

# Heterocyclic Compounds

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## Lecture 1

## Heterocyclic Compounds

A cyclic organic compound containing all carbon atoms in ring formation is referred to as a *carbocyclic compound*. If at least one atom other than carbon, forms a part of the ring system then it is designated as a *heterocyclic compound*. Nitrogen, oxygen and sulfur are the most common heteroatoms

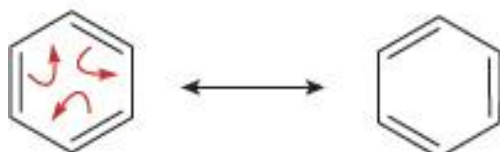
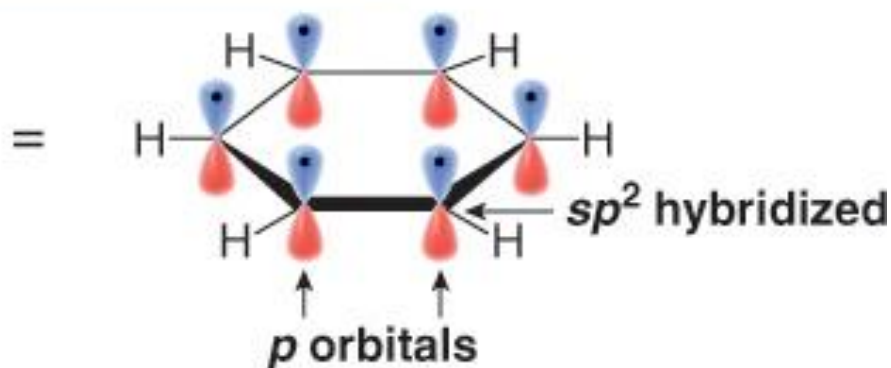
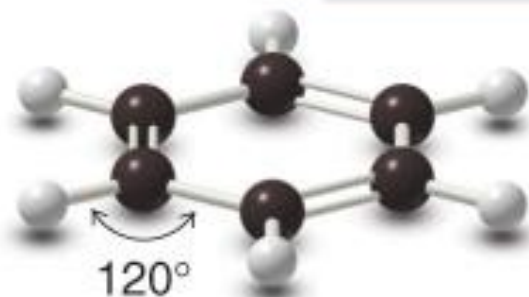
**Heterocyclic compounds may be classified into:**

**1. aliphatic heterocyclic compounds. Are the cyclic analogues of amines, ethers, thioethers, etc. Their properties are particularly influenced by the presence of strain in the ring. These compounds generally consist of small (3- and 4-membered) and common (5 to 7 membered) ring systems.**

2. aromatic heterocyclic compounds. Are those which have a heteroatom in the ring and behave in a manner similar to benzene in some of their properties. Furthermore, these compounds also comply with the general rule proposed by Hückel. *This rule states that aromaticity is obtained in cyclic conjugated and planar systems containing  $(4n + 2) \pi$  electrons .*

- Because each  $\pi$  bond has two electrons, benzene has six  $\pi$  electrons.

