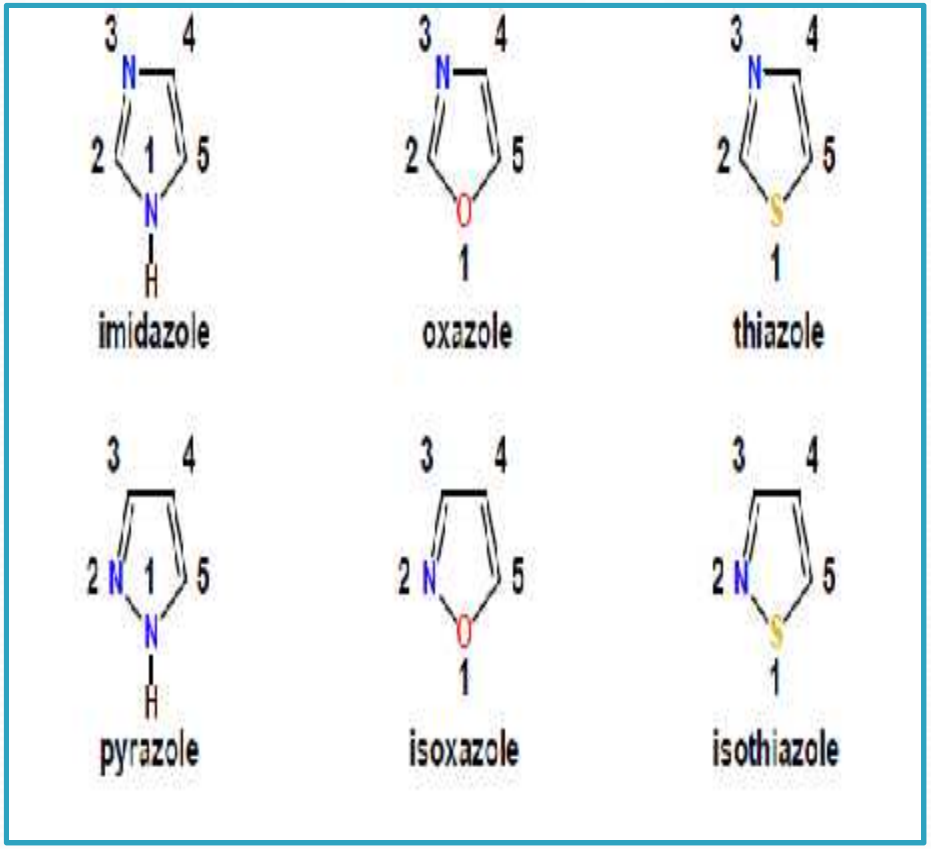
Five member rings heterocyclic with two hetero atoms (1,3-azole)

Dr.ayad

- Introduction of second heteroatom create azole (nitrogen is one of the heteroatoms.
- -No. of the ring start from the heteroatom with higher atomic no.
- -Like pyrrole, furane and thiophene all ring are aromatic.
- -All the compounds have group =N- (azomethine , like N in pyridine) which have one unpaired of electron



1,3 azole : Imidazole, Oxazole & Thiazole

- Fivemember ring containe two hetero atoms one of which is nitrogen.
- The other hetero atoms are NH, O & S
- All have a characterization of aromatic compound.

Physical properties

1- Basicity

- Imidazole is the most basic compounds pKa= 7.0
- Oxazole = 0.8
- Thiazole = 2.5
- The 1,3 azole are more basic than pyrrole (pKa= -3.8)
- Imidazole is more basic than pyridine (pKa= 5.2)

