BINF 653 - Spring 2005

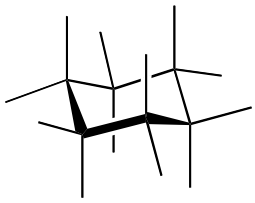
Sybyl Laboratory

Molecular Mechanics - force field energy terms

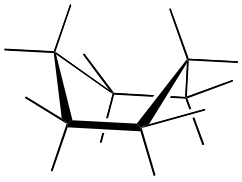
1. Sketch and minimize cyclohexane.

Build/Edit, Sketch Molecule, OK, *click six point ending with a click one the first to form a cyclic structure,* ***ADDH, End Select****.* ***Compute, Minimize, Modify, Charges, Gasteiger-Huckel, OK,*** *change the gradient to 0.005, and Max Iterations to 100,000,* ***OK.***

Note whether your minimized structure is the chair or boat conformation.



Chair



Boat

Record the energy of your minimized structure then convert it into the opposite conformer:

Chair form : _____ Boat form : _____

Build/Edit, Sketch Molecule, OK, MOVE, *click on one of the carbons in the ring, move the mouse in the direction opposite from the atoms starting position and click again* ***End Select****.* ***Compute, Minimize, OK*** *(the settings you changed before are now default).*

Record the energy of the new conformer. Which is more stable? Which is experimentally known to be more stable? Why is it more stable?

_____

_____

_____

2. Relative Conformational Stabilities of Cyclohexanol and 5-Hydroxy-1,3-dioxane.

Make and minimize the two cyclohexanol conformers

Start with the minimized boat form of cyclohexane generated above.

Build/Edit, Sketch Molecule, OK, *click on the O in the lower right hand box then click on one of the axial hydrogens,* ***ADDH, End Select.***

Minimize the structure as before. Note the direction that the hydrogen of the alcohol points, i.e., does it point away from the ring (exo) or toward it (endo)? What is its energy?

_____

_____

_____

Save the structure.

File, Save As, *click the file box and type the name (either cexo or cendo),* ***Save.***

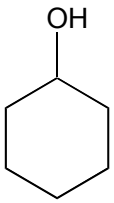
Change the C-OH torsion angle to the opposite conformer.

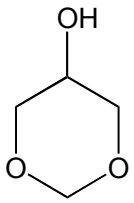
Click the rotate bond icon on the left vertical tool bar, click the first empty box under Q, click the carbon attached to the oxygen, click the oxygen. Change the dihedral angle by pressing > or < until the opposite conformer is generated. Click "Rot Bonds (M1), then "Twist Freeze." Click Q to quit rotating.

Minimize and save as "cexo" or "cendo".

What is its energy?

_____





Make and minimize the two 5-Hydroxy-1,3-dioxane conformers.

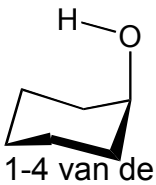
Start with which ever conformer of cyclohexanol you have on the screen and convert it to the corresponding dioxane.

> ***Build/Edit, Sketch Molecule, OK, REMOVE_H,*** *click on the O in the lower right hand box then click on two carbons to be changed to oxygens,* ***ADDH, End Select.***

Note that no matter which conformer you started with, you now get exo. Minimize as before and save as "oexo." Convert this to the endo conformer as before, minimize and save as "oendo."

Clear the screen ***Build/Edit, Zap.***

Read in each of the four compounds one at a time, minimize and fill in the table with the values for total energy and the values of the selected terms in the energy expression.



1-4 van der Waals Energy _____

van der Waals Energy _____

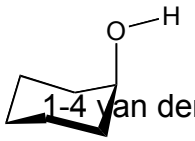
Sum _____

1-4 Electrostatic Energy _____

Electrostatic Energy _____

Sum _____

Total Energy_____



1-4 van der Waals Energy _____

van der Waals Energy _____

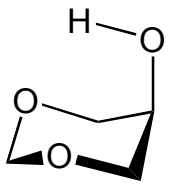
Sum _____

1-4 Electrostatic Energy _____

Electrostatic Energy _____

Sum _____

Total Energy_____



1-4 van der Waals Energy _____

van der Waals Energy _____

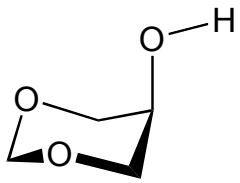
Sum _____

1-4 Electrostatic Energy _____

Electrostatic Energy _____

Sum _____

Total Energy_____



1-4 van der Waals Energy _____

van der Waals Energy _____

Sum _____

1-4 Electrostatic Energy _____

Electrostatic Energy _____

Sum _____

Total Energy_____

3. Additional Structure Creation Exercises

Build/Edit, Sketch Molecule, OK, draw structure as a carbon skeleton, change the appropriate carbons to the correct heteroatom.

ADDH, End Select.

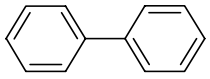
Compute, Minimize, Modify, Charges, Gasteiger-Huckel, OK, change the gradient to 0.005, and Max Iterations to 100,000, OK.

File, Save As…, etc.

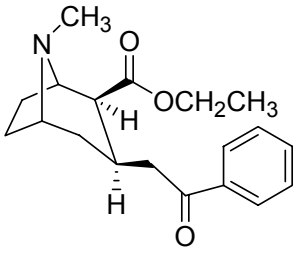
Where relevant, check stereochemistry.

Build/Edit, Other Tools, Find Chirality, RS, All, OK.

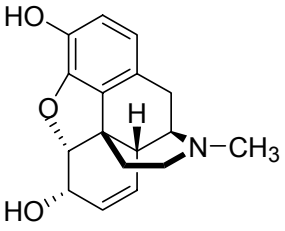
Biphenyl - what is the orientation of the two aromatic rings?_____

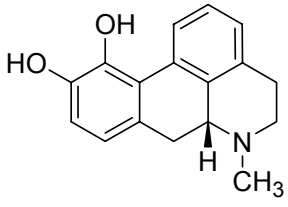


Cocaine - Is it flat? Check stereochemistry and change if incorrect. _____



Morphine (an opiate agonist) and Apomorphine (an opiate antagonist) - Are they similar in 3D structure?
_____





Morphine Apomorphine

Consider the following questions:

1. Which is more stable for cyclohexanol, the endo or exo form? By how much?

2. Which is more stable for 5-Hydroxy-1,3-dioxane, the endo or exo form? By how much? How do you account for the differences in behavior between the two compounds?

3. Are the differences attributable to steric or electronic factors?

4. Steric factors are not sensitive to dielectric constant (solvent polarity) but electronic ones are. Given this, how could you computationally test your theory?