# CH-2

# Nomenclature of Heterocyclic compounds

# Nomenclature of heterocyclic compounds

There are three systems for naming heterocylic compounds:

1. The common nomenclature: which convey little or no structural information but it still widely used.

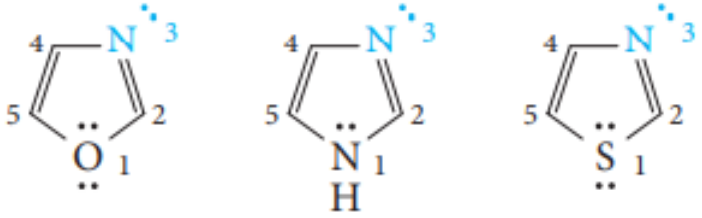
2. The replacement method.

3. The Hantzsch-Widman (IUPAC or Systematic) method which in contrast is designed so that one may deduce from it the structure of the compound.

# 1-Common Nomenclature

- Each compound is given the corresponding trivial name (which should be memorized, see the following slides). This usually originates from the compounds occurrence, its first preparation or its special properties.

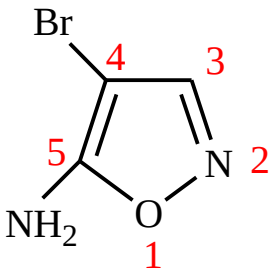
- If there is more than one hetroatom of the same type numbering starts at the saturated one.




- 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.

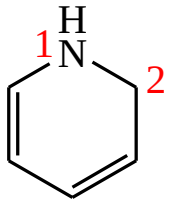
# 1- Common Nomenclature

- If substituents 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

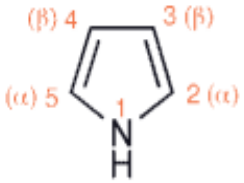
- The words dihydro or trihydro or tetrahydro are used if two or three or four atoms are saturated. These words are preceded by numbers indicate the position of saturated atoms as low as possible and followed by the corresponding fully unsaturated trivial name.



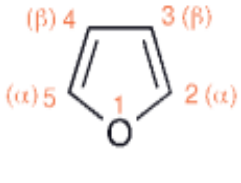

1,2-Dihydro-pyridine

# Trivial names

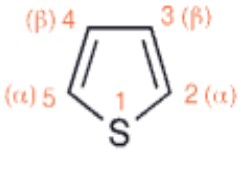
## 5-membered heterocycles with one or two heteroatoms



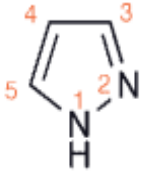
pyrrole



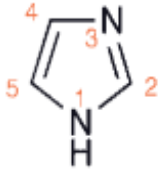
furan



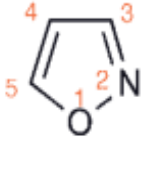
thiophene



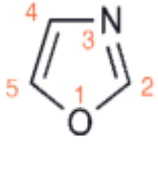
pyrazole



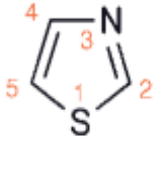
imidazole



isoxazole

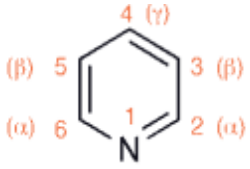


oxazole

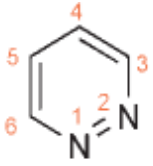


thiazole

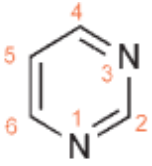
## 6-membered heterocycles with one or two heteroatoms



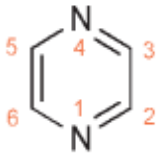
pyridine



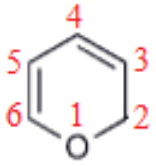
pyridazine



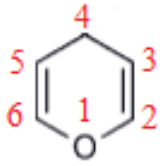
pyrimidine



pyrazine



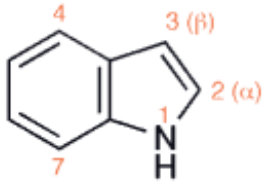
2*H*-pyran



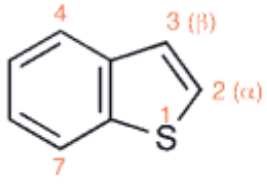
4*H*-pyran

# Fused heterocycles

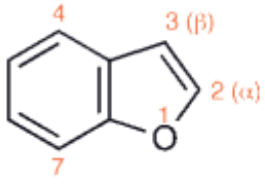
## Common ring-fused azoles



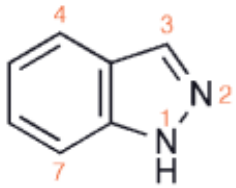
indole



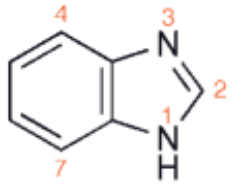
benzothiophene
[benzo[*b*]thiophene]



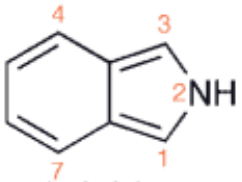
benzofuran
[benzo[*b*]furan]