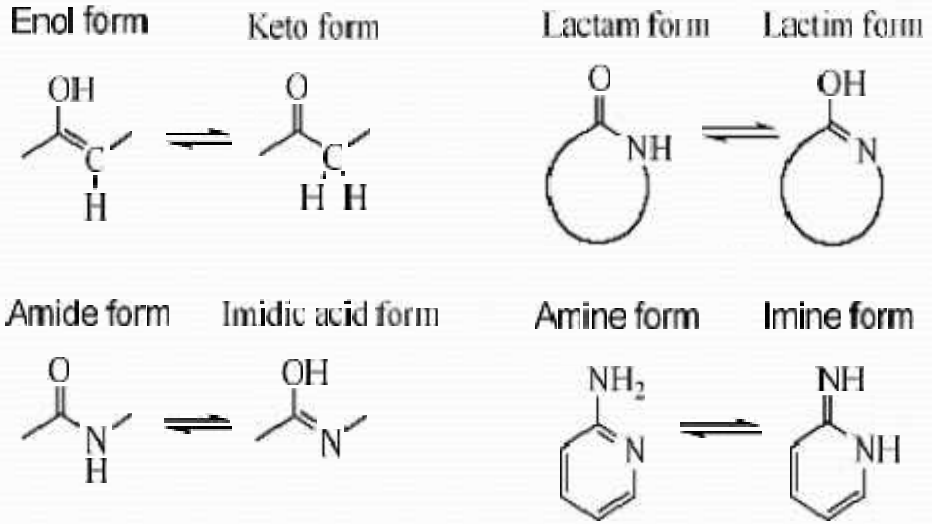
2- Boiling point

- Imidazole 250-255C
- Oxazole 69-70C
- Thiazole 116- 118 C

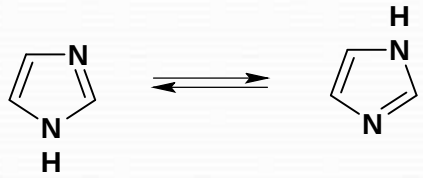
3- solubility

- imidazole soluble in water, oxazole & thiazole springly soluble in water

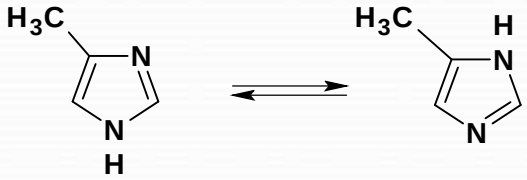
Tautomers are isomers (structural isomers) of organic compounds that readily interconvert by a chemical reaction called **tautomerization**. This reaction commonly results in the formal migration of a hydrogen atom or proton, accompanied by a switch of a single bond and adjacent double bond. The concept of tautomerizations is called **tautomerism.** Because of the rapid interconversion, tautomers are generally considered to be the same chemical compound.



It exists in two equivalent tautomeric forms, because the proton can be located on either of the two nitrogen atoms Imidazole .

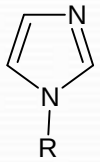


unsymmetrically substituted imidazole



4- methyl imidazole **5- methyl imidazole**

this compound is 4(5) methyl imidazole

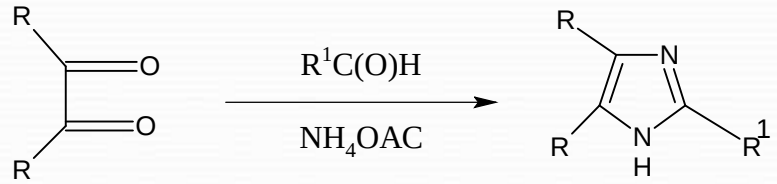


N-substituted imidazole, tautomerism not possible

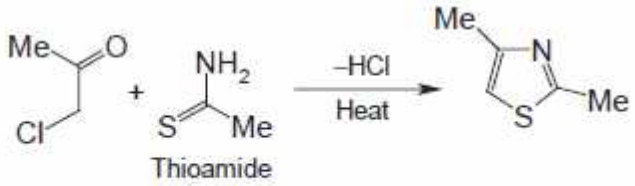
oxazole and thiazole tautomerism not possible also

Preparation of 1,3 azole

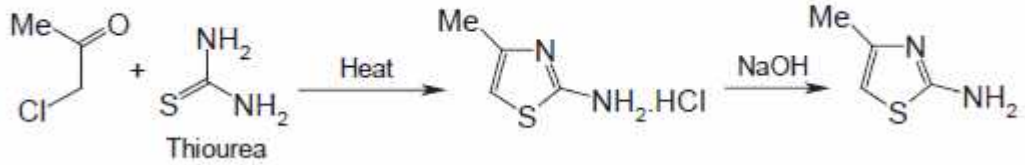
Preparation of imidazole The condensation of a 1,2-dicarbonyl compound with ammonium acetate and an aldehyde results in the formation of an imidazole



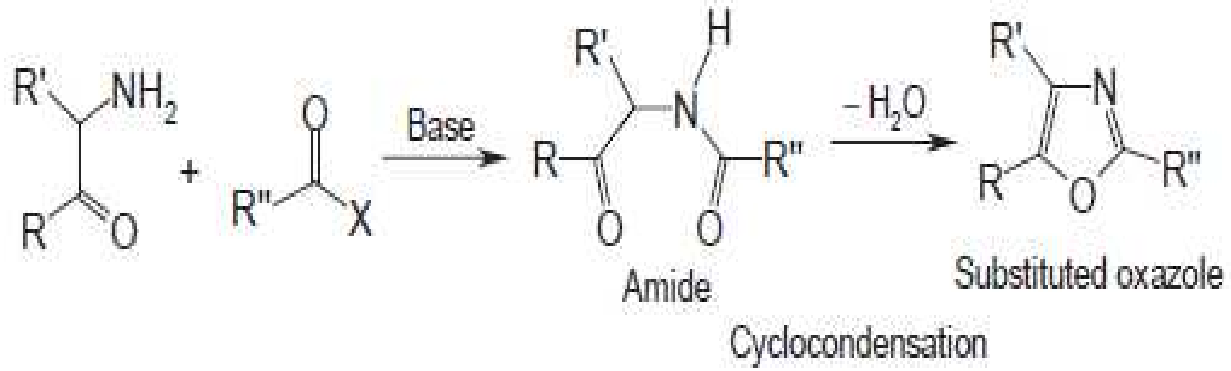
Preparation of thiazole Hantzsch synthesis can be applied to synthesize the thiazole system from thioamides. The



