Heterocyclic Nomenclature (from Gilchrist, T. L. *Heterocyclic Chemistry*; Longman; London, 1992)

The Hantzsch-Widman nomenclature system is the standard method for naming heterocyclic rings. A heterocycle is defined as a ring that contains one or more atoms that is different from ('hetero') carbon. We will most commonly see nitrogen heterocycles. Just as with all cyclic compounds, heterocycles may be aromatic or not aromatic based on the Hückel's rule ($4n+2$).

The Hantzsch-Widman system accomplishes several tasks. First, the identity of the different atoms is established by placing different prefixes for each type of non-carbon atom. The three prefixes we will encounter are oxa-, thia-, and aza- for oxygen, sulfur, and nitrogen, respectively. Second, the position of the heteroatoms is denoted by ring atom numbers. Third, the size and degree of unsaturation of the ring is determined by the suffix at the end.

Table. Listing of common Hantzsch-Widman suffixes.

ring size	unsaturated ring	unsaturated ring with nitrogen	saturated ring	saturated ring with nitrogen
3	-irene	-irine	-irane	-iridine
4	-ete		-etane	-etidine
5	-ole		-olane	-olidine
6	-ine		-inane (-ane)	
7	-epine		-epane	
8	-ocine		-ocane	
9	-onine		-onane	
10	-ecine		-ecane	

A few examples of applying these nomenclature ideas are shown below.

1.  , aziridine

   This ring contains nitrogen (prefix is aza-) and is a three-membered ring that is completely saturated (-iridine). Remember that nitrogen-containing rings often require a slightly different suffix. When combining the prefixes and suffixes, two vowels can end up together. In this case we seem to have azairidine. When this happens, drop the vowel on the end of the first part. This gives aziridine after dropping the second 'a' of aziridine.

2.  , 1,2-oxazetidine

   This ring contains nitrogen (aza-) and oxygen (oxa-) and is a fully saturated four-membered ring (-etidine). Atom prefixes have a strict order in which they are to be listed. For the three atoms we will see, the order is oxygen followed by sulfur followed by nitrogen. So, after dropping the appropriate vowels, we get oxazetidine. Note that if there are two atom prefixes, vowels will be dropped by the earlier prefix. The numbers are placed in order of the prefixes with priority of the numbers being the same as the order of the prefixes. Oxygen is in position 1, and nitrogen is next door and is therefore in position 2. This gives 1,2-oxazetidine.

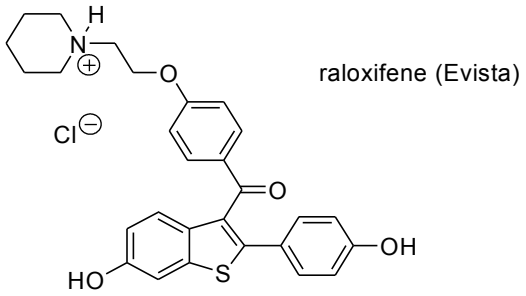
3.  , 1,2,5-oxadiazole

Again, we have nitrogen (aza-) and oxygen (oxa-). Unsaturated five-membered rings with nitrogen have the –ole suffix. Since there are two nitrogens, we need a di- in front of aza-. Oxygen comes before nitrogen, so we have oxadiazole. Note that the 'a' in oxa- is not dropped since there are not two vowels together. Oxygen is higher priority than nitrogen, so it is in position 1 by default. The two nitrogens are therefore at positions 2 and 5. This gives 1,2,5-oxadiazole.

4.  , 1,3-oxathiolane

Prefixes of oxa- and thia- with a suffix of –olane initially gives oxathiolane. Oxygen takes priority in numbering to give 1,3-oxathiolane.

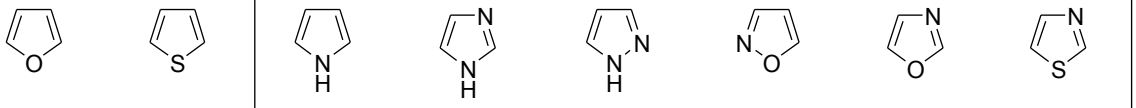
While drugs are not named by Hantzsch-Widman rules, bits and pieces of the naming system are often apparent in the common name of a drug. The trade names of drugs rarely have any relationship to the structure since the trade names are created by marketing departments. For example, Eli Lilly's osteoporosis drug has a common name of raloxifene while the trade name is Evista. In this case, the 'fene' in the common name is almost certainly a carry over from the thiophene ring in the structure of the drug. This example is fairly subtle. The common names of many drugs have –ole or some other Hantzsch-Widman prefix that will give a clue to the size of rings or atoms in the drug structure.



raloxifene (Evista)

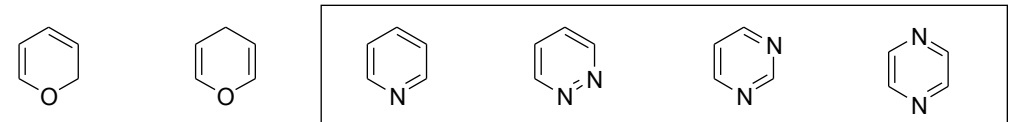
Not all heterocyclic rings follow the Hantzsch-Widman rules listed above. These trivial names typically show traces of the systematic nomenclature, but do not completely follow the rules. Examples of names and structures of these compounds are on the following page. The aromatic nitrogen five- and six-membered rings still have the correct suffixes, -ole and -ine, respectively. Thiazole only lacks the atom numbers to get to the systematic name, 1,3-thiazole. Other examples are completely different. Thiophene would be thiole under the systematic nomenclature.

common azoles - five-membered aromatic nitrogen heterocycles



furan | thiophene | pyrrole | imidazole | pyrazole | isoxazole | oxazole | thiazole

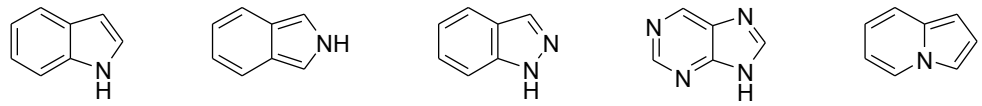
common azines - six-membered aromatic nitrogen heterocycles



furan (2*H*-furan) | 4*H*-furan | pyridine | pyridazine | pyrimidine (DNA/RNA base) | pyrazine

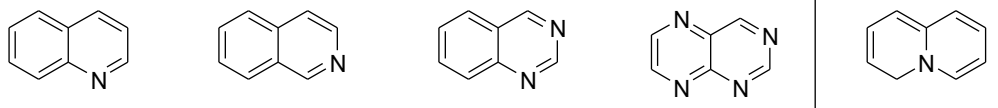
These are examples of tautomers. Neither is aromatic.

common ring-fused azoles



indole (found in the amino acid tryptophan) | isoindole | indazole | purine (DNA/RNA base) | indolizidine

common ring-fused azines



quinoline | isoquinoline | quinazoline | pteridine (found in the B vitamin riboflavin) | quinolizidine

pyrrolidine | piperidine | piperazine | morpholine