

Nucleophiles & Electrophiles

Created with: Release 2021-3

Prerequisites: working knowledge of Maestro

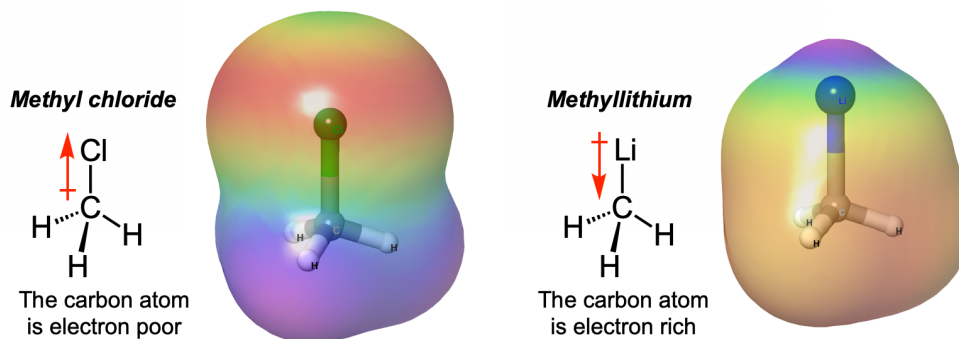
Files Supplied: Chemical_bonding_worksheet

Categories: organic chemistry

About this Lesson

In this lesson plan, students will examine the behavior of nucleophiles and electrophiles. Students will learn about inductive effects and how to identify nucleophilic and electrophilic centers in a molecule. This will help with predicting where electron density can be found and where it is likely to flow during a reaction.

Using Maestro, students will create a map of electrostatic potential (ESP) of various nucleophiles and electrophiles with Jaguar and examine the electrostatic potential on the molecular surface. These renderings will help with visualizing sites of high and low electron density.



Learning Objectives

- Differentiate between nucleophilic and electrophilic centers
- Identify electron-rich and electron-poor regions by mapping electrostatic potential surfaces onto molecules

Standards:

- ACS Guidelines
 - Properties of Molecules ([Conceptual Topics](#))
- ETS Chemistry GRE
 - Organic Chemistry – Structure, Bonding, and Nomenclature ([3.A](#))
- AAMC MCAT
 - Nature of molecules and intermolecular interactions ([5B](#))

Assessments

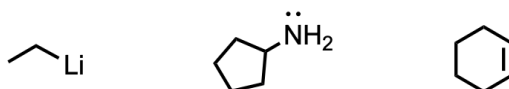
The following types of formative assessments are embedded in this lesson:

- Assessment of student understanding through discussion of warm-up questions and filling in any knowledge gaps of inductive effects
- Visual assessment of student-generated electrostatic potential surfaces of nucleophilic and electrophilic centers

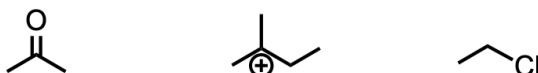
Warm-Up Questions: To be done on their own or at the beginning of class

Watch the [Khan Academy videos](#) on nucleophilicity and basicity.

- 1) Identify the nucleophilic center of each molecule.




- 2) Identify the electrophilic center of each molecule.



Lesson Outline

1. [What you will need for this lesson](#) - p. 3
2. [Polar Bonds, Induction, and Electronegativity](#) - p. 5
3. [Nucleophiles](#) - p. 7
4. [Electrophiles](#) - p. 20
5. [Individual Exercise](#) - p. 33
6. [Summary, Additional Resources, and References](#) - p. 34
7. [Glossary of Terms](#) - p. 34

1. What you will need for this lesson

	<ol style="list-style-type: none">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 "Nucleophiles" and copy folder to Desktop<ul style="list-style-type: none">• Here, you will find the lesson plan, worksheet, and any additional resources
 <p>Maestro</p> <p>Figure 1-1. Open Maestro.</p>	<ol style="list-style-type: none">3. Open Maestro<ol style="list-style-type: none">a. See Starting Maestro if you need help

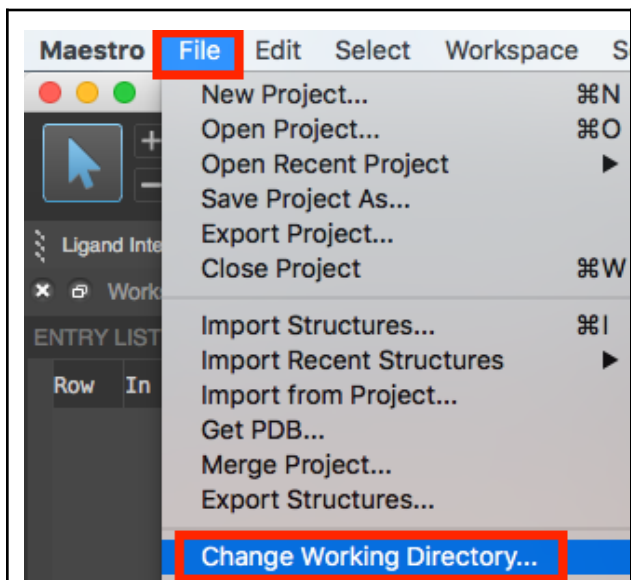


Figure 1-2. Change Working Directory option.

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

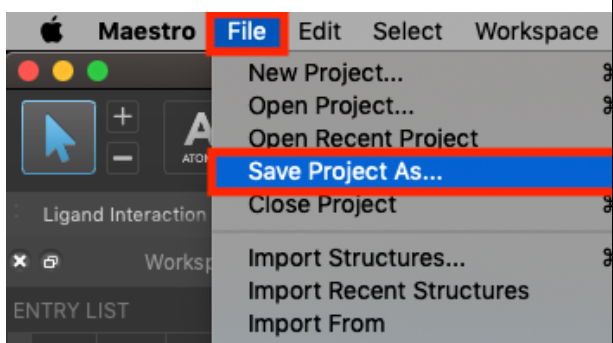


Figure 1-3. Save Project panel.

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

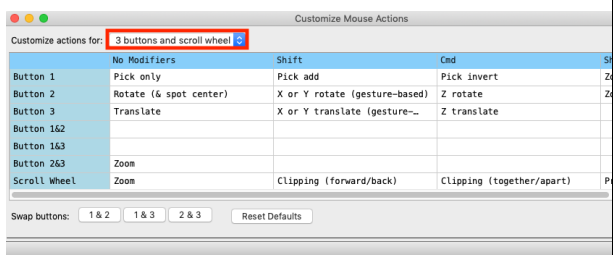


Figure 1-4. Choose the best mouse option for your set up.

8. Finally, check your **Mouse Actions**
 - a. PC : **Edit > Customize Mouse Actions**
 - b. Mac : **Workspace > 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. Polar Bonds, Induction, and Electronegativity

Bond polarity is a measure of how equally or unequally the electrons in any covalent bond are shared. A **nonpolar covalent bond** is one in which the electrons are shared equally, like in Cl₂, N₂, or H₂. In the case of Cl₂, each atom starts off with seven valence electrons, and each Cl shares one electron with each other forming one covalent bond.



Figure 2-1. Nonpolar covalent bond of Cl₂

The total number of electrons around each individual atom consists of six nonbonding electrons and two shared, bonding electrons for eight total electrons. This matches the number of valence electrons in the closest noble gas argon (Ar). Since the bonding atoms are identical, Cl₂ contains a nonpolar covalent bond.

In a **polar covalent bond**, there is an unequal distribution of electrons which is characterized by a partial positive charge on one atom and a partial negative charge on the other. The atom that attracts the electrons more strongly acquires the partial negative charge and vice versa. For example, the electrons in the H–Cl bond of a hydrogen chloride atom spend more time near the more electronegative chlorine atom than near the hydrogen atom. Therefore, the chlorine atom carries a partial negative charge while the hydrogen atom has a partial positive charge. We can represent this charge distribution as:

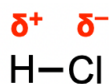


Figure 2-2. Polar covalent bond of H–Cl

The δ^+ (delta plus) and δ^- (delta minus) symbolize the partial positive and negative charges, respectively. In a polar bond, these numbers are less than a full charge of the ions.

Electronegativity is the ability of an atom in a molecule to attract electrons to itself and is used to estimate whether a given bond is nonpolar covalent, polar covalent, or ionic. The greater an atom's electronegativity, the greater its ability to attract electrons to itself. American chemist Linus Pauling developed an electronegativity scale, which is based on thermochemical data shown below.

