Objective 7. Apply addition and elimination concepts to predict electrophilic aromatic substitution reactions (EAS) for benzene and monosubstituted benzenes.

EAS with benzene

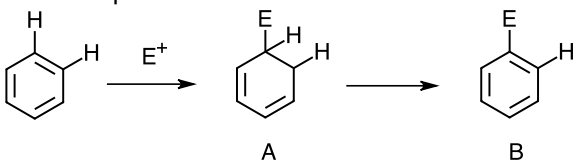
1. Compare cyclohexene, 1,3-cyclohexadiene, and benzene.

a. Rank each compound in order of stability. Give reasons.

b. Which compound is the most reactive? Give reasons.

c. Which compound is the least reactive? Give reasons.

2. Electrophilic aromatic substitution involves two steps: addition followed by elimination.



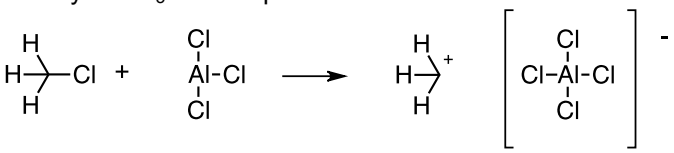
a. Use curved arrows to show how E^+ reacts with benzene to form Structure A. On which C does the + charge go in Structure A?

b. Draw resonance structures of Structure A. Which resonance structure is the most stable?

c. What type of reagent reacts with Structure A to form Structure B? Use curved arrows to show how this reaction occurs.

3. Benzene reacts with $CH_3Cl/AlCl_3$. In this reaction, CH_3Cl reacts with $AlCl_3$ to form CH_3^+ and $AlCl_4^-$.

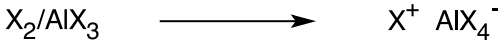
a. Why is CH_3^+ electrophilic?



b. Show how CH_3^+ reacts with benzene to form toluene. Use curved arrows to show bonds breaking and forming. Draw intermediates.

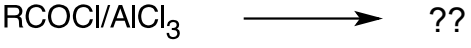
4. Aromatic pi bonds are poor nucleophiles. A strong electrophile is needed to react with an aromatic pi bond.

a. X_2 is non-polar. But at one instant in time, there are more electrons (electron density) around one X and fewer electrons around the other X. This gives one X a partial negative charge and the other X a partial positive charge. The X with the partial negative charge is attracted to the the Al^{3+} in $AlCl_3$. Show how X^+/AlX_4^- forms.



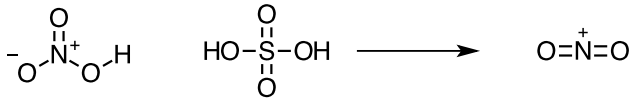
Then, use curved arrows to show how X^+ reacts with benzene to form C_6H_5X. How many resonance structures of the intermediate are there? Which resonance structure is the major contributor?

b. RCOCl reacts with $AlCl_3$ similar to how X_2 reacts with $AlCl_3$. Draw the intermediate that forms when RCOCl reacts with $AlCl_3$ to form $(RCO)^+$ (AlX_4^-). On which atom is the (+) charge on $(RCO)^+$? Would you expect this ion to be a good electrophile?



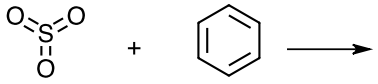
Then, use curved arrows to show how RCO^+ reacts with benzene to form C_6H_5COR. How many resonance structures of the intermediate are there? Which resonance structure is the major contributor?

c. HNO_3 reacts with H_2SO_4. A H from H_2SO_4 reacts with the O bonded to the H in HNO_3 to form $O_2NOH_2^+$. The H_2O is a leaving group. Use curved arrows to show how NO_2^+ forms from $O_2NOH_2^+$.

