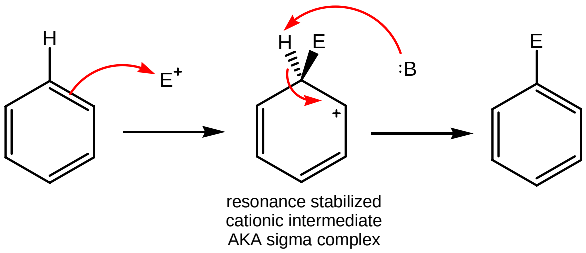
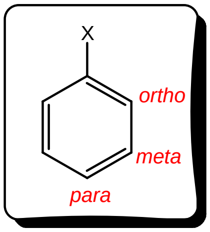
Computational Chemistry and Electrophilic Aromatic Substitution

Background: Electrophilic aromatic substitution (Ege, pp. 366-382)

Objectives: (1) The nature of the cationic intermediate formed during electrophilic aromatic substitution will be investigated computationally using the computational package Spartan. (2) The directing effects of substituents on the outcome of an electrophilic aromatic substitution will be examined. Semi-empirical calculations will be used to predict the preferred orientation (*o*, *m*, or *p*) when toluene, aniline, nitrobenzene, and trifluorotoluene react with nitronium cation (NO_2^+).

General mechanism for electrophilic aromatic substitution:





Part A Procedure:

Building Molecules. *We will begin our study by using Spartan to build the basic sigma complex (shown above) where E =* NO_2*.*

1. From the Desktop menu choose Spartan '04.

2. Before performing a calculation, you must build a molecule then save it. Click on **File** and choose **New**. This opens the building tools so can construct the molecule. The basic building tools are shown on the right side of the screen.

3. Build the sigma complex with the nitro group. The following instructions will make this easier.

   Start building the sigma complex by choosing the sp^2 carbon from the model kit. Click the left mouse button to add the sp^2 carbon to the screen.

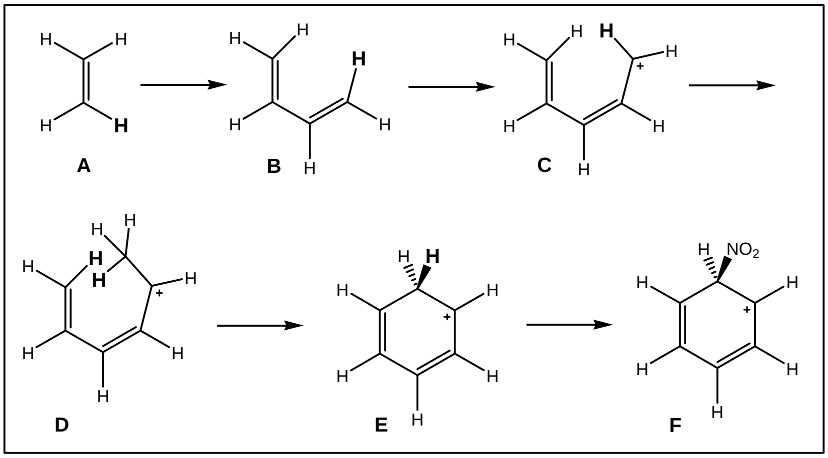
   Next, click on the half of the double bond that you just installed to complete the double bond. This will add a second sp^2 carbon on the molecule you are building, giving you the molecule ethene ($CH_2{=}CH_2$) on the screen (see **A** below). Grey = C. Yellow or white = H.

   Next, click on one of hydrogens of ethene. This starts another double bond. Complete it by clicking on the unfinished half of the double bond. At this point, you have built the molecule butadiene ($CH_2{=}CH{-}CH{=}CH_2$), see **B**.

   Now you need to add an sp^2 carbon that has only 3 valences (e.g. a carbocation). To do this, you need to go to the expert tool kit. Click the **Exp** tab at the top-right. Highlight C. Highlight the three valence button. Now click on a cis hydrogen of butadiene (bold in **B**). You have now built the pentadienyl cation (**C**).

   Complete the sigma complex by switching back to the entry level model kit (**Ent**). Highlight the sp^3 carbon and add it to the molecule (**D** is now built). Now the ring needs to be closed. Click on "bond" (button at top of screen that looks like a bond is being formed) and then click on an sp^3 hydrogen and the appropriate sp^2 hydrogen (bolded H's in **D**). You have now built **E**.

Finally you need to add the nitro group on the sp^3 carbon. Choose “groups” then “nitro” then click on one of the two sp^3 hydrogens in **E**. Your molecule should now look somewhat like **F**.



The following mouse commands are useful as you are building in Spartan:

Left mouse: rotate molecule
Right mouse: translate molecule
Shift-left mouse: rotate molecule in plane of screen
Shift-right mouse: enlarge/shrink molecule
Alt-left mouse (when bond is highlighted): rotate torsion angle
Alt-right mouse (when bond is highlighted): stretch/shrink bond length

4. Before performing a semi-empirical calculation (time intensive), you will “clean-up” the molecule you built using a quick minimization. Click the **Minimize** button at the top of the screen. (*E with down arrow*).

5. Save the molecule. Under the **File** menu, choose **Save As** and save the file with an appropriate name.

Semi-Empirical Calculations. *After building your molecule, it is now time to do some computation! We will set up a semi-empirical calculation that will allow us to obtain an optimized geometry for the intermediate and its energy. Finally, we will produce a surface that helps us visualize the electron distribution in the ion.*

10. Choose **Semi-Empirical** under the **Setup-Calculations** menu. The Setup Semi-Empirical Dialog box appears; set the tasks as follows:

    Calculate: Equilibrium Geometry (pull down menu)
    with: Semiempirical AM1
    Start from: initial geometry
    Options: leave this box blank

    Total Charge: +1
    Multiplicity: singlet

11. Click the submit button. When the job is finished and you click OK, the molecule’s structure is updated.

***Displaying the Results**. It is now time to visualize the charge distribution in this charged ion. How is the +1 charge distributed in this molecule?*

12. Choose **Setup**, then **Surfaces**. In the surfaces dialog box choose **Add**. Select **density** from the **Surface** menu, select **LUMO** from the **Property** menu, and **low** from the **Resolution** menu.

