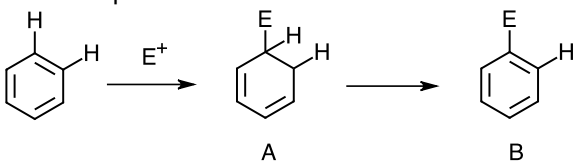
Objective 7 Practice Problem solutions
EAS with benzene

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.

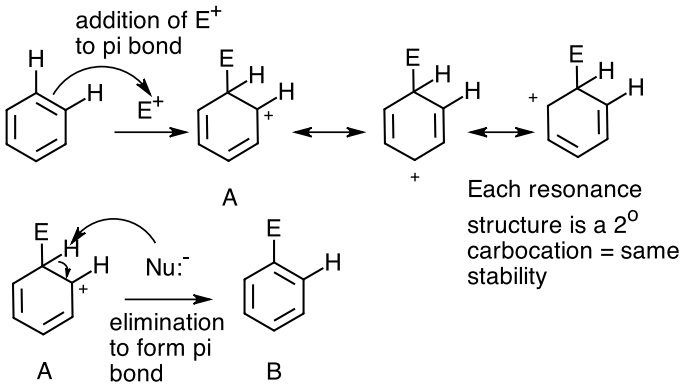
Answers: a. Benzene (aromatic) is more stable than 1,3-cyclohexadiene (conjugated diene). Cyclohexene is the least stable.
b. Cyclohexene is the least stable and most reactive.
c. Benzene (aromatic) is more stable and least reactive.

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

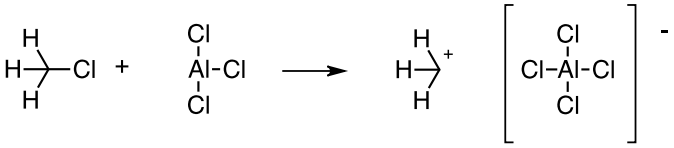


a. Use curved arrows to show how E^+ reacts with benzene to form Structure A. On which C does the + charge go in Structure A?
b. Draw resonance structures of Structure A. Which resonance structure is the most stable?
c. What type of reagent reacts with Structure A to form Structure B? Use curved arrows to show how this reaction occurs.

Answers: Note three resonance structures tells us the intermediate is a low energy, stable intermediate. More resonance structures means more delocalization (spreading out) of pi electrons and charge.

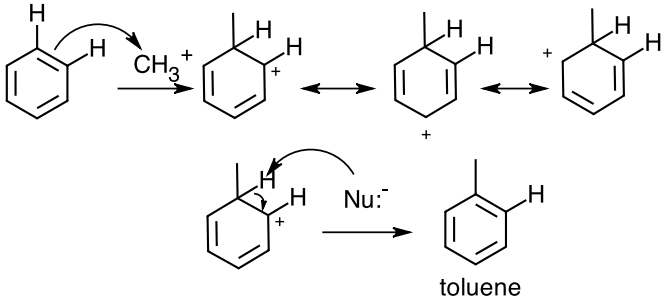


3. Benzene reacts with $CH_3Cl/AlCl_3$. In this reaction, CH_3Cl reacts with $AlCl_3$ to form CH_3^+ and $AlCl_4^-$.
a. Why is CH_3^+ electrophilic?



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

Answers: a. CH_3^+ is electrophilic because it is a carbocation - an electron deficient species.
b. What $Nu:^-$ reacts with H in the elimination step?

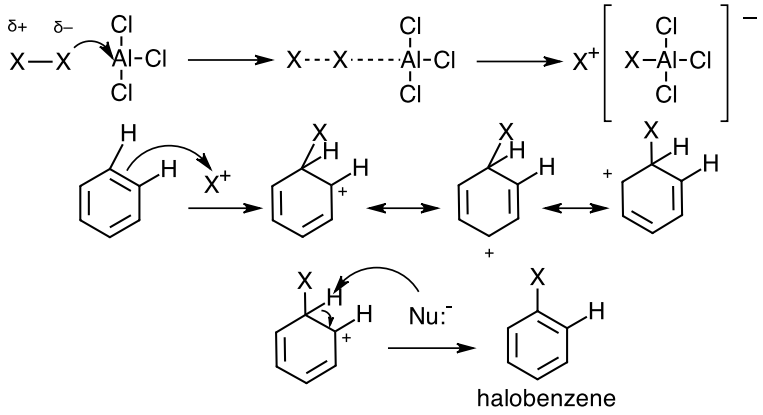


4. Aromatic pi bonds are poor nucleophiles. A strong electrophile is needed to react with an aromatic pi bond.

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.

