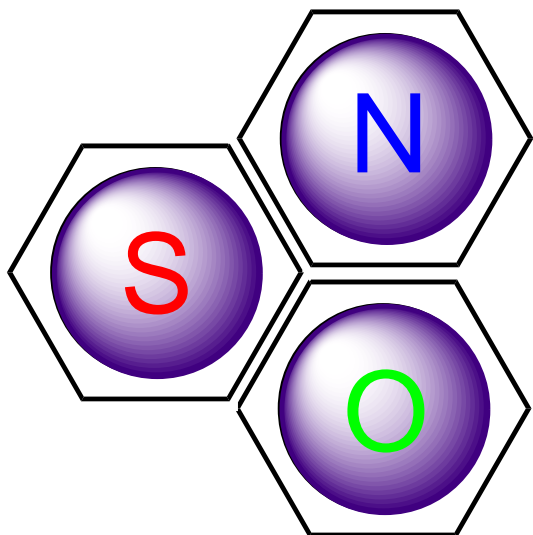


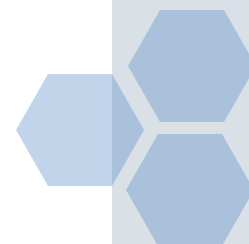


# Heterocyclic Chemistry



**Five-membered Heterocycles**

**Pyrrole, Furan and Thiophene**

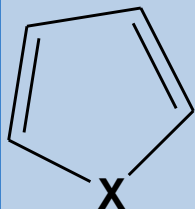




# Hetero-Monocyclic Compounds

## A. Five-membered Rings with one Heteroatom

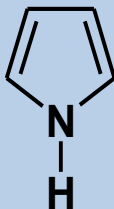
- ❖ The main reason for the study of pyrrole came from the work on the structure of **haem**; the blood respiratory pigment, and the **chlorophyll**; the green photosynthetic pigment of plants.
- ❖ Thiophene and its derivatives occurs in petroleum.
- ❖ **Furan occurs widely in secondary plant metabolites, especially in terpenoids.**
- ❖ **Unsubstituted pyrrole, furan, and thiophene are usually obtained from petroleum.**



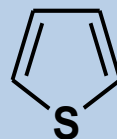
X = NH Pyrrole

= O Furan

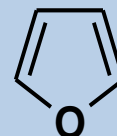
= S Thiophene



Pyrrole



Thiophene



Furan



# Hetero-Monocyclic Compounds

## Structure and Aromaticity

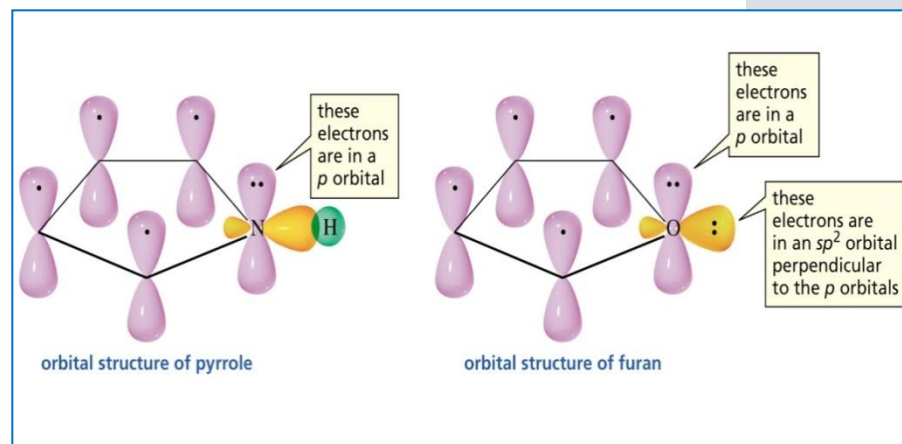
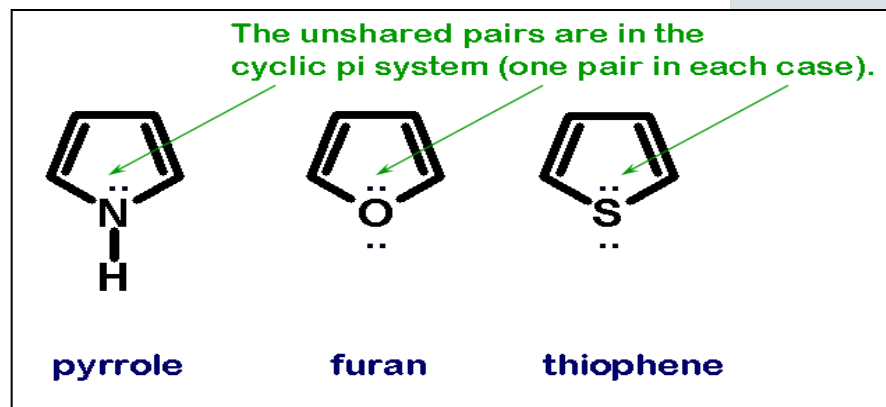
❖ Pyrrole furan and thiophene are aromatic because:

1) they fulfill the criteria for aromaticity, the extent of delocalization of the nonbonding electron pair is decisive for the aromaticity, thus the grading of aromaticity is in the order of:

**Furan < Pyrrole < Thiophene < Benzene**

this order is consistent with the order of electronegativity values for oxygen (3.44), nitrogen (3.04) and thiophene (2.56).

