

Chemistry of Heterocyclic Compounds

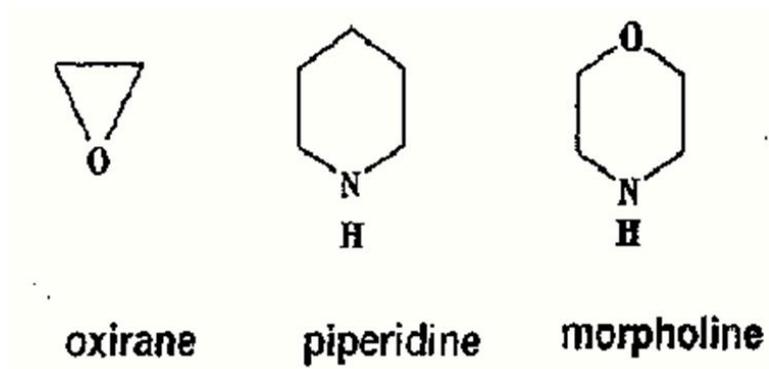
What's Heterocyclic Compound?

A heterocyclic compound is one that contains rings made up, in addition to carbon, one or more heteroatoms like O, N, S, P.... etc.

Heterocyclic compounds can be classified into

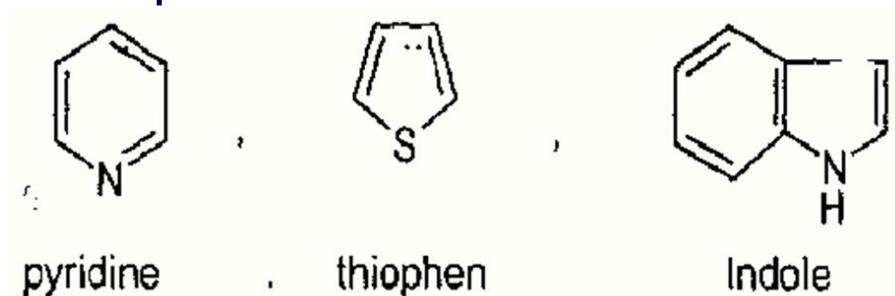
1) aliphatic heterocycles::

Examples



2) Aromatic heterocycles:

Examples



NOMENCLATURE OF HETEROCYCLES

type of the heteroatom, their

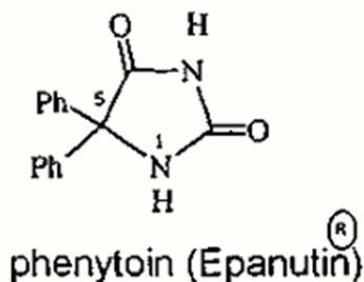
numbers and their positions. (Table I):

When two or more heteroatom of same type are present, the prefix di, tri,...etc. is used.

If the heteroatoms are different, their order of citation start with the heteroatom of as high a group in the periodic table and as low an atomic number in that group. Thus the order of naming will be: O > S > Se > N > P > Si > B > Hg etc (see table I):

a- Trivial names:

b- Generic names, and Trade names:



C- IUPAC (or systemic or chemical name):

B-Nomenclature of non Fused Heterocycles

Prefix + stem + suffix

1- The Prefix

Table I : prefix name of heteroatoms and their order of priority:

Heteroatom	Prefix name	order of priority
Oxygen	Oxa	1
Sulphure	thia	2
Selenium	selena	3
Nitrogen	aza	4
Phosphorus	phospha	5
Silicon	sil	6
Boron	Bora	7
Mercury	mercura	8

A Reference book of such IUPAC nomenclature outlined here is:
 CRC Handbook of Chemistry and Physics by Robert. C.W and Melvin.
 J. A. 60th edition. 1979-1980 p. (C33-C44)

2-The stem

It determines the ring-size from 3 membered ring to 10

membered ring.

Table II:

Ring Size	stem
3:	ir (from tri)
4:	et (from tetra)
5:	ol
6:	in
7:	ep (from hepta)
8:	oc (from octa)
9:	on (from nona)
10:	ec (from deca)

3- The Suffix

It determines the state of saturation or unsaturation which depends upon

(i) the presence or absence of N and

(ii) the ring size.

saturation or unsaturation state

(Table III): saturation and unsaturation state.

