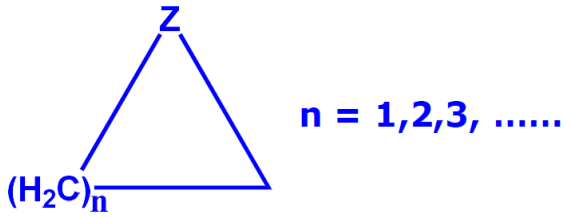
NOMENCLATURE OF HETEROCYCLES WITH ONE ATOM

Nomenclature of Heterocycles

- In medieval ages, names of organic compounds were based on their natural occurrence or common uses as a means of identifying them, usually before their structures were determined.
- Such names, devised based on natural occurrence or uses, are called common or trivial names.
- Systematic (IUPAC) nomenclature allows for the structure of the compound to be deduced from its name.
- The systematic nomenclature of heterocycles allows the use of several different systems of nomenclature:
  i. Common nomenclature for aromatic heterocycles.
  ii. Hantzsch-Widman nomenclature: This is recommended for 3-10 membered heterocycles.
  iii. Replacement nomenclature: Ideal for spiroheterocycles, bridged heterocycles and other heterocycles greater than 10-membered.

Hantzsch-Widman Nomenclature of Heterocycles



- This is the most widely used systematic nomenclature for three to ten-membered heterocyclic systems with various degrees of unsaturation.
- This nomenclature specifies the type and position(s) of the heteroatom (Z), ring size and sense of unsaturation (whether saturated or unsaturated).
- The parent name of a heterocycle based on Hantzsch-Widman nomenclature is generated by combining a prefix, a stem and a relevant suffix.
- Whereas the prefix-identifies the heteroatom, the stem identifies the ring size, while the suffix specifies the sense of unsaturation.

Hantzsch-Widman Nomenclature of Heterocycles

- The prefixes for the common heteroatoms in the order of their priorities are:

Heteroatom	Valence	Group	Atomic #	Prefix
Oxygen	**II**	**6**	**8**	**Oxa**
Sulphur	**II**	**6**	**16**	**Thia**
Nitrogen	**III**	**5**	**7**	**Aza**
Phosphorous	**III**	**5**	**15**	**Phospha**
Silicon	**IV**	**4**	**14**	**Sila**
Boron	**III**	**3**	**5**	**Bora**

- Note that the order of citation begins with atoms as high in a group in the periodic table and as low in atomic number in the group.

Hantzsch-Widman Nomenclature of Heterocycles

- The stems for the ring systems and the suffixes for sense of saturation/unsaturation are tabulated below:

Ring Size	Stem	Saturated (N) Suffix	Saturated Suffix	Unsaturated Suffix
Three	ir	idine	ane	ene
Four	et	idine	ane	e
Five	ol	idine	ane	e
Six	-	inane	ane	ine
Seven	ep	-	ane	ine
Eight	oc	-	ane	ine
Nine	on	-	ane	ine
Ten	ec	-	ane	ine

Hantzsch-Widman Nomenclature of Heterocycles

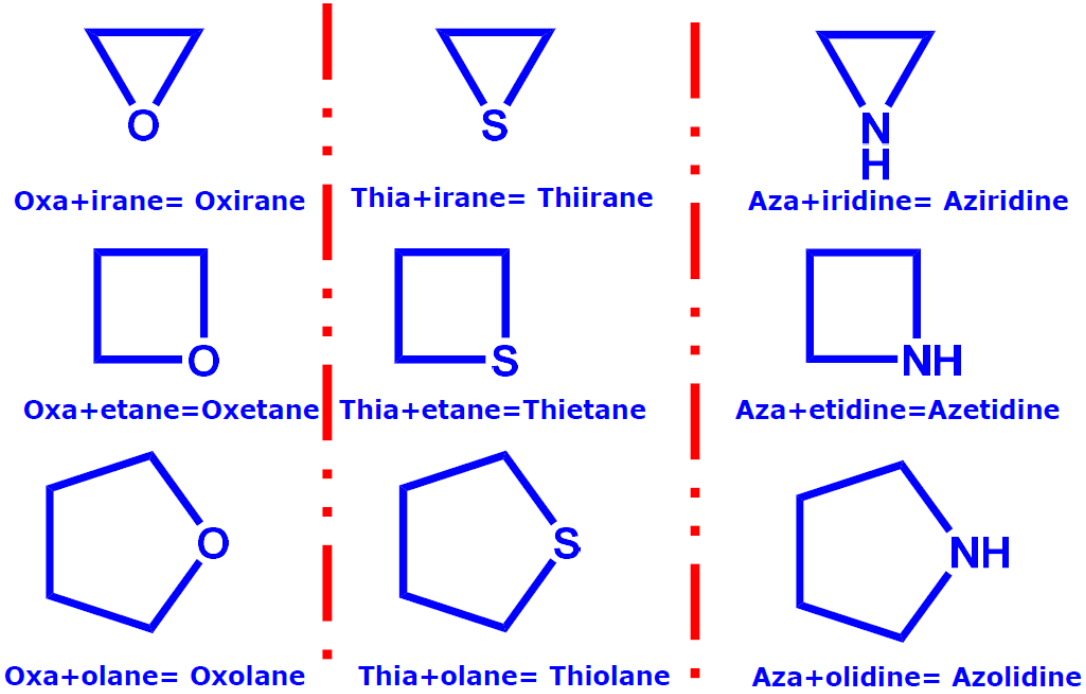
- Note that some of the syllables of the stem (ring size) are derived from Latin numerals, e.g. ir from tri, et from tetra, ep from hepta, oc from octa, on from nona, ec from deca.
- An exception in suffixes applies for saturated 3, 4 and 5-membered nitrogen heterocycles, for which the traditional "iridine", "etidine" and "olidine“ stem-suffixes are used, respectively .

