Getting started with HyperChem. Program description.

In this project you will create simple organic molecules and learn how to manipulate them. However, before starting you should create your home directory (under D:/comp_lab) in which you will place all your files. In this directory you should create sub-directories for each lab exercise (for example, for the first exercise of HyperChem lab, you should save your files under the directory D:/comp_lab/user_name/Hyper/ex_1).

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Introduction:

Computer programs that calculate the energy of various conformations of molecules and predict the lowest energy conformation are called *molecular modeling programs*. In this brief introduction you will learn how to construct (draw) representations of molecules using a molecular modeling program called *HyperChem* (HyperCube, Inc.) and to perform geometry optimizations (energy minimizations) to determine the lowest energy conformations of molecules.
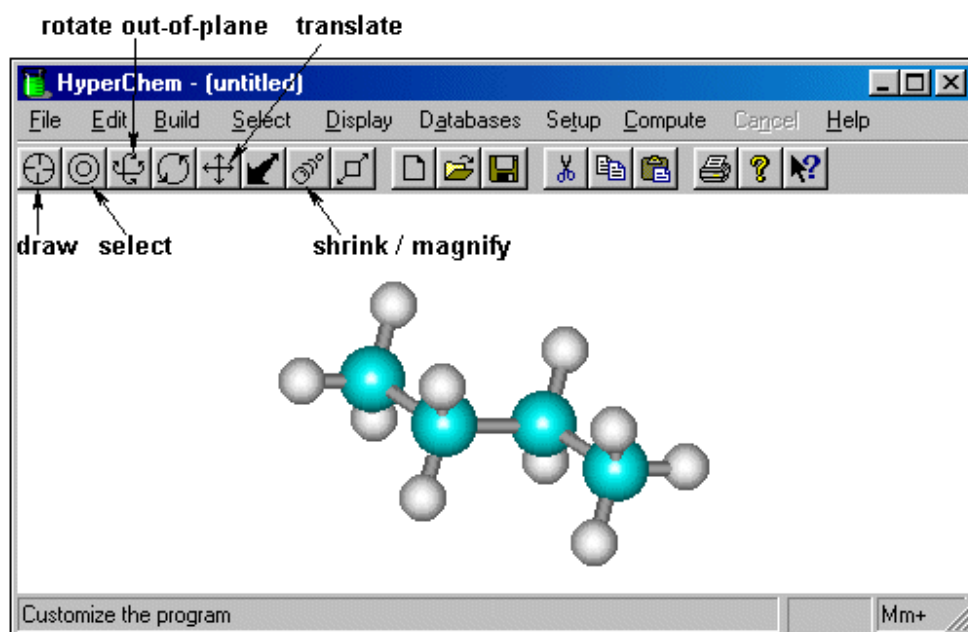
1. Building a molecular model

Exercise A.1

Use the instructions below in order to **build a model** of the following molecules:
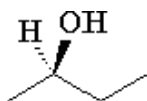
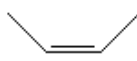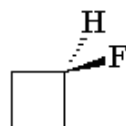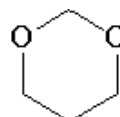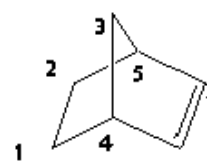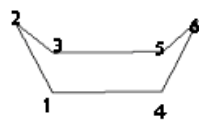Note: In order to build a model of chiral molecules (e.g. A), draw a planar molecule perpendicular to one of the chiral bonds, then rotate the molecule out of plane and add the last substituent.

For the *cis 2-butene* one should Select the dihedral (torsion) angle (L-click the Select button and then L-click the first carbon atom, draw and L-click the fourth carbon atom). Set the dihedral angle to zero (L-click the Edit button and select Set Bond Torsion, insert 0 bond torsion and OK).

In order to build a model for the boat configuration of *cyclohexane*, one should Build a model of the chair configuration, L-click the Select button on HyperChem toolbar. Then, select Multiple Selections. L-click the select tool and then select the four carbon atoms located in the same plane. L-click the Select button and L-click Name Selection, select PLANE and OK. Now deselect the plane, by R-clicking somewhere outside the structure. Select, three carbon atoms and six hydrogen atoms that you want to reflect through the defined plane. Then, L-click the Edit button and select Reflect. Save the models in files with meaningful names in a separate directory (For example,

In *HyperChem*, both the left mouse button (L-click) and the right mouse button (R-click) are used. Often the left button has the opposite effect as the right button. The left button is the default and is the one to use if you are simply told to click on an object.

Open the *HyperChem* window by pressing the start, then programs and then HyperChem.

Before creating a structure, use the mouse to select the **draw tool** , located in the upper left corner of the *HyperChem* window, by clicking on it. (Briefly holding the mouse over any of the icons in the tool bar will show you the icon's function. Each tool that is selected will produce a cursor with a different shape.) Double L-click on the **draw tool** in order to open the Element Table dialog box. Select carbon from the periodic table if it does not already appear in the box at the top. Close the periodic table window.

Place the cursor on the screen and L-click to draw a carbon atom. L-click and drag the mouse to where you wish to draw another carbon atom. Let up on the button and another carbon atom will be drawn with a bond connecting it to the first carbon atom. Continue clicking and dragging until you have constructed the carbon skeleton of the molecule you wish to model. Now, double L-click on the **select tool** just to the right of the draw tool. This causes the program to add the appropriate number of hydrogen atoms and do a preliminary "model build," which means to use preset bond angles and bond lengths to create a trial structure[1]. Give the file containing this structure a name by selecting File, Save As, and then entering the name. The default extension *.hin* will be appended unless you choose to save the file in a different file format.