### A. Five-membered Rings with one Heteroatom



### The order of aromaticity

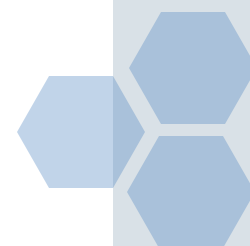
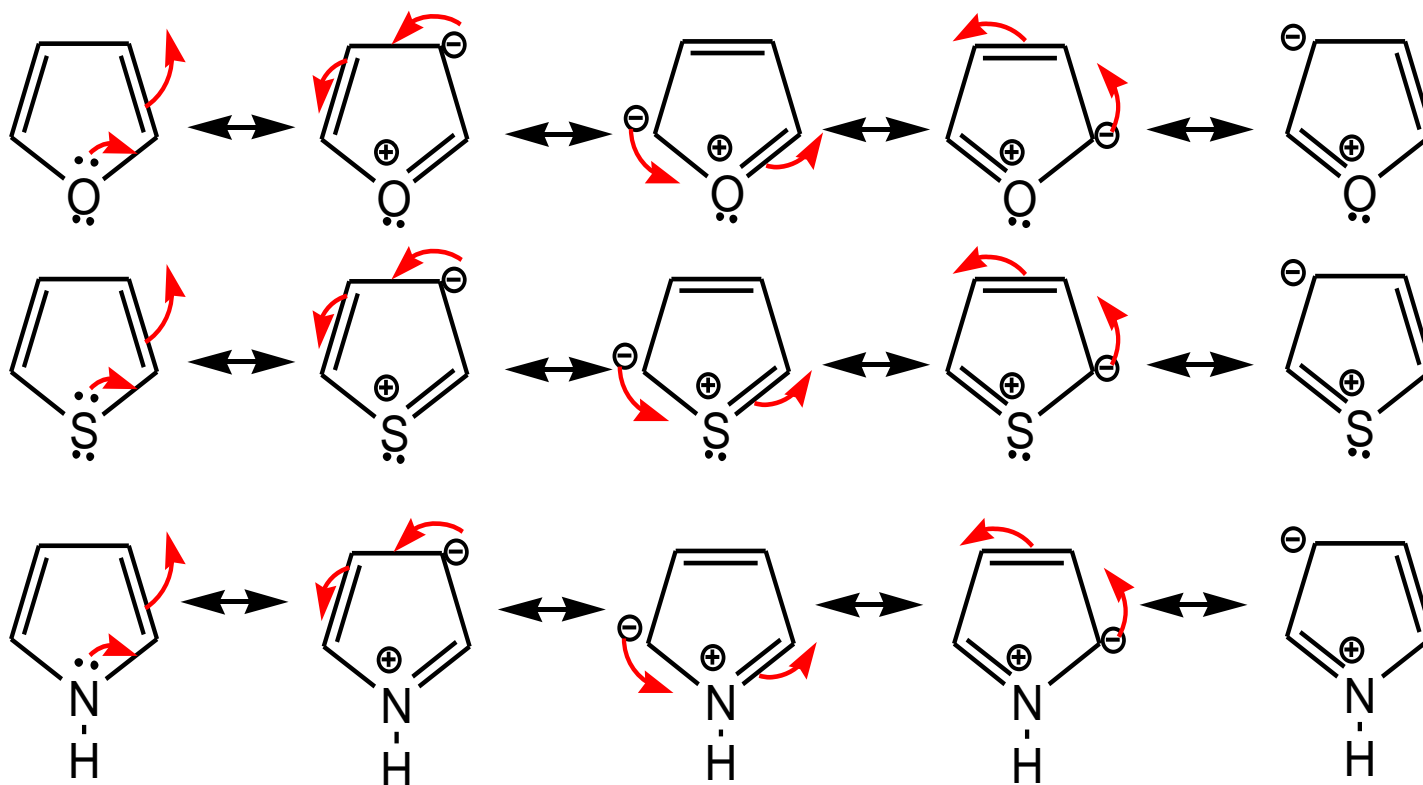
**Benzene > Thiophene > Pyrrole > Furan**



## Structure and Aromaticity

### A. Five-membered Rings with one Heteroatom

2) They tend to react by **electrophilic substitution** due appearance of **-ve charge** on carbon atoms due to delocalization as shown in the following **resonance structures**





# Hetero-Monocyclic Compounds

## Structure and Aromaticity

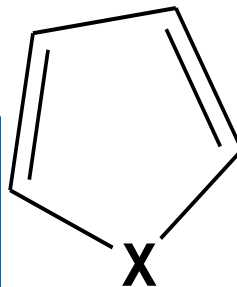
3- Electrons not available for protonation—hence **not basic**

4- 6  $\pi$  electrons over 5 ring atoms .....  
Electron rich... so more reactive than benzene towards electrophilic substitution.

The order of reactivity is:

**Pyrrole > Furan > Thiophene > Benzene**

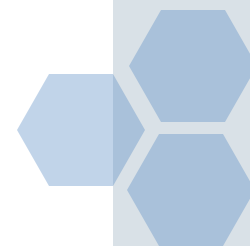
### A. Five-membered Rings with one Heteroatom



**X = NH Pyrrole**

**= O Furan**

**= S Thiophene**





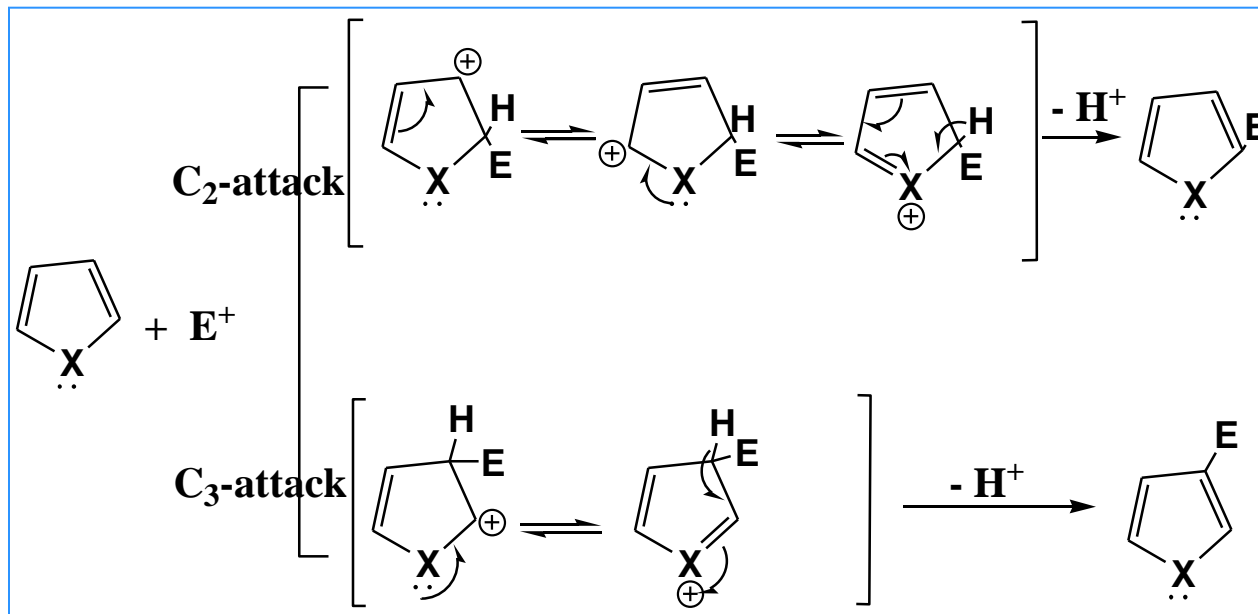
## Structure and Aromaticity

### A. Five-membered Rings with one Heteroatom

#### 5- The pattern of reactivity with Electrophilic reagents.

Aromatic compounds ..... By substitution  
addition followed by proton loss  
[ onium intermediate ]