Hantzsch-Widman Nomenclature

Combining Prefixes, Stems and Suffixes

- When combining one or more prefixes for the heteroatom(s) with the stem-suffix for the size of the ring and unsaturation: If the stem-suffix begins with vowel, the terminal letter ‘a’ of the prefix is dropped.

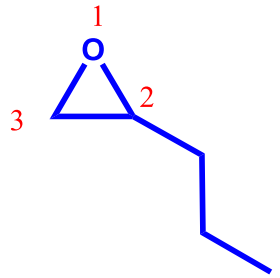
Examples



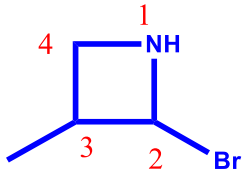
Hantzsch-Widman Nomenclature

Substituted Saturated Heterocycles

- If the saturated heterocycle is substituted, the heteroatom is designated number 1, and the ring is numbered proceeding in the direction that gives the substituents the lowest possible location number (locant).

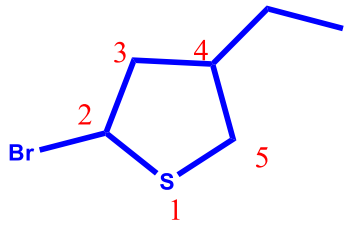


2-Propyloxirane

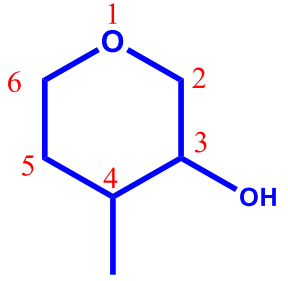


5

2-Bromo-3-methylazetidine



2-Bromo-4-ethylthiolane

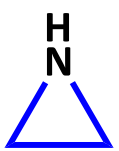


3-Hydroxy-4-methyloxane

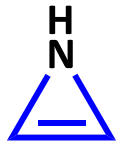
Hantzsch-Widman Nomenclature

Saturated vs Unsaturated Heterocycles

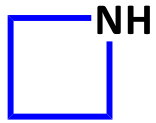
- It is important to recognize that the saturated suffix applies only to completely saturated ring systems.
- For unsaturated heterocycles, the parent compound is the monocyclic system of a given ring size with a maximum number of noncumulative double bonds.



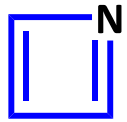
Aziridine



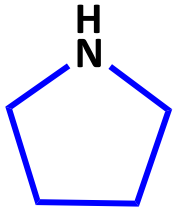
Azirine



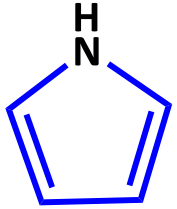
Azetidine



Azete

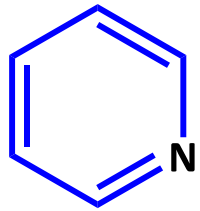


Azolidine



Azole

Azinane

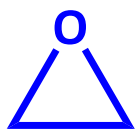


Azine

Hantzsch-Widman Nomenclature

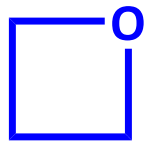
Saturated vs Unsaturated Heterocycles

- The saturated and unsaturated oxygen and sulphur heterocycles are depicted below.

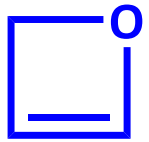


Oxirane

Oxirene



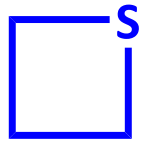
Oxetane



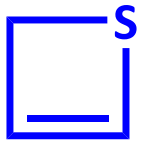
Oxete

Thiirane

Thiirene



Thietane



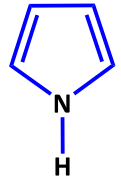
Thiete

Hantzsch-Widman Nomenclature

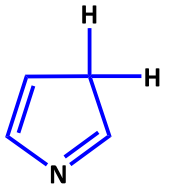
Unsaturated Heterocycles

- Some unsaturated heterocycles with a maximum number of double bonds can exist in more than one form.
- For example, azole and oxine can exist in the three and two regio-isomers shown below, respectively.

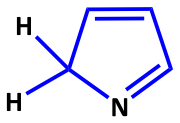
Azole



Double bonds @ 2 and 4

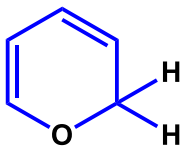


Double bonds @ 1 and 4

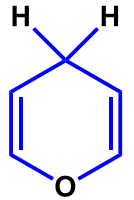


Double bonds @ 1 and 3

Oxine



Double bonds @ 2 and 4



Double bonds @ 2 and 5

- Since these regio-isomers are different compounds, how would they be named so that it is clear which structure is implied?

Hantzsch-Widman Nomenclature

Unsaturated Regio-isomeric Heterocycles

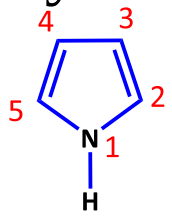
- The regio-isomeric unsaturated heterocycles resulting from the shifting position of saturation (sometimes referred to as “extra-hydrogen” or obligatory saturation) are named by adding a prefix that indicates the number of the ring atom that is saturated (possesses the extra hydrogen) using italic capital ‘*1H*’ ‘*2H*’ ‘*3H*’, etc.
- The numerals indicate the ring atom position of these unsaturated heterocycles having the extra hydrogen atom.
- How then can the three azole and two oxine regio-isomers be named?

Hantzsch-Widman Nomenclature

Unsaturated Regio-isomeric Heterocycles

- To name the regio-isomers, number the ring system from the heteroatom in the direction that gives the saturated position priority in numbering.