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[1] You can invoke a model builder by double L-clicking the select tool or by selecting Add H & Model Build on the Build menu in the toolbar.

2. Additional Procedures and Options:

> Exercise A.2
>
> Report <HCO bond angle of molecule A (report with accuracy of $\pm 0.1^0$).

2.1 Labeling atoms: Select **Labels** on the **Display** menu. In the Atoms option box, L-click on Symbol and press OK.

2.2 Editing individual atoms. Change one of the carbon atoms to oxygen: (a) Double-click on the draw tool to open the Element Table dialog box. (b) Choose Oxygen, then close the dialog box. The dialog box disappears and oxygen is set as the new default element. (c) L-click on a carbon atom. The atom symbol C changes to an O and the oxygen end of the bond turns from cyan to red (if you are using the default colors).

2.3 To change bond order, select the draw tool, then R-click the mouse on a carbon-carbon bond (for example) to erase the bond. The right mouse button erases a bond, whereas the left mouse button creates a bond.

2.4 XY translation. You use the XY translate tool to move molecules or selected atoms

along the plane of the computer screen. (a) L-click on the XY translate tool . (b) Move the cursor into the workspace. The cursor assumes the shape of the XY translate tool. (b) L-drag until the molecule on the screen. (c) Double-click on the translate tool button gives the Translate dialog box, in which you can manually set the translation (in Angstrom).

2.5 Z translation. Here you move the molecule toward and away from you (along the z axis) using the Z-translate tool.

(a) On the **Display** menu, choose **Rendering**, select **sticks** tab and make sure **Perspective** is on (i.e. marked with 'v'). With **Perspective** view, all molecules appear to be in perspective: closer atoms appear larger. (b) You must turn **Perspective** on before you use the Z translation tool to see any effect. Choose **OK** to close this dialog box.

(c) L-click on the **Z-translate tool** . Move the pointer into the workspace. The pointer assumes the shape of the Z-translate tool.

(d) L-drag slowly toward the bottom of the workspace – the molecule moves closer to you. Continue moving the molecule until it completely disappears.

2.6 Using the Zoom Tool. To increase or decrease the magnification of a molecule, use the **Magnify/Shrink tool (Zoom tool)** . This is useful, for instance, when you want to examine structural details of a large molecule. (a) Press the tool icon . Move the pointer into the workspace. The pointer assumes the shape of the zoom tool. (b) Magnify the molecule by L-drag slowly toward the bottom of the workspace. To shrink, L-drag in the opposite direction. (c) Double-click on the zoom tool gives a zoom dialog-box, in which you can specify the zoom factor. A zoom factor of 1 corresponds to scaling the molecule to properly fit the workspace window.

2.7 Centering and Scaling. When a molecular system is first loaded from the file system, it is centered in the workspace in a standard size. After you use the Translation or Zoom tools on the molecule, you can return it to its original size and center it in the workspace. **Scale to Fit** uses the current selection of atoms or the whole system if there is no selection.

Select **Scale to Fit** on the **Display** menu, or alternatively, press the space bar. The molecule returns to its original size and is positioned at the center of the workspace.

2.8 Z Rotation (in the screen plane) With the **Z rotation (Rotate in-plane) tool**, you can rotate molecules around the z-axis, defined as the direction perpendicular to the screen plane. The resulting rotation is in the screen plane. (a) L-click on the Z rotation tool and L-drag horizontally to the right in the workspace. The molecule moves in the clockwise direction. (b) L-drag horizontally to the left - the molecule moves in the counterclockwise direction.

Note: L-click-dragging vertically has no effect.

2.9 XY Rotation (out of screen plane) To rotate one or more molecules around the *x* or *y-axis* or both, use the XY rotation tool. (a) L-click on the **XY rotation (Rotate out of plane) tool** and move the cursor into the workspace. You may use the **Labels** dialog on the **Display** menu to add symbols to the atoms, for clarity. (b) L-drag horizontally - the molecule rotates around the y-axis. (c) L-drag vertically - the molecule rotates around the x-axis. (d) L-drag diagonally to rotate the molecule around both x and y-axes.

2.10 To display bond lengths and bond angles, (a) Make sure that atoms are selected in the select menu in the tool bar. (b) L-click on the **select tool** and then L-click and drag between two bonded atoms. The bond length will be displayed in the status bar. (c) To display the angle formed between three bonded atoms, L-click and drag between the two end atoms. These procedures are illustrated below. To cancel a selection, R-click the **select tool** anywhere outside the region occupied by the molecular structure within the *HyperChem* window.

