

Electrophilic Aromatic Substitution in Monosubstituted Benzene

Developed By: Wallace D. Derricotte

Email(s): wallace.derricotte@entos.ai

Appropriate Course(s): Organic Chemistry

Description

Electrophilic aromatic substitution is a common organic reaction in which an electrophile replaces a substituent attached to an aromatic system. Many important organic reactions of aromatic compounds fall under this category, including alkylation, halogenation, and nitration. Understanding its mechanism is of critical importance, and computational tools can help predict the likely sites of substitution in a molecule.

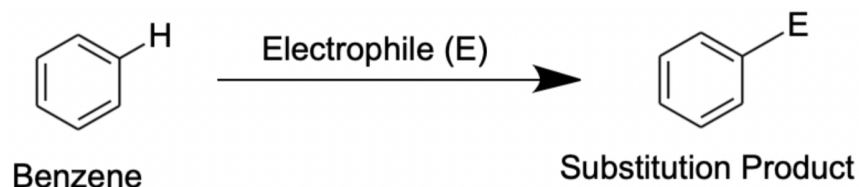


Figure 1: General electrophilic aromatic substitution involving an electrophile (E) and benzene.

In this exercise, **Orbital Maps** will be utilized in order to make predictions on the likely sites of electrophilic aromatic substitution in monosubstituted benzene derivatives. Orbital maps take the absolute value of the molecular orbitals and map them onto the total electron density of the molecule.

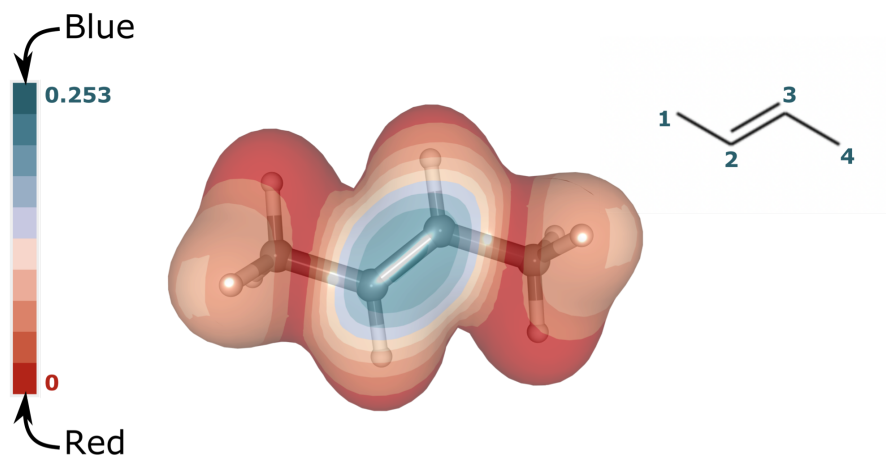


Figure 2: HOMO orbital map of 2-butene.

For the highest occupied molecular orbital (HOMO) and the lowest unoccupied molecular orbital (LUMO), these maps indicate likely regions of electrophilic and nucleophilic reactivity, respectively. Figure 2 shows the HOMO orbital map for 2-butene; for this molecule, we expect that the most likely site of electrophilic reactivity will be along with the central double bond between C2 and C3. This is reflected in the HOMO map, where the blue color indicates a region of high electrophilic reactivity, and a region of red indicates a site of low electrophilic reactivity.

You are going to investigate the likely sites of electrophilic aromatic substitution in a series of monosubstituted benzenes. In these molecules, the electrophile can add at the ortho, meta, or para position relative to the substituent on the benzene ring.

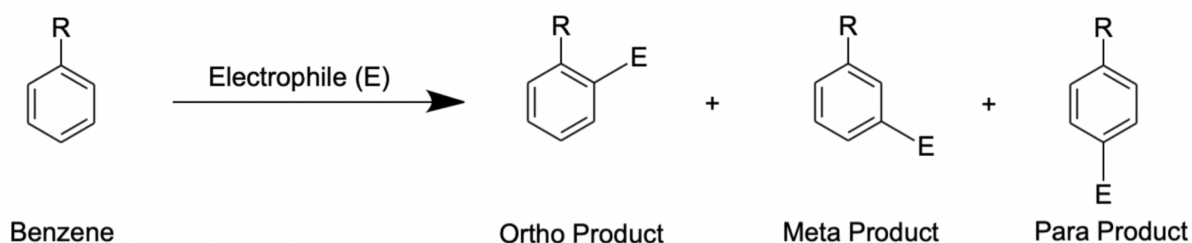


Figure 3: Different products of electrophilic aromatic substitution for monosubstituted benzenes.

Based on where the electrophile attaches in the major substitution product(s), the substituent is known as an **ortho-, para-director** or a **meta-director**. The HOMO map of the substituted benzene can be used in order to predict the likely sites of electrophilic reactivity and classify the substituent as either a meta-director or an ortho-, para-director. In this activity, you are going to investigate a series of monosubstituted benzenes, predict the likely sites of electrophilic reactivity, and classify the substituent as a meta director or an ortho-, para- director.

Learning Objective(s)

- Use the HOMO orbital map to identify likely sites of electrophilic reactivity.
- Understand the mechanism of electrophilic aromatic substitution.
- Discern the connection between a substituents character as an electron donor/acceptor and where it directs electrophilic substitution.

