

# UNIT 1

## INTRODUCTION TO HETEROCYCLIC COMPOUNDS

### Structure

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### 1.1 INTRODUCTION

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This is the first unit of this course and Vol. 1 which is based on Heterocyclic compounds. These compounds are biologically very active and exhibit a large variety of structures. You will come across many such compounds during the study of this volume.

This unit, however, exposes you to the nomenclature of heterocyclic compounds in the very beginning. There are several systems of naming these compounds. We will discuss *trivial* or *common* nomenclature, *Hantzsch-Widman nomenclature*, *fusion nomenclature* and *replacement nomenclature*. It would be interesting to know how a single compound can be named differently under such different systems.

In addition to the nomenclature, you will learn about the spectral characteristics of heterocyclic compounds. The spectral characteristics are important in knowing and understanding the structural aspects of a compound. We will also describe here the reactivity and aromaticity of heterocyclic compounds, in general. The specific structures and reactivities of different types of heterocyclic compounds will be explained in the forthcoming units related to different categories of such compounds.

### Expected Learning Outcomes

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After studying this unit you should be able to:

- ❖ name various systems used for the nomenclature of heterocyclic compounds;

- ❖ state the rules used in different systems and give their appropriate examples;
- ❖ write the systematic name of a given compound from its structure and write the structure of the compound from its systematic name;
- ❖ describe the important spectral characteristics of the heterocyclic compounds;
- ❖ discuss the general aromatic nature of aromatic heterocyclic compounds and their characteristics; and
- ❖ explain the reactivity of heterocyclic compounds.

## 1.2 NOMENCLATURE

The nomenclature of heterocyclic compounds is challenging and is full of variety of names as there is a vast variety in the structures of these compounds. The range includes different sizes of the rings from three membered onwards, including different heteroatoms such as O, N, S, Se, Si, Sn, As etc. and the number of heteroatoms (1,2 or 3 or more) in one or more rings. The saturated and unsaturated nature of rings as well as the aromatic and non-aromatic type of rings, constitute an immense variety in the structures of heterocyclic compounds.

Different systems have been used for the nomenclature of heterocyclic compounds. These are as follows:

- (i) Trivial or Common names
- (ii) Hantzsch-Widman System
- (iii) Fusion Nomenclature
- (iv) Replacement Nomenclature

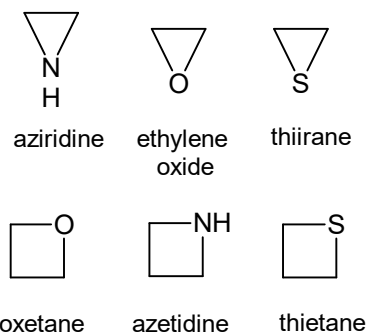
We will now discuss these systems one by one.

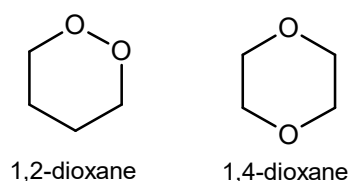
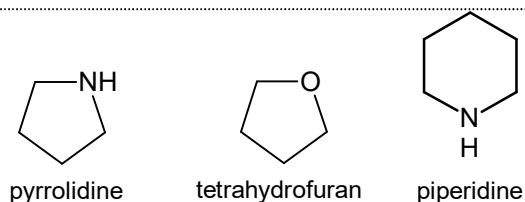
### (i) Trivial or Common Names

The trivial or common names of heterocyclic compounds originated on the basis of their sources or characteristic properties. These names are retained by IUPAC and are given below for some common and simple heterocyclic compounds.

Some examples of different structural types are presented below.

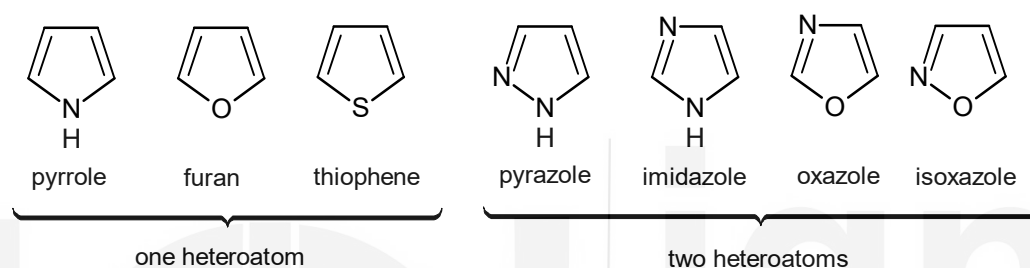
#### Saturated Compounds



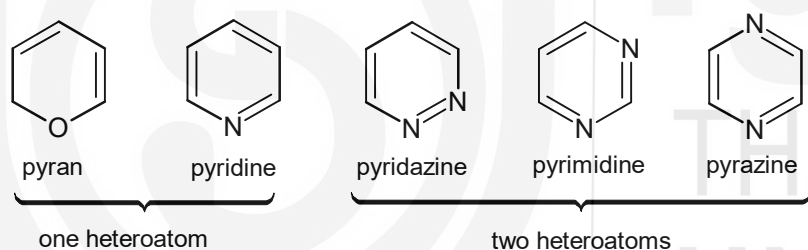


## Aromatic Compounds

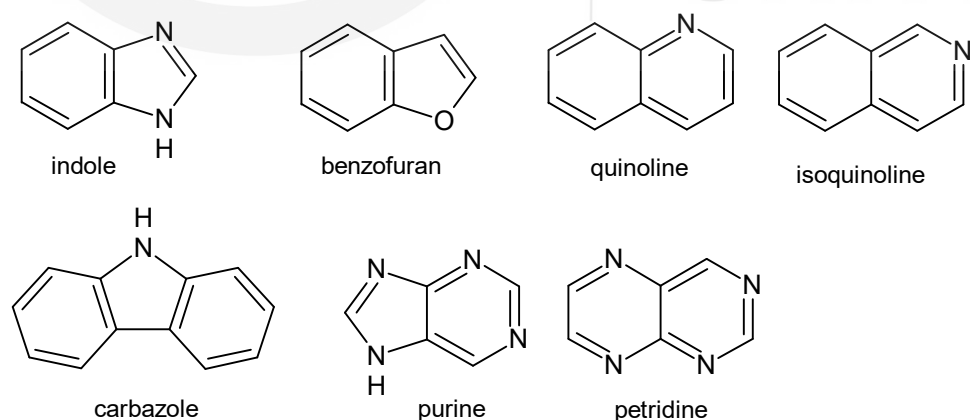
### Five-membered rings



### Six-membered rings



### Condensed or Fused Heterocyclic Compounds

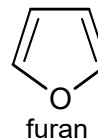
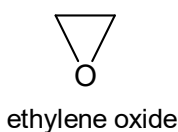


When we move from trivial to systematic nomenclature, the prefixes are used for different heteroatoms as given in Table 1.1.

**Table 1.1: Prefixes for different heteroatoms**

Heteroatom	Oxygen	Sulphur	Selenium	Nitrogen	Phosphorous	Silicon	Boron
Prefix	Oxa	Thia	Selena	Aza	Phospha	Sila	Bora

The increasing priority order of atoms is from right to left of the table. The prefix as given in Table is followed by the carbocyclic name of the compound to give its systematic name.



Thus, ethylene oxide is named as oxacyclopropane and furan is called oxacyclopenta-2,4-diene.

Another systematic nomenclature which is most widely used is **Hantzsch-Widman** system. Let us now study about it in detail.

### (ii) Hantzsch-Widman System

This system uses the prefixes given in Table 1.1 (without final *a*) and the suffix given in Table 1.2 for naming different compounds according to their ring size and the saturated or the unsaturated nature.

**Table 1.2: Suffixes for different heterocyclic compounds**

Ring size	Saturated	Unsaturated
3	<i>irane</i>	<i>irene</i>
4	<i>etane</i>	<i>ete</i>
5	<i>olane</i>	<i>ole</i>
6	<i>inane</i>	<i>ine</i>
7	<i>epane</i>	<i>epine</i>
8	<i>ocane</i>	<i>ocine</i>
9	<i>onane</i>	<i>onine</i>
10	<i>ecane</i>	<i>ecine</i>

Note that the first two letters of the suffix denote the ring size and are common to both saturated and unsaturated type of the compounds.

