

Organic Chemistry

Computational Modeling Experiment

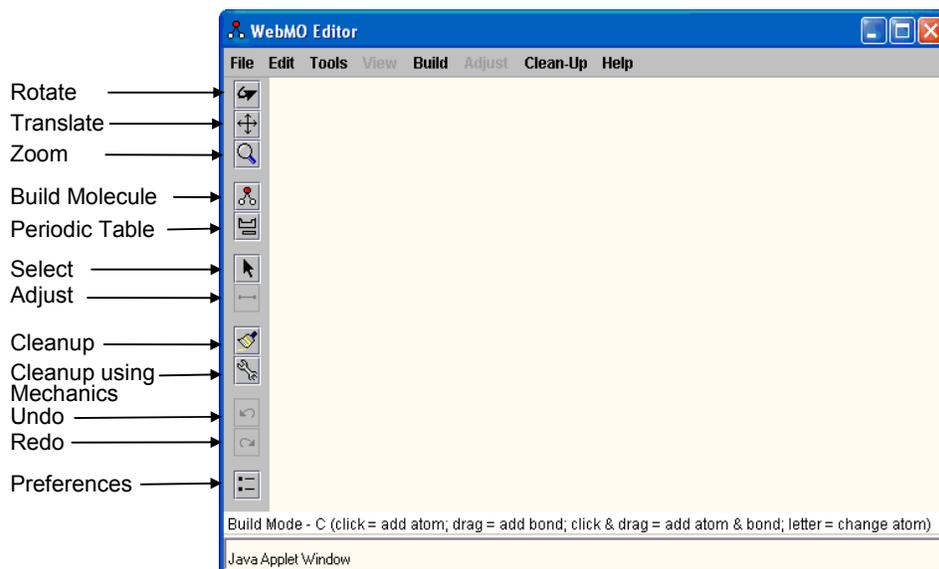
Introduction

This laboratory exercise is designed to introduce students to the capabilities of computational chemistry and its usefulness as an aide in modeling organic molecules. Through the simplified interface of WebMO, students will access several powerful computational engines to perform geometry optimizations, molecular orbital calculations, and more. Students are introduced to the computational process piecewise, as they are required to build increasingly complicated molecules and perform increasingly detailed calculations. This exercise covers a variety of key organic concepts, with an emphasis on drawing both linear organic molecules and the various conformations of cyclohexane. Students will determine strain energies to compare the relative stability of the anti and eclipsed conformations in ethane as well as axial and equatorial substitution in cyclic structures. Upon completion of this exercise, students should be well acquainted with the effect of conformation on stability and with the technique of drawing organic molecules.

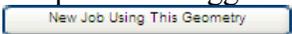
Procedure

Ethane

1. Follow your instructor's directions to access the WebMO Job Manager. This is the central hub of the WebMO program. From here you can create new jobs, view completed jobs, delete unwanted data, and organize your work.
2. Click on the New Job tab to enter the Build Molecule page. Open the editor.



Build the carbon backbone of ethane, C_2H_6 . To start, click , the build button. To add a carbon atom, simply click in the editor window. Clicking on an atom and