$X_2/AlX_3 \longrightarrow X^+ \ AlX_4^-$

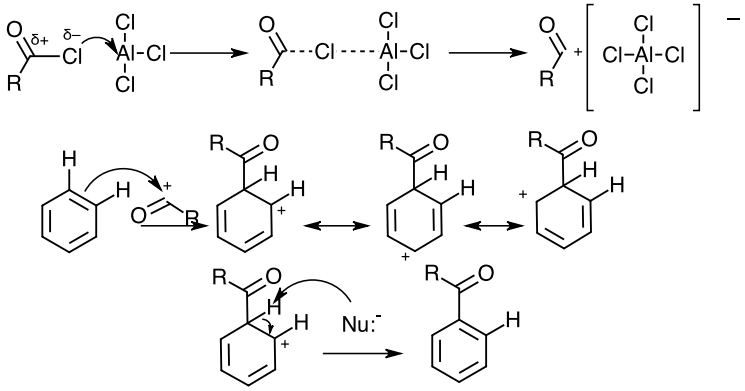
Then, use curved arrows to show how X^+ reacts with benzene to form C_6H_5X. How many resonance structures of the intermediate are there? Which resonance structure is the major contributor?
Answer: three resonance structures are equivalent (each are 2° carbocations so same stability).



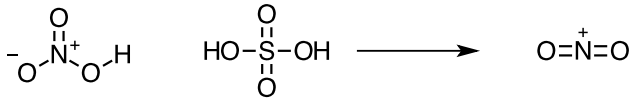
b. RCOCl reacts with $AlCl_3$ similar to how X_2 reacts with $AlCl_3$. Draw the intermediate that forms when RCOCl reacts with $AlCl_3$ to form $(RCO)^+$ (AlX_4^-). On which atom is the (+) charge on $(RCO)^+$? Would you expect this ion to be a good electrophile?

$RCOCl/AlCl_3 \longrightarrow$??

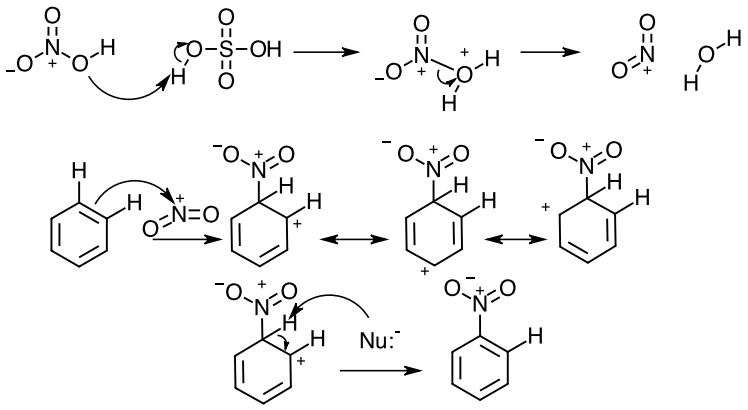
Then, use curved arrows to show how RCO^+ reacts with benzene to form C_6H_5COR. How many resonance structures of the intermediate are there? Which resonance structure is the major contributor?
Answer: three resonance structures are equivalent (each are 2° carbocations so same stability).



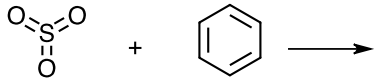
c. HNO_3 reacts with H_2SO_4. A H from H_2SO_4 reacts with the O bonded to the H in HNO_3 to form $O_2NOH_2^+$. The H_2O is a leaving group. Use curved arrows to show how NO_2^+ forms from $O_2NOH_2^+$.



