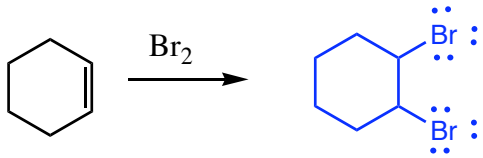
Learning Guide for Chapter 18 - Aromatic Compounds II

I. Electrophilic aromatic substitution
- Introduction
- Mechanism
- Reagents and Products
- Electrophiles
- Effects of Substituents
- Friedel-Crafts alkylation and acylation

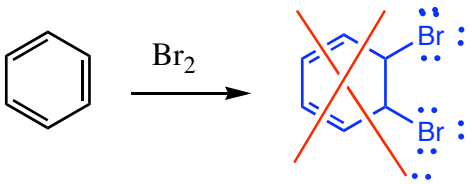
I. Electrophilic Aromatic Substitution

Introduction

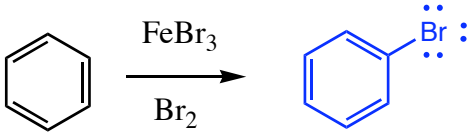
Which of the following reactions will give product?



addition — Br atoms added to the molecule without taking anything away



no reaction — addition would destroy aromaticity



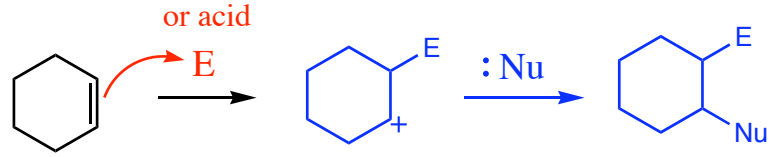
substitution — H is replaced by Br; product is still aromatic

What can you conclude?

aromatic rings undergo substitution instead of addition to preserve aromaticity
different reagents are needed

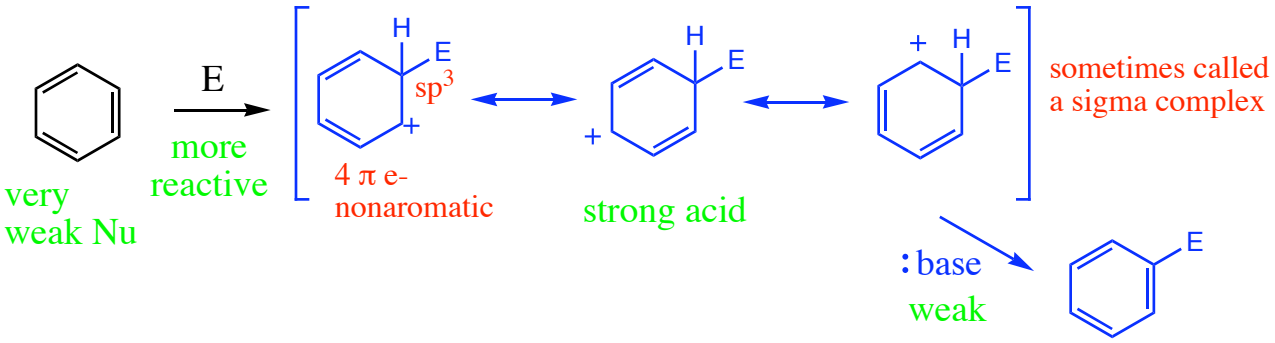
Mechanism

In addition reactions of alkenes, how does the C=C react? weak Nu or base



weak Nu — strong E

When an aromatic ring reacts, it is a very weak nucleophile. What will be formed?



How would the activation energy of the first steps compare?

C+ formed in both, has resonance in the second
but aromaticity destroyed in the second - much higher

How would the two electrophiles compare?

second one is much stronger, more reactive

Why does the C+ react as an acid rather than an electrophile at the end?

to restore aromaticity

What would you predict about the strength the acid and the base in the second step?

weak

summing up:

Why is the reaction call "electrophilic aromatic substitution"?

reagent is an E
starting material must be aromatic
H is replaced by E

What are the two steps involved?

1 - ring attacks E, forms non-aromatic C+ w/ resonance structures

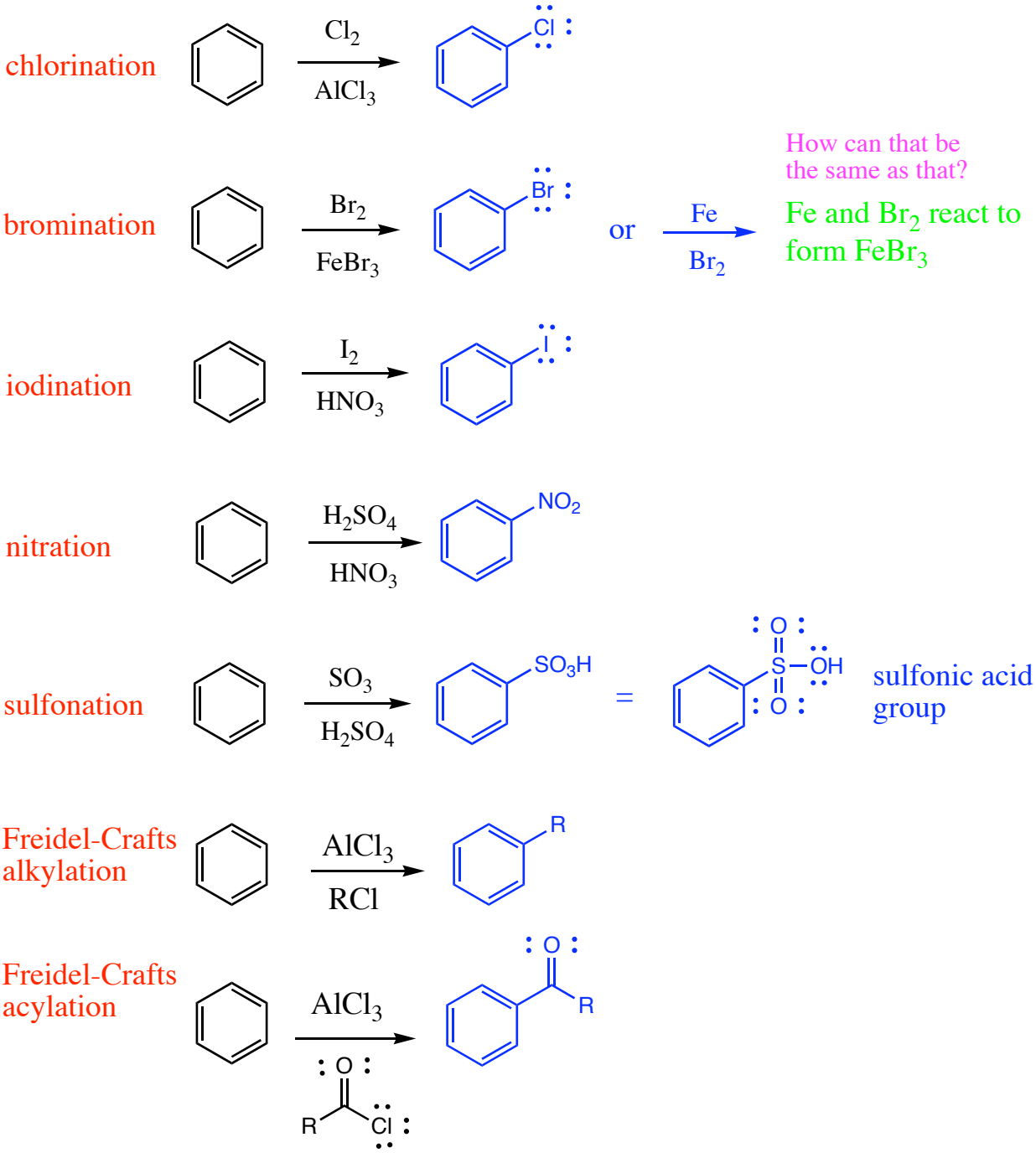
2 - weak base pulls off H on same C as E, restoring aromaticity

How does this reaction compare to the reactions we studied in the last section?

don't have to start with aryl halides
benzene attacks, rather than being attacked

Reagents and Products

What are the names and products in the following reactions?