- dragging to an empty space creates a bond to a new atom. Bonds can also be made by dragging a line between two existing atoms.
3. Click  to perform a “comprehensive cleanup using mechanics” operation. This places hydrogens in the unfilled valencies, hybridizes each atom, and idealizes all bond lengths, bond angles, and dihedral angles. You should now see ethane in the staggered conformation. If you do not, click  again.
 4. To rotate the molecule, first click . Now click and drag the molecule to rotate it. Rotate it so you are looking down the carbon-carbon bond. **Draw a Newman projection of what you see.**
 5. Rotate the molecule so that the carbon-carbon bond is in the plane of the screen. **Draw the molecule as it appears now, using wedged and dashed lines to represent bonds coming out from or going into the page.**
 6. Close the editor to return to the Build Molecule page. Click  to proceed to the Choose Computational Engine page. Select the Tinker engine and click  to continue. At the Job Options page, give your job a unique name *beginning with your initials*. Choose the Geometry Optimization calculation and the MM3 force field. Click  once more to start the calculation. This will also return you to the Job Manager.
 7. To check to see if the job is finished, click the refresh tab. Once the job is completed, open up the View Job page by clicking on the job’s name. **Find and record the total potential energy (strain energy).**
 8. The molecule can be analyzed within the window on the View Job page. Click , the select arrow. Now select any atom. Its hybridization and charge will be displayed at the bottom of the window. Once one atom is selected, hold the Shift key to select more. Notice that if you select two atoms, the distance between them is displayed. If three or four atoms are selected, you are given a bond angle or dihedral angle. If you no longer want to select a group of atoms, click away from the molecule. **Find and record the following properties of ethane.**
 - a. The distance between closest H atoms attached to different carbons.
 - b. The H-C-C bond angle
 - c. The H-C-C-H dihedral angle (choose two H atoms that are anti to each other)
 9. Now we’ll compare the staggered and eclipsed conformations. Start another job by clicking . Open the editor. To switch between staggered and eclipsed, we’ll need to change the dihedral H-C-C-H angle. Determine what this dihedral angle should be. (It may help to think of what a Newman projection would look like.) Open the editor. Using , choose the four atoms that define this angle. The button beneath the Select arrow should now look like . Click it to open a window that allows you to change the dihedral angle. Adjust it so the ethane is now in the eclipsed conformation.
 10. Repeat steps 4-8 for the new conformation. (In Step 8c, choose two H atoms that eclipse each other.) **Decide which conformation of ethane is the most stable. Record this on the answer sheet.** When finished, return to the Job Manager by clicking either blue arrow.

Ethylene

11. Create a new job. Build ethylene, C_2H_4 . To make a double bond, simply drag a second line in between the two carbons. Do a comprehensive cleanup using mechanics. **Draw a Newman projection and wedge drawing.** Continue to the next screen. This time, choose Mopac for the computational engine. On the Job Options page, choose a Molecular Orbital calculation. Remember to give this job a unique name starting with your initials.
12. Once the job is complete, open it. Scroll down to the table titled “Molecular Orbitals” and click the magnifying glass next to “Electrostatic potential.” This should open MOViewer and a picture of an electrostatic potential map for ethylene. (The browser’s security features may ask if you are sure you want to download this file. Continue with the download.)
13. An electrostatic potential map displays different electron densities in different colors. Red portions of the map correspond to high density; blue portions correspond to low density. The intermediate colors fill in this spectrum: red > orange > yellow > green > blue. To zoom in and out of the map, hold Shift and move the mouse. To switch to a see-through map, click . In the Preferences window, change the opacity to around 50%. **Draw a picture of the model and indicate the region with the highest electron density with shading. Why is the density so high here? If an electrophile, such as H^+ , were to attack ethylene, where would it do so? Mark this spot on your drawing.** Close the MOViewer window.

Butane

14. Return to the Job Manager, create a new job and use the editor to build butane, C_4H_{10} . Do a comprehensive cleanup using mechanics.
15. Use the Select arrow to select the four carbons. Make sure you select them linearly (i.e., C1-C2-C3-C4). From the Adjust menu choose Scan Coordinate. Set Start at -180 , Stop at 180 , and # Steps at 36. This will allow us to create an animation sequence with 36 steps, showing the dihedral angle change from -180 to 180 degrees.
16. Close the editor and proceed to the next page. Choose the Mopac engine. Proceed to the Job Option page, and choose the Coordinate Scan calculation. Perform the calculation. This job may take 10-15 seconds.
17. Open the job and scroll down to the Coordinate Scan table. Click the magnifying glass next to the Energy column. This graph shows how energy is affected by the changing dihedral angle. **Sketch it on the answer sheet.**
18. Click the filmstrip icon in the Geometry Sequence table to begin the animation. You can control the animation with the five bottom buttons on the toolbar. The third button, , is particularly useful, as it advances one frame at a time. Note how the energy (heat of formation) changes as the molecule changes shape. **Draw a Newman projection of butane in its eclipsed, gauche, and anti conformations. Record the heat of formation at each. Find and record the**

C1-C4 distance and the C1-C2-C3 bond angle for each conformer. Why is the bond angle different in the gauche and anti conformations?