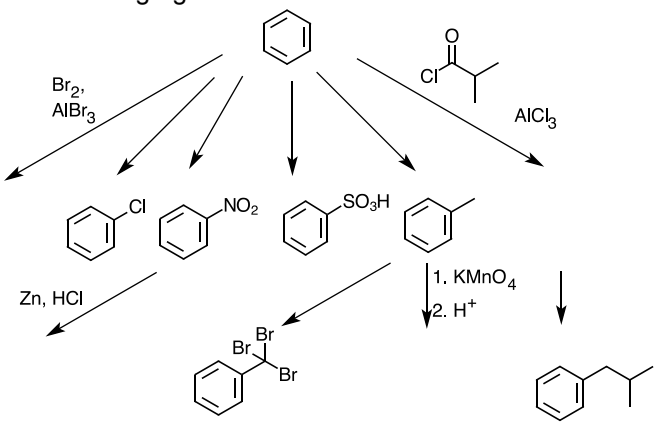


Then, use curved arrows to show how NO_2^+ reacts with benzene to form nitrobenzene. How many resonance structures of the intermediate are there? Which resonance structure is the major contributor?

d. Fuming sulfuric acid contains H_2SO_4 and SO_3. SO_3 is a strong electrophile. Draw a resonance structure of SO_3. Which resonance structure is the major contributor? Use curved arrows to show how SO_3 reacts with benzene to form $C_6H_5SO_3H$. Draw resonance structures of the carbocation intermediate. How is H_2SO_4 used in this reaction?



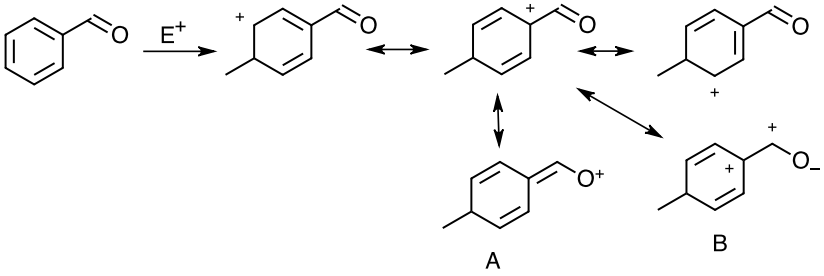
5. Draw structure of product or determine reaction conditions. Identify the structural features in each compound. Note: Zn is a reducing agent.



EAS with monosubstituted benzene

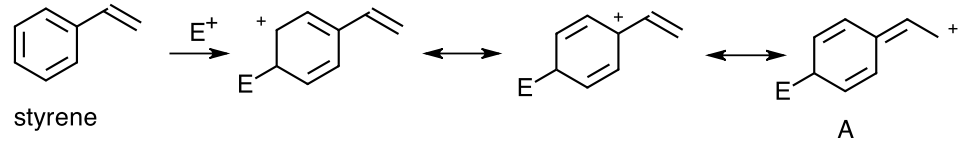
1. Benzene and substituted benzene compounds undergo electrophilic aromatic substitution reactions. Relative to H,
a. list the groups that are electron donating. What does it mean to "activate the ring"?
b. list the groups that are electron withdrawing. What does it mean to "de-activate the ring"?

2. Benzaldehyde (smells like almonds) reacts with electrophile, E^+, in a EAS reaction.
a. Draw the curved arrows to show how E^+ reacts at the para position. Draw in E in each structure.
Draw curved arrows to show how to go from resonance structure to another.



Which resonance structure is the most stable? Give reasons.
Which resonance structure is the least stable? Give reasons.
b. Use curved arrows to show how E^+ reacts at the meta position. Draw the resonance structures.
The aldehyde group deactivates the ring and is a meta director. Explain why the resonance structures in part a (para) are less stable than your resonance structures (meta).

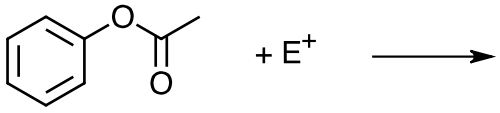
c. Styrene (used to make plastics) reacts with electrophile, E^+, in a EAS reaction.



styrene

Draw the curved arrows to show how E^+ reacts at the para position.
Draw curved arrows to show how to go from resonance structure to another.
One resonance structure is missing. Draw this resonance structure.
Compare Intermediate A from part a to Intermediate A from this part. Why does A form in styrene but not benzaldehyde? (Hint: Formal charge of +1 on O is not likely because ____.)