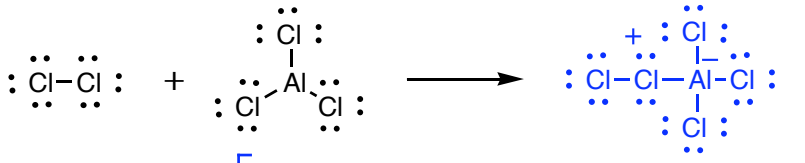
We will focus on the first 5, then come back to the last 2.

You will need to memorize these reagents and the products that they form; however, you should also be able to use some reasoning based on their mechanisms to help you.

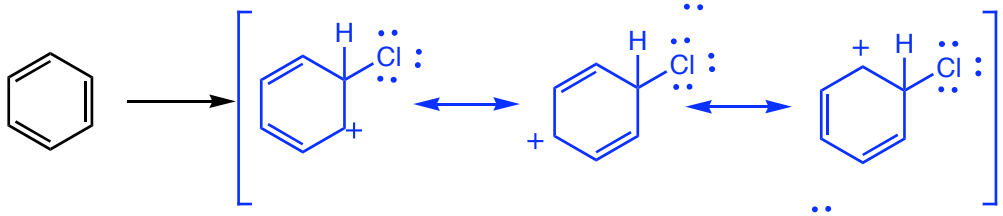
Electrophiles

Most of the reagents require a preliminary reaction in order to form a highly reactive nucleophile. The base required for the second step will be different for each reaction.

chlorination: reactive complex forms between Cl_2 and $AlCl_3$

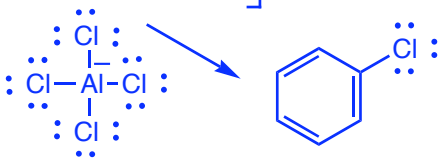


where would this complex be attacked?

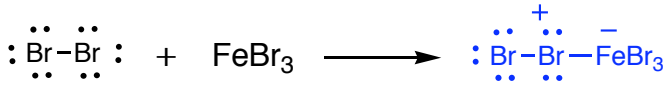


What reagents are being used up, and which are catalytic?

benzene, Cl_2 used up to make chlorobenzene
$AlCl_3$ catalytic



bromination: reactive complex forms between Br_2 and $FeBr_3$.

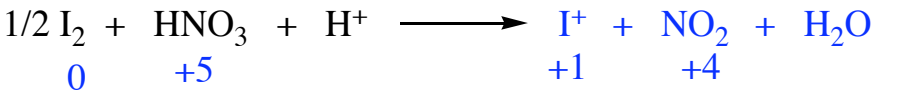


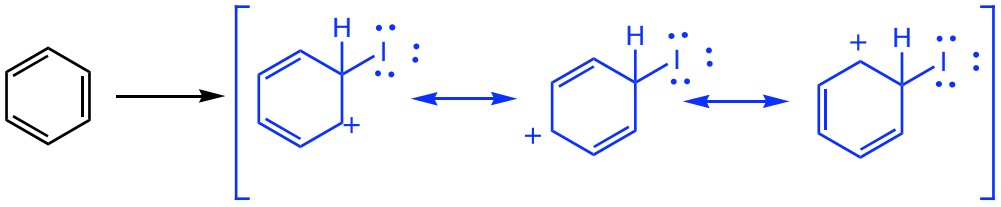
$FeBr_3$ is ionic;
is ne Fe-Br bond truly covalent?

same kind of mechanism as above

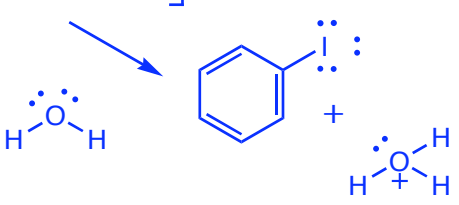
pair of e- in benzene ring attacks Br on the end, forming C+ w/ 3 resonance structures
bromine takes a H to give bromobenzene and HBr

iodination: redox reaction between iodine, nitric acid, and some additional acid



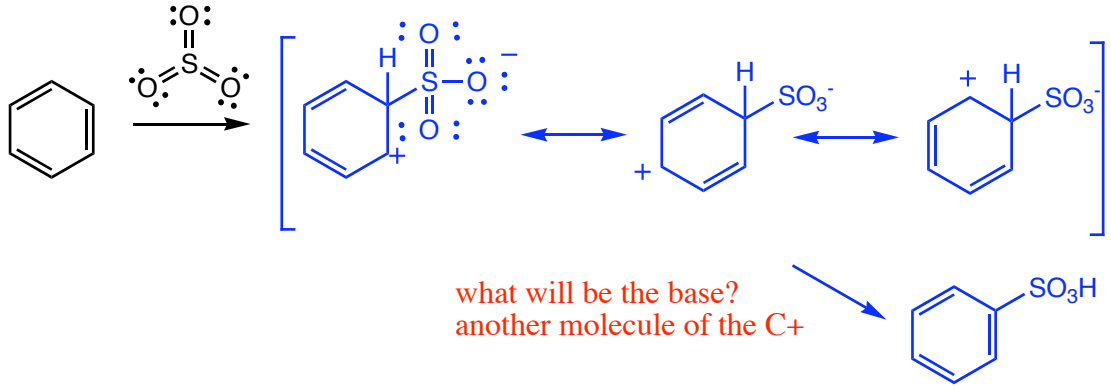


what will be the base?