Instructions

1. Go to [Envision](https://envision.entos.ai) and type "methylbenzene" into the search bar.

- Let's add a few more monosubstituted benzenes to our workspace. Navigate to the bottom left corner of the screen and click the **+** button to add a new molecule to your workspace.
- Type "methoxybenzene" into the search window and press enter.
- Repeat Step 2, in order to add benzoic acid and nitrobenzene to the workspace.
- Once you have all these molecules in your workspace, click the **👁** icon next to each molecule name in order to add them to the grid view.
- Click on the methylbenzene molecule in the grid, navigate to the bottom of the Properties list and click Surfaces. Click on the dropdown menu for Surface Coloring and change this to Orbital Map. From the table click the HOMO orbital.
- Repeat step 6 in order to display the HOMO map for methoxybenzene, benzoic acid, and nitrobenzene.
- Now all HOMO orbital maps should be displayed for the molecules simultaneously, inspect them and note the similarities/differences between them. (Note: for the sake of comparison, it is helpful to orient the molecules such that the substituent is pointing up in all cases, see Figure 4 for an example):

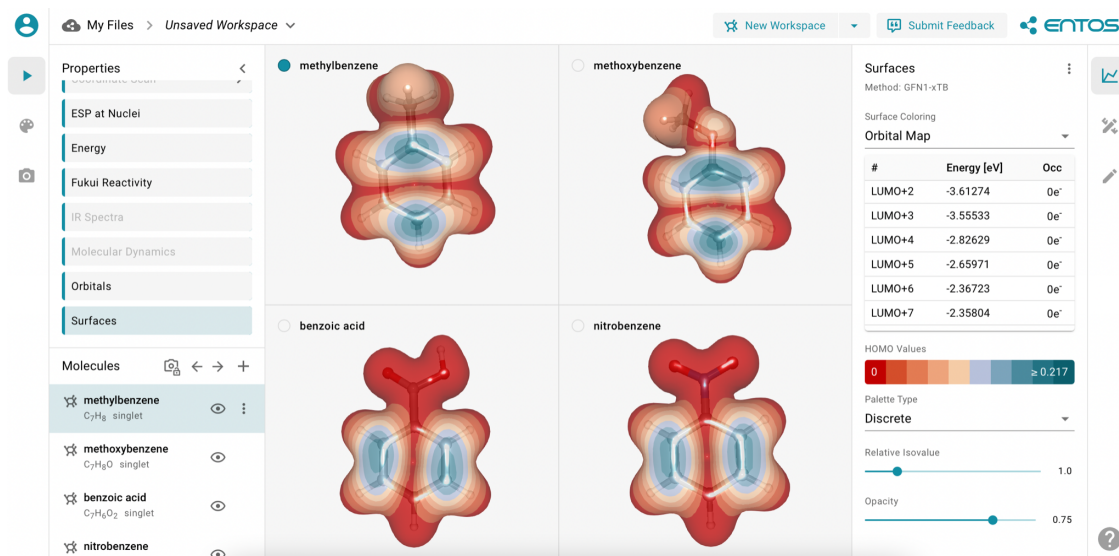
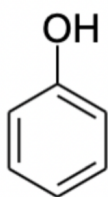


Figure 4: HOMO orbital maps of the four monosubstituted benzenes mentioned.

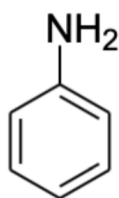
- Fill in the table below for each molecule, predicting the likely sites of electrophilic aromatic substitution and labeling the substituent as either an ortho-, para-director or meta-director.

Molecule Name	Carbon Atoms Likely for Substitution (ex. C2, C3, etc)	Meta-Director or Ortho-, Para-Director ?
methylbenzene		
methoxybenzene		
nitrobenzene		
benzoic acid		

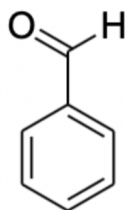
10. Below are structures for additional monosubstituted benzenes. Click the structure to open the molecule in Envision and plot the HOMO orbital map to predict the likely sites of electrophilic aromatic substitution:



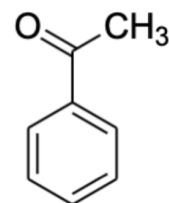
Phenol



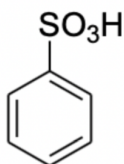
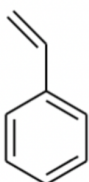
Aniline



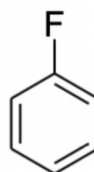
Benzaldehyde



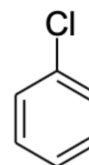
Acetophenone

Benzenesulfonic
Acid

Styrene



Fluorobenzene



Chlorobenzene

Molecule Name	Carbon Atoms Likely for Substitution (ex. C2, C3, etc)	Meta-Director or Ortho-, Para-Director ?
phenol		
aniline		
benzaldehyde		
acetophenone		

benzenesulfonic acid		
styrene		
fluorobenzene		
chlorobenzene		

Discussion Questions

1. For all of the monosubstituted benzenes studied, classify the substituent as either an electron donating or electron withdrawing group. Do you notice a trend between this property and whether the substituent is a meta-director or ortho-,para-director? Explain.
2. For those molecules where the meta product is highly likely, there are still relatively high HOMO values located at the ortho carbon. Explain this observation, what consequence will this have on the observed products of electrophilic aromatic substitution?
3. Take 3 examples of the molecules studied in this activity. Draw resonance forms of the substitution intermediates in order to explain the observed substitution.