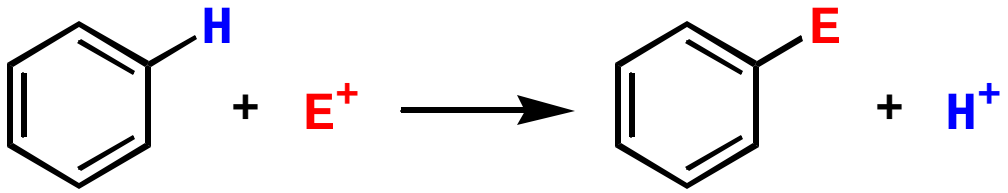
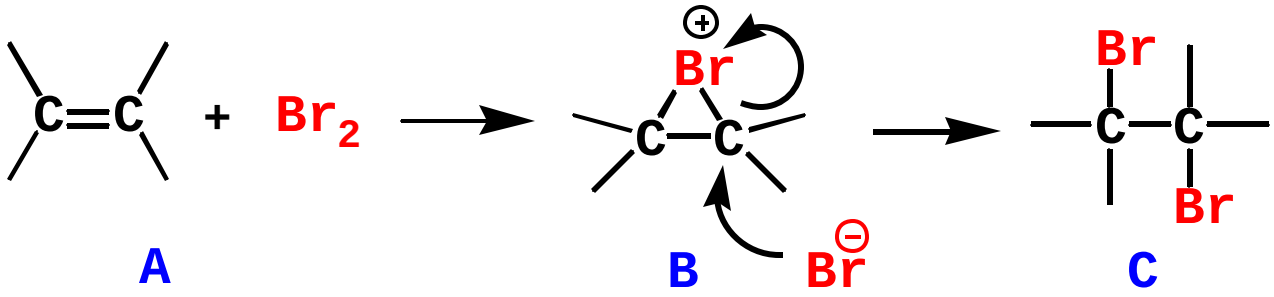
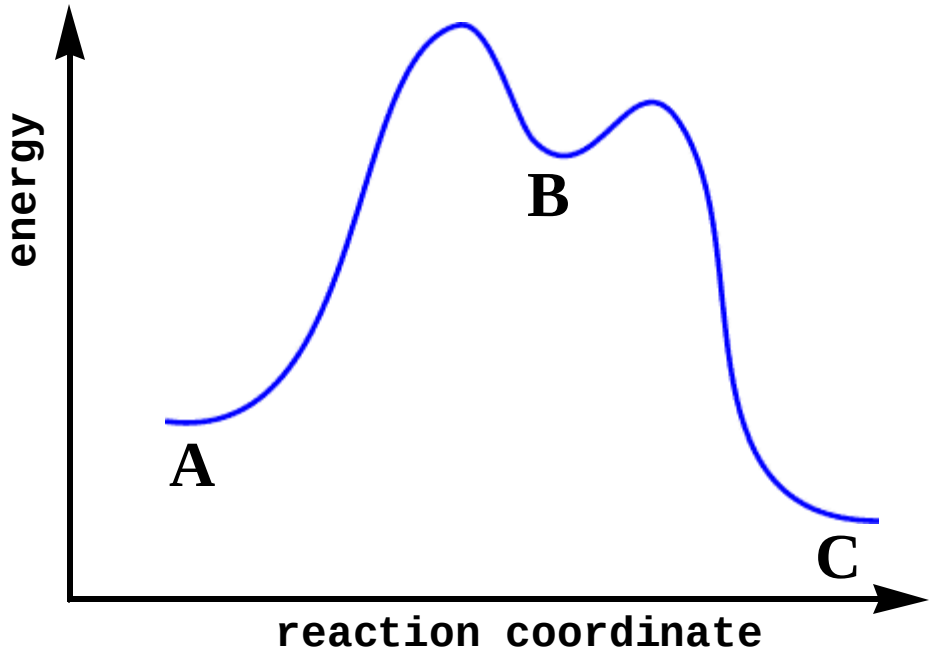
Chapter 16 - Chemistry of Benzene - Electrophilic Aromatic Substitution

Electrophilic aromatic substitution -> reaction in which hydrogen atom is replaced by an electrophile

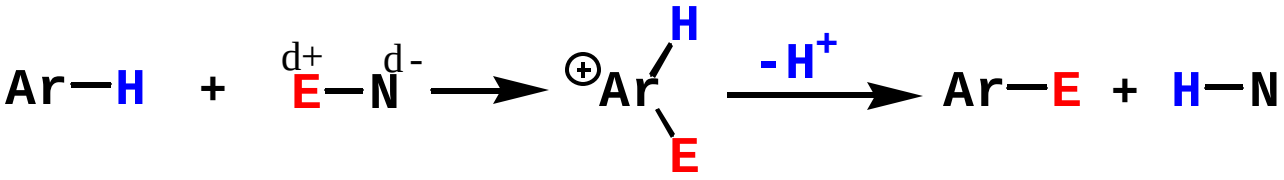


Alkenes undergo electrophilic addition reactions…



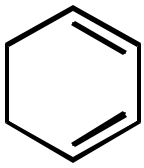


Arenes undergo electrophilic substitution reactions…



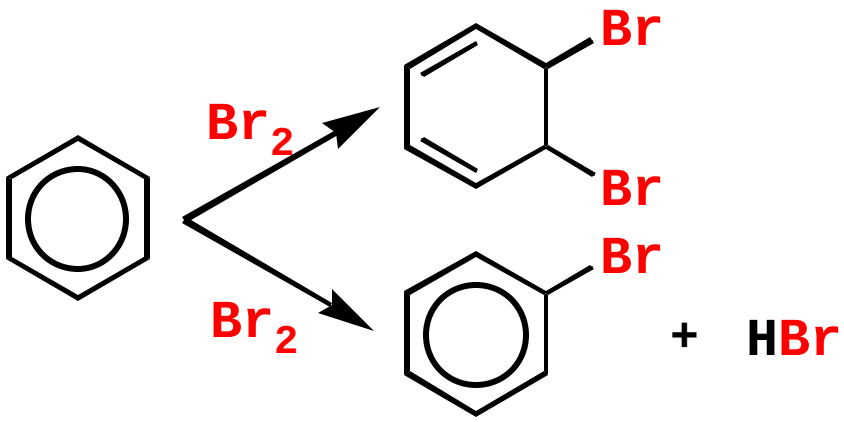
Double bonds in aromatic compounds behave differently from isolated double bonds…