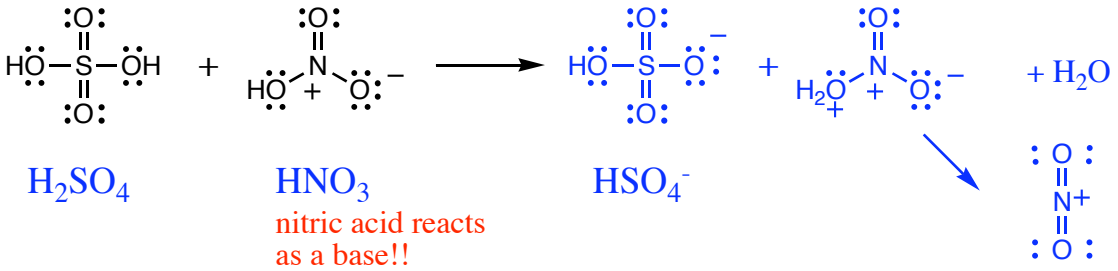


SO_3 is a gas; ir is also the anhydride of sulfuric acid
the mixture is called "fuming sulfuric acid" because it reacts w/ water vapor
to form clouds of sulfuric acid when opened

sulfonation: SO_3 is the electrophile; sulfuric acid is the solvent



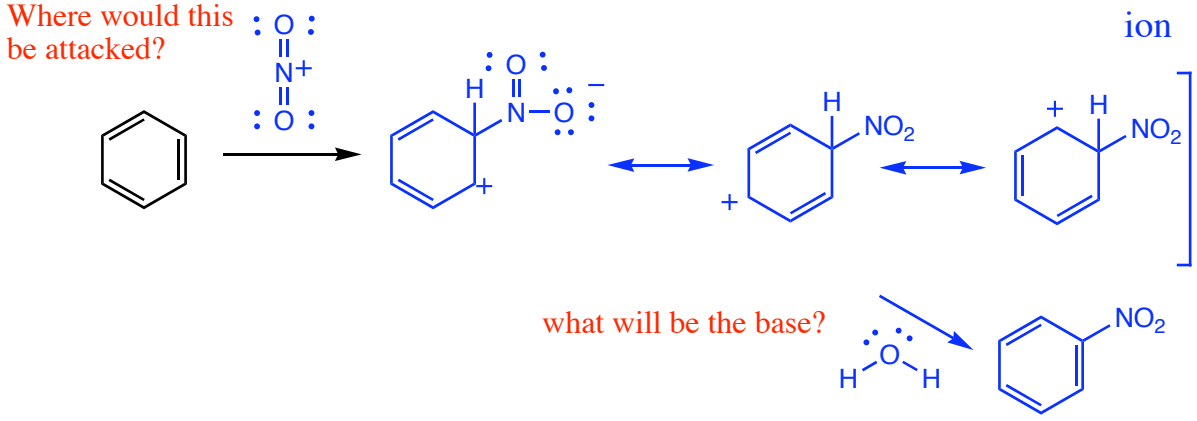
nitration: sulfuric and nitric acid react to form nitronium ion



H_2SO_4 HNO_3 HSO_4^-

nitric acid reacts
as a base!!

nitronium
ion



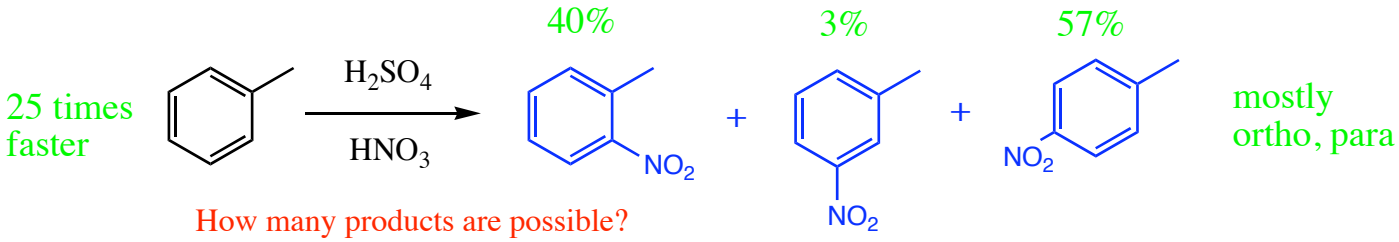
What are the reactive electrophiles and bases in each reaction?

chlorination - Cl_2-$AlCl_3$ complex; $AlCl_4^-$
bromination - Br_2-$FeBr_3$ complex; $FeBr_4^-$
iodination - I^+ ion; H_2O
sulfonation - sulfur trioxide; $PhSO_3^-$
nitration - nitronium ion; H_2O

Effects of Substituents

In order for electrophilic aromatic substitution reactions to be useful, they must work on a variety of aromatic compounds. However, when we do the reaction on a ring which already contains some other substituent, some complications come up.

First of all, more than one isomer is possible.



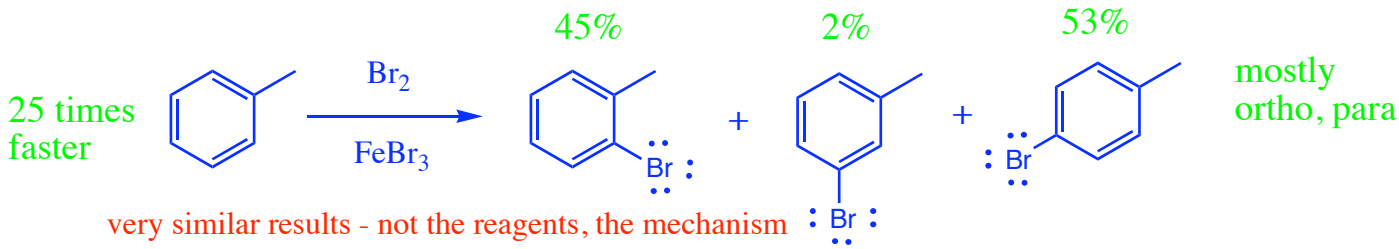
How many products are possible?

When you isolate these products, you will find that they are present in different amounts. Secondly, the reaction is about 25 times faster with toluene than with benzene.

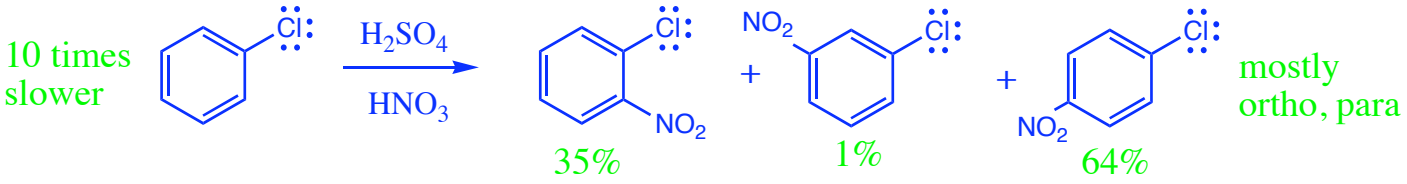
To understand why these ratios of products are formed, and why the reaction is faster, we need to get some more data. What other reactions could we try?

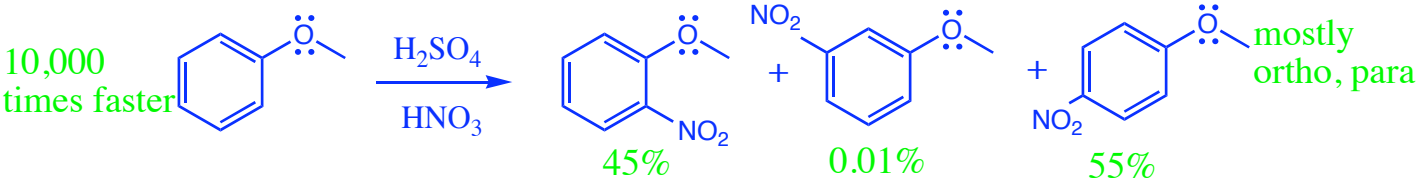
different reagents

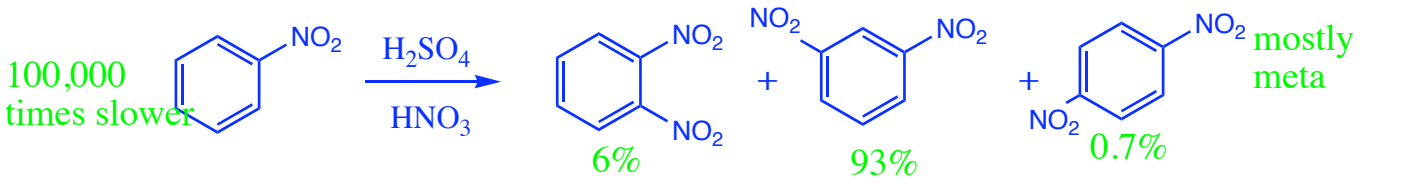
try aromatic rings with different substituents