Cyclohexane

19. Return to the Job Manager, create a new job and open the editor. Enter the Build menu and choose the Fragment option. In the new window that opens, change the category to Rings and the fragment to Cyclohexane – Chair. Once you have done this, you can place the chair in the window the same way you placed carbon atoms previously. Perform a comprehensive cleanup using mechanics operation on the molecule. Notice that the strain energy has been calculated by the editor and is displayed at the bottom of the window. Rotate the molecule so you can see the chair. (If you click  before clicking , you can rotate the molecule without having the strain energy display disappear.) **Record the strain energy and draw the chair (with all hydrogens) in the box provided.**
20. Under the File menu, select New to clear the editor. Create a Cyclohexane – Boat fragment. The strain energy for this conformation is already given in the answer sheet. **Draw the boat in the box provided. Include all hydrogens.** Perform a comprehensive cleanup using mechanics on the molecule. It will relax to a twist-boat conformation. **Record the energy of the conformation and draw a twist-boat in the box provided. Include all hydrogens.**
21. Open the Cyclohexane-Half Chair fragment. **Draw the half-chair in the box with all hydrogens attached. Have an instructor check your drawings before proceeding.**
22. Cyclohexane changes its conformation through a ring-flipping process, which involves rotation around several C-C bonds. An energy diagram of this process is provided on the answer sheet. Each minimum or maximum corresponds to a different conformation of the ring. **On the graph, indicate which extremes correspond to which conformations by drawing the structures in the boxes provided.** Make sure to draw the structures in a way that represents the movement from one chair to the opposite (flipped) chair. You do not need to draw hydrogens. It may help to consider which of those conformations are stable and which ones are not. The energies from steps 19-21 will also be useful.

Substituted Cyclohexanes

23. Clear the editor. Using the Cyclohexane – Chair fragment, build an axial-substituted methylcyclohexane. To change a hydrogen atom to a methyl group, first enter the Build menu and select C. Then click on an axial hydrogen to replace it with a carbon. Use  to add the methyl hydrogens and minimize the energy. **Draw the molecule. Record the strain energy and the shortest distance between a methyl-group hydrogen and a ring hydrogen.**
24. Now make an equatorial-substituted methylcyclohexane. To delete a portion of a molecule, use  to select the group of atoms you no longer need and press the delete key. **Record the strain energy and the shortest distance between a**

methyl-group hydrogen and a ring hydrogen. What is the difference in the strain energies?

25. Use the same strategy to compare the two different chair conformations for *trans*-1,2-dimethylcyclohexane. **Draw each conformation, record the strain energies, and label which, if any, is more stable.**
26. Repeat step 25 for the following molecules:
 - a. *cis*-1,2-dimethylcyclohexane
 - b. *trans*-1,3-dimethylcyclohexane
 - c. *cis*-1,3-dimethylcyclohexane

Larger Molecules

27. Use the WebMO editor to draw the two chair conformations of menthol (see Figure 1 on the next page). To add non-carbon atoms to your structure, go to the Build menu and choose the desired atom. **For each conformation,**
 - a. **Record the strain energy on the answer sheet.** Use the strain energy displayed after a comprehensive cleanup using mechanics. You do not need to run any calculations for this problem.
 - b. Close the editor and click  in the viewer on the Build Molecule page. This opens a new Internet Explorer window. Hit Alt+Print Screen on the keyboard to take a screenshot of this window. Paste the screenshot in Microsoft Word. Put screenshots of both conformations in the same document, but do not print it out yet.
Explain why one conformation has a higher strain energy than the other.
28. Use the WebMO editor to construct a model of morphine (figure 2 on the next page). Minimize the energy. **Record this energy on the answer sheet.** Using the same procedure as in step 27b, put a picture of morphine into the same document that has your pictures of menthol. **Print the document and attach it to your answer sheet. Label all of the functional groups within morphine on your picture.**

