Chapter 1

INTRODUCTION

General concepts about heterocyclic chemistry

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SUMMARY

- Heterocyclic compound: Definition.
- Uses and Relevance of heterocyclic compounds.
- Classes of heterocycles.
  - $\pi$-Deficient aromatic heterocycles
  - $\pi$-Excedent aromatic heterocycles
  - Other aromatic heterocycles
  - Non-aromatic heterocycles
- Nomenclature of heterocyclic compounds
**HETEROCYCLIC COMPOUNDS: DEFINITION**

**CYCLIC COMPOUNDS**

**ISO CYCLIC COMPOUNDS:** Cyclic compounds in which the cycle is formed by atoms of the same element

- Benzene
- Pentazole

**Carbocycles:** Isocyclic compounds formed exclusively by carbon atoms

- Benzene
- Cyclopentadiene
- Cycloheptane

**HETEROCYCLIC COMPOUNDS:** Cyclic compounds which are formed by atoms of at least two different elements

- Inorganic heterocycles: Heterocycles which *do not contain* any carbon atom on the cyclic scaffold

- Organic heterocycles: Heterocycles which *contain at least* one carbon atom on the cyclic scaffold

- Piperidine
ORGANIC HETEROCYCLES

Most common heteroatoms: Nitrogen (the most abundant and important), Oxygen and Sulfur (rather abundant)

Other heteroatoms: Se, Te, P, As, Sb, Bi, Si, Ge, Sn, Pb, B (less common not easily found among natural products but useful as synthetic intermediates and/or chemical reagents)

Metal atoms: Pd, Ru, Co... etc. (Metalacycles)

Lawesson Reagent
(Used for sulfur transfer reactions)

An intermediate in the OsO₄-mediated dihydroxylation of alkenes
USES AND RELEVANCE OF HETEROCYCLIC COMPOUNDS

Natural products:

- Palitoxin (neurotoxin)
- Vancomycin (antibiotic)
- Coniine (cicuta leaves)
- Nicotin (tobacco leaves)
- Strichnine (poison)
- Quinine (antimalaria)
- Codeine (analgesic)
- Heroine (allucinogen)
USES AND RELEVANCE OF HETEROCYCLIC COMPOUNDS

Synthetic Drugs:
- Tetrahydrolipstatin (xenical®) (obesity treatment)
- Taxol® (intitumoral)
- Crixivan® (anti-HIV)

Food additives and health-care consumables:
- Abrox® (Chanel N.5)
- Saccharin (sweetener)

Structural Biomolecules:
- Carbohydrates
- Nucleic acids
- Vitamins
- Several aminoacids and proteins
- Co-enzymes (porphirin, chlorophile...)
  And so on.
Heterocycles can be classified into three general groups:

- **Saturated**
- **Partially saturated**
- **Aromatic**

### SATURATED HETEROCYCLES

- **Oxepane** ($X=O$)
- **Azepane** ($X=NH$)
- **Oxane** ($X=O$)
- **Thiane** ($X=S$)
- **Piperidine** ($X=NH$)
- **1,4-Dioxane** ($X=O$)
- **1,4-Dithiane** ($X=S$)
- **Piperazine** ($X=NH$)
- **tetrahydrofurane** ($X=O$)
- **tetrahydrothiophene** ($X=S$)
- **Pyrrolidine** ($X=NH$)
- **Oxetane** ($X=O$)
- **Azetidine** ($X=NH$)

**Non-planar structure** (sp$^3$ hybridization of C atoms and heteroatoms)

Different conformations

- **More stable**

**Reactivity:** Similar behaviour than that of the corresponding open-chain analogues

- Oxane like dialkylethers
- Thiane like dialkylsulfides
- Piperidine like a secondary amine

Consider bond-angle strain and lack of conformational freedom for reactivity (e.g. pyrrolidine is more basic than Et$_2$NH)
CLASSES OF HETEROCYCLES

PARTIALLY SATURATED HETEROCYCLES

→ **C-C double bond**: React essentially as alkenes

- Electron-rich alkene
  - (X=N: enamine)
  - (X=O: Enol)
  - Nucleophilic character

  X=O: 3,4-Dihydro-2H-pyrane
  X=NH: 1,2,3,4-Tetrahydropyridine

- “Standard” alkene
  - Typical alkene reactivity
    - (halogenation, hydroalogenation, hydration, hydroboration, oxymercuration, cycloadditions...)

