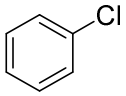
Loudon Chapter 16 Review: Chemistry of Benzene

Jacquie Richardson, CU Boulder – Last updated 2/5/2020

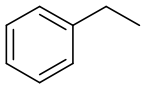
This chapter is all about aromatic rings and the reactions that they undergo. They differ a lot from normal reactions of alkenes, because the aromatic ring is so stable that we need pretty severe conditions to make it do anything.

Nomenclature

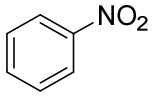
Aromatic rings are named under the IUPAC system, similar to other alkenes and alkanes. Substituents are named along with their locations, but if there's only a single substituent then it's assumed to be at carbon 1. One substituent that shows up commonly here is the nitro group, which we haven't seen much of before.



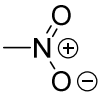
Chlorobenzene



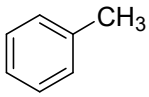
Ethylbenzene



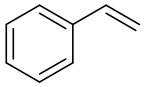
Nitrobenzene

Nitro group: 

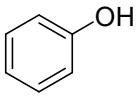
There are several common names for benzene derivatives that you should know.



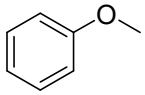
Toluene



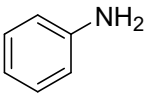
Styrene



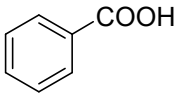
Phenol



Anisole

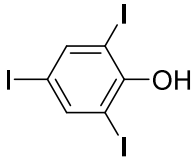


Aniline

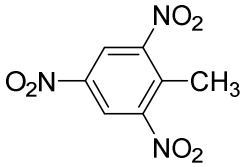


Benzoic acid

Versions of these molecules with additional substituents can be named after them, with the main substituent (for example, the CH_3 group in toluene) assumed to be at position 1.

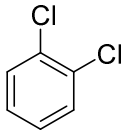


2,4,6-triiodophenol

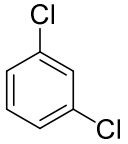


2,4,6-trinitrotoluene (TNT)

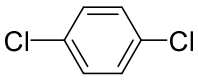
If a ring has two substituents, it can be named either with the usual substituent numbers or with *ortho*/*meta*/*para* (abbreviated as *o*/*m*/*p*).



1,2-dichlorobenzene
o-dichlorobenzene

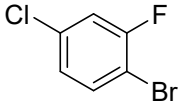


1,3-dichlorobenzene
m-dichlorobenzene



1,4-dichlorobenzene
p-dichlorobenzene

Any more than two substituents though, and numbers are the only valid way to name the compound. However, the relationship between any two groups can still be described as *ortho*/*meta*/*para*, similar to how we could still describe groups as *cis*/*trans* to each other in a cyclohexane with multiple substituents.



1-bromo-4-chloro-2-fluorobenzene
(Cl & F are *meta* to each other,
F & Br are *ortho* to each other,
Br & Cl are *para* to each other)

There are also some common names for disubstituted rings: two CH_3 groups is a xylene, and a CH_3 plus an OH is a cresol.

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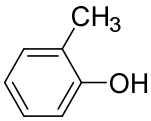
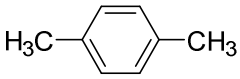
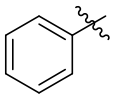


o-cresol

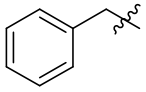


p-xylene

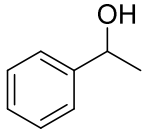
Benzene can also be named as a substituent, if the parent chain is not the benzene ring (perhaps due to having principal functional groups). The benzene ring itself is named "phenyl", and benzene plus a methylene group is "benzyl".