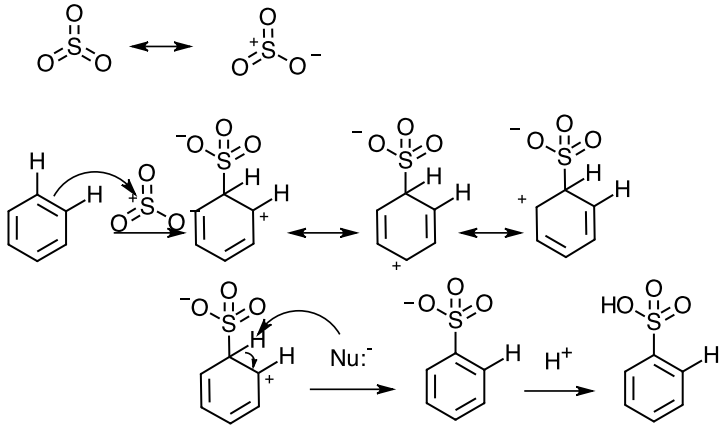
Then, use curved arrows to show how NO_2^+ reacts with benzene to form nitrobenzene. How many resonance structures of the intermediate are there? Which resonance structure is the major contributor?
Answer: three resonance structures are equivalent (each are 2° carbocations so same stability).



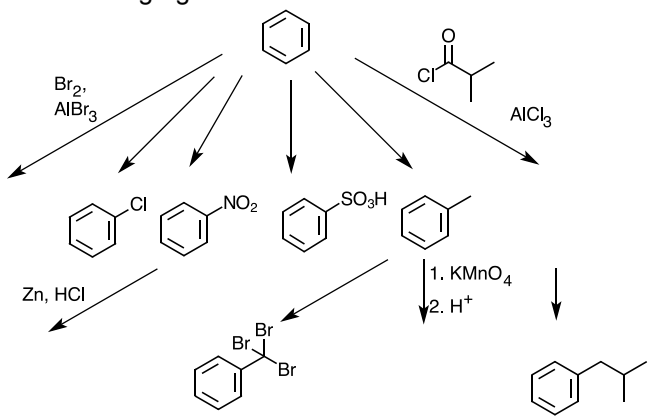
d. Fuming sulfuric acid contains H_2SO_4 and SO_3. SO_3 is a strong electrophile. Draw a resonance structure of SO_3. Which resonance structure is the major contributor? Use curved arrows to show how SO_3 reacts with benzene to form $C_6H_5SO_3H$. Draw resonance structures of the carbocation intermediate.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



Answer: three resonance structures are equivalent (each are 2^o carbocations so same stability).

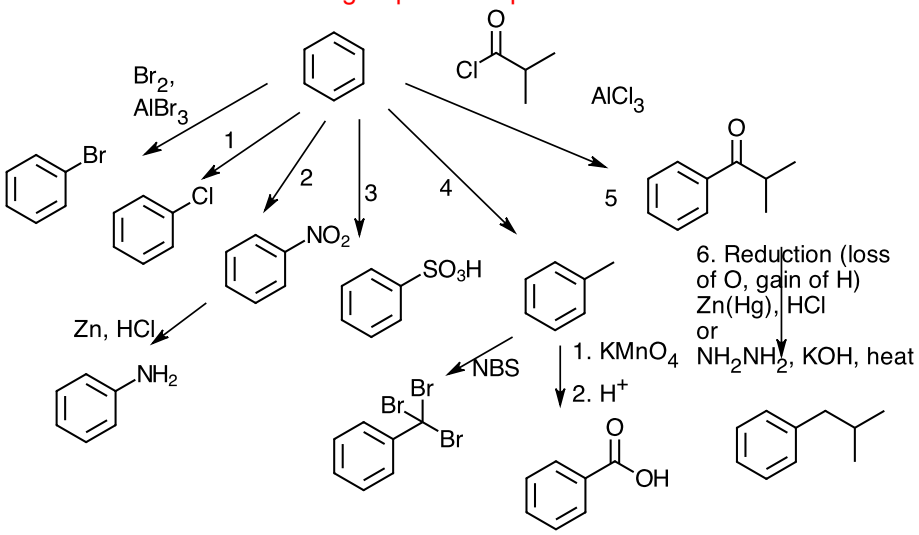


5. Draw structure of product or determine reaction conditions. Identify the structural features in each compound. Note: Zn is a reducing agent.