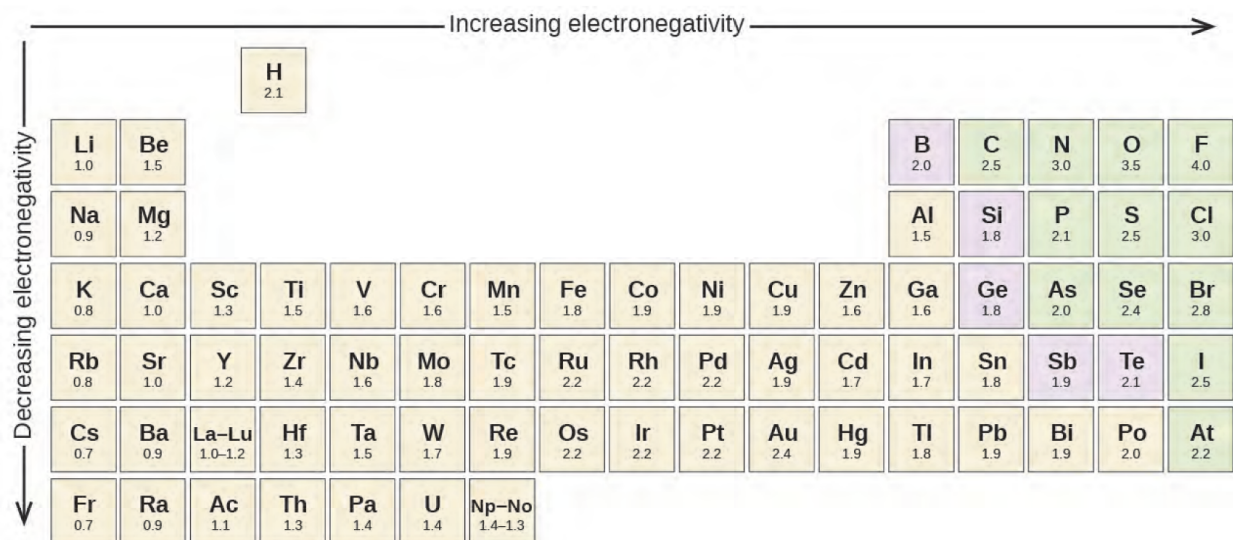


Figure 2-3. Linus Pauling's Electronegativity Scale

The absolute value of the difference in electronegativity (ΔEN) of two bonded atoms provides a rough approximation of the polarity to be expected in the bond and, thus, the bond type. Note that electronegativity values have no units. When the difference is very small or zero, the bond is nonpolar covalent. When the difference is between 0.4 and 1.8, the bond is polar covalent. When the difference is above 1.8, the bond is ionic. A table summarizing electronegativity differences and bond types is shown below.

Bond Type	Electronegativity Difference
Nonpolar covalent	< 0.4
Polar covalent	0.4 – 1.8
Ionic	> 1.8

Table 2-1. Summary of bond types based on electronegativity differences

Induction (or inductive effect) is due to the difference in electronegativity of atoms bonded together. A bond between two atoms is polarized if there is a difference between their electronegativities. This **polarization** of the bond causes the appearance of partial charges (δ^+ and δ^-), which may have effects on close-by neighboring bonds. Some effects may be electron withdrawal which often occurs on atoms that are more electronegative than carbon (O, N, F, etc.), or electron repelling which often occurs on

atoms that are less electronegative than carbon (Mg, Al, etc.). We will visualize inductive effects in various nucleophiles and electrophiles using calculated electrostatic potential maps later in this lesson.

3. Nucleophiles

A **nucleophile** contains an electron-rich center and comes from the Greek meaning “nucleus lover”. Nucleophiles provide the electrons to make a new bond in a substitution reaction (either S_N1 or S_N2). A nucleophilic center is characterized by its ability to react with a positive charge or partial positive charge by donating a pair of electrons. There are three different kinds of electron-rich regions:

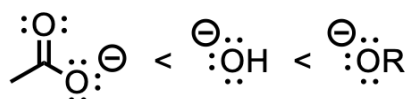
- 1) nonbonding electrons (present on oxygen, nitrogen, and negatively charged carbon atoms called carbanions) – Atoms that possess nonbonding lone pairs of electrons are nucleophilic. Note that lone pairs of electrons may not always be drawn in molecular structures so be aware of the octet rule and feel free to draw them in if they are not shown.
- 2) a carbon atom bonded to a metal, such as a Grignard/organomagnesium or organolithium – A carbon atom bonded to a metal has a strong negative character which can be shown through writing a resonance structure. The carbanion is considered to be a strong nucleophile.
- 3) π bonds – A π bond is also a region of high electron density. Since π bonds are not as strong as σ bonds, π electrons are more available to react in a reaction because π bonds can break more easily. Molecules containing π bonds are considered to be weak nucleophiles and can react with strong acids or electrophiles.

Nucleophilicity is a kinetic property measured by the rate at which a nucleophile causes a substitution reaction to occur. Certain reactions are better with strong nucleophiles while others are better with weak nucleophiles. Some factors that contribute to nucleophilicity include:

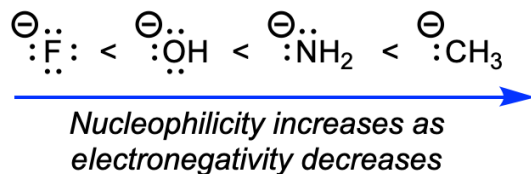
- 1) **Charge** – As electron density on an atom increases, so does nucleophilicity



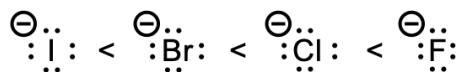
- 2) **Basicity** – The stronger the base, the greater the nucleophilicity



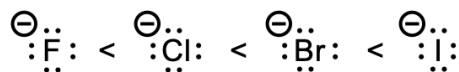
- 3) **Electronegativity** – For atoms in the same row of the periodic table, as electronegativity increases, nucleophilicity decreases



- 4) **Solvation effect** – Depends on whether the reaction is in polar protic or polar aprotic solvent. In polar protic solvents, nucleophilicity increases going down the periodic table. In polar aprotic solvents, nucleophilicity increases going up the periodic table

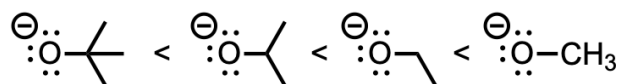


*In polar protic solvent
(i.e. H₂O, MeOH, etc.)*

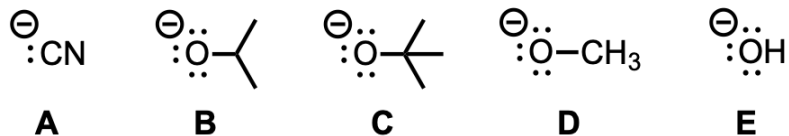


*In polar aprotic solvent
(i.e. DMSO, THF, etc.)*

- 5) **Steric hindrance** (or bulkiness) – The less bulky, the better the nucleophile since it is easier for the nucleophile to backside attack



Example #1: Rank the following compounds in order of increasing nucleophilicity.



Computational Exercise #1: Generating Electrostatic Potential (ESP) Maps on the Molecular Surface

Now we will calculate the electrostatic potential surfaces of ethanol and ethoxide to visually identify which nucleophile is strong and which is weak. ESP maps will show the electron-density distribution on the surface of the molecules. This exercise involves three parts:

- 1) Build the molecules and minimize their geometries
- 2) Generate surfaces of the molecules
- 3) Map the electrostatic potentials to the molecular surfaces

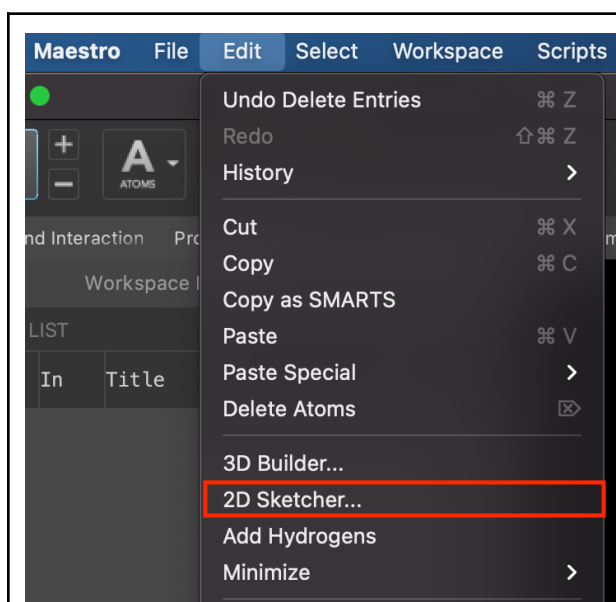


Figure 3-1. Open 2D Sketcher.

Part 1. Build the molecules and minimize their geometries

Before generating any surfaces, build and minimize the structures for ethanol and ethoxide

- 4) Go to **Edit > 2D Sketcher**

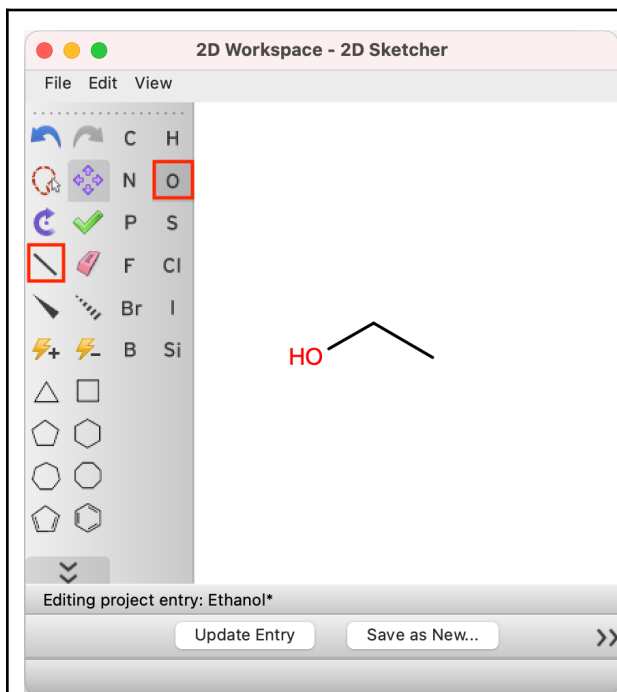


Figure 3-2. Drawing ethanol.