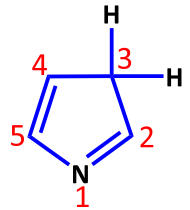
Azole



1*H*-Azole

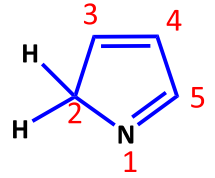
1*H*-Pyrrole

(Pyrrole)



3*H*-Azole

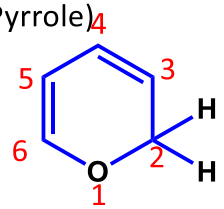
3H-Pyrrole



2*H*-Azole

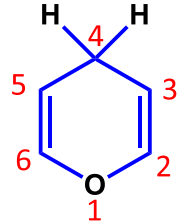
2H-Pyrrole

Oxine



2*H*-Oxine

***2H*-Pyran**



4*H*-Oxine

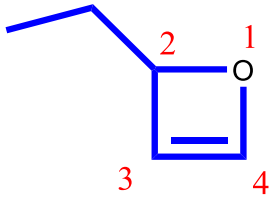
***4H*-Pyran**

- Among the three regio-isomers of azole (common name: pyrrole), which is the most stable? Refer to the concept of aromaticity to rationalize the stability among the regiomers of pyrrole.

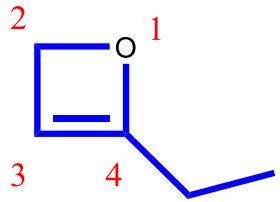
Hantzsch-Widman Nomenclature

Substituted Unsaturated Heterocycles

- When an unsaturated heterocycle with a maximum number of noncumulative double bonds contains a saturated atom, its position is given the lowest possible locant and is numerically indicated by an italic capital *H* before the name of heterocyclic ring system.
- The heteroatom, however, remains designated number 1.



2-Ethyl-2*H*-oxete



4-Ethyl-2*H*-oxete

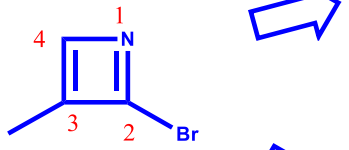
- Note that the position of unsaturation takes precedence in adopting the lowest possible location number (locant) starting at the heteroatom.

Hantzsch-Widman Nomenclature

Partially Unsaturated Heterocycles

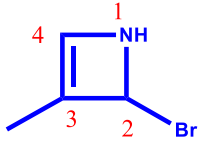
- The naming of heterocycles with a lesser degree of unsaturation (number of double bonds is less than the maximum) requires adding the prefixes "dihydro"or "tetrahydro“, (as appropriate for the degree of unsaturation) to the same name of unsaturated state.
- The position of saturation is again given the lowest possible location number (locant) after the heteroatom.

Full Unsaturation

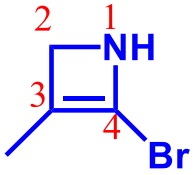


2-Bromo-3-methylazete

Partial Unsaturation



2-Bromo-3-methyl-1,2-dihydroazete

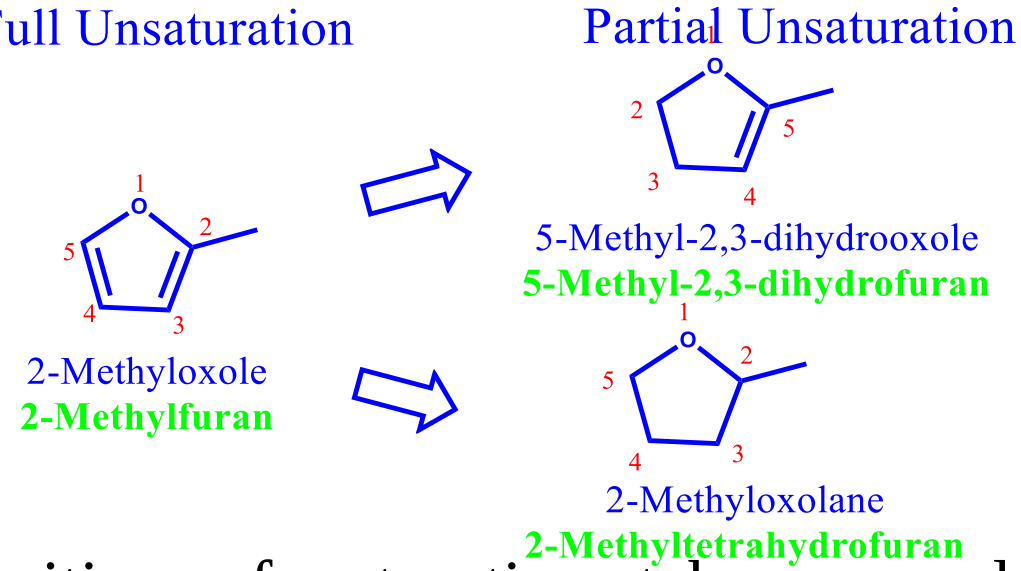


4-Bromo-3-methyl-1,2-dihydroazete

Hantzsch-Widman Nomenclature

Substituted Unsaturated Heterocycles

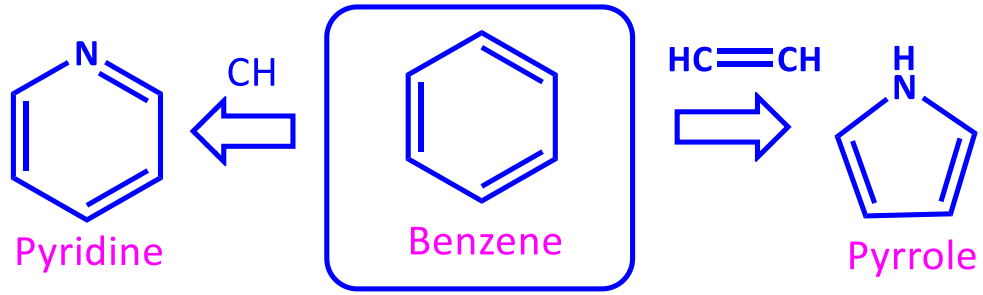
- The “dihydro” and “tetrahydro” prefixes are used in the nomenclature of partially and fully saturated derivatives of furans.