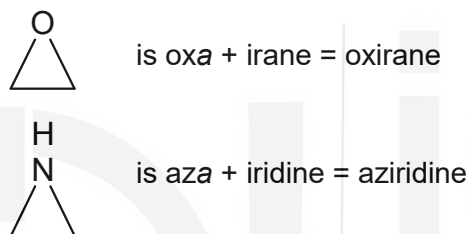
Before, we actually understand the examples of naming the compounds according to the above nomenclature, following details/exceptions are also to be kept in mind.

- (i) The suffix '*irine*' is used for nitrogen containing three-membered unsaturated heterocyclic compounds.
- (ii) For three-, four- and five-membered saturated nitrogen containing heterocyclic compounds *iridine*, *etidine* and *olidine*, respectively are used as *suffixes*.
- (iii) In case of unsaturated heterocyclic compounds, the suffixes given are used for rings having maximum number of non-cumulative possible double bonds. These suffixes are *not* used for partially or completely saturated heterocycles where the 'dihydro'-, 'tetrahydro'- etc. prefixes are used.

- (iv) The terminal 'e' suggested in the rules is optional. For example, in CAS index nomenclature, names for non-nitrogenous heterocycles such as dioxin, dithiin and oxathiin are used.
- (v) The use of suffixes '*etine*' and '*oline*' which are earlier used for four and five membered nitrogen containing compounds is *not* recommended by IUPAC.
- (vi) For pyran, *axine* cannot be used as it is a trivial name of quinolin-8-ol. Similarly, for pyridine, *azine* should not be used as it is class name for compounds having =N–N= group.
- (vii) The IUPAC accepts trivial names for some heterocyclic compounds. These are pyrrole, pyrazole, pyridine, pyrimidine, imidazole etc.

Let us now understand some examples given below to understand the nomenclature based on these rules for different heterocyclic compounds.

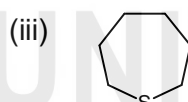
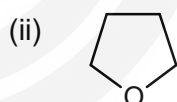
Thus,



Note here that a of oxa and aza is has been omitted in the name of the compound.

### SAQ 1

How will you name the following compounds based on Hantzsch-Widman system?



### SAQ 2

Write the structures of the following compounds:

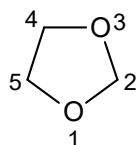
(i) azirine

(ii) azepine

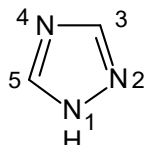
Let us see what happens when more than one heteroatom is present in the ring. Two situations arise here:

**(i) When the same heteroatom is present**

Then, the prefixes *di-*, *tri-*, etc. are used as per the situation. See the examples given below:

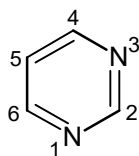


1,3-dioxolane



1,2,4-triazole

And, pyrimidine, having the following structure,

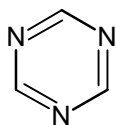


pyrimidine

is named as 1,3-*diazine*.

### SAQ 3

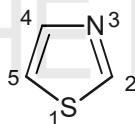
Can you name the following compound?



#### (ii) When the heteroatoms present are different

When different heteroatoms are present in the same ring, as the order of atoms is  $O > S > N > P > As > Si > B$  etc., the name is a *combination of prefixes in the order of above priority order*.

Thus, in the following compound,



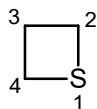
the priority of  $S > N$ . Therefore, we write thia + aza + ole.

Thus, the name of this compound is 1, 3-thiazole.

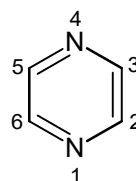
(Note that *a* is written only once in the name).

Let us now study about the *numbering of atoms* in the heterocyclic ring.

The heterocyclic atom is always numbered as 1 when present in a ring in case of compounds having only one heteroatom.



thietane

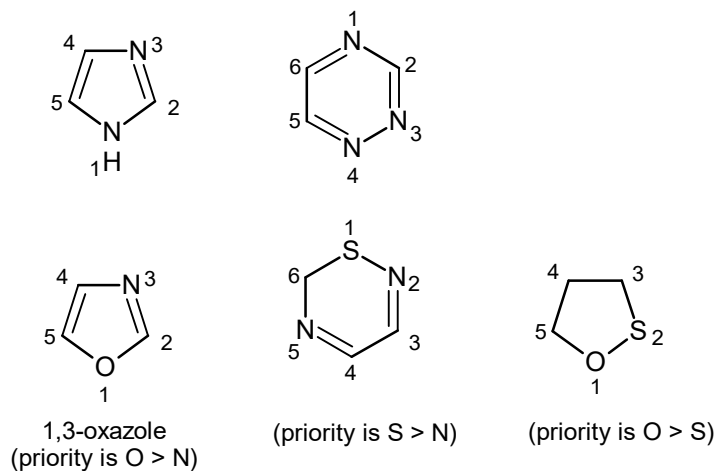


pyridine

But, in case two or more than two heteroatoms are present in the ring, then, they may be *same* or *different*.

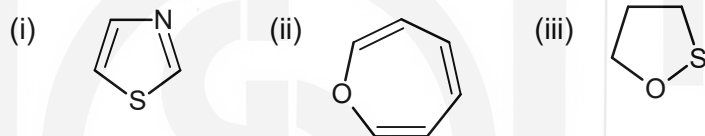
When the heteroatoms are *same*, then the numbering is done in such a way that these atoms get the lowest possible numbers.

But when the atoms are *different*, then first we have to look for which atom has the highest/higher priority. This atom is then given as number 1 and the rest of the heteroatoms are given the lowest possible numbers. The priority order is  $O > S > N \dots$  which was given earlier in Table 1.1. Some examples for both the above types of compounds are given below.

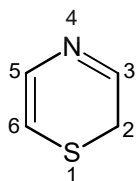


### SAQ 4

Can you number the heteroatoms present in the following compounds?



Let us now explore what happens when a *saturated atom* is present in the heterocyclic ring which contains the maximum number of non-cumulative double bonds. In such a situation, that saturated atom is given the lowest possible number which is indicated by italic *H* along with it and is written before the name of the heterocyclic ring in the beginning of the name of the compound. For example, in the following compound,

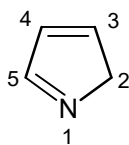
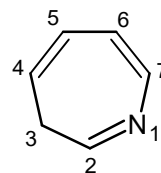


a saturated carbon is present at 2 position, so we indicate this in the beginning of the name as *2H* followed by the numbers given to the heteroatoms S and N, i.e., 1, 4 which are separated by a dash after *2H*.

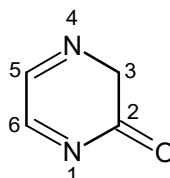
So,  $2H-1,4$ -thia + aza + ine  
 thiazine  
 remove a

which gives *2H-1,4-thiazine* as the name.

Some more examples of saturated carbon atoms in the heterocyclic ring are as follows:

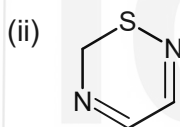
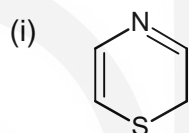
2*H*-pyrrole3*H*-azepine

In case, a carbonyl group is also present in the heterocyclic ring, then *H* is indicated in the bracket after the position of the carbonyl group. For example, the name of the following compound, is, pyrazin-2(3*H*)-one.



### SAQ 5

Give the names of the following compounds:

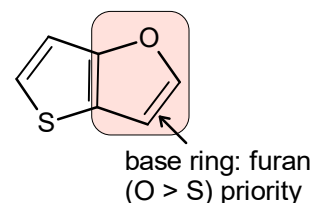
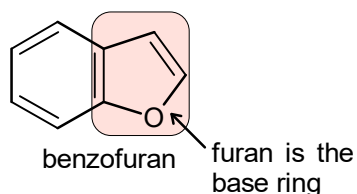


Let us now understand the **Fusion Nomenclature** in detail.

