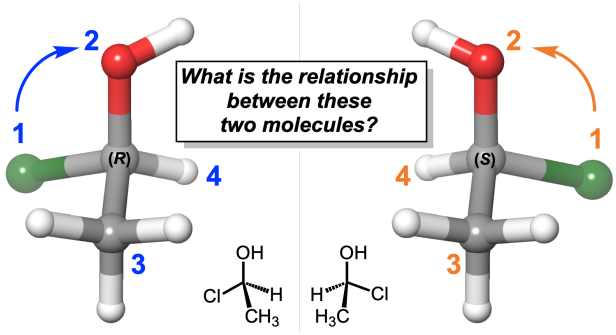
Stereoisomers

Created with: Release 2021-3
Prerequisites: working knowledge of Maestro
Files Supplied: Stereoisomers_worksheet
Categories: organic chemistry

About this Lesson

In this lesson plan, students will explore compounds called stereoisomers that differ from each other only in the three-dimensional, spatial arrangement of their atoms, but not in the connectivity of their atoms. The connection between stereoisomerism and drug action will also be discussed.

Using Maestro, students will use the 2D Sketcher and 3D Builder tools to learn how to draw different kinds of stereoisomers. Energy minimizations and geometry optimization calculations will be performed using Jaguar. The tile function will be used to compare stereoisomeric relationships between pairs of molecules to determine if they are enantiomers or diastereomers.



Learning Objectives

- Designate configuration of a stereocenter using the Cahn-Ingold-Prelog (CIP) system
- Determine the stereochemical relationship between a pair of molecules

Standards

- *ACS Guidelines:*
  - Understand molecular structure and bonding (Section 5.2)
- *ETS Chemistry GRE:*
  - Structure, Bonding and Nomenclature – Stereochemical Notation (3.A)
- *AAMC MCAT:*
  - Stereochemistry of covalently bonded molecules (5B)

Assessments

The following types of formative assessments are embedded in this lesson:

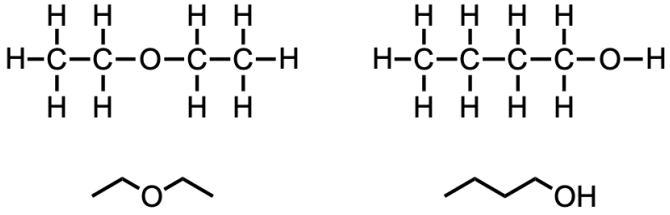
- Assessment of student understanding through discussion of warm-up questions and filling in any knowledge gaps about constitutional isomers
- Visual assessment of student-generated enantiomers and diastereomers

Warm-Up Questions: To be done on their own or at the beginning of class

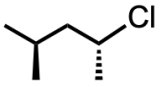
Watch the Khan Academy videos on stereochemistry.

1) What is the difference between constitutional isomers and stereoisomers?

2) Label the following pair of molecules as either constitutional isomers or stereoisomers. Both the skeletal structure and bond line structure of each molecule have been provided.



3) How many chiral center(s) does the following molecule have?



Lesson Outline

1. What you will need for this lesson

	1. Go to the 'Data' folder and open your Class Folder found on the virtual cluster's desktop. 2. Right-click on the folder called "Stereoisomers" and copy folder to Desktop ● Here, you will find the lesson plan, worksheet, and any additional resources
 *Figure 1-1. Open Maestro.*	3. Open **Maestro** a. See Starting Maestro if you need help

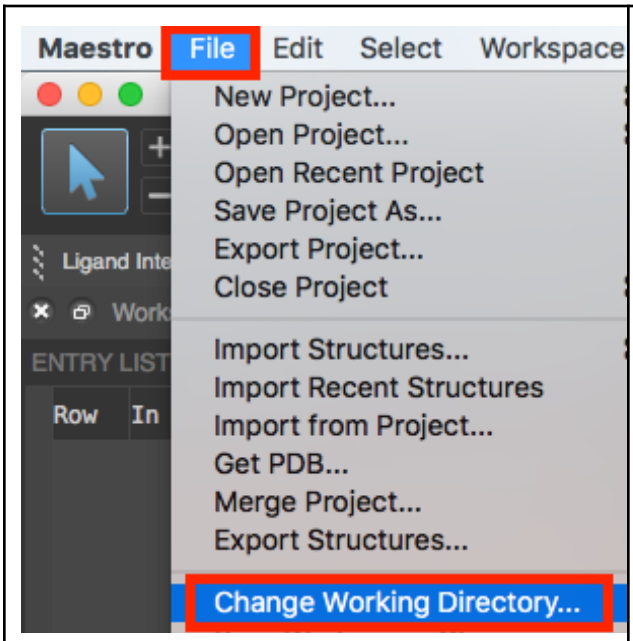


Figure 1-2. Change Working Directory option.

4. Go to **File > Change Working Directory**
5. Find your “Stereoisomers” folder that you duplicated to your Desktop, and click **Choose**

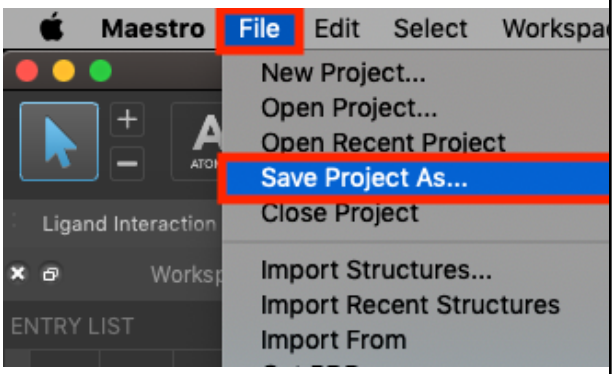


Figure 1-3. Save Project panel.

6. Next, go to **File > Save Project As**
7. Type “**Stereoisomers_tutorial**” and click **Save**
    - The project will be titled stereoisomers_tutorial.prj

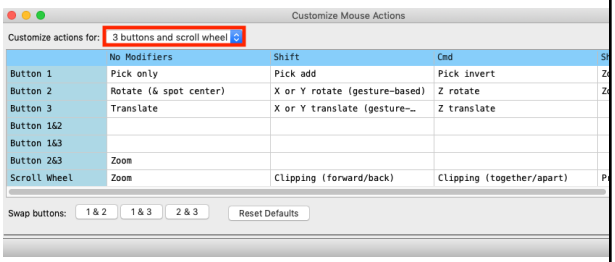


Figure 1-4. Choose the best mouse option for your set up.

8. Finally, check your **Mouse Actions**
    - **Edit > Customize Mouse Actions**

9. Make sure you have **the best option chosen for your set up**. This lesson was written with a three-button mouse with a scroll wheel. If you do not have a mouse, choose **Trackpad**.

2. Introduction to Stereoisomers

Isomers are molecules that have the same molecular formula but have differing structural arrangements in space. Though they are made up of the same components, distinct isomers do not necessarily bear resemblance to each other both visually and in terms of their properties. Isomers can be broken into two types: constitutional isomers and stereoisomers.

Constitutional isomers are when two molecules share the same chemical formula but differ in structural arrangement. For example, butane (or *n*-butane) and 2-methylpropane (or isobutane) both have a molecular formula of C_4H_{10}, but they differ in connectivity. *N*-butane is more linear whereas isobutane is more branched, yet they have the same number of carbon and hydrogen atoms in each isomer.