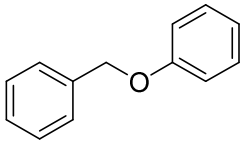
Phenyl
(Ph or ϕ)



Benzyl
(Bn or ϕ-CH_2)



1-phenylethanol

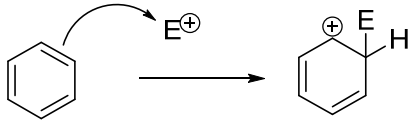


Benzyl phenyl ether

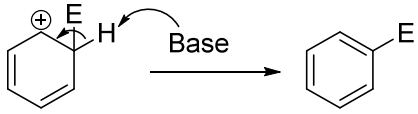
Electrophilic Aromatic Substitution (EAS)

This category of reactions takes up almost the entire chapter. The good news is that all reactions in this category fit into the same pattern, with minor variations.

1. Generate the electrophile: This is the part that varies from one reaction to another.
2. Have the benzene ring attack the electrophile: This always happens when one of the double bonds goes out and attacks the electrophile, breaking the aromaticity of the ring. After this happens, the ring is in a cationic state (an arenium ion) and has several resonance forms – the positive charge can be placed in a few different locations. This becomes important later in the chapter.



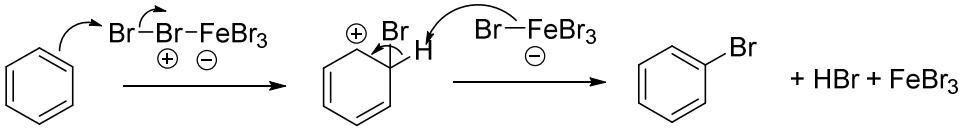
3. Reestablish aromaticity: To do this, we need to pull the H off the atom that got the electrophile attached to it. (Remember, if the ring's aromatic then each carbon can only have one other bond coming off of it.) What acts as the "base" depends on what's left over from generating the electrophile.



Halogenation

This can be done with chlorine or bromine. Halogen electrophiles are generated when the dihalogen attacks an iron trihalide ($FeBr_3$ or $FeCl_3$).

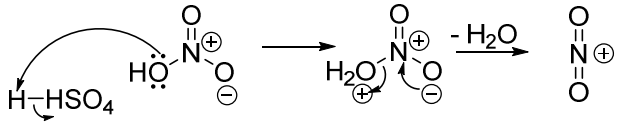
Then, the ring attacks the outermost halogen atom. It's kind of tempting to attack the middle one since it has the positive charge. But since the middle halogen still has a full octet, it wouldn't get any benefit by being attacked directly. The next two steps happen as part of the general EAS pattern. This mechanism is the same for bromine and chlorine.



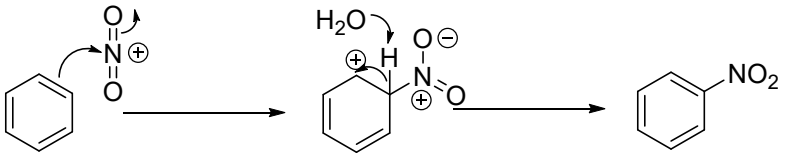
Note that this regenerates the $FeBr_3$ catalyst and gives HBr as a waste product. Overall the reaction is written as:

Nitration

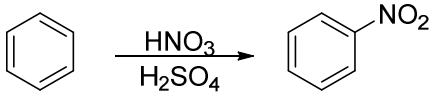
In this case, the generation of the electrophile is a little more complicated. You can sort of think of it as being like the acid-catalyzed elimination of water from back in chapter 10 – protonate the OH group to turn it into a better leaving group. You need H_2SO_4 around for this to happen. NO_2^+ is called the nitronium ion.



Then the attack and rearomatization happen just like before.