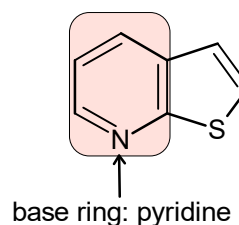
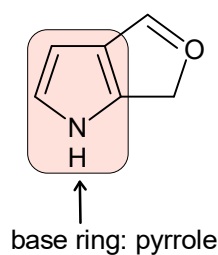
#### (iii) Fusion Nomenclature

It is used for those systems which contain two or more cyclic units joined by a common bond. In these compounds, the heterocyclic ring is chosen as the base ring. Some structures of different heterocyclic compounds are illustrated below.

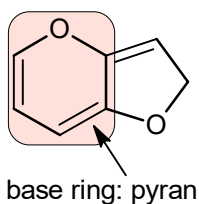
##### (i) Compounds without N



##### (ii) Compounds containing N

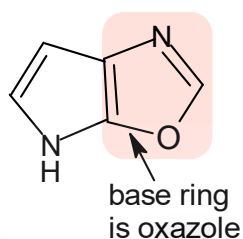


- (iii) In case, the rings of **unequal size** are there which contain the heteroatoms, the ring of larger size is taken as the base ring.



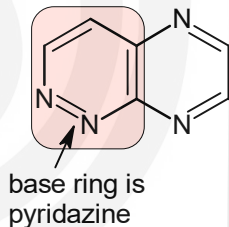
- (iv) When rings of **same size** are present, then the following situations may occur:

- (a) When *number of heteroatoms is different*, the base ring is that ring which contains *more* number of heteroatoms.



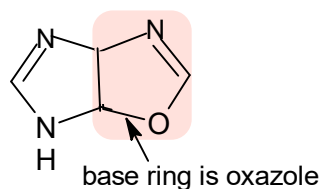
- (b) When *equal number of heteroatoms* are present

- When these atoms are *same*: The ring having the lowest numbers given to the heteroatoms forms the base ring.

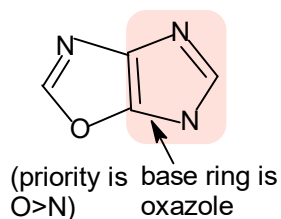


- When these atoms are *different*, then

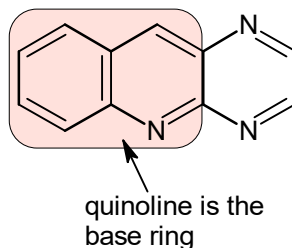
- ring with a greater variety of heteroatoms is the base ring



- ring with the priority order given earlier for heteroatoms is the base ring.



- (v) Bicyclic or polycyclic systems can also be chosen as the base rings and their common or trivial name can be used for this purpose, e.g,



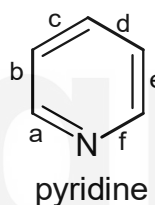
- (vi) The sides of the base ring are labelled as a, b, c,... as shown below:

a – for 1,2-bond

b – for 2,3-bond

c – for 3,4-bond

and so on.



The atoms of the other ring are also numbered as 1,2,3,... etc. according to the lowest possible numbers.

- (vii) The attached ring is indicated as a prefix and its ending *e* is changed to *o*. For example, for benzene attachment, the compound will be named with *benzo* prefix.

Similarly, for pyrazole ring, prefix *pyrazolo* is added before the base ring for naming the compound. Some exceptions exist which are given below:

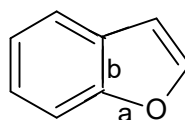
*pyrido-* for pyridine

*furo-* for furan

*quino-* for quinoline

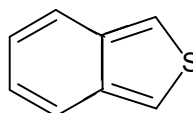
*thieno-* for thiophene

Let us now understand the names with some examples. In the following compound, a benzene ring is attached to the *b* side of the furan base ring,

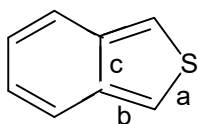


So, the name is *benzo[b]furan*.

Similarly, another compound shown below has a benzene ring attached to thiophene.



But which side of thiophene? Let us see.



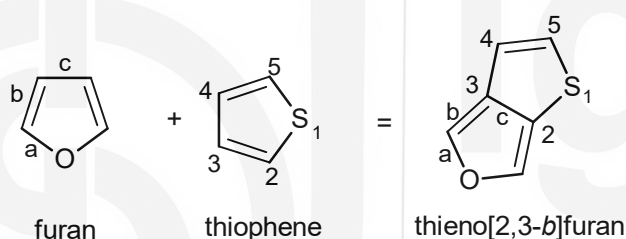
It is *c* side. So, its name will be benzo[*c*]thiophene.

## SAQ 6

Can you now write the structures of the following compounds according to the fusion nomenclature?

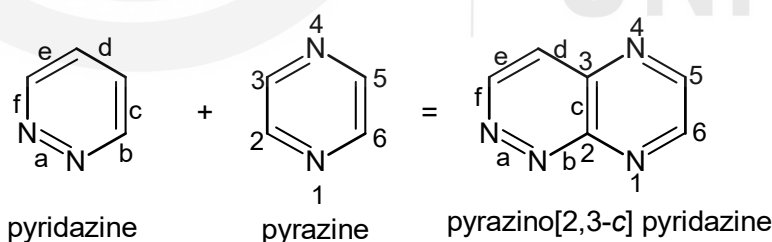
- (i) Benzo[*b*]pyridine      (ii) Benzo[*d*]thiepine

In addition to the side of the base ring, the numbers of attachment of the other ring are also included in the square bracket to clearly indicate the fusion when the other ring attached also contains a hetero atom. For example, if thiophene is attached by its 2,3 position to the furan ring on its *c* side, then we can write its structure and name as follows:



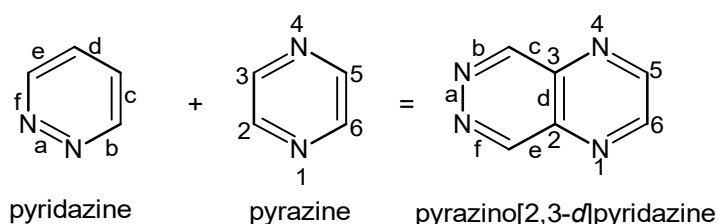
Note that in the square bracket, a *comma* (,) is placed between the numbers and a *dash* separates the side of the other ring.

Let us take the examples of two more compounds and see what the difference in them is.



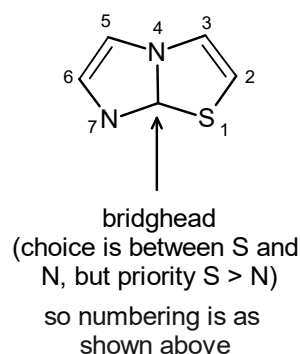
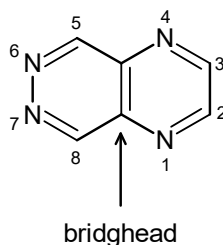
Clearly, here the base ring is pyridazine. If the *c* side of pyridazine is fused with 2, 3 side of pyrazine, we get the above structure.

But, if instead of *c* side, *d* side of the pyridazine is fused with 2, 3-side of pyrazine whose structure would be written as



- (viii) Before we close the discussion on fusion nomenclature, an important aspect of *numbering* the fused compound is to be understood clearly. The heteroatom next to the bridgehead is numbered as 1. Needless to say, that if more than one such options of heteroatoms are there, obviously the order of preference would be as stated earlier ( $O > S > N > P > \dots$ ).

Some examples are as follows:



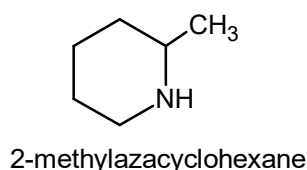
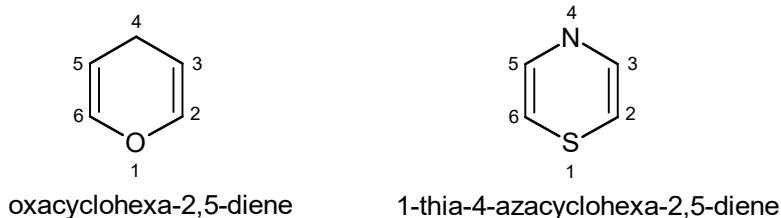
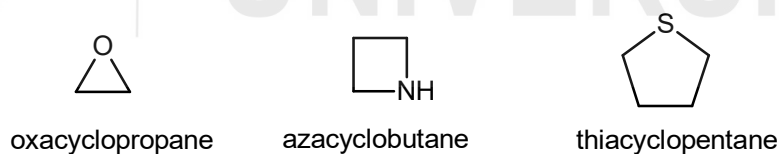
Note here that the heteroatoms present in the rings are numbered but the carbon atoms are *not*.