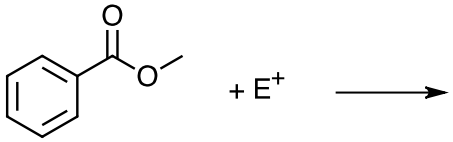
3. The substituted benzene reacts with E^+:



a. What functional group is the side group?
b. Use curved arrows to show how E^+ reacts at the ortho position. Draw resonance structures of the intermediate. Which resonance structure is the most stable?
c. Use curved arrows to show how E^+ reacts at the meta position. Draw resonance structures of the intermediate. Which resonance structure is the most stable?

d. Use curved arrows to show how E^+ reacts at the para position. Draw resonance structures of the intermediate. Which resonance structure is the most stable?
e. Compare the resonance structures in b, c, and d. Which structure shows how the functional group activates the ring?
f. Explain why the ortho and para products form rather than the meta product.

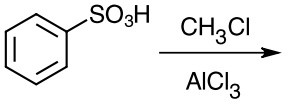
4. Methyl benzoate ($C_6H_5COOCH_3$) reacts with E^+:



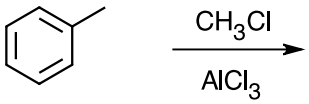
a. What functional group is the side group?
b. Use curved arrows to show how E^+ reacts at the ortho position. Draw resonance structures of the intermediate (4 resonance structures). Which resonance structure is the most stable?
c. Use curved arrows to show how E^+ reacts at the meta position. Draw resonance structures of the intermediate (3 resonance structures). Which resonance structure is the most stable?
d. Use curved arrows to show how E^+ reacts at the para position. Draw resonance structures of the intermediate (4 resonance structures). Which resonance structure is the most stable?
e. Compare the resonance structures in b, c, and d. Which structure shows how the functional group deactivates the ring?
f. Explain why the meta product forms rather than the ortho and para products.

5. The aromatic compounds in Questions 3 and 4 are esters.
a. Why does one compound activate the ring whereas the other deactivates the ring?
b. Fill in the blanks based on the resonances structures you drew in Questions 3 and 4.
(i) The ____ on the O ____ electron density to the ring and activates the ring.
(ii) A ____ charge on the C bonded to the ring deactivates the ring by _____.
c. The activating groups are ____ and are ____ directors.
d. The deactivating groups are ____ and are ____ directors.
e. List any exceptions to (c) and (d).

6. Predict the product of each reaction. Hint: The atom or group bonded to benzene tells me ____.
a.

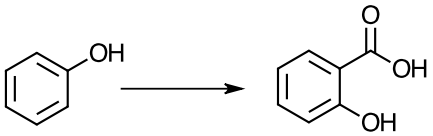


b.

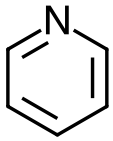


c. Which reaction occurs faster? Give reasons.
d. Bromination of aniline usually produces the trisubstituted tribromoaniline as the product. Explain why it is difficult to control the number of substitutions when aniline undergoes EAS.
e. What product would you expect for the bromination of anisole? Would you expect difficulty controlling the number of substitutions when anisole undergoes EAS? Give reasons.

7. a. Starting from phenol (used to be used in Listerine mouth wash), synthesize salicylic acid (precursor to aspirin).



b. Pellagra is a disease caused by a deficiency of niacin ($C_6H_5NO_2$) in the diet. Niacin can be synthesized in the lab by the side chain oxidation of 3-methylpyridine with chromic acid or potassium permanganate. Suggest a reasonable structure for niacin.



pyridine (note: it stinks)

c. The following synthesis will not produce the desired product. Identify the flaw in the synthesis.