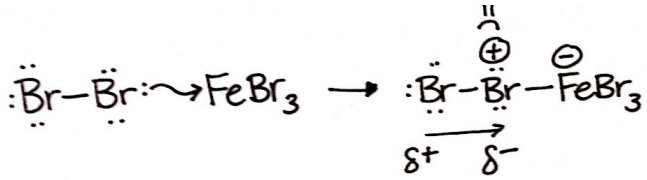
12BL Experiment 9: Directive Effects in Vanillin Bromination – An EAS Rxn

Safety: Proper lab goggles/glasses must be worn (even over prescription glasses). As always, ask where organic waste containers are located in the lab.

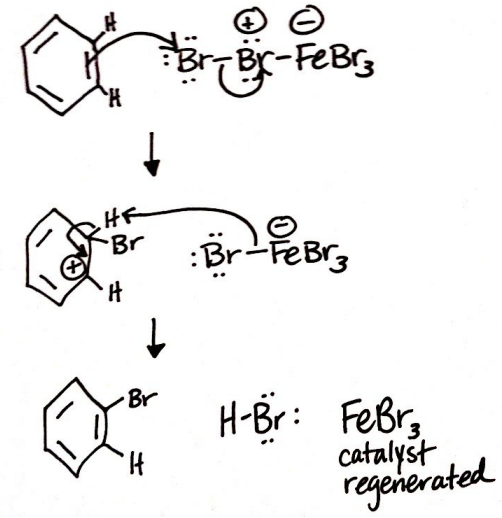
Background:

An Electrophilic Aromatic Substitution (EAS) reaction is one in which an electrophile is substituted onto a nucleophilic aromatic ring. Classic EAS reactions learned in lecture include halogenation, nitration, sulfonation, akylation, and acylation. Today you will be performing a bromination – the specifics of which we will cover shortly. In classic bromination, a catalyst, $FeBr_3$, is used to create an electrophile out of the neutral species Br_2. Recall that an electrophile is a "lover of electrons" and so the electrophile itself must be electron deficient (which equates to slightly positive or even completely positive).



Because interacting with bromine and its vapors is a hazard, you will be generating bromine in solution.

Once the electrophile has been generated, the nucleophilic aromatic pi electrons will attack – once again the common theme throughout reaction mechanisms occurs, "negatives attack positives."



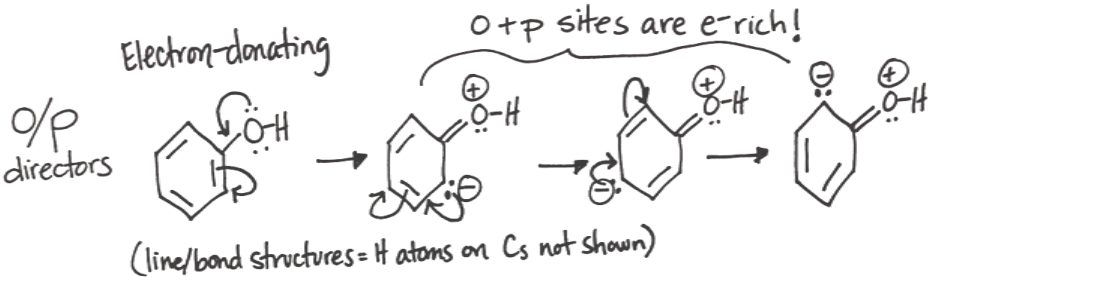
We have just seen a basic example of EAS on an ***UNsubstituted*** aromatic ring. Will the presence of substituents on an aromatic ring affect further substitution? You betcha!

Substituents on an aromatic ring have unique directing effects on incoming groups. In a nutshell, an existing functional group will tell a new functional group where it is allowed to bond on the aromatic ring.

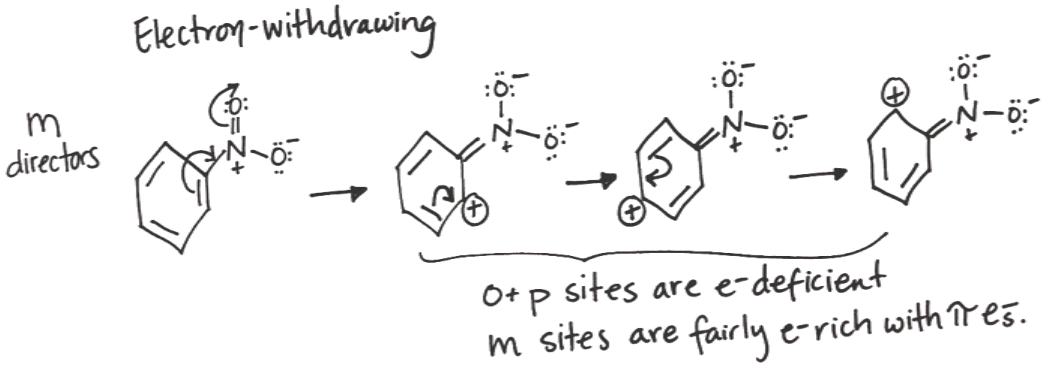
First we must consider how many substituents are already on the ring and identify their strength of directing – are they an activator or a deactivator of EAS. Activators help the EAS reaction to occur by increasing the nucleophilicity of the ring; deactivators slow down EAS reactions and if too many deactivators are present, the reaction may not occur at all.

