Organic chemistry

Heterocyclic Chemistry (1)

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1. Introduction to Heterocycles

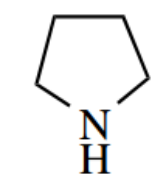
- **A heterocycle** is a ring that contains atoms of more than one element.
- Common organic heterocycles are comprised of carbon and either nitrogen, oxygen, or sulfur.
- Many different kinds of heterocycles are commonly found in the structures of biological molecules and pharmaceuticals.

1. Introduction to Heterocycles

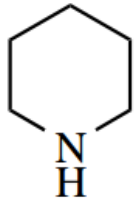
Heterocycles are divided into:

a) Aliphatic heterocycles:

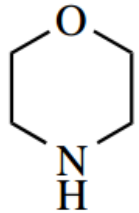
They are very similar to their open-chain aliphatic analogues



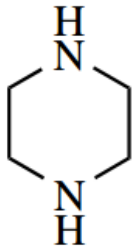
pyrrolidine



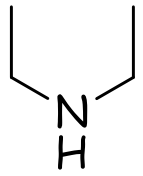
piperidine



morpholine

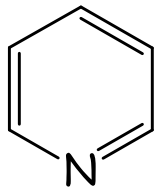


piperazine

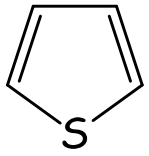


diethylamine

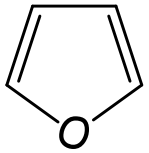
b) Aromatic Heterocycles:



pyridine



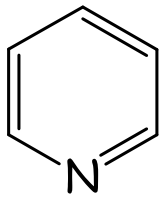
thiophene

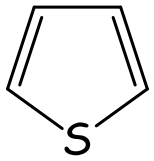


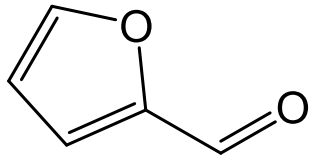
furan

2. Nomenclature of Heterocycles

- **Trivial names**: long time ago some heterocyclic compounds were given names related to their natural source or method of preparation (e.g. furfural), properties (e.g. thiophene) or both (e.g. pyridine).
- **IUPAC** (systematic or chemical) names.







Trivial name:	Pyridine	Thiophene	Furfural
IUPAC name:	(azine)	(Thiole)	(furan-2-carbaldehyde)

- IUPAC rules still permit the use of several trivial names

2. Nomenclature of Heterocycles

Nomenclature of Monocyclic Heterocycles

The name of monocyclic Heterocycles consists of three parts:

1- Prefix 2- stem 3-suffix

1-the prefix:

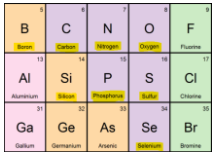
- It indicates the type, numbers and positions of the heteroatom,
- If the heteroatoms are different, their order of naming will be according this priority: **O** > **S** > Se > **N** > P > Si >…..etc.

2-the stem: It determines the ring size. OSmaN

3-the suffix: It determines the degree of unsaturation

2. Nomenclature of Heterocycles

Table 1: Prefixes in Descending Priority order



Element	Valence	Prefix	Order of priority
Oxygen	2	Oxa	1
Sulfur	2	Thia	2
Selenium	2	Selena	3
Nitrogen	3	Aza	4
Phosphorus	3	Phospha	5
Silicon	4	Sila	6
Boron	3	Bora	7

The last letter (a) in oxa, thia, aza…..etc is omitted if followed by a vowel.

2. Nomenclature of Heterocycles

Table 2: (Stem + suffix) indicating ring size and unsaturation

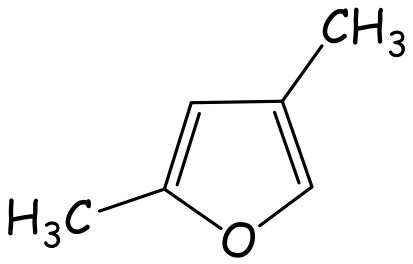
Ring size	Stem	Stem + suffix			
		Containing nitrogen		Containing no nitrogen	
		Maximum unsaturation	Saturation	Maximum unsaturation	Saturation
3	ir	irine	iridine	irene	irane
4	et	ete	etidine	ete	etane
5	ol	ole	olidine	ole	olane
6	in	ine	Perhydro[a]	ine	ane
7	ep	epine	Perhydro[a]	epine	epane

[a] The prefix “Perhydro” is attached to the name of the corresponding unsaturated compound.