→ **C-Heteroatom double bond**: React essentially as carbonyls, azomethine or related derivatives

- C=X polar bond
  - Electrophilic character,
  - Confer high acidity to α-H

X=O+: 2,3,4-Tetrahydropyrilium cation
X=N: 2,3,4,5-Tetrahydropyridine
AROMATIC HETEROCYCLES

- **Aromaticity confers high stability (lower reactivity)**
  - Difficult to oxidize or reduce
  - **REACTIVITY:** Aromatic electrophilic substitution ($S_{E}\text{Ar}$)/Aromatic nucleophilic substitution ($S_{N}\text{Ar}$)/ or aromatic radical substitutions ($S_{R}\text{Ar}$) (addition/elimination mechanism retaining aromaticity)

- **Aromaticity: Hückel rule**
  - For a molecule to be aromatic it must:
    - Be cyclic
    - Have a $p$-orbital on every atom in ring
    - Be planar
    - Possess $4n+2\pi$ electrons ($n = \text{any integer}$)

- Benzene $6\pi\text{e}^-\ (4\times1\ +\ 2)$
- Pyridine $6\pi\text{e}^-\ (4\times1\ +\ 2)$
- Naphtalene $10\pi\text{e}^-\ (4\times2\ +\ 2)$
- Furane $6\pi\text{e}^-\ (4\times1\ +\ 2)$
- Cyclopentadienyl anion $6\pi\text{e}^-\ (4\times1\ +\ 2)$
- Cyclopropenyl cation $2\pi\text{e}^-\ (4\times0\ +\ 2)$
- [14]-Annulene $14\pi\text{e}^-\ (4\times3\ +\ 2)$

- Erich Hückel (1886-1980)
CLASSES OF HETEROCYCLES

AROMATIC HETEROCYCLES

- **π-Deficient aromatic heterocycles:**
  
  These result from replacing one or more CH units from an aromatic hydrocarbon with (one) heteroatom(s).

  - Pyridine
  - Pyrillium cation
  - Pyrimidine
  - Quinoline

- **π-Excedent aromatic heterocycles:**
  
  These result from replacing one or more CH=CH units from an aromatic hydrocarbon with (one) heteroatom(s).

  - Furane
  - Pyrrol
  - Pyrimidine
  - Indole
**PI-DEFICIENT AROMATIC HETEROCYCLES**

**PYRIDINE vs BENZENE**

**SIMILARITIES**
- Both fullfil Hückel rule
- All atoms in the ring are sp²-hybridized
- σ-bond skeleton formeb by sp²-sp² orbital interactions
- π-Framework formed by a single electron of each atom at pₓ orbital

**DIFFERENCES**
- Nitrogen lone pair on sp2 orbital
- Lone pair lies perpendicular to the molecule axis (coplanar with the ring)
- Different electronegativities of C and N distort electronic distribution

Distortion of electronic distribution:

Nitrogen is more electronegative than carbon and attracts electrons, therefore increasing the electron density on N and C3 and C5 (>1), while electron density is decreased on C2, C4 and C6 (<1).
This can be explained in terms of resonance structures:

Pyridine vs Benzene

These forms have the less contribution (positive charge on N).
π-DEFICIENT AROMATIC HETEROCYCLES

PYRIDINE vs BENZENE

Molecular orbitals of Benzene

- LUMO
- HOMO
- Antibonding molecular orbitals
- Bonding molecular orbitals
- Six 2p atomic orbitals
- Six π molecular orbitals
**PYRIDINE vs BENZENE**

Molecular orbitals of Benzene vs Pyridine

**HOMO:** π-MO’s are lower in energy in pyridine compared with benzene (π-deficient)

**LUMO:** π*-MO’s are lower in energy in pyridine compared with benzene (more tendency to accept electrons, more reactive towards aromatic electrophilic substitution)
**π-DEFICIENT AROMATIC HETEROCYCLES**

**Shape of Molecular orbitals**

(6) (5) (3) (2) (1) (4)

**PYRIDINE vs BENZENE**

- **Bonding**
  - (2) $A_{1}$ $B_{1}$
  - (3) $A_{2}$

- **Valence orbitals**
  - (1) $B_{1}$

- **Anti-bonding**
  - (4) $A_{1}$ $B_{3}$
  - (5) $A_{2}$

- **π-backbonds**
  - (6)
One heteroatom (pyridine-like):

Behave essentially like pyridine. Differences arise from the different electronegativity of the heteroatom.