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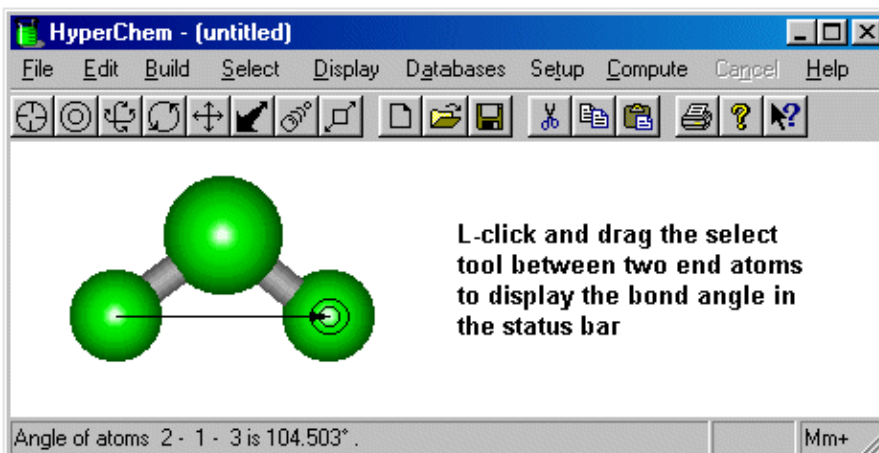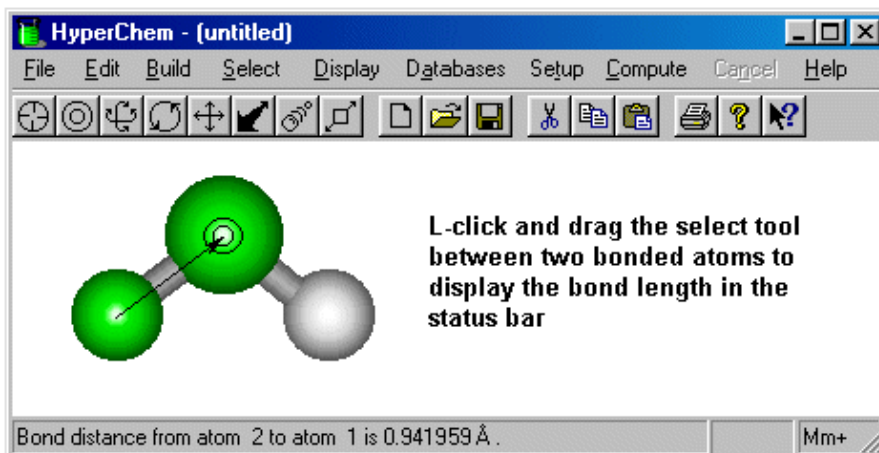
2.11 Atom characteristics. (a) On the Select menu, make sure that Atoms is chosen and that Multiple Selections is not. (b) L-click on the Select tool ⊚ and L-click on the oxygen atom. The selected atom is highlighted and the atom characteristics appear in the status line. The status line shows the atom's serial number in the molecule, the name of the element, the force field type, the atom's symbol within the molecular structure[2], the force field charge[3] and spatial coordinates. It also shows the x, y, and z coordinates of the atom. The Build menu items Set Atom Type, Set Charge, and Constrain Geometry become active. This lets you specify non-default atomic properties for the Model Builder, like a given charge or geometry. (c) Select other atoms and compare atom characteristics shown in the status line.

2.12 To display a structure in different renderings, L-click on the Display menu and select "Rendering…". You will be presented with a list of six different ways your structure can be rendered. The list is shown below.

| Stick | Balls | Balls and Cylinders | Overlapping Spheres | Dots | Sticks and Dots |

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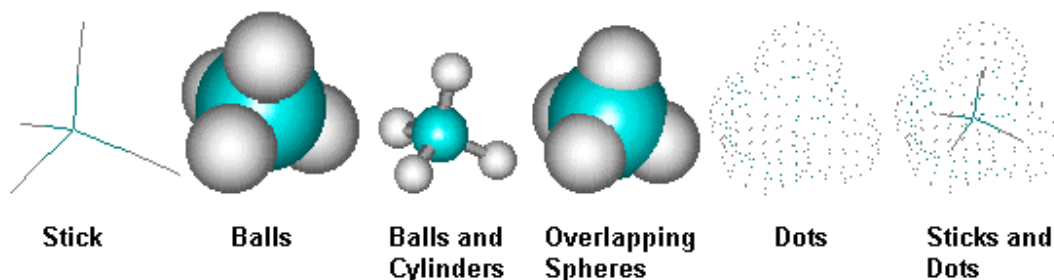
[2] E.g. H bonded to an O may is denoted in MM+ force field as 'HO' and has specific parameters, different the an H bonded to a carbon. This notation may change in other force fields.
[3] Charge assigned to the atom by the force field model.

Tool Summary:

Tool	Name	Action
	Draw	L-click: place atom in drawing area
		L-click-drag: draw bonds between atoms
		L-click on bond: create multiple bond
		Dbl-L-click on bond: create aromatic bond(s)
		R-click on bond: erase bond
		L-click on atom: replace atom with another element
		Dbl-L-click on icon: display periodic table
	Select	L-click: select atom (name of atom and position displayed in status bar)
		L-click-drag: display bond length or bond angle in status bar)
		R-click: cancel selection
		Dbl-L-click on icon: perform preliminary model build and add hydrogen atoms
	Rotate out-of-plane	L-click-drag: rotate structure in three dimensions
	Rotate in-plane	L-click-drag: rotate structure in plane of screen
	Translate	L-click-drag: move structure around the screen
	Magnify/shrink	L-click-drag: structure gets larger and smaller

3. Selecting a calculation method

To perform a calculation in HyperChem one first has to choose a method. There are three kinds of methods available in HyperChem: Molecular Mechanics, Ab-initio and Semi-empirical methods[4].

Molecular mechanics

A variety of models exists for the potential energy of molecular systems as a function of the coordinates of their atomic nuclei. These models treat the nuclei as Newtonian particles under the influence of a potential energy function or a force field. All models use empirical data to *parameterize the force field*, that is - to set the parameters (like charges, dipoles, bond parameters) that determine the potential energy as a function of the configuration. HyperChem provides the following models: MM+, AMBER, BIO+, and OPLS .

Ab-initio methods

Ab-initio methods are characterized by the introduction of an arbitrary basis set for expanding the molecular orbitals and then the explicit calculation of all required integrals involving this basis set .

Ab-initio calculations can be performed at the Hartree-Fock self-consistent field level of approximation. The post Hartree-Fock level includes the effects of correlation, which are not included at the Hartree-Fock level of approximation of a non-relativistic solution to the Schrödinger equation.