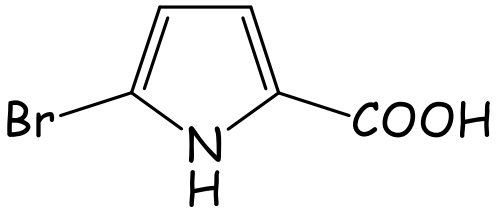
2. Nomenclature of Heterocycles

Numbering of the monocycles

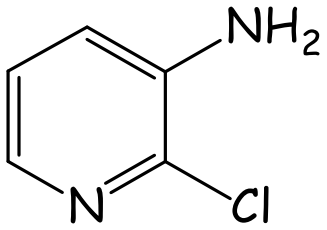
1. Numbering starts from heteroatom and proceeds around the ring so as to give substituents the least possible number. Substituents are indicated in alphabetical order.



2,4-dimethyloxole



5-bromo-1*H*-pyrrole
-2-carboxylic acid

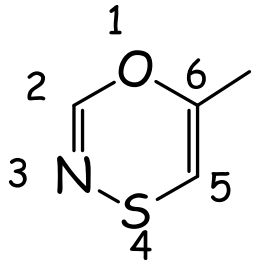


3-amino-2-chloroazine

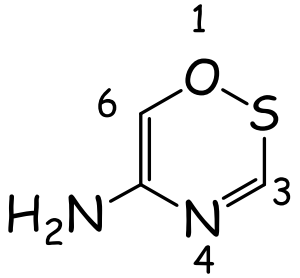


2. Nomenclature of Heterocycles

2. Numbering begins at the atom of higher order of priority (O > S > N) and proceeds to give the second heteroatom the lowest possible number.



6-methyl-1,4,3-oxathiazine



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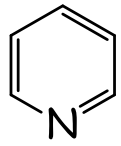
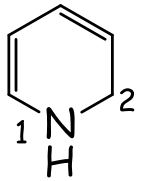
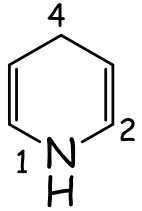
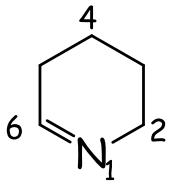
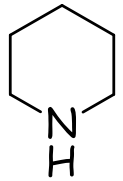
3. In partially unsaturated rings, prefix 1,2-dihydro, trihydro, …etc. is added to the name of unsaturated ring. The saturated positions are given the lowest numbers after the heteroatom.







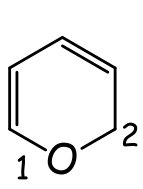


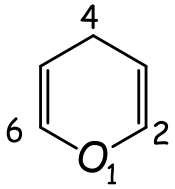


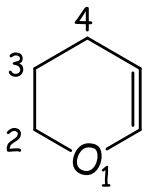
IUPAC:	Azine	1,2-dihydroazine	1,4-dihydroazine	----------	Perhydroazine
Trivial:	Pyridine	1,2-dihydropyridine	1,4-dihydropyridine		Piperdine

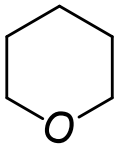
2. Nomenclature of Heterocycles

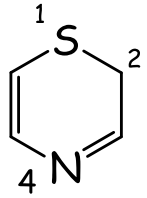
4. Obligatory saturation of a <u>single</u> position is indicated by its number followed by the symbol *H* (e.g. 1*H*, 2*H*, 3*H*, ….etc).