Benzene—A planar molecule

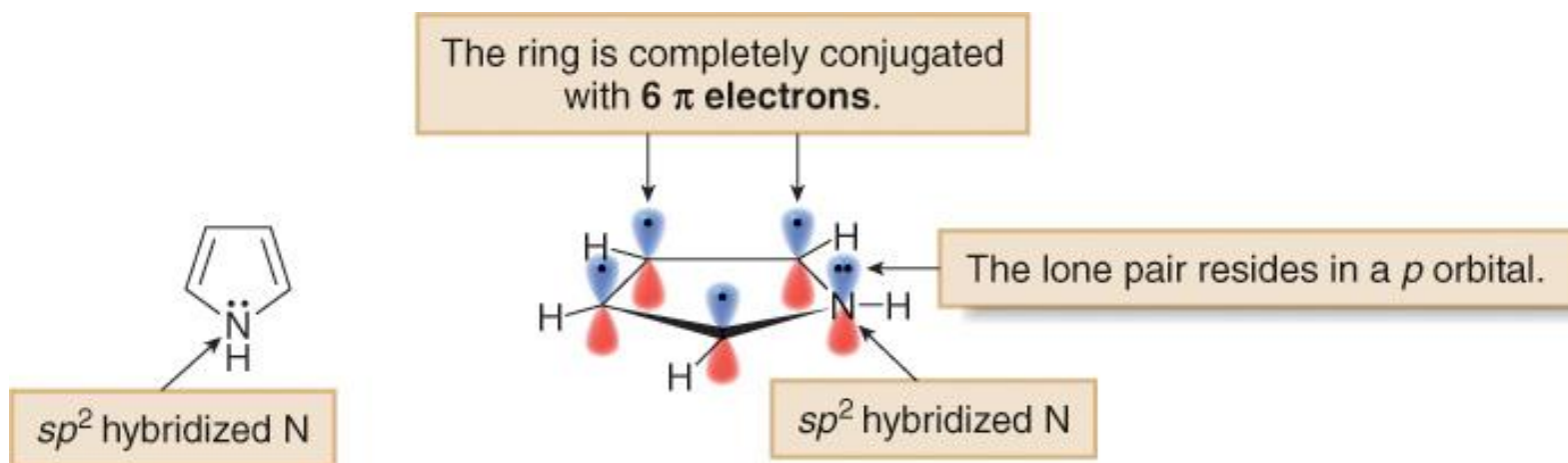


The hybrid



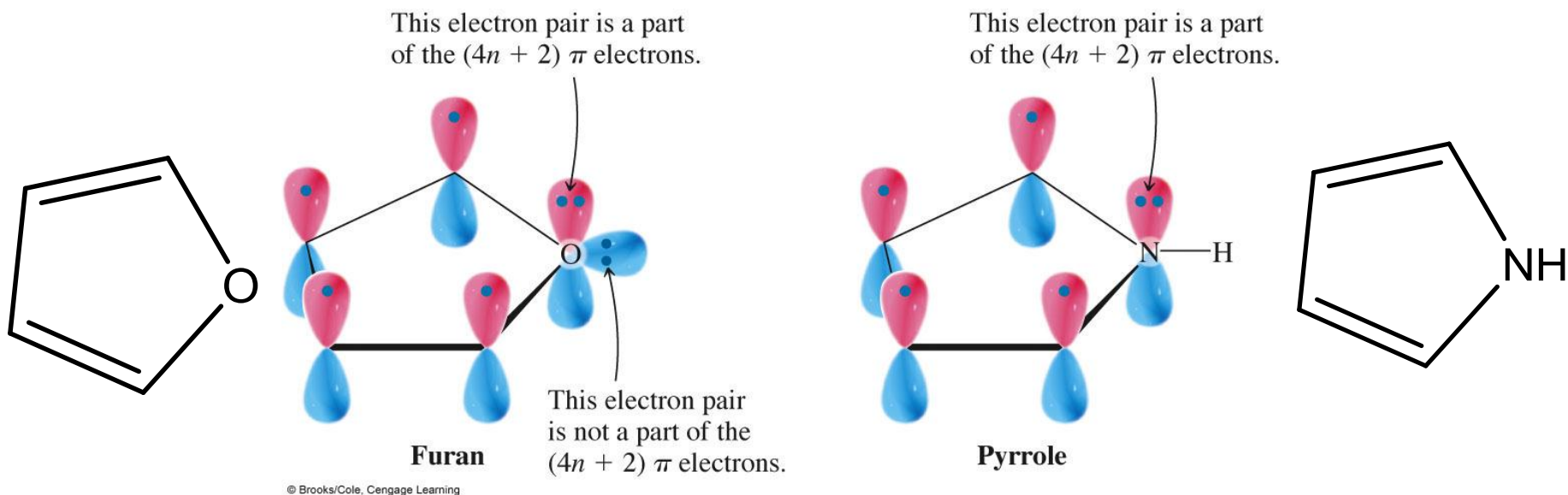
The electrons in the  $\pi$  bonds are **delocalized** around the ring.

- **Pyrrole** is an example of an aromatic heterocycle. It contains a five-membered ring with two  $\pi$  bonds and one nitrogen atom.
- Pyrrole has a  $p$  orbital on every adjacent atom, so it is completely conjugated.
- **Pyrrole** has six  $\pi$  electrons—four from the  $\pi$  bonds and two from the lone pair.