Constitutional isomers of C_4H_{10}

butane ***isobutane***

Figure 2-1. Constitutional isomers of C_4H_{10}

Stereoisomers have an identical molecular formula and atomic sequence but differ in how they are spatially arranged. *Cis-trans* stereoisomerism can be used to denote disubstituted cycloalkanes. For example, *cis*-1,2,-dimethylcyclohexane and *trans*-1,2-dimethylcyclohexane both have the same molecular formula of C_8H_{16} as well as the same connectivity of atoms, but the spatial arrangement of the methyl groups differ. The *cis* stereoisomer shows the two methyl groups on the same side of the ring, while the *trans* stereoisomer shows the two groups on opposite sides of the ring.

cis-trans stereoisomers of C_8H_{16}

***cis*-**
1,2-dimethylcyclohexane

***trans*-**
1,2-dimethylcyclohexane

Figure 2-2. *Cis-Trans* isomers of C_8H_{16}

Furthermore, the terms *cis* and *trans* are also used to describe stereoisomerism in double bonds. For example, *cis*-2-butene and *trans*-2-butene both have the same

molecular formula of C_4H_8 as well as the same connectivity of atoms, but the spatial arrangement of the methyl groups differ. The *cis* stereoisomer shows the groups on the same side of the double bond, while the *trans* stereoisomer exhibits groups on opposite sides of the double bond. These two molecules have two different physical properties because the double bond does not have free rotation like single bonds do at room temperature.

cis-trans stereoisomers of C_4H_8

***cis*-2-butene**
Boiling point: 4ºC

***trans*-2-butene**
Boiling point: 1ºC

Figure 2-3. *Cis-Trans* isomers of C_4H_8

The last type of stereoisomer delves into a specific property called **chirality**. Chiral objects are **not superimposable** on their mirror images. The most common source of molecular chirality is the presence of a chiral center which is a carbon atom with four unique, or different, substituents attached to it. The tetrahedral sp^3-hybridized carbon atom in bromochloroethanol shown below is chiral because it contains four different substituents: –OH, –Cl, –Br, and $–CH_3$. We will go into much more detail on how to assign chirality and how to label stereoisomeric relationships of two chiral molecules later in this lesson.

Stereoisomers of C_2H_4OClBr

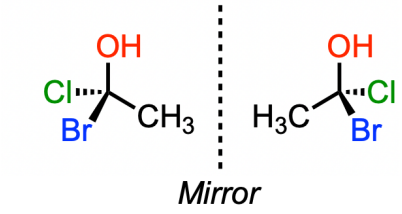


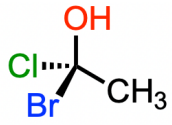
Figure 2-4. Stereoisomers of C_2H_4OClBr

3. Assigning Configuration using the Cahn-Ingold-Prelog (CIP) Rules

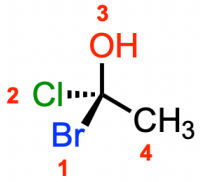
In order to determine the specific configuration of a stereocenter, a system developed by three chemists named Cahn, Ingold, and Prelog, was developed.

- Step 1: Identify the chiral center and rank the substituents around the chiral center. The higher that atomic number, the higher the priority.
    - If priority can't be assigned by the direct atoms bonded to the chiral center, look to the next set of atoms. Priority is assigned at the first point of difference
    - Atoms in a double or triple bond are considered to be bonded to an equivalent number of similar atoms by single bonds
- Step 2: Orient or rotate the molecule so the lowest ranked atom or group points towards the back (on a dashed bond).
- Step 3: Read the 3 highest priority groups.
    - If the 3 groups are read clockwise, the configuration is (*R*).
    - If the 3 groups are read counterclockwise, the configuration is (*S*).

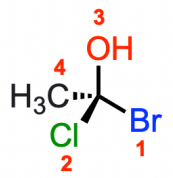
Example #1. Assign configuration of (*R*) or (*S*) to the following chiral molecule.



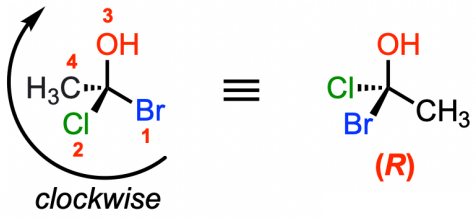
- Step 1: After looking at the periodic table, Br has the highest atomic number of 35, then Cl has the second highest atomic number of 17, then O has the third highest atomic number of 8, and C has the lowest atomic number of 6.



- Step 2: Since C has the lowest atomic number making it the lowest priority group, we have to rotate the methyl group to the back (on a dashed bond). Then we can relabel our priority groups.



- Step 3: The sequence 1 > 2 > 3 follows a clockwise configuration, so we can assign the chiral center as (*R*).



Computational Exercise #1: Geometry Optimization using Maestro

Even though we draw bonds coming towards us as wedged bonds and bonds going away from us as dashed bonds, sometimes it is still difficult to visualize the three-dimensionality of a molecule when it is drawn on a flat piece of paper. Now we are going to learn how to build a three-dimensional structure of a chiral molecule, optimize its geometry using Maestro, and use the CIP rules to assign its stereochemical configuration. Visualizing the molecular structure can be done in three different ways:

1) Through the 2D Sketcher
2) Through the 3D Builder
3) Or, by importing pre-built molecules

We will be using the 2D Sketcher tool in Maestro.

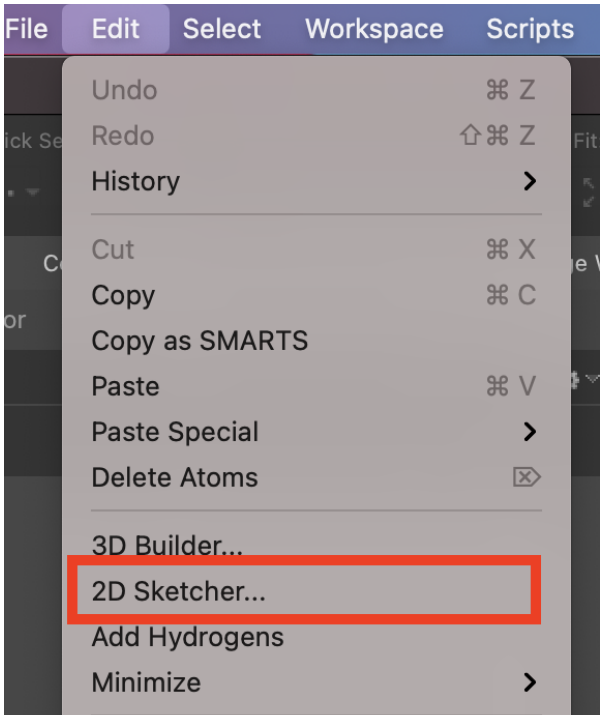


Figure 3-1. Opening 2D Sketcher

Part 1. Build (*R*)-1-bromo-1-chloroethane using 2D Sketcher

Before optimizing any molecular geometry, you will need a starting molecule in your workspace. Let's draw the structure of 1-bromo-1-chloroethane using the 2D sketcher.

1. Go to **Edit** > **2D Sketcher**

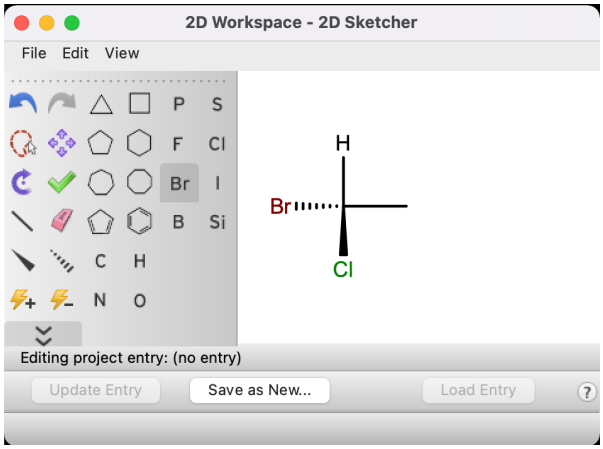


Figure 3-2. Drawing 1-bromo-1-chloroethane.