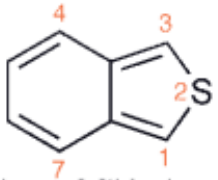
1*H*-indazole



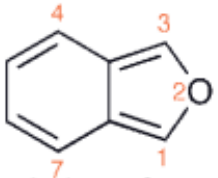
1*H*-benzimidazole



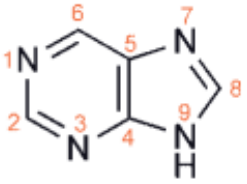
isoindole



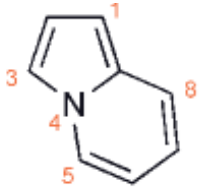
benzo[*c*]thiophene



isobenzofuran

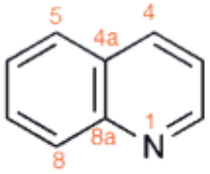


purine
[9*H*-purine]

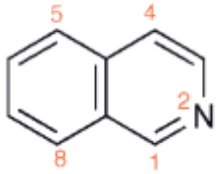


indolizine

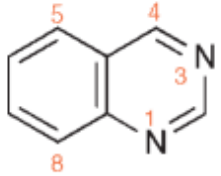
## Common ring-fused azines



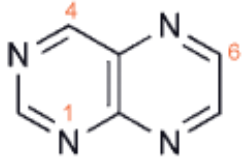
quinoline



isoquinoline



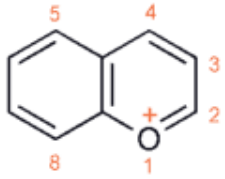
quinazoline



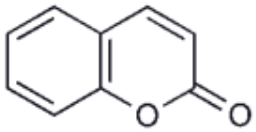
pteridine

# Trivial Names

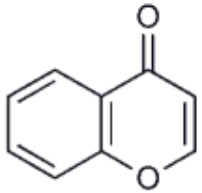
chromylium
(benzo[*b*]pyrylium)
[1-benzopyrylium]



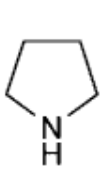

coumarin
[2*H*-1-benzopyran-2-one]



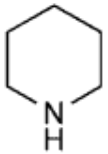

chromone
[4*H*-1-benzopyran-4-one]



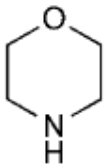

## Saturated heterocycles



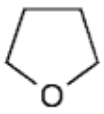

pyrrolidine



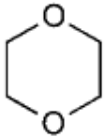

piperidine



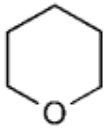

morpholine




tetrahydrofuran
THF




dioxane
[1,4-dioxane]




tetrahydropyran

# 2-Replacement nomenclature

- In replacement nomenclature, the heterocycle's name is composed of the corresponding carbocycle's name and an elemental prefix for the heteroatom introduced (if more than one heteroatom is present they should be listed according to the priority order shown in table (1). According to this nomenclature, tetrahydrofuran, for instance, is called oxacyclopentane.

Table-2

Priority decreases

| Atom | Prefix |
|---|---|
| O | oxa |
| Se | selena |
| S | thia |
| N | aza |
| P | phospha |

# 2- Replacement nomenclature


Benzene


1,3-Cyclopentadiene

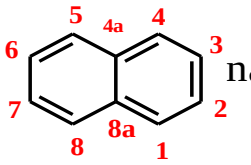

1,3-Cyclopentadiene


Cyclopropane

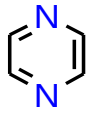

Cyclopropene


1,3-Cyclopentadiene


Cyclohexane

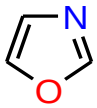


naphthalene

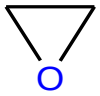


1,4-Diazabenzene

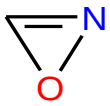
Oxacyclopenta-2,4-diene



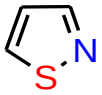
1-Oxa-3-azacyclopenta-2,4-diene



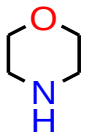
Oxacyclopropane



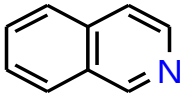
Oxazacyclopropene



1-Thia-2-azacyclopenta-2,4-diene



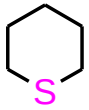
1-Oxa-4-azacyclohexane



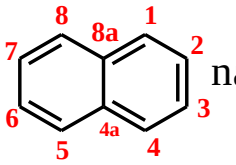
2-Azanaphthalene

# 2- Replacement nomenclature

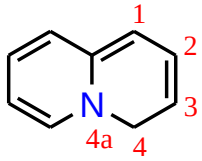
cyclohexane



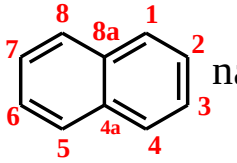

Thiacyclohexane



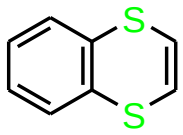

naphthalene



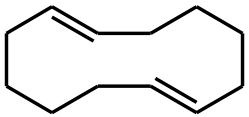

4*H*-4a-azanaphthalene



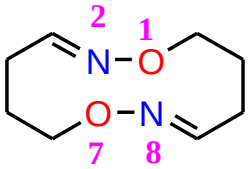

naphthalene




1,4-dithianaphthalene



cyclododecadiene




1,7-Dioxa-2,8-diazacyclododeca-2,8-diene

# 3- Hantzsch-Widman nomenclature (IUPAC)

- Hantzsch-Widman nomenclature is named after the German chemists Arthur Hantzsch and Oskar Widman, who proposed similar methods for the systematic naming of heterocyclic compounds in 1887 and 1888 respectively.

