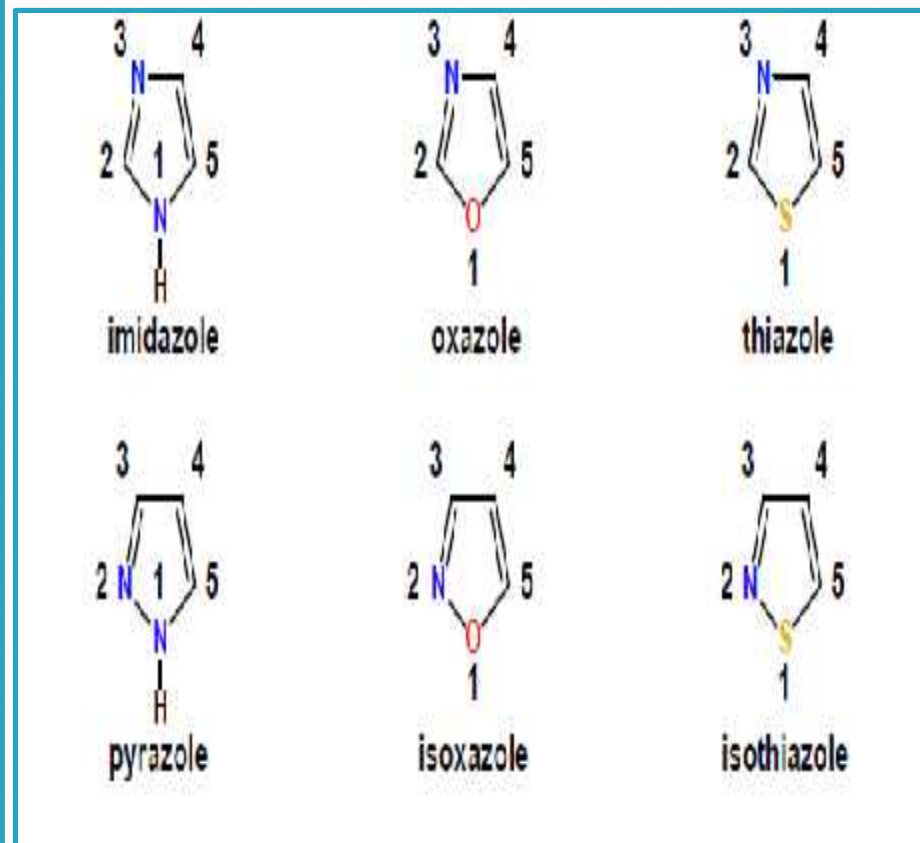




Five member rings heterocyclic  
with two hetero atoms (1,2-azole)

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



# 1,2 azole : pyrazole, Isoxazole & Isothiazole

- Five member ring contain two hetero atoms one of which is nitrogen.
- The other hetero atoms are NH, O & S
- All have a characterization of aromatic compound.
- Like 1,3-azole, =N- carries lone pair of electrons
- 1,2 azole are basic compounds due to the lone pair of electrons on =N- group but it is less basic than 1,3 azole

## Physical properties

### 1- Basicity

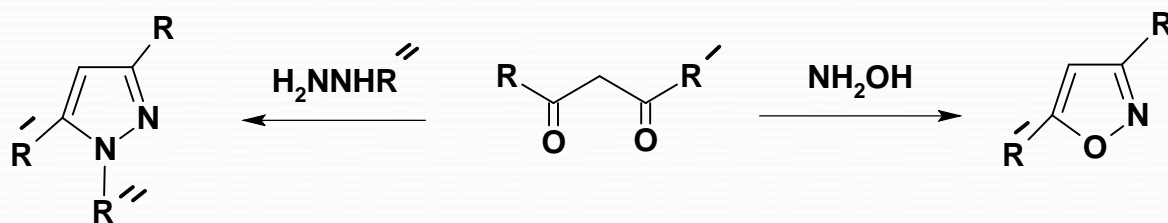
- pyrazole is the most basic compounds  
pKa= 2.5
- isoxazole = -3.0
- isothiazole = -0.5
- Owing to the electron with drawing effect of the adjacent hetero atom 1,3 azole are more basic than 1,2 azole.

### 2- Boiling point

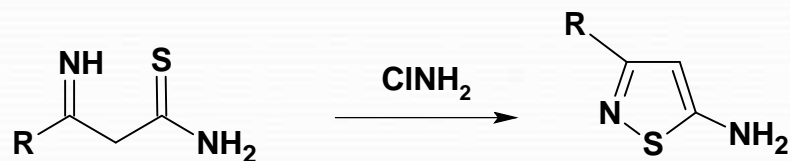
- pyrazole 186-188C
- isoxazole 95C
- isothiazole 114 C

## Preparation of 1,2 azole

While, 1,3 diketone undergo condensation with hydroxyl amine to produce isoxazole, with hydrazine they yield corresponding pyrazole



