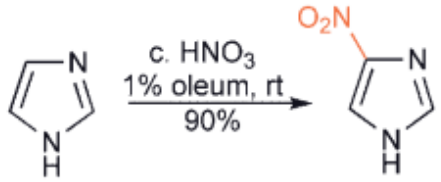
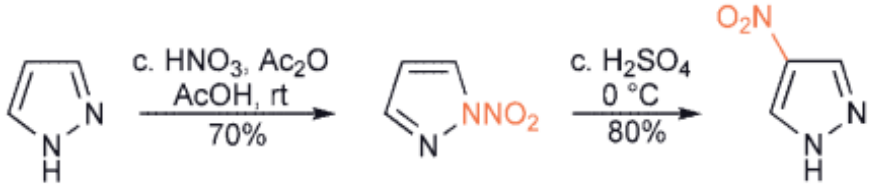
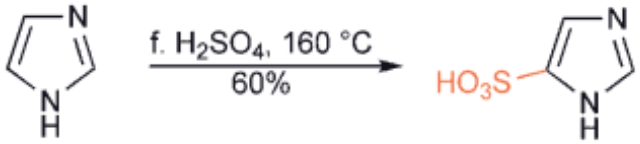
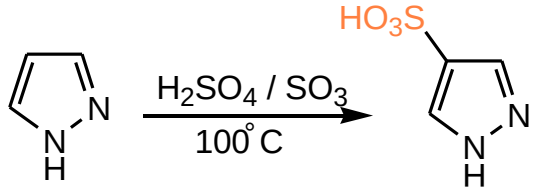




2) Sulfonation





3) Halogenation