- The position of saturation takes precedence in the numbering and the positions to which the hydrogens are added are specified in the name of the partially saturated heterocycle.

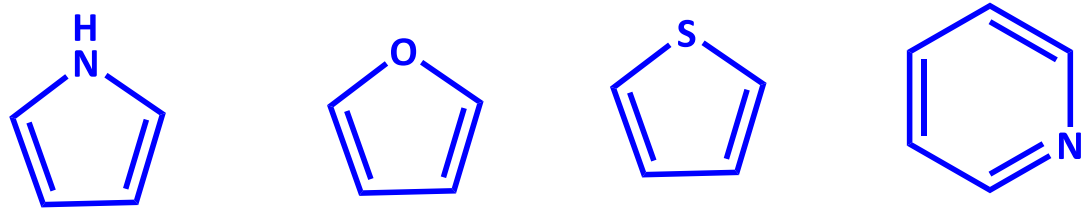
Aromatic Heterocycles

- The concept of aromaticity also applies in heterocyclic compounds.
- Aromaticity applies in systems that:
  - ✓ Are cyclic and planar
  - ✓ Have conjugated (sp^2 hybridized) p-orbitals on every atom in the ring
  - ✓ Satisfy Huckels rule of 4n+2 p delocalized electrons (n = any integer)
- Replacing a CH or CH=CH unit of benzene, the quintessential carbocyclic aromatic compound, with a N atom provides aromatic heterocycles, pyridine and pyrrole, respectively.



Hantzsch-Widman Nomenclature Aromatic Heterocycles

- Replacing a CH=CH unit of benzene with an O or S atom also provides five membered aromatic heterocycles, furan and thiophene, respectively.
- For nomenclature of aromatic heterocycles, a hybrid of trivial and Hantzsch-Widman nomenclature is accepted.
- Generally, the nomenclature of aromatic heterocycles prefers trivial names eg: pyrrole, furan, thiophene, pyridine etc., over their Hantzsch-Widman names.

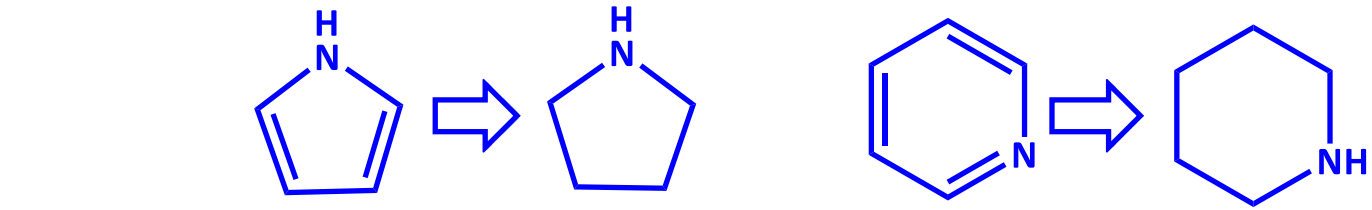


Systematic	Azole	Oxole	Thiole	**Azine**
Trivial	Pyrrole	Furan	Thiophene	Pyridine

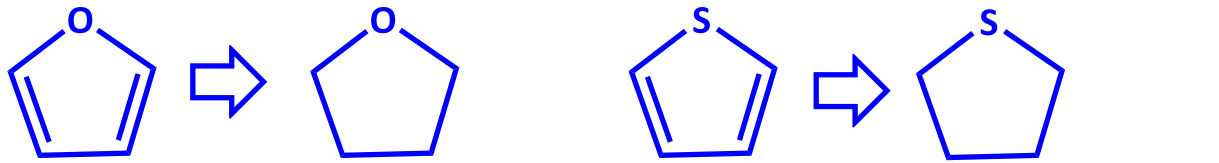
- Azine is not used as a name for pyridine because of its use as a class name of compounds with =N—N= group.

Hantzsch-Widman Nomenclature Aromatic Heterocycles

- Some of these trivial or common names of aromatic heterocycles, have also informed the formulation of names of derived saturated heterocycles.



Trivial	Pyrrole	Pyrrolidine	Pyridine	Piperidine
Systematic	Azole	Azolidine	**Azine**	**Azinane**



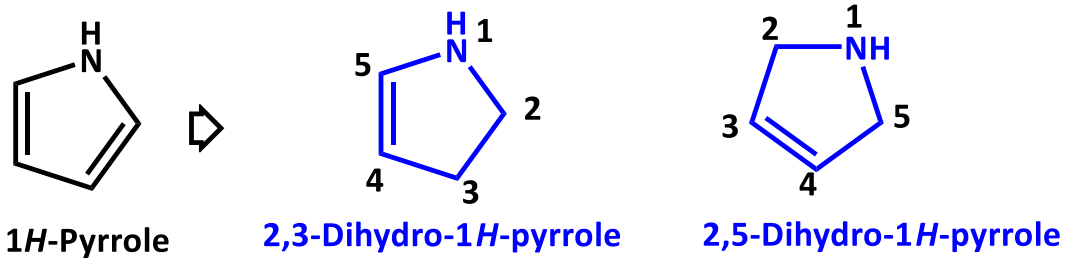
Trivial	Furan	Tetrahydrofuran	Thiophene	Tetrahydrothiophene
Systematic	Oxole	Oxolane	**Thiole**	**Thiolane**