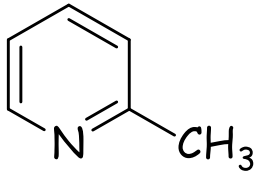




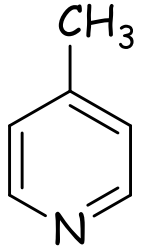
IUPAC: 2*H*-oxine 4*H*-oxine 3,4-dihydro-2*H*-oxine Oxane 2*H*-1,4-thiazine

Trivial: 2*H*-Pyran 4*H*-Pyran

5. Monomethylpyridines are called **picolines.**



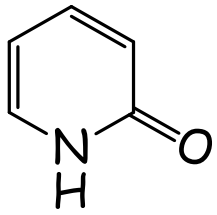
α-Picoline



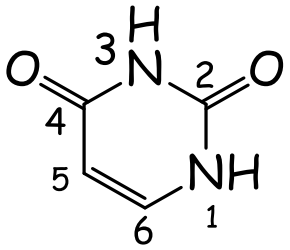
γ -Picoline

2. Nomenclature of Heterocycles

6. The presence of a carbonyl group is indicated by a suffix one and its position by a number.



Dihydropyridin-2-one



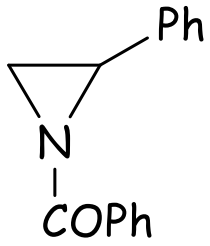
1,2,3,4-Tetrahydropyrimidine-2,4-dione
(Uracil)

2. Nomenclature of Heterocycles

- More examples of **3** and **4** membered rings heterocycles:





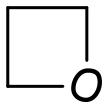


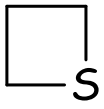
IUPAC: Oxirane

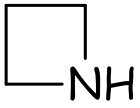
Trivial: (ethylene oxide)

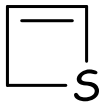
(ethylene imine)

1-Benzoyl-2-phenyl aziridine



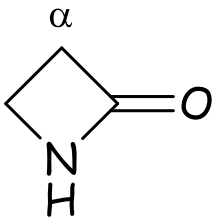


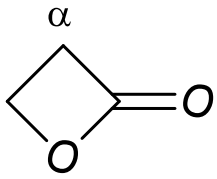




Oxetane

Azetidine





IUPAC: Azetidine-2-one

Trivial: (β- propiolactam)

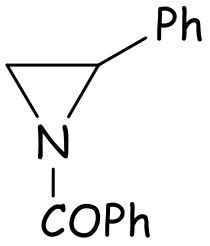
(β- propiolactone)

2. Nomenclature of Heterocycles

- More examples of **3** and **4** membered rings heterocycles:



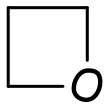


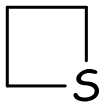


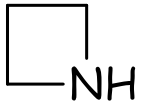
IUPAC: Oxirane
Trivial: (ethylene oxide)

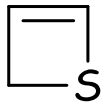
Aziridine
(ethylene imine)

1-Benzoyl-2-phenyl aziridine







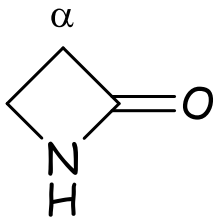


Oxetane

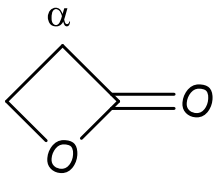
Thietane

Azetidine

2*H*-thiete



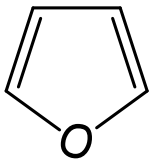
IUPAC: Azetidine-2-one
Trivial: (β- propiolactam)

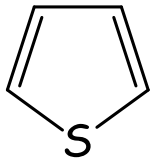


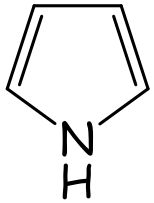
Oxetane-2-one
(β- propiolactone)

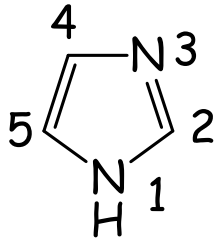
2. Nomenclature of Heterocycles

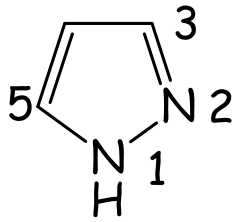
- More examples of <u>unsaturated</u> **5** membered rings heterocycles:





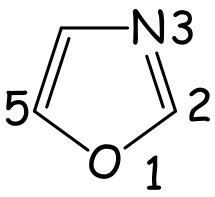


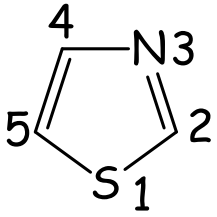


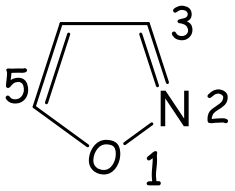


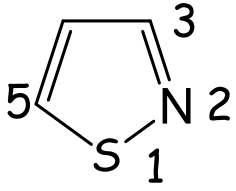
IUPAC: Oxole ..... 1*H*-Azole 1*H*-1,2-diazole

Trivial: (furan) (thiophene) (pyrrole) (imidazole) (Pyrazole)







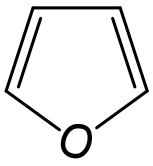


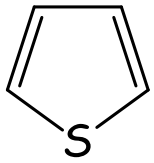
IUPAC: 1,3-oxazole 1,2-thiazole

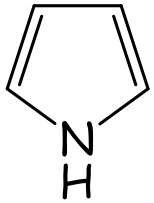
Trivial: (oxazole) (thiazole) (Isoxazole) (Isothiazole)

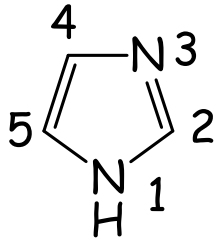
2. Nomenclature of Heterocycles

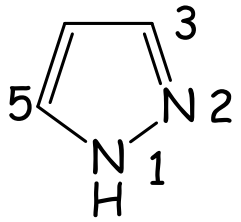
- More examples of <u>unsaturated</u> **5** membered rings heterocycles:





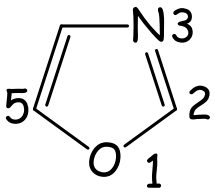


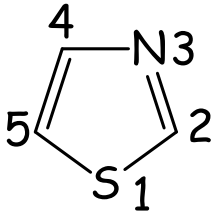


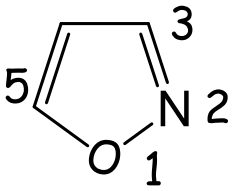


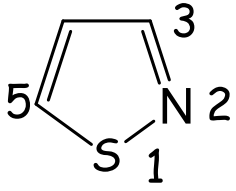
IUPAC: Oxole — Thiole — 1*H*-Azole — 1*H*-1,3-diazole — 1*H*-1,2-diazole

Trivial: (furan) — (thiophene) — (pyrrole) — (imidazole) — (Pyrazole)







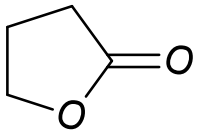


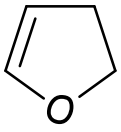
IUPAC: 1,3-oxazole — 1,3-thiazole — 1,2-Oxazole — 1,2-thiazole

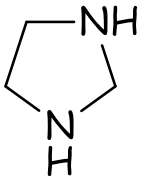
Trivial: (oxazole) — (thiazole) — (Isoxazole) — (Isothiazole)

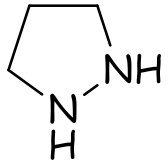
2. Nomenclature of Heterocycles

- More examples of <u>saturated</u> **5** membered rings heterocycles:



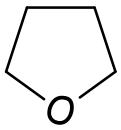


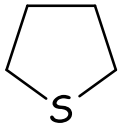


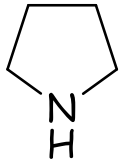


IUPAC: Oxolane-2-one ..... 1,3-diazolidine .....