Ring size	Stem	stem + Suffix			
		N: present		N: absent	
		unsat.	sat.	unsat	sat.
3	ir	irine	iridine	irene	irane
4	et	ete	etidine	ete	etane
5	ol	ole	olidine	ole	olane
6	in	ine	a	in ^(b)	ane ^(c)
7	ep	epine	a	epin	epane
8	oc	ocine	a	ocin	ocane
9	on	onine	a	onin	onane
10	ec	ecine	a	ecin	ecane

Table III (cont):

a: The complete saturation is indicated by prefixing "perhydro " added before the total name of the unsaturated state.

b: no suffix

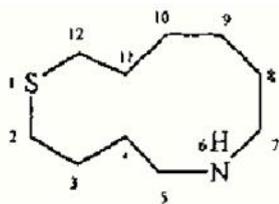
c: no stem

N.B: If the ring size is more than 10, use the carbocyclic

monocyclic name and the heteroatom is indicated by prefixes:

Oxa, thia, aza

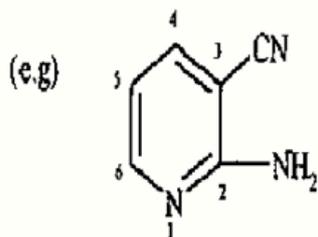
Example



1 - Thia - 6 - azacyclododecane
(1, 6 - Thiazacyclododecane)

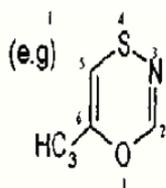
Manner of numbering of the monocycles

Monocycles containing one heteroatom, are numbered beginning at the heteroatom and the substituents takes the least possible number:

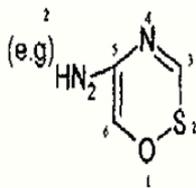


Rule 2

Cycles containing more than one different heteroatoms the numbering begins at the atoms of the higher order of priority (shown in table I) and proceeds round the ring in order to give other heteroatoms the least possible numbers without regards to the substituents;



6-Methyl-1,4,3-oxathiazine

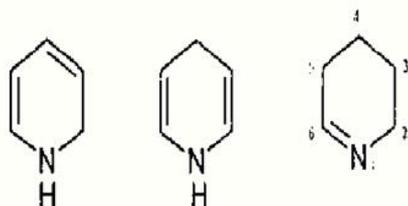


5-Amino-1,2,4-oxathiazine

Nomenclature of Partially Saturated Ring

Rule 1

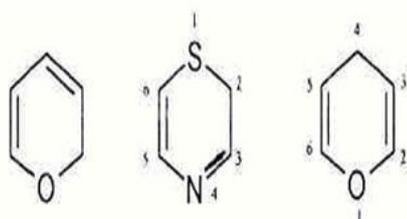
If the number of double bonds is less than the maximum, prefix dihydro tetrahydro,.... etc are added to the same name of unsaturated state. The saturated positions are given the least numbers after the hetero atom.



1,2-dihydroazine 1,4-dihydroazine 2,4,5,6-tetrahydroazine

Rule 2

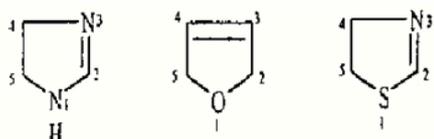
Obligatory saturation of a single position is indicated by a symbol 1H, 2H, 3H... etc. according to the position of the saturated atom