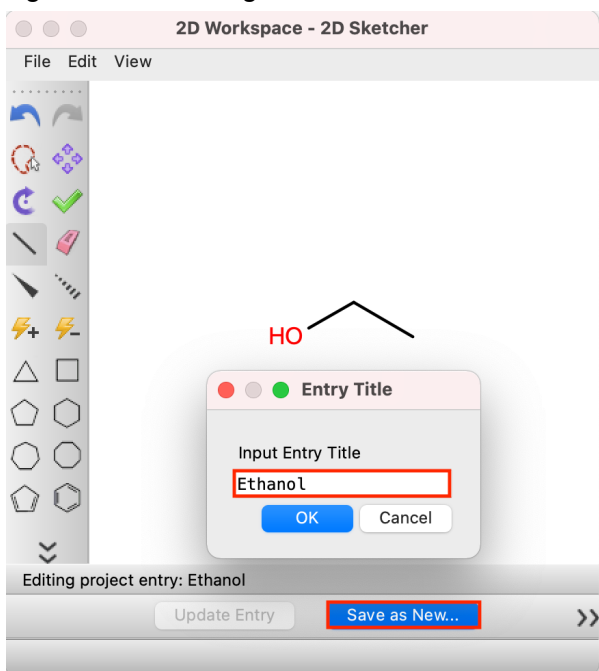


Figure 3-3. Saving Ethanol.

- 5) **Draw ethanol**
 - a) Go to the selection bar on the left
 - b) Choose the single bond button
 - c) Click and drag in the workspace to form ethane
 - d) Click and drag again from one of the carbon atoms to form propane (linear 3-carbon chain)
 - e) Click "O" in the selection bar and click the end of the single bond to change a carbon to OH at the end
- 6) Click on **Save as New** and for *Input Entry Title* write **Ethanol**. Click **OK**.

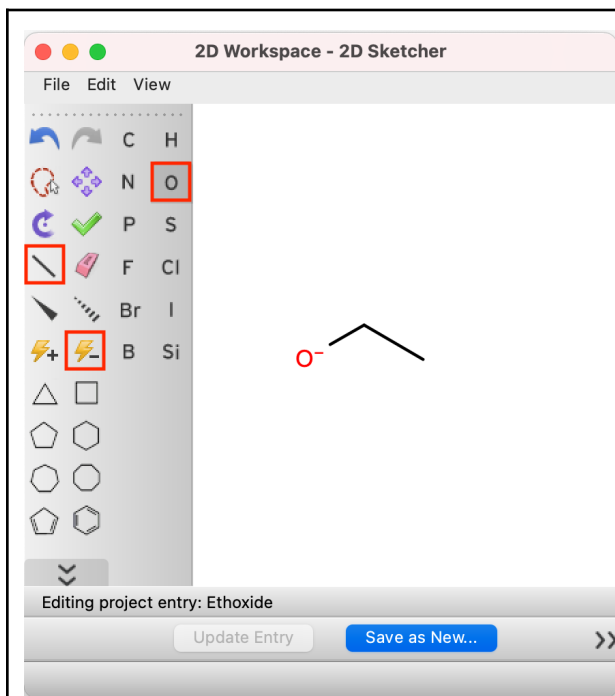


Figure 3-4. Drawing Ethoxide.

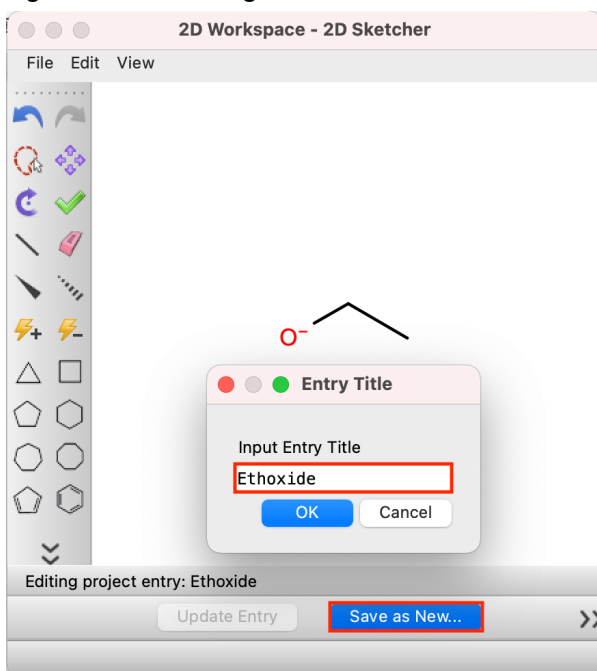
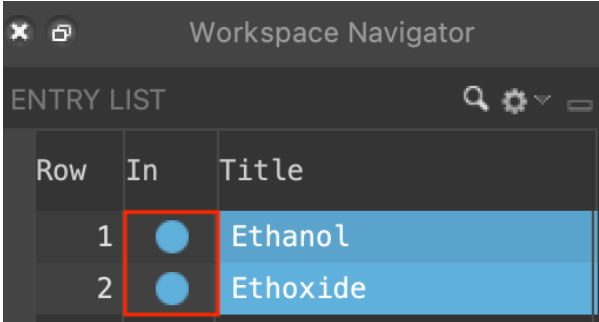
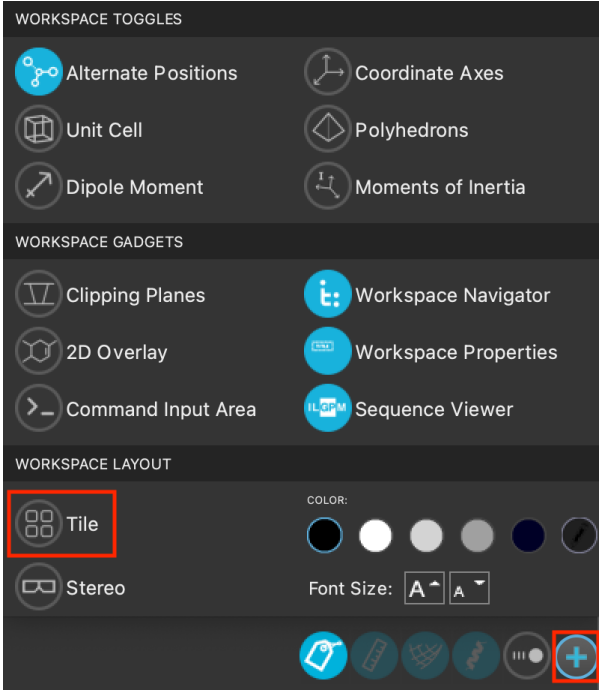


Figure 3-5. Saving Ethoxide.

- 7) **Draw ethoxide**
 - a) Go to the selection bar on the left
 - b) Choose the single bond button
 - c) Click and drag in the workspace to form ethane
 - d) Click and drag again from one of the carbon atoms to form propane (linear 3-carbon chain)
 - e) Click "O" in the selection bar and click the end of the single bond to change a carbon to OH at the end
 - f) Click the lightning bolt *Decrease Charge* button then click the Oxygen atom in your molecule. This removes the H from OH and adds a negative charge to O.
- 8) Click on **Save as New** and for *Input Entry Title* write **Ethoxide**. Click **OK**.

 <p>Figure 3-6. Including both molecules.</p>	<p>Viewing multiple molecules at the same time can be important for comparing and contrasting them. We will show ethanol and ethoxide side by side so we can easily see how they differ.</p> <p>9) Simultaneously include (control + click or command + click) all molecules</p>
 <p>Figure 3-7. Tiling both molecules.</p>	<p>10) Show workspace configuration panel by clicking the Plus symbol at the bottom right corner</p> <p>11) Click Workspace Layout > Tile</p>

ENTRY LIST		
Row	In	Title
1		Ethanol
2		Ethoxide

Figure 3-8. Selecting both entries.

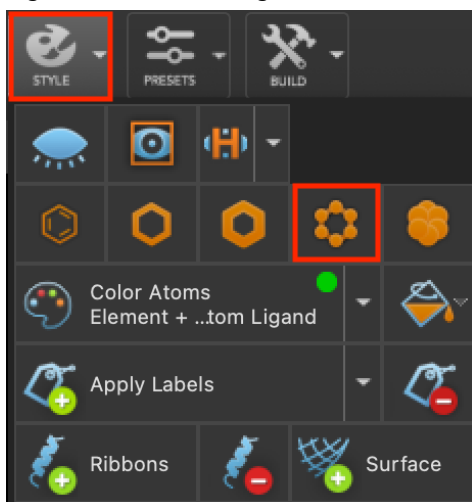


Figure 3-9. Applying ball-and-stick style to all entries.