2. **Draw** 1-bromo-1-chloroethane exactly how it is shown in Figure 3-2.
    a. Go to the selection bar on the left
    b. Create a methyl group by choosing the "draw line" and **clicking** in the 2D Workspace
    c. Drag rightwards from the methyl group to add another carbon
    d. Create a wedge bond by choosing the wedge bond and dragging down from the central carbon
    e. Put your cursor over the end of the wedge and type Cl to add a chlorine
    f. Create a dashed bond by choosing the dashed bond and dragging to the left from the

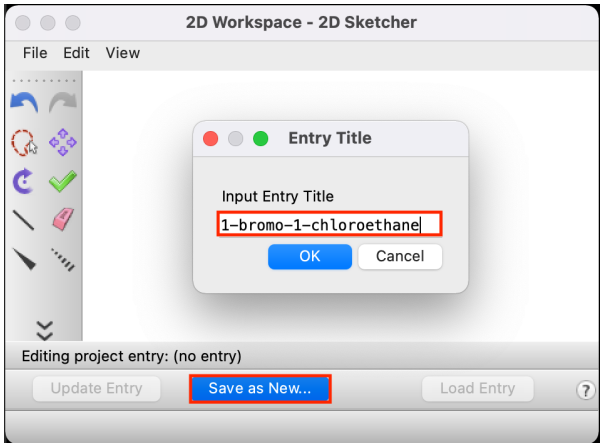


Figure 3-3. Saving 1-bromo-1-chloroethane.

central carbon

g. Put your cursor over the end of the wedge and type Br to add a bromine
h. Once again click on the “draw line” and click on the “H”. Drag upwards from the central carbon
i. Try to replicate the sketch shown in the figure as closely as possible

3. Click on **Save as New** and for *Input Entry Title* write **1-bromo-1-chloroethane**. Click **OK**.

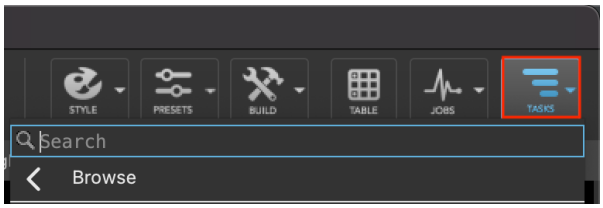


Figure 3-4. Clicking the Tasks button in the upper righthand corner.

Part 2. Optimize the Geometry using Quantum Mechanic DFT

Now let’s optimize the molecule at the quantum mechanical level.

4. With the 1-bromo-1-chloroethane entry selected and included, go to **Tasks > Optimization** using Jaguar
   a. The Jaguar Optimization panel opens
5. Use structures from **Project Table (1 selected entry)**

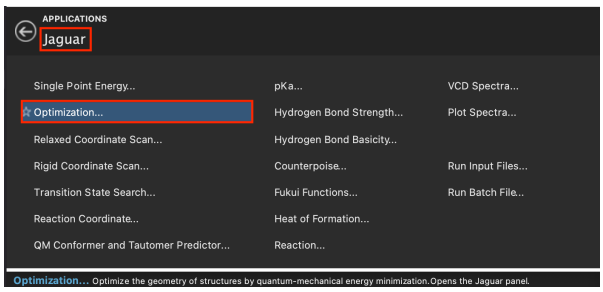


Figure 3-5. Opening the Jaguar Optimization panel.

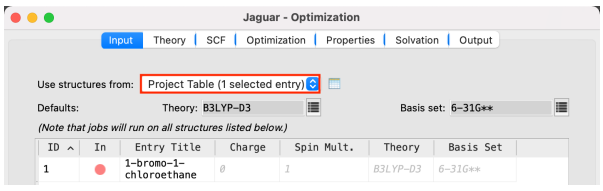


Figure 3-6. Setting the Jaguar Optimization panel to optimization.

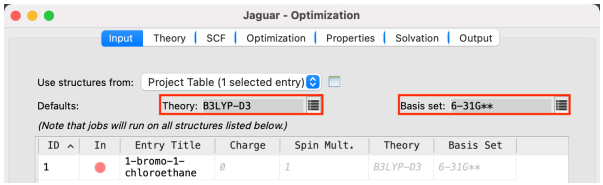


Figure 3-7. Setting the QM parameters for optimization.

Various settings can be altered depending on the specific use case. We will only adjust the *Input* tab for this example.

6. For *Theory*, select B3LYP-D3
7. For *Basis set*, select 6-31G**

A few additional comments about preparing for an optimization calculation:

- If you hover the mouse over the basis set in the table, you can see the number of basis functions associated with the basis set. This is useful to know since the quality of the basis set *usually* improves as the number of functions increases, noting again the trade-off between quality and computational expense
- Always make sure the charge and the spin multiplicity are correct (in this case, 1-bromo-1-chloroethane is a neutral, singlet, so charge = 0 and spin multiplicity = 1). Multiplicity is defined as 2S + 1, where S is the total orbital spin of the molecule. For instance, a system with one unpaired electron is a doublet (multiplicity = 2), since the total orbital spin S = ½.
- Use the *Atom-Level Settings* button to define per-atom basis sets
- Constraints can be defined on the *Optimization* tab
- Properties, such as atomic charges, vibrational frequencies, surfaces and more can be requested on the *Properties* tab
- Solvent can be defined via several implicit solvation models on the *Solvation* tab. Note that this example is a gas-phase geometry optimization
- Read more about geometry optimization with Jaguar here

8. Change the *Job name* to **1-bromo-1-chloroethane_opt_B3LYP-D3_6-31Gss**
    a. Usually we incorporate stars (*) and pluses (+) into file

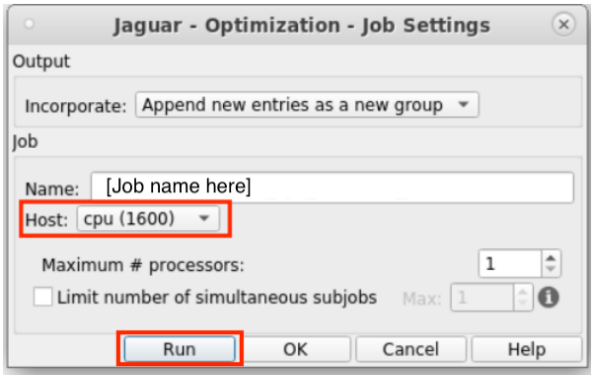


Figure 3-8. Naming and running the job.

names with S and P, respectively

9. Adjust the job settings ( ) by clicking the gear button to the right of the Job name
    - Choose CPU (1600) as your host with 1 processor
10. Click **Run**

Figure 3-9. Banner that shows the job is finished – Result has been incorporated.

When the job finishes, a banner will appear indicating that the result has been incorporated. At this time, the molecule with the optimized geometry is now shown in the workspace

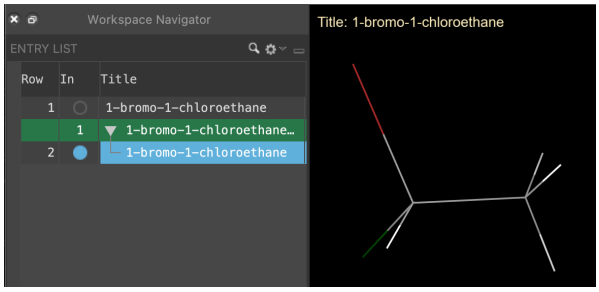


Figure 3-10. The output molecule of 1-bromo-1-chloroethane.

11. A new entry group is added to the entry list titled 1-bromo-1-chloroethane_opt_B3LYP-D3_6-31GSS.011 (1). Select and include the molecule titled 1-bromo-1-chloroethane in this subgroup. This is your optimized structure.

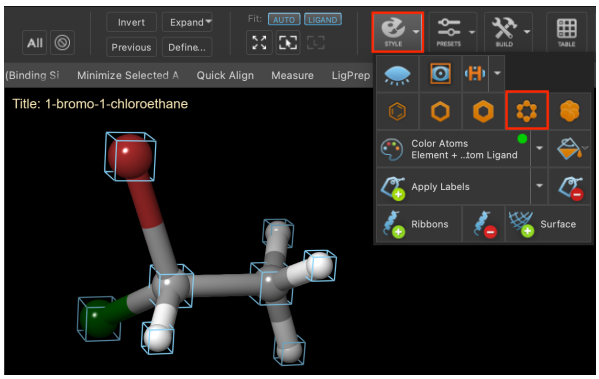


Figure 3-11. Viewing and styling 1-bromo-1-chloroethane.