Let us next study another system of nomenclature called *replacement* nomenclature.

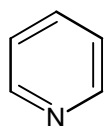
#### (iv) Replacement Nomenclature

This system is based on name of the related carbocyclic compound to which the appropriate prefix for the heteroatoms such as aza, oxa, thia etc. are prefixed. Here also, the heteroatom is given the lowest possible number.

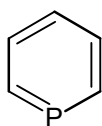
Some examples are given below.



In case, all the three double bonds similar to benzene are present, the compound is named according to the replacement of CH of benzene. Thus,

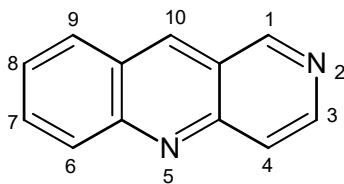


is azabenzene and



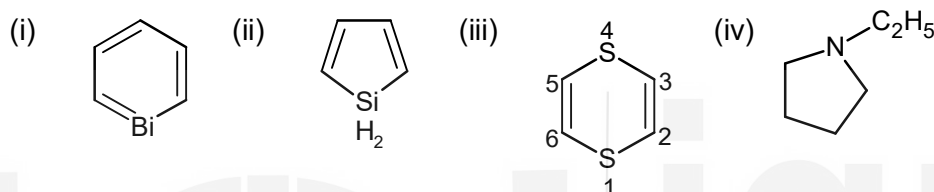
is phosphabenzene.

Similarly, 2, 5-diazaanthracene has the following structure:



## SAQ 7

Write the names of the following heterocyclic compounds according to the replacement nomenclature.



Although fused heterocycles and spiro compounds can be named according to this system; a detailed discussion of same is beyond the scope of this unit.

After a detailed study of the nomenclature of heterocyclic compounds, we will now focus our attention on the spectral characteristics, reactivity and aromaticity of these compounds in the remaining part of this unit. So, let us begin with the spectral characteristics.

## 1.3 SPECTRAL CHARACTERISTICS OF HETEROCYCLIC COMPOUNDS

The spectral signals in UV, IR and NMR can be studied to know the structure and nature of heterocyclic compounds. Let us briefly analyse different spectral signals.

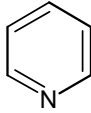
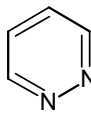
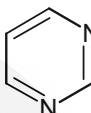
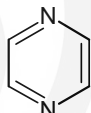
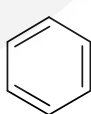
### (i) UV spectra of heterocyclic compounds

In the UV spectrum, the different bands obtained are correlated with the electronic transitions qualitatively. The comparisons are done with their carbocyclic analogs to get some idea of the aromatic nature.

The unsubstituted system such as furan shows a band in the UV spectrum at about 200 nm whereas that of pyridazine shows the band at 346 nm.

The monocyclic azines exhibits two bands in their UV spectra: one between 240-260 nm due to  $\pi \rightarrow \pi^*$  transitions and the other at longer wave length occurs between 270-340 nm due to  $n \rightarrow \pi^*$ . The transitions that occur at longer wave length are solvent dependent and are absent in the corresponding carbocyclic systems.

Table 1:3 UV Spectral data of azaheterocycles

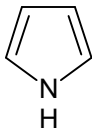


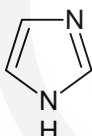
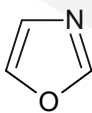
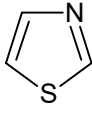
Compound	$\pi \rightarrow \pi^*$ $\lambda_{\max}$ (nm)	Bands $\log \epsilon$	$n \rightarrow \pi^*$ $\lambda_{\max}$ (nm)	Bands $\log \epsilon$
 pyridine	251	3.30	270	2.65
 pyridazine	246	3.11	340	2.50
 pyrimidine	243	3.31	298	2.51
 pyrazine	260	3.75	328	3.02
 benzene	254	2.04	–	–

Protonation of the nitrogen atom of the ring eliminates  $n \rightarrow \pi^*$  band from the spectrum but increases the intensity of the  $\pi \rightarrow \pi^*$  band without changing its position. Bicyclic systems such as isoquinoline exhibits more complex structure in their UV spectra as the  $n \rightarrow \pi^*$  and  $\pi \rightarrow \pi^*$  bands overlap.

For pyridine, the  $n \rightarrow \pi^*$  band is observed only in hexane as the solvent because in alcohol it shifts towards shorter wavelength and is masked by the  $\pi \rightarrow \pi^*$  band.

The UV spectra of five membered heteroaromatic systems are simple and show only a single medium to strong band at low wavelength. It also does not have any fine structure.

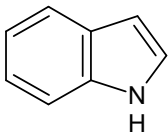
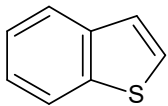
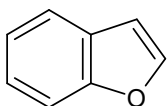
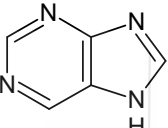
**Table 1.4: UV spectral data of Monocyclic Five-membered Heterocyclic Compounds**

Compound	$\pi \rightarrow \pi^*$ $\lambda_{\max}$ (nm)	$n \rightarrow \pi^*$ $\lambda_{\max}$ (nm)	$\epsilon/\log \epsilon$	$\epsilon'/\log \epsilon'$
 Pyrrole	210	–	5100/4.20	–
 Furan	200	–	10000/3.90	–
 Thiophene	235	–	4300/3.87	–
 Imidazole	206	–	3500	–
 Oxazole	205	–	3900	–
 Thiazole	200	239	10000	3400

The  $n \rightarrow \pi^*$  transition is not observed in them because of large s-character and the smaller ring size.

UV spectra of bicyclic heterocyclic compounds having five-membered heterocyclic ring are complex and normally show three or more bands.

**Table 1.5: UV Spectra of Bicyclic compounds with Five-membered Heterocyclic rings**

Heterocycle	$\lambda_{\max}$ (nm)	$\lambda_{\max}$ (nm)	$\lambda_{\max}$ (nm)
 Indole	288	261	213
 Benzo[b]thiophene	288	257	227
 Benzo[b]furan	281	–	244
 Purine	263	–	7950

In case of benzofused systems, the  $\lambda_{\max}$  values shift towards higher wavelengths. For example, benzo[b] thiophene absorbed at 288 (2000), 257 (5500) and 227 (28000) as compared to thiophene which absorbs at 235 nm (4300).

Benzo[b]heterocycles absorb at lower wavelength as compared to benzo[c]heterocycles indicating lower aromaticity of benzo[b] compounds. Thus, benzo[c] thiophene shows  $\pi \rightarrow \pi^*$  transitions in the region 445-465 nm.

### (ii) Infra-red spectra of heterocyclic compounds

You already know that the vibrational frequency of a bond is given by the following expression:

$$\bar{\nu} = \frac{1}{2\pi c} \sqrt{\frac{k}{\mu}}$$

where  $k$  is the force constant and is related to the bond strength and  $\mu$  is the reduced mass. Also

$$\mu = \frac{m_1 \times m_2}{m_1 + m_2}$$

where  $m_1$  and  $m_2$  are the masses of the two atoms involved in the bond formation. Here,  $c$  is the velocity of light.

Thus, the stronger the bond between two atoms, more will be its vibrational frequency. The bond strengths in turn, are related to the bond lengths. Hence, if the vibrational frequency is more, more strong (or partial double bond) character is indicated. In other words, we can say that the decrease in the vibrational frequency indicates reduction in the bond order. Hence, partial double bond character or conjugation and delocalisation can be understood by using the change in the vibrational frequency.