HyperChem performs ab-initio SCF calculations as a standard. It also can calculate the correlation energy (to be added to the total SCF energy) by a post Hartree-Fock procedure called MP2 that does a Møller-Plesset second-order perturbation calculation.

Semi-empirical methods

These calculations solve the Schrödinger equation, with certain approximations, to describe the electron properties of atoms and molecules. To simplify and shorten these calculations, semi-empirical methods make many simplifications, for example, including only the valence electrons in the calculation; neglecting the integrals for certain interactions; using standard, non-optimized, electron orbital basis functions; and using parameters derived from experiments. Experimental parameters eliminate the need to calculate certain quantities and to correct for errors resulting from approximations.

3.1 MM+ force field calculation setup:

(a) L-click Molecular mechanics in the Setup menu.

(b) Select MM+ force field and options to open a dialog box:

Option	Details
Electrostatics	Non-bonded electrostatic interactions are calculated using bond dipole interactions or partial atomic charges.
Cutoffs	This option determines the distance limits for calculating non-bonded interactions.
None	Calculates all non-bonded interactions
Switched	A smoothing function, applied from the inner radius to the outer radius gradually reduces non-bonded interactions to zero.
Shifted	A smoothing function applied over the whole non-bonded radius from zero to outer radius, gradually reduces non-bonded interactions to zero.
Outer radius (for switched and shifted cutoffs only)	The minimum distance in which non-bonded interactions are set to zero.
Inner radius (for switched and shifted cutoffs only)	This is the maximum inter-atomic distance for full non-bonded interactions

(c) L-Click OK and OK.

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[4] For more information about these methods, see the theoretical background.

3.2 AMBER, OPLS and BIO+ force field calculation setups:

(a) L-click Molecular mechanics in the Setup menu.

(b) Select a force field (AMBER or OPLS or BIO+) and options to open a
dialog box:

Option	Details
Dielectric	Modifies the magnitude of Coulombic interactions between atoms separated by three bonds.
Constant	Makes epsilon constant. Use this form for gas phase systems, or systems with an explicit solvent .
Scale factor	For Constant, epsilon = (permittivity of free space) x (Scale factor). For Distance dependent, epsilon = (permittivity of free space) x (Scale factor) x (inter-atomic separation). Scale factor must be greater than or equal to 1.0. The default of 1.0 is appropriate for most systems .
1-4 scale factor	Non-bonded interactions (van der-Waals and electrostatic) between atoms separated by only three bonds are multiplied by this factor. This option is not available for MM+.
Electrostatic	This modifies the magnitude of charge interactions between atoms separated by three bonds. The range is 0 to 1. For AMBER and OPLS, use 0.5. For BIO+, use 1.0, 0.5, or 0.4 depending on the parameter set .
van der-Waals	This modifies the magnitude of van der-Waals interactions between atoms separated by three bonds. The range is 0 to 1. For AMBER, use 0.5; for OPLS, 0.125; for BIO+, the value is fixed at 1.0 .
Cutoffs	These options determine the distance limits for calculating non-bonded interactions. Choosing Periodic Box on the Setup menu automatically sets Switched with default values. Cutoffs are necessary to prevent calculating interactions with neighboring periodic images. Cutoffs are available for MM .+

	The Cutoffs settings return to their default values if you place a new molecular system in the workspace . Options: See table above.

(c) L-Click OK and OK.

3.3 PM3 Semi-empirical method or ab-initio set ups:

(a) L-click Semi-empirical (or ab-initio) in the Setup menu.

Option	Details
Total charge	This is the net excess of nuclear charge over electronic charge. It is zero for a neutral system, a positive integer for a cation, and a negative integer for an anion .
Spin multiplicity	This is the total spin multiplicity, 2S+1, where S is the total electron spin of the system. Each unpaired electron counts for a spin of +1/2. A closed-shell system has a multiplicity of 1 (singlet). An open-shell system can have a multiplicity of 2, 3, 4 (doublet, triplet, quartet), or higher. Use integers from 1 to 4 .
Convergence limit	An SCF calculation ends when the difference in energy between two consecutive iterations is less than this amount. This is the convergence limit for total electron energy during iterations of an SCF calculation. The default is 0.01 kcal/mol. The practical range is 1 to 10^{-3}. The calculation might not reach values less than 10^{-3} because of round-off errors .
Iteration limit	This sets the maximum number of iterations for a SCF calculation. The calculation ends after this iteration, even if it has not reached the Convergence limit. The results might be incorrect if the calculation was far from convergence or the energy of the system is oscillating. The default of 50 should be adequate for most cases. The practical range is 50 to 200 .

Spin pairing	This sets the method for calculating spin interactions, of which there are two : UHF, the Unrestricted Hartree-Fock method provides separate spatial orbitals (alpha and beta) for electrons with each type of spin. This method is useful for open-shell systems, and to accommodate dissociation reactions in closed-shell systems. Takes longer than an RHF calculation . RHF, the Restricted Hartree-Fock method requires that a spin pair of electrons occupy the same spatial orbital. This method is useful for open- and closed-shell systems .
State	This describes the excitation state of the valence electrons in the system . Lowest, the lowest electronic state of a given spin multiplicity. Next lowest, this is the first electronically excited state of a given spin multiplicity (singlet, doublet, triplet, or quartet).

4. Performing a calculation

4.1 Single point calculations

These calculations determine the total energy (in Kcal/mole) and the gradient[5] of a molecular system or of selected atoms in one particular configuration. With a semi-empirical or ab-initio method, a single point calculation also determines the electron (charge) distribution in the system. The name "single point" reflects the fact that we calculate a single pre-selected configuration. Before starting, make sure you *deselect* any selection; otherwise the calculation will be *only for the selected atoms*.