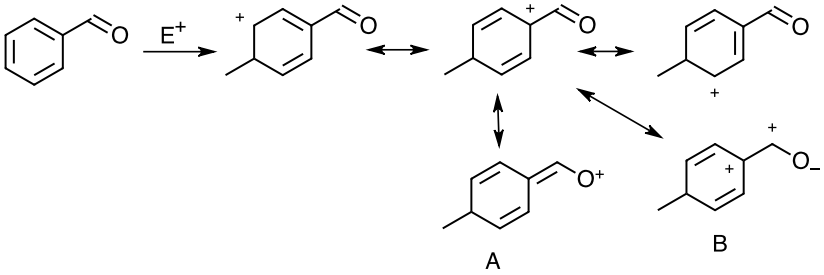
Answers: 1. Cl_2, $AlCl_3$
2. HNO_3, H_2SO_4
3. fuming H_2SO_4
4. CH_3Cl, $AlCl_3$. Friedel-Crafts alkylation occurs by carbocation intermediate. But carbocation can undergo rearrangement. Also, Friedel-Crafts alkylation may substitute additional R groups because R is an activating group.
Toluene has benzylic C so can use NBS or Br_2, light to substitute Br for H.
5. Friedel-Crafts acylation to form ketone.
Can't use this reaction to make an aldehyde because HCOCl decomposes under reaction conditions to form CO and HCl.
Friedel-Crafts acylation will not substitute additional acyl groups because acyl group (ketone) is a deactivating group.
6. Ketone to alkyl group is a reduction reaction (loss of O, gain of H).

Zn(Hg), HCl (Clemmensen reduction - acidic conditions)
NH_2NH_2, KOH, heat (Wolff-Kishner reduction –basic conditions)
NOTE: Friedel-Crafts acylation followed by reduction to form R group avoids rearrangement from Friedel-Crafts alkylation. But have to make sure other groups in compound are not reduced.

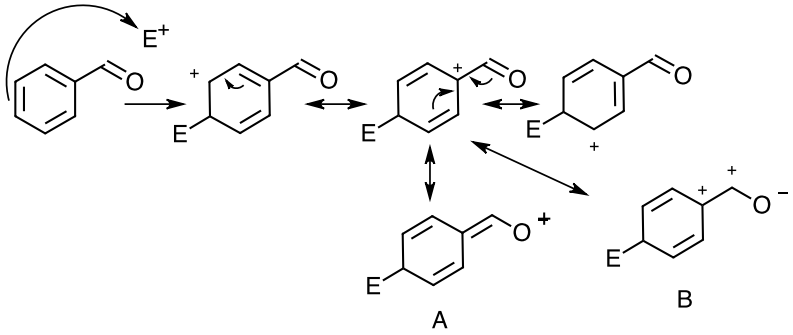


EAS with monosubstituted benzene
1. Benzene and substituted benzene compounds undergo electrophilic aromatic substitution reactions. Relative to H,
a. list the groups that are electron donating. What does it mean to "activate the ring"?
b. list the groups that are electron withdrawing. What does it mean to "de-activate the ring"?
Answer: See Objective 7 Lecture Slides 13 and 18 for electron donating groups and electron withdrawing groups.
electron donating groups: NH_2, OH, OR, OCOR, R
electron withdrawing groups: X, COR, CHO, COOH, COOR, CN, NO_2

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.

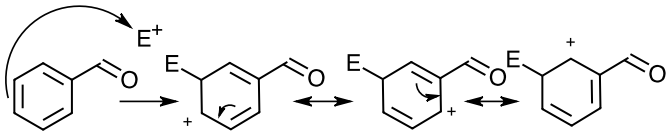


Which resonance structure is the most stable? Give reasons.
Answer: 3^o carbocation but see next answer.
Which resonance structure is the least stable? Give reasons.
Answer: Structure B with 3 charges (see formal charge rules from CHM 12A) and 2 (+) charges on adjacent atoms means the two (+) charges repel each other ==> very unstable.