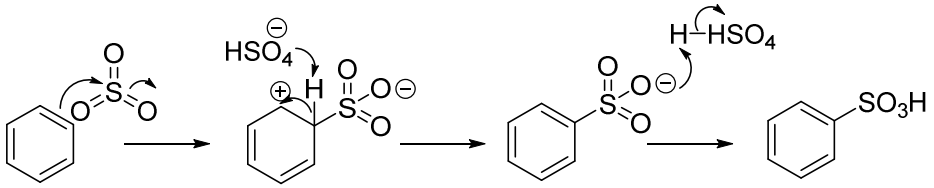


The overall reaction is written as this:

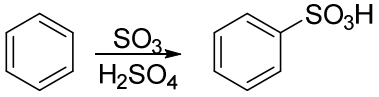


Sulfonation

There are a few different ways this could happen, but the most likely way involves straight sulfur trioxide (SO_3). Normally this is already present as part of the reaction mixture, along with H_2SO_4. Even though SO_3 doesn't officially have a positive charge, there's such a huge delta positive on the sulfur that it acts just like any other electrophile. This does mean that it needs to neutralize itself later by picking up a proton though.



There are several ways of writing the overall reaction. All of them use a mixture of H_2SO_4 and SO_3, but this mixture can go by the name of "fuming sulfuric acid" or "oleum".



Friedel-Crafts Alkylation

This is one of the more useful reactions in this chapter, since it gives us a way to makes new carbon-carbon bonds. The electrophile can be either a carbocation created by using $AlCl_3$ to pull off a chlorine atom (more likely if the carbon is secondary or tertiary), or a molecule that looks a lot like the electrophiles used in halogenations above (more likely if the carbon is primary, and cannot rearrange to get a secondary or tertiary carbocation).

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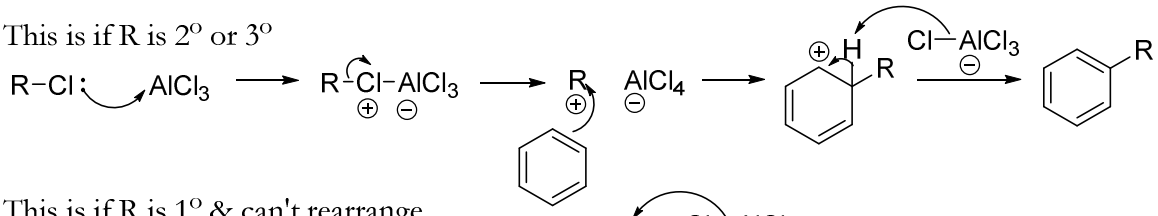
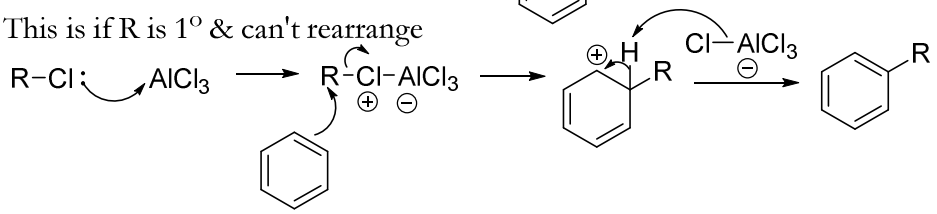
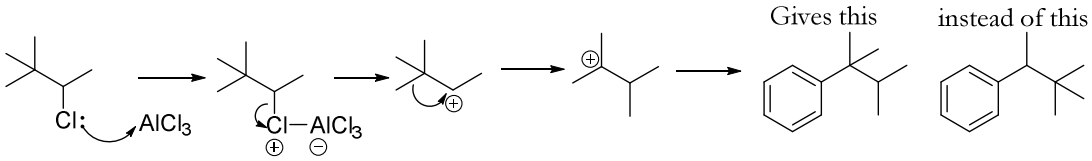
This is if R is 2° or 3°