Order of reactivity : **Pyrrole** > **Furan** > **Thiophene** > **Benzene**





# Hetero-Monocyclic Compounds

## Structure and Aromaticity

ne

### 6-The order of aromaticity

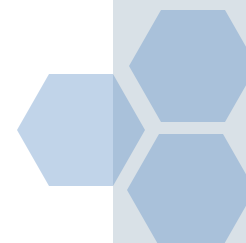
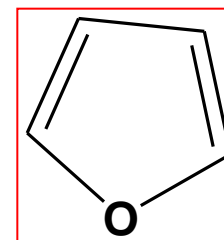
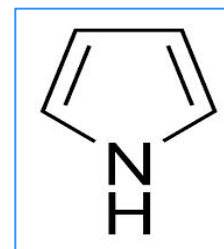
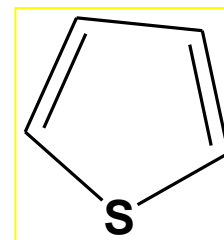
**Benzene > Thiophene > Pyrrole > Furan**

In case of Thiophene [S] donate & accept electrons..... so delocalization as complete as benzene

In case of Pyrrole [N] -Diene-like character  
 $\text{CH}_2=\text{CH}-\text{CH}=\text{CH}_2$

In case of Furan [O] electronegativity more .... Diene-like character  
 $\text{CH}_2=\text{CH}-\text{CH}=\text{CH}_2$

## A. Five-membered Rings with one Heteroatom





## A. Five-membered Rings with one Heteroatom

### Sources & Synthesis

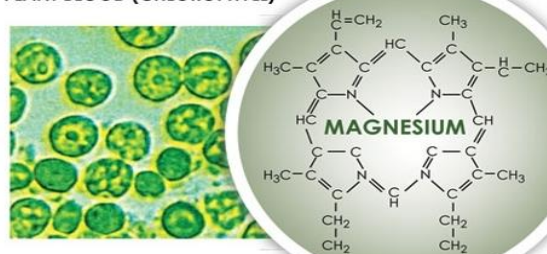
#### A) Sources

Pyrrole & Thiophene .... Coal Tar



Pyrrole ring ....  
Porphyrin system.....  
**Chlorophyll &  
Hemoglobin**

PLANT BLOOD (CHLOROPHYLL)



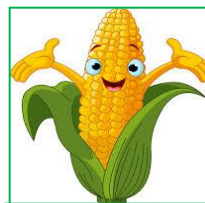
HUMAN BLOOD (HEMOGLOBIN)



Furan ..... Decarbonylation of  
Furfuraldehyde .....  
Oat hulls, corn cobs or rice hulls