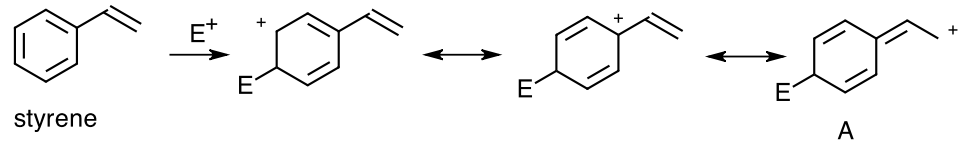


b. Use curved arrows to show how E^+ reacts at the meta position. Draw the resonance structures.
The aldehyde group deactivates the ring and is a meta director. Explain why the resonance structures in part a (para) are less stable than your resonance structures (meta).

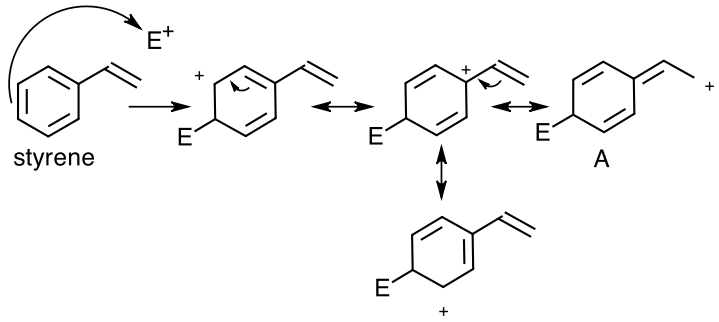
Answer: Each meta intermediate is a 2° carbocation.



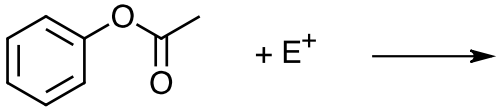
c. Styrene (used to make plastics) reacts with electrophile, E^+, in a EAS reaction.



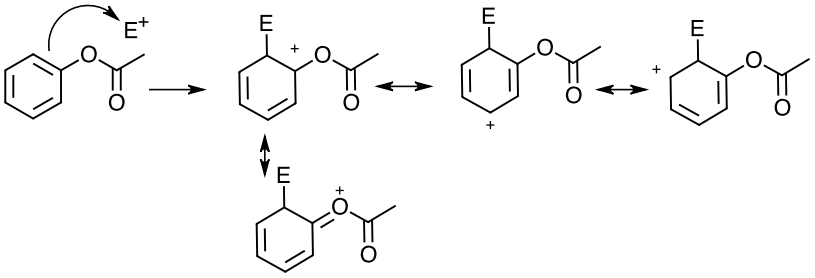
Draw the curved arrows to show how E^+ reacts at the para position.
Draw curved arrows to show how to go from resonance structure to another.
One resonance structure is missing. Draw this resonance structure.
Compare Intermediate A from part a to Intermediate A from this part. Why does A form in styrene but not benzaldehyde? (Hint: Formal charge of +1 on O is not likely because ____.)
Answer: Intermediate A is allylic carbocation.
Intermediate A from part a does not form because a +1 charge is very unlikely on the electronegative O. (See formal charge rules from CHM 12A).



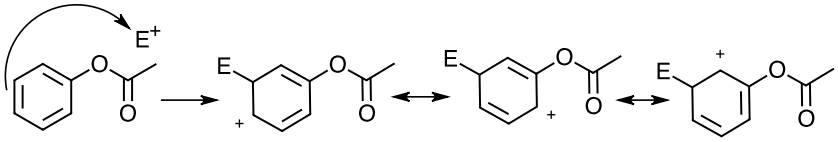
3. The substituted benzene reacts with E^+:



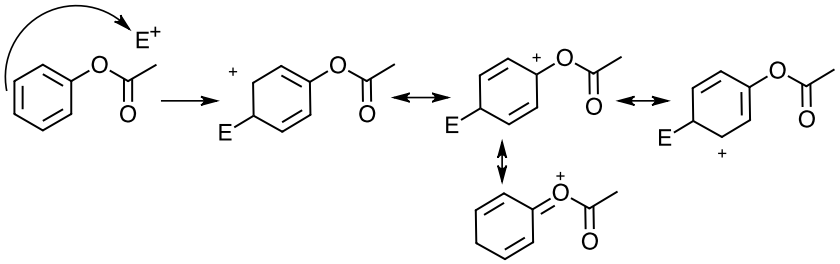
a. What functional group is the side group? Answer: ester
b. Use curved arrows to show how E^+ reacts at the ortho position. Draw resonance structures of the intermediate. Which resonance structure is the most stable?



