STRUCTURAL FEATURES OF ORGANIC MEDICINAL AGENTS

I. Atomic and Molecular Structures of Organic Medicinal Agents (OMAs)

A. Atomic Structure

Organic medicinal agents are compounds (molecules) composed of individual atoms linked via chemical bonds. The primary elements of OMAs are carbon (C) and hydrogen (H). Other elements found in lesser abundance in OMA structures include nitrogen (N), oxygen (O), sulfur (S), phosphorous (P) and halogens (F, Cl, Br, I). Examples of the contributions of these atoms in various drug molecules are shown in the Functional group Tutorials.

The properties of OMAs are derived from their composite elements and atomic structure:

- **Atom**: Composed of a positively charged nucleus (protons and neutrons) surrounded by a negatively charged electron cloud (electrons). **Example Carbon: 6Ps, 6Ns and 6 e's.**

- **Atomic Number**: Assigned to an atom as a number that is equal to the number of positive charges on the nucleus, which in turn is equal to the number of electrons around the nucleus of the neutral atom. **Example Carbon: 6Ps, 6 e's, Atomic Number = 6.**

- **Electron shell**: A spherical region containing electrons that surrounds the nucleus of an atom. Shells are designated by their level from the nucleus 1, 2, 3, etc. **Example Carbon: Shell 1 (2 electrons), Shell 2 (4 electrons).**

- **Valence shell**: The outermost shell of electrons in the structure of an atom; these electrons are employed in bonding of atoms. **Example Carbon: has four valence electrons: 2s^2, 2p^2.**

- **Electron orbital**: The smaller regions containing electrons into which shells are subdivided; designated as s, p, d, etc. **Example Carbon (6 electrons): 1s^2, 2s^2, 2p^2.**

- Since different atoms have different numbers of electrons in the corresponding orbitals, it is important to understand how the orbitals are filled – the electronic configuration. The table below gives the electronic configuration of a number of atoms. **Example Carbon: 1s^2, 2s^2, 2p^2.**

<table>
<thead>
<tr>
<th>Shell</th>
<th>H</th>
<th>He</th>
<th>Li</th>
<th>Be</th>
<th>B</th>
<th>C</th>
<th>N</th>
<th>O</th>
<th>F</th>
<th>Ne</th>
</tr>
</thead>
<tbody>
<tr>
<td>1s</td>
<td>1</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>2s</td>
<td></td>
<td>1</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>2p</td>
<td></td>
<td></td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td>6</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
The following rules apply to the filling of electron orbitals in the creation of atoms:

- Electrons are distributed one each among orbitals as long as equivalent orbitals remain (a single electron in an orbital is called an **unpaired electron**). Example Carbon: **Paired electrons in 1s^2 and 2s^2. Unpaired electrons in two p orbitals (2p^2)**

- Only after every equivalent orbital contains a one electron is a second electron added to form an electron pair in an orbital.

- **Octet Rule**: the tendency of atoms to attain an outer shell content of 8 electrons (attain a “rare gas electron configuration”). The most common exception to this rule is hydrogen (H) which attains an outer shell of 2 electrons.

Most of the important characteristics of the atoms mentioned above are determined by the valence electrons of those atoms. Since these are the electrons located in the outermost shell, they determine the number of bonds that each atom will form with other atoms.

The number of valence electrons in the relevant atoms is presented in the table below:

<table>
<thead>
<tr>
<th>Atom</th>
<th>H</th>
<th>C</th>
<th>N</th>
<th>P</th>
<th>O</th>
<th>S</th>
<th>F</th>
<th>Cl</th>
<th>Br</th>
<th>I</th>
</tr>
</thead>
<tbody>
<tr>
<td>Valence Electrons</td>
<td>1</td>
<td>4</td>
<td>5</td>
<td>5</td>
<td>6</td>
<td>6</td>
<td>7</td>
<td>7</td>
<td>7</td>
<td>7</td>
</tr>
</tbody>
</table>

It is helpful to look at the position of each of these atoms in the Periodic table in order to understand the origin of these numbers. A portion of the Periodic table is presented below:

<table>
<thead>
<tr>
<th>Boron</th>
<th>Carbon</th>
<th>Nitrogen</th>
<th>Oxygen</th>
<th>Fluorine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aluminum</td>
<td>Silicon</td>
<td>Phosphorus</td>
<td>Sulfur</td>
<td>Chlorine</td>
</tr>
<tr>
<td>Gallium</td>
<td>Germanium</td>
<td>Arsenic</td>
<td>Selenium</td>
<td>Bromine</td>
</tr>
<tr>
<td>Indium</td>
<td>Tin</td>
<td>Antimony</td>
<td>Tellurium</td>
<td>Iodine</td>
</tr>
</tbody>
</table>

Utilizing the octet rule the number of bonds each atom will form can then be predicted in the following manner:

\[
8 - \# \text{ of valence electrons} = \text{number of bonds an atom will normally form in the neutral (uncharged) state}^* \\
\]

* Recall H does not obey the octet rule (there are other exceptions as well such as B, Al and transition metals among others).
B. Molecular Structure

Molecules/compounds are formed as a result of the establishment of a bond between atoms. The driving force for bonding among atoms is that bonding permits these atoms to comply with the octet rule and thereby achieve a more stable state. These bonds may be of two types:

1. **Ionic bond**: formed by complete transfer of electron(s) from one atom to the other resulting in the formation of a cation/anion pair which is effectively bonded by the attractive force between opposite charges. Atoms that tend to give up a valence electron in forming an ionic bond are the **electropositive** atoms (left side of periodic table including Group I and II) while those that accept a donated electron are the **electronegative** atoms (right side of periodic table including Group IV, V, VI and VII). The property of **electronegativity** of an atom is its tendency to attract electrons toward itself (atoms at the top of Group VI and VII have the highest electronegativity).

2. **Covalent bond**: formed by the sharing of an electron pair between atoms. Each atom provides an electron for the bond -note that each atom comprising the bond fulfills the octet rule.

As a general rule, ionic bonds are formed between atoms that differ widely in electronegativity while covalent bonds are generally formed between atoms of similar or identical electronegativity.

<table>
<thead>
<tr>
<th>ATOM</th>
<th>ATOMIC NUMBER</th>
<th>ELECTRONEGATIVITY</th>
</tr>
</thead>
<tbody>
<tr>
<td>H</td>
<td>1</td>
<td>2.1</td>
</tr>
<tr>
<td>C</td>
<td>6</td>
<td>2.5</td>
</tr>
<tr>
<td>N</td>
<td>7</td>
<td>3.0</td>
</tr>
<tr>
<td>O</td>
<td>8</td>
<td>3.5</td>
</tr>
<tr>
<td>F</td>
<td>9</td>
<td>4.0</td>
</tr>
<tr>
<td>Si</td>
<td>14</td>
<td>1.8</td>
</tr>
<tr>
<td>P</td>
<td>15</td>
<td>2.1</td>
</tr>
<tr>
<td>S</td>
<td>16</td>
<td>2.5</td>
</tr>
<tr>
<td>Cl</td>
<td>17</td>
<td>3.0</td>
</tr>
<tr>
<td>Br</td>
<td>35</td>
<td>2.8</td>
</tr>
<tr>
<td>I</td>
<td>53</td>
<td>2.5</td>
</tr>
</tbody>
</table>
Examples of compound formation via covalent bond formation:

\[ \text{H}_2, \text{N}_2, \text{Cl}_2, \text{H}_2\text{O}, \text{HCl}, \text{CH}_3\text{CH}_3 : \text{Structure represented by “line” bonds: H-H} \]

Examples of compound formation via ionic bond formation:

\[ \text{NaBr, KCl, NaOH: Structures represented by ionic bonds, Na}^+ \text{ Br}^- \]

Examples of compound formation via ionic and covalent bond formation:

\[ \text{CH}_3\text{COO-Na}^+ \]

Bonding in OMAs is primarily of the covalent type since the atoms commonly comprising OMA structure are of similar electronegativities. The atoms, C, N and O, have to be prepared for bonding ("hybridized") prior to the formation of covalent bonds.

1. Bonding in Carbon

In order to form four single bonds, carbon utilizes the four electrons in its valence shell (2s\(^2\), 2p\(^2\)). It does this through a process of hybridization which utilizes outer s orbital (the 2s) and 3 p orbitals (2sp\(_{x,y,z}\)). This type of hybridization is therefore known as sp\(^3\). Each of these bonds is referred to as a sigma (\(\sigma\)) bond.

\[
\text{C: } 1s^22s^22p^2 \xrightarrow{\text{Hybridization}} \text{C: } 1s^22sp^3 \xrightarrow{\text{sp}^3 \text{ tetrahedron}}
\]

According to the valence shell electron pair repulsion theory (VESP) electron pairs seek to orient themselves as far away from each other as possible. This translates into a tetrahedral geometry for sp\(^3\) carbon.