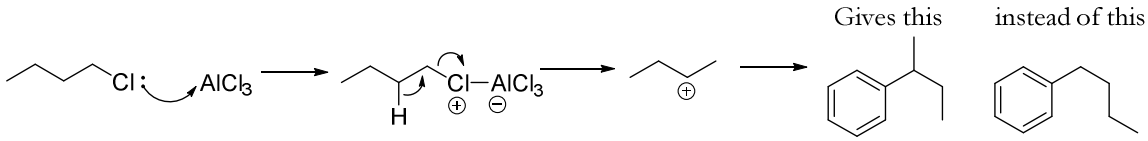


This is if R is 1° & can't rearrange

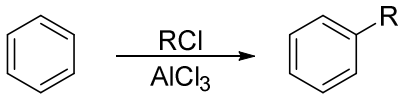


All the normal rules for carbocations apply: more substituted is more stable, and if it's not completely stable it can rearrange. In fact, whether it goes through a true carbocation or not, it can still rearrange carbocation-style! This means that the R group you intend to attach is not always what you get, which is a big drawback to this reaction.



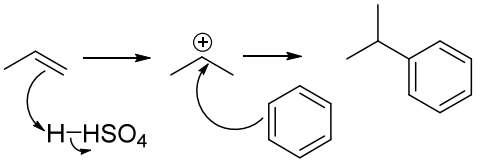


The overall reaction is:

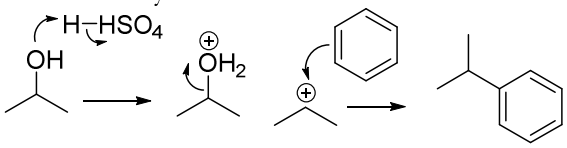


We can use other methods of generating a carbocation to do this reaction as well. We've seen at least two examples in the past: acid-catalyzed addition to an alkene, and acid-catalyzed dehydration of an alcohol.

Acid-cat addition to alkenes:



Acid-cat dehydration of alcohols:



Again, both of these have all the problems associated with carbocations. If we want to avoid these problems, we have to use acylation instead. There's another problem involving the molecule doing this reaction multiple times in a row, which we'll cover later in this chapter.

Friedel-Crafts Acylation

Again, this is a way of creating new carbon-carbon bonds. The biggest difference between FC alkylation and FC acylation is that acylation means we're attaching a group that has a carbonyl at the point of attachment. Since there's something with a lone pair attached to the carbon where the reaction occurs, we never actually generate a carbocation. Instead we generate an acylium ion, with a C-O triple bond. This is much more stable than a carbocation so there's no chance of rearrangement.

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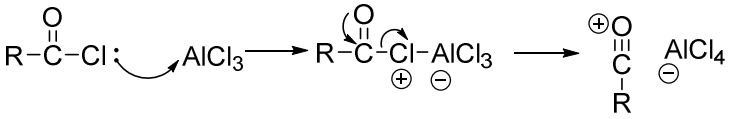
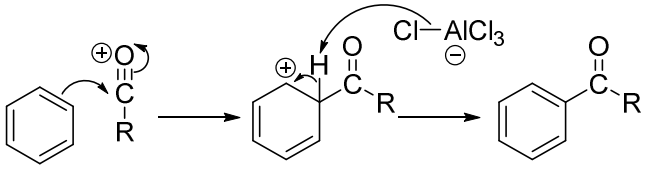
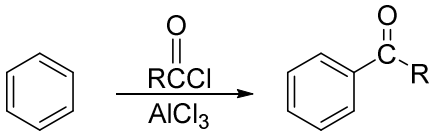


This acylium ion is safe from rearrangements.

From here, the reaction proceeds just like all other EAS reactions.



So the overall reaction is:

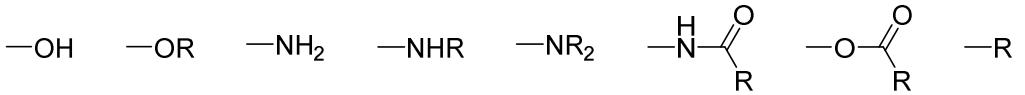


One limitation here: this reaction doesn't work if R is a hydrogen. For that, you need a special reaction called Gattermann-Koch formylation, which we won't cover.