Answer: 3° carbocation
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?



Answer: Same stability. Each meta intermediate is a 2° carbocation.
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?

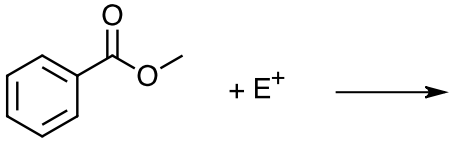


Answer: 3° carbocation

e. Compare the resonance structures in b, c, and d. Which structure shows how the functional group activates the ring?
Answer: in the ortho and para intermediates, the resonance structures with the pi bond between the O and C in the ring. The lone pair on the O donates electron density into the ring.

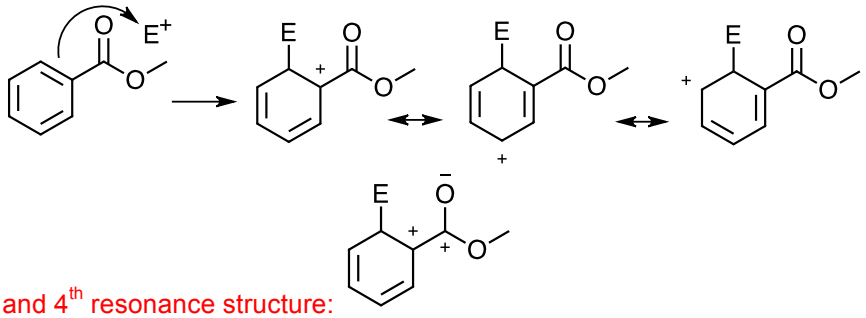
f. Explain why the ortho and para products form rather than the meta product.
Answer: the ortho and para intermediates are more stable and form faster than the meta intermediate so more product forms from the ortho and para intermediates.

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



a. What functional group is the side group? Answer: ester

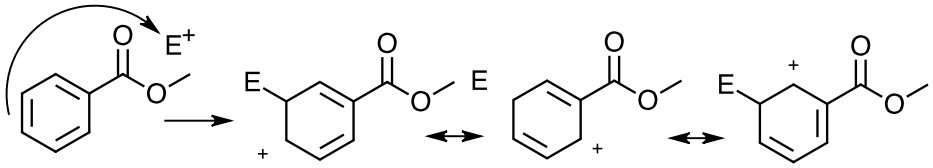
b. Use curved arrows to show how E^+ reacts at the ortho position. Draw resonance structures of the intermediate (4 resonance structures). Which resonance structure is the most stable?



and 4th resonance structure:

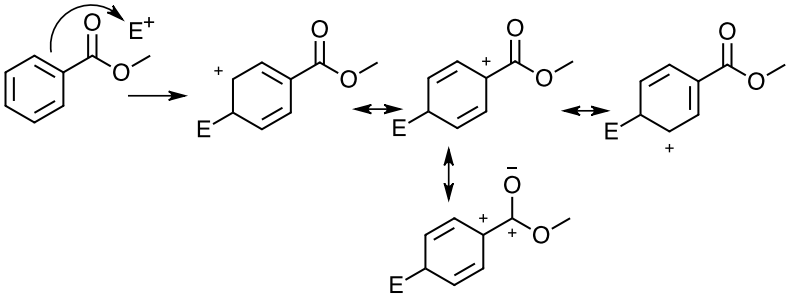
Answer: Top three are the same stability. Each ortho intermediate is a 2° carbocation. 4th resonance structure is unstable – 3 charges with 2 (+) charges on adjacent atoms.

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?