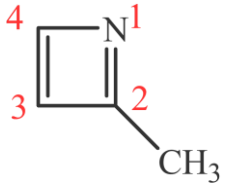
- According to this system three to ten-membered rings are named by combining the appropriate prefix (or prefixes) that denotes the type and position of the heteroatom present in the ring with suffix that determines both the ring size (depending on the total number of atoms in the ring) and the degree of unsaturation (note that fully saturated and fully unsaturated have certain rules for nomenclature while partially unsaturation will be indicated in certain ways). In addition, the suffixes distinguish between nitrogen-containing heterocycles and heterocycles that do not contain nitrogen

**IUPAC name = locants +Prefix + suffix**

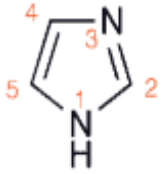
# Hantzsch-Widman rules for fully saturated and fully unsaturated heterocycles

1) Identify the hetroatom present in the ring and choose from (table 1 on slide 9) the corresponding prefix (e.g. thia for sulfur, aza for nitrogen and oxa for oxygen).

2) The position of a single heteroatom control the numbering in a monocyclic compound. The heteroatom is always assigned position 1 and if substituents present are then counted around the ring in a manner so as to take the lowest possible numbers.




3) A multiplicative prefix (di, tri, ect.) and locants are used when two or more similar heteroatoms contained in the ring( two nitrogen indicated by diaza) and the numbering preferably commenced at a saturated rather than an unsaturated atom, as depicted in the following example: 1,3-diazole



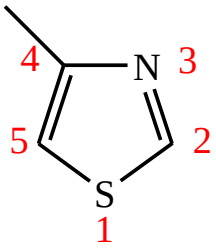
imidazole

# Hantzsch-Widman rules

4) If more than one type of hetroatoms present in the ring the name will include more than one prefix with locants to indicate the relative position of the heteroatoms.

- Atom prefixes have a strict order of priority (preference) in which they are to be listed. For example,‘’Oxa’’(for oxygen) always comes before ‘’aza’’ (for nitrogen) in a name (see table 1).
- When combining the prefixes (e.g. oxa and aza) two vowels may end up together, therefore the vowel on the end of the first part should be omitted (oxaza).
- The numbering is started from the heteroatom of the highest priority in such a way so as to give the smallest possible numbers to the other heteroatoms in the ring (the substituents are irrelevant).

For example :




4-Methyl-1,3-Thiazaole

# Hantzsch-Widman rules

5) Choose the appropriate suffix from (table 2) depending on the ring size.

Table-2

| Ring size | Suffix |
|---|---|
| 3 | ir |
| 4 | et |
| 5 | ol |
| 6 | in |
| 7 | ep |
| 8 | oc |
| 9 | on |
| 10 | ec |

# Hantzsch-Widman rules

6) The endings indicate the size and degree of unsaturation of the ring.

Tabel-2

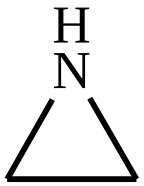
| Ring size | With N | | Without N | |
|---|---|---|---|---|
| | Unsat. | Sat. | Unsat. | Sat. |
| 3 | irine | iridine | irene | irane |
| 4 | ete | etidine | ete | etane |
| 5 | ole | olidine | ole | olane |
| 6 | ine | a | in | inane |
| 7 | epine | a | epin | epane |
| 8 | ocine | a | ocin | ocane |
| 9 | onine | a | onin | onane |
| 10 | ecine | a | ecin | ecane |

a : means use the prefix perhydro followed by the fully unsaturated name

7) Combine the prefix (s) and suffix together and drop the first vowel if two vowels came together.

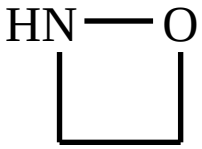
# Hantzsch-Widman rules

## Examples:




**Aziridine**

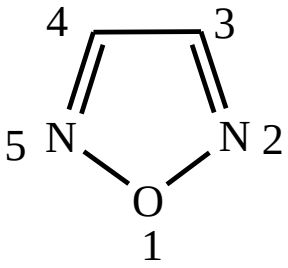
- This ring contains (N): Prefix is aza
- The ring is 3-membered and fully saturated: suffix is iridine
- By combining the prefix and suffix, two vowels ended up together (azairidine), therefore the vowel on the end of the first part should be dropped. This gives the correct name: Aziridine



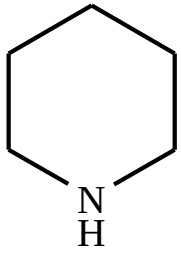

**1,2-oxazetidine**

- This ring contains (O and N) (O has higher priority than (N) and by starting numbering the ring at (O): Prefix is 1,2-Oxaaza, but the first vowel must be omitted to give: 1,2-Oxaza
- The ring is 4-membered and fully saturated: suffix is etidine
- By combining the prefix and suffix, two vowels ended up together (1,2-oaxazaetidine), therefore the vowel on the end of the first part should be dropped. This gives the correct name:1,2-oxazetidine