13. Select **Submit** from **Setup** menu. A dialog appears telling you that your calculation has been submitted. Click on **OK** to remove it from the screen.

14. When the calculation has completed you will be notified. Click on **OK** to remove the dialog from the screen.

15. Select **Surfaces** from the **Display** menu. Check the yellow box next to the word density. You can click on the colorful surface of the molecule. A dialog box at the bottom right corner will appear. You then select **Transparent** under **Style**. Note: Red represents regions of high electron density. Blue represents regions of low electron density.

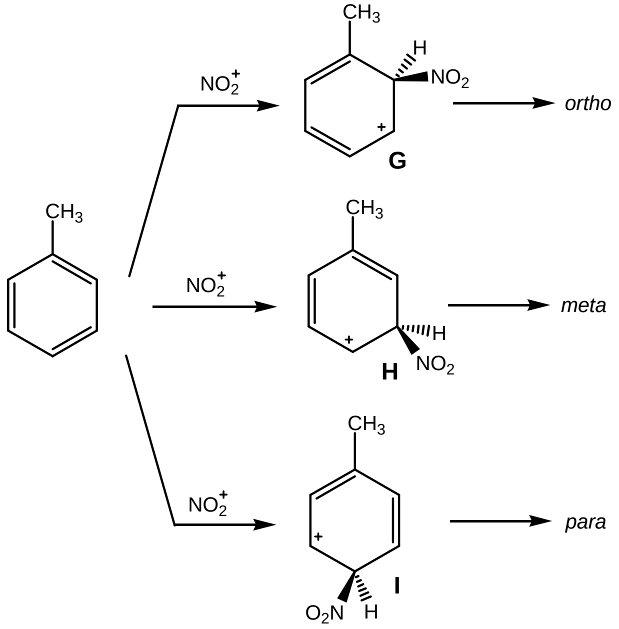
Points of Discussion (to be completed in your notebook):

1. Draw a picture of the sigma complex with its calculated electrostatic potential.
2. Which ring positions show buildup of positive charge? Briefly explain how you arrived at your choice.
3. Draw the important resonance contributors for the sigma complex you built.
4. Does your interpretation of the electrostatic potential (question 2) match the classic resonance description of the sigma complex (question 3)?

Part B Procedure:

***Nitration of Substituted Benzene Rings: Stabilities of Substituted Sigma Complexes**. We will now turn our attention to substituted sigma complexes. Our goal is to determine relative stabilities of a series sigma complexes formed from nitration of toluene, aniline, nitrobenzene, and trifluorotoluene. The example shown below illustrates that nitration of toluene can occur at the ortho, meta, or para position. You are to compare the calculated energies of the three possible sigma complexes.*

Nitration of toluene can give rise to *ortho*, *meta*, or *para* sigma complexes:



1. The calculation from Part A should still be on the screen. Uncheck the surface box to remove the surface, then close the surface dialog box. Leave your sigma complex on the screen, and bring up the model kit by choosing the **+** button at the top of the screen.

2. Instead of starting from scratch, we are going to save time by recycling the existing sigma complex. Here's how to modify the existing sigma complex to build sigma complex **G** (shown above). Chose the sp^3 carbon from the model kit and click on the ortho hydrogen of the sigma complex. At this point, your structure should look like **G**.

3. Minimize the sigma complex, and save it under a unique file name. Perform a semi-empirical AM1 calculation as before (refer to Part A, #10-11).

4. The calculated energy can be found under **Display**, then **Properties**. Record this energy in the table below (copy this table into your notebook).

5. To build the meta structure, you can delete the methyl group you added in step 2, and then add a methyl group at the meta position. Save the structure and calculate its energy.

6. Repeat this modification procedure for each of the remaining sigma complexes indicated in the table below. Record their respective energies in your notebook as you proceed.

7. Copy three sigma complexes (one *ortho*, one *meta*, one *para*) you have constructed to one page in Microsoft Word. In Spartan, go to **Edit** and **Copy**. Open a new Word file and **Paste** the image onto the new page. You can adjust the size of the image by clicking on it and using the border around the image to reduce or enlarge. Add your name and label to the pictures. Email the word file to your instructor.

AM1 Energy (kcal/mol)			
Sigma complex resulting from nitration of:	*ortho*	*meta*	*para*
toluene			
aniline			
nitrobenzene			
trifluorotoluene			

Points of Discussion (to be completed in your notebook):

1. According to your calculations, which substituents direct attack to the *meta* position and which substituents direct attack to the *ortho* or *para* positions?
2. Are your conclusions from question 1 in accord with what is expected for these substituents? Briefly explain. Include a description of the general characteristics of a *meta* director and general characteristics of an *ortho/para* director in your explanation.
3. Which substituent shows the greatest preference for *meta* versus *ortho/para*? What properties of this substituent cause it to have such a large preference.
4. Which substituent shows the greatest preference for *ortho/para* versus *meta*? What properties of this substituent cause it to have such a large preference.
5. For those substituents which direct *ortho/para*, which position (*ortho* or *para*) is preferred? What effect is causing one position (*ortho* or *para*) to be preferred over the other.