Oat hulls



corn cobs



rice hulls



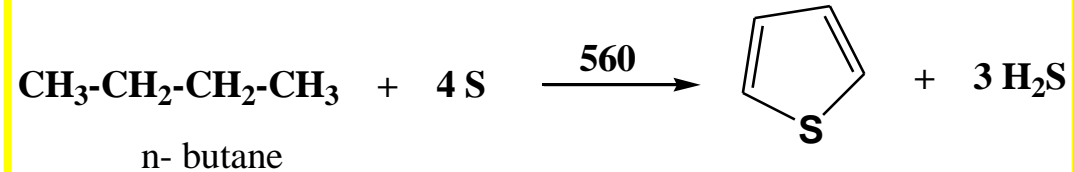




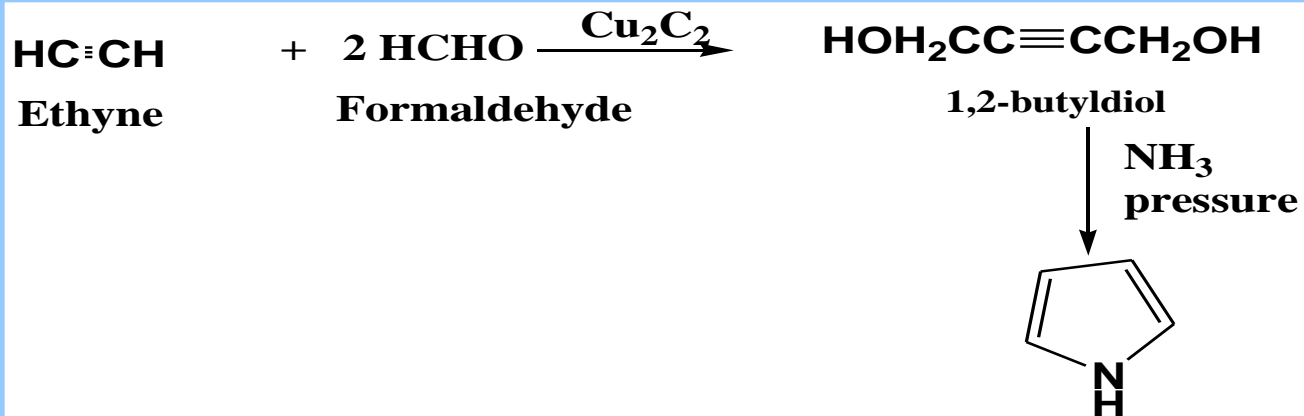
## B) Synthesis

### A. Five-membered Rings with one Heteroatom

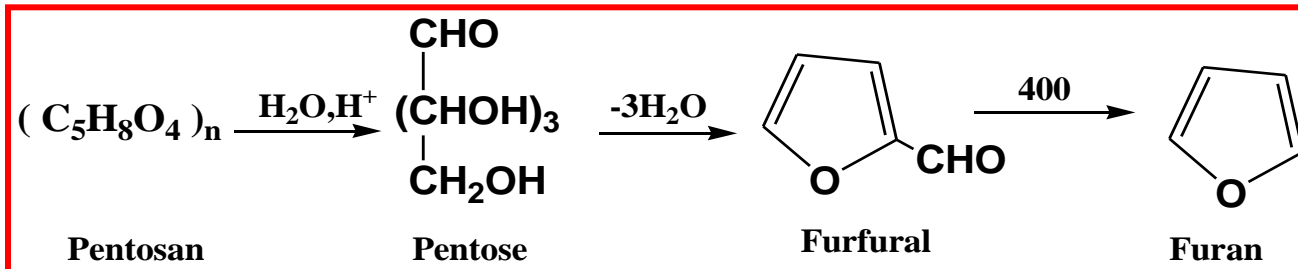
#### Thiophene



#### Pyrrole



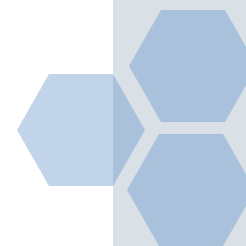
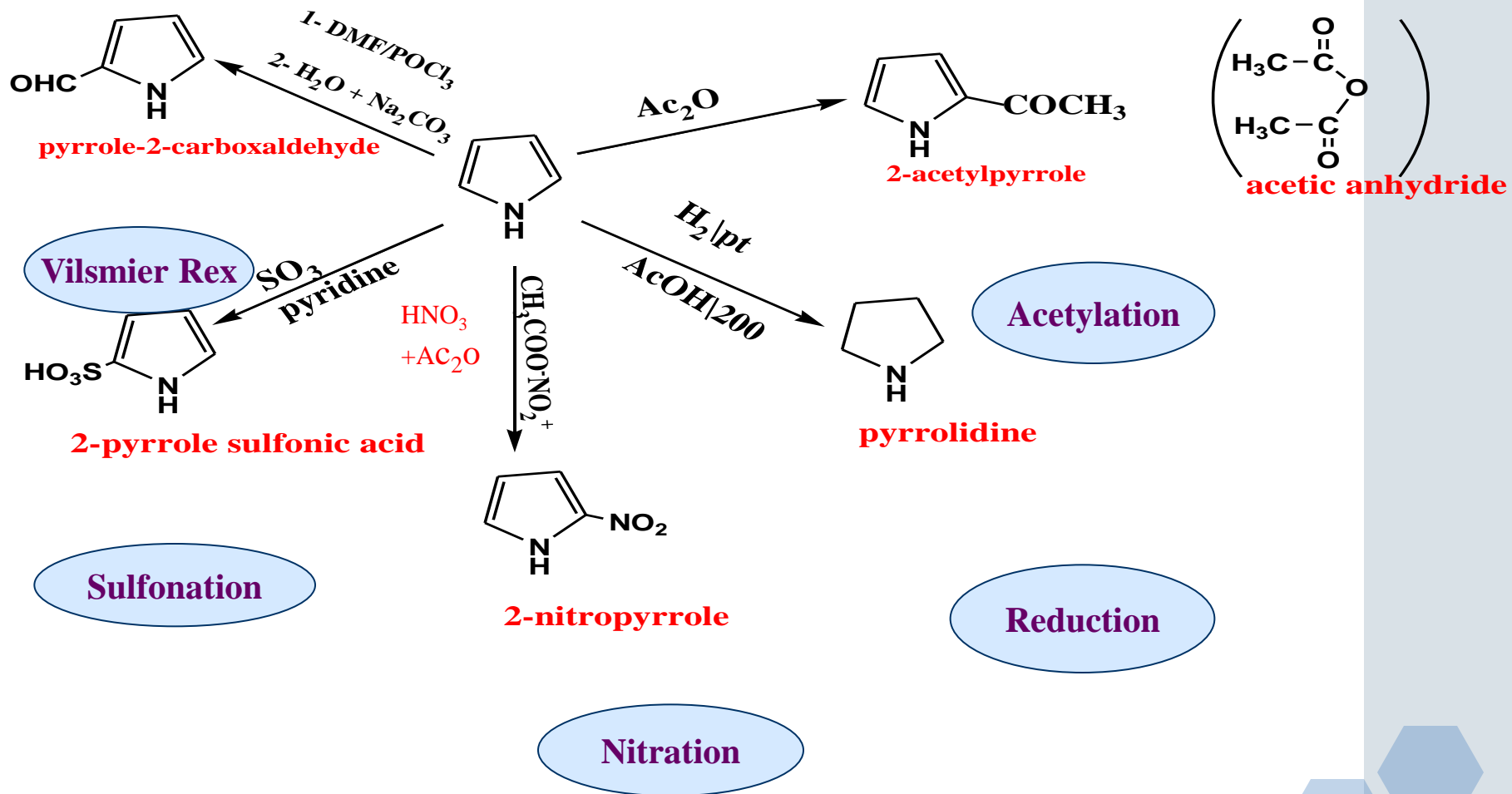
#### Furan





## Reactions of pyrrole

### A. Five-membered Rings with one Heteroatom

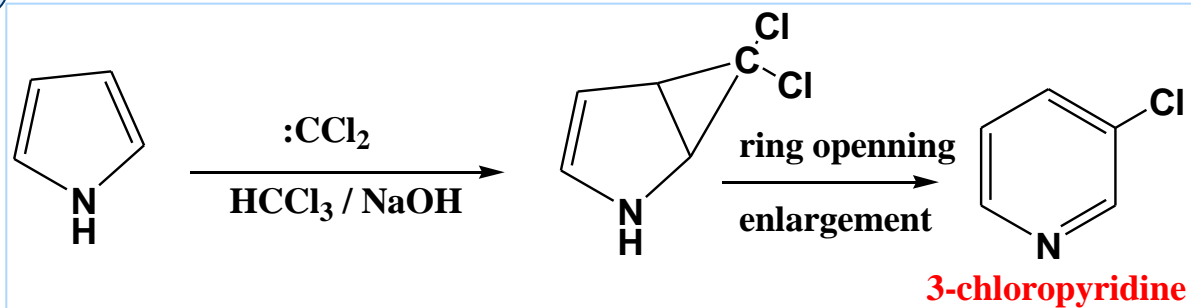




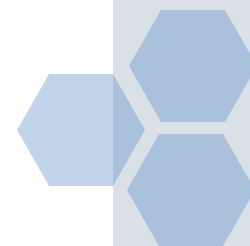
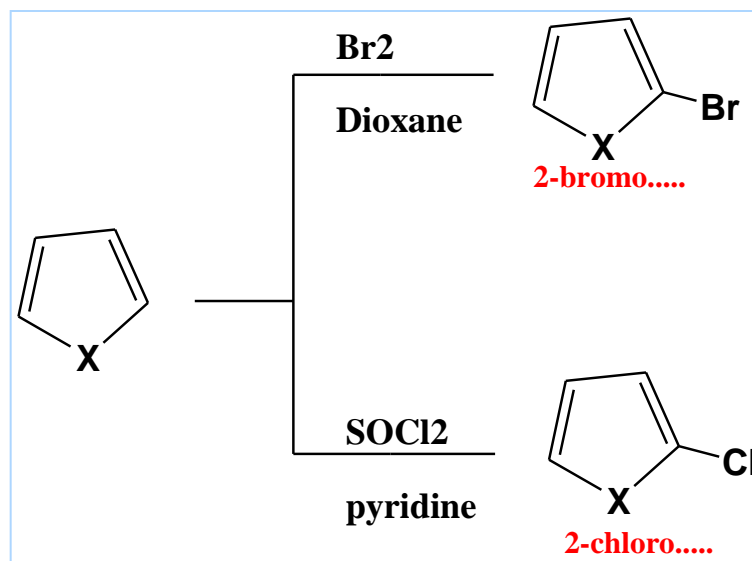
## Reactions of Pyrrole