To perform a single point calculation:

 (a) Select a method of calculation in the Setup menu (as explained above).

 (b) Choose Single Point on the Compute menu.

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[5] Gradient: The rate of change (first derivative) of the energy of a molecular system as a function of atomic positions. A gradient of zero indicates a configuration with minimum energy (a local or global minimum or a transition state). When HyperChem reports a single value for Gradient, this is the RMS gradient of the forces on all atoms.

4.2 Geometry optimization calculations

These calculation uses one of the methods: molecular mechanics, semi-empirical, or ab-initio methods, to find a minimum-energy (stable) configuration for a molecular system. The calculation adjusts atomic coordinates in steps to find a configuration in which net forces on each atom are reduced to zero. This is usually a local minimum on the potential surface, but is not necessarily the global minimum for a molecular system .

(a) Before starting, make sure you *deselect* any selection[6]; otherwise the calculation will be *only for the selected atoms*.

(b) Go to the **File** menu and select **Start Log** ….   Give the log file a significant name (usually the same name you will use for the structure file) and note its directory location.

(c) Select a method of calculation in the Setup menu (as explained above).

(d) L-click the Compute menu and select geometry optimization.

Option	Details
Steepest Descent	Moves directly down the steepest slope of inter-atomic forces on the potential energy surface . This method makes limited changes to the molecular structure and is useful for correcting bad starting geometry or removing bad contacts. It is most effective when the molecular system is far from minimum, and it is less satisfactory for macro-molecular systems .
Fletcher-Reeves	A conjugate gradient method using one-dimensional searches. This algorithm converges better than the Steepest Descent method .
Polak-Ribiere	A conjugate gradient method using one-dimensional searches, converging more quickly than Fletcher-Reeves but using slightly more memory .

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[6] You can deselect selected atoms by R-clicking the Select tool somewhere outside the structure.

Eigenvector-Following	Available for semi-empirical and ab-initio quantum mechanical methods (Setup/Semi-empirical and Setup/ Ab-initio), this method moves the atoms of a molecular system based on the eigenvector of the Hessian (the second derivatives of the total energy with respect to displacements). The initial guess of the Hessian is computed empirically .
Termination Conditions	RMS gradient - Set the root-mean-square (RMS) gradient to determine the end of the calculations. When the RMS gradient is less than the value you enter, the calculation ends . Cycles - Enter a number to limit the number of search directions. The default value is 15 times the number of atoms . In vacuo - Removes the periodic boundaries from the calculation .
Periodic boundary conditions	Uses the periodic boundary conditions that exist for the molecular system. You can turn this off by specifying In vacuo.

(e) L-click OK. The calculation will begin, and the progress will be displayed at the bottom of the screen in the status bar. Notice that the shape of the molecule you are modeling changes as the calculation proceeds. When the calculation is completed, the program will display Converged = YES in the status bar. The "steric" energy is the number given as "Energy =" and the units are kcal/mol. The zero energy is defined as a system where all nuclei and electrons are at infinity. This is the sum of the contributions to the energy from bond stretching or compression, bond angle deformation, dihedral angle (torsional) strain, Van der-Waals repulsion, combination stretch-bend, and electrostatic repulsion. It does not include the contributions to the molecular energy from covalent bonds. Depending on

the calculation method, the energy which appears in the status line might not be the total energy. All of the energy terms can be read from the log file, or from within HyperChem by going to the **Compute** menu and choosing **Properties** and then **Energy Details**. The units can be changed under **Preferences** in the **File** menu.

(f) The optimized structure should be saved by selecting File, Save.

(g) When the energy geometry optimization is completed, go to the **File** menu and select **Stop Log**. The log file can be read with any word processing program including Windows Notepad.

Important remark about selecting a convergence criterion and about reporting calculated properties

*The "chemical accuracy" is a concept used to express our subjective feeling about the accuracy of the numbers (e.g. energies, bond lengths, bond angles, etc.) we use to express the calculated properties. Naturally, it should be small (e.g. 1 percent) of typical molecular numbers. Typical chemical energies are of order 1eV (~ 23Kcal/mole) so the accuracy we seek is ~ 0.23 Kcal/mole. This has two implications for your work: First the convergence parameters that are used should be of the same order, or smaller, than the accuracy we seek, e.g. 0.001eV (or 0.01 Kcal/mole). Second, results should be reported at the same accuracy of the convergence parameter that is used. Similarly, for calculated **bond lengths** a reasonable choice for the required accuracy is ± 0.01**Angstrom** for bond length and $\pm 0.1^0$ for **bond angles**.*

Exercise A.3

Use the MM+ molecular mechanics force field to calculate the energies of molecules B and C (single point energy calculation).

Steps of calculation:

- Open the file of the model you built for the molecule.
- Use section 3.1 to setup the MM+ force field in the setup menu (select default parameters).
- Use section 4.1 to perform a single point calculation of the molecule.
- Report the energy of the molecules according to the above calculation (report with accuracy of ± 0.01 Kcal/mol).

Exercise A.4

Use the Restricted Hartree-Fock (ab-initio) method and a minimal basis set to perform another single point calculation of molecules B and C.

Steps of calculation:

- Open the file of the model you built for the molecule.

- Use section 3.3 to setup RHF method (select ab-initio in the setup menu, Basis-set-minimal (STO-3G), total charge – 0, multiplicity –1, spin pairing – RHF, convergence limit – 10^{-2}, iterations limit – default).

- Report the energy of the molecule according to the above calculation (see section (e) on the previous page, report with accuracy of ± 0.01 Kcal/mol).

- Compare the total energy as calculated using RHF (ab-initio) and MM+ (molecular mechanics) methods. Explain the major difference in energy (pay attention to the sign of the calculated energy).