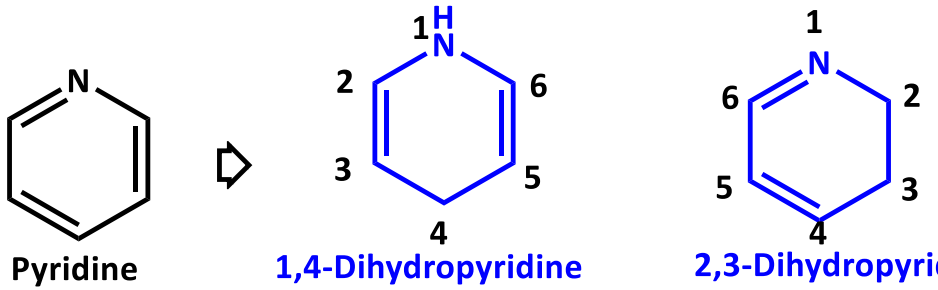
- The surviving trivial names are important because they are used as a basis for constructing more systematic names for simple derivatives and polycyclic systems.

Hantzsch-Widman Nomenclature

Partially Saturated Aromatic Heterocycles

- Just like the unsaturated heterocycles, systems that appear to be derived from aromatic heteromonocycles by partial saturation are also named using the trivial names as the parent name alongside prefixes "dihydro"or "tetrahydro“, as appropriate for the degree of saturation.

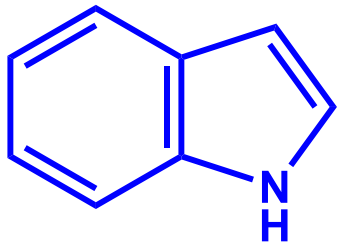




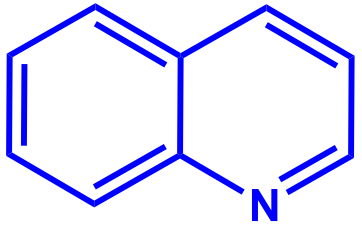
Hantzsch-Widman Nomenclature

Common Names of Aromatic Heterocycles

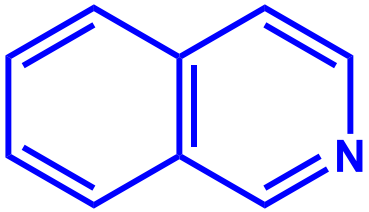
- Other aromatic heterocyclic systems with one heteroatom that have trivial names are shown below.



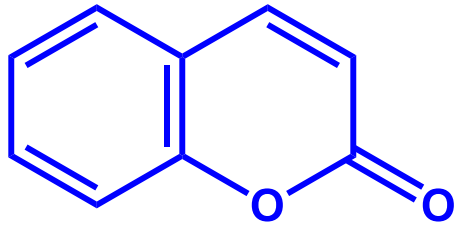
Indole



Quinoline



Isoquinoline



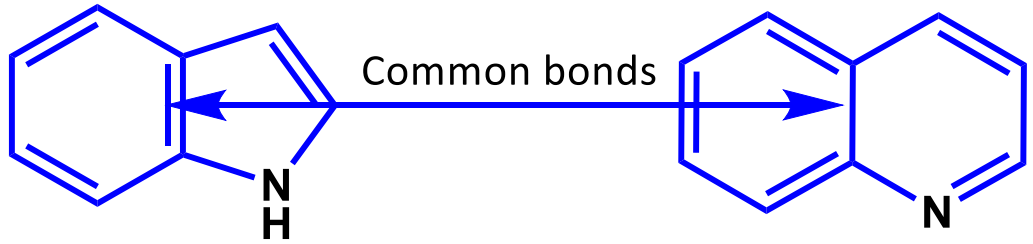
Coumarin

- Some of these heterocyclic systems with trivial names comprise of fused ring systems.
- What are fused ring systems?

Hantzsch-Widman Nomenclature

Fused Ring Heterocycles

- Fused heterocycles are systems constructed by combining two or more cyclic systems.
- The rings are fused if they are linked in such a way that each structural unit has one bond common to each other.
- Moreover, each of the fused ring units should contain a maximum number of non-cumulative double bonds.



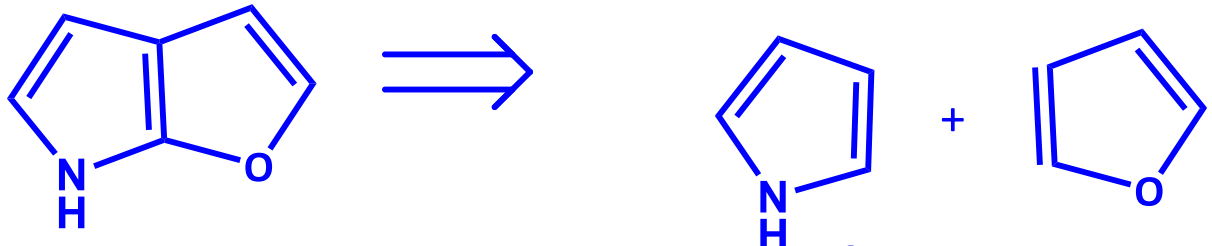
Indole Quinoline

- Can you identify the aromatic rings that fuse to generate indole and quinoline, respectively?
- Suppose indole and quinoline did not have a trivial name, how would one name them and how could this process be extended to name other fused heterocycles?