Examples:

- Methane (CH\(_3\)):

\[
\begin{array}{c}
\text{H} \\
\text{H} \\
\text{H} \\
\text{H}
\end{array}
\]

- Ethane (CH\(_3\)CH\(_3\)):

\[
\begin{array}{c}
\text{H} \\
\text{H} \\
\text{H} \\
\text{H}
\end{array}
\]

Carbon may also form double bonds (commonly accompanied by 2 single bonds). In order to accomplish this carbon uses the outer s orbital (2s) and 2 p orbitals to generate an sp\(^2\) orbital which

![Diagram of sp\(^3\) and sp\(^2\) hybridization]
possesses trigonal geometry. The remaining p orbital is located perpendicular to the plane and is involved in pi (π) bonding.

\[
\begin{align*}
\text{C: } & 1s^22s^22p^2 \quad \text{Hybridization} \\
\rightarrow & \quad \text{C: } 1s^22sp^2(2\pi) \\
\text{sp}^2 \text{ trigonal (planar)}
\end{align*}
\]

Examples:

- Ethene (CH₂CH₂):

\[
\text{H} \quad \text{C} \equiv \text{C} \quad \text{H}
\]

- Formaldehyde (CH₂O):

\[
\text{H} \quad \text{C} \equiv \text{O}
\]

Carbon may also form \textbf{triple bonds} by utilizing the outer s orbital (2s) and 1p orbital (2p) to give \textit{2} sp orbitals with linear geometry. The remaining p orbitals are located perpendicular to the plane and are involved in pi (π) bonding:

\[
\begin{align*}
\text{C: } & 1s^22s^22p^2 \quad \text{Hybridization} \\
\rightarrow & \quad \text{C: } 1s^22sp(2\pi) \\
\text{sp linear} \quad \text{planar}
\end{align*}
\]

Examples

- Acetylene (HCCH):

\[
\text{H} \quad \text{C} \equiv \text{C} \quad \text{H}
\]

- Hydrogen cyanide (HCN):

\[
\text{H} \quad \text{C} \equiv \text{N}
\]

The bonding states of carbon are summarized on the next page along with the properties of various bonding states:
The Bonding States of Carbon

**sp³ Hybridization**

\[ \text{sp}^3 \text{ Hybridization} \]

\[ \begin{array}{c}
\text{σ} \\
\text{σ} \\
\text{σ} \\
\text{σ}
\end{array} \]

**sp² Hybridization**

\[ \text{sp}^2 \text{ Hybridization} \]

\[ \begin{array}{c}
\text{σ} \\
\text{π} \\
\text{π}
\end{array} \]

**sp Hybridization**

\[ \text{sp} \text{ Hybridization} \]

\[ \begin{array}{c}
\text{π} \\
\text{π} \\
\text{π}
\end{array} \]

**Carbon:** 1s² 2s² 2p² (Valence electrons: 2s² + 2p² = 4)

Will form four bonds in the neutral bonding state

**sp³ Hybridized Carbon (Tetrahedral)**

\[ \text{sp}^3 \text{ tetrahedron} \]

**sp² Hybridized Carbon (Trigonal, Planar)**

\[ \text{sp}^2 \text{ trigonal (planar)} \]

**sp Hybridized Carbon (Linear)**

\[ \text{sp linear} \]

**Alkane:** Free radical rxns

\[ \text{Alkene: Addition and reduction rxns} \]

\[ \text{Alkyne: Addition and reduction rxns} \]

Chirality Possible: R and S Enantiomers

No chirality but Geometric Isomerism Possible: E and Z Isomers

No chirality or Geometric Isomerism Possible:
2. **Covalent bonding by N**

Nitrogen has five electrons in its valence shell and thus will form three bonds in the neutral state and one pair of non-bonded electrons. Nitrogen is capable of forming single, double and triple bonds and commonly does so with one pair of electrons remaining associated only with nitrogen.