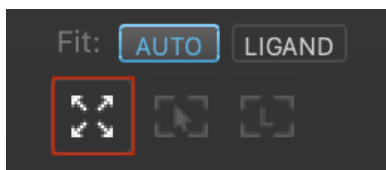


Figure 3-10. Centering the views of all three entries.

- 12) Simultaneously **select** (control + click or command + click) all molecules
- 13) Change their representations to ball-and-stick by clicking on the **Style** menu and choosing **Apply ball-and-stick representation**
- 14) Include atom labels if you'd like by clicking **Apply Labels > Custom Label**

- 15) To center all the molecules within their respective areas, click **Fit view to all visible objects**

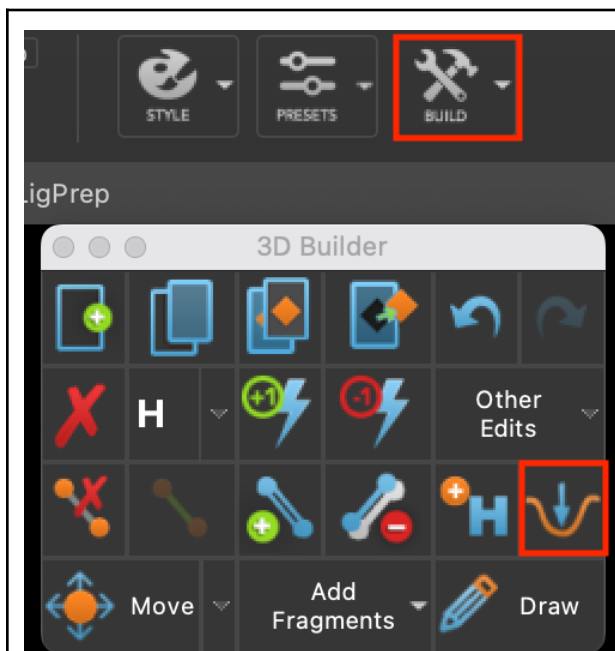


Figure 3-11. Performing force field minimization on all entries

- 16) **Select** all three molecules in the workspace (there are many approaches to do so: Main Menu, Select > All; Toolbar, Quick Select, All, Shift + Click + Drag and more)
- 17) In the **Build** dropdown from the toolbar (3D Builder panel), select **Minimize selected atoms**
 - The molecule is minimized, and the parameters adjust slightly

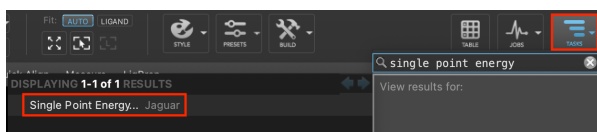


Figure 3-12. Open the Jaguar - Single Point Energy Panel.

Part 2. Generate surfaces for the molecules

- 18) **Select** all three molecules – we will be running the next calculations in parallel
- 19) Open the **Jaguar - Single Point Energy** panel from the *Task* button
 - a) Click **Browse > Jaguar > Single Point Energy**
 - b) Or, type **Single Point Energy** in the search bar

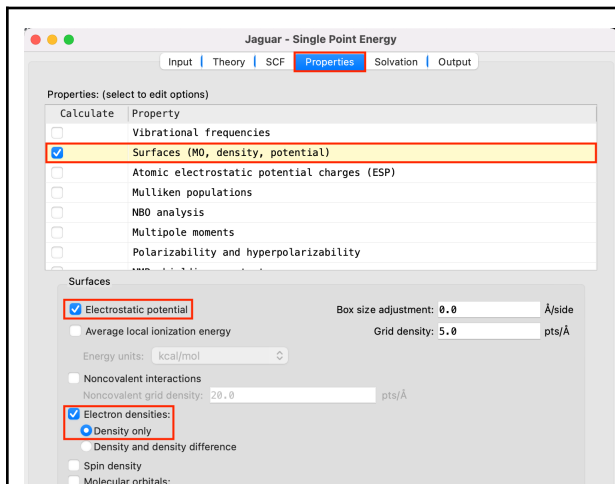


Figure 3-13. Choosing the surface controls under the Properties tab.

- 20) In the **Properties** tab, select the row for **Surfaces** and click the check box
 - a) The **Surfaces** controls are displayed
- 21) In the **Surfaces** section, select **Electrostatic potential** and **Electron densities**, and ensure that no other surface types are selected
- 22) Ensure that **Density only** is selected under **Electron densities**

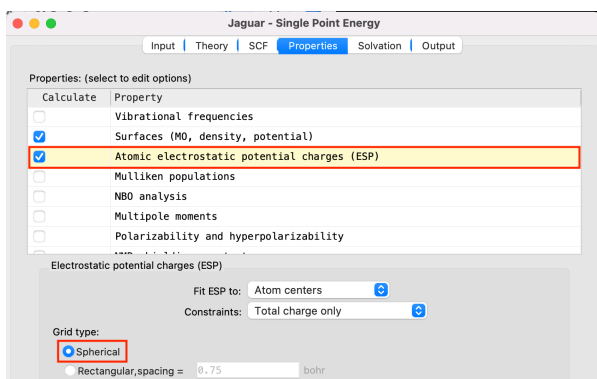


Figure 3-14. Choosing atomic electrostatic potential charges under the Properties tab.

- 23) Check the box for **Atomic electrostatic potential charges (ESP)** in the Properties table



Figure 3-15. Running the ESP jobs in parallel.

- 24) Name the job **ESP**
- 25) Adjust the settings by clicking the gear icon
- 26) Choose **localhost (4)** as the Job Host
- 27) Click **Run**
 - a) When the jobs finish, the structures are imported and the electron density surfaces may be displayed
 - b) The incorporated jobs will be shown in a separate Entry Group in the Entry List

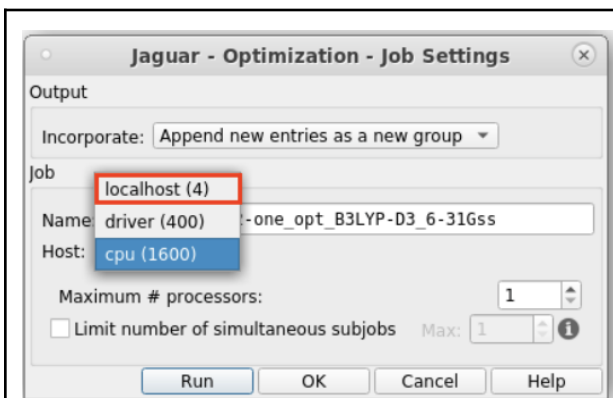


Figure 3-16. Adjusting the job settings.

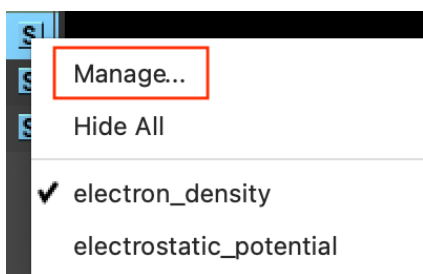
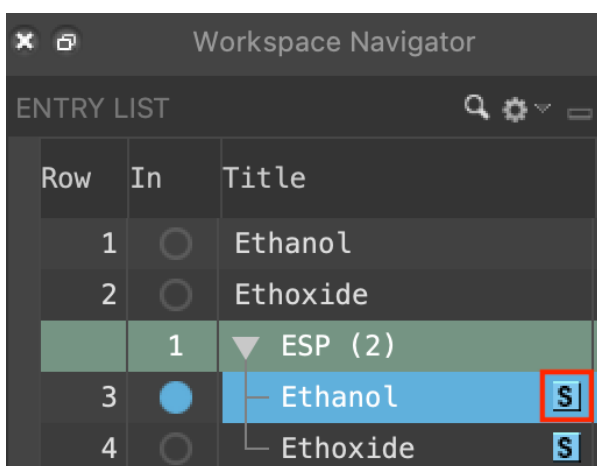


Figure 3-17. Clicking the S button in the Entry List and choosing Manage.