The detailed study of IR spectra of individual compounds is beyond the scope of this course and you will study more about them at higher levels.

As the vibrational frequency of a particular bond depends on the structural features of the molecule, the electronic effects as well as hydrogen bonding, the exact IR spectrum of an individual molecule is unique. Nevertheless, we can correlate the IR vibrational frequencies with the structural features present in the molecule and correlate the changes in the vibrational frequencies of different molecules on the basis of the electronic effects operating in them.

If we analyse the vibrational frequencies in the IR spectrum of benzene and six-membered heterocyclic compounds pyridine and pyrimidine, we find that they occur at similar frequencies.

**Table 1.6: IR spectral data for benzene, pyridine and pyrimidine**

	Benzene (monosubstituted)	Pyridine	Pyrimidine
Ring stretching frequencies	1610-1600	1610-1595	1600-1545
	1590-1580	1570-1550	1575-1540
	1520-1417	1520-1480	1510-1410
	1460-1440	1420-1410	1470-1330

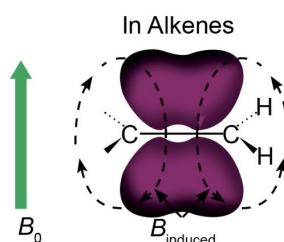
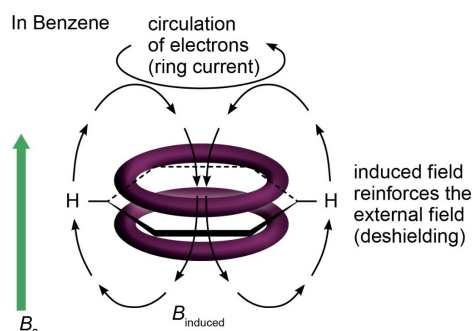
The aromatic C–H saturated stretching frequencies appear above  $3000\text{ cm}^{-1}$ . The C-H bending vibrations are observed at  $1300\text{--}1000\text{ cm}^{-1}$  (in plane bending) and  $700\text{--}1000\text{ cm}^{-1}$  (out of plane bending).

### NMR Spectra of Heterocyclic Compounds

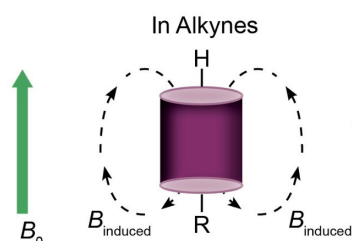
You have studied in your earlier classes that delocalisation of the  $\pi$  electrons in aromatic compounds results in the deshielding of the proton leading to the appearance of its signal in the low field i.e., around  $\delta 7.24$  ppm for benzene, in the NMR spectra.

When the magnetic field is applied for recording NMR spectrum, the induced magnetic field due to ring current, strengthens the applied field around the protons outside the ring making them resonate at high  $\delta$  values. On the other hand, the protons lying in the region of the low electron density appear at high field with low  $\delta$  value.

The ring current effects increase with the size of the ring and are higher for six-membered ring than five-membered ring.



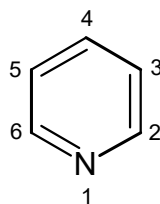
The induced magnetic field  $B_{\text{induced}}$  reinforces the external magnetic field,  $B_0$  in the vicinity of protons. Hence, the protons are deshielding and appear downfield at 4.5-6 ppm.



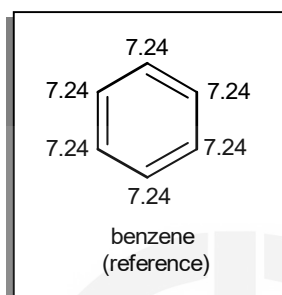
The induced magnetic field  $B_{\text{induced}}$  opposes the external magnetic field. this causes shielding of proton and hence, the appear upfield at  $\sim 2.5$  ppm.

The chemical shift value is related to the electron density of the ring carbon to which hydrogen is attached.

If a nitrogen atom is present as in case of pyridine,  $\alpha$ -protons are deshielded and absorb at lower field. The  $\gamma$ -protons also experience the deshielding but lesser than  $\alpha$ -protons. However the  $\beta$ -protons appear slightly upfield.



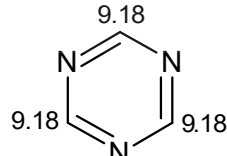
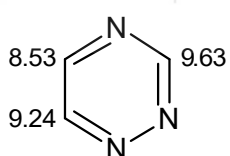
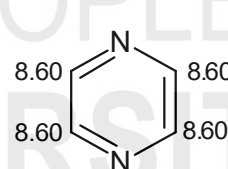
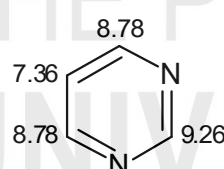
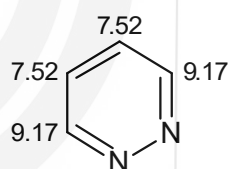
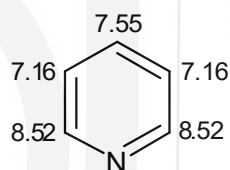
Thus, H2 and H6 protons appear at  $\delta$  8.52 ppm and H4 appears at  $\delta$  7.55 ppm. H3 and H5 protons absorb at  $\delta$  7.16 which is slightly upfield.



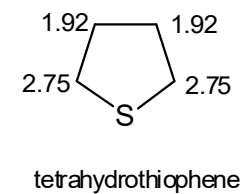
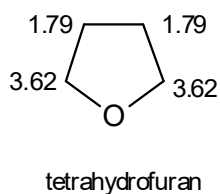
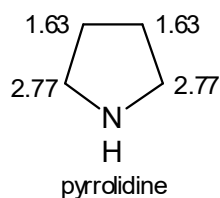
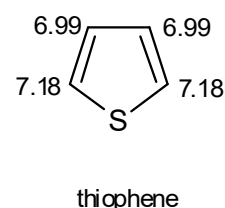
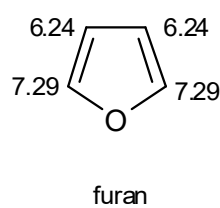
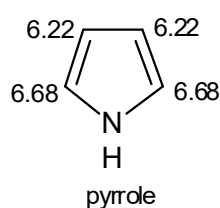
With the increase in the number of nitrogen atoms in the ring, the effect becomes stronger.

Some examples of six-membered heterocyclic compounds along with the chemical shift values (in  $\delta$  units) of different protons at different positions of the ring are given below:

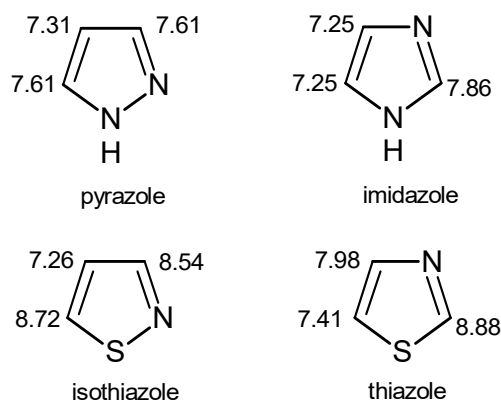
### Six-membered Heterocyclic Compounds



### Five-membered Compounds with One Heteroatom



## Five-membered Heterocycles with Two Heteroatoms

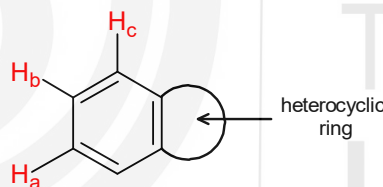


You can see that the signal for the  $\alpha$ -proton next to the heteroatom appears downfield at high  $\delta$  values. Also, the higher the electronegativity of the heteroatom, the lower would be chemical shift of the  $\beta$ -proton (pyrrole is an exception to this).

If you compare thiazole and imidazole, the protons appear relatively downfield in thiazole.

## 1.4 AROMATICITY AND REACTIVITY

The aromaticity of five-membered and six-membered heterocyclic compounds can be judged by vicinal coupling constants. Consider the following heterocyclic compound in which a benzene ring is fused with the heterocyclic ring.

