CHM1321 Stereochemistry and Molecular Models Assignment

Note: A significant amount of background information is provided in the following sections. More detail is found in the Mechanistic Patterns textbook in Chapters 4 and 5.

Introduction

A key aspect of modern organic chemistry is the consideration and analysis of the three-dimensional structure of molecules. Shape and stereochemistry are extremely important in medicinal chemistry and biochemistry because enzymes, proteins and other molecular machines inside our bodies are three-dimensional entities. Any interactions between biological molecules or between biological molecules and drugs will be based on overall geometry. Stereochemistry is also very important in chemical reactivity. Chemical reactions require that molecules and atoms interact to achieve favourable orbital overlap. This can only be done if the orbitals have the proper geometry to overlap.

Understanding the three dimensional shape and reactivity of organic compounds is very difficult to do using two-dimensional drawings. To properly understand organic structure and reactivity, it is necessary to consider the molecules in three dimensions. Today this can be done on a computer; however the best way to work in three dimensions is to use plastic molecular models. Models are cheaper, more rugged and are easier to visualize with.

An example of the types of reactivity differences you can expect when stereochemistry is considered is shown in Scheme 1. This is a cyclization reaction in which an epoxide is formed by displacement of a halogen in an \(S_N2\) process. When seen in two dimensions, the reaction is simple. An example of a flat representation of a reaction is the conversion of 1 to 2. The introduction of stereochemistry complicates matters. Notice that the \(trans\) product 3 is readily closed to produce epoxide 4 whereas the \(cis\) product 5 does not easily react. The reason for this is that the nucleophile and leaving group cannot become antiperiplanar to one another in structure 5 because of the relative configurations of the groups. Antiperiplanar alignment is necessary in this reaction so that the unpaired electrons of the nucleophile can interact with the \(\sigma^*\) orbital of the leaving group to produce a new bond. On paper, this relationship is difficult to see, but becomes obvious when molecular models are used.

Darling Molecular Models

In this assignment, you will use your molecular models to construct a set of compounds from a list your instructor will provide. For best results, Darling molecular models should be used, although other types may be permitted. Consult your instructor if you wish to use an alternate model kit.
The models you will use for the assignment are made of variously coloured plastic parts. The most common “organic” elements and the colors associated with them are shown in Table 1. Other elements can be various colors depending on need. Hydrogen is assumed on the “empty” bonds of carbon. On heteroatoms (O, N, etc.), it is usually convenient to use one of the small ball markers to represent a hydrogen atom. Empty bonds on heteroatoms are normally interpreted as lone pairs of electrons. When making models, the bonds should slide together easily. Do not force the models, or try to make small rings (3 or 4 atoms). See the instruction booklet that came with your models.

You will be using framework models. In this type of molecular model, the “sticks” represent bonds between atoms or lone pairs of electrons. Atoms are assumed to lie at the point at which the “sticks” come together (vertices) or at the ends of “empty sticks”. Most of the atom parts in your kits are designed to form tetrahedral atoms that consist of the central atom surrounded by 4 equally distributed bonds. It is important to always build tetrahedral atoms so that overall molecular geometries can be visualized. This includes heteroatoms. The bonds converge at the vertices of a tetrahedron centered on each atom.

![Figure 1: Two model pieces (a) when connected (b) form a tetrahedral geometry.](image)

You create a tetrahedral atom by joining together two V-shaped parts (Figure 1). Slide the pieces together at right angles so that the V-shaped openings point towards each other. Pinch the pieces together until they click. Double bonds are made using the sp² pieces (Figure 2), which look like elongated oval rings. Triple bonds are represented by the linearly shaped pieces.
Figure 2: (a) A double bond piece and two model pieces labelled sp², when connected, form a double bond (b), with trigonal planar geometry. (c) A triple bond piece, showing 180° linear geometry.

It is usually easiest to assemble models by preparing the required number of tetrahedral atoms and then joining them together. As much as possible, try to make your models look like your drawings, this will make it easier to build models. Similarly, making drawings look like models makes it easier to transfer information to paper.

Structural Representations

Scheme 2 shows some of the various ways to depict the structures of compounds in two dimensions. Each of these notations has been designed to convey structural information for different purposes. More detail on these representations can be found in your textbook.