### A. Five-membered Rings with one Heteroatom

with carbene



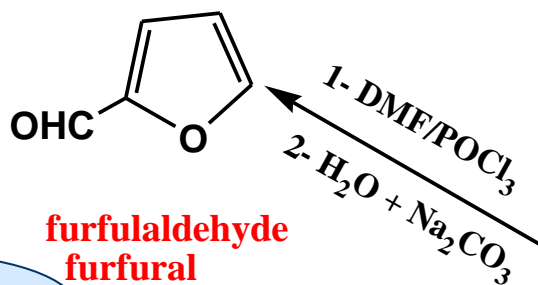
Halogenation



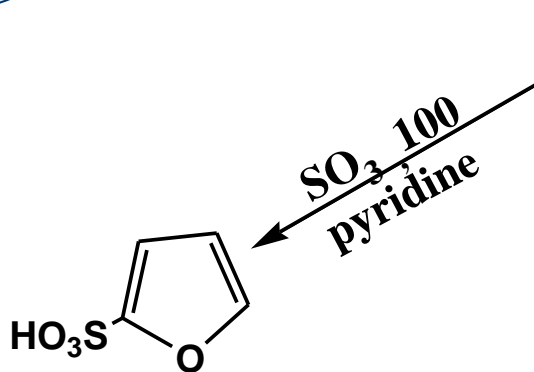


## Reactions of Furan

### A. Five-membered Rings with one Heteroatom

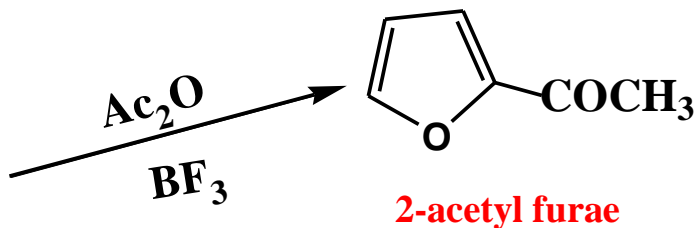
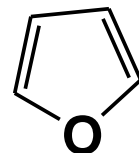