Examples:

- Methylamine (CH₃-NH₂): ![Methylamine](image)

- Formaldehyde imine (CH₂NH): ![Formaldehyde Imine](image)

- Acetonitrile (CH₃-CN): ![Acetonitrile](image)

Under the bonding conditions in the examples above, nitrogen is neutral. If however the non-bonded electron pair becomes involved in bonding a positive charge results (based on formal charge calculations). This is illustrated in the example below for methylamine, a covalent compound converted to methylamine hydrochloride, a compound with additional ionic bonding. The ability of nitrogen’s electron pair to participate in bonding of this type is a measure of its basicity and nucleophilicity as described in the Amine Tutorial.

Example: Methylamine to methylamine hydrochloride

![Methylamine to Methylamine Hydrochloride](image)

The bonding states of nitrogen are summarized on the next page along with the properties of various bonding states:
The Bonding States of Nitrogen

Nucleus (7 protons + 7 neutrons)
1s Orbital (2 electrons)
2s Orbital (2 electrons)
2p Orbital (3 electrons)

Nitrogen: $1s^2 2s^2 2p^3$ (Valence electrons: $2s^2 + 2p^3 = 5$)
Will form three bonds in the neutral bonding state

**sp$^3$ Hybridization**

- **sp$^3$ Hybridized Nitrogen (Tetrahedral-Trigonal)**
  - sp$^3$ tetrahedron
  - HHH \(\text{C} = \text{N}^{+} \text{H}^{+}\)
  - Amine: Basicity and Nucleophilicity
  - Rapid inversion at nitrogen masks chirality

**sp$^2$ Hybridization**

- **sp$^2$ Hybridized Carbon (Trigonal, Planar)**
  - sp$^2$ trigonal (planar)
  - HHH \(\text{C} = \text{N}^{+} \text{H}^{+}\)
  - Imine: Weak basicity and nucleophilicity. Carbon is electrophilic

- **sp Hybridization**
  - sp linear
  - HHH \(\text{C} = \text{N}^{+} \text{H}^{+}\)
  - Nitrile: Very weak basicity and nucleophilicity. Carbon is electrophilic
  - No chirality or Geometric Isomerism Possible:
3. Covalent bonding by O:

Carbon has eight electrons with 6 in the valence shell. Thus it can form two bonds in the neutral state and have two pairs of non-bonded electrons. Just as carbon can form single and double bonds, oxygen is also capable of forming these types of bonds. Unlike carbon however, oxygen in its neutral state forms two bonds and retains two pairs of electrons in nonbonding orbitals. As will be seen later, these electrons are free to participate in a number of interactions with other molecules (H-bonding):

Examples

- Methanol (CH₃OH):

- Oxygen (O₂):

- Acetic acid (CH₃COOCH₃):

The bonding states of oxygen are summarized on the next page along with the properties of various bonding states:
The Bonding States of Oxygen

Oxygen: $1s^2 2s^2 2p^4$ (Valence electrons: $2s^2 + 2p^4 = 6$)
Will form two bonds in the neutral bonding state

$sp^3$ Hybridization

$sp^3$ Hybridized Nitrogen
(Tetrahedral-Trigonal)

$sp^2$ Hybridization

$sp^2$ Hybridized Carbon
(Trigonal, Planar)

Alcohol: Low Basicity
but good Nucleophilicity

Carbonyl (Aldehyde/Ketone)
Very weak basicity but carbon
is electrophilic

No Stereochemistry
at oxygen

No Stereochemistry
at oxygen
II. Noncovalent Intermolecular Bonds

Attractive forces among molecules are established as a result of the presence of polarized covalent bonds within these structures. Polarization of the bonding electron pair occurs because of differences in electronegativities of the two atoms involved in the covalent bond. Hence, the bonding electron pair will orient themselves closer to the more electronegative atom of the bonding atoms.

The presence of polarized covalent bonds in OMA structures gives rise to local dipoles or charges within these structures. These dipoles are then capable of interacting via dipolar-type interactions with dipoles of other molecules. The dipoles may be permanent or they may be transient (sometimes referred to as induced or transient dipoles).

A. Van Der Waals Interactions (induced dipole interaction, hydrophobic bonding)

- the weakest intermolecular bond (0.5 - 1.0 Kcal/mole)
- occurs between nonpolar portions of two molecules
- results from a mutual distortion of electron clouds making up the covalent bond
- distance and temperature dependent occurring at lower temperatures where molecules are able to come in close proximity to each other.

B. Dipole-dipole interactions (Hydrogen bonds)

- occurs when at least one dipole contains an electropositive hydrogen, strength = 1.0 to 10 kcal/mole,
- electropositive H occurs when it is covalently bonded to an electronegative atom such as O, S or N,
- classical H-bonding is seen in water - the unexpectedly high boiling point of H₂O is due to its strong intermolecular association via H-bonds.