# Hantzsch-Widman rules




**Oxa + diaza + ole = 1,2,5-Oxadiazole**

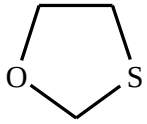


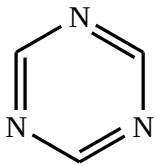

**Perhydro + aza + ine = perhydroazine**

# Hantzsch-Widman rules

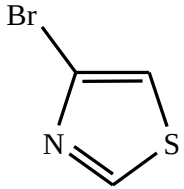
**Exercise:**

Explain how can you name the following heterocycles.



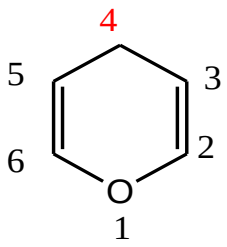




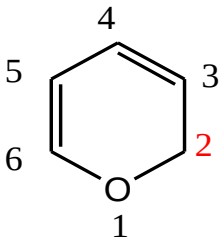
# Hantzsch-Widman rules for partially unsaturated heterocycles

- Partial unsaturation in heterocyclic compounds can be indicated by one of the following methods:

a) The position of nitrogen or carbon atoms which bear extra hydrogen atoms must be indicated by numbers and italic capital H (e.g. 1*H*, 2*H*, etc.) followed by the name of maximally unsaturated ring.

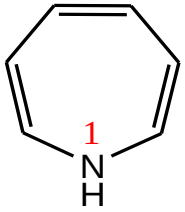



4*H*-Oxin

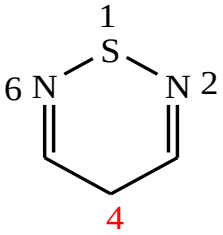



2*H*-Oxin

Not 6*H*-Oxin



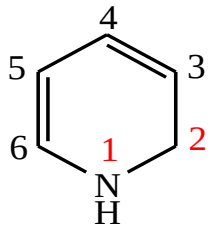

1*H*-Azepine




4*H*-1,2,6-Thiadiazine

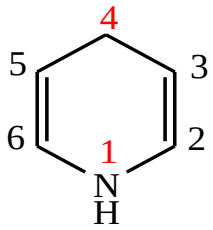
# Hantzsch-Widman rules for partially unsaturated heterocycles

b) The words dihydro, or trihydro, or tetrahydro are used if two or three or four atoms are saturated. These words are preceded by numbers indicate the position of saturated atoms as low as possible and followed by the corresponding fully unsaturated Hantzsch-Widman name.

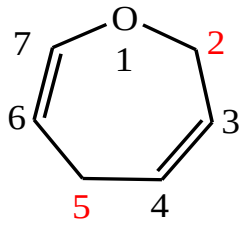



1,2-Dihydroazine

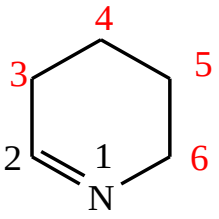
Not 1,6-Dihydroazine




1,4-Dihydroazine

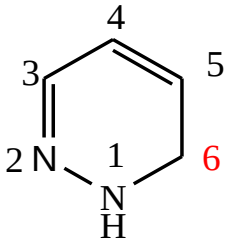



2,5-Dihydrooxepin



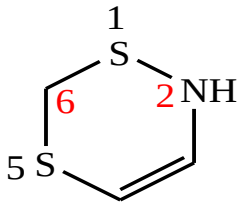

3,4,5,6-Tetrahydroazine

Not 2,3,4,5-Terahydroazine




1,6-Dihydro-1,2-diazine

Hint:



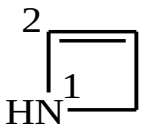

2*H*,6*H*-1,5,2-Dithiazine

# Hantzsch-Widman rules for partially unsaturated heterocycles

c) Alternatively, the partially unsaturated 4 and 5 rings (i.e. rings contain one double bond) are given special Hantzsch-Widman suffixes as in table 3 and the double bond is specified as $\Delta^1$, $\Delta^2$, $\Delta^3$, etc.. Which indicates 1 and 2 ; 2 and 3; 3 and 4 atoms respectively have a double bond.