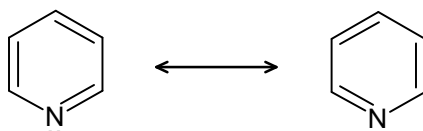


If the ratio of the *ortho* coupling constants  $J_{(\text{ratio})} = J_{ab} : J_{bc} = 1$ , for the complete delocalisation and if this value is 0.55 then this is the reference value for localisation. These constants are affected by ring angles and inductive effects and effects of the heteroatoms.

This ratio is qualitatively co-related with Resonance Energy Per  $\pi$  Electron (REPE) to know about cyclic delocalisation in heteroaromatic system. There is a linear relationship between  $J_{(\text{ratio})}$  and REPE. This relationship indicates delocalisation of electrons.

You are familiar with the terms *aromatic* and *non-aromatic* from your earlier classes. Benzene is aromatic as it is *planar*, *conjugated*, *cyclic* and obeys *Huckel's rule*. Similarly, we used to interpret for other carbocyclic systems. But, let us see what happens when a heteroatom is present in the ring.

In pyridine, the following resonance structures are possible

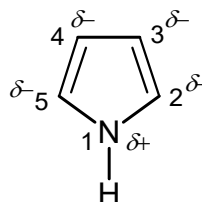


The pyridine, all C atoms and N atom, are  $sp^2$  hybridised.

Thus, a nucleophilic attack is possible at C-2 and an electrophilic attack is possible at C-3 in pyridine.

The C–N bonds are shorter and a lone pair of electrons makes it basic. Hence, N bears a partial negative charge whereas carbon atoms 2, 4 and 6 are electron deficient. The positions 3 and 5 are neutral. Thus, electron density at ring carbons is less, so such systems are called  $\pi$ -deficient. Also, as the number of N atoms increase, in the ring the energies of HOMOs of such systems also decrease.

Similarly, in case of pyrrole, the following structure emerges from various canonical forms.



The attack of an electrophile, thus, takes place preferably at 3 position as compared to 2. Thus, it is a  $\pi$ -excessive system.

Many such  $\pi$ -excessive systems can be obtained by replacing one or more of CH group in pyrrole by O or S. Similar to pyrrole, all these are aromatic as the lone pair of the heteroatom forms a part of the ring. The additional N atoms, however, makes the respective system less electron-rich.

Normally, the heterocyclic systems can be regarded as pyrrole like or pyridine like.

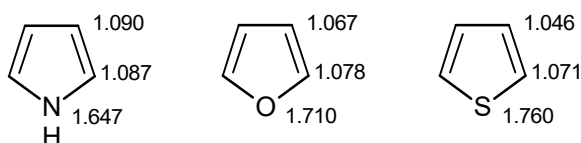
In furan, oxygen is highly electronegative and it holds the electron pair tightly than N in pyrrole.

However, in thiophene, the S is less electronegative. The order of aromaticity of these compounds is



and their resonance energies are 121      88      67      (in kJ mol<sup>-1</sup>)

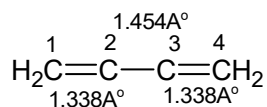
The electron densities at respective atoms are as shown below:



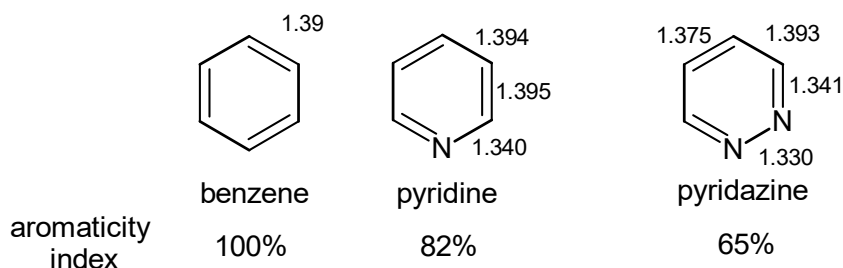
Let us now consider aromaticity in little more detail. There are certain criteria such as bond lengths (structural aspect), ring current (electromagnetic aspects) and chemical behavior (electrophilic substitution reactions) to be examined.

### (i) Bond lengths

You already know that in benzene all C–C bond lengths (1.39 Å) are equal and their value ranges between C–C single bonds and C=C double bonds. However, in conjugated polyenes, such as butadiene, which are non-aromatic in nature, the bond length values alternate between C<sub>1</sub>–C<sub>2</sub> and C<sub>2</sub>–C<sub>3</sub> bonds.

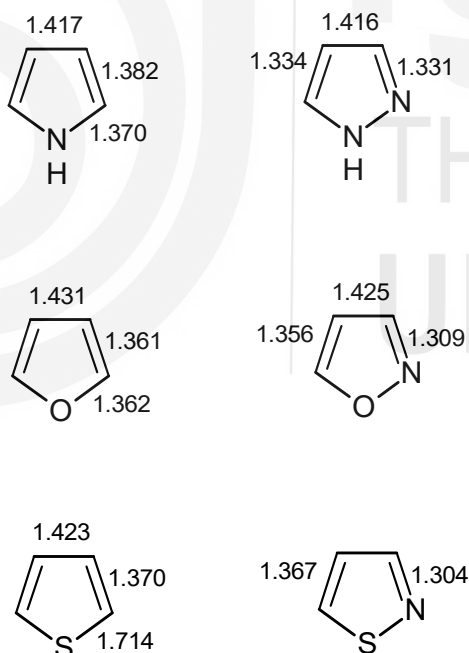


Thus, bond lengths in non-aromatic and aromatic compounds give an indication about the nature of the compound. The bond lengths of some heterocyclic compounds and their percentage aromaticity indices are given below.



The values of bond lengths in pyridine and pyridazine are similar to that of benzene and do not show much alternation. So, we conclude these two compounds to be *aromatic*.

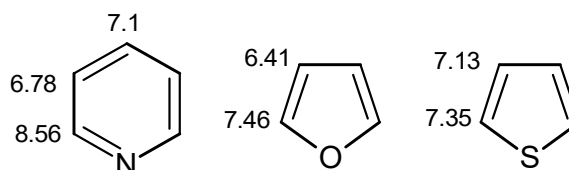
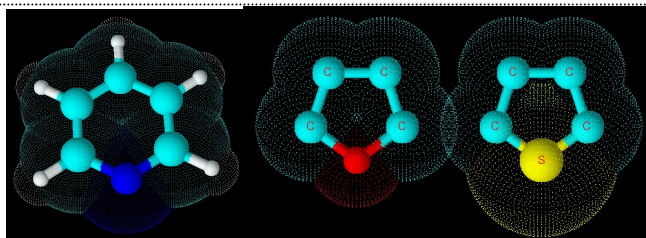
However, in case of five membered heterocyclic compounds, bond localisation are observed and since different heteroatoms are involved, no clear cut inferences can be drawn.



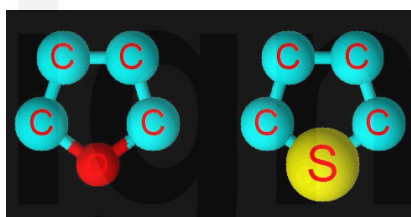
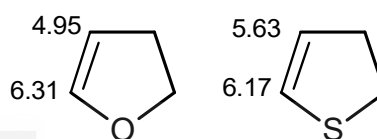
You can see that delocalisation is lesser in five membered rings as compared to six membered heterocycles.

## (ii) Ring Current Effects

You have studied that diamagnetic ring current causes shielding or deshielding of protons lying in different areas which leads to the upfield or downfield positions of the signals in the  $^1\text{H}$ -NMR spectrum. The aromatic protons typically appear downfield. The chemical shift values of some compounds are shown below:



These chemical shift values indicate aromatic nature. On the other hand, the following compounds are non-aromatic as indicated by their chemical shift ( $\delta$ ) values.