Answer: Same stability. Each meta intermediate is a 2° carbocation.

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?



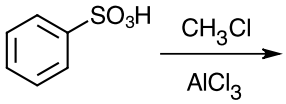
Answer: Top three are the same stability. Each ortho intermediate is a 2° carbocation. 4th resonance structure is unstable – 3 charges with 2 (+) charges on adjacent atoms.

e. Compare the resonance structures in b, c, and d. Which structure shows how the functional group deactivates the ring?

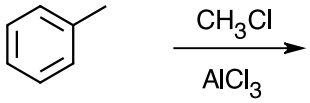
Answer: See the resonance structure with the (+) charge on the carbon bonded to the ring and two oxygens (carbonyl carbon). The (+) charge withdraws electron density from the ring.
f. Explain why the meta product forms rather than the ortho and para products.
Answer: the meta intermediates are more stable and form faster than the ortho and para intermediates so more product forms from the meta intermediates.

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).
Answer: a. Lone pair on O adjacent to ring can donate electron density to the ring. See resonance structures. Carbonyl C (C=O) adjacent to ring can have (+) charge and withdraws electron density from ring. See resonance structures.
(i) The __lone pair__ on the O __ donates _ electron density to the ring and activates the ring.
(ii) A _(+) _ charge on the C bonded to the ring deactivates the ring by ___ withdrawing electron density __.
c. The activating groups are __NH_2, OH, OR, OCOR, R__ and are _ ortho, para_ directors.
d. The deactivating groups are __X, COR, CHO, COOH, COOR, CN, NO_2 __ and are __meta __ directors.
e. List any exceptions to (c) and (d). X is deactivating but is an ortho, para director.

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

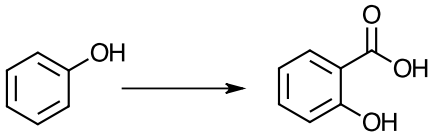


Answer: SO_3H is a meta director. Cl substitutes meta to SO_3H group.
b.



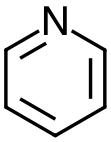
Answer: CH_3 is an ortho, para director. CH_3 substitutes ortho or para to CH_3 group.
c. Which reaction occurs faster? Give reasons.
Answer: Reaction b because CH_3 is an activating group.
d. Bromination of aniline usually produces the trisubstituted tribromoaniline as the product. Explain why it is difficult to control the number of substitutions when aniline undergoes EAS.
Answer: The NH_2 group in Aniline ($C_6H_5NH_2$) is a strongly activating group so it is difficult to control the number of Br substitutions in 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.
Answer: Predict trisubstituted tribromoanisole. The OCH_3 group in anisole ($C_6H_5OCH_3$) is a strongly activating group so it is difficult to control the number of Br substitutions in EAS.

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



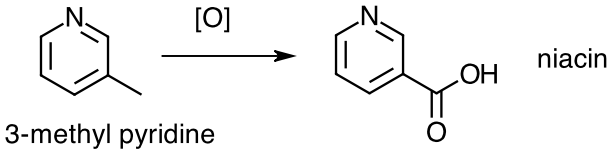
Answer: OH is o,p director. 1. CH_3Cl, $AlCl_3$ to form ortho-methyl phenol; 2. Use $KMnO_4$ to oxidize methyl group to acid group.
Can block substitution at para position by substituting $–SO_3H$ in para position (use concentrated H_2SO_4) and then doing steps 1 and 2. Remove SO_3H in para position with dilute H_2SO_4.

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)

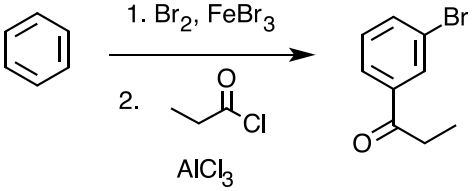
Answer: N is position 1. Oxidize R group to acid group. (See Objective 6 reactions at side chain in aromatics.)



3-methyl pyridine

niacin

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



Answer: Step 1 produces bromobenzene. Br is a deactivating group but is an ortho, para director (the exception). So Step 2 substitutes the ketone (acyl group) ortho or para to Br instead of meta.