**Condensed structures** show no three-dimensional structure. They are used when composition is important, or when you are trying to convey a structure using a word-processor. These structures provide information about how each atom in a compound is connected. Condensed formulas make assumptions about how many atoms can be connected to a given atom. To understand these formulas, you need to know how many connections each type of atom can make. Carbons normally form four bonds, nitrogen forms three, oxygen two and halogens one. All of the hydrogens that are attached to an atom are written immediately after that atom. The groups that are attached to a given atom are frequently surrounded by parentheses. Some examples are shown below:

a) CH₃CH₂CH₂CH₃  
b) CH₃CHClCH₂CH₃  
c) CH₃CH₂OH  
d) CH₃OCH₃  
e) OHCH(CH₃)₂
In the first example (a), all 4 carbons are connected in a linear chain. The first carbon is surrounded by three hydrogens, the second and third carbons by two hydrogens each, and the fourth carbon by three hydrogens. Note that each carbon is bonded to four other atoms. In the example (b), the first carbon is connected to three hydrogens and is also connected to the second carbon. This second carbon is connected to one hydrogen, a chlorine atom and to the third carbon. The third carbon is connected to two more hydrogens and to the last carbon, which is bonded to three hydrogens.

Compounds (c) and (d) illustrate the bonding of heteroatoms. In the third molecule, the first carbon is connected to three hydrogens and to the second carbon. This carbon is connected to two hydrogens and to the oxygen. The final hydrogen is connected to the oxygen. In the fourth structure, the first carbon is connected to three hydrogens and to the oxygen. The oxygen is connected to the second carbon, which is connected to three hydrogens.

The fifth compound shows an example of groups. In this case, the oxygen is connected to a hydrogen and to the first carbon. This carbon is connected to a hydrogen and to two CH₃ groups. The connection to these groups is a carbon-carbon bond in each case.

The structure shown at right provides an example of a condensed formula containing a double bond. The first carbon is connected to three hydrogens and to the second carbon. The second carbon is connected to one hydrogen and to the third carbon. This third carbon is connected to a hydrogen and to the final CH₃ group. Drawing this structure with bonds clearly shows that the second and third carbons each now have three bonds. Since it is understood that carbon normally makes four bonds, it is implied that these two carbons must be connected by a double bond.

**Zig-zag structures** convey stereochemical information in a compact manner. In these structures, carbons and hydrogens are not explicitly written. Instead only the bonds connecting the carbons are drawn. carbons are assumed at each vertex and terminus. The atomic symbols for heteroatoms are shown. Hydrogens are not explicitly shown unless bonded to a drawn atom. In these structures, it is important to remember that carbon always forms a maximum of four bonds. Any time a vertex or terminus has less than four bonds, the remaining bonds (to a maximum of four) are assumed to be to hydrogens. Shown in Scheme 4 are some condensed structures, with the corresponding zig-zag structure on the right.

In the first example, three carbons are connected in a linear chain. This chain is drawn as a zig-zag. The termini and vertexes represent the carbons. It is assumed that the first and third carbons each carry three hydrogens, while the middle carbon is bonded to two hydrogens (total of four bonds).
In the second example, five carbons are connected in a ring. Each vertex represents a carbon, and each line represents a bond. The number of hydrogens bonded to each carbon can be deduced by remembering that each carbon can bond to a maximum of four other atoms.

In the final example, three carbons are connected in a chain. The third is connected to two oxygens. Note that because the oxygens are heteroatoms, that the symbol for oxygen is explicitly drawn. The final hydrogen is written after an oxygen and so must be connected to the oxygen. The first oxygen must be doubly bonded since it is not followed by a hydrogen. This double bond can only be to the carbon preceding it.

The models in your kit naturally form zig-zags because of the tetrahedral geometry of the atoms. This can be helpful when drawing structures or building models because you can make your models look like your drawings and vice-versa. In the sections below, you will be asked to build models from condensed structures and then draw the zig-zags. Build each model and place it on the desktop in a zig-zag fashion, then simply draw what you see. This method helps to reduce errors when you convert models to drawings and vice-versa.

Zig-zag structures often feature bonds that look like wedges or hashes. These bonds are used to show the three-dimensional tetrahedral shape of an atom. Bonds drawn as simple lines are assumed to be in the plane of the paper. Wedge bonds are assumed to project above the plane of the paper. Hash bonds are assumed to project below the plane of the paper.