Hantzsch-Widman Nomenclature

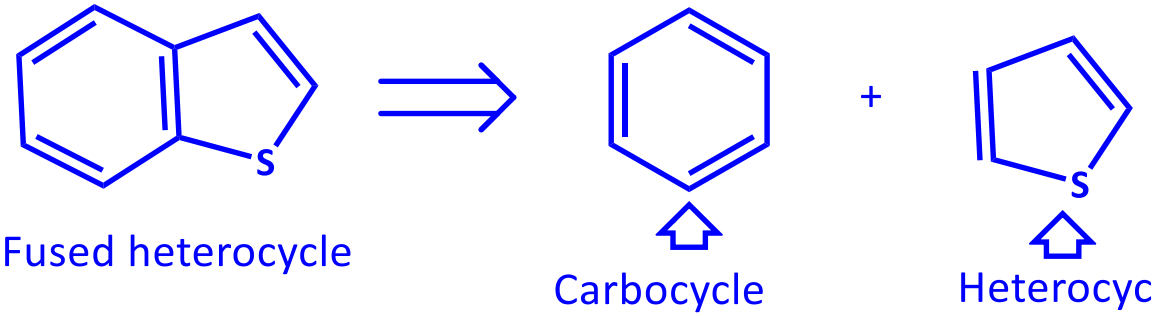
Rules for Fused Aromatic Heterocycles

- To name a fused heterocycle, dissect it into its components to set one as its base component and the other(s) will be designated as attached component(s).



Fused system Components

- The base component should always be a heterocyclic system. The components are given their recognized trivial names (if possible) else, systematic name is used.



Fused heterocycle Carbocycle Heterocycle

Base component = Thiophene

Hantzsch-Widman Nomenclature

Rules for Naming Fused Heterocycles

- To derive the name of the fused heterocycle, the attached component is added as a prefix to the name of the base component.
- The prefix in such names is generated by replacing the terminal ‘e’ in the name of the attached component by ‘o’, i.e. benzo, naphtho and so on.
- The bonds of the base component are alphabetalized with consecutive italic letters starting with ‘*a*’ for the 1,2-bond headed towards the bond of fusion etc.
- The general format for the name of the fused heterocycle is as outlined below.

Name of fused heterocycle = Prefix + [alphabet] + Suffix

Prefix: Attached component; [alphabet]: Fusion bond; Suffix: Base component

Hantzsch-Widman Nomenclature

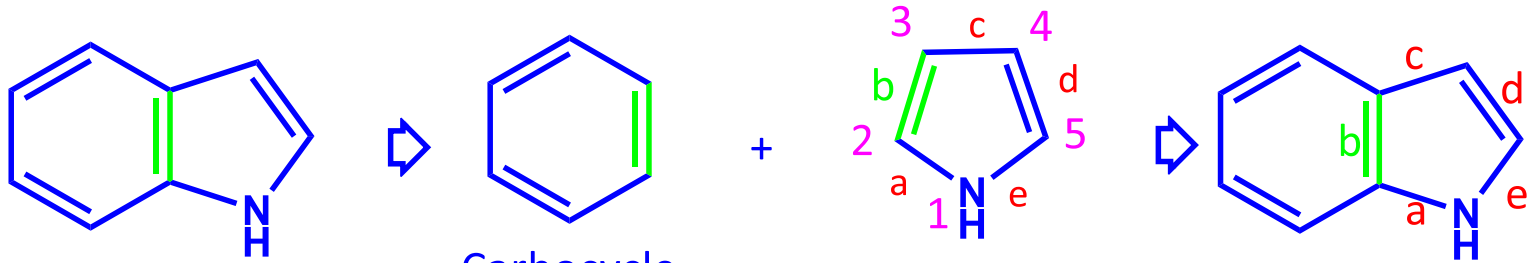
Carbocycle Fused to Heterocycle

- To name a fused heterocycle, derived from the fusion of a carbocycle to a heterocycle:
  i. Derive the parent name (written at the end) from the name of the heterocyclic ring (base component).
  ii. Generate the attached name (written first) from the name of the attached benzene (i.e Benzo).
  iii. The bond of fusion of the parent ring with the attached benzene ring is indicated using alphabetical letters (a, b, c etc) placed in square brackets between the prefix and parent name.
  iv. To determine the alphabet for the bond of fusion, number the parent ring from the heteroatom to the fusion bond such that side 1,2, takes letter (a), side 2,3 takes letter (b), side 3, 4 takes letter (c) etc.

Hantzsch-Widman Nomenclature

Carbocycle Fused to Heterocycle

- To name a fused heterocycle derived from the fusion of a carbocycle to a heterocycle, determine the parent name, the prefix of the attached component and the alphabet of the bond of fusion as illustrated below:



Parent name = Pyrrole

Prefix = Benzo

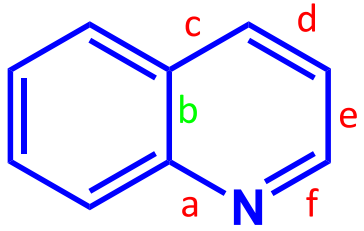
Fusion side = [*b*]

Full name = Benzo[*b*]pyrrole

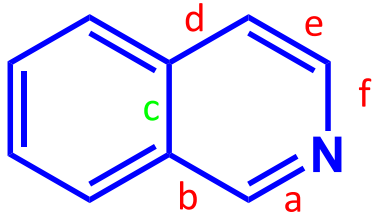
(Trivial name = Indole)

Hantzsch-Widman Nomenclature
Carbocycle Fused to Heterocycle

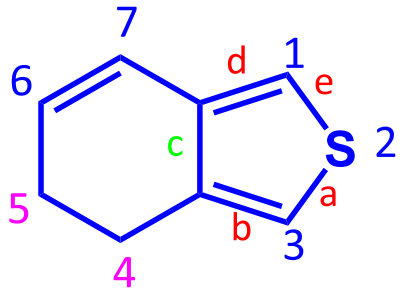
- Following a similar approach, confirm the naming of the fused heterocycles below:



Benzo[*b*]pyridine (Quinoline)



Benzo[*c*]pyridine (Isoquinoline)



4,5-Dihydrobenzo[*c*]thiophene

- Note that when the fused heterocycles are partially saturated or substituted, the total numbering of the complete fused system in done to determine the positions of saturations or substitutions.
- The numbering starts from the atom next to the fusion point giving the hetero atom the least possible numbering and the fused carbons are given the fusion number adding to it letters (a, b, c, etc).