very similar results - not the reagents, the mechanism







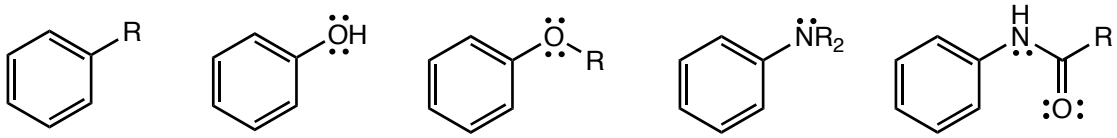
all kinds of results - substituent is affecting the rate-determining step in different ways for different isomers

After doing hundreds of these reactions, you can sumarize the results as follows:

1 - All of the reagents give the same results for a given starting material.

2 - Substituents on the aromatic ring can be divided into three groups:

Group 1 Activating, Ortho/Para-directing Groups



mildly activating ——— strongly activating

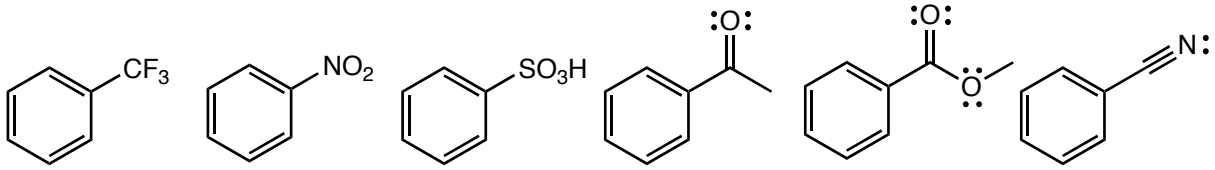
alkyl groups or atoms with electron pairs on an atom connected to the ring

all give mostly ortho and para products

alkyl groups moderately speed up the reaction

groups with electron pairs dramatically speed up the reaction

Group 2 Deactivating, Meta-directing Groups



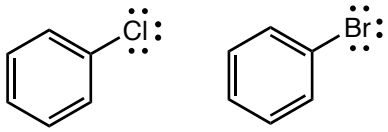
——— strongly deactivating ———

all have atoms with full or partial charges connected to the ring

all give mostly meta products

all slow down the reaction

Group 3 Mildly deactivating, Ortho/Para-directing Groups



mildly deactivating

halogens

moderately slow the reaction

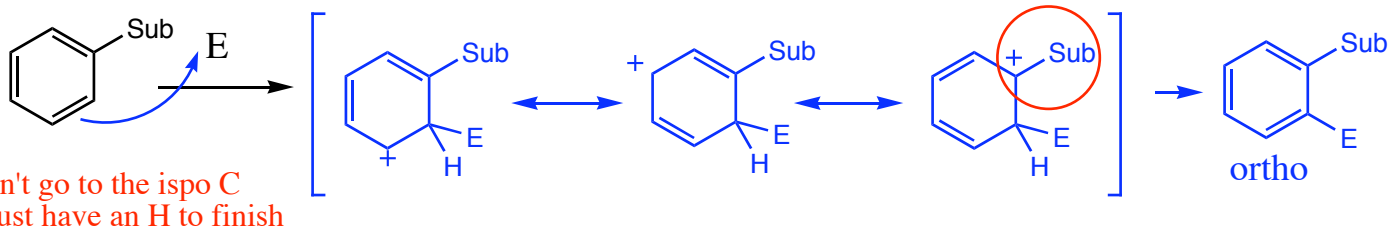
give ortho/para products

To answer the question why, we must look at how the presence of a substituent affects the rate-limiting step.

Which step will be rate limiting? formation of C+ with resonance structures

preliminary steps - can't be, results don't change
final step should be fast - restores aromaticity

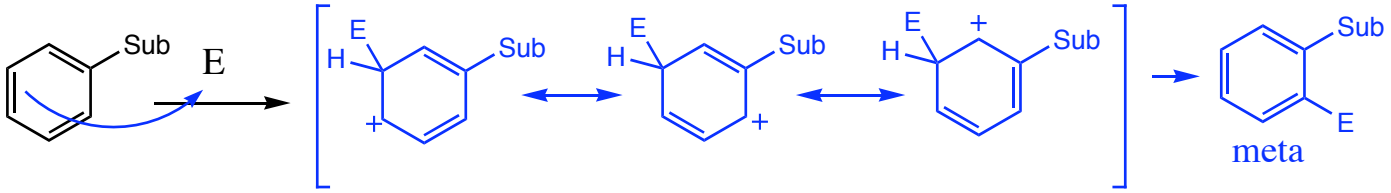
Ortho:



can't go to the ispo C
must have an H to finish

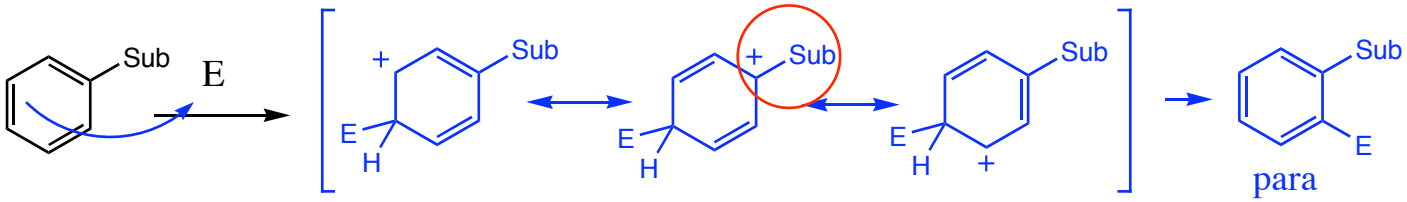
ortho - positive charge has density on C with substituent

Meta:



meta - positive charge does not have density on C with substituent

Para:



para - positive charge has density on C with substituent

If the substituent can stabilize the positive charge, what will happen to the energy of the intermediate?

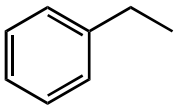
it will go down, the reaction will be faster

If the substituent destabilizes the negative charge, what will happen to the energy of the intermediate?