Exercise A.5

Perform a geometry optimization calculation of molecules E and F with OPLS (molecular mechanics).

- Open the file of the model you built for the molecule.

- Use section 3.2 to setup the OPLS force field in the setup menu (use default parameters).

- Use section 4.1 to perform a single point calculation of the molecule.

- Use section 1 to report the following bond lengths and bond angles of molecule E (before the geometry optimization calculation, report bond length with accuracy of ± 0.01 Å and bond angle with accuracy of $\pm 0.1^0$):

  C_1-C_2, C_3-C_4, C_6-C_7, C_3-H and $\angle C_4 C_3 C_5$.

- Use section 1 to report the following bond lengths and bond angles of molecule F (before the geometry optimization calculation):

  C_3-C_5, C_1-C_4, C_3-H, $\angle C_1 C_2 C_3$ and $\angle C_2 C_1 C_4$.

- Record the total energy of the molecules before the geometry optimization calculation (with accuracy of ± 0.01 Kcal/mol).

- Use section 4.2 to setup and perform the geometry optimization calculation (Use the Polak-Ribiere algorithm, RMS gradient of $0.01 \, \text{Kcal}/(\text{Å} \cdot mol)$ or default cycles, select In vacuo).

- Compare the total energy of the molecules before and after the geometry optimization calculation.

- Compare the above bond lengths and bond angles of the molecules before and after the geometry optimization calculation.

5. Displaying calculated properties

5.1 Dipole moment of a molecule, L-click on the Display menu and select "Show Dipole Moment". The value of the dipole moment (Debyes) will be displayed in the status bar (total and x, y, z components). This procedure must be performed immediately following an energy minimization. The value of the dipole is also given in the **Compute** menu **Properties** section, and its components can be accessed by clicking **Details** next to the dipole.

5.2 Atomic charges. There are various ways to define atomic charges. HyperChem uses Mulliken atomic charges[7], which are commonly used in Molecular Orbital theory. After a geometry optimization or single point energy calculation with a Semi-empirical or ab-initio method:

(a) L-click display menu. (b) L-click Labels (c) Select charge and OK (atomic units).

5.3 Bond orders. The bond order is an approximate quantitative descriptor for the amount of bonding between two (bonded) atoms. The bond order is initially 1 for single bonds, 2 for double bonds, 3 for triple bonds, and 1.5 for aromatic bonds. After a quantum mechanical calculation (semi-empirical or ab-initio), the bond order, as displayed by a requested label, will be a computed measure of the amount of bonding. To display bond order: (a) L-click the Display button and open the Labels dialog box. (b) Select bond order and OK.

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[7] It is a method of assigning a fictitious charge to each atom in the molecule, based on the relative contribution of the atomic orbitals (located on each atom) to the molecular wave function.

5.4 Plotting calculated molecular orbitals

After you have performed a semi-empirical or ab-initio geometry optimization or single point energy calculation, you can L-click Compute and choose Orbitals to display the contours of the energy levels for all orbitals or an orbital you specify. Use the Orbitals dialog box to see degeneracies and near degeneracies, HOMO-LUMO gaps, orbital occupation scheme, alpha and beta spin manifolds separately (for UHF calculations of open shell systems). The Isosurface-rendering tab which appears once under Options allows you to change the appearance of the contour, when it is too small or too big.

Exercise A.6

Use the Restricted Hartree-Fock method (ab-initio) and a minimal basis set to perform a geometry optimization calculation of water and propene (a) Report and compare the dipole moment of the optimized molecules. (b) Plot the Highest occupied molecular orbital, what is the significance of the two colors in the plot? what is the energy and occupation number of the HOMO? (c) What is the significance of the two colors in the plot? (these are violet and green by default) (d) In Compute/Orbitals/Options, select the Isosurface-rendering tab and change the iso-value of the orbital contour. Re-plot and explain what the effect of the change is. (e) Report the total electronic energy of the molecules according to your calculations.

- Build a model for the molecule.
- Use section 3.3 to setup RHF method (select ab-initio in the setup menu, Basis-set-minimal (STO-3G), total charge – 0, multiplicity –1, spin pairing – RHF, convergence limit – 10^{-2}, iterations limit – default).
- Use section 4.2 to setup and perform a geometry optimization calculation (Use the Polak-Ribiere algorithm, RMS gradient of $0.01 \, \text{Kcal}/(\text{Å} \cdot mol)$ or default cycles, select In vacuo).
- Use section 5.1 to report the dipole moment of the optimized structure.
- Use section 5.4 to plot the HOMO, report the energy and occupation of the Homo (for occupation number select labels in the Compute Orbitals dialog box).
- Open your saved log file to report the electronic energy of the molecule.

Exercise A.7

Use the PM3 (Semi-empirical) method to perform a geometry optimization calculation of molecules E, F and G.
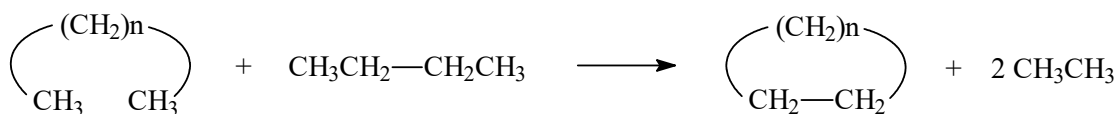
- Open the file of the model you built for the molecule.

- Use section 3.3 to setup the PM3 (Semi-empirical) calculation method (Select PM3 method, total charge – 0, multiplicity – 1, spin pairing – RHF, state – lowest, SCF controls: convergence limit – 0.01, iterations limit - default).