Hantzsch-Widman Nomenclature

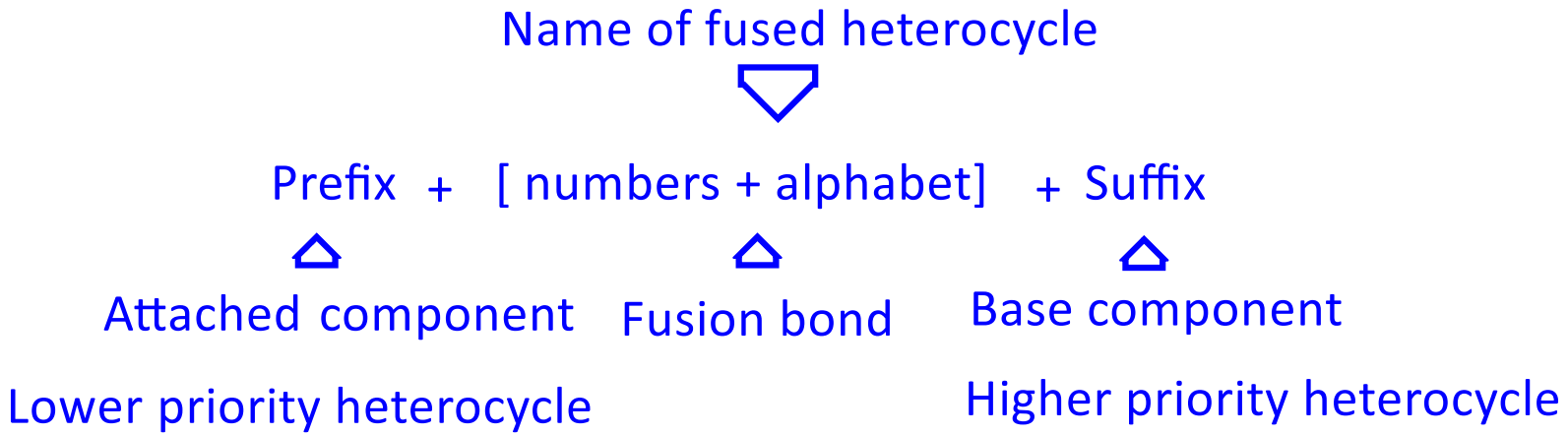
Heterocycle Fused to Another Heterocycle

- The IUPAC nomenclature of such systems is based on:
  i. The parent name (suffix) is given by the higher priority heterocycle.
  ii. The attached ring (s) name is the lower priority ring and is used as the prefix.
- The atoms common to both rings (side of fusion) are indicated by appropriate letters and numbers enclosed in a square bracket and placed immediately after the prefix.
- The numbers (positions of attachment) of the attached component are placed in the sequence in which they are attached to the base component.
- For substituted systems, the numbering of atoms of the attached component is in the normal way 1,2,3….based on the principle of lowest possible numbering.

Hantzsch-Widman Nomenclature

Heterocycle Fused to Another Heterocycle

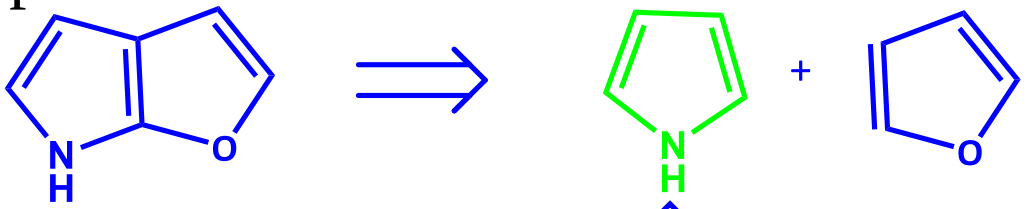
- The general format for capturing the name of a fused heterocycle combining a heterocycle fused to another heterocycle is summarized below:
  i. The parent name given by the higher priority heterocycle is used as suffix.
  ii. The fused ring (s) name is the lower priority ring and is used as prefix.



Hantzsch-Widman Nomenclature

Rules for Fused Aromatic Heterocycles

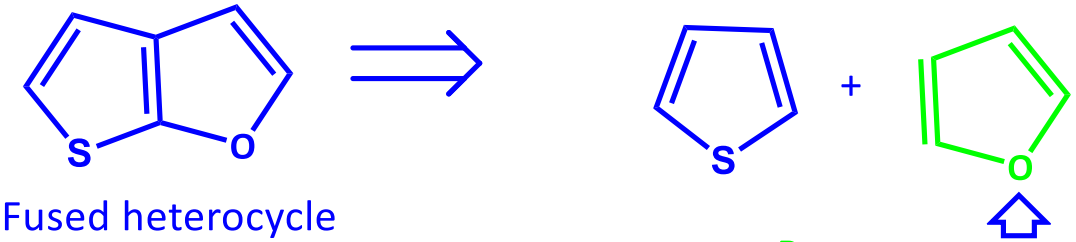
- If there is a choice between different heterocyclic components, nitrogen-containing components take singular precedence over all other heterocycles as the base component.



Fused heterocycle

Base component = Pyrrole

- If nitrogen is absent, then the ring with other heteroatom(s) is selected as base component based on the order of preference (oxygen > sulphur).