A modification of the above method involves the use of thiourea instead of a thioamide.



Preparation of oxazole Cyclocondensation of amides, through dehydration, leads to the formation of corresponding oxazoles. This synthesis is known as *Robinson-Gabriel synthesis*. A number of acids or acid anhydrides, e.g. phosphoric acid, phosphorus oxychloride, phosgene and thionyl chloride, can bring about this dehydration.



Reactions of oxazole, imidazole and thiazole

The presence of the pyridine-like nitrogen deactivates the 1,3-azoles toward electrophilic attack, and increases their affinity towards nucleophilic attack.

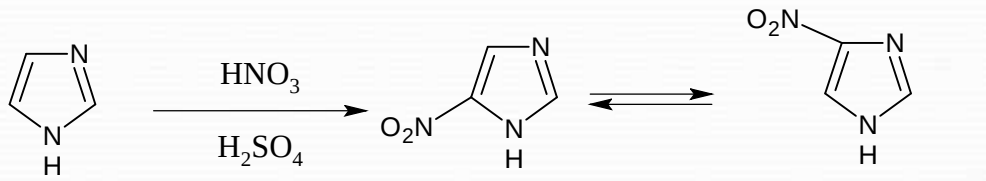
1,3 Azole are much less reactive to ESR than pyrrole, furan & thiophene, but more reactive than pyridine.

Imidazole is most reactive than thioazole & oxazole toward ESR.

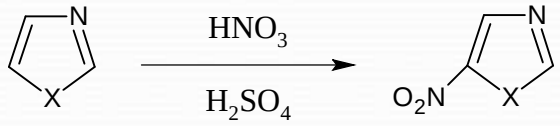
Any electron donating group on the ring can faciliate ESR.

ESR occurs at C-5.

Tautomerism in imidazole leads to the 4(5)mixture

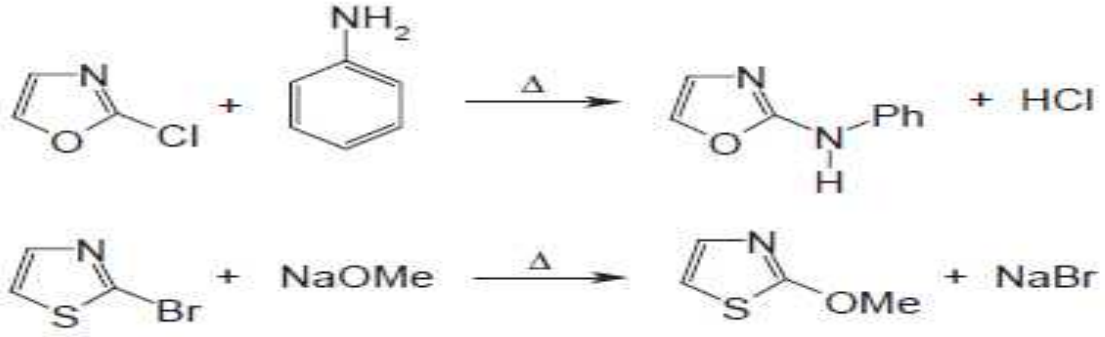


5- Nitroimidazole 4-Nitroimidazole

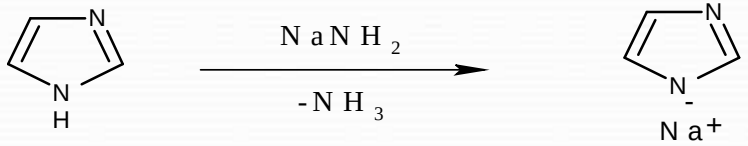


X = O, S

Nucleophilic aromatic substitutions 1,3-azoles are more reactive than pyrrole, furan or thiaphene towards nucleophilic attack. Some examples



In case of imidazole the strong base can remove the NH proton



but in oxazole and thiazole donot have any NH , so the most acidic proto is that at C-2

X = O , S