- Pyrrole is cyclic, planar, completely conjugated, and has  $4n + 2$   $\pi$  electrons, so it is aromatic.

The oxygen atom of **furan** is  $sp^2$  hybridized. one unshared pairs of electrons on oxygen lies in an unhybridized  $2p$  orbital and is a part of the aromatic sextet. The other unshared pair lies in an  $sp^2$  hybrid orbital and is not a part of the aromatic system.



**A heterocyclic ring may comprise of three or more atoms which may be saturated or unsaturated. Also the ring may contain more than one hetero atom which may be similar or dissimilar.**



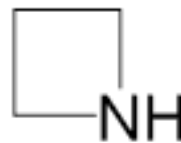
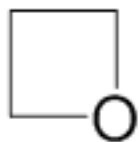
## 1-Three member ring

1-Ethylene oxide      2-Ethylene imine



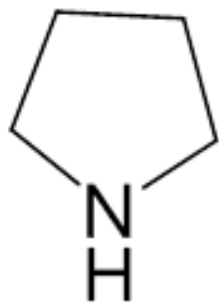
## 2-Four member ring

1-Trimethylene oxide      2-Trimethylene sulfide      3-Trimethylene imine

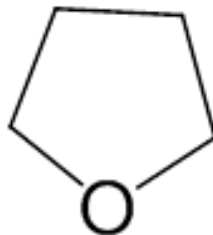


Five member ring

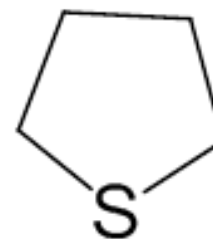
1-Saturated compounds



Pyrrolidine



Tetrahydrofuran



Thiolane

## Unsaturated compounds contain one or two heteroatoms

*common azoles - five-membered aromatic nitrogen heterocycles*



furan



thiophene



pyrrole



imidazole



pyrazole



isoxazole



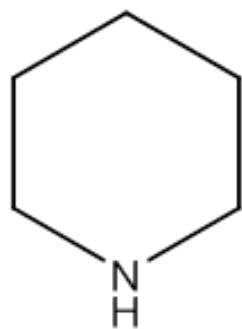
oxazole



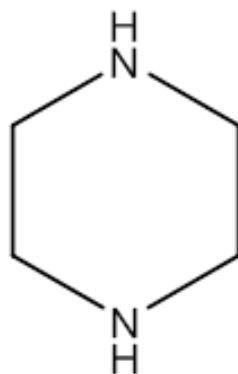
thiazole

Six member compounds

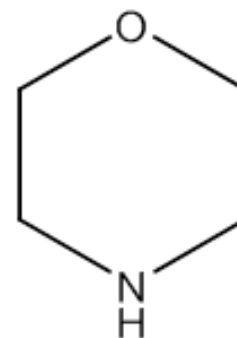
Saturated compounds contain one or two heteroatoms



Piperidine

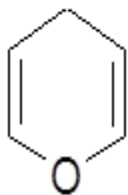
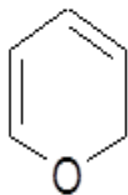


Piprazine



Morpholine

## Unsaturated compounds contain one or two heteroatoms

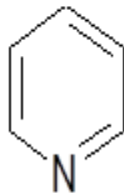


**2H-Pyran**

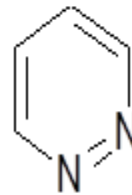
**4H-Pyran**

These are tautomers  
Both are not aromatic

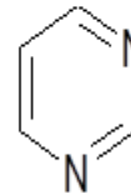
### *Common azines-six-membered aromatic nitrogen heterocycles*