Trivial: (imidazolidine) (pyrazolidine)

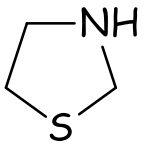


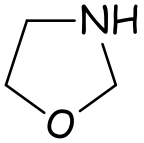


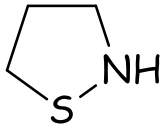


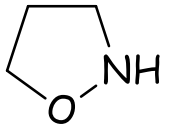
IUPAC: ..... Thiolane .....

Trivial: (tetrahydrofuran) (pyrrolidine)







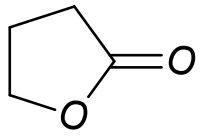


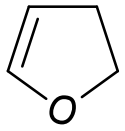
IUPAC: 1,3-thiazolidine ..... 1,2-thiazolidine .....

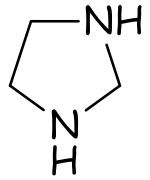
Trivial: (thiazolidine) (oxazolidine) (isothiazolidine) (isoxazolidine)

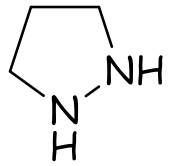
2. Nomenclature of Heterocycles

- More examples of <u>saturated</u> **5** membered rings heterocycles:







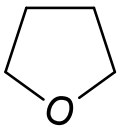


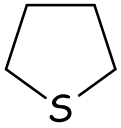
IUPAC: Oxolane-2-one
Trivial: (γ-butyrolactone)

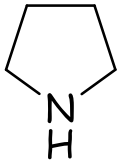
2,3-Dihydrofuran

1,3-diazolidine
(imidazolidine)

1,2-diazolidine
(pyrazolidine)



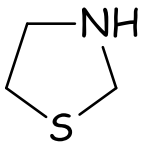


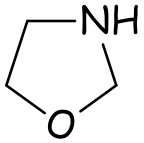


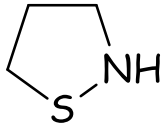
IUPAC:
Trivial: Oxolane
(tetrahydrofuran)

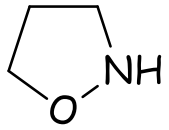
Thiolane

Azolidine
(pyrrolidine)









IUPAC: 1,3-thiazolidine
Trivial: (thiazolidine)

1,3-oxazolidine
(oxazolidine)

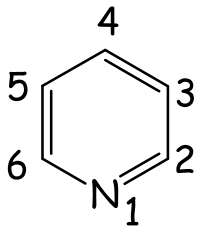
1,2-thiazolidine
(isothiazolidine)

1,2-oxazolidine
(isoxazolidine)

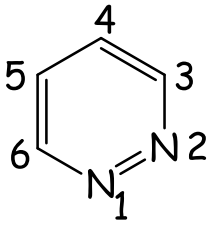
2. Nomenclature of Heterocycles

- More examples of **6** membered rings heterocycles:

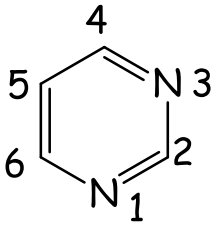
Unsaturated



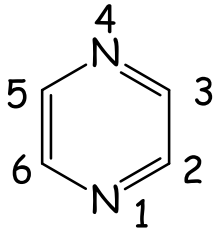
azine
(pyridine)



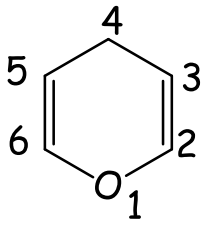
(pyridazine)



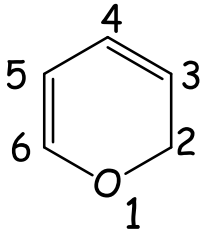
1,3-diazine
(pyrimidine)



(pyrazine)

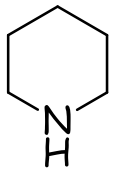


4*H*-oxin
(4*H*-pyran)

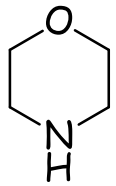


(2*H*-pyran)

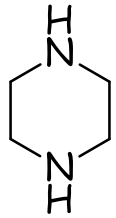
Saturated



perhydroazine
(Piperidine)



(morpholine)