2H-Oxin (2H-pyran) 2H-1,4-thiazine 4H-pyran

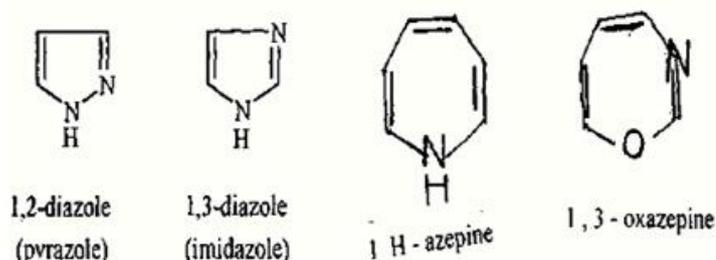
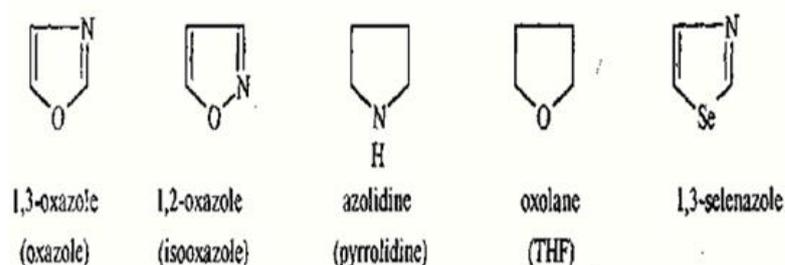
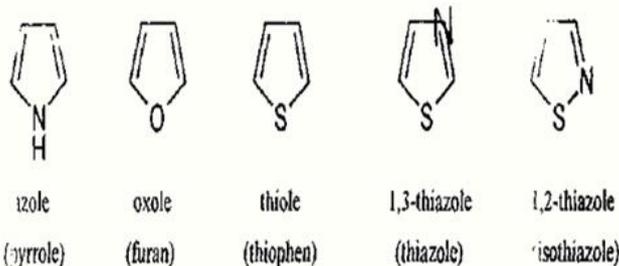
Rule 3

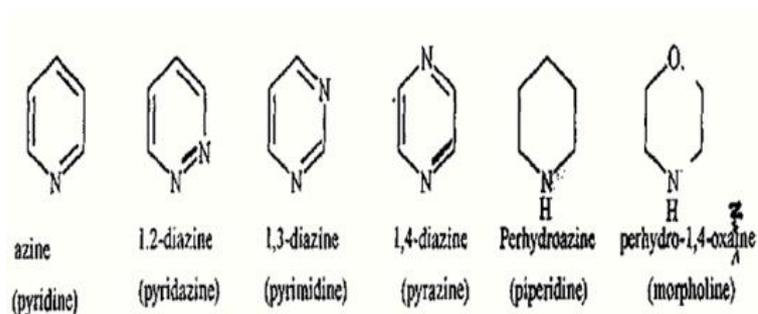
In case of 4 & 5 membered rings with partial saturation (i.e) contain only one double bond. The suffix will be (ine) when N is present and (ene) when N is absent, and indicate the position of the double bond over A symbol.



Δ^2 -1,3-diazoline Δ^2 -oxolene Δ^2 -thiazoline
(Δ^2 -imidazoline)

The following are the IUPAC and trivial names of most monocycles





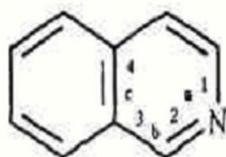
B-Nomenclature of Fused Heterocycles

(B I) Carbocycle fused with heterocyclic system.

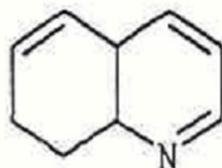
(B II) Heterocycle fused with another heterocyclic system

I-Nomenclature of Carbocycle fused with Heterocycles IUPAC name:

1. The Parent name (written at the end) is the name of the heterocyclic ring.
2. The fused name (written at first) is the name of the fused benzene called (Benzo)
3. The Side of fusion of the parent ring with the fused benzene ring is indicated by alphabetical numbering and put such letter (a, b, c, ... etc) between square brackets in between the prefix and parent name. In this case the parent ring is numbered as usual (p 5) and the sides 1,2, take letter (a), side 2,3 takes letter (b), side 3, 4 takes letter (c), ... etc



benzo (C) pyridine



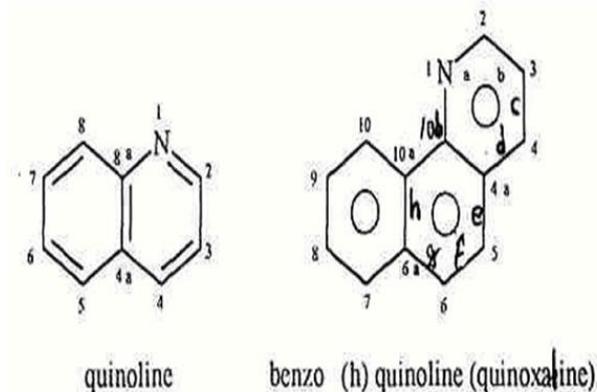
benzo (b) pyridine

- 4- The total numbering of the complete fused system is done to determine the positions of saturations or substitutions according to the following rules:

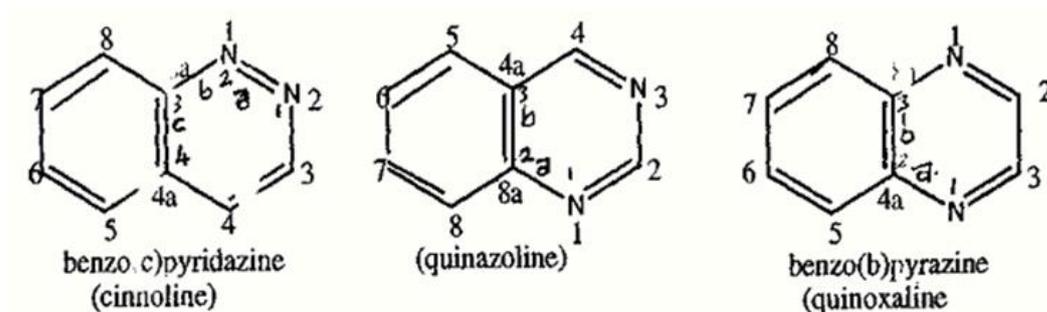
a- The fused system is oriented so that:
The greatest number of ring is in a horizontal row, and the remaining rings above the right of this horizontal row.

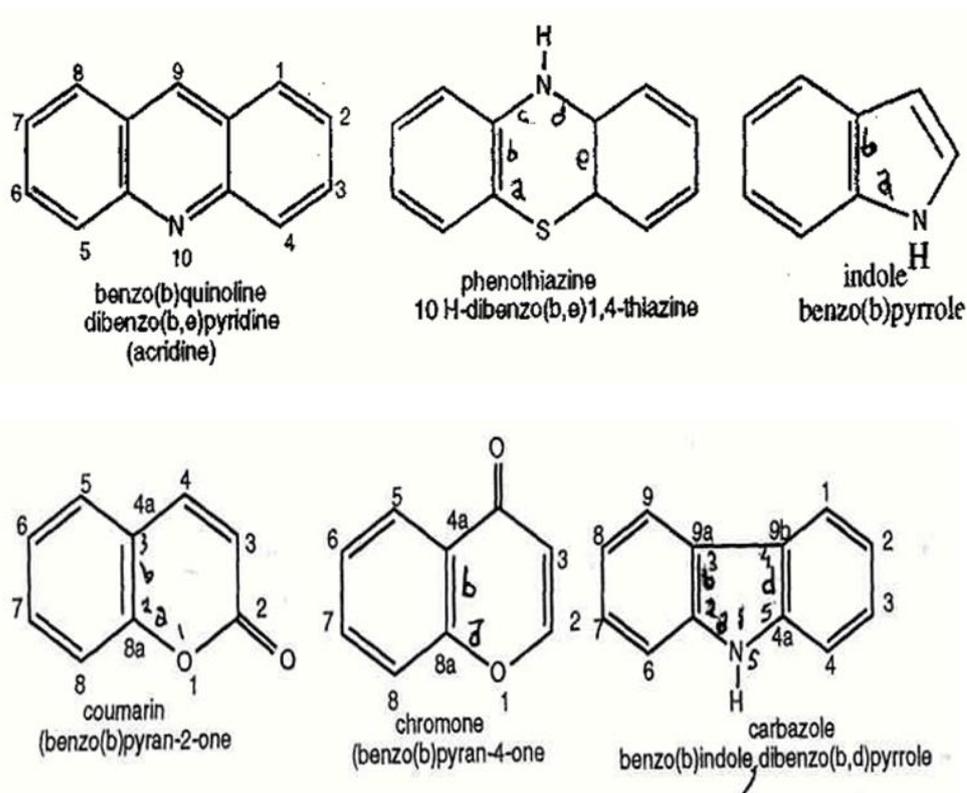
b- The numbering starts from the atom next to the fusion giving the hetero atom the least possible numbering and continue numbering in clockwise direction (whenever possible) and the fused carbons are given the same previous number adding to it letters (a, b, c, etc).

c- In case of poly cycles, the parent name is given to the largest heterocycles containing many rings (provided it has a famous trivial name).



The following are the agreed trivial and IUPAC names of the some of the famous carbocycles fused with hetero cycle :





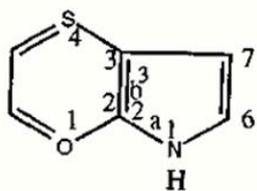
(II) Nomenclature of Heterocycle fused with another Heterocycles

The IUPAC rules for naming such systems are also composed of 4 points:

- 1- The Parent name given to the more prior heterocycle(s), is used as suffix.
- 2- The fused ring (s) name is the less prior rings and is used as prefix.
- 3- The side of fusion for both rings.
- 4- The numbering of the total system.