**Pyridine**

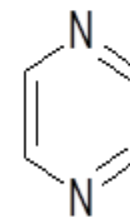


**Pyridazine**



**Pyrimidine**

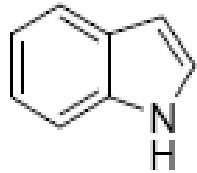
**DNA/RNA bases**



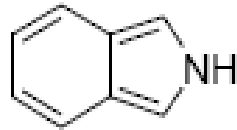
**Pyrazine**

## Fused ring

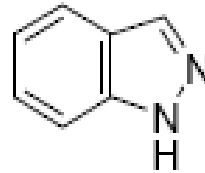
*common ring-fused azoles*



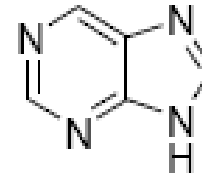
indole  
(found in the amino acid tryptophan)



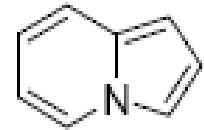
isoindole



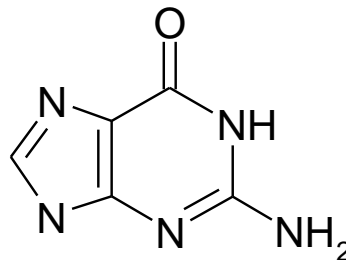
indazole



purine  
(DNA/RNA base)

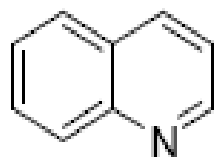


indolizidine

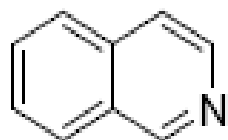


Guanine

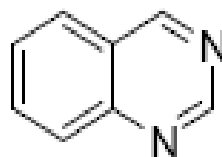
*common ring-fused azines*



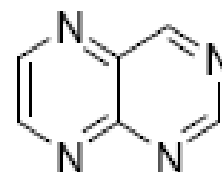
quinoline



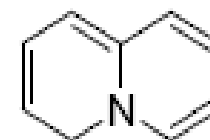
isoquinoline



quinazoline



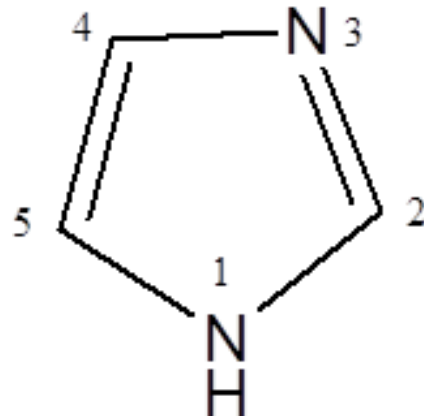
pteridine  
(found in the  
B vitamin  
riboflavin)



quinolizidine

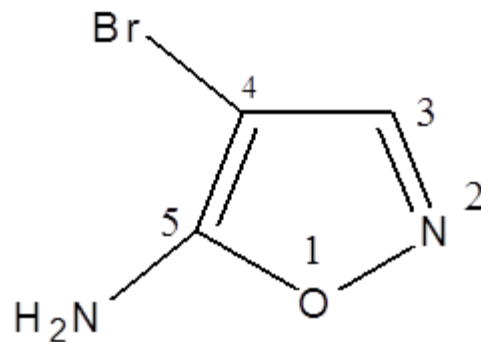
## Numbering of heterocyclic compounds.

1. If there is more than one hetroatom of the same type numbering starts at the saturated one, e.g. imidazole.

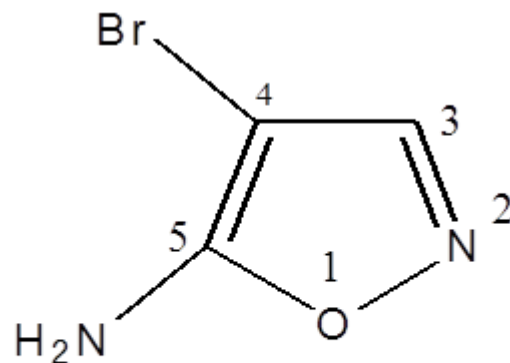




**2. If there is more than one type of the heteroatoms, the ring is numbered starting at the hetroatom of the higher priority (**O>S>N**) and it continues in the direction to give the other hetroatoms the lower numbers as possible.**



**3. If substituents are present, their position should be identified by the number of the atoms bearing them and then they should be listed in alphabetical order.**



5-Amino-4-bromoisoxazole