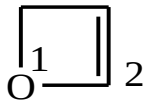
**Name : $\Delta^x$ + Prefix + special suffix** ( x= locant of the double bond)

| Ring size | With N | Without N |
|---|---|---|
| 4 | etine | etene |
| 5 | oline | olene |



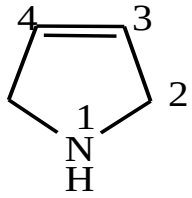

$\Delta^2$ -Azetine

2-Azetine



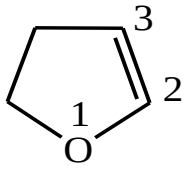

$\Delta^2$ -Oxetene

2-Oxetene




$\Delta^3$ -Azoline

3-Azoline



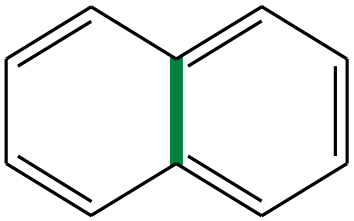

$\Delta^2$-Oxolene

2-Oxolene

# Nomenclature of Fused Systems

**Definitions:**

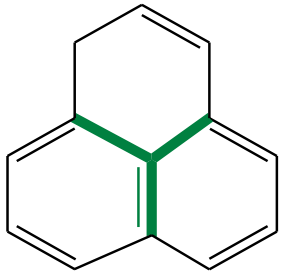
- Fusion: This term is used to describe the process of joining two separate rings with the maximum number of non-cumulative double bonds *via* two atoms and one common bond.
- *Ortho-fused* rings: are those rings that have only two common atoms and one bond, example; Naphthalene



Naphthalene

# Nomenclature of Fused Systems

- *Ortho-and peri-fused rings:* are those found in a polycyclic compound with a ring that is *ortho*- fused to different sides of two other rings that are themselves ortho-fused together (i.e. there are three common atoms between the first ring and the other two), example; 1*H*-phenalene is considered as being composed of three benzene rings, each is *ortho-peri*-fused to the other two.



1*H*-Phenalene

- Polycyclic compounds incorporating one heterocyclic ring or fused heterocylic system fused to benzene are known benzoheterocycles.
- Also bicyclic compounds with two fused heterocyclic rings are well known.
- Both types can be named according to certain rules.

# Nomenclature of Fused Heterocyles

A. Nomenclature of benzofused compounds:

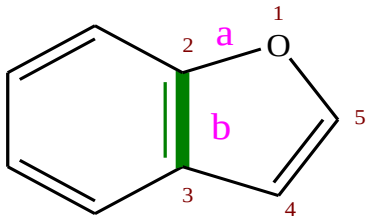
- Unless listed as a trivially named heterobicycle (see slide 6), a benzene ring fused to a heteromonocycle of five or more members or a heterobicylcle is named by prefixing the word benzo to a letter indicating the position of fusion in square brackets by the name of heterocyclic ring (common or IUPAC or modified replacement name).

Name = Benzo [letter] name of heterocyclic ring

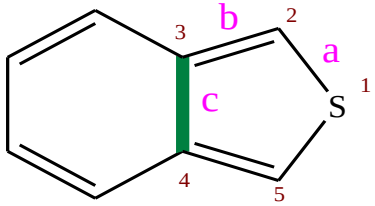
- For designating the position of fusion, the peripheral bonds of the heterocyclic ring are consecutively assigned alphabetical letters staring with the 1,2-bond as a side and the labeling is continued around the ring to give the common bond the lowest order.

# Nomenclature of Fused Heterocyles

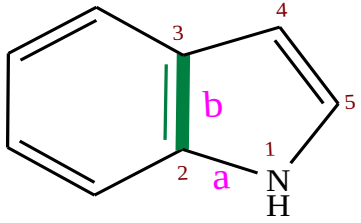
Examples:



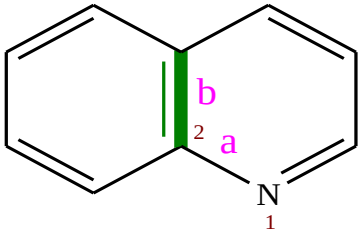

Benzo[*b*]furan



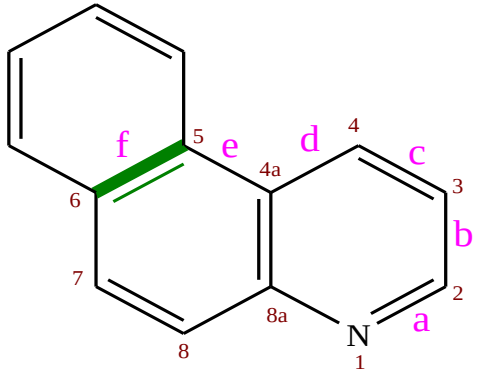

Benzo[*c*]thiophene




Benzo[*b*]pyrrole
Indole




Benzo[*b*]pyidine
Qunioline

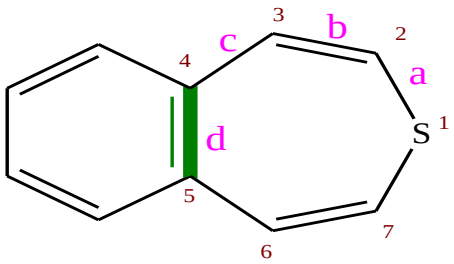



Benzo[*f*]qunioline

# Nomenclature of Fused Heterocyles

- There is An exception to the two ring systems in which a benzene ring is fused to a hetero ring (which doesn't have a known common name) may be named by prefixing numbers indicating the positions of the hetero atoms to benzo followed by the name of the heterocyclic component.
- Numbering is assigned according to priority order of the hetero atoms i.e.