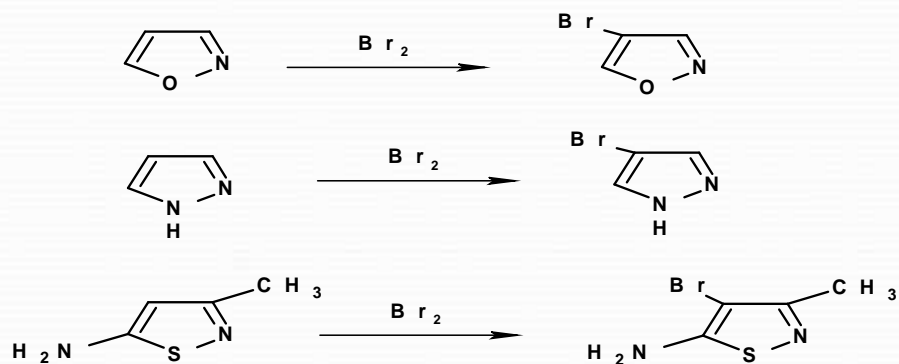
Isothiazole can be prepared from thioamides in the following way



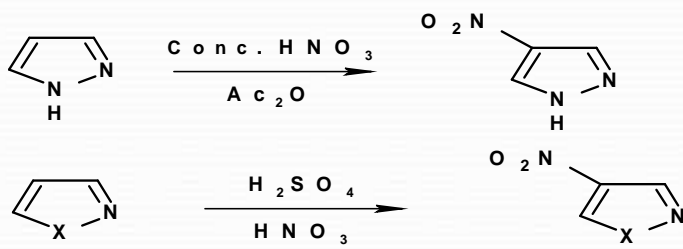
# Reaction of 1,2 azole

- Like 1,3 azole, due to the presence of =N- group in the ring 1,2 azole are **much less** reactive towards ES reactions than furan, pyrrole and thiophene.
- 1,2 azole undergo ES reactions under appropriate reaction condition
- The main substitution takes place at the C-4 position.
- Pyrazole reactivity like phenol, but isoxazole & isothiazole reactivity like benzene

## Bromination

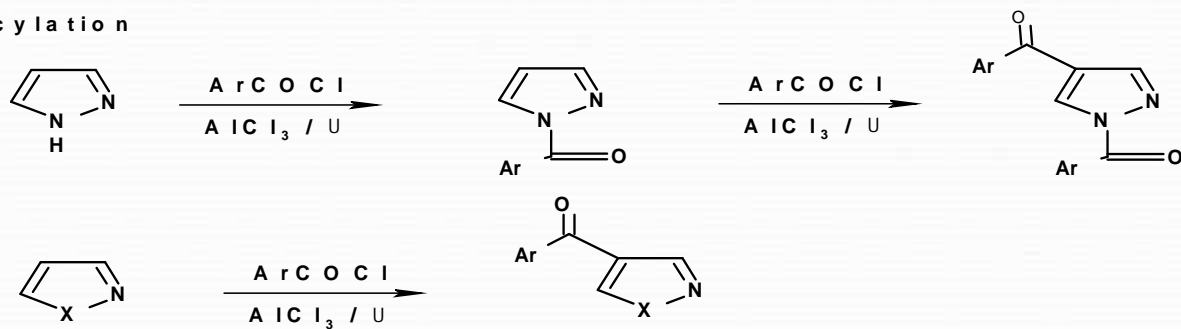


## Nitration

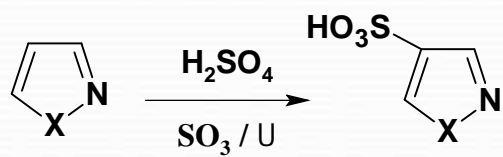


$x = O \text{ \& \ } S$

## Acylation

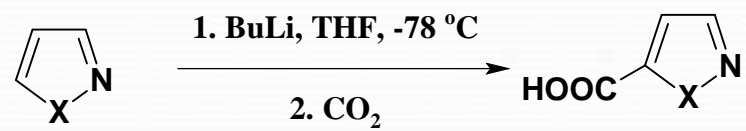
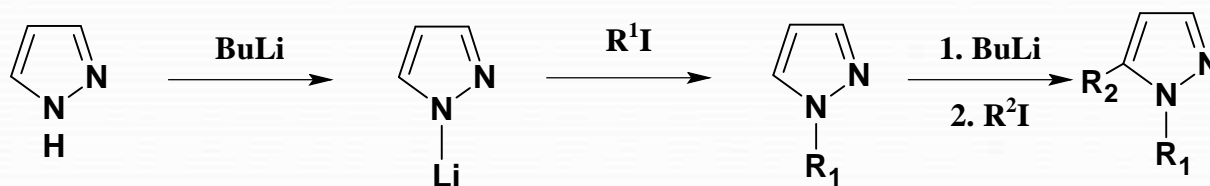


## Sulfonation



x = NH, O & S

## Metallation



x = O & S