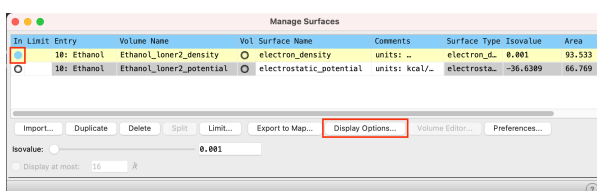


Figure 3-18. Choosing settings in the Manage

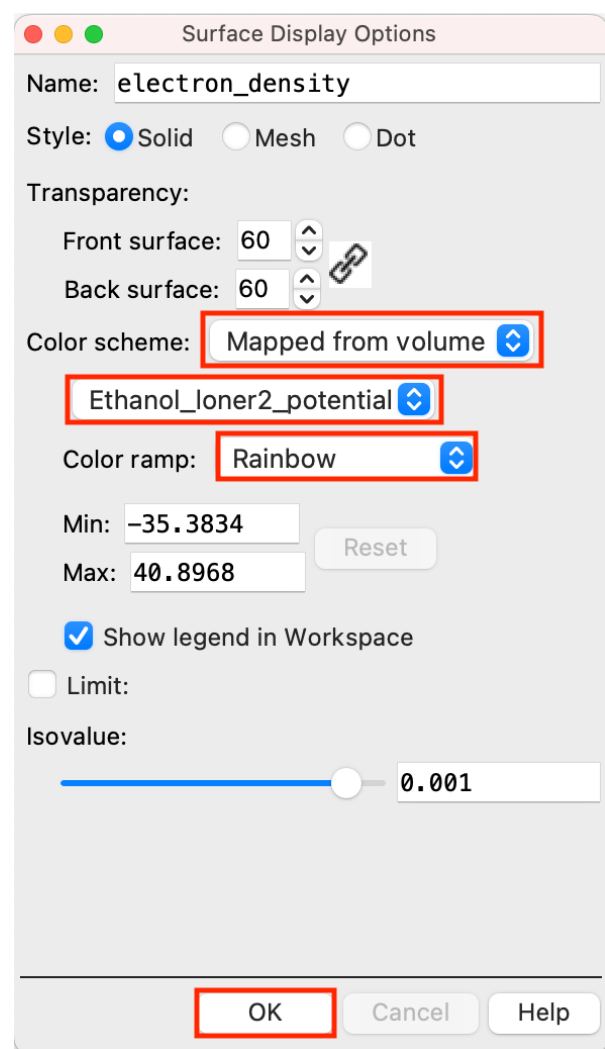
Part 3. Map the electrostatic potential to the molecular surfaces

- 28) Click the **S** button in the **Entry List** for **Ethanol** and choose **Manage**
 - a) The **Manage Surfaces** panel opens

- 29) Click the **In** column for the electron density surface to include it in the Workspace
- 30) Click **Display Options**

Surfaces panel.

a) The **Surface Display Options** panel opens



- 31) For **Color scheme**, select **Mapped from volume**
- 32) Select **Ethanol_loner2_potential** from the volume data list
- 33) From the **Color ramp** option menu, choose **Rainbow**
- 34) Click **OK**
- 35) Repeat steps 25-31 for Ethoxide.

Figure 3-19. Choosing settings in the Surface Display Options panel

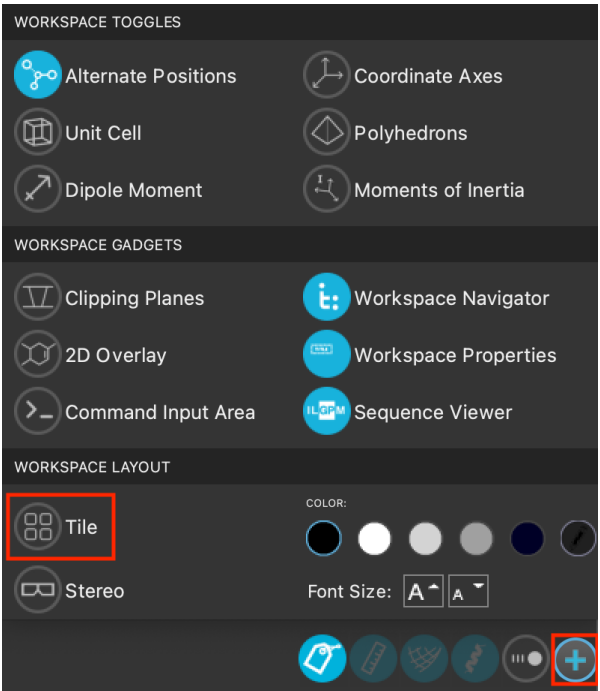


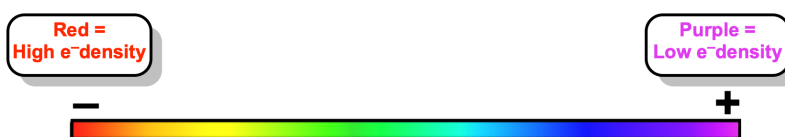
Figure 3-20. Tile both electrostatic potential surfaces.

36) Once you have displayed both electrostatic potential surfaces, tile the molecules so we can compare them

a) Click **Workspace Layout > Tile**

37) Feel free to play around with them and notice any similarities or differences between each molecule

When analyzing electrostatic potential surfaces, red represents regions of high electron density while purple represents regions of low electron density. See the range shown below:



Take a screenshot of the two electrostatic potential maps of ethanol and ethoxide and put it into your worksheet. In a few sentences, analyze any differences you see between the two surfaces. Determine which regions of each nucleophile dictate its strength, or lack thereof, towards attack of an electrophile.

Both ethanol and ethoxide contain oxygen atoms with lone pairs, so both molecules can act as nucleophiles. The ethoxide ion contains a negative charge on the oxygen atom making it a stronger nucleophile than the neutral ethanol molecule. This is indicative in their electrostatic potential maps – the red, more electron dense region is larger in ethoxide whereas the red region in ethanol is more localized to only the oxygen atom. Ethanol is a weak nucleophile because it is overall neutral whereas ethoxide is a strong nucleophile because it is negatively charged.

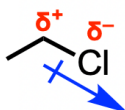
The strength of ethoxide is affected by **polarizability**. Polarizability is the ability of an atom to distribute its electron density unevenly in response to external influences. For example, HS^- is a particularly strong nucleophile because sulfur is a large atom with many electrons distant from the nucleus. Sulfur's polarizability causes its electron density to be unevenly distributed as it attacks an electrophile.

This example represents a standalone comparison of these two nucleophiles; it is important to note that the solvent in which these two nucleophiles may react in may change its nucleophilicity towards a given substrate.

4. Electrophiles

An **electrophile** is an “electron loving” species that is typically either positively charged or has a partial positive charge (δ^+). An electrophilic center is an electron-deficient atom that is capable of accepting a pair of electrons, similar to that of a Lewis acid. Two examples of electrophiles are:

- 1) An electrophilic carbon atom from inductive effects of a halide

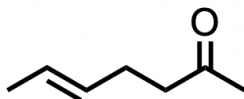


- 2) A carbocation which is a positively charged carbon atom – a carbocation has an empty p orbital that functions as a site that can accept a pair of electrons.



Electrophiles may have electron-withdrawing groups which is a group containing electronegative elements pulling the electron density towards them. Furthermore, electrophiles may also have polarizable π -bonds such as $\text{C}=\text{O}$ or $\text{C}=\text{N}$ bonds where partial charges can be drawn in.

Example #2: Predict where the nucleophilic and electrophilic centers are in the following molecule (*E*)-hept-5-en-2-one. Draw in any partial charges if applicable.



Computational Exercise #2: Optimizing the Geometry and Generating an Electrostatic Potential (ESP) Map on the Molecular Surface on (*E*)-hept-5-en-2-one

Now we will optimize the geometry of (*E*)-hept-5-en-2-one and calculate the electrostatic potential surfaces to visually show the electron-density distribution on the surface of the molecule. This exercise involves four parts:

- 1) Build the molecule and minimize its geometry
- 2) Optimize the geometry using quantum mechanical DFT
- 3) Generate surface of the molecule
- 4) Map the electrostatic potentials to the molecular surfaces

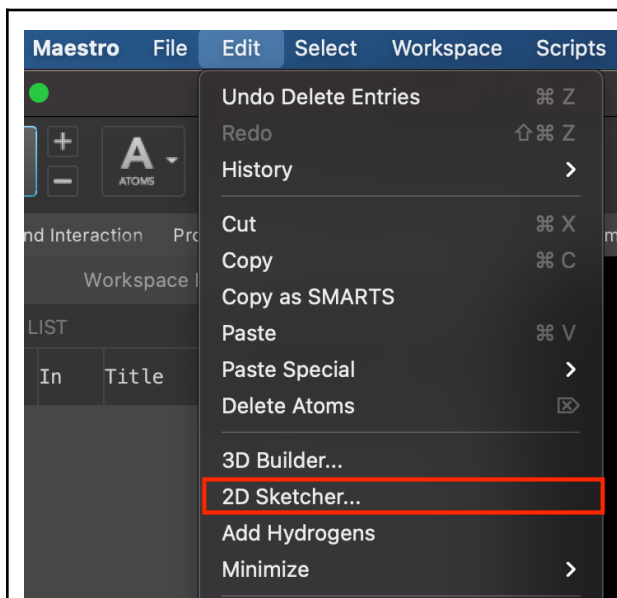


Figure 4-1. Open 2D Sketcher.

Part 1. Build (*E*)-hept-5-en-2-one using 2D Sketcher

Before optimizing any molecular geometry, you will need a starting molecule in your workspace. Let's draw the structure of (*E*)-hept-5-en-2-one using the 2D sketcher.