- Use section 4.2 to setup and perform a geometry optimization calculation (Use the Polak-Ribiere algorithm, RMS gradient of $0.01\,\text{Kcal}/(\text{Å}\cdot mol)$ or default cycles, select In vacuo).

- Use section 5.2 to report the atomic charges (Mulliken) of the molecule G.

- Use section 5.4 to plot the HOMO, report the energy and occupation of the Homo (for occupation number select labels in the Compute Orbitals dialog box) of molecules E and F.

Exercise B – Calculation of ring strain in Cyclo-Alkanes

Background

In this lab you will use PM3 semi-empirical method to determine the amount of "ring strain" in cyclo-alkanes as a function of ring size. "Ring strain" arises in small ring structures from the deviation of bond angles from their "ideal" (tetrahedral) values and from the more severe eclipsing (torsional) interactions in small rings (because they are not flexible enough to twist to avoid these interactions.)

The method that you will use is to employ an **isodesmic reaction scheme**, that is, the reaction in which the number and type of bonds broken on the reactants side is identical to the number of formed bonds in the products side of the equation. This approach tends to cancel out systematic errors and leads to more accurate results than direct comparison between the ring and the open chain. It should always be employed when comparing the energies of several structures. The isodesmic reaction scheme that you will employ is shown below.

$$\text{cyclo-}(CH_2)n\text{ with } CH_3, CH_3 \quad + \quad CH_3CH_2\!-\!CH_2CH_3 \quad \longrightarrow \quad \text{cyclo-}(CH_2)n \text{ with } CH_2\!-\!CH_2 \quad + \quad 2\ CH_3CH_3$$

B.1 Construct models of each of the following molecules in *HyperChem,* add hydrogen atoms and model build: cyclopropane, cyclobutane, cyclopentane, cyclohexane, cycloheptane, ethane, propane, butane, pentane, hexane and heptane.

B.2 Perform a geometry optimization using the PM3 semi-empirical method. *Make sure you keep a log file for each such molecule, since you will need its Heat of Formation (which is also available from the menu at Compute/Properties/Energies at 0K/Details).*

- Use section 3.3 to setup the PM3 (semi-empirical) calculation method (Select PM3 method, total charge – 0, multiplicity – 1, spin pairing – RHF, state – lowest, SCF controls: convergence limit – 0.01, iterations limit –use default).

- Use section 4.2 to setup and perform a geometry optimization calculation (Use the Polak-Ribiere algorithm, RMS gradient of 0.01 Kcal/(Ang·*mol*) or default number of cycles, select In vacuo).

B.3 What are the heats of formation of each of the molecules? Note that the heats of formation are stored in the log file, and you can access the data there with any simple text editor (like Notepad).

B.4 Calculate the energy of the isodesmic reaction shown above separately for n = 1, 2, 3, 4 and 5. Recall that Hess's law allows you to determine the heat of formation of the reaction from the heat of formation difference values of the products and the reactants:

$$\Delta H_{reaction} = \sum_{i\ product} \Delta H_{formation,i} - \sum_{j\ reactant} \Delta H_{formation,j}$$

B.5 In order to calculate the strain energy, a reference standard must be employed. Select as your standard the isodesmic reaction that gives the most favorable $\Delta H_{reaction}$ (the greatest negative, or the smallest positive value). It is reasonable to expect to use as a standard the $\Delta H_{reaction}$ for the isodesmic reaction involving hexane-cyclohexane, since it is generally known that a six-membered ring in a chair conformation is devoid of the usual kinds of strain associated with small ring compounds. Thus, subtract the $\Delta H_{reaction}$ for the isodesmic reaction involving hexane-cyclohexane from the $\Delta H_{reaction}$ for the isodesmic reaction involving the other pairs.

B.6 Which cyclo-alkane ring size (3, 4, 5, 6 or 7 member) has the most strain, according to your calculation?

B.7 Which ring size has the least strain, according to your calculation?

B.8 Plot ring strain vs. ring size (3-7). What do you observe?

B.9 Calculate the ring strain per CH2 group. Which ring size has the most strain per CH2?

B.10 Compare the following experimental values of strain energy and your calculated strain energy:

Molecule	Strain energy (Kcal/mol)
cyclo-propane	27
cyclobutane	26
cyclopentane	7
cyclohexane	0
cycloheptane	6

Exercise C - Mechanisms of electrophilic addition of Bromine to alkenes

In this lab, we will explore the mechanism of addition of bromine to alkenes.

An example for such an addition is the following
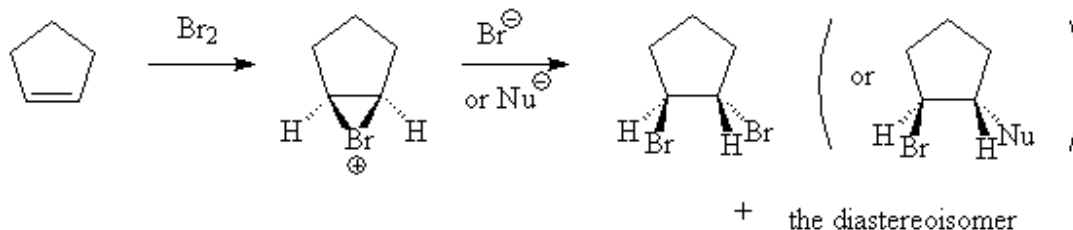
The above reaction includes two steps. In the first step the electron pair from the double bond attacks the polarized bromine, forming a cyclic intermediate bromonium ion[8] and causing the Br-Br bond to be break. Bromide ion departs with both electrons from the former Br-Br bond. In the second step, the bromide ion uses an electron pair to attack the intermediate bromonium, breaking one C-Br bond, forming another C-Br bond and giving a neutral addition product.