Directing Effects

Up until now we've only looked at regular benzene doing these reactions. Things get more complicated when the aromatic ring has substituents attached to it already. The general idea is that if there's already a group attached to a ring, it gets to decide where the new group sticks on (*ortho*, *meta*, or *para*). There are two different factors to take into account: whether a group is activating or deactivating (meaning it makes the molecule react faster or slower than plain benzene would), and whether it's *ortho/para*-directing or *meta*-directing. Everything depends on stabilization of the carbocation ring intermediate. Is the group that already on the ring going to make the positively-charged carbon more or less stable? And which positions around the ring get their positive charges stabilized better or worse? Generally, groups are described as either electron-donating groups (EDGs) or electron-withdrawing groups (EWGs). You can break down substituents into three basic categories. The book has a table on pg. 812 that lists a lot of them.

1. Activating and *ortho/para*-directing: This group includes any EDGs. Anything that has a lone pair on the atom attached directly to the ring (unless it's a halogen – see below) and anything that's weakly electron-donating through hyperconjugation like an R group fit into this category. These speed up the reaction at all sites in the ring, but the *ortho* and *para* positions feel the effect more strongly so they become the major products.



2. Deactivating and *meta*-directing: This covers any EWGS, which have either a positive charge or a delta-positive charge at the point of attachment. Usually the tip-off that you're dealing with something from this group is that the atom attached to the ring has a double or triple bond to something more electronegative. These slow down the reaction at all sites in the ring, but again the *ortho* and *para* positions feel the effects more strongly. So the major product results at the *meta* position.

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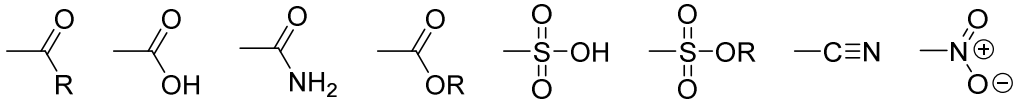
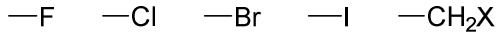
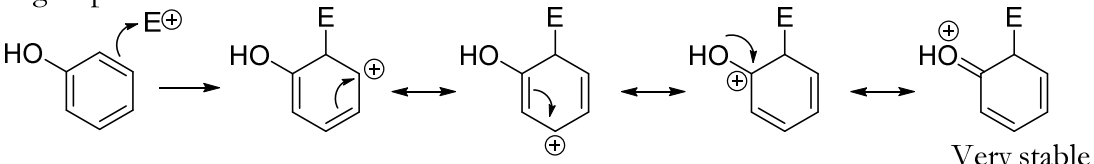


3. Slightly deactivating and ortho/para-directing: The main part of this group is the halogens, along with halomethyl groups. The reason for this is that they're sort of straddling the divide – they're EDGs by resonance, because they have multiple lone pairs they can donate into the ring. But they're EWGs by inductance, because they're pulling electron density towards themselves. Overall these two effects nearly cancel out, so they are usually only weakly deactivating.



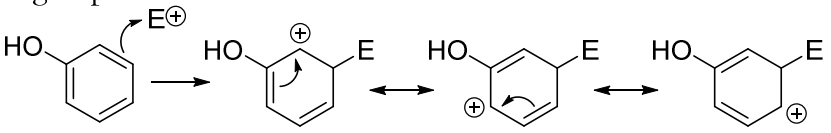
As for why the groups break down into these categories, it helps to start with one molecule and show it going through EAS at each of the three positions, then comparing which ones are best. Here's an -OH group as an example (should be activating and *ortho/para*-directing, based on the list above.) It doesn't even matter which EAS reaction you do, since the new group doesn't usually get a say on where it attaches.