C. Ion-dipole interactions

- occurs between an ion, either cation or anion, and a formal dipole,
- cations show bonding to a region of high electron density while anions will bond to an electron-deficient site
- a relatively strong noncovalent intermolecular attraction that is relatively insensitive to temperature.
III. Physicochemical Properties of OMAs

The physicochemical properties of OMAs that are of general pharmaceutical and pharmacological interest include reactivity and solubility. Reactions of OMAs of interest are those that occur under relatively mild conditions such as those found during pharmaceutical manufacture, dosage formulation, storages, administration, etc. The other reactivity of OMAs of interest is the property of acidity or basicity.

The relative solubility of an OMA in aqueous vs. lipid media is of both pharmaceutical and pharmacological interest with respect to dosage formulation, route of administration as well as drug biodisposition. The solubility of OMAs is usually expressed in terms of relative water solubility with those compounds having high water solubility listed as being **hydrophilic** while those of low water solubility listed as being **hydrophobic**. These latter compounds are more commonly referred to as being **lipophilic**.

The solubility of OMAs in water is largely dependent on the ability of the OMA to establish noncovalent interactions (usually H-bonds) with molecules of H$_2$O as illustrated below for the interaction of water-soluble NaCl in water.

![Interaction of water-soluble NaCl in water](image)

Hydrocarbons are unable to establish significant interactions with H$_2$O molecules since these nonpolar compounds, at best, interact with other molecules via weak van der Waals forces. Therefore hydrocarbons will not be soluble in (miscible) H$_2$O but will be compatible with other hydrocarbons. Low molecular weight hydrocarbons (1-4 C) are usually gases while those with 5 to 20 C are low boiling liquids (see “Hydrocarbon Tutorials”)

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Addition of atoms other than C and H to the structure of OMAs produces functional compounds. Atoms usually included are O, N, S and sometimes P. Addition of these so-called *heteroatoms* significantly alters the physicochemical properties of functional organic compounds as compared to the simpler hydrocarbons.