Figure 1: Menthol

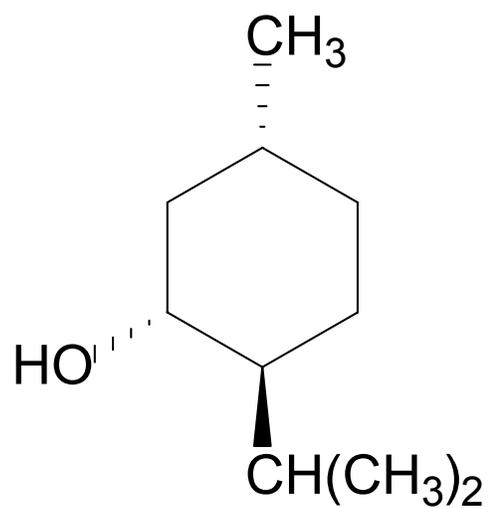
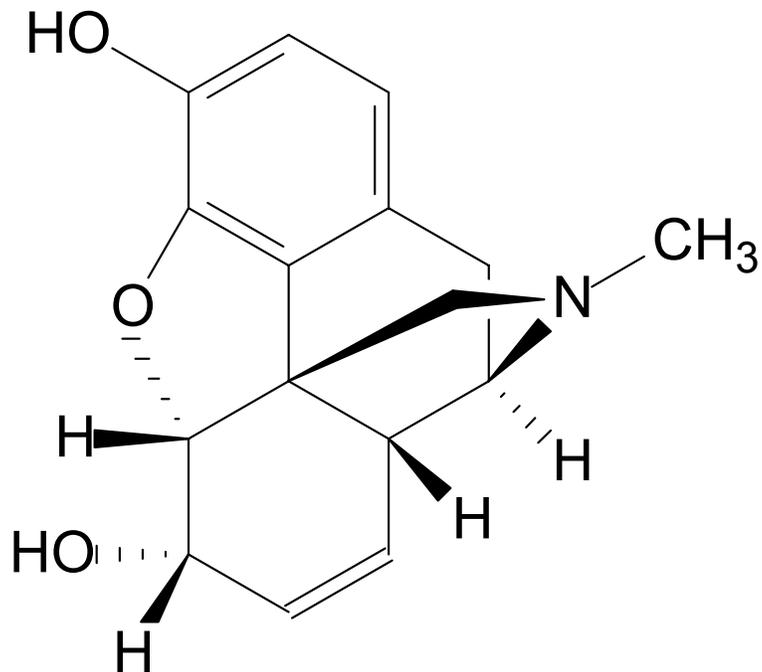


Figure 2: Morphine



Ethane

	Staggered	Eclipsed
Newman Projection		
Wedge Drawing		
Strain Energy		
H-H distance		
H-C-C bond angle		
H-C-C-H dihedral		