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

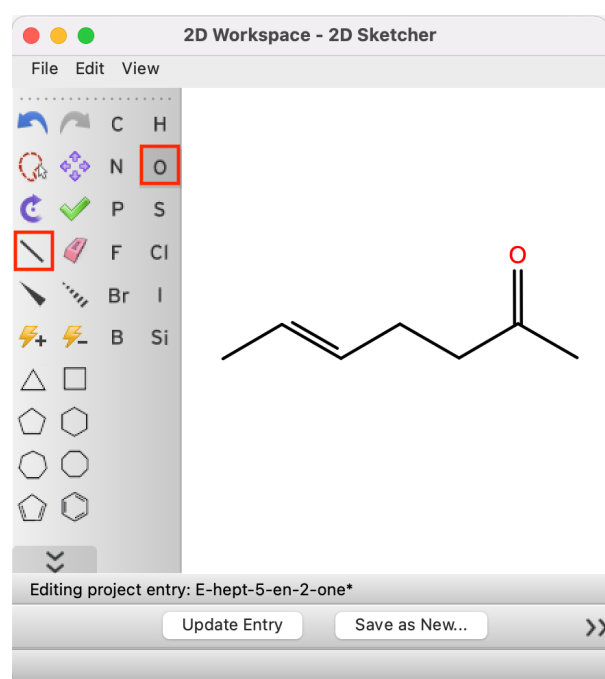


Figure 4-2. Draw (*E*)-hept-5-en-2-one

2. **Draw** the structure of (*E*)-hept-5-en-2-one. You do not need to draw in any lone pair of electrons; only show the bonds.
 - Go to the selection bar on the left
 - Choose the single bond button
 - Click and drag in your workspace to form ethane
 - Continue to click and drag until you form heptane (7-carbon linear chain)
 - Click and drag at the C2 position from the right to draw a methyl group
 - Click the center of this bond to form an alkene
 - Click the Oxygen atom to add an O to the end of the alkene you just made; this makes a carbonyl

- Choose the single bond button again and click the center of the C5–C6 bond to form a double bond

Note: You could also use **O** on your keyboard for atom assignments.

The 2D sketcher functions like many standard 2D molecular drawing tools. For a complete overview of using the sketcher panel, see the [2D Sketcher Panel documentation](#).

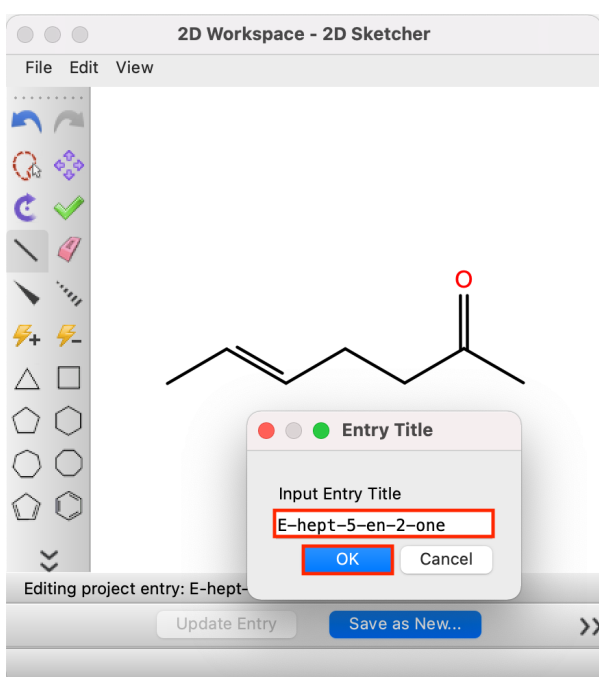
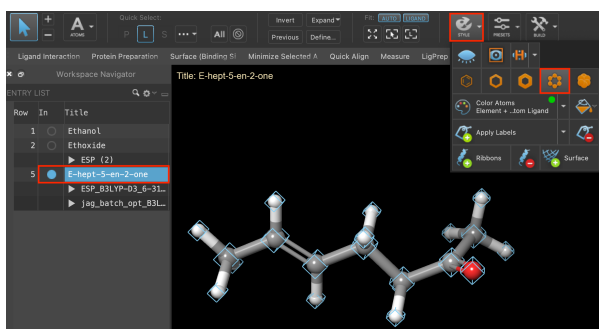


Figure 4-3. Saving (E)-hept-5-en-2-one

3. Click on **Save as New**
4. For *Input Entry Title*, write **E-hept-5-en-2-one**. Click **OK**.

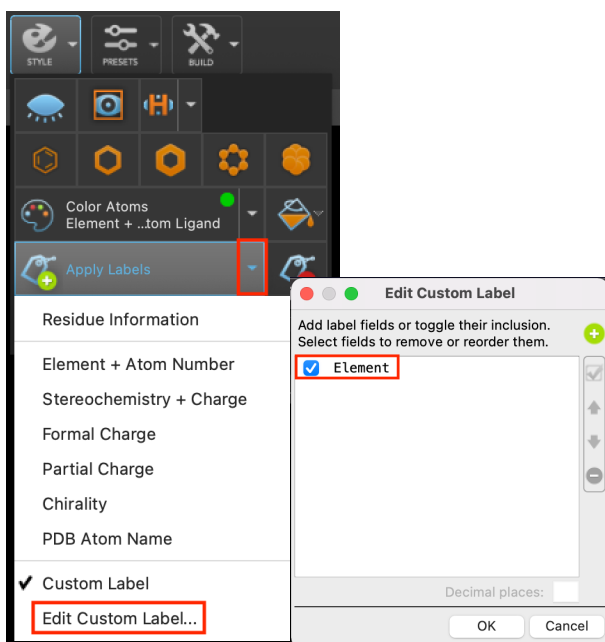


6. Close the 2D Sketcher panel
 - The (E)-hept-5-en-2-one molecule is selected in the entry list and included in the workspace
7. Change the representation to ball-and-stick by clicking on the **Style**

Figure 4-4. Viewing and styling
(E)-hept-5-en-2-one

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 atom labels, click **Style > Apply Labels** then click the drop down arrow on the right side
10. Click **Edit Custom Labeling**
11. Checkbox **Element** and press **OK**
12. 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 4-5. Labeling atoms.

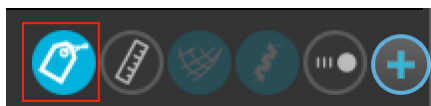


Figure 4-6. Toggling labels on.



Figure 4-7. Toggling labels off.

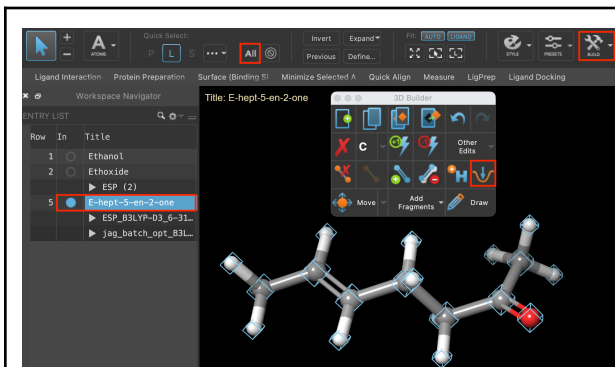


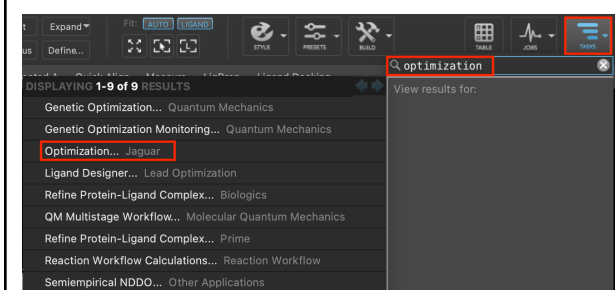
Figure 4-8. Force field minimization.

Part 2. Force Field Minimization

We can improve upon this starting structure by using a force field minimization. The molecule will still not be optimized by quantum mechanics (QM), but it will improve the starting geometry.

13. **Select** all atoms in the workspace (there are many approaches to do so: Main Menu, Select > All; Toolbar, Quick Select, All, Shift + Click + Drag and more)
14. In the **Build** dropdown from the toolbar (3D Builder panel), select **Minimize selected atoms**
 - The molecule is minimized, and the parameters adjust slightly

Note: Force fields are usually good at generating structures of molecules with common functional groups and elements. When it comes to more exotic atomic arrangements and less frequent elements (such as transition metals) or simply large molecules, force fields can yield structures with inaccurate or even unphysical geometries, and in those cases, quantum mechanical geometry optimizations become absolutely indispensable.



Part 3. Optimize the Geometry using Quantum Mechanic DFT

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

Figure 4-9. Opening the Jaguar Optimization panel.

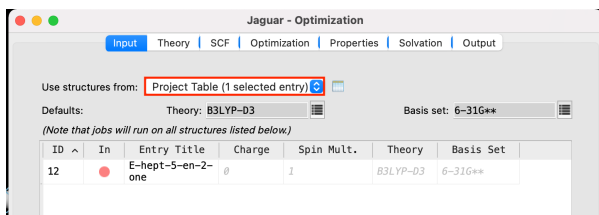


Figure 4-10. Setting the Jaguar Optimization panel to optimization.

15. With the (E)-hept-5-en-2-one entry selected and included, go to **Tasks > Optimization** using Jaguar
 - Type optimization in the Tasks search bar
 - The Jaguar Optimization panel opens
16. Use structures from **Project Table (1 selected entry)**

Note: We are optimizing one molecule, (E)-hept-5-en-2-one. By selecting many molecules in the entry list, we can optimize as many molecules as we would like concurrently with the same QM settings.