- Pyridine
- Pyrilium cation
- Phosphinine
- Siline

$O^+$ is more electronegative than N (Carbon atoms at ring more electron-deficient)
P and Si are less electronegative than N (Carbon atoms at ring less electron-deficient)

Two or more heteroatoms:

The higher the number of heteroatoms on the structure, the more electron-deficient the heterocycle will become.

- Pyridine
- Pyridazine
- Pyrimidine
- Pyrazine
- 1,3,5-Triazine
These result from replacing one or more CH=CH units from an aromatic hydrocarbon with (one) heteroatoms. Isoelectronic with cyclopentadienyl anion.

- All atoms in the ring are sp²-hybridized
- σ-bond skeleton formed by sp²-sp² orbital interactions
- π-framework formed by a single electron of each atom at pₓ orbital
- The heteroatom lone pair that participates on the aromatic π-system lies perpendicular to the molecule axis (coplanar with the ring)
- Heteroatom bonds to adjacent atoms by single bonds

**FEATURES**

- **ELECTRON DENSITY**: Six π-electrons shared by five atoms
- **ELECTRON DENSITY**: The carbon atoms of the ring have more electron density compared with benzene but less than the heteroatom

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**Examples**

- Cyclopentadienyl anion
- Furane
- Pyrrol
- Thiophene
- Indole
- Pyrrol
- Furane

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**Dihedral Angles (in degrees)**

- Pyrrol: 1,090, 1,090
- Furane: 1,078, 1,078
- Indole: 1,078
- Thiophene: 1,067, 1,067

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**Bond Lengths (in Ångstroms)**

- Pyrrol: 1.647, 1.087
- Furane: 1.078

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Can be understood in terms of resonance structures

- **Pyrrol**:
  - Resonance hybrid

- **Furane**:
  - Resonance hybrid

- **Thiophene**:
  - Resonance hybrid
  - Additional resonance structure (d orbital participation)

- Thiophene has a **more aromatic** character (contribution of additional resonance structure without charge separation)
- Furane has the **less aromatic** character (unstability of resonance structures with a positively charged oxygen atom.)
**π-EXCEDENT AROMATIC HETEROCYCLES**

**PYRROL vs CYCLOPENTADIENYL ANION**

- **HOMO in pyrrole is less energetic** (more accessible and therefore with more tendency to donate electrons: π-excedent)
- **GEOMETRY OF HOMO**: Largest coefficients at C2 and C5: More reactive positions
**OTHER AROMATIC HETEROCYCLES**

**Monocyclic heterocycles:**
- Can be pyridine-like (C=heteroatom double bond) or pyrrol-like (heteroatom participates with two electrons in the π system).
- Most frequently found: N-heterocycles

![Pyrrol-like Heterocycles](image)

1,4-dihydro-1,4-diazocine (Hückel: $4\times2 + 2 = 10\ \pi\ e^-$)
1H-azonine (Hückel: $4\times2 + 2 = 10\ \pi\ e^-$)
Aza-[18]-annulene (Hückel: $4\times4 + 2 = 18\ \pi\ e^-$)

**Pyridine-like Heterocycles**

![Pyridine-like Heterocycles](image)

azecine (Hückel: $4\times2 + 2 = 10\ \pi\ e^-$)

**Fused polycyclic heterocycles:**
- Incorporate both pyridine-like or pyrrol-like heterocyclic moieties sharing one or more bonds.