  O > S > N




Benzo[*d*]thiepine

# Nomenclature of Fused Heterocyles

## B. Nomenclature of fused heterocylic compounds:

- Naming a fused heterocyclic systems composed of two monoheterocyclic units or benzoheterocycles (e.g. chromene) fused with another hetrocycle ring is based upon considering one system as the parent (base) and the second is considered as substituent.

**Name : name of minor ring [number, number-letter] name of major ring**

- The name of the minor ring is derived by writing a contracted prefix for the substituent ring present. In an attached component prefix the terminal 'e' is changed to 'o' with exception of:

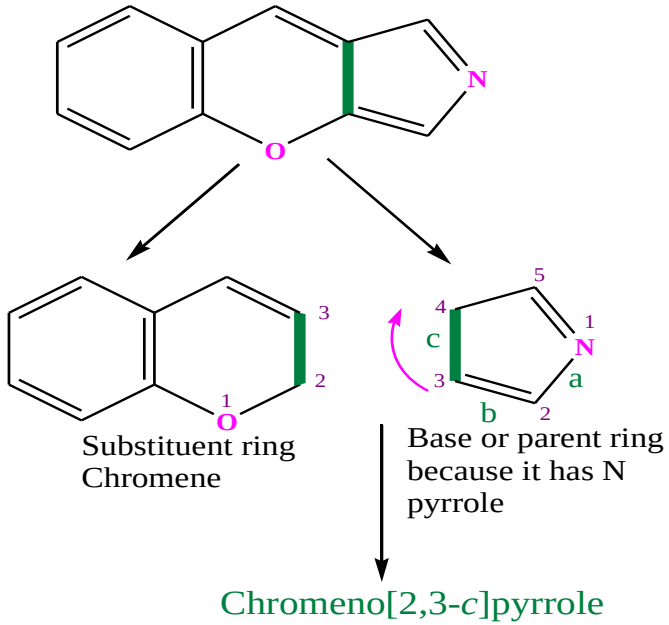
| | |
|---|---|
| Furo | From Furan |
| Imidazo | From Imidazole |
| Thieno | From Thiophene |
| pyrido | From Pyridine |
| Pyrimido | From Pyrimidine |
| Quino | From Quinoline |
| Isoquino | From Isoquinoline |

# Nomenclature of Fused Heterocyles

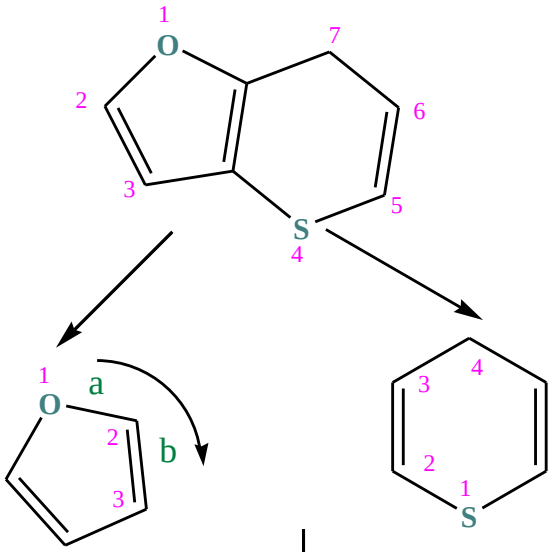
- The numbers indicate which atoms in the minor ring are common to the major ring (fusion sites in minor ring).
- The order of the numbers indicates which atom of the minor ring is encountered closest to atom 1 in the major numbering system (i.e. these numbers may be written in ascending or descending order e.g.2,3 or 3,2 )
- The letter defines the position of attachment of the minor ring to the major ring (fusion sites in base component).
- Finally a suffix indicate the name of the base ring is written.
- The numbering system for the whole fused system is not the same as the numbers in the square brackets (i.e. there are three numbering systems; one for minor ring, one for major ring and the third is for the system as a whole).
- Priority order of component ring systems: Selection of a parent component or attached component is based on the following rules which are applied in order:

# Nomenclature of Fused Heterocyles

Rule 1: A heterocyclic ring containing the heteroatom occuring earlist in the order N, F, Cl, Br, I, O, S, Se,..
(i.e. ring containing N preferred to the rings does not contain N or containing O, or S)



# Nomenclature of Fused Heterocyles



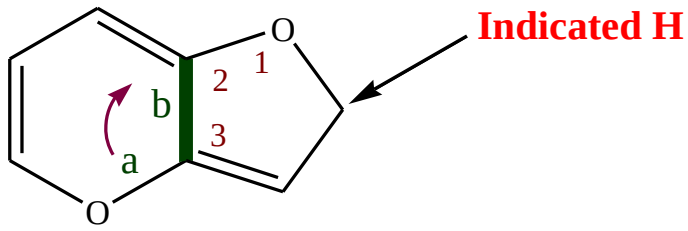

**Parent ring**
O preferred to S
Furan

**Substituent ring**
Thiopyrano with one satrated C that take locant 7 when the system is numbered as a whole (starting from O to give the two heteroatoms locants 1,4 while starting from S gives them locants 1,5)