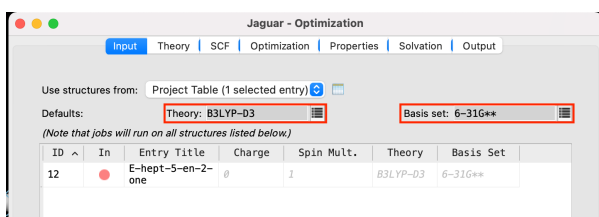


Figure 4-11. Setting the QM parameters for optimization.

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

17. For *Theory*, select B3LYP-D3
18. 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, (E)-hept-5-en-2-one 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 $S = \frac{1}{2}$.

- 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](#)

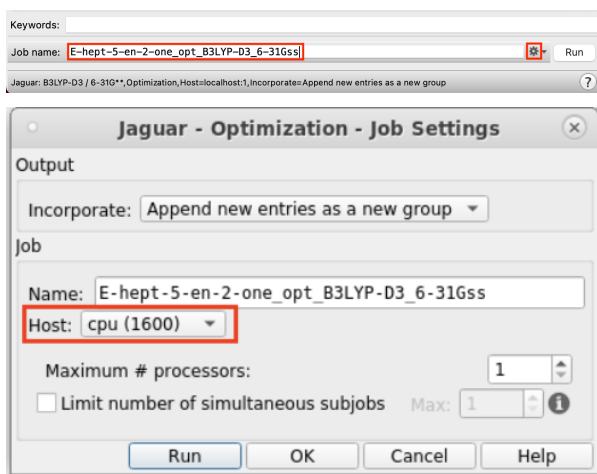
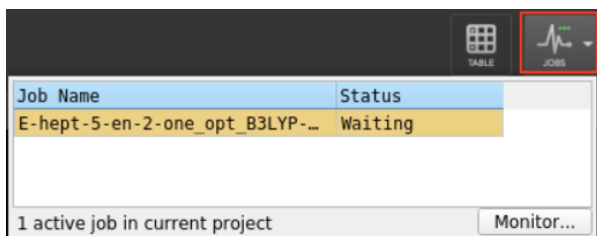


Figure 4-12. Naming and running the job.

19. Change the *Job name* to **E-hept-5-en-2-one_opt_B3LYP-D3_6-31GSS**
 - Usually we incorporate stars (*) and pluses (+) into file names with S and P, respectively
20. Adjust the job settings (⚙️)
 - This job requires a CPU host and should complete in under 5 minutes
21. Click **Run**

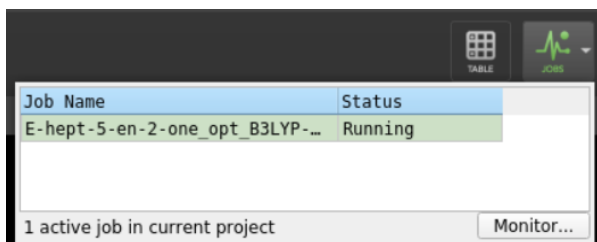
Note: It is advised to also add in a *Vibrational frequencies* calculation (from the *Properties* tab). This involves a bit more computational expense, but is a useful way to be sure that your output is a minimum (as opposed to a maximum) on the Potential Energy Surface (PES). For more detail, see the [Locating Transition States](#) tutorial.



When a job is submitted to the queue, you can check its status by clicking the Jobs button in the upper right-hand corner

- If the job is in the queue, it will say 'Waiting'

Figure 4-13. Status when a job is in the queue.



Job Name	Status
E-hept-5-en-2-one_opt_B3LYP-...	Running

1 active job in current project Monitor...

Figure 4-14. Status when a job is running.

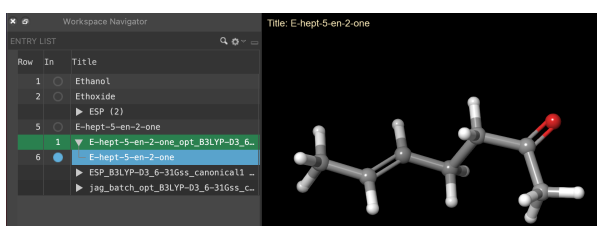


Figure 4-15. The output molecule of PCl_3 .

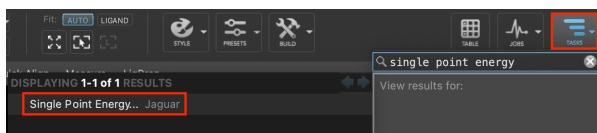


Figure 4-16. Open the Jaguar - Single Point Energy Panel.

- If the job is in progress, it will say 'Running'

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

22. A new entry group is added to the entry list titled E-hept-5-en-2-one_opt_B3LYP-D3_6-31GSS.011 (1). This is your optimized structure.

- Your structure may look a bit different because you may have built a different conformer. This is okay and you can still proceed to the next step as it will not change your ESP results.

Part 3. Generate the ESP surface for the molecule

23. **Select** the optimized molecule
24. Open the **Jaguar - Single Point Energy** panel from the *Task* button
 - Click **Browse > Jaguar > Single Point Energy**
 - Or, type **Single Point Energy** in the search bar

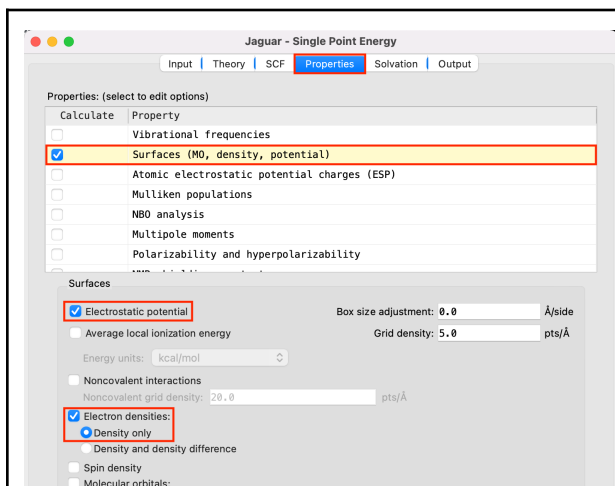


Figure 4-17. Choosing the surface controls under the Properties tab.

25. In the **Properties** tab, select the row for **Surfaces** and click the check box
 - The **Surfaces** controls are displayed
26. In the **Surfaces** section, select **Electrostatic potential** and **Electron densities**, and ensure that no other surface types are selected
27. Ensure that **Density only** is selected under **Electron densities**

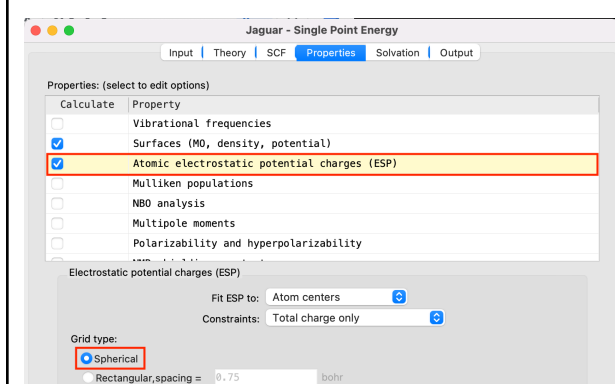


Figure 4-18. Choosing atomic electrostatic potential charges under the Properties tab.

28. Check the box for **Atomic electrostatic potential charges (ESP)** in the Properties table

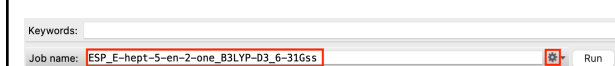


Figure 4-19. Running the ESP job.

29. Name the job
ESP_E-hept-5-en-2-one_B3LYP-D3_6-31Gss
30. Adjust the settings by clicking the gear icon
31. Choose **localhost (4)** as the Job Host
32. Click **Run**
 - When the jobs finish, the structures are imported and the electron density surfaces may be displayed

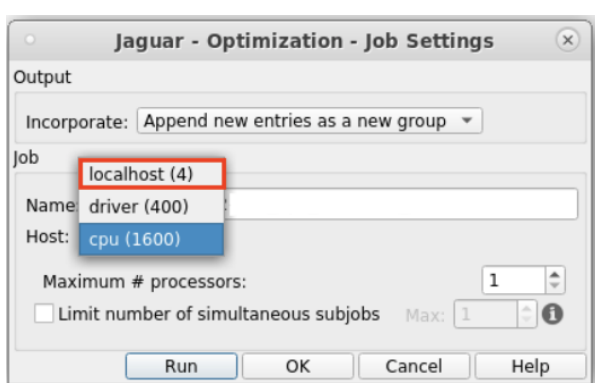


Figure 4-20. Adjusting the job settings.