If group attaches ortho:



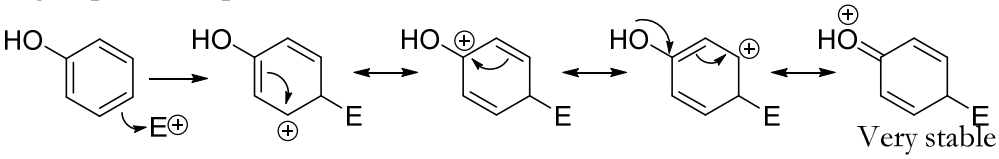
Very stable

If group attaches meta:



No way to get charge onto O, so not as stable

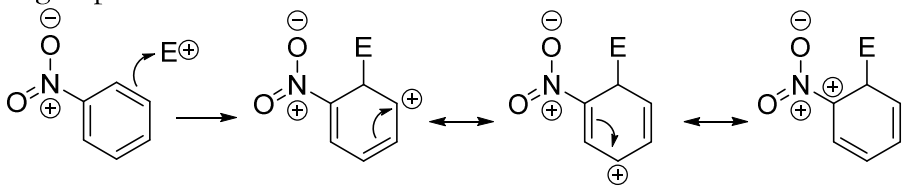
If group attaches para:



Very stable

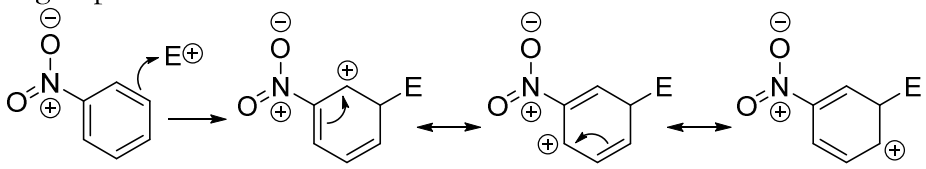
By contrast, if we do this for a *meta*-directing group like nitro, the *ortho* and *para* mechanisms at some point have two positive charges adjacent to each other (or a positive charge and a delta positive charge, for carbonyl groups).

If group attaches ortho:



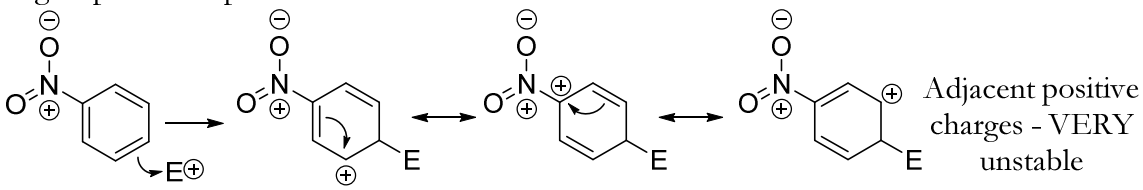
Adjacent positive charges - VERY unstable

If group attaches meta:

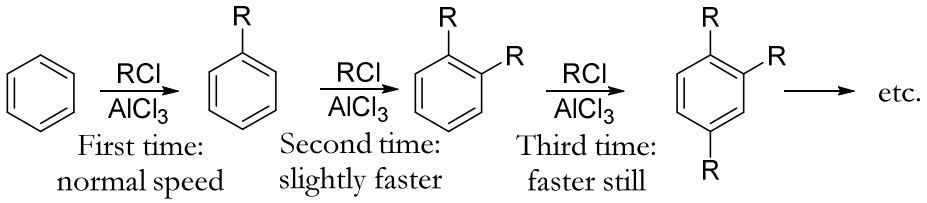


Not as unstable

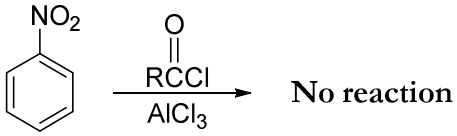
If group attaches para:



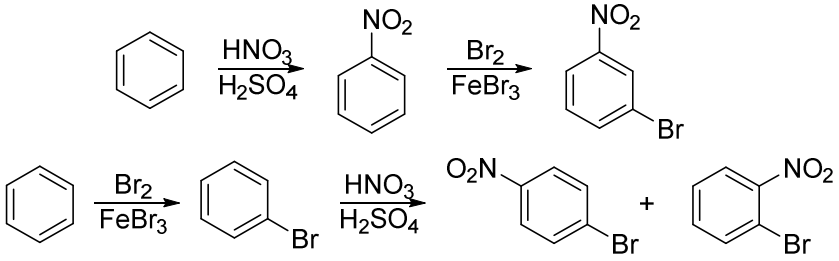
This also explains the second problem that we have with Friedel-Crafts alkylation: R groups are activating, so once you stick on one R group, it becomes a lot easier for the molecule to add a second one. This is called overalkylation. You can get around this problem by using a huge excess of aromatic starting material, so there just aren't enough R groups to overalkylate all of them.



On the flip side of this, when you're adding deactivating groups it's easy to get it to stop after a single addition, since the reaction gets harder each time. In fact, all of the groups listed above as deactivating groups are too deactivating to permit alkylation or acylation to occur in a reasonable time, and are considered no reaction for Friedel-Crafts (but not for any other EAS reactions).



Depending on the geometry we want in the final product, we can use directing effects to decide which groups to add to the ring first. If we need *meta* geometry we have to add a *m*-director first, but if we want *ortho* or *para* then we need to add an *o*/*p*-director first.

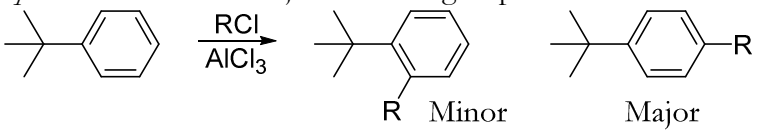


Sometimes there is no good way to perform a synthesis, either because both groups have the wrong directing ability, or for some other reason like Friedel-Crafts getting shut down by deactivators. In these cases, we might have to use a few workarounds that will be covered in future chapters.

Ortho vs. *Para* for *o,p*-Directors

Normally it's hard to get purely *ortho* or purely *para* molecules since *o,p*-directors favor a mixture of these two products. In a lot of cases, we just have to synthesize both, and then rely on separations techniques to isolate them from each other. However, there are a few ways to bias the outcome towards one side or another. To favor *para*, we need to use sterics

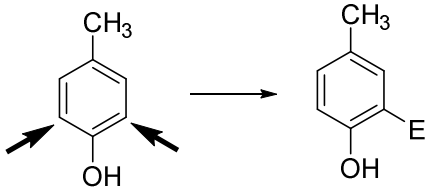
to your advantage. For instance, even though *t*-butyl is an *o,p*-director, the product we get will be almost all *para* since it's hard to jam another group in next to it.



Biasing towards just *ortho* is more difficult. Some reactions are so favorable that the electrophile will attach every time it encounters the ring, which gives a 2:1 *ortho/para* ratio (just because there are twice as many *ortho* positions).

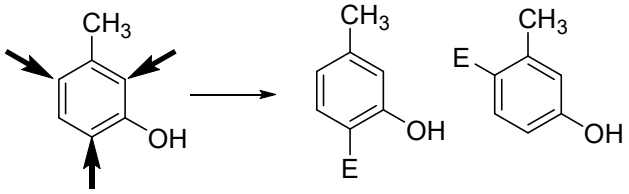
Multiple Substituent Effects

If you have multiple groups on the ring to begin with, it gets even more complicated. Usually the rule is that the strongest activating group gets to decide, but it's common to get a mixture of products.



OH is the stronger activator and it wants *o/p*

One more factor involves two groups that start *meta*. It's unlikely that a new group will add in between them, because that position is sterically too hard to get to.



Both groups agree on where they want E to add, but the position between them is too hindered.

Hydrogenation of Aromatics

This is the one reaction in this chapter that isn't EAS. It turns out the double bonds in benzene can be hydrogenated, like an alkene. But since the aromatic ring is so stable, it takes much harsher conditions to make it happen – huge pressures and temperatures. Also the catalyst is slightly different – Ni instead of Pd/C.