7*H*-Thiopyrano[3,2-*b*]furan

# Nomenclature of Fused Heterocyles

Rule 2: A heterocyclic component containing the largest possible individual ring

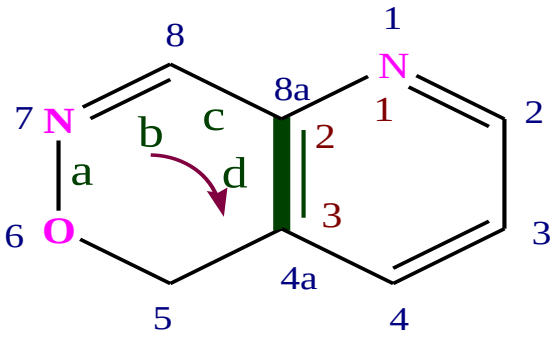



2*H*-Furo[3,2-*b*]pyran
(pyran [6] preferred to furan [5])

Numbering the whole system is started from O in furan ring to give the two heteroatoms locants 1,4 while starting from O in pyran ring gives them locants 1,5, thus the indicated H takes locant 2

# Nomenclature of Fused Heterocyles

Rule 3: A heterocyclic component containing the greater number of hetroatoms of any kind

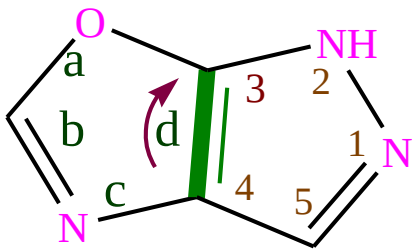



5*H*-Pyrido[2,3-*d*][1,2]oxazine
(Oxazine preferred to pyridine)

N.B. The whole molecule is numbered starting from pyridine ring to give the three heteratoms the lowest locants (1,6,7), however, stating from oxazine ring will give them locants (2,3,5) or (2,3,8).

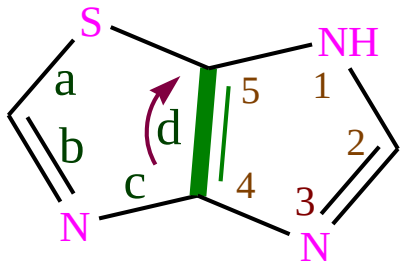
# Nomenclature of Fused Heterocyles

Rule 4: A heterocyclic component containing the greater variety of hetroatoms




1*H*-Pyrazolo[4,3-*d*][1,3]oxazole

(O & N preferred to N only)

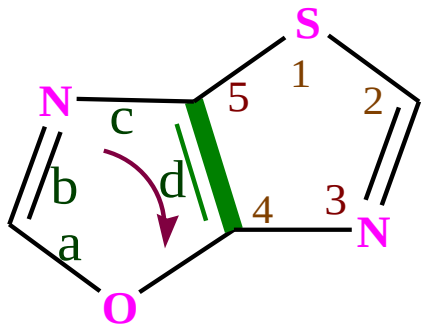



1*H*-Imidazo[4,5-*d*][1,3]thiazole

N.B. The whole molecule is numbered starting from pyrazole ring to give the four heteratoms the lowest locants (1,2,4,6). While starting from oxazole ring give them locants (1,3,4,5) or (1,3,5,6).

# Nomenclature of Fused Heterocyles

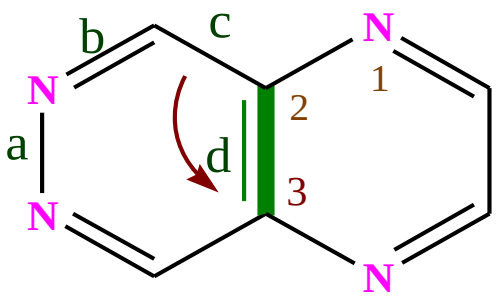
Rule 5: A heterocyclic component containing the greater number of heteroatoms most preferred when considered in order F, Cl, Br, I, O, S, Se, Te, N, P, As, Sb, Bi, Si, Ge, Sn Pb, B, Hg




[1,3]Thiazolo[5,4-*d*][1,3]oxazole
(N & O preferred to N & S)

# Nomenclature of Fused Heterocyles

Rule 6: A heterocyclic component with the lower locants for heteroatoms

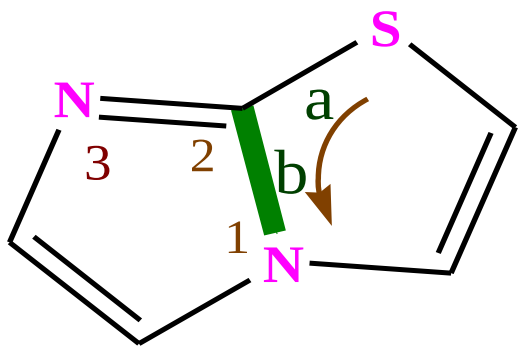



Pyrazino[2,3-*d*]pyridazine

(pyridazine [2N-1,2] preferred to pyrazine [2N-1,4]

# Nomenclature of Fused Heterocyles

Rule 7: If a position of fusion is occupied by a heteroatom the name of the component rings to be used are so chosen as both to contain the heteroatom.