In this lab, we will use the PM3 semi-empirical method to explore bromine addition to different alkenes. We will start with an initial (cyclic bromonium) guess of the intermediate structure and perform a geometry optimization calculation. Then, we will use the optimized bond orders, atomic charges and calculated molecular orbitals to conclude whether the structure of the intermediate is cyclic or not and to predict the product of the reaction (syn or anti stereoisomers).

C.1 Use the HyperChem program in order to build a model of the five cations shown bellow. Select Allow Arbitrary Valence in the Build menu.
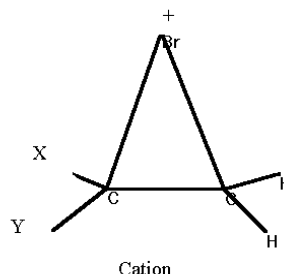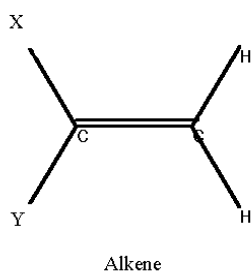
Alkene   Cation


[8] In bromonium ion the brome atom has a partial positive charge.

Alkene/ Cation	X	Y
1	H	H
2	H	OH
3	H	C_6H_5
4	CH_3	CH_3
5	CF_3	CF_3

C.2 Perform an energy optimization calculation for all five cations:

- Use section 3.3 to setup the PM3 (Semi-empirical) calculation method (Select PM3 method, **total charge 1**, multiplicity – 1, spin pairing – RHF, state – lowest, SCF controls: convergence limit – 0.01, iterations limit –use default).

- Use section 4.2 to setup and perform a geometry optimization calculation (Use the Polak-Ribiere algorithm, RMS gradient $0.01 \, Kcal/(Å \cdot mol)$ or default number of cycles, select In vacuo).

C.3 Use sections 5.2 and 5.3 to display the bond orders and the atomic charges of each optimized cation. Tabulate the following properties for each cation: Both C-Br bond orders, C-Y bond order, atomic charges on both C atoms and on the Br. According to the calculated bond orders and atomic charges, to which type of structure (A, B, C, or D) does each of the five optimized intermediate structures most resembles?
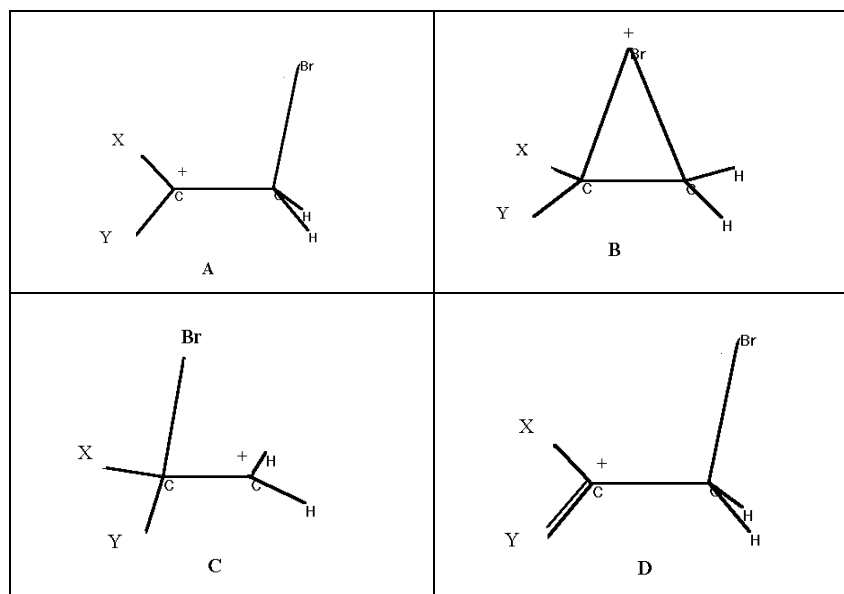
C.4 Report the two calculated C-Br bond orders and the calculated atomic charges on both carbon atoms and conclude to which carbon atom will the (second) bromide ion attach? Explain your conclusions.

C.5 Use steric considerations and the optimized geometry of the intermediate cation to predict which isomer will be formed (syn or anti)? Explain.

C.6 Use section 5.4 to calculate the HOMO and LUMO. Plot the densities of the HOMO and LUMO orbitals, as well as the molecular electronic density. Recalling that the attacking Bromine ion is a nucleophile, and according to the calculated molecular orbitals, to which carbon atom will the second bromide ion be attached? Justify your conclusions.

C.7 Use the calculated molecular orbitals to predict which isomer product will be formed (syn or anti)? Explain your results.

C.8 Use the PM3 method to perform a geometry optimization calculation of both isomers products (syn and anti).

- Build a model for each isomer (select the dihedral angle, Br-C-C-Br, and press the Edit button and select Set Bond Torsion to zero for syn isomer and 180 for anti-isomer).

- Deselect the dihedral bond by R-clicking somewhere outside the structure.

- Use section 3.3 to setup the PM3 (Semi-empirical) calculation method (Select PM3 method, total charge - 0, multiplicity – 1, spin pairing – RHF, state – lowest, SCF controls: convergence limit – 0.01, iterations limit –use default).

- Use section 4.2 to setup and perform a geometry optimization calculation (Use the Polak-Ribiere algorithm, RMS gradient $0.01\ Kcal/(\text{Å}\cdot mol)$ or default number of cycles, select In vacuo).

Report the energy and optimized dihedral angle of each optimized isomer.

C.9 Use the energy calculation to predict which isomer product will be formed (syn or anti)? Explain. Compare your conclusions with steric considerations and with calculated molecular orbital theory.