When drawing wedges and hashes, it is important to respect the tetrahedron shape. A tetrahedron is formed from two V shapes, joined at their vertexes and twisted 90° to each other. When drawing stereochemistry (wedges or hashes), you should always draw the atoms to show the two V shapes joining at the vertex (see above). Two of the bonds should lie in the plane of the paper (single lines), one should be up and the other down.

A Newman projection is a cartoon showing the dihedral angle of a bond. The dihedral angle is defined by 4 atoms, and the bond in question is assumed to be the one between the second and third atom of the four atoms specified. Newman projections are very useful in determining reactivity and overall shape.

In the line structure shown in Figure 3, ethane is depicted with all the hydrogens drawn in stereochemical notation. If you look along the axis of the carbon-carbon bond, you will see the projection of this bond and the dispersal of the hydrogen atoms. To illustrate this dispersion of atoms, the Newman projection is used.

In the Newman projection, the carbon atom that is in back is represented as a circle. Each of the hydrogens that are bonded to this carbon are represented by lines, spaced 120° apart. Notice that these lines stop at the outside of the circle that represents the rear carbon.
Figure 3: (a) How to construct a Newman Projection of ethane. Newman projections for the staggered (b) and eclipsed (c) conformers of ethane.

The three carbon-hydrogen bonds connected to the front carbon are depicted as lines spaced 120° apart. The carbon is assumed to be the vertex formed by these lines. The Newman projection is formed by combining the representation of the front and back carbons. This shows the conformation that the molecule is in. The angle between a hydrogen on the front carbon, and a hydrogen on the back carbon is called the dihedral angle, Φ. It is defined by the four atoms that make up the angle (H-C-C-H).

Your model kit contains small plastic spheres that are designed to fit over tetrahedral atoms. The sphere can be used to make Newman projections easier to see. Place a sphere on the back atom of the bond you are viewing. As you look down the bond, you will see the Newman projection. The sphere represents the circle shown in the Newman projection. Using a sphere that contrasts the color of the atom in front can often make the Newman projection easier to see.

The dihedral angle defined by atoms gives rise to specific conformations in a molecule. A conformation is simply a shape that a compound can adopt by the rotation of bonds. Figure 3 shows two types of conformation that are of particular importance. In the first example (Figure 3b), the dihedral angle shown is 60°. This conformation, in which the hydrogens are maximally separated, is called a staggered conformation. Figure 3c shows a conformation in which the dihedral angle is 0°. This conformation, in which the carbon-hydrogen bonds of the front and back carbons overlap, is called an eclipsed conformation. In addition to these conformations, there are two types of staggered conformer, the anti-staggered and the gauche-staggered. You should consult your text for descriptions of these conformations.

Absolute configuration

The shape of chiral compounds is conveyed by a naming system that provides the absolute configuration of each of the stereogenic centers in the compound. This system is analogous to naming our hands right or left. The system that is used is called the Cahn-Ingold-Prelog system or simply the R,S-system. Details are given in the course text. To name a stereogenic center using this system, the following steps are carried out.
1. Each of the four groups attached to a stereogenic atom is assigned a priority (1, 2, 3, 4) based on the atomic number of the directly attached atoms. Priority #1 goes to the atom with the highest atomic number.

2. In the case of a tie (same atomic number), the next directly attached atom in each of the groups in question is examined. This process continues, examining each of the atoms at the branch point until the tie is broken. Atoms are examined according to the order highest-to-lowest atomic number.

3. For double or triple bonds, the group is re-drawn duplicating the atoms at each end of the π-bond. Note that only the directly attached atoms are duplicated, not entire groups.

4. For isotopes, break ties using atomic masses (highest mass = highest priority).

5. Rotate the structure so that the lowest priority group points away from you. The molecule is named according to the direction of rotation of the three highest priority groups in the order of 1-2-3. **Clockwise** rotation means that the stereogenic center is called R, **counter-clockwise** rotation gives the S designation.