It is worth mentioning here that resonance energy per  $\pi$ -electron (REPE) can be correlated to the aromaticity. The values for some heterocyclic compounds are shown below:

**Table 1.7: REPE of some heterocyclic compounds**

Compound	REPE
Benzene	0.065
Pyridine	0.058
Pyrimidine	0.49
Pyrazine	0.49
Quinoline	0.052
Isoquinoline	0.051
Imidazole	0.042
Pyrrole	0.039
Furan	0.007
Thiophene	0.032

### (iii) Chemical behavior of Reactivity

Aromatic compounds generally undergo substitution reactions and retain the aromatic ring. The reactivities of various compounds are different towards different reagents about which you will study in their different reactions in the forthcoming units.

The reactivity of a compound is reflected by the difference in energy between its ground state and the transition state. The electronic features also govern the reactivity towards different reagents and selectivities for specific positions of the ring are exhibited. The energies of the different resonance intermediates resulting in a particular reaction are compared and the final position of favoured attack of the electrophile is arrived at/explained as obtained in the experimental product.

We would keep in mind the above discussed aspects and explore the nature of compounds, their structural aspects, reactions and reactivities for different classes of heterocyclic compounds in the rest of the units of this volume.

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### SAQ 8

Write the intermediates of protonation of pyrrole at different positions.

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### SAQ 9

Which position is most likely to be protonated in pyrrole? Why?

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## 1.5 SUMMARY

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In this unit, you learnt that

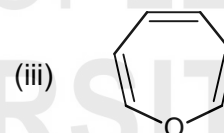
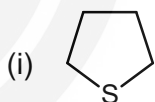
- The heterocyclic compounds exhibit a large variety of structures and biological activities.
- They can be both aromatic and non-aromatic.
- They can be named according to different systems of nomenclature.
- They have trivial names which are accepted by IUPAC and are still used commonly.
- The table below summarises various prefixes for different categories of heterocyclic compounds.

Ring size	Saturated	Unsaturated	Saturated (with nitrogen)
3	-irane	-Irine	-iridine
4	-etane	-ete	-etidine
5	-olane	-ole	-olidine
6	-inane	-ine	
7	-epane	-epine	
8	-ocane	-ocine	
9	-onane	-onine	
10	-ecane	-ecine	

- Heterocyclic compounds exhibit characteristic spectral signals in UV, IR and NMR spectra.
- The  $\pi \rightarrow \pi^*$  transitions depend upon the nature of solvent used. However, on protonation, the  $n \rightarrow \pi^*$  transition is not observed as the lone pair of electrons is not available. But, protonation increases the intensity of the  $\pi \rightarrow \pi^*$  bond.
- The UV spectra of bicyclic systems (similar to naphthalene) are complex and in these spectra,  $\pi \rightarrow \pi^*$  and  $n \rightarrow \pi^*$  transitions overlap. Here, the  $\pi \rightarrow \pi^*$  transitions being stronger over the  $n \rightarrow \pi^*$  transitions.
- The vibrational bands in IR spectra are related to bond strengths and therefore, to bond lengths. The vibrational frequency of a bond increases if it acquires a double bond character by conjugation and *vice-versa*. Also, the conjugation and delocalisation of electrons reflects on the aromatic nature of the compound.
- The chemical shift value is related to the electron density of the ring carbon to which hydrogen is attached.
- Normally, the heterocyclic systems can be regarded as pyrrole like or pyridine like.
- Heterocyclic compounds show interesting and important chemical reactions.

## 1.6 TERMINAL QUESTIONS

1. Give the name of the following compounds:

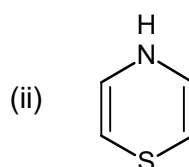
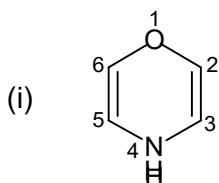


2. Write the structures of the following compounds:

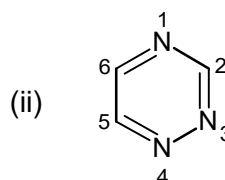
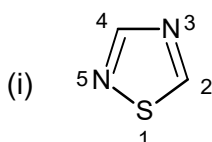
(i) thiocane

(ii) 2,3-dihydroazete

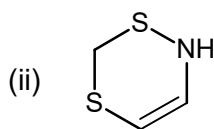
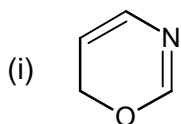
3. Can you give the names of the following compounds?



4. Why are the following ways of numbering the heterocyclic compounds incorrect?



5. Name the following compounds:



6. Write the structure of the following compounds:

(i) 4*H*-1,4-Thiazine (ii) 1,4-thiazepine (iii) 4*H*-thiopyran

7. Fill in the blanks in the following

(i) (a) oxa + \_\_\_\_\_ = (b) \_\_\_\_\_ + irane = (c) aza + iridine =



\_\_\_\_\_

(ii) (a) \_\_\_\_\_ + etane = (b) thia + \_\_\_\_\_ = (c) aza + \_\_\_\_\_ =

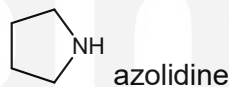
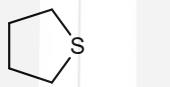


\_\_\_\_\_ thietane

\_\_\_\_\_

(iii) (a) oxa + olane = (b) \_\_\_\_\_ + olane = (c) \_\_\_\_\_ + \_\_\_\_\_ =

\_\_\_\_\_



8. Write the structures of the following compounds:

(i) Pyridine (ii) 1,4-Dihydropyridine (iii) 2,3-Dihydropyridine

9. Write the structures of the following compounds:

(i) Pyrrole or 1*H*-pyrrole (ii) 2*H*-pyrrole (iii) 3*H*-pyrrole

10. Can you write the names of the following compounds according to fusion nomenclature?

(i) Quinoline (ii) Isoquinoline (iii) Indole

11. Write the structures of the following compounds:

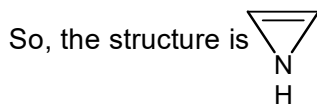
(i) 1,3-Diazacyclopenta-2,4-diene  
(ii) 1-Oxa-3-azacyclopenta-2,4-diene

## 1.7 SOLUTIONS AND ANSWERS

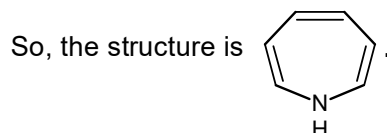
### Self Assessment Questions

- (i) thia + etane → thietane  
(ii) oxa + olane → oxolane  
(iii) thia + epane → thiepane

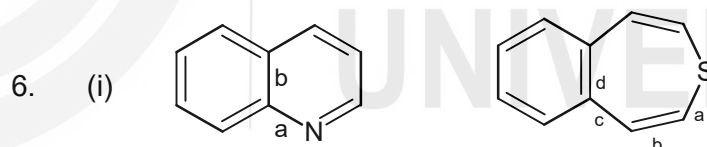
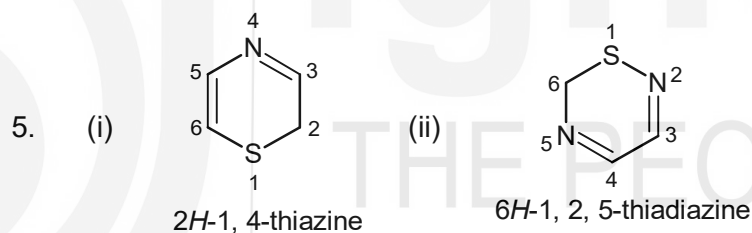
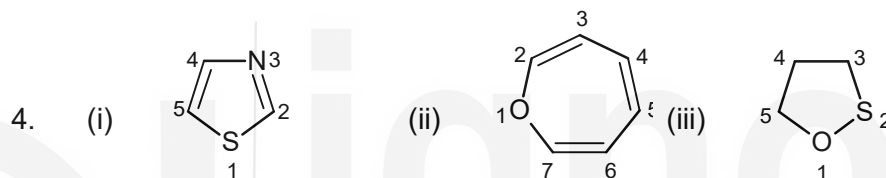
2. (i) azirine = aza + irine  
 ↓ ↓  
 nitrogen + 3 membered  
 unsaturated ring