An activator is defined as an ***electron-donating*** group: it must have a **lone pair** bearing atom attached to the ring OR it is an **alkyl** group (***any*** carbon/hydrogen group). A deactivator is defined as an ***electron-withdrawing*** group: basically any polar, electronegative group will pull electron density AWAY from the ring decreasing its nucleophilicity; a classic deactivator CANNOT have a lone pair bearing atom attached to the ring (with the exception of halogens).

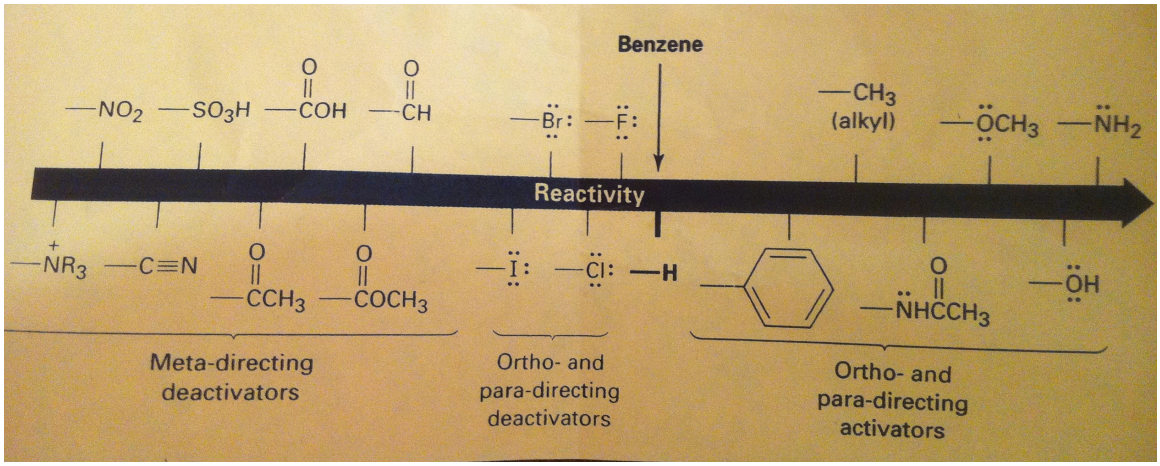
Activators are ortho/para directors – they direct incoming groups to ortho and para positions. If you take a look at the resonance contributers for the existing molecule, you will see that the ortho and para positions are extremely electron rich.



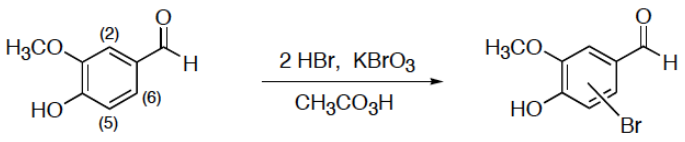
Deactivators are meta directors – they direct incoming groups to metal positions. If you take a look at the resonance contributers for the existing molecule, you will see that the ortho and para positions are extremely positive – thus these sites would repel a positive electrophile from bonding, leaving it to attach to the meta sites.



Halogens are a unique class – because they are electronegative, they are deactivators. BUT, they also have lone pairs to donate to the ring, which will make the ortho and para sites electron rich at times. So halogens are moderate deactivators and ortho/para directors.



To predict your major organic product you must consider a couple of other interactions in order to make your decision. First we know that Activators trump Deactivators in controlling directing. In general, the strongest activator will control the directing to the ortho and para sites. But what if we have to decide what the one major product is? Well, you need to consider steric constraints (crowding). The most stable product is one that is not crowded because large substituents near one another will repel, ultimately destabilizing the molecule.



Compound	mp (°C)
2-bromovanillin	154-155
5-bromovanillin	164-166
6-bromovanillin	177-178

Finally, to limit the exposure to bromine, we will not be using bromine and the $FeBr_3$ catalyst as discussed in lecture. Instead, we will be generating bromine in solution (equation 1); then an electrophilic bromonium cation will be formed by reaction by bromine's reaction with acetic acid (equation 2).