12. Change the representation to ball-and-stick by clicking on the **Style** menu and choosing **Apply ball-and-stick representation**
13. Change the color of the atoms by clicking on the **Style > Color Atoms > Element + Custom Ligand**

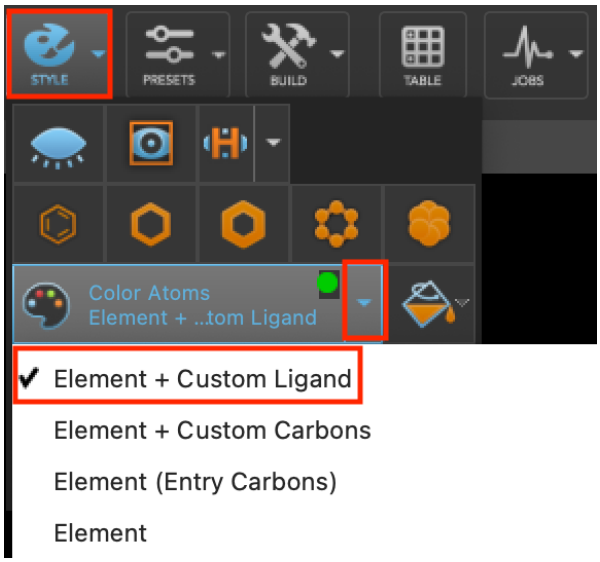


Figure 3-12. Changing atom colors for 1-bromo-1-chloroethane.

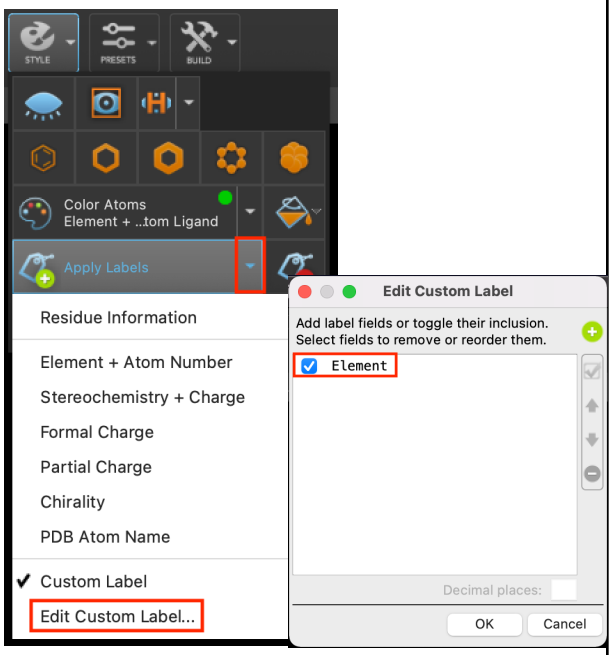
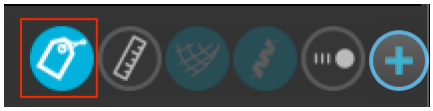


Figure 3-13. Labeling atoms.



14. To display atom labels, click **Style > Apply Labels** then click the drop down arrow on the right side
15. Click **Edit Custom Labeling**
16. Checkbox **Element** and press **OK**
17. Go back to **Style > Apply Labels > Custom Label** and now each atom in your workspace should be labeled

Note: You can toggle the atom labels on and off by clicking Annotations label button in the Workspace toggle on the bottom right corner

Figure 3-14. Toggling labels on.

Figure 3-15. Toggling labels off.

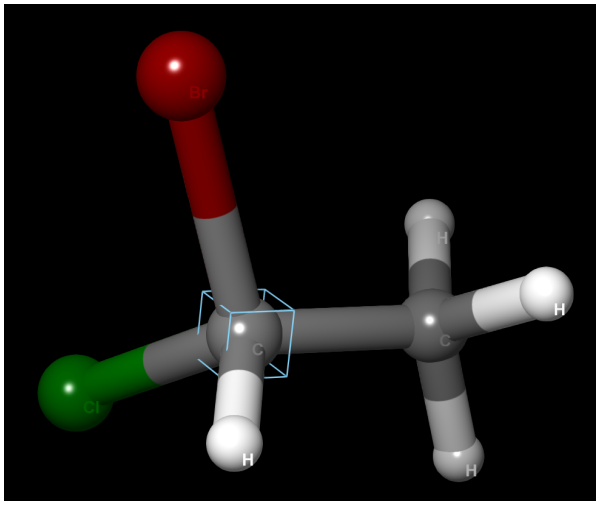


Figure 3-16. Determining where the chiral center is.

Part 3. Assign stereochemical configuration using CIP rules

Now that we optimized the geometry of 1-bromo-1-chloroethane, let's go through the CIP rules to determine its stereochemical configuration.

18. Determine which carbon atom is the chiral center. Remember that a chiral carbon has 4 unique, or different, substituents around it

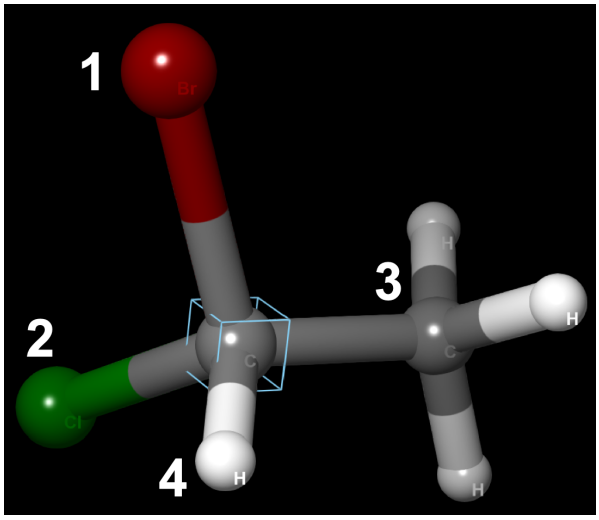


Figure 3-17. Labeling priorities of each substituent around the chiral center.

19. Label the priorities of each atom surrounding the chiral center based on atomic number (this can be found from a periodic table). Feel free to take note of these priorities on a separate piece of paper

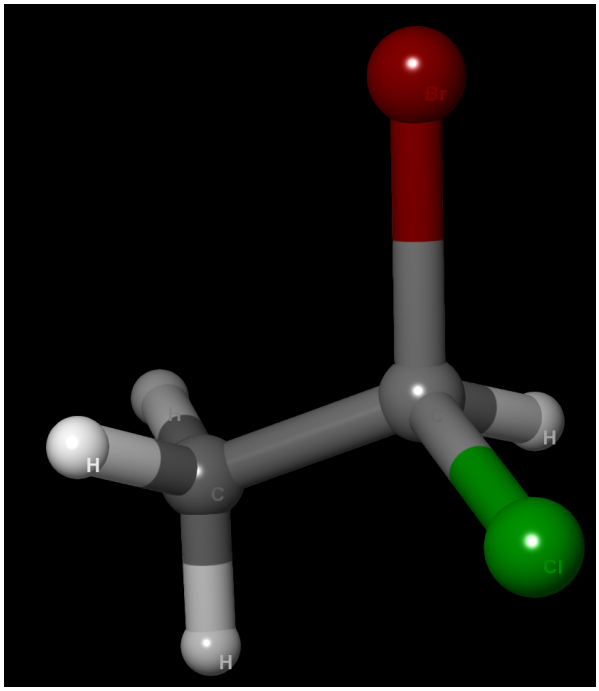


Figure 3-18. Rotating the molecule to the lowest priority group is facing the back.

20. Rotate the molecule so the lowest priority group is facing the back

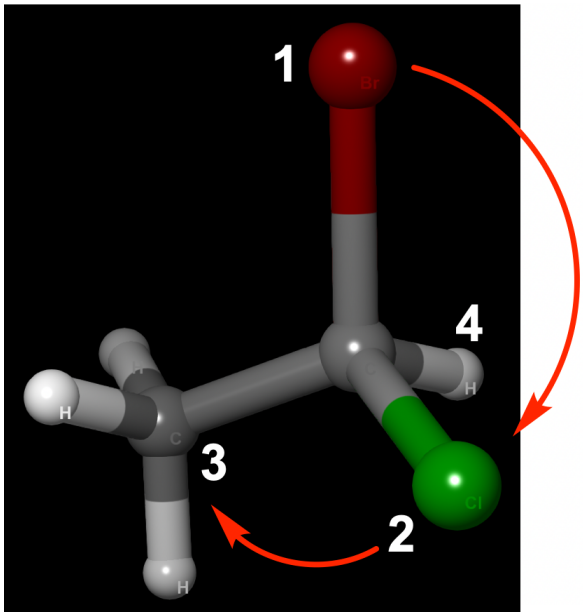


Figure 3-19. Assigning configuration based on either clockwise or counterclockwise sequence of the first 3 priority groups.