![Fused Heterocycles](image)

Quinoline (Hückel: $4\times2 + 2 = 10\ \pi\ e^-$)
Acridine (Hückel: $4\times3 + 2 = 14\ \pi\ e^-$)
Pteridine (Hückel: $4\times2 + 2 = 10\ \pi\ e^-$)
Isoquinoline (Hückel: $4\times2 + 2 = 10\ \pi\ e^-$)

Indole (Hückel: $4\times2 + 2 = 10\ \pi\ e^-$)
Benzofurane (Hückel: $4\times2 + 2 = 10\ \pi\ e^-$)
Purine (Hückel: $4\times2 + 2 = 10\ \pi\ e^-$)
Benzotriazole (Hückel: $4\times2 + 2 = 10\ \pi\ e^-$)
NON-AROMATIC HETEROCYCLES

- Heterocycles in which the p-ring system is partially or completely saturated.
- Behave chemically like the corresponding acyclic analogues but taking into account the STRAIN (angle strain, steric strain and torsional strain)
- Because of Angle strain, small-size rings tend to react by ring-opening processes, releasing strain and reaching to a more stable situation.

ANGLE STRAIN

Baeyer Strain Theory:

- Explains specific behavior of chemical compounds in terms of bond angle strain.
- It was proposed by Adolf von Baeyer in 1885 to account for the unusual chemical reactivity in ring-opening reactions of cyclopropanes and cyclobutanes where this angle strain is relieved.

On ring strain he noted in 1885:

“The four valences of the carbon atom act in the directions that connect the center of a sphere with the corners of a tetrahedron and that form an angle of 109.28’ with each other. The direction of the attraction can experience a deviation that will, however, cause an increase in strain correlating with the degree of this deviation”
Johann Friedrich Wilhelm Adolf von Baeyer was born on October 31, 1835, in Berlin, as the son of Johann Jakob Baeyer and Eugenie née Hitzig. He came from a family distinguished both in literature and the natural sciences. His father, a lieutenant-general, was the originator of the European system of geodetic measurement. Even as a child Baeyer was interested in chemical experiments and at the age of twelve found a new double salt of copper. Baeyer devoted his first two years as a student at the University of Berlin (1853-1855) chiefly to physics and mathematics. By 1856, however, his old love for chemistry re-awakened and drew him to Bunsen’s laboratory in Heidelberg. His studies here on methyl chloride resulted in his first published work which came out in 1857. During the next year he worked in Kekulé’s private laboratory in Heidelberg and was associated with his ingenious structure theory. Baeyer’s life work was soon to bring this indeed most brilliant of chemical theories much resounding success. In 1858, in Berlin, he received his doctorate for his work on cacodyl compounds which had been done in Kekulé’s laboratory.

For the next year or two Baeyer was again working with Kekulé who had meanwhile become Professor at Ghent. A study of uric acid, which also led him to the discovery of barbituric acid, provided the thesis by which he qualified as a university teacher in 1860. In the same year he became a lecturer in organic chemistry at the "Gewerbe-Akademie" (Trade Academy) in Berlin. He received little money but was given a spacious laboratory. In 1866 the University of Berlin, at the suggestion of A.W. Hofmann, conferred on him a senior lectureship, which, however, was unpaid.

It was during the Berlin period that Baeyer began most of the work that was to bring him fame later. In 1865 he started his work on indigo - the blue dye had fascinated him since his youth-and this soon led to the discovery of indole and to the partial synthesis of indigotin. His pupils Graebe and Liebermann, with the help of the zinc-dust distillation developed by Baeyer, clarified the structure of alizarin and worked out the synthesis used industrially. Studies were initiated on condensation reactions which, after Baeyer had gone to Strassburg as Professor in the newly established University (1871) brought to light that important category of dyestuffs - the phthaleins. Baeyer’s theory of carbon-dioxide assimilation in formaldehyde also belongs to this period.

On the death of Justus von Liebig in 1873, Baeyer was called to his Chair in the University of Munich and there, over many years, built up an excellent new chemical laboratory. With his tenure at Munich came elegant total syntheses of indigo, as well as work on acetylene and polyacetylene, and from this derived the famous Baeyer strain theory of the carbon rings; there were studies of the constitution of benzene as well as comprehensive investigations into cyclic terpene. In this connexion the Baeyer-Villiger oxidation of ketones by means of per-acids was discovered. Special interest was aroused theoretically by his work on organic peroxides and oxonium compounds and on the connexion between constitution and colour.
**NON-AROMATIC HETEROCYCLES**

**ANGLE STRAIN**

*Coulson and Moffit Model*

“The maximum overlap between molecular orbitals is not an absolute requisite for bond formation if this leads to significant deviation from the natural angles associated to hybridization”