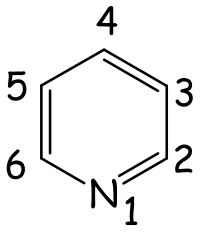


perhydro-1,4-diazine
(piperazine)

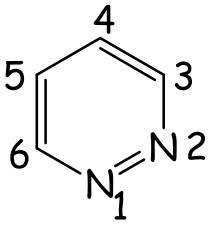
2. Nomenclature of Heterocycles

- More examples of **6** membered rings heterocycles:

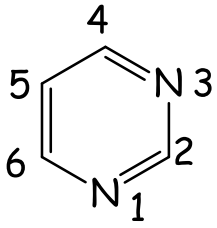
Unsaturated



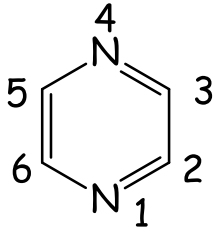
azine
(pyridine)



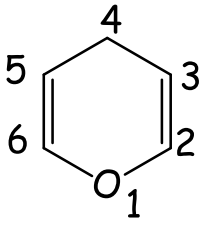
1,2-diazine
(pyridazine)



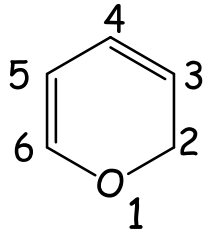
1,3-diazine
(pyrimidine)



1,4-diazine
(pyrazine)

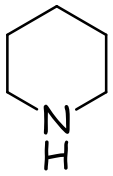


4*H*-oxin
(4*H*-pyran)

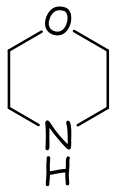


2*H*-oxin
(2*H*-pyran)

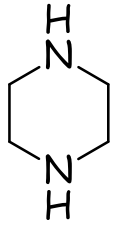
Saturated



perhydroazine
(Piperidine)



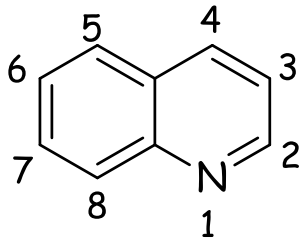
1.4-oxazinane
(morpholine)



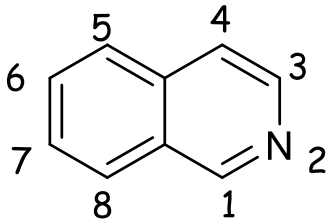
perhydro-1,4-diazine
(piperazine)

2. Nomenclature of Heterocycles

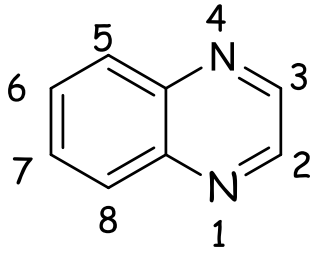
- The most important heterocycles having accepted trivial names are the following:



(Quinoline)



(Isoquinoline)



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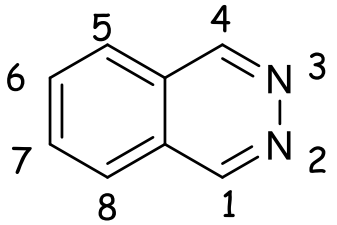
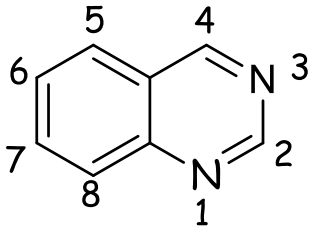


(Phthalazine)



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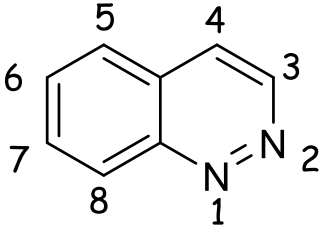
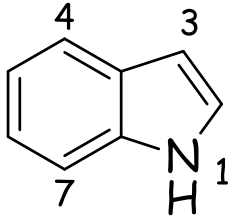


(cinnoline)



(1*H*-Indole)