- The incorporated jobs will be shown in a separate Entry Group in the Entry List

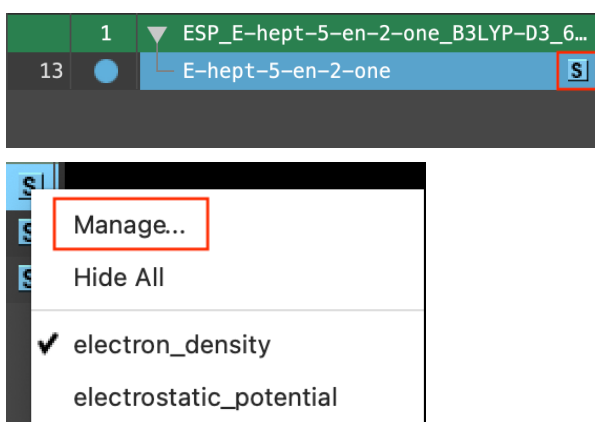


Figure 4-21. Clicking the S button in the Entry List and choosing Manage.

Part 4. Map the electrostatic potential to the molecular surfaces

33. Click the **S** button in the **Entry List** for **Ethanol** and choose **Manage**
 - The **Manage Surfaces** panel opens

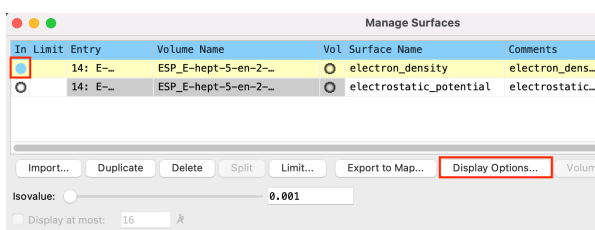
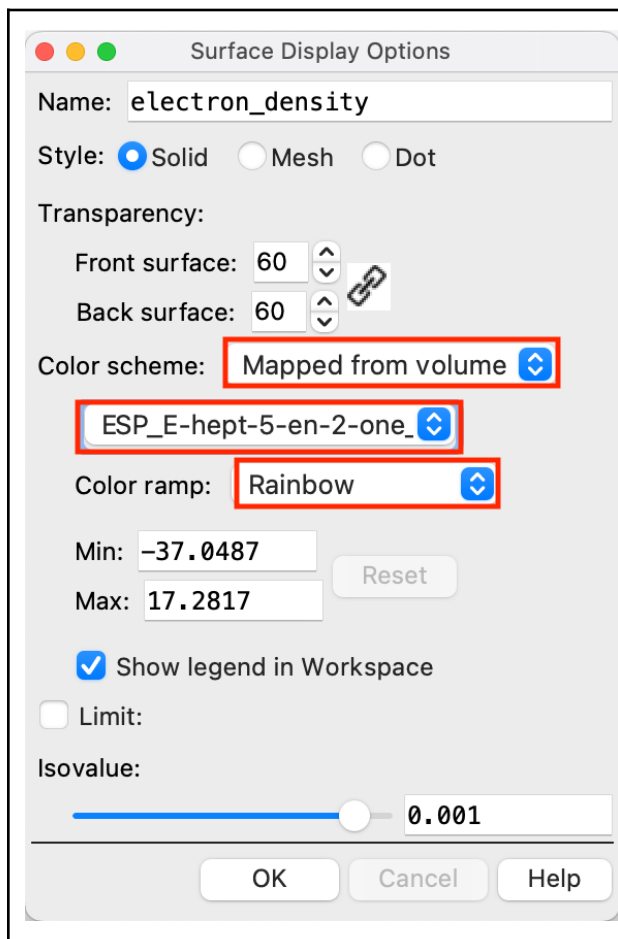
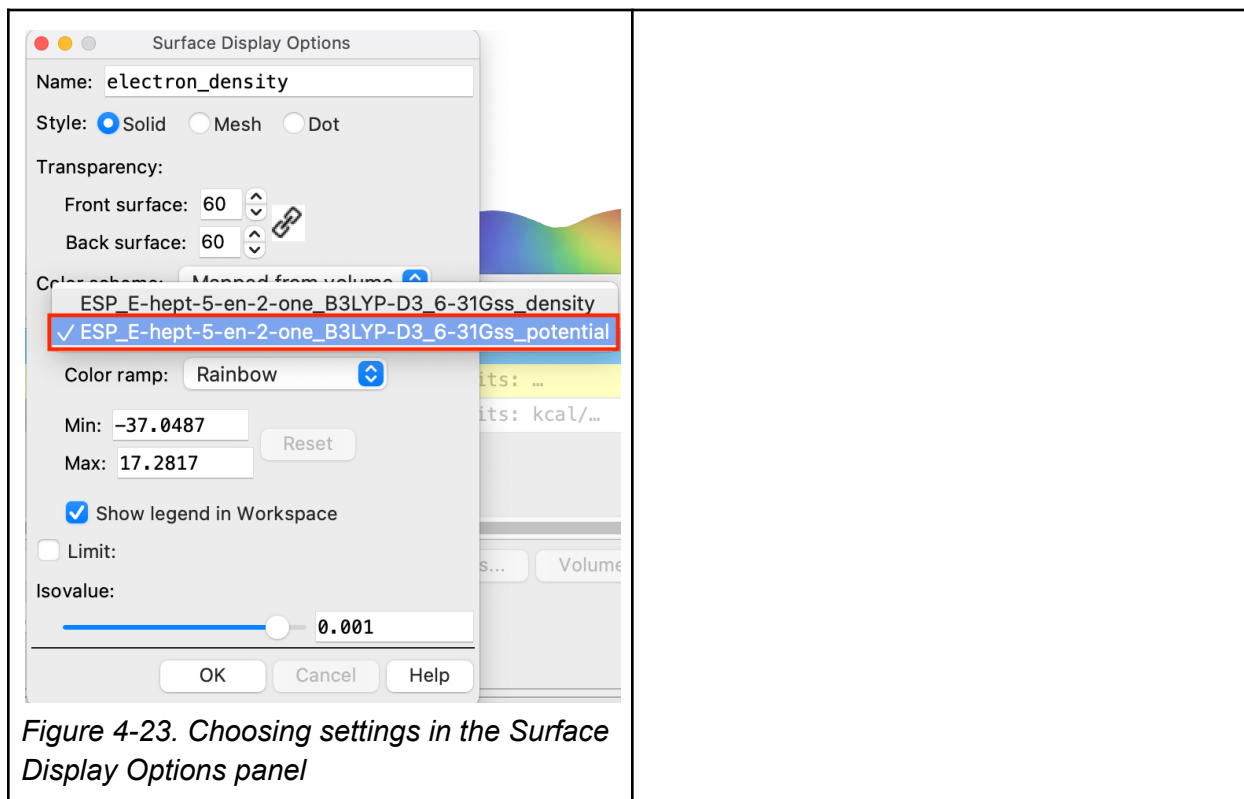


Figure 4-22. Choosing settings in the Manage Surfaces panel.

34. Click the **In** column for the electron density surface to include it in the Workspace
35. Click **Display Options**
 - The **Surface Display Options** panel opens



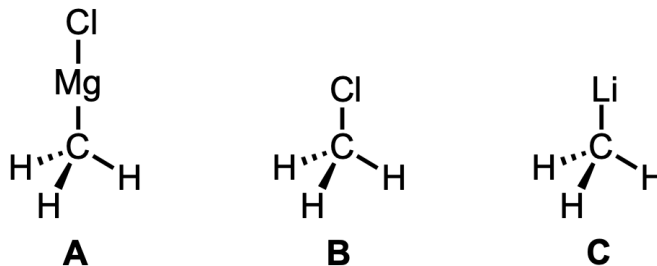
36. For **Color scheme**, select **Mapped from volume from volume**
37. Select **ESP_E-hept-5-en-2-one_B3LYP-D3_6-31Gss_potential** from the volume data list
38. From the **Color ramp** option menu, choose **Rainbow**
39. Click **OK**



Take a screenshot of your electrostatic potential map and analyze the nucleophilic and electrophilic regions of (*E*)-hept-5-en-2-one.

5. Individual Exercise

All three molecules below contain carbon atoms but some act as a nucleophile while some act as an electrophile.



For each of the molecules:

- a) Build the molecules in Maestro using the 2D sketcher and minimize the structures.
- b) Optimize their geometries using Jaguar. Take screenshots of your optimized structures with a ball-and-stick representation (from the Style toolbar).
 - Theory: B3LYP-D3, Basis set: 6-31gss
 - Use local host to run the jobs
- c) Run single point calculations using Jaguar to generate electrostatic potential maps. Take screenshots of each ESP map.
 - Theory: B3LYP-D3, Basis set: 6-31gss
 - Use local host to run the jobs
- d) Determine whether the carbon atoms are nucleophilic and electrophilic centers.

6. Summary, Additional Resources, and References

In this lesson, you learned about nucleophiles and electrophiles. A nucleophile is a reactant that provides a pair of electrons to form a new covalent bond whereas an electrophile is a reactant that accepts a pair of electrons. You learned about inductive effects and how to identify nucleophilic and electrophilic centers in a molecule. Understanding how electrons flow from electron-rich regions to electron-poor regions is essential in learning organic chemical reactions.

Using Maestro, a simple geometry optimization using Jaguar can be performed to show a molecule's structure. Electrostatic potential surfaces can also be generated to visualize electron-poor and electron-rich regions in both nucleophiles and electrophiles.

For further learning:

- Exploring potential energy surface for chemical reactions: An overview of some practical methods. [DOI:10.1002/jcc.10231](https://doi.org/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](#)

7. Glossary of Terms

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