- Ring strain is reduced if internal sp² orbitals acquire higher p character.
- sp² Orbitals with a higher p character implies that bond lengths are shorter, with a bond angle closer to 90° and with a curvy geometry (also known as banana bonds)
- The external sp2 orbitals (those linked to H in cyclopropane) acquire less p character (more spherical) and this leads to distorted bond angles (φ = 116° and not 109°)

**Consequences of Angle Strain:** The angle strain of cyclopropane renders the molecule unstable and highly reactive due to the large amount of potential energy stored in the molecule. Cyclopropane, when burned, releases substantially more energy than when propane is burned. This difference cannot be explained solely by the fact that there are two additional hydrogens in propane. The higher heat of combustion of cyclopropane is due to the angle strain. It is known that cyclohexane does not undergo hydrogenation reactions. However, cyclopropane does readily undergo hydrogenation reactions. This difference in reactivity is due to the high potential energy stored in cyclopropane, whereas there is little potential energy in cyclohexane.
STERIC STRAIN

- Steric strain results from the electron-electron repulsion of atoms (or groups of atoms) that are too close together.
- Steric strain stores potential energy in a molecule by forcing repelling groups together.

E.g.: 1,3-diaxial interactions in cyclohexanes

E.g.: s-cis conformation in butadiene
Steric strain that occurs when there are eclipsed interactions.

E.g.: conformations of n-butane.
NON-AROMATIC HETEROCYCLES

THREE-MEMBERED HETEROCYCLES

- Consequences of angle strain and torsional strain.
  - Higher reactivity: Ring opens quite easy (C-X bonds are also polarized)

\[
\begin{array}{c}
\text{R}^1 \quad \text{X} \\
\delta^- \\
\delta^- \\
\end{array}
\quad \text{X} \\
\delta^+ \\
\delta^- \\
\quad \text{R}^3 \quad \text{R}^2
\]

\[
\text{Nu}^- \quad \text{Nu}^- \quad \text{Nu}^- \\
\rightarrow \\
\rightarrow \\
\rightarrow \\
\end{array}
\]

- Attack on less-hindered carbon atom (steric control)
- Inversion of configuration at the attacked carbon atom
- Retention of configuration at the other carbon atom.

- Less basicity of the heteroatom lone pair: Aziridines are less basic than other secondary amines because the curved bonds make the sp\(^2\) orbital which contains the lone pair to have more s-character (more spherical) and therefore electrons remain closer to nucleus and more tightly bonded.

- Increased energy barrier for nitrogen inversion in aziridines: Nitrogen atom in aziridines is highly pyramidal and the required energy to undergo pyramidal inversion is relatively high because the molecule has to go through a highly strained planar intermediate. As a consequence, rotamers can be in some cases isolated.
NON-AROMATIC HETEROCYCLES

FOUR- AND FIVE-MEMBERED HETEROCYCLES

Azetidine:
- Non-planar molecule: Twisted conformation in order to minimize strain.

The most stable conformation places the nitrogen lone pair in a pseudoaxial position.

Oxetane:
- Planar structure: The lack of substituents at oxygen atom makes torsional strain to be minimal and the energies between twisted and planar structures are very close to each other.

Pyrrolidine and tetrahydrofurane:
- Non-planar molecules: Envelope-like conformations to avoid torsional strain (*no angle strain in five-membered cycles*).
- Heteroatom goes to the out-of-plane position to avoid gauche interactions.

Pyrrolidine is more basic than acyclic secondary amines (lone pair more exposed on a molecular orbital with full sp$^3$ character (*no angle strain*).
Non-planar molecules: Chair conformation is the most stable one
Heteroatom lone pair preferably on axial position (minimizing 1,3-diaxial strain)
Other issues to take care of when carrying out conformational analysis:

- Pyramidal inversion of nitrogen atom.
- The two interchanging chair conformations

The Van der Waals interactions between substituents and the lone pairs of the heteroatoms. These are very important on highly electronegative atoms such as oxygen (electrons are closer to the nuclei and electrostatic repulsions become more important)
Interactions between contiguous lone pairs: Preference for gauche conformation (lone-pair containing orbitals almost perpendicular) because of the possibility for existing overlaps between $\sigma^*$ molecular orbitals which contribute to the stabilization of electron density by delocalization. Maximum energy on eclipsed conformation in which both lone pairs are eclipsed to each other because of electrostatic repulsion.

i, ii, vi, vii: pyramidal inversion
iii, iv, v: cycle flip

Conformation of maximum energy
Anomeric effect: Orbital interactions through $\sigma$-bonds.