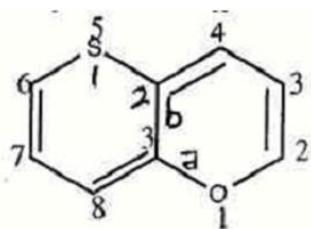
1. The selection of the parent ring(s) (as suffix) should be according to the following order of preferences

i- The Nitrogen containing ring must be taken as a parent ring:



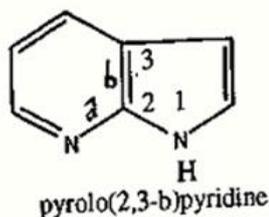
1,4-oxathiazino(2,3-b)pyrrole

ii- If no Nitrogen, the ring contain the more prior heteratom (according to table I), is considered as a parent ring:

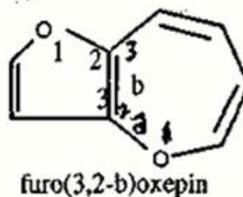


thiino(2,3-b)pyran

iii) The largest ring size is taken as a parent ring if the two rings contain N or does not contain N.

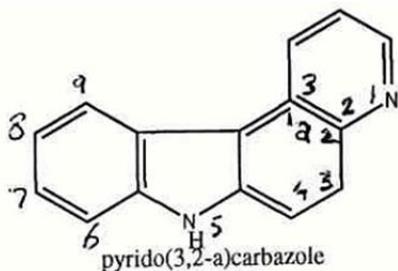


pyrolo(2,3-b)pyridine



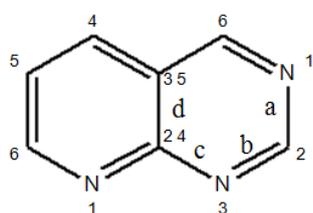
furo(3,2-b)oxepin

iv) The largest number of rings with famous trivial name is always used as parent name:

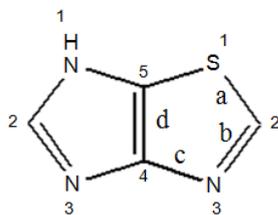


pyrido(3,2-a)carbazole

v) The ring containing the greatest number of hetero atoms or greatest varieties of heteroatoms is the parent ring:

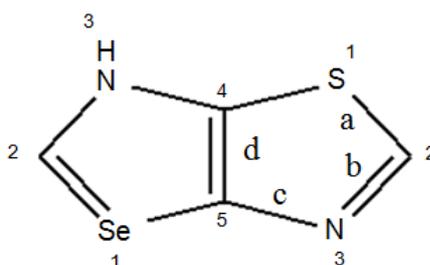


pyrido(2,3-d)pyrimidine



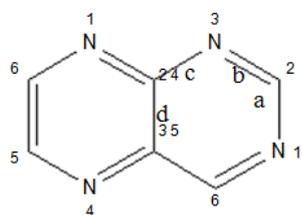
imidazo(4,5-d)thiazole

vi) A component ring having the more prior heteroatom (according table I) is the parent ring:

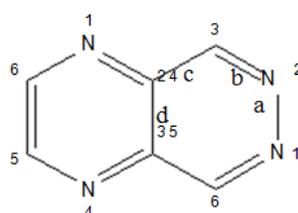


selenazolo(5,4-d)thiazole

vii) The parent ring is the ring containing a more number of carbon atoms adjacent to the fusion:



pyrazino(2,3-d)pyrimidine



pyrazino(2,3-d)pyridazine

2- The naming of the prefix of fused (less prior) heterocycles is given as such:

Furan = furo

Thiophene = thieno

Pyridine = pyrido

Pyrrole = pyrrolo

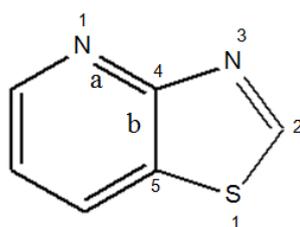
Imidazole = imidazo

Quinoline = quino

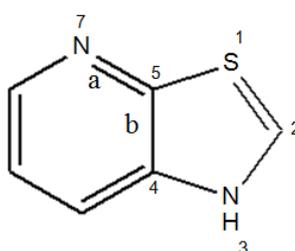
3- Determination of the sides of fusion for both sides of the two fused heterocycles as such:

a- The side of fusion with the parent ring is numbered alphabetically and the letter of fusion is placed between square brackets at its end.

b- The side of fusion of the prefix ring is indicated by two numbers denoting the two positions of fusion with the parent ring, these two numbers are also placed at first in the square brackets. The order of writing these two numbers conforms the direction of lettering of the parent ring.