<table>
<thead>
<tr>
<th>Functional Group</th>
<th>Name</th>
<th>Systematic Name</th>
<th>Common Name</th>
</tr>
</thead>
<tbody>
<tr>
<td>R-CH₂OH</td>
<td>Primary alcohol</td>
<td>Alkanol</td>
<td>Alkyl alcohol</td>
</tr>
<tr>
<td>R₂-CHOH</td>
<td>Secondary alcohol</td>
<td>---</td>
<td>---</td>
</tr>
<tr>
<td>R₃C-OH</td>
<td>Tertiary alcohol</td>
<td>---</td>
<td>---</td>
</tr>
<tr>
<td>Ar-OH</td>
<td>Phenol</td>
<td>Phenol</td>
<td>Phenol</td>
</tr>
<tr>
<td>R-O-R</td>
<td>Aliphatic ether</td>
<td>Alkoxy alkane</td>
<td>Alkyl ether</td>
</tr>
<tr>
<td>R-O-Ar</td>
<td>Mixed ether</td>
<td>Alkoxy benzene</td>
<td>---</td>
</tr>
<tr>
<td>Ar-O-Ar</td>
<td>Aromatic ether</td>
<td>Aryloxy benzene</td>
<td>---</td>
</tr>
<tr>
<td>R-CH₂NH₂</td>
<td>Primary amine</td>
<td>Aminoalkane</td>
<td>Alkyl amine</td>
</tr>
<tr>
<td>R-CH₂NH-R</td>
<td>Secondary amine</td>
<td>Aminodialkane</td>
<td>Dialkyl amine</td>
</tr>
<tr>
<td>R-CH₂N-R₂</td>
<td>Tertiary amine</td>
<td>Aminotrialkane</td>
<td>Trialkylamine</td>
</tr>
<tr>
<td>Ar-NH₂</td>
<td>Aromatic amine</td>
<td>Aniline</td>
<td>Aniline</td>
</tr>
<tr>
<td>R₄N⁺ Cl⁻</td>
<td>Quaternary ammonium chloride</td>
<td>Alkyl(aryl) ammonium chloride</td>
<td>Alkyl(aryl) ammonium chloride</td>
</tr>
<tr>
<td>RCHO</td>
<td>Aldehyde</td>
<td>Alkanal</td>
<td>-aldehyde</td>
</tr>
<tr>
<td>RCOOR</td>
<td>Ketone</td>
<td>Alkanone</td>
<td>Alkyl ketone</td>
</tr>
<tr>
<td>RCOOH</td>
<td>Carboxylic acid</td>
<td>Alkanoic acid</td>
<td>RCO + ic acid</td>
</tr>
<tr>
<td>RCOOR</td>
<td>Ester</td>
<td>Alkyl alkanoate</td>
<td>Alkyl RCO-ate</td>
</tr>
<tr>
<td>RCONHR</td>
<td>Amide</td>
<td>Alkanamide</td>
<td>RCO + amide</td>
</tr>
<tr>
<td>R-CO-NH-CO-R</td>
<td>Imide</td>
<td>Alkanimide</td>
<td>---</td>
</tr>
<tr>
<td>RCN</td>
<td>Nitrile</td>
<td>Alkanonitrile</td>
<td>RCO + nitrile or Cyanooalkane</td>
</tr>
<tr>
<td>RSH</td>
<td>Thiol</td>
<td>Alkanethiol</td>
<td>Alkyl mercaptan</td>
</tr>
<tr>
<td>R-S-R</td>
<td>Sulfide</td>
<td>Alkylthiolalkane</td>
<td>Alkyl sulfide</td>
</tr>
<tr>
<td>R-SO₂-R</td>
<td>Sulfoxide</td>
<td>Alkylsulfinyl alkane</td>
<td>Alkylsulfoxide</td>
</tr>
<tr>
<td>R-SO₂-R</td>
<td>Sulfone</td>
<td>Alkylsulfonyl alkane</td>
<td>Alkylsulfone</td>
</tr>
<tr>
<td>R-SO₃H</td>
<td>Sulfonic acid</td>
<td>Alkylsulfonic acid</td>
<td>---</td>
</tr>
<tr>
<td>R-SO₂NH₂</td>
<td>Sulfonamide</td>
<td>Alkylsulfonamide</td>
<td>---</td>
</tr>
<tr>
<td>R-X (X = F, Cl, Br, I)</td>
<td>Halide</td>
<td>Haloalkane</td>
<td>Alkyl halide</td>
</tr>
</tbody>
</table>
The following rules may be followed in naming an OMA containing functional groups:

1. Multiple functionality is indicated by *di, tri, tetra, etc.*

2. The parent hydrocarbon chain should contain all functionality. The position of the functionality should be designated by the lowest possible number.

3. In cases of mixed functionality, the following priority list should be used in numbering functionality position on the parent hydrocarbon chain:

   (a) COOH, CONH₂, or COOR  
   (b) CHO  
   (c) CN  
   (d) Ketone  
   (e) -OH  
   (f) -NR₂  
   (g) -OR  
   (h) -C₂R  
   (i) -CH=CR₂  
   (j) -R

Heterocyclic Systems - cyclic organic compounds containing an atom other than C within the ring structure are termed **heterocycles**. Heterocyclic OMAs usually contain O, N or S in addition to C.

1. Three- and four-membered heterocycles:
2. Five-membered heterocycles:
3. Six-membered heterocycles:
4. Fused heterocycles:
5. Miscellaneous heterocycles commonly found in OMAs:
V. Problems

1. Provide the electronic configuration for the following atoms (use a periodic table). See the example for carbon below. Also provide the valence and number of bonds each atom would form:

   H:
   Na:
   Ca:
   Mg:
   Al:
   C: 1s^2 2s^2 2p^2  Valence = 4, Bonds formed = 4
   N:
   O:
   S:
   F:
   Cl:

2. Draw the “lewis dot structure formulas” for the following molecules and indicate if the bonds formed are ionic or covalent. Also show all charges. See the example below and examples worked in class:

   \[
   \text{CH}_3\text{OH} = \begin{array}{c}
   \text{H} \\
   \vdots \\
   \vdots \\
   \vdots \\
   \text{H} \\
   \end{array}
   \]

   Example: No charge

   \[
   \text{NaOH} \quad \text{C}_2\text{H}_6 \quad \text{CH}_3\text{COONa} \quad \text{CH}_2\text{O} \quad \text{Mg(Cl)}_2
   \]

3. Identify the bonds labeled “a”, “b” and “c” in the structure below. Also rank these bonds in terms of relative energy (highest to lowest).