The anomeric effect, also known as Edward-Lemieux effect is a stereoelectronic effect that describes the tendency of heteroatomic substituents adjacent to a heteroatom within a cyclohexane ring to prefer the axial orientation instead of the less hindered equatorial orientation that would be expected from steric considerations.

The most widely accepted explanation is that there is a stabilizing interaction (hyperconjugation) between the unshared electron pair on the one heteroatom (the endocyclic one in a sugar ring) and the $\sigma^*$ orbital for the axial (exocyclic) C–X bond.

In terms of resonance structures:

- Antiperiplanar to axial polarised $\sigma$–$\sigma^*$ bond
- Antiperiplanar to polarised pyran $\pi$ bond
- One stabilising interaction
- Two stabilising interactions
### Anomeric effect:

**β-D-glucose 64%**  
**α-D-glucose 36%**

\[
K = \frac{64}{36} = 0.56  
\Delta G = -RT \ln K = 1.48 \text{ kJ mol}^{-1}
\]

<table>
<thead>
<tr>
<th>In cyclohexanes</th>
<th>In tetrahydropyrans</th>
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<tbody>
<tr>
<td><img src="image1.png" alt="structure" /></td>
<td><img src="image2.png" alt="structure" /></td>
</tr>
<tr>
<td>94.5%</td>
<td>99.3%</td>
</tr>
<tr>
<td>(\Delta G = 7 \text{ kJ mol}^{-1})</td>
<td>(\Delta G = 12 \text{ kJ mol}^{-1})</td>
</tr>
<tr>
<td>5.5%</td>
<td>0.7%</td>
</tr>
<tr>
<td>84%</td>
<td>46%</td>
</tr>
<tr>
<td>(\Delta G = 4.1 \text{ kJ mol}^{-1})</td>
<td>(\Delta G = -0.4 \text{ kJ mol}^{-1})</td>
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<tr>
<td>16%</td>
<td>54%</td>
</tr>
<tr>
<td>77%</td>
<td>30%</td>
</tr>
<tr>
<td>(\Delta G = 3.0 \text{ kJ mol}^{-1})</td>
<td>(\Delta G = -2.1 \text{ kJ mol}^{-1})</td>
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<td>23%</td>
<td>70%</td>
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<td>72.5%</td>
<td>5%</td>
</tr>
<tr>
<td>(\Delta G = 2.4 \text{ kJ mol}^{-1})</td>
<td>(\Delta G = -7.3 \text{ kJ mol}^{-1})</td>
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<tr>
<td>27.5%</td>
<td>95%</td>
</tr>
</tbody>
</table>

**K roughly constant**

**K increases with electronegativity**
OTHER FACTORS INFLUENCING CONFORMATION

Other different types of interactions can also influence the preferred conformation for non-aromatic heterocycles

- **Intramolecular H-bonding interactions:** Can fix a hypothetically strained conformation because of the stabilizing effect of the intramolecular bond.

  ![Intramolecular H-bonding interactions](image)

  More stable

- **Ring-chain tautomerism:**
  - Tautomers are isomers of organic compounds that readily interconvert by a chemical reaction. Because of the rapid interconversion, tautomers are generally considered to be the same chemical compound.
  - Ring-chain tautomerism occurs when the movement of the atoms (generally a proton) is accompanied by a change from an open structure to a ring

  ![Ring-chain tautomerism](image)
GENERAL RULES (adopted by IUPAC)

- Hetero-atom is to be counted as 1 or as low as possible.
- When there is more than one hetero-atom, preference is given to O, then S, then N, then C. Also N-H presides over N=.
- When there is more than one hetero-atom, numbering should be as direct as possible from one to the other.
- Substituents are numbered as low as possible.
- Acceptable prefixes include O=Oxa; S=Thia; N=Aza.
- Common suffixes for N- and non-N-heterocycles: For partially unsaturated systems, H is(are) used to indicate the location of saturation.
- Hantzsch-Widman System of systematic name of heterocyclic compounds.