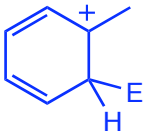
it will go up, the reaction will be slower

Group 1 - alkyl substituents and substituents with electron pairs on the atom next to the ring

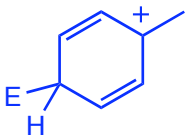
alkyl



ortho

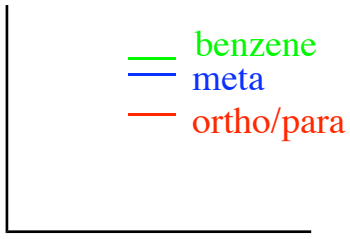


para



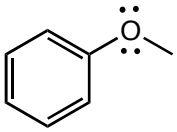
more stable - 3º C+

energy diagram

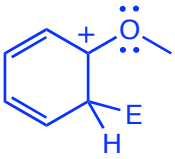


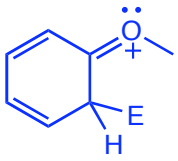
reaction takes lower pathway
goes faster, gives o,p products

electron-donating



ortho

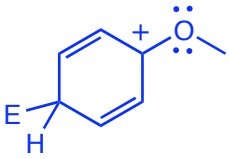


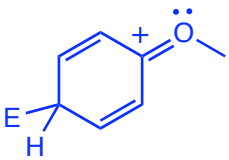


O is electroneg
less stable

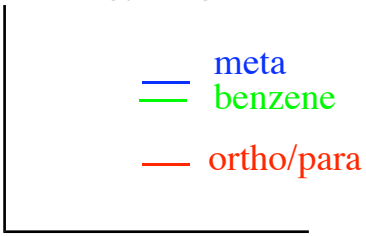
new resonance
structure!

para

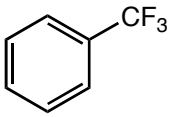




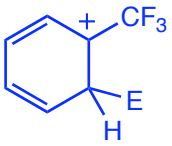
energy diagram



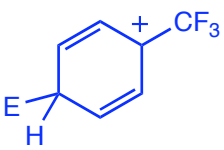
Group 2: substituents with fully or partially positively charged atoms on the benzene ring



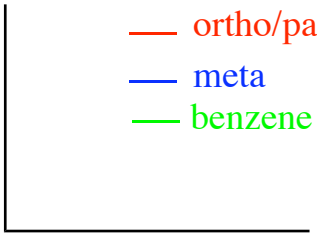
ortho



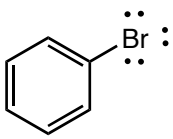
para



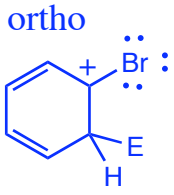
energy diagram

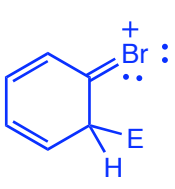


Group 3: halogen substituents

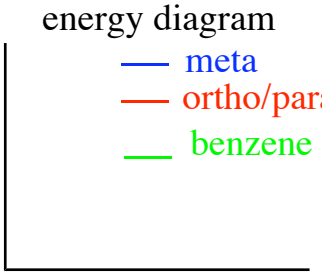


ortho

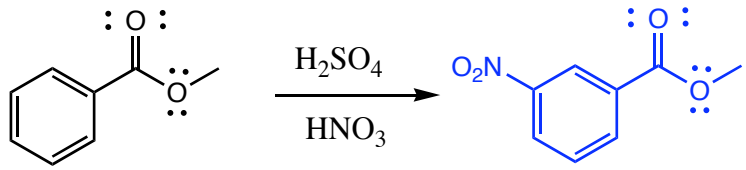




energy diagram



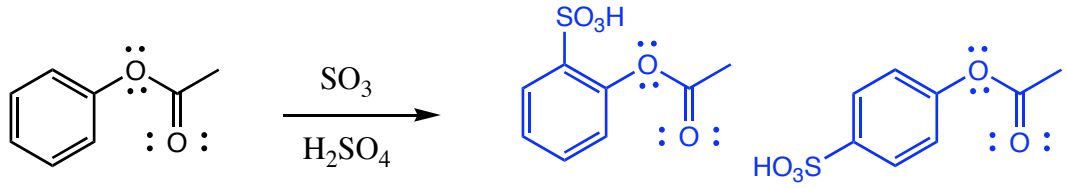
What products will predominate in each of the following cases, and why? Will they be slower or faster than the same reaction on a benzene ring?



deactivating, meta directing

nitration adds NO_2

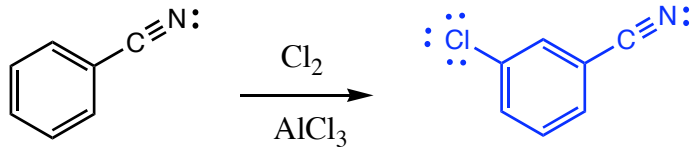
all reactions are slower, but o/p are slowest - meta wins



activating, o/p directing

sulfonation adds SO_3H

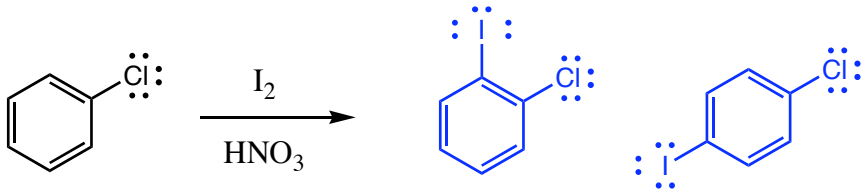
o/p reactions are faster, meta are slower



deactivating, meta directing

chlorination adds Cl

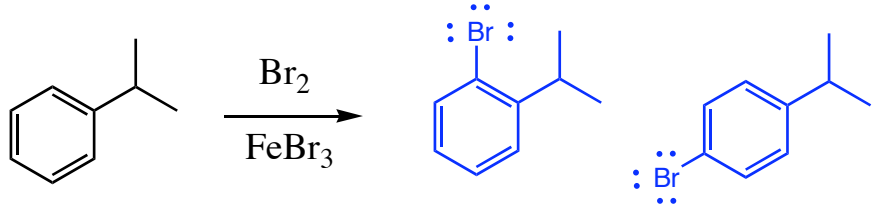
all reactions are slower, but o/p are slowest - meta wins