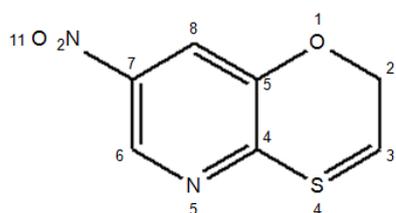
thiazolo(4,5-b)pyridine



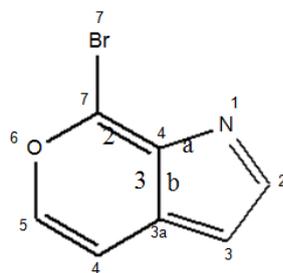
thiazolo(5,4-b)pyridine

4-The peripheral numbering of the total heterocyclic fused molecule is by the same discussed rule (page 5), and considering the following other rules

A) Give the lowest number to the more prior heteroatom (according to table I) especially when present just after fusion. But, if the more prior heteroatom is not the nearest to the fusion side the other nearest heteroatoms after fusion must take the least possible numbering regardless of priority of table I.

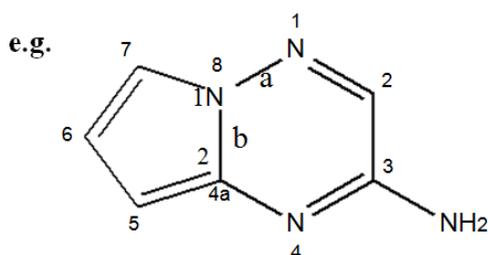


7-nitro-[1,4]oxathiino[3,2-b]pyridine



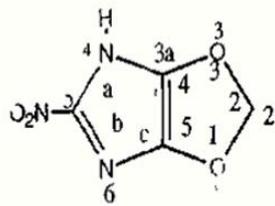
7-bromo pyrano[3,4-b]pyrrole

b) The heteroatoms in the fusion side are numbered according to the sequence of numbering, but when carbon atoms in the fusion take the previous number plus letter a, b, c,...etc. and also such carbon atom follow the least possible numbering:

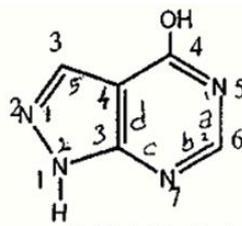


3-amino pyrolo[1,2-b][1,2,4]triazine

c) The saturated atoms take the least possible numbering before other substituents.

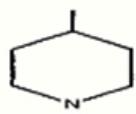


5-nitro-2H,4H,1,3-dioxo[4,5-d]imidazole

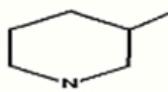


1H-pyrazolo[3,4-d]pyrimidin-4-ol
(Zyluric or Nouric)

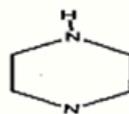
Radicals Derived from Heterocyclic Compounds



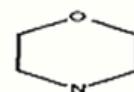
4-piperidinyl



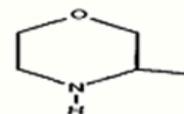
3-piperidinyl



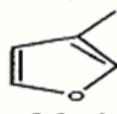
piperazino



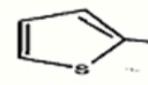
morpholino
4-morpholinyl



3-morpholinyl

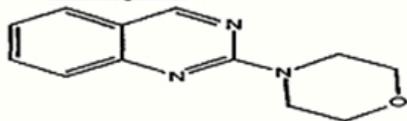


3-furyl

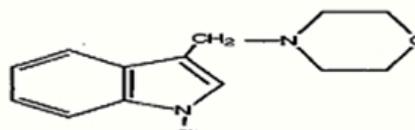


2-thienyl

Examples:



2-morpholino quinazoline



3-(morpholinomethyl) indole



Nor-nicotine
3(2-pyrolidinyl) pyridine