Equation 1 $5\ HBr + KBrO_3 + CH_3CO_2H \rightarrow 3\ Br_2 + 3H_2O + CH_3CO_2^- + K^+$

Equation 2 $CH_3CO_2H + Br_2 \rightarrow HBr + Br^+ + CH_3CO_2^-$

Images: http://www.nvcc.edu/alexandria/stb/chm/246/46_vanillin.pdf

Objective: 1. To understand how substituents affect the outcome of an Electrophilic Aromatic Substituation reaction. 2. To predict products of EAS. 3. To write out the mechanisms and resonances involved in EAS. 4. To synthesize "bromovanillin" and determine which "bromovanillin" was formed.

Procedure:

Reaction:
1) Under the hood, dissolve 0.304 g of vanillin in 4.0 mL of acetic acid using a 10 mL Erlenmeyer flask and micro stir bar.

2.) Add 0.15 g of potassium bromate, followed by 0.40 mL of 48 % hydrobromic acid. Your solution should turn a dark orange color.

3) Stir the reaction mixture for 45 minutes. NOTE: what are the visual clues that the reaction is complete? Is it exothermic or endothermic?

Isolation:
4) Pour the mixture into an Erlenmeyer flask containing 30 mL of ice cold water, stir for an additional 15-20 minutes with stir bar. NOTE: You should see lots of insoluble bromovanillin during this part of the procedure.

5) *IF* your liquid is an orange color still, add 30% sodium thiosulfate solution (drop wise while stirring) until it turns yellow. This will destroy any residual bromine in the reaction mixture.

6.) Isolate the white solid obtained by vacuum filtration, washing with ice-cold water.

Purification:
7) Recrystallize the crude solid using 50% ethanol/water to remove impurities. NOTE: The solid may not dissolve completely.

8.) Let the solution cool, crystals form, and re-filter.

Characterization:

9.) Take the melting point range of the *dry* product and compare it to the melting points of the possible products. Determine which regioisomer was made. Did this confirm your original hypothesis?

10.) Obtain the mass of your final product and calculate the percent yield.

Procedure adapted by Shasta Ott
http://people.smu.edu/ahumason/1084/Supplemental%20Packet%20-%20Summer%202%202008.pdf
http://www.nvcc.edu/alexandria/stb/chm/246/46_vanillin.pdf

12BL Prelab Experiment 9: Directive Effects in Vanillin Bromination

1. Explain what an Electrophilic Aromatic Substitution (EAS) reaction is?

2. What species is the nucleophile in an EAS reaction?

3. What are the all the reagents/catalysts/etc… that you need to put the following groups onto a benzene ring?

a. benzene—**Br**

b. benzene—**SO_3H**

c. benzene—**NO_2**

d. benzene—**$COCH_3$**

4. For substituents already on a benzene ring….

What is meant by Activators? How do you recognize Activators? Example?

What is meant by Deactivators? How do you recognize Deactivators? Example?

What is meant by O/P Directors? How do you recognize O/P Directors? Example?

What is meant by M Directors? How do you recognize M Directors? Example?

5. Explain why halogens are deactivators, and yet they are also o/p directors?

6. Show the EAS mechanism for the bromination of phenol using $Br_2/FeBr_3$. (If more than one product can be formed, show the mechanism for the major product AND briefly indicate your choice). Your mechanism should be clear showing all structures/reagents/catalysts/arrows/charges/etc…

12BL Postlab Experiment 9: Directive Effects in Vanillin Bromination

***Results**

*Calculation of Limiting Reactant & Theoretical Yield of Product:
(use dimensional analysis clearly labeling all units & chemicals)

*% Yield Calculation:

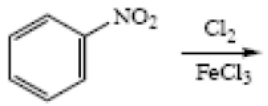
*Record the Experimental Melting Pt. Range of your product _____˚C

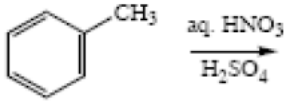
*What is the identity of your product? Product Name_____

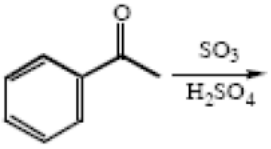
Theoretical MP_____

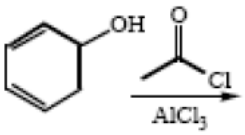
Questions

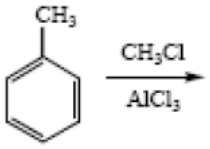
1. Give the major product(s) of the following rxns. Briefly indicate why it is major.



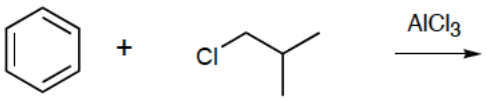








2. Show the complete mechanism (all arrows, charges, etc…) for the formation of the major product in the following reaction. Be careful – you should be confident in carbocation mechanisms in determining the major product.



3. Give the major product that forms from the di-substituted aromatic molecules below. Briefly indicate why it is major.