deactivating, o/p directing

iodination adds I

all reactions are slower, but o/p are a little faster

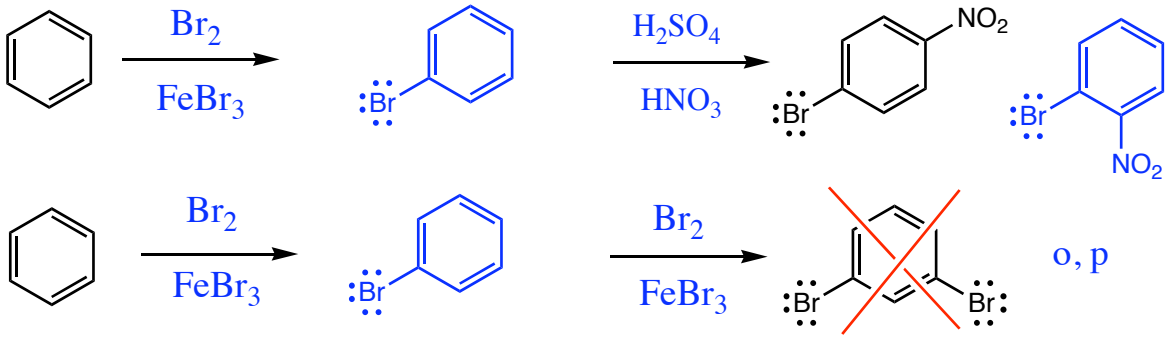


activating, o/p directing

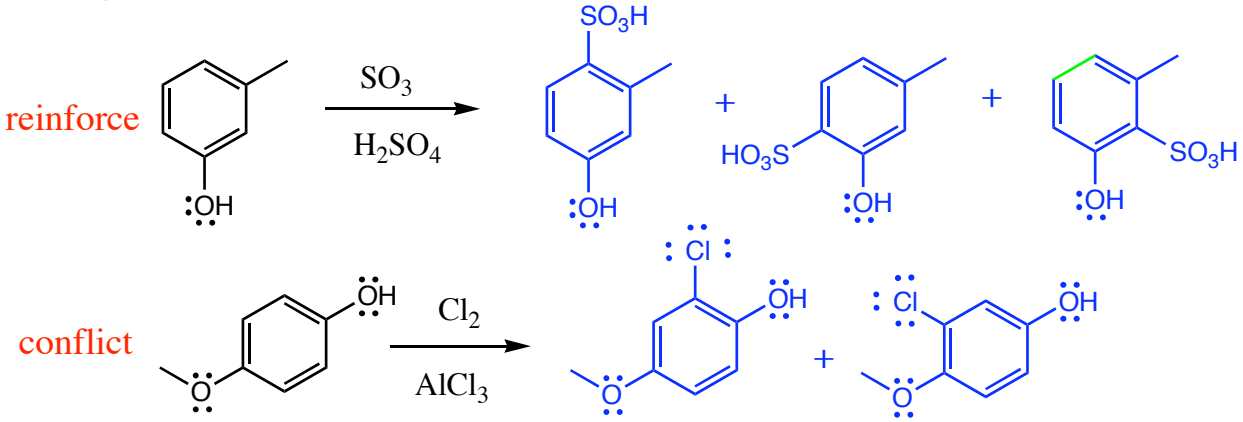
bromination adds Br

all reactions a little faster, o/p more than meta

When combining reactions to form syntheses, the directing effect of substituents must be taken into account.



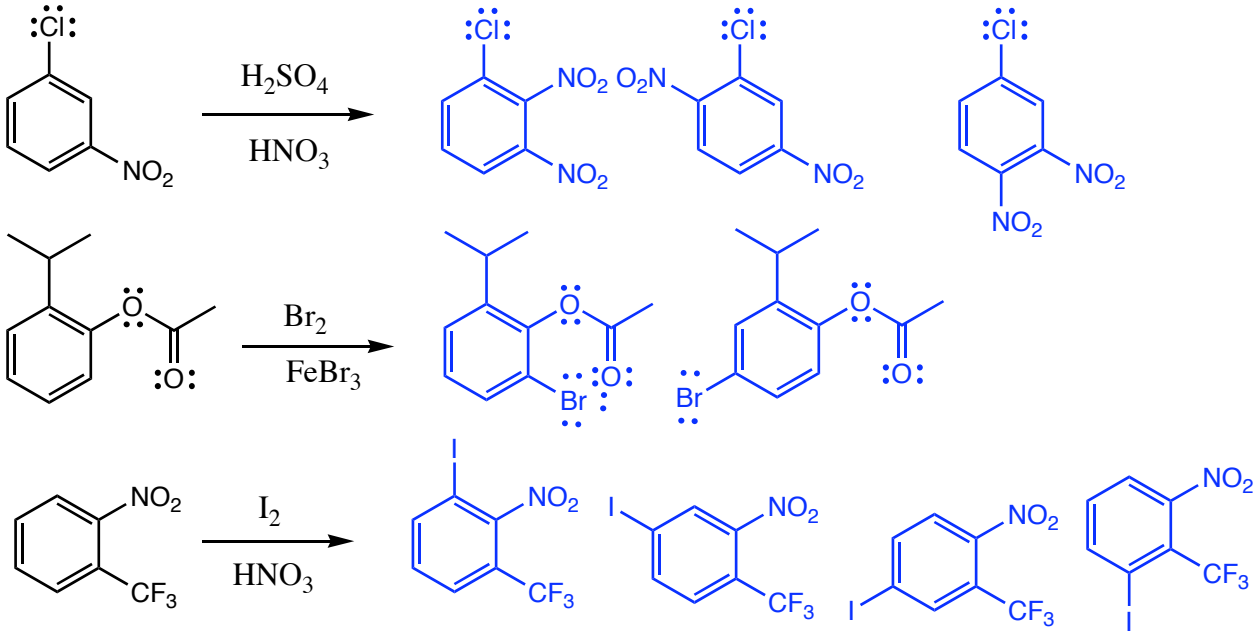
When more than one substituent is present, they may reinforce the directing effect, or they may conflict.



When conflicts occur, what takes priority?

same priority - mixtures

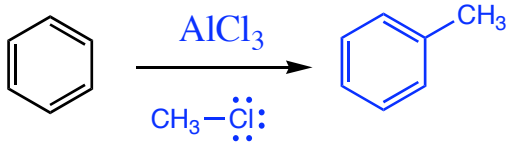
1. strong o/p directing groups
2. mild o/p directing groups
3. all meta directing groups



Friedel-Crafts Alkylation and Acylation

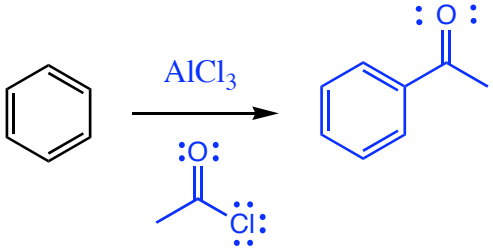
What reagents are needed for Freidel-Crafts alkylation and acylation reactions? What substituent is added?

alkylation



reagents: $AlCl_3$, alkyl chloride
product: alkyl group added

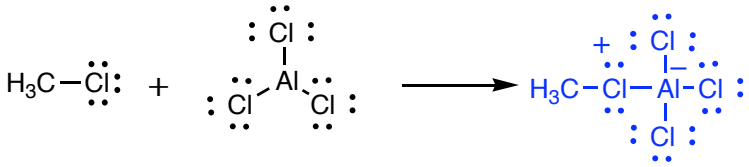
acylation



reagents: $AlCl_3$, acid chloride
product: ketone added

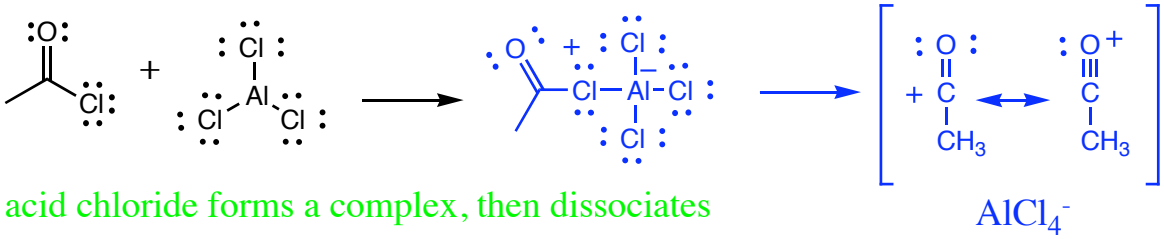
How do the reactive electrophiles form?