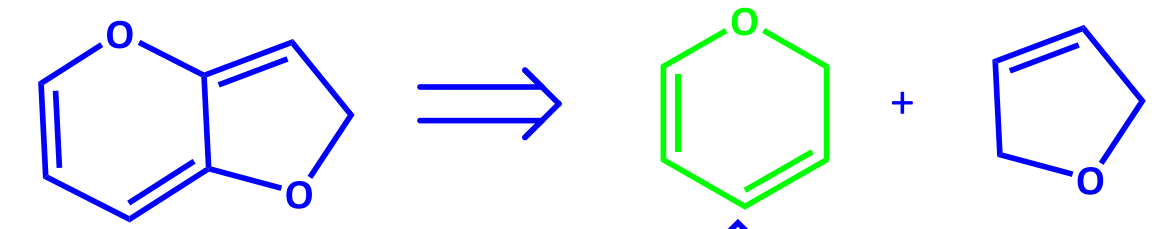
Fused heterocycle

Base component = Furan

Hantzsch-Widman Nomenclature

Rules for Fused Aromatic Heterocycles

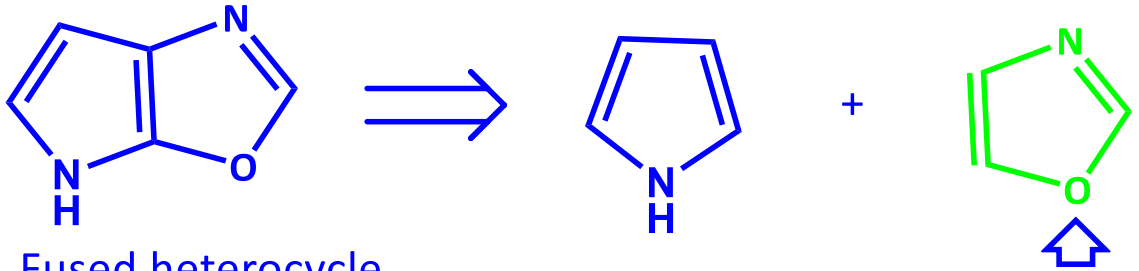
- If components have the same heteroatom, but rings of unequal size are present, then the one with largest size of the ring is selected.



Fused heterocycle

Base component = Pyran

- If rings of equal size with different number of heteroatoms are present, then the ring with greater number of heteroatoms of any kind is considered as a base component.



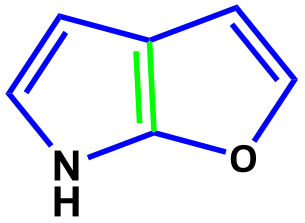
Fused heterocycle

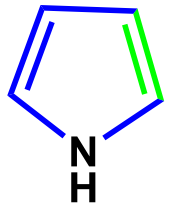
Base component = Oxazole

Hantzsch-Widman Nomenclature

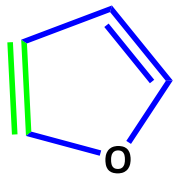
Heterocycle Fused to Another Heterocycle

- Illustrated below is the process of naming a fused heterocycle combining a heterocycle to another heterocycle.



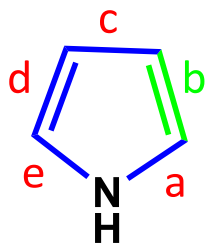


+



Base component

Attached component

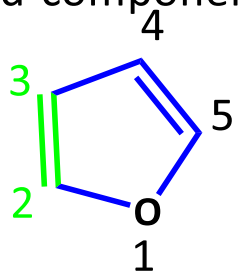


Fusion bond letter

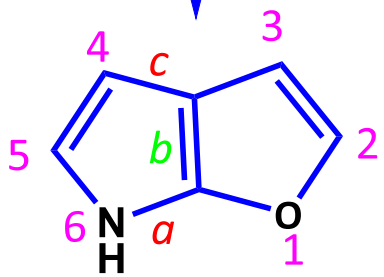
Parent name = Pyrrole

Prefix = Furo

Fusion point= [2.3-*b*]



Fusion bond number

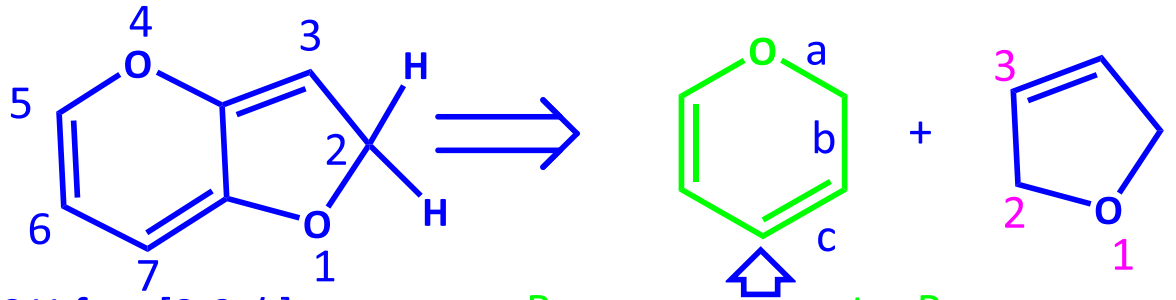


6*H*-furo[2,3-*b*]pyrrole

Hantzsch-Widman Nomenclature

Fused Aromatic Heterocycles

- The common prefixes for the heterocycles are:
  - ✓Furan = furo
  - ✓Thiophene = thieno
  - ✓Pyridine = pyrido
  - ✓Pyrrole = pyrrolo
  - ✓Imidazole = imidazo
- If the fused heterocycle comprises of a partially saturated heterocycle, the position of the saturated atom is indicated by an italicized hydrogen and is given the lowest possible number locant.



2*H*-furo[3,2-*b*]pyran

Base component = Pyran