21. Relabel priorities and determine whether 1 > 2 > 3 is clockwise (*R*) or counterclockwise (*S*)
22. Since groups 1 > 2 > 3 are going clockwise, this particular isomer is (*R*)-1-bromo-1-chloroethane

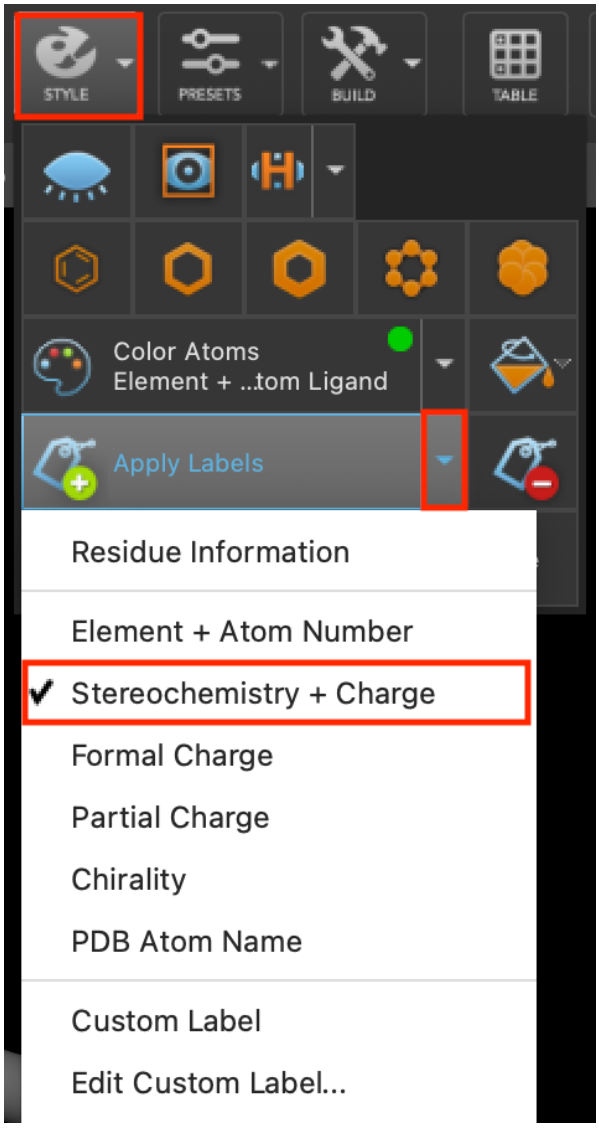


Figure 3-20. Applying the Stereochemistry + Charge Label to the molecule.

23. To double-check your answer and display stereochemistry labels, click **Style > Apply Labels** then click the drop down arrow on the right side
24. Click **Stereochemistry + Charge** and you will find that indeed, this stereocenter is (*R*)
25. Double-click the entry name in the entry list and change the name to R-1-bromo-1-chloroethane.

4. Enantiomers

A pair of compounds with the same atom connectivity, molecular formula, and only 1 chiral center can either be identical or enantiomers with one another. If they are identical, they would have the same exact stereochemical configuration. If they have completely opposite configurations (i.e. one molecule is (*R*) while the other is (*S*)), then they would be enantiomers. Enantiomers are stereoisomers that are nonsuperimposable, mirror images of one another and exhibit identical physical properties. When exposed to plane-polarized light, however, enantiomers exhibit different behavior. An enantiomer that rotates plane-polarized light in the positive direction is called dextrorotatory [(+), or d-], while the enantiomer that rotates the light in the negative direction is called levorotatory [(-), or l-]. When both d- and l- isomers are present in equal amounts, the mixture is called a **racemic mixture**. To learn more about the optical activity of enantiomers, you can read more about it here.

To better understand and visualize a pair of enantiomers, let's draw the enantiomer of (*R*)-1-bromo-1-chloroethane in Maestro.

Computational Exercise #2: Compare Multiple Molecules by Tiling

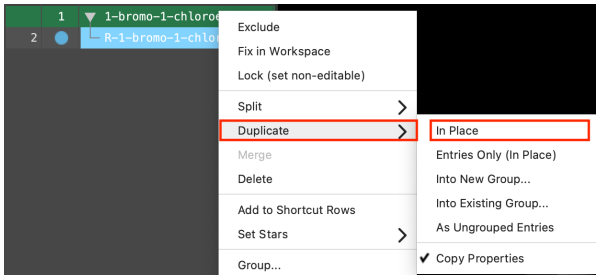
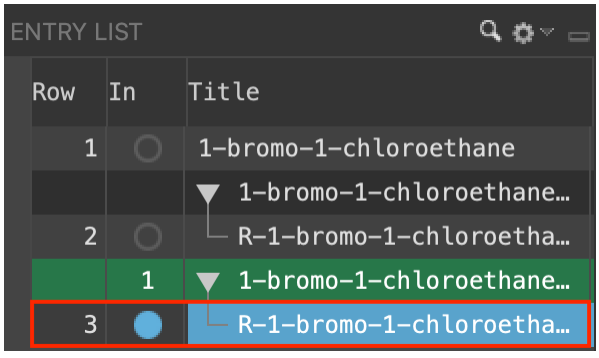


Figure 4-1. Duplicating R-1-bromo-1-chloroethane in the Entry List.

1. **Right-click** the entry R-1-bromo-1-chloroethane
2. Click **Duplicate > In Place** and you will see a new entry appear in the entry list



3. Include and select the new entry

Figure 4-2. Including and selecting the new entry.

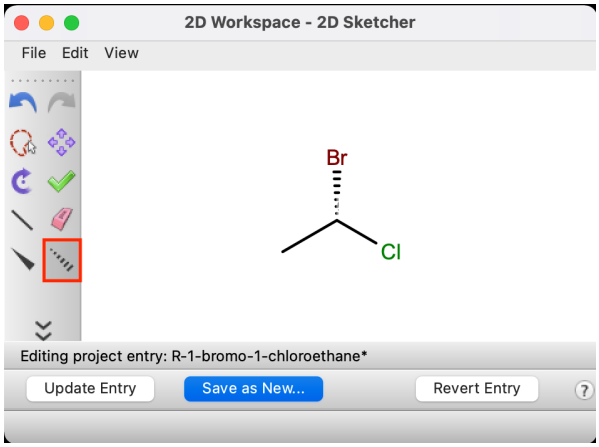


Figure 4-3. Changing the wedged bond to a dashed bond.

4. Go to **Edit** > **2D Sketcher**
5. Change the wedged C–Br bond to a dashed C–Br bond

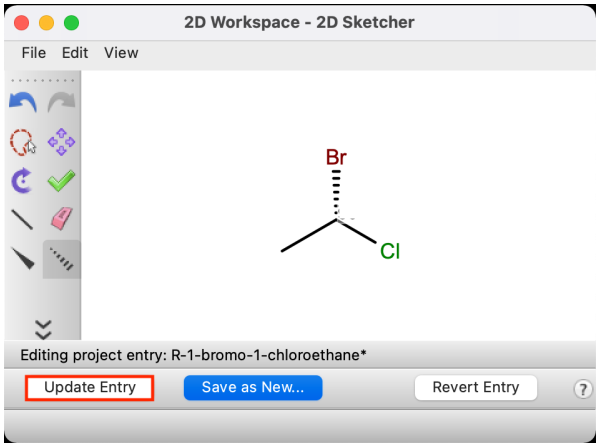


Figure 4-4. Update Entry.