alkylation



RCl forms a complex with $AlCl_3$ (just like Cl_2 does)

acylation

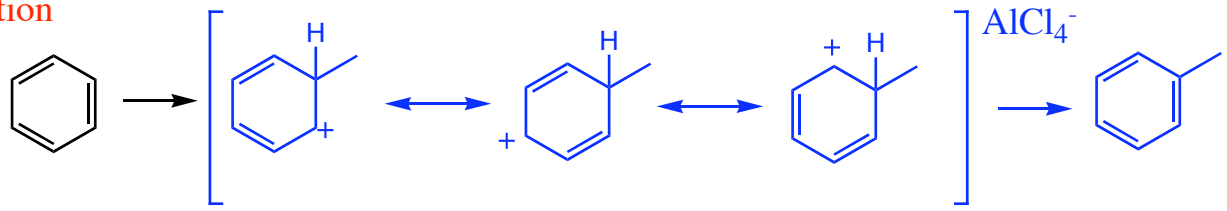


acid chloride forms a complex, then dissociates

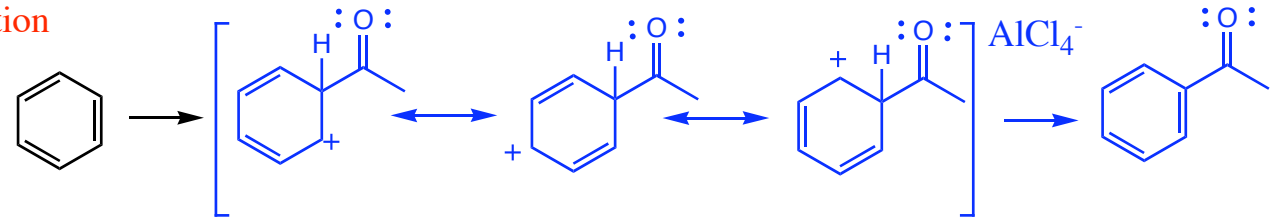
How does the aromatic ring react with these electrophiles?

benzene ring attacks, base pulls off a H

alkylation



acylation



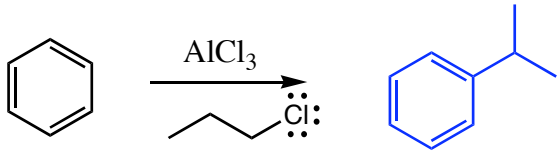
What are the three major limitations of the Freidel-Crafts alkylation reaction?

1) rearrangements

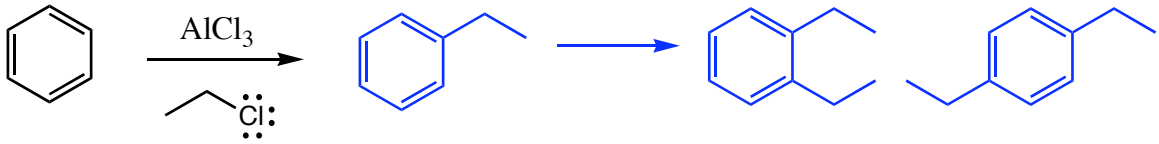
2) multiple substitutions

3) won't work on strongly deactivated rings

1) primary alkyl halides always give rearranged products

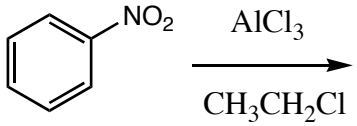


2) the product is more reactive than the staring material, so multiple products form



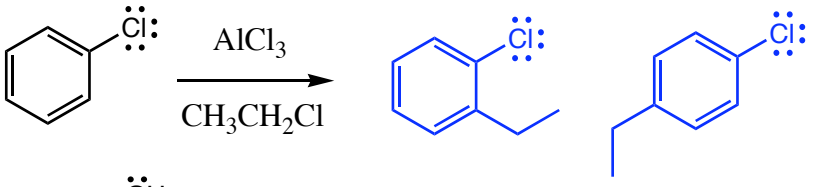
3) if a ring contains a strong deactivating group, the reaction is too slow (electrophile isn't strong enough)

strongly deactivating

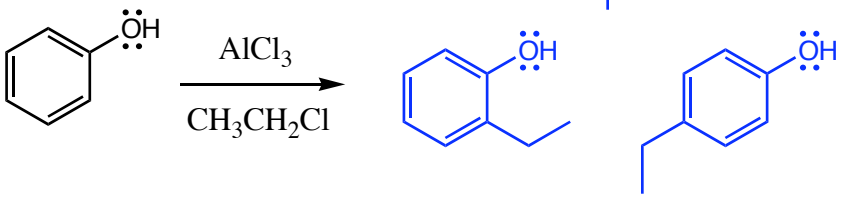


no reaction

mildly deactivating



activating



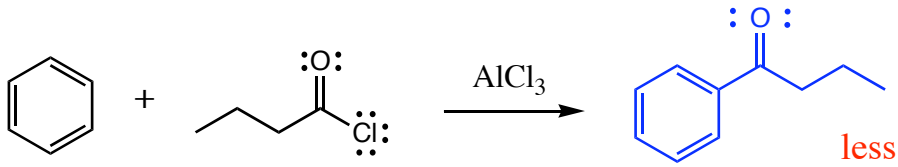
Which of these limitations does acylation overcome?

1) no rearrangements

2) no multiple substitutions

3) still won't work on strongly deactivated rings

1) acylium ions have resonance, so they don't rearrange

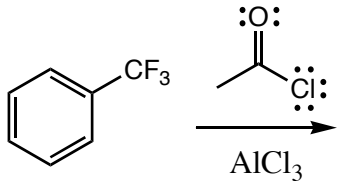


less reactive
no more products

2) the product is less reactive than the starting material

(use reaction above)

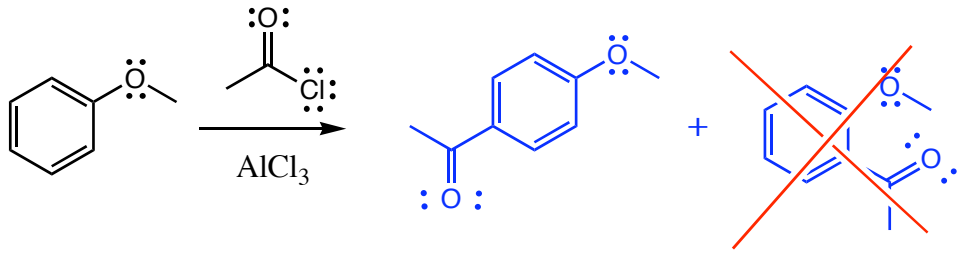
3) if the ring has a strong deactivating group, it is still too slow



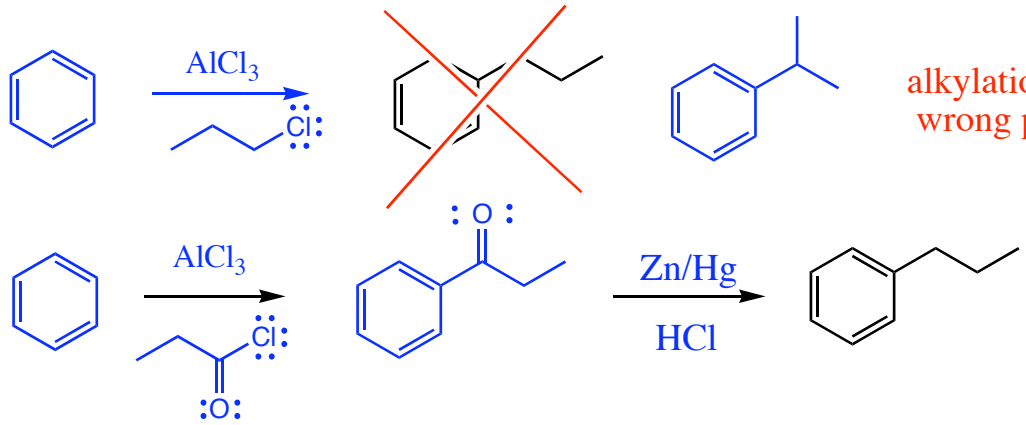
no reaction

How are acylation product distributions different from other electrophilic aromatic substitutions?