Vilsmier Rex

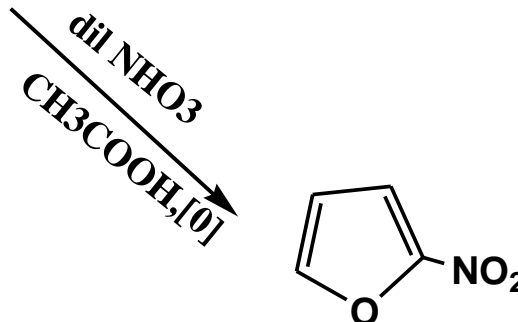


**2-furan sulfonic acid**

Sulfonation



Acetylation



**2-nitrofuran**

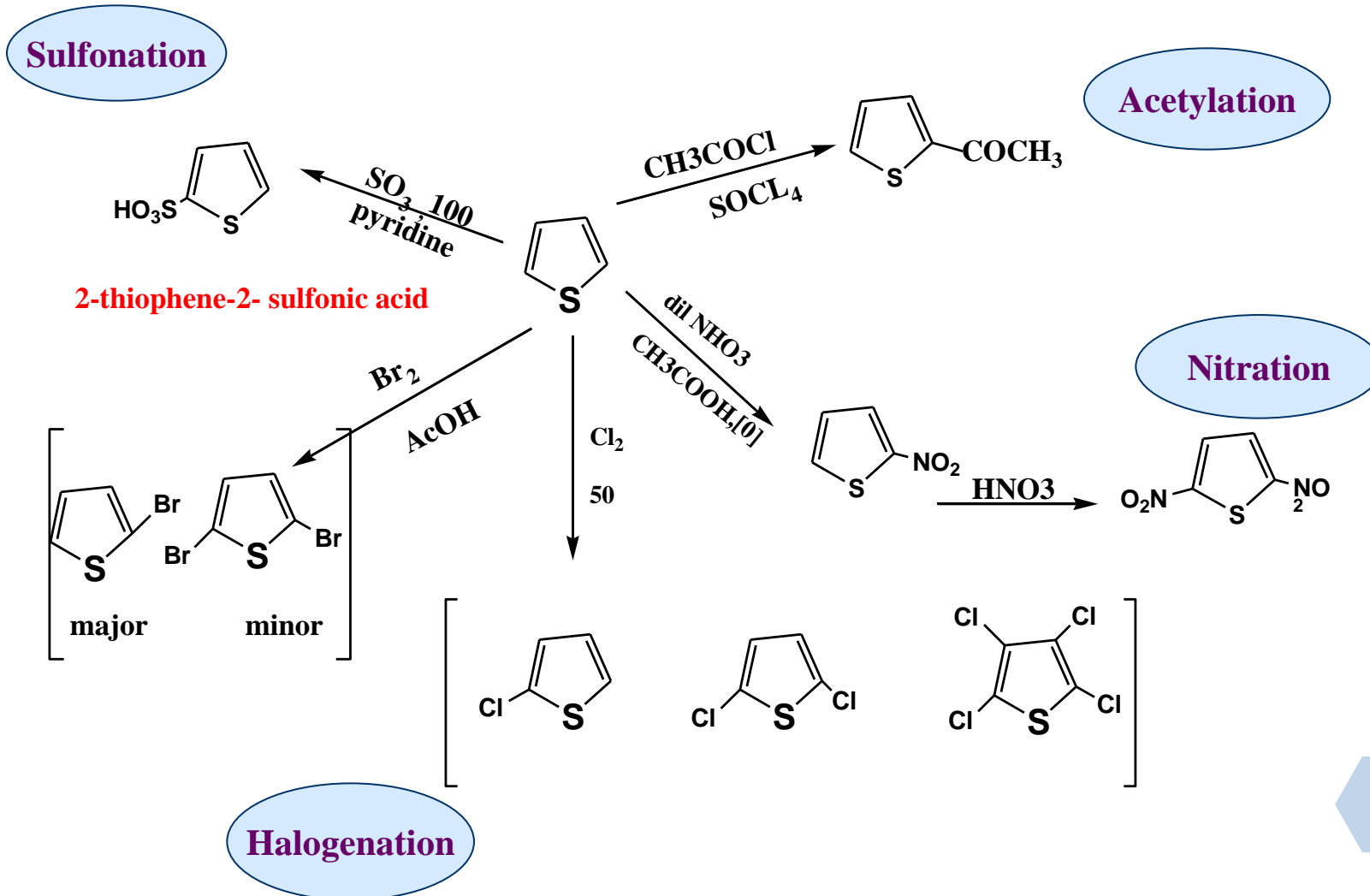
Nitration





## Reactions of Thiophene

### A. Five-membered Rings with one Heteroatom

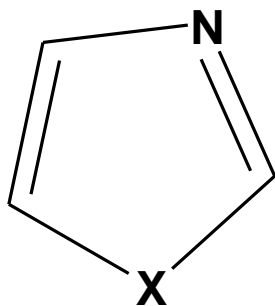




# Hetero-Monocyclic Compounds

## A. Five-membered Rings with one Heteroatom

**Five Membered Heteroaromatic Rings**  
Containing **2X** , at least one **nitrogen**



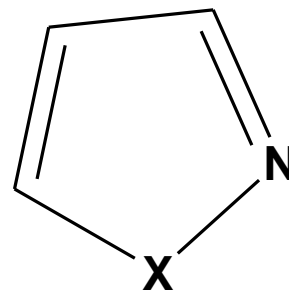
**1,3-Azoles**

**Thiazole [ 1,3-thiazole]**

**Oxazole [ 1,3-oxazole]**

**Imidazole [ 1,3-diazole]**

**X = S ,O ,or N**

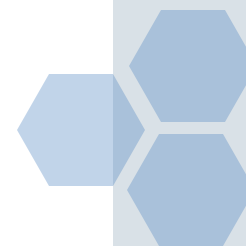


**1,2-Azoles**

**Isothiazole [ 1,2-thiazole]**

**Isoxazole [ 1,2-oxazole]**

**Pyrazole [ 1,2-diazole]**





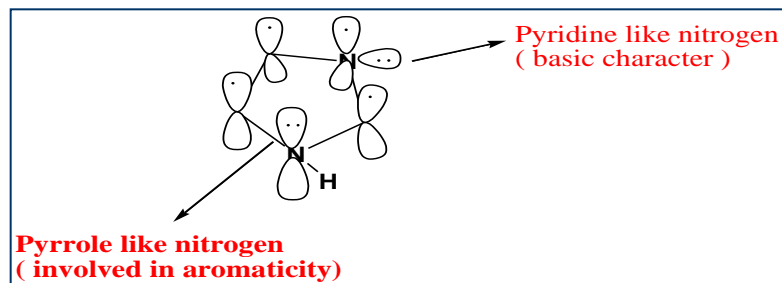
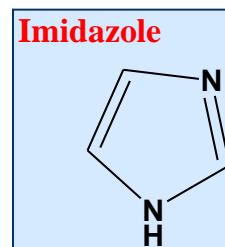
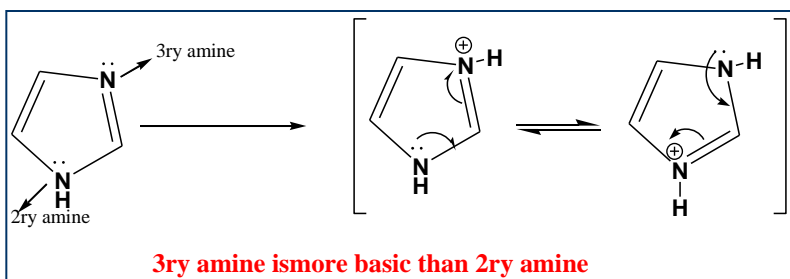
# Hetero-Monocyclic Compounds

## A. Five-membered Rings with one Heteroatom

Five Membered Heteroaromatic Rings  
Containing **2X**, at least one **nitrogen**

### Aromaticity & Basicity

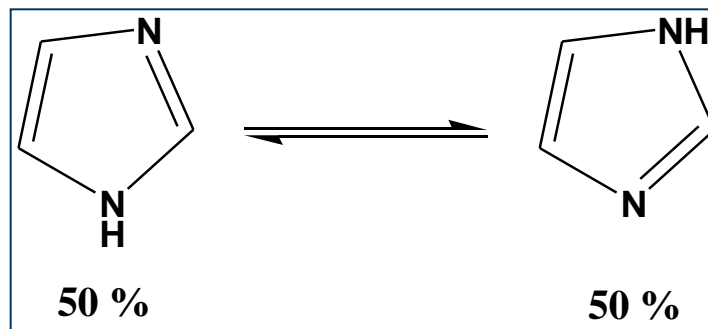
Strong base, due to the greater electron releasing capacity of the two nitrogen's



### Importance of the ring

Building blocks as **Histidine** and **Histamine**

It exist in two tautomeric forms .....

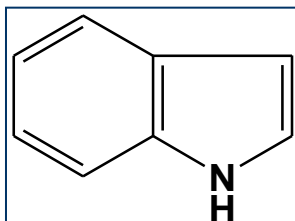




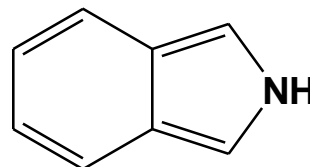
# Hetero-Monocyclic Compounds

## Fused Five Membered Heteroaromatic Rings With one X

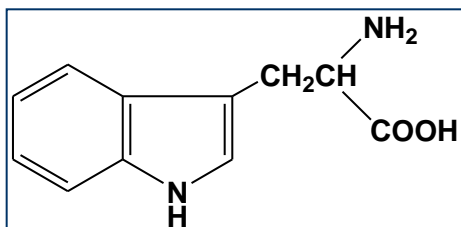
### A. Five-membered Rings with one Heteroatom