6. Click **Update Entry**
7. Change the representation to ball-and-stick by clicking on the **Style** menu and choosing **Apply ball-and-stick representation**
8. Change the color of the atoms by clicking on the **Style > Color Atoms > Element + Custom Ligand**
9. To display stereochemistry labels, click **Style > Apply Labels > Stereochemistry + Charge Number**

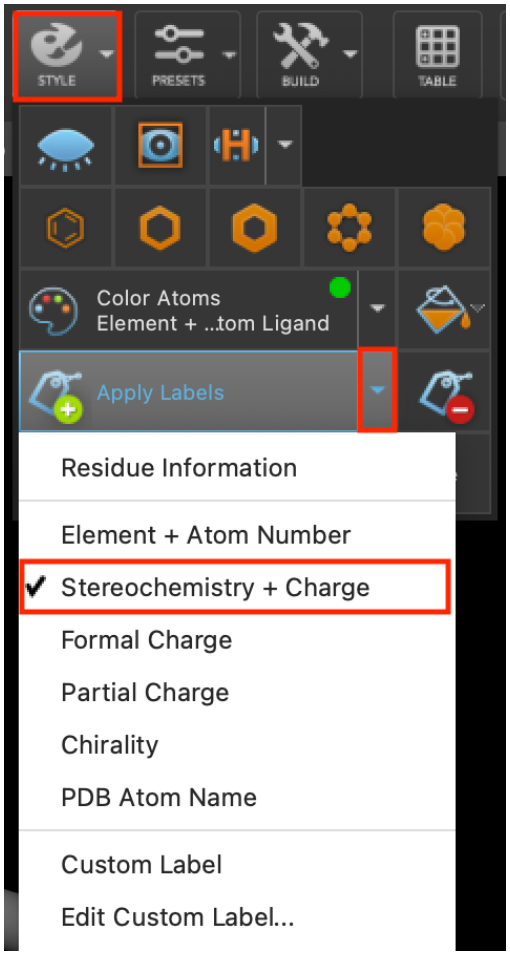


Figure 4-5. Applying the Stereochemistry + Charge label to the molecule.

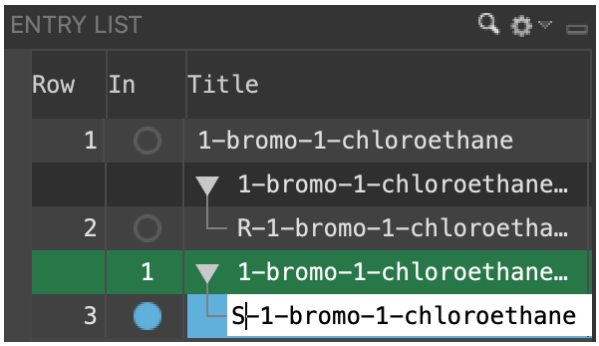


Figure 4-6. Changing the Entry Name.

10. Change the Entry name to S-1-bromo-1-chloroethane by double-clicking on the name.

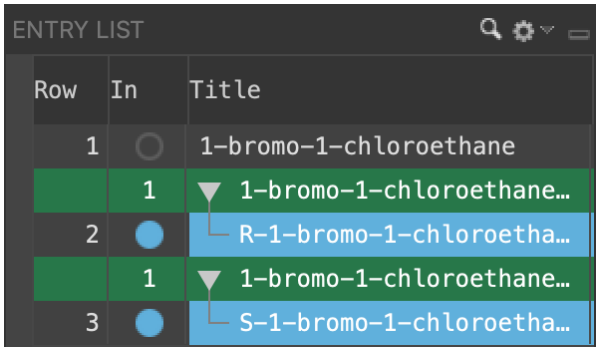


Figure 4-7. Including both molecules in the Entry List.

Now let's view our molecules side by side.

11. Simultaneously **include** (control + click or command + click) both the R-1-bromo-1-chloroethane and the S-1-bromo-1-chloroethane

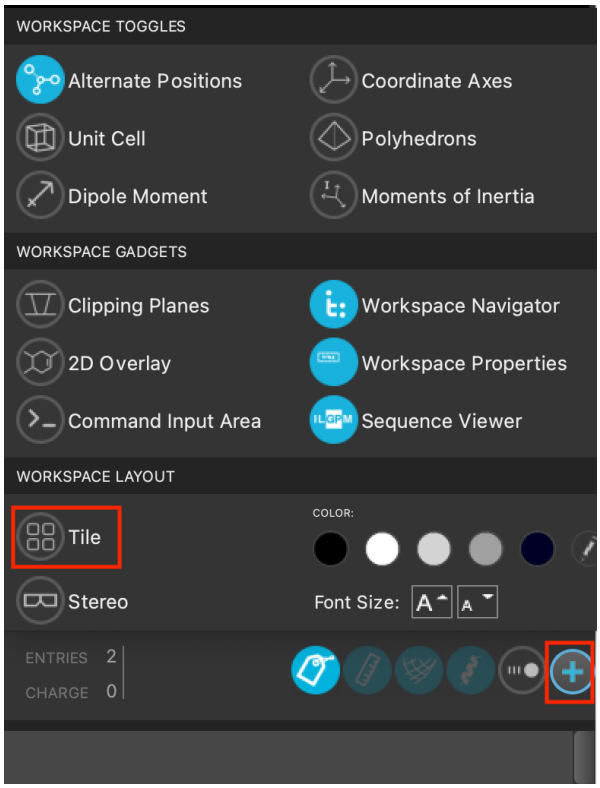


Figure 4-8. Opening the Workspace Configuration Panel

12. Click the + symbol in the bottom left-hand corner to show workspace configuration panel
13. Click **Tile** under the Workspace Layout

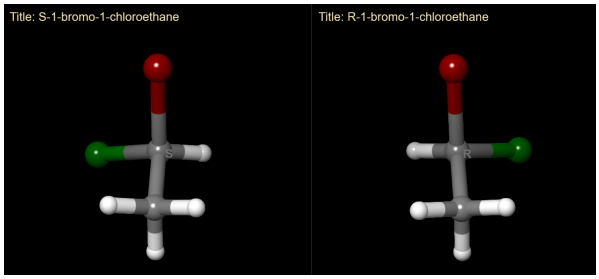


Figure 4-9. Tiling the two enantiomers side-by-side.

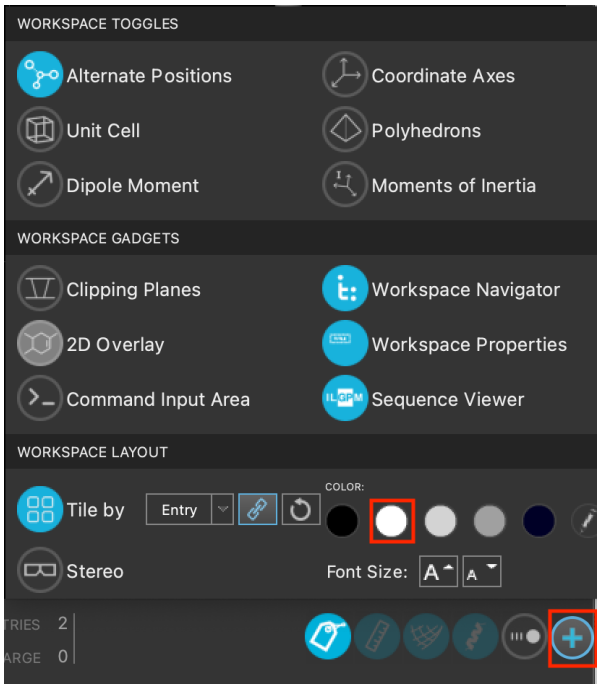
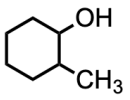


Figure 4-10. Changing the background color to white.

14. Change the background color to white by clicking on the + symbol in the bottom right-hand corner
15. You can take a screenshot of your molecules to input into the Stereoisomers worksheet.

5. Diastereomers

Diastereomers are stereoisomers that are not mirror images of one another. The difference between enantiomers and diastereomers is more apparent when we compare compounds with more than one chiral center. For example, let's take a look at the structure of 2-methylcyclohexanol.



2-methylcyclohexanol

Figure 5-1. Structure of 2-methylcyclohexanol

This molecule contains two chiral centers where each one can either have the (*R*) configuration or the (*S*) configuration. A molecule can have 2^n number of possible stereoisomers where *n* is the number of chiral centers. Since 2-methylcyclohexanol has 2 chiral centers, it has a total of $2^2 = 4$ possible stereoisomers, as shown below.

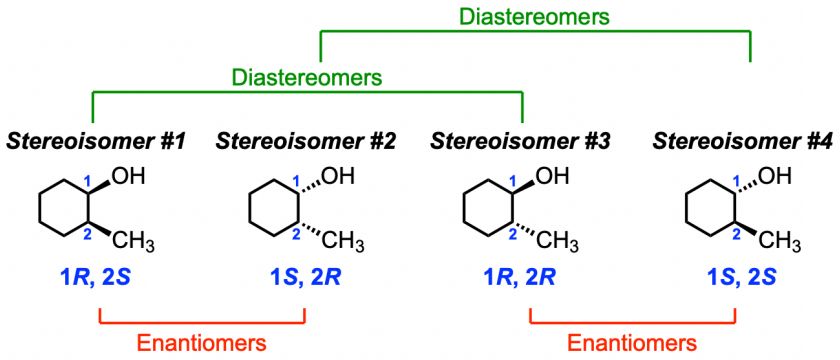


Figure 5-2. The possible stereoisomers of 2-methylcyclohexanol

Stereoisomers #1 and #2 are enantiomers because both chiral centers completely inverted to the opposite configuration. The same goes for stereoisomers #3 and #4 where the two chiral centers in stereoisomer #3 were (1*R*, 2*R*) and they both inverted to the opposite configuration of (1*S*, 2*S*) in stereoisomer #4. Now if we compare stereoisomer #1 to stereoisomer #3, notice that one chiral center stayed the same (1*R*) whereas the second chiral center inverted from (2*S*) to (2*R*). Since only one chiral center inverted, these two isomers are no longer mirror images from one another, making them diastereomers. And the same goes for stereoisomers #2 and #4 where they are both diastereomers as well.

As previously mentioned, *cis-trans* isomers of alkenes are also considered to be diastereomers because they too are not mirror images of one another. Let's build a few diastereomeric alkenes to visually compare their differences.

Computational Exercise #3: Build Diastereomeric Alkenes

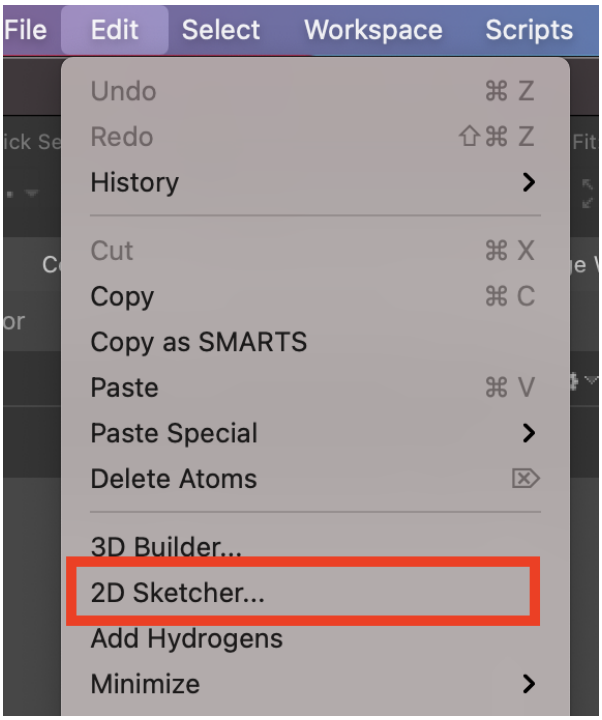


Figure 5-3. Open 2D Sketcher.

In order to visualize the molecules and compare isomers in three dimensions, we first have to draw models of the molecules. This can be done either through the 2D Sketcher, the 3D builder, or by importing pre-built molecules. We will be using the 2D Sketcher tool:

1. Go to **Edit → 2D Sketcher**

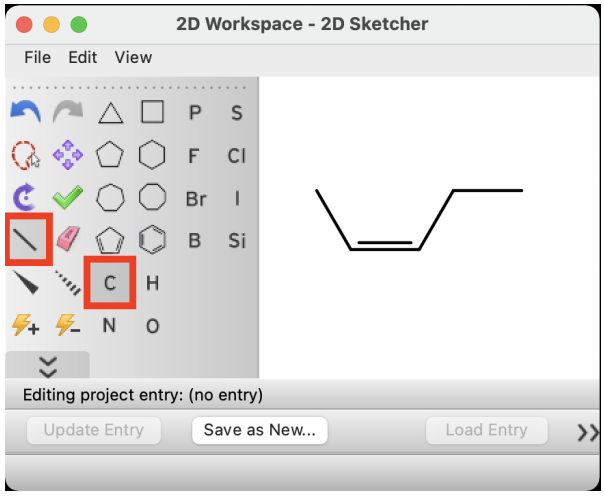


Figure 5-4. Drawing cis-2-pentene.

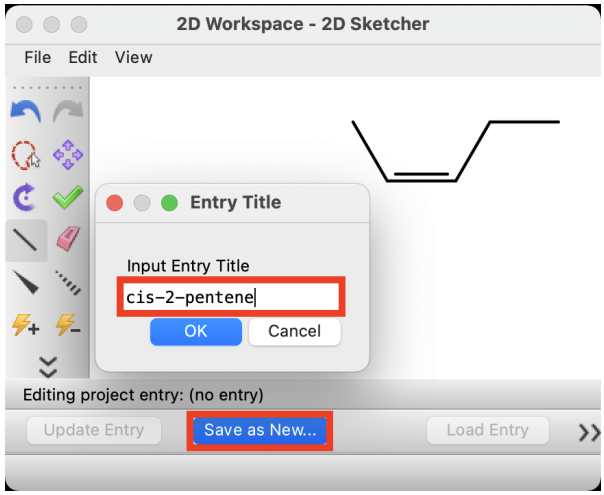


Figure 5-5. Saving cis-2-pentene

2. **Draw** cis-2-pentene
    - Go to the selection bar on the left
    - Create a methyl group by choosing the “C” or the draw line and **clicking** in the 2D Workspace
    - Drag from the methyl group to add more
    - Click on the bond between methyl groups to make it a double bond
    - Try to replicate the sketch shown in the figure as closely as possible
3. Click on **Save as New** and for *Input Entry Title* write **cis-2-pentene**. Click **OK**.

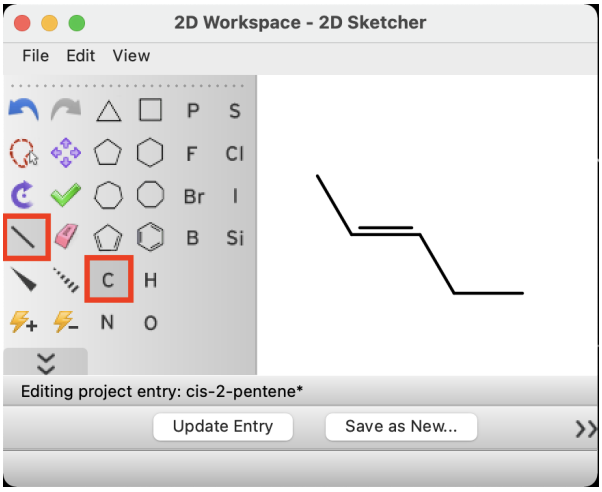


Figure 5-6. Drawing trans-2-pentene.

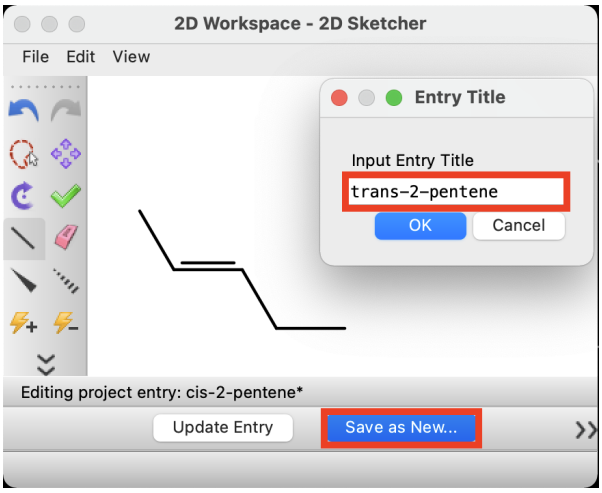


Figure 5-7. Saving trans-2-pentene.

4. **Draw** trans-2-pentene
    - Reference the instructions for cis-2-pentene in step 1
    - Try to replicate the sketch shown in the figure as closely as possible
5. Click on **Save as New** and for *Input Entry Title* write **trans-2-pentene**. Click **OK**.

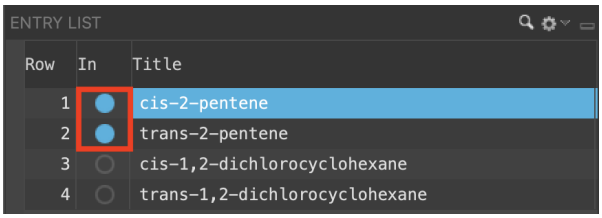


Figure 5-8. Including the cis/trans molecules.

Oftentimes, viewing multiple molecules simultaneously can be important for comparing and contrasting them. We will show our cis and trans isomer molecules side by side so that we can easily see how they differ.

1. Simultaneously **include** (control + click or command + click) both the cis-2-pentene and the trans-2-pentene

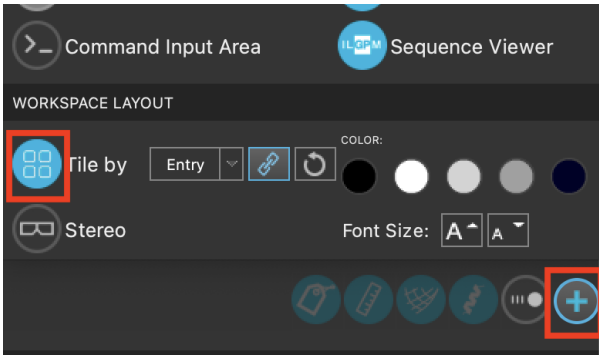


Figure 5-9. Tiling the cis/trans entries.

2. Show workspace configuration panel → Workspace Layout → Tile

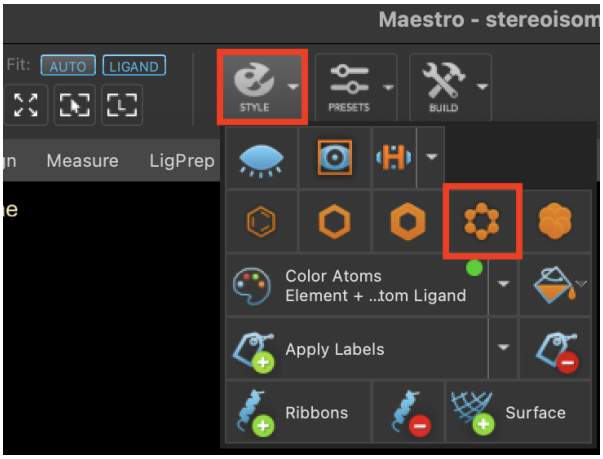


Figure 5-10. Applying ball-and-stick style to cis/trans entries.

3. Change the representation to ball-and-stick by clicking on the **Style** menu and choosing **Apply ball-and-stick representation**

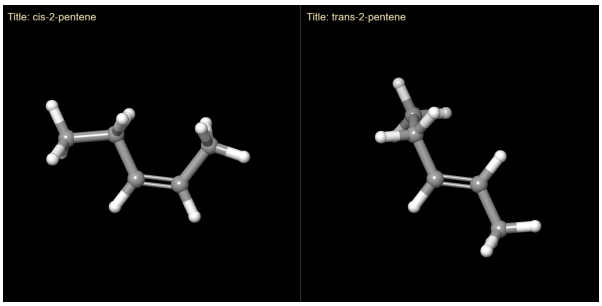


Figure 5-11. Viewing 2-pentene isomers.

4. Feel free to pan around, zoom in, and look at your molecules
5. Change the background to white and take a screenshot of your molecules to put in the Stereoisomers worksheet.

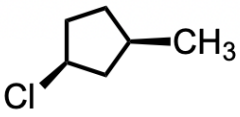
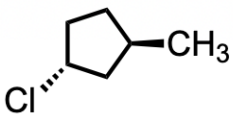
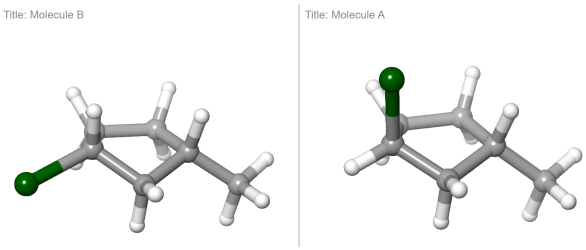
For 2-pentene, notice that the *cis* configuration shows the methyl and the ethyl substituents on the same side of the double bond. The *trans* configuration has the methyl and ethyl on opposite sides of the double bond.

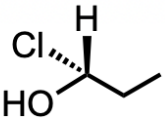
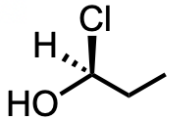
6. Individual Exercises

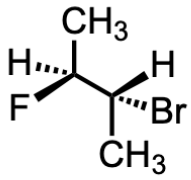
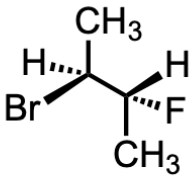
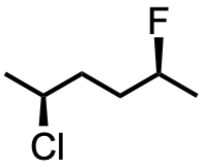
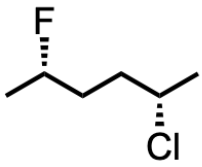
For each pair of molecules:

1) Build the molecules using 2D sketcher in Maestro and Optimize their geometries by running Optimization Jaguar calculations. Attach screenshots of your optimized molecules tiled next to each other in the worksheet
2) Determine the stereochemical configuration using CIP rules
3) Determine whether the pair of molecules are identical, enantiomers, or diastereomers

Here is an example:

 **Molecule A**  **Molecule B**	1)  2) Molecule A: (1*S*, 3*R*)-1-chloro-3-methylcyclopentane Molecule B: (1*R*, 2*R*)-1-chloro-3-methylcyclopentane 3) Diastereomers because one chiral center inverted while the other chiral center stayed the same

 **Molecule A**  **Molecule B**	1) 2) 3)

 **Molecule A**  **Molecule B**	1) 2) 3)
 **Molecule A**  **Molecule B**	1) 2) 3)

7. Conclusion and References

The overarching objective of this tutorial was to introduce or reinforce concepts about different types of stereoisomers. To better understand how pairs of stereoisomers differ from one another, we used Maestro to model the isomers in three dimensions. By using Maestro's computational tools, we learned to use the 2D Sketcher to conveniently build our molecules in 3D and how to optimize a structure's geometry using quantum mechanical DFT. Additionally, we changed the style of our molecules, applied labels to them, and arranged them in a tiled formation to easily compare a set of molecules.

For some related practice, proceed to explore other relevant tutorials:

- Introduction to Geometry Optimizations, Functionals, and Basis Sets

For further reading:

- Exploring potential energy surface for chemical reactions: An overview of some practical methods. DOI:10.1002/jcc.10231
- Introduction to Computational Chemistry, 3rd Edition
- Essentials of Computational Chemistry: Theories and Models, 2nd Edition
- Molecular Modelling: Principles and Applications, 2nd Edition
- See the Jaguar help documentation

8. Glossary

Entry List - a simplified view of the Project Table that allows you to perform basic operations such as selection and inclusion

Included - the entry is represented in the Workspace, the circle in the In column is blue

Project Table - displays the contents of a project and is also an interface for performing operations on selected entries, viewing properties, and organizing structures and data

Recent actions - This is a list of your recent actions, which you can use to reopen a panel, displayed below the Browse row. (Right-click to delete.)

Scratch Project - a temporary project in which work is not saved. Closing a scratch project removes all current work and begins a new scratch project

Selected - (1) the atoms are chosen in the Workspace. These atoms are referred to as "the selection" or "the atom selection". Workspace operations are performed on the selected atoms.

(2) The entry is chosen in the Entry List (and Project Table) and the row for the entry is highlighted. Project operations are performed on all selected entries

Working Directory - the location that files are saved

Workspace - the 3D display area in the center of the main window, where molecular structures are displayed

2D Workspace - the 2D panel that opens from the “edit” dropdown that allows for the construction of molecules using a 2D sketcher

Tile - if multiple entries are included, included entries are displayed side by side in individual boxes rather than being overlaid in the same space