<table>
<thead>
<tr>
<th>Ring Size</th>
<th>Saturated</th>
<th>Partly Saturated</th>
<th>Unsaturated</th>
</tr>
</thead>
<tbody>
<tr>
<td>3</td>
<td>-irane</td>
<td>-</td>
<td>-irene</td>
</tr>
<tr>
<td>4</td>
<td>-etane</td>
<td>(dihydro)</td>
<td>-ete</td>
</tr>
<tr>
<td>5</td>
<td>-olane</td>
<td>(dihydro)</td>
<td>-ole</td>
</tr>
<tr>
<td>6</td>
<td>-inane</td>
<td>(di or tetrahydro)</td>
<td>-ine</td>
</tr>
<tr>
<td>7</td>
<td>-epane</td>
<td>(di or tetrahydro)</td>
<td>-epine</td>
</tr>
<tr>
<td>8</td>
<td>-ocane</td>
<td>(di, tetra, or hexahydro)</td>
<td>-ocine</td>
</tr>
</tbody>
</table>
**NOMENCLATURE OF HETEROCYCLIC COMPOUNDS**

**Hantzsch – Widman Nomenclature (adopted by IUPAC)**

<table>
<thead>
<tr>
<th>Ring Size</th>
<th>Saturated</th>
<th>Partly Saturated</th>
<th>Unsaturated</th>
</tr>
</thead>
<tbody>
<tr>
<td>3</td>
<td>-irane</td>
<td>-</td>
<td>-irene</td>
</tr>
<tr>
<td>4</td>
<td>-etane</td>
<td>(dihydro)</td>
<td>-ete</td>
</tr>
<tr>
<td>5</td>
<td>-olane</td>
<td>(dihydro)</td>
<td>-ole</td>
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<td>-ine</td>
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<tr>
<td>7</td>
<td>-epane</td>
<td>(di or tetrahydro)</td>
<td>-epine</td>
</tr>
<tr>
<td>8</td>
<td>-ocane</td>
<td>(di, tetra, or hexahydro)</td>
<td>-ocine</td>
</tr>
</tbody>
</table>

Common name: ethylene oxide  
Systematic name: Oxa + irane .... Oxirane

Common name: furan  
Systematic name: Oxa + ole .... Oxole

Common name: pyrrole  
Systematic name: H at 1 position + Aza + ole .... 1H-Azole

Common name: piperidine  
Systematic name: Aza + inane .... 1H-Azinane

Common name: pyrimidine  
Systematic name: two aza at 1, 3 positions + ine .... [1,3]-diazine
### Hantzsch – Widman Nomenclature (adopted by IUPAC)

<table>
<thead>
<tr>
<th>Ring Size</th>
<th>Saturated</th>
<th>Partly Saturated</th>
<th>Unsaturated</th>
</tr>
</thead>
<tbody>
<tr>
<td>3</td>
<td>-irane</td>
<td>-</td>
<td>-irene</td>
</tr>
<tr>
<td>4</td>
<td>-etane</td>
<td>(dihydro)</td>
<td>-ete</td>
</tr>
<tr>
<td>5</td>
<td>-olane</td>
<td>(dihydro)</td>
<td>-ole</td>
</tr>
<tr>
<td>6</td>
<td>-inane</td>
<td>(di or tetrahydro)</td>
<td>-ine</td>
</tr>
<tr>
<td>7</td>
<td>-epane</td>
<td>(di or tetrahydro)</td>
<td>-epine</td>
</tr>
<tr>
<td>8</td>
<td>-ocane</td>
<td>(di, tetra, or hexahydro)</td>
<td>-ocine</td>
</tr>
</tbody>
</table>

**Examples:**
- **Azocane**
- [1,3]-**Oxazocane**
- [1,3,7]-**Oxathiazocane**
- 4,5-**dihydro-2H,8H-[1,3,7]-oxathiazocine**
- 6-Methyl-2-phenyl-2H,8H-[1,3,7]-oxathiazocine
- 6-Methyl-2-phenyl-2H,3H,8H-oxocine