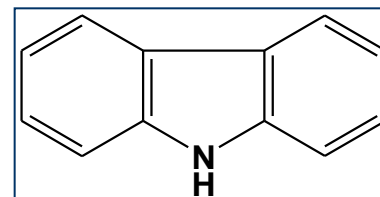
**benzo[b]pyrrole**  
**Indole**



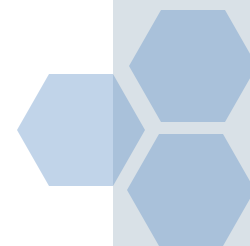
**benzo[c]pyrrole**  
**Isoindole**



**Tryptophan**



**Carbazole**





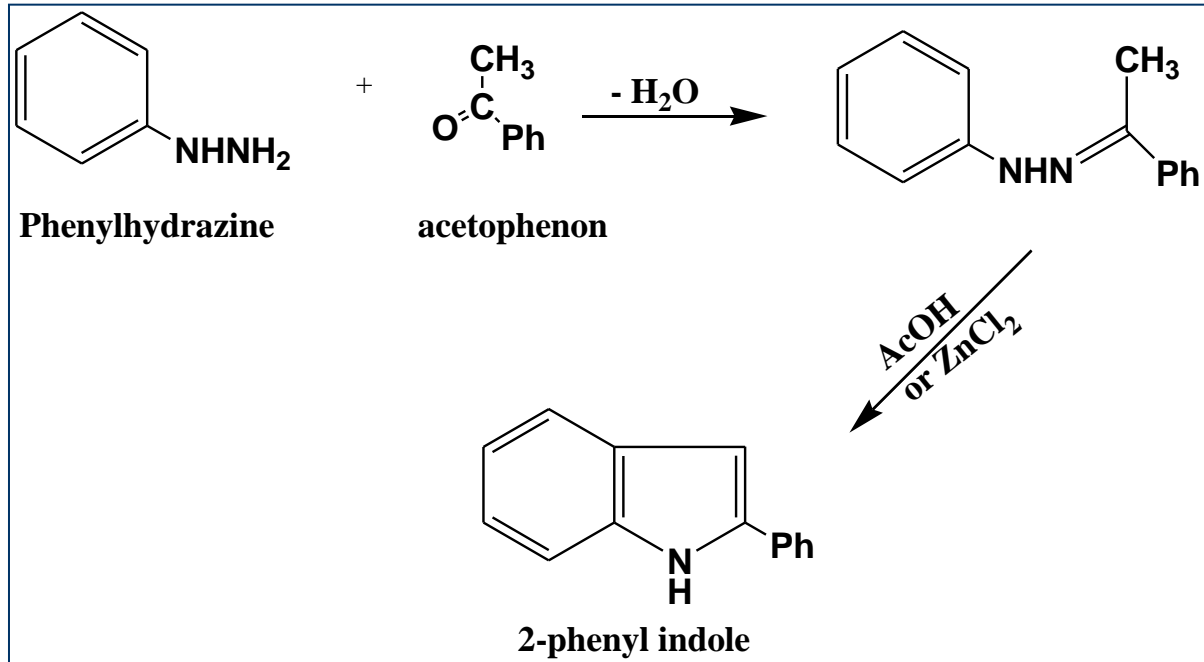


## Fused Five Membered Heteroaromatic Rings With one X

### A. Five-membered Rings with one Heteroatom

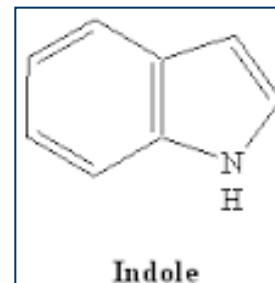
## Indole

### Fischer Synthesis



### Basicity of Indole

Not basic because lone pair is delocalized and contributed to the Aromatic system





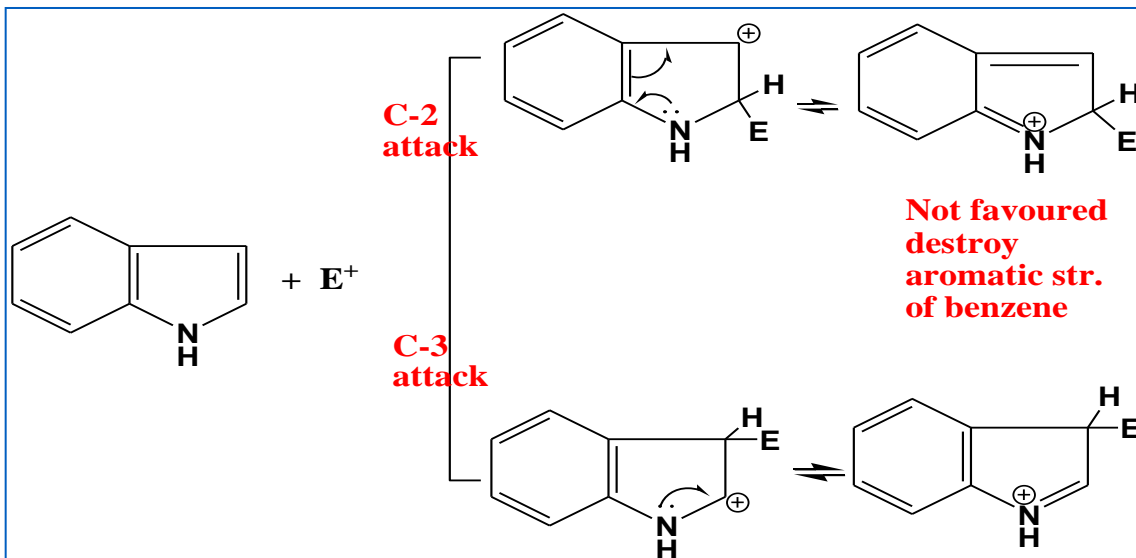
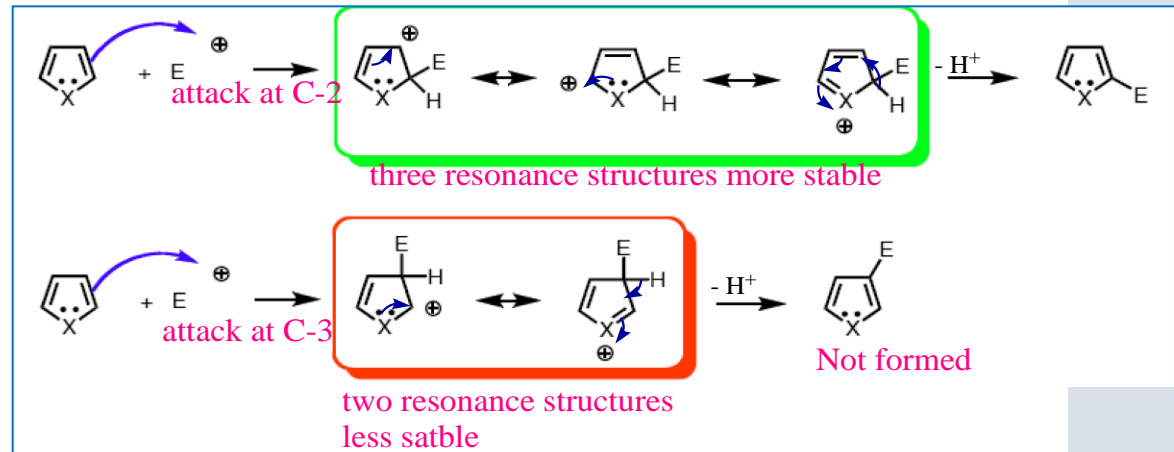
# Hetero-Monocyclic Compounds