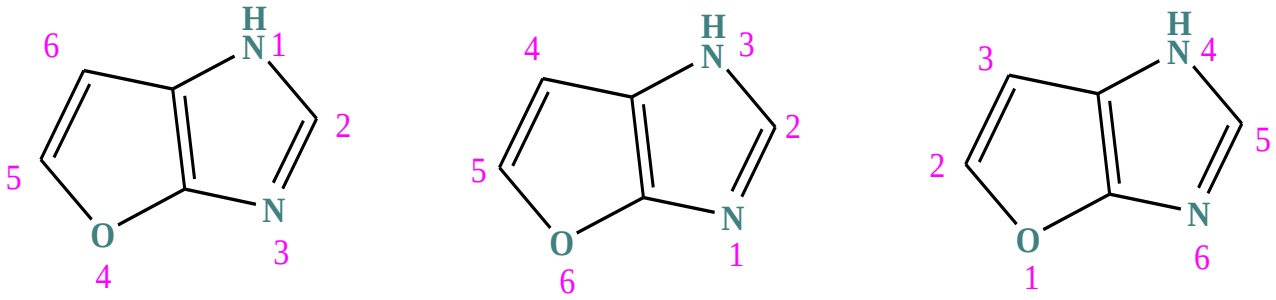



Imidazo[2,1-*b*][1,3]thiazole

# Order of preference between alternative numbering system of the whole molecule

- Numbering the whole fused system should start from the first atom after fusion in any direction to fulfill the following rules in order:

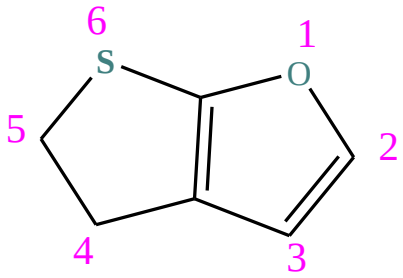
a) Give low numbers for the heteroatoms as a set




1*H*-Furo[2,3-*d*]imidazole

(heteroatoms 1,3,4 is preferred to 1,3,6 or 1,4,6)

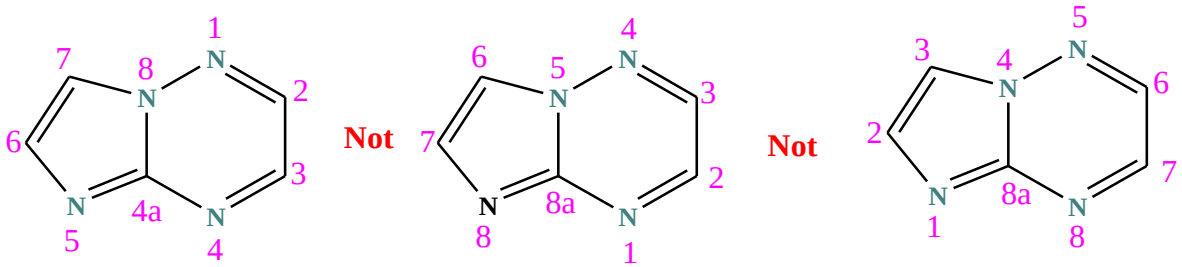
b) Give low numbers for heteroatoms of higher priority i.e. O,S, N




4,5-Dihydro-thieno[2,3-*b*]furan

# Order of preference between alternative numbering system of the whole molecule

c) Give low numbers to fusion carbon atoms




Imidazo[1,2-*b*][1,2,4]triazine

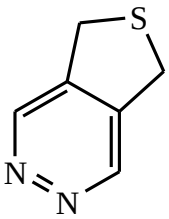
fusion C -4a is preferred to 8a

d) Give low numbers to indicated hydrogen atom

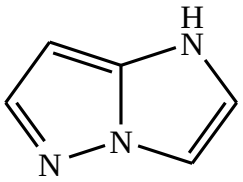

2*H*,4*H*-[1,3]dioxol[4,5-*d*]imidazole

Indicated hydrogens 4 not 6

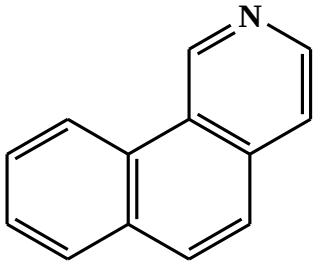
Exercise : Name the following compounds.



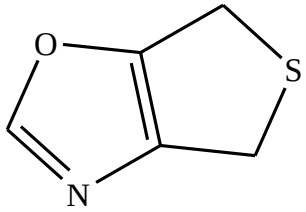

(a)




(b)




(c)




(d)

# Summary of Nomenclatures Rules

## Scheme for deriving the base component of a fused ring system

- Is there only one ring which contains nitrogen?

Yes: choose this as base component

- Are the two rings have the same heteroatoms but their size is different ?

Yes: choose the larger one

- Are the two rings of the same size but have different heteroatoms?

Yes: choose the ring containing a heteroatom of the highest priority i.e. O >S

- Are the rings of the same size but contain different numbers of heteroatoms?

Yes: choose the ring with the greater number

- Are the two rings of the same size and the same number of different heteroatoms?

Yes: choose the ring with the greatest variety of heteroatoms

- Are the two rings have the same size and the same number and type of heteroatoms?

Yes: choose the ring with the lower numbers for heteroatoms