**Chair Structures**

Cyclohexane is a special structure in organic chemistry, because this is the only cyclic hydrocarbon that has a strain-free conformation. This conformation is called a chair conformation because a line-representation resembles a reclining chair. When cyclohexane is viewed from the top, the molecule looks like a hexagon. However, if this structure is rotated slightly and viewed from the side, a three-dimensional shape appears that is called a chair. Details on chair conformations are given in the textbook in Chapter 3.
**The Assignment**

Your instructor will provide you with a list of molecules – follow the instructions below for each compound.

**Part A: Enantiomers and Diastereomers.**

1. Construct a model of Molecule A, as well as the model of its mirror image. Take a photo of the two models with your student card visible in the photo. The photo should clearly show that the two models are mirror images. You may repeat this step with the other compounds, but it is not necessary to take photos of each model, only Molecule A.
2. Carefully draw the structures of the models that you have made using proper stereochemical notation. The mirror images should be drawn side-by-side indicating the mirror plane. Structures should be drawn using the zig-zag style, either by hand or using ChemDraw (see note below).
3. Determine if the mirror images can be superposed and therefore if they are enantiomers and/or diastereomers.
4. Identify the stereogenic centre(s) of the molecule.
5. Determine the configuration at each stereogenic centre (R or S).
6. For compounds that have more than one stereogenic centre, prepare all the possible stereoisomers of the compound, including all mirror images. You should try to prepare all of the isomers of a given compound at the same time.
7. Carefully draw the models that you have made using proper stereochemical notation. The mirror images should be drawn side-by-side indicating the mirror plane. Models should be drawn using the zig-zag style.
8. If there are more than 2 stereoisomers, perform a full stereochemical analysis of your structures, indicating which pairs are enantiomers and/or diastereomers. Identify the stereogenic centre(s) of the molecule and determine the configuration at each stereogenic centre.

**Part B: Newman projections.**

1. Construct a model of the provided molecule (match the configuration exactly) and look down the indicated bond. Take a photo from this perspective with your student card visible in the photo.
2. Using your model, construct an energy diagram to show the variation in the free energy of the molecule as the FRONT ATOM is rotated CLOCKWISE from 0° to 360° in 60° increments. In your energy diagram, you should clearly show the relative energies of each conformer.
3. Draw Newman projections for each conformation on the bottom of your diagram.
Part C: Chair conformations
1. Build a model of the molecule in one chair form.
2. Draw your model properly using the chair convention.
3. Indicate all of the axial and equatorial substituents (including hydrogens).
4. Without breaking any bonds, convert your model to the other chair form. Be careful not to rotate the overall molecule.
5. Draw your model properly and indicate all of the axial and equatorial substituents (including hydrogens).
6. Indicate which of the two chair conformations you expect to be more stable.

Notes:
Assignments must be uploaded as a single digital document to the course website (we will accept the usual formats, such as .docx, .pdf etc.) before the deadline. It is your responsibility to ensure that the file is readable and submitted properly on time; late submissions or corrupted files will not be graded. Your assignment must include the two photos (from Parts A and B) as well as your structures.

If you are drawing your structures and Newman Projections by hand, they must be drawn in pen and be clear and legible – if we can’t see/understand what you have drawn, it will not be graded. To submit your assignment, you can either scan or take a photo of your written answers and attach your model photos to form a single document, using the software of your choice.

If you are using ChemDraw for your structures, please follow these steps:
- open a new document
- go to File → Apply Document Settings from… → ACS Document 1996

This will apply the necessary pre-sets so that your structures can be copy-pasted easily and neatly into most applications (e.g., Microsoft Word), along with your answers and photos.

A warning: using ChemDraw generally provides much neater-looking structures; however, it takes much longer to draw molecules using this program than simply drawing them by hand.
### CHM1321 STEREOCHEMISTRY ASSIGNMENT – LIST OF COMPOUNDS

### CHM1721 DEVOIR DE STÉRÉOCHIMIE – LISTE DE COMPOSÉS

#### Part A / Partie A:

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<tbody>
<tr>
<td>A</td>
<td>H₂NCH(CH₃)CH₂CH₃</td>
</tr>
<tr>
<td>B</td>
<td>CH₃ClBr(CH(OH))CH₃</td>
</tr>
<tr>
<td>C</td>
<td>CH₃CH₂CH(CH₂OH)CH₂OH</td>
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<tr>
<td>D</td>
<td><img src="image.png" alt="Image" /></td>
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#### Part B / Partie B:

![Image](image.png)

#### Part C / Partie C:

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