because of steric hindrance, little para product forms



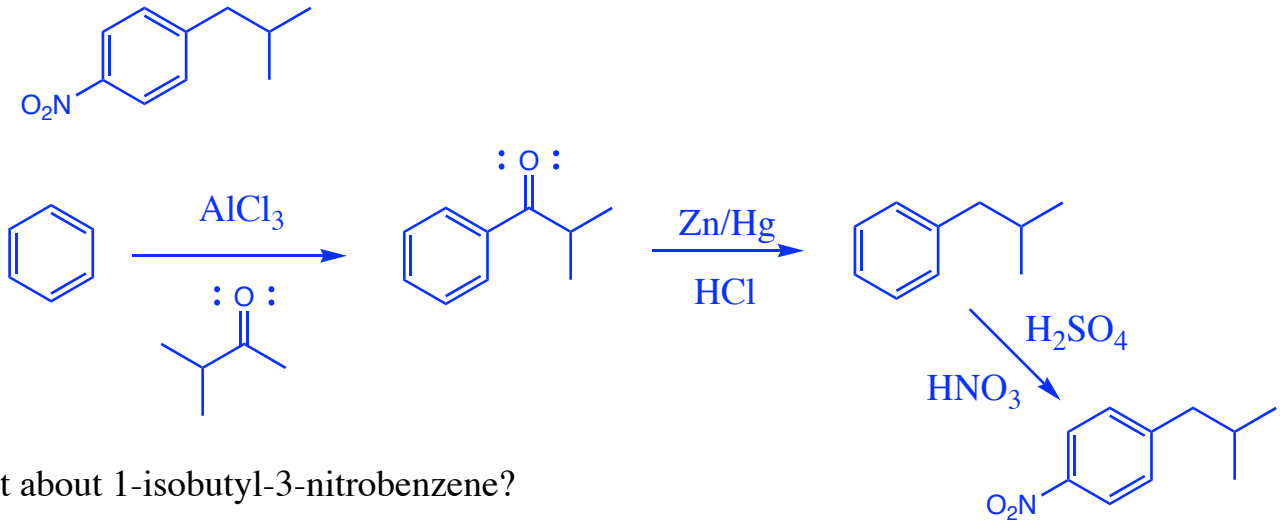
How can the Clemmenson reaction be used with Freidel-Crafts acylation to give products that could not be made with Friedel Crafts alkylation?



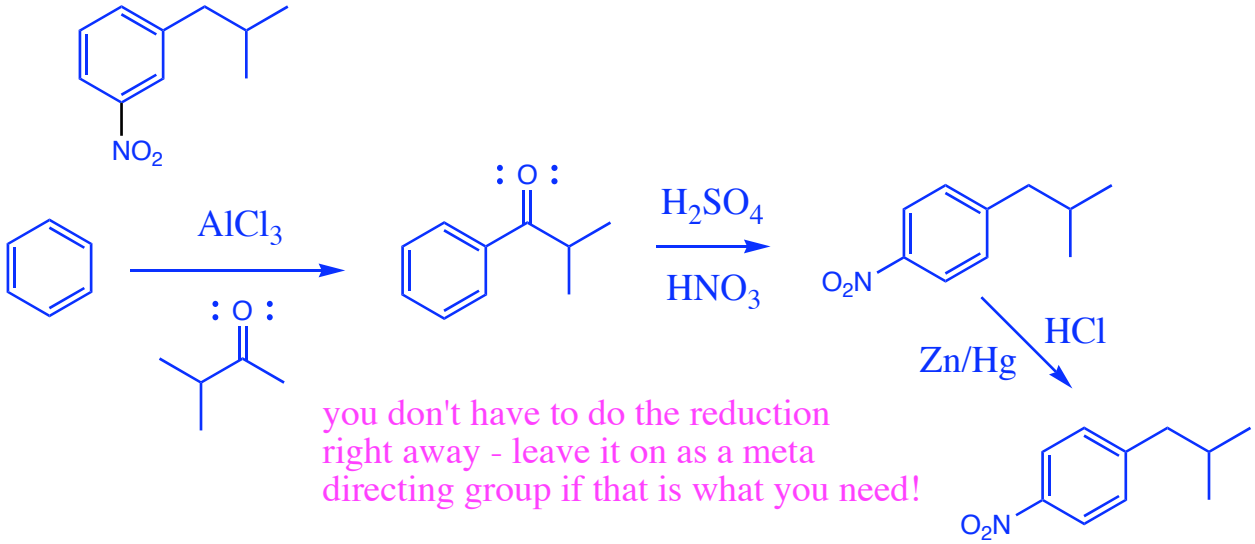
alkylation -
wrong product

use acylation, then remove C=O with Clemmensen reduction

How could 1-isobutyl-4-nitrobenzene be synthesized from benzene?

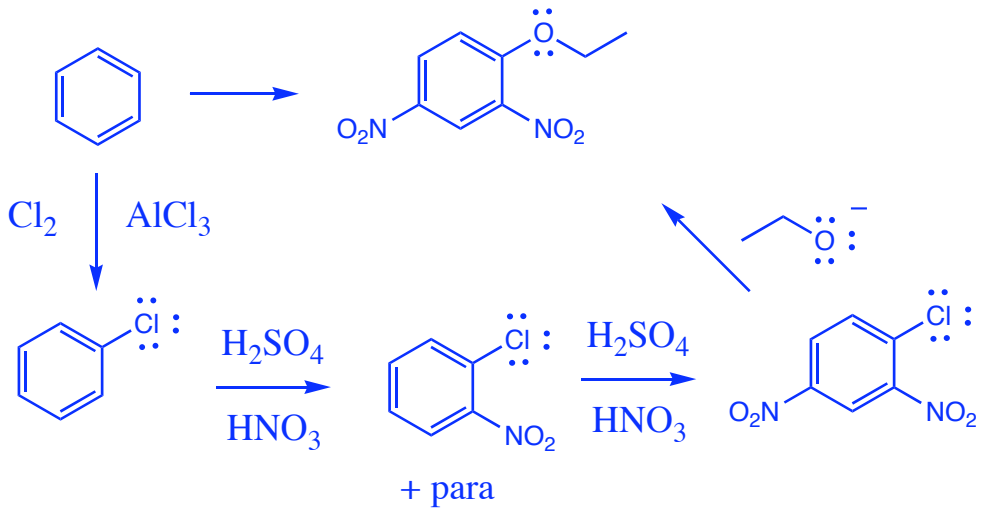


What about 1-isobutyl-3-nitrobenzene?



you don't have to do the reduction right away - leave it on as a meta directing group if that is what you need!

Synthesize 1-ethoxy-2,4-dinitrobenzene from benzene.



+ para