## Fused Five Membered Heteroaromatic Rings With one X

### A. Five-membered Rings with one Heteroatom

## Indole

It undergoes Electrophilic Substitution at Position 3

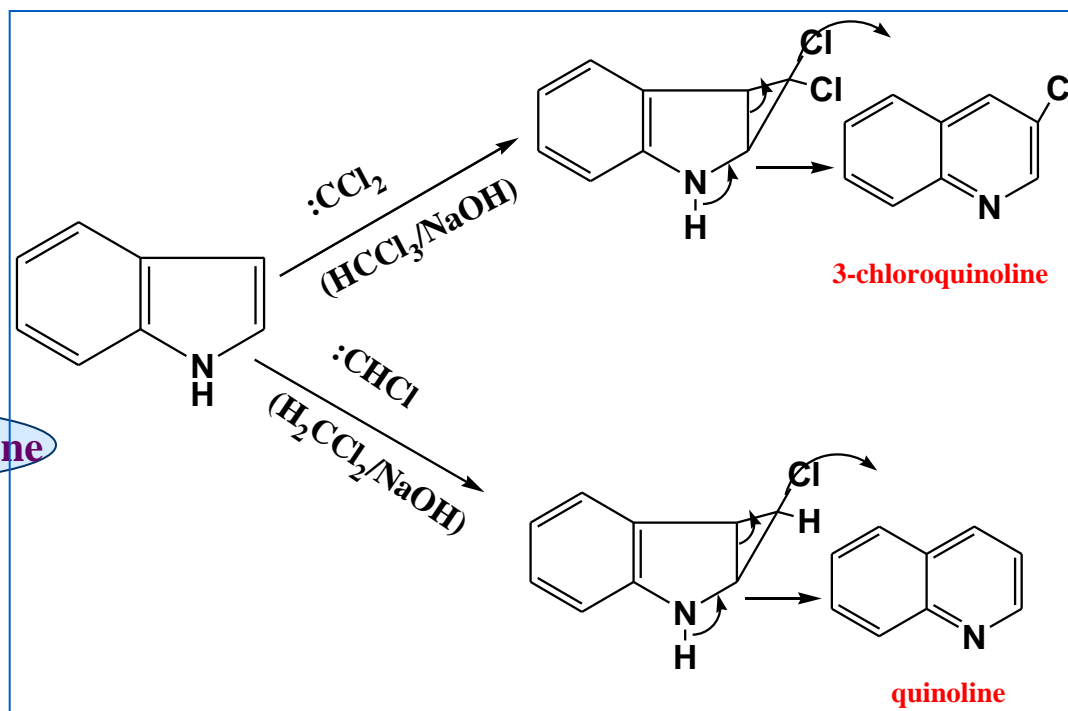
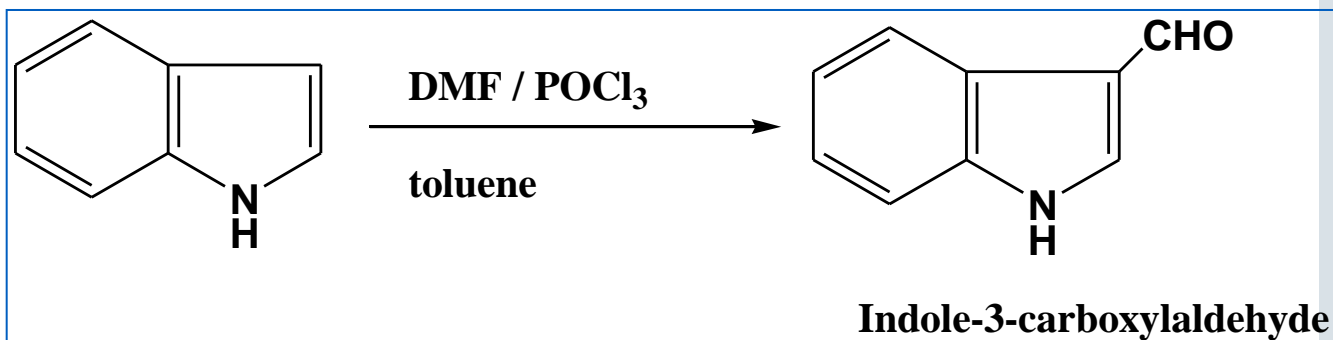




# Hetero-Monocyclic Compounds

## A. Five-membered Rings with one Heteroatom

### Vilsmier Rex



### Reaction with carbene





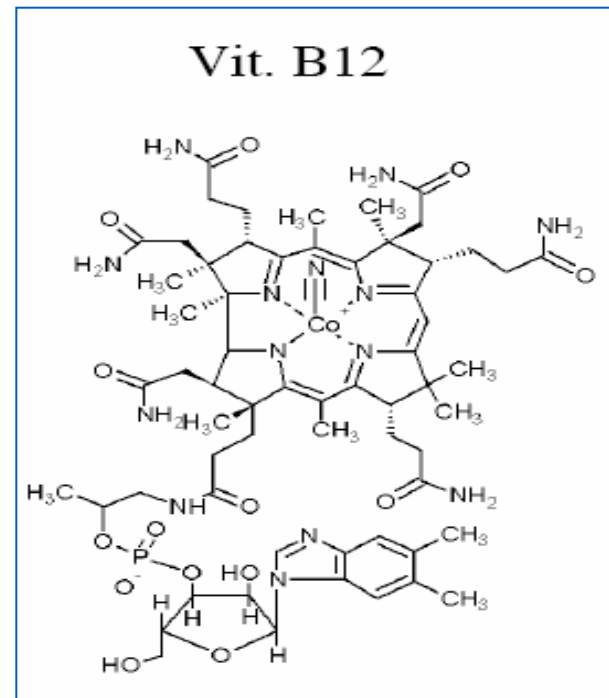
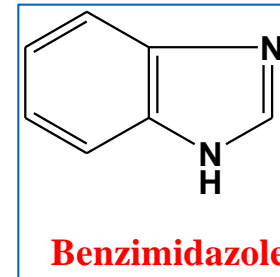
# Hetero-Monocyclic Compounds

## A. Five-membered Rings with one Heteroatom

### Fused Five Membered Hetero aromatic Rings With two X

Benzimidazole ...

In Vit B12 : Commercially as an parasiticide





**Thank you!**