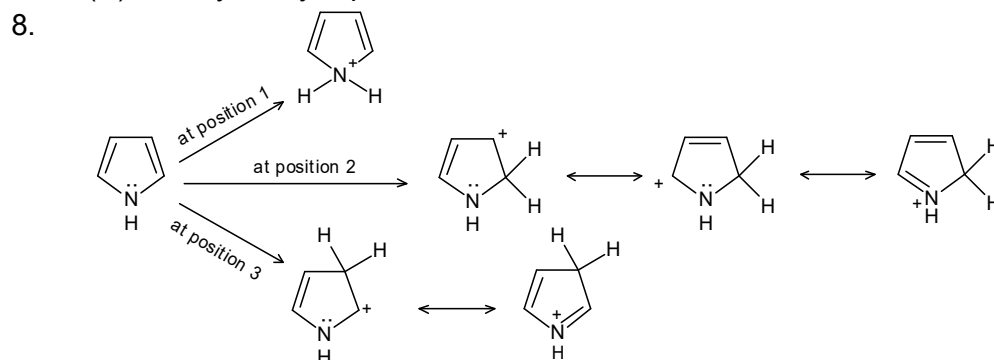
- (ii) azepine = aza + epine  
 ↓ ↓  
 nitrogen + seven membered  
 unsaturated ring



3. It is 1, 3, 5-triazine.



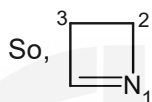
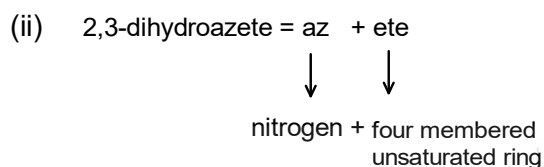
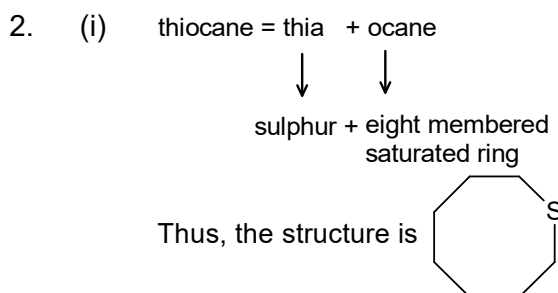
- 7.. (i) Bismabenzene  
 (ii) Silabenzene  
 (iii) 1,4-Dithiacyclohexa-2,5-diene  
 (iv) *N*-ethylazacyclopentane



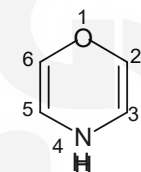
9. The position 2 is likely to be protonated. The reason being the more number possible of resonance structures.

**Terminal Questions**

1. (i) thia + olane  $\rightarrow$  thiolane  
 (ii) phosphate + ole  $\rightarrow$  phosphole  
 (iii) oxa + epine  $\rightarrow$  oxepine

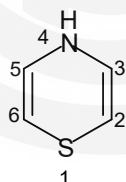


3. (i) The priority is O > N; so



oxa + aza + ine  $\rightarrow$  oxazine  
 and it is 1, 4-oxazine

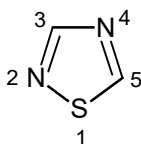
- (ii) Here, the priority is S > N, so



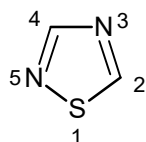
thia + aza + ine  $\rightarrow$  thiazine  
 Hence, the name is 1, 4-thiazine.

Also, note that the two rings in compounds (i) and (ii) are differently written but the names are not affected by that.

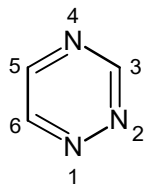
4. (i) The numbering is incorrect because if we number the other way round as shown below,



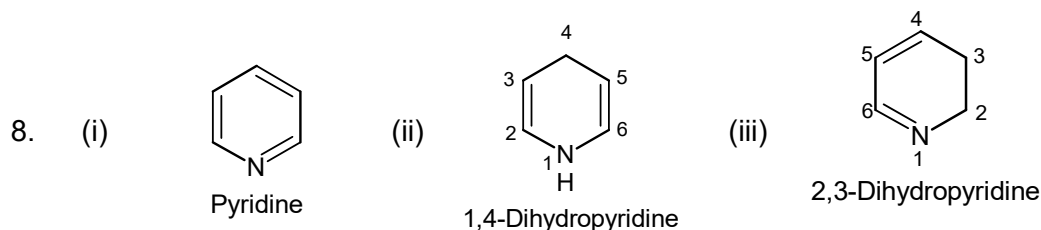
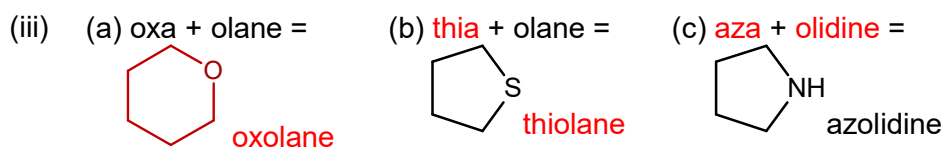
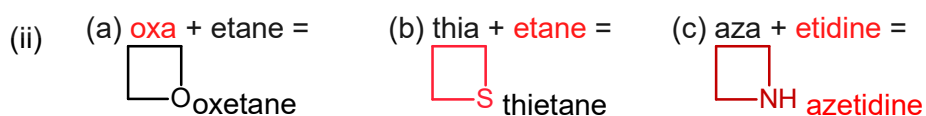
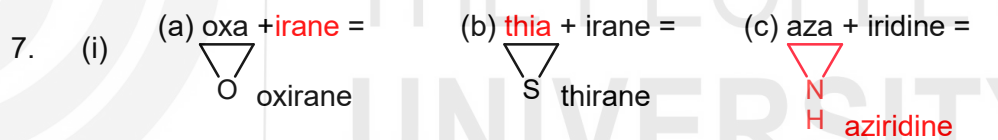
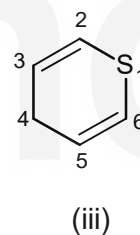
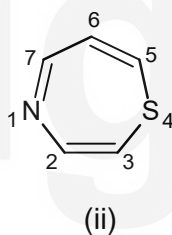
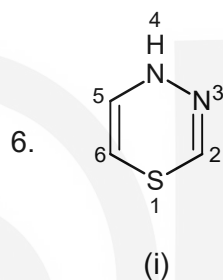
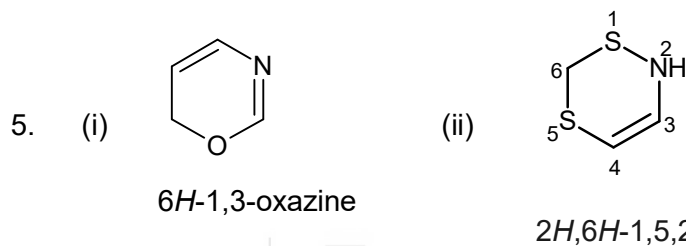
then, the nitrogen atoms get the lower numbers, i.e. 2 and 4 but not 3 and 5 as given in the question.



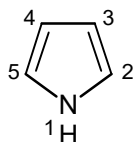
- (ii) Here also, the numbers given to the N atoms are 1,3 and 4. If we alternatively number them as shown below:



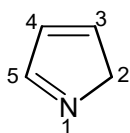
We get the N atoms at 1, 2 and 4 positions and these are lower numbers than those given in questions. Hence, the correct numbering will be 1, 2, 4 as given above.



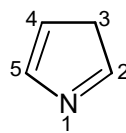
9. (i)



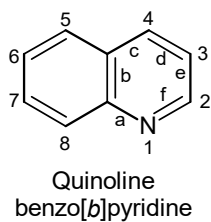
(ii)



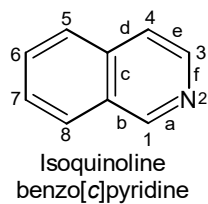
(iii)



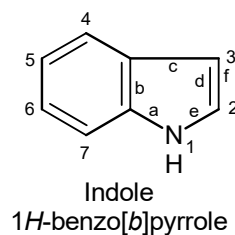
10. (i)



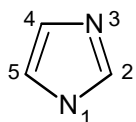
(ii)



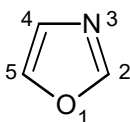
(iii)



11. (i)



(ii)



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