Which conformation is more stable? _____ Why? _____

Ethylene

Newman Projection	Wedged Drawing

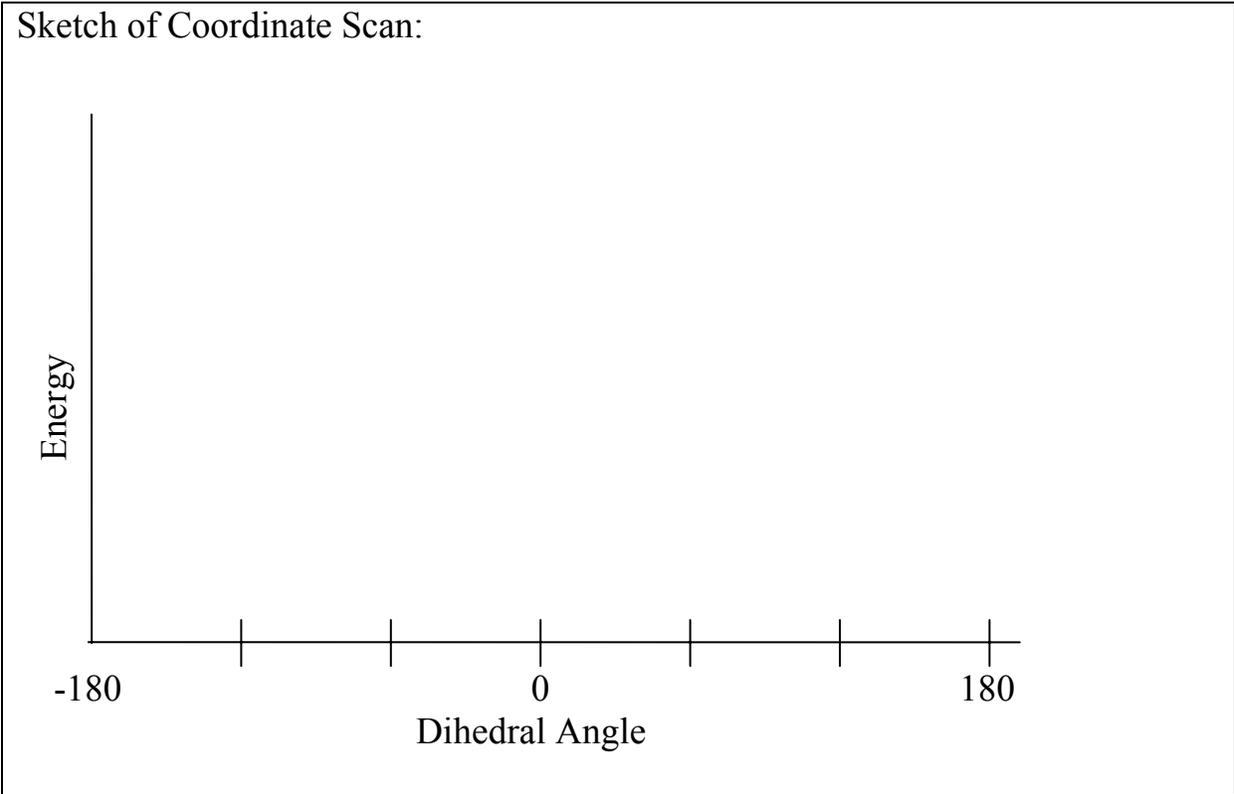
Electrostatic Potential Map

What region has the highest electron density? _____

Why? _____

Where would an electrophile attack ethylene? _____

Butane



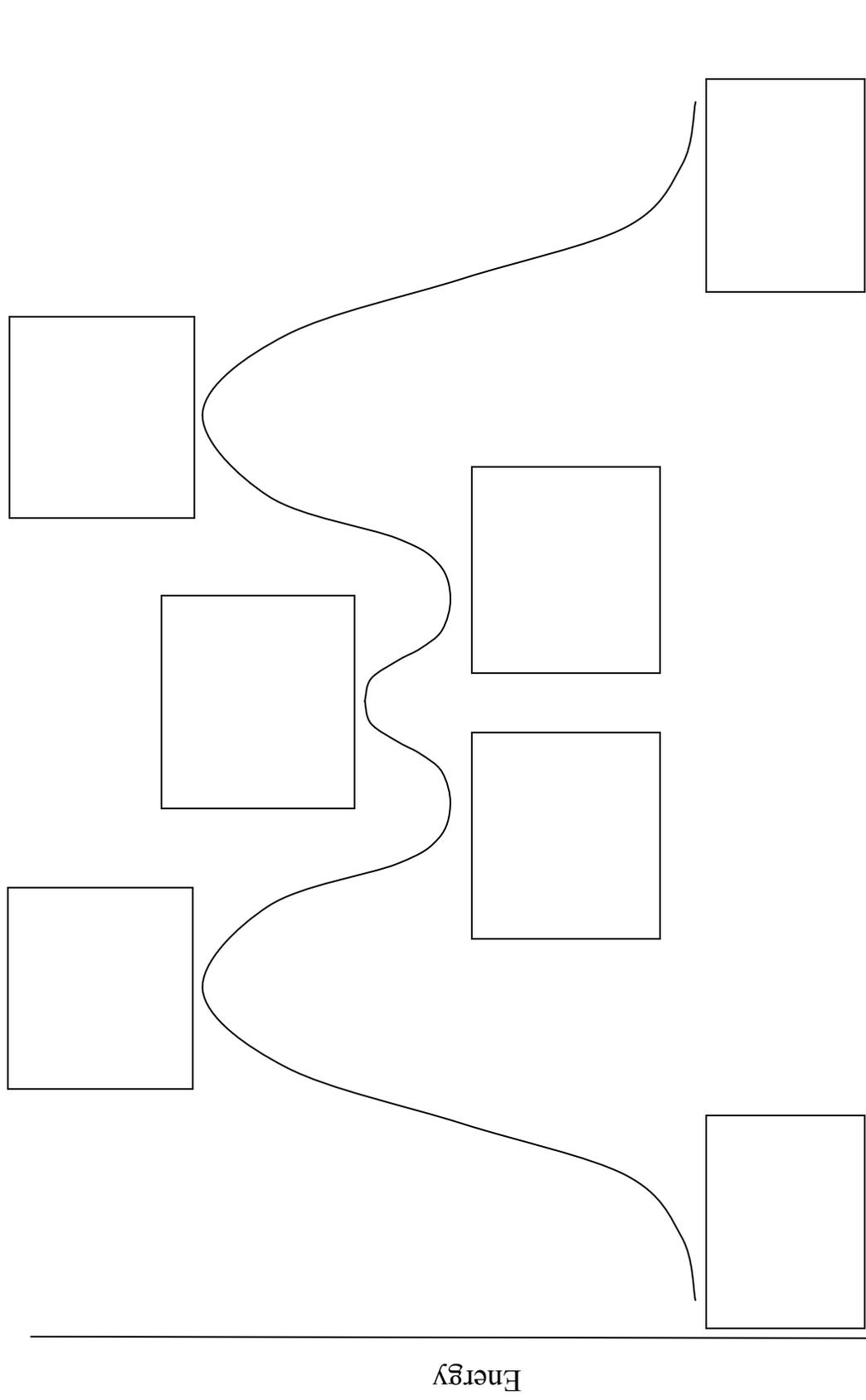
	Eclipsed	Gauche	Anti
Newman Projection			
Heat of Formation			
C1-C4 Distance			
C1-C2-C3 Bond Angle			

Why is the bond angle different in the gauche and anti conformations? _____

Cyclohexane

Chair	Boat
Strain Energy:	Strain Energy: 13.8 kcal/mol
Twist-Boat	Half-Chair
Strain Energy:	Strain Energy: 17.7 kcal/mol

Potential Energy Diagram



Methylcyclohexane

Axial	Equatorial
Strain Energy: Shortest Methyl H – Ring H Distance:	Strain Energy: Shortest Methyl H – Ring H Distance:

What is the difference in strain energy? _____

Dimethylcyclohexanes

trans-1,2-dimethylcyclohexane

Strain Energy:	Strain Energy:
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cis-1,2-dimethylcyclohexane

Strain Energy:	Strain Energy:
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trans-1,3-dimethylcyclohexane

Strain Energy:	Strain Energy:
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cis-1,3-dimethylcyclohexane

Strain Energy:	Strain Energy:
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Analyze these results, taking into account the number of axial and equatorial substituents each conformation has. Make a statement describing which form of substitution is energetically favored. _____

Larger Molecules

Strain energy of menthol with axial substituents: _____

Strain energy of menthol with equatorial substituents: _____

Why does one conformation have higher strain energy? _____

Strain energy of morphine: _____

Attach your printout with the pictures of menthol and morphine.