Unit-I
Nomenclature of Heterocyclic compounds

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Subject: Pharmaceutical Organic chemistry-III (B.Pharm II/I sem, 15R00303)
Nomenclature of heterocyclic compounds

• Three systems for naming heterocyclic compounds:

1) The common nomenclature: no structural information but it still widely used.

2) The replacement method

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

Each compound is given the corresponding trivial name. This usually originates from the compounds occurrence, its first preparation or its special properties.

If there is more than one heteroatom of the same type numbering starts at the saturated one, e.g. imidazole.

If there is more than one type of the heteroatoms, the ring is numbered starting at the heteroatom of the higher priority (O>S>N) and it continues in the direction to give the other heteroatoms the lower numbers as possible.
If substituents present, their position should be identified by the number of the atoms bearing them and then they should be listed in alphabetical order.

The words dihydro, or trihydro, or tetrahydro are used if two or three or four atoms are saturated. These words are preceded by numbers indicate the position of saturated atoms as low as possible and followed by the corresponding fully unsaturated trivial name.
1) 5-membered heterocycles with one or two heteroatoms

- Furan
- Thiophene
- Pyrrole
- Imidazole
- Pyrazole
- Isoxazole
- Oxazole
- Thiazole

2) 6-membered heterocycles with one or two heteroatoms

- Pyridine
- Pyridazine
- Pyrimidine
- Pyrazine

These are tautomers
Both are not aromatic

Common azines-six-membered aromatic nitrogen heterocycles

DNA/RNA bases
3) Fused heterocycles

**common ring-fused azoles**

- Indole (found in the amino acid tryptophan)
- Indoxyl
- Indazole
- Purine (DNA/RNA base)
- Indolizidine

**common ring-fused azines**

- Quinoline
- Isoquinoline
- Quinazoline
- Pteridine (found in the B vitamin riboflavin)
- Quinolizidine

Guanine
4) Saturated heterocycles

pyrrolidine  piperidine  piperazine  morpholine
II- Replacement nomenclature

- Heterocycle’s name is composed of the corresponding carbocycle’s name and an elemental prefix for the heteroatom introduced (if more than one heteroatom is present they should be listed according to the priority order shown in (table 1).

Table 1

<table>
<thead>
<tr>
<th>Atom</th>
<th>Prefix</th>
</tr>
</thead>
<tbody>
<tr>
<td>O</td>
<td>oxa</td>
</tr>
<tr>
<td>Se</td>
<td>selena</td>
</tr>
<tr>
<td>S</td>
<td>thia</td>
</tr>
<tr>
<td>N</td>
<td>aza</td>
</tr>
<tr>
<td>P</td>
<td>phospha</td>
</tr>
</tbody>
</table>
II- Replacement nomenclature

- Benzene
- Cyclopentadiene
- Cyclopentadiene
- Cyclopropane
- Cyclopropene
- Cyclopentadiene
- Cyclohexane
- Naphthalene

1,4-Diazabenzenne
Oxacyclopenta-2,4-diene
1-Oxa-3-azacyclopenta-2,4-diene
Oxacyclopropane
Oxazacyclopentene
1-Thia-2-azacyclopenta-2,4-diene
1-Oxa-4-azacyclohexane
2-Azanaphthalene
German chemists Arthur Hantzsch and Oskar Widman, proposed similar systematic naming of heterocyclic compounds in 1887 and 1888 respectively.

three to ten-membered rings named by combining the appropriate prefix (or prefixes) that denotes the type and position of the heteroatom present in the ring with suffix that determines both the ring size and the degree of unsaturation

In addition, the suffixes distinguish between nitrogen-containing heterocycles and heterocycles that do not contain nitrogen

IUPAC name = locants+ prefix + suffix
Hantzsch-Widman rules for fully saturated and fully unsaturated heterocycles

1) Identify the heteroatom present in the ring and choose from (table 1 on slide 8) the corresponding prefix.

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

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

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

- When combining the prefixes (e.g. oxa and aza) two vowels may end up together, therefore the vowel on the end of the first part should be omitted (oxaza).
Hantzsch-Widman rules

- The numbering is started from the heteroatom of the highest priority in such a way so as to give the smallest possible numbers to the other heteroatoms in the ring (the substituents are irrelevant). For example, the prefix corresponding to the following compound is 4-Methyl-1,3-Thiaza....

5) Choose the appropriate suffix from (table 2) depending on whether or not nitrogen atom is present in the ring, the size of the ring and presence or absence of any double bonds.

6) Combine the prefix(s) and suffix together and drop the first vowel if two vowels came together.
a: means use the prefix perhydro followed by the fully unsaturated name
Hantzsch-Widman rules

- Examples

This ring contains (N) Prefix is aza

The ring is 3-membered and fully saturated suffix is iridine

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

• The ring is 4-membered and fully saturated suffix is etidine

• By combining the prefix and suffix, two vowels ended up together (1,2-oaxazaetidine), therefore the vowel on the end of the first part should be dropped. This gives the correct name: 1,2-oxazetidine
This ring contains (O) prefix1 (oxa), and two (N) prefix2 diaza

Locants, since (O) is higher priority than (N) so it is in position 1 by default and the two (N) are therefore at positions 2 and 5, this gives the combined prefixes as 1,2,5-oxadiaza (note that the a in oxa is not dropped)

It is 5-membered, fully unsaturated ring with (N) the suffix is ole

By combining the prefixes and the suffix and dropping the appropriate vowels we get the correct name as 1,2,5-Oxadiazole
The ring is 6-membered, fully saturated with nitrogen. Prefix perhydro followed by the name of fully unsaturated 6-membered ring with nitrogen azine.

Thus the full name is perhydroazine.
Partial unsaturation in heterocyclic compounds can be indicated by one of the following methods:

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

\[
\begin{align*}
2H, 3H-\text{Oxole} & \quad \quad 1H-\text{Azepine} & \quad 5H-1,2,3-\text{Oxathiazole} & \quad 4H-\text{Oxin}
\end{align*}
\]
b) The words dihydro, or trihydro, or tetrahydro are used if two or three or four atoms are saturated. These words are preceded by numbers indicate the position of saturated atoms as low as possible and followed by the corresponding fully unsaturated Hantzsch-Widman name.

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

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

<table>
<thead>
<tr>
<th>Ring size</th>
<th>With N</th>
<th>Without N</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>-etine</td>
<td>-etene</td>
</tr>
<tr>
<td></td>
<td>-oline</td>
<td>-olene</td>
</tr>
</tbody>
</table>
Hantzsche-Widman rules for partially unsaturated heterocycles

- **Examples**

  \[ \Delta^2 \text{-Azetine} \]

  \[ \Delta^2 \text{-Oxetene} \]

  \[ \Delta^3 \text{-Azoline} \]

  \[ \Delta^2 \text{-Oxolene} \]

  \[ \Delta^4 \text{-1,3-Thiazoline} \]

  \[ \Delta^2 \text{-1,3-Diazoline} \]
Exercise:
Explain how can you name the following heterocycles.

1,3-Oxathiolane  1,3,5 triazine  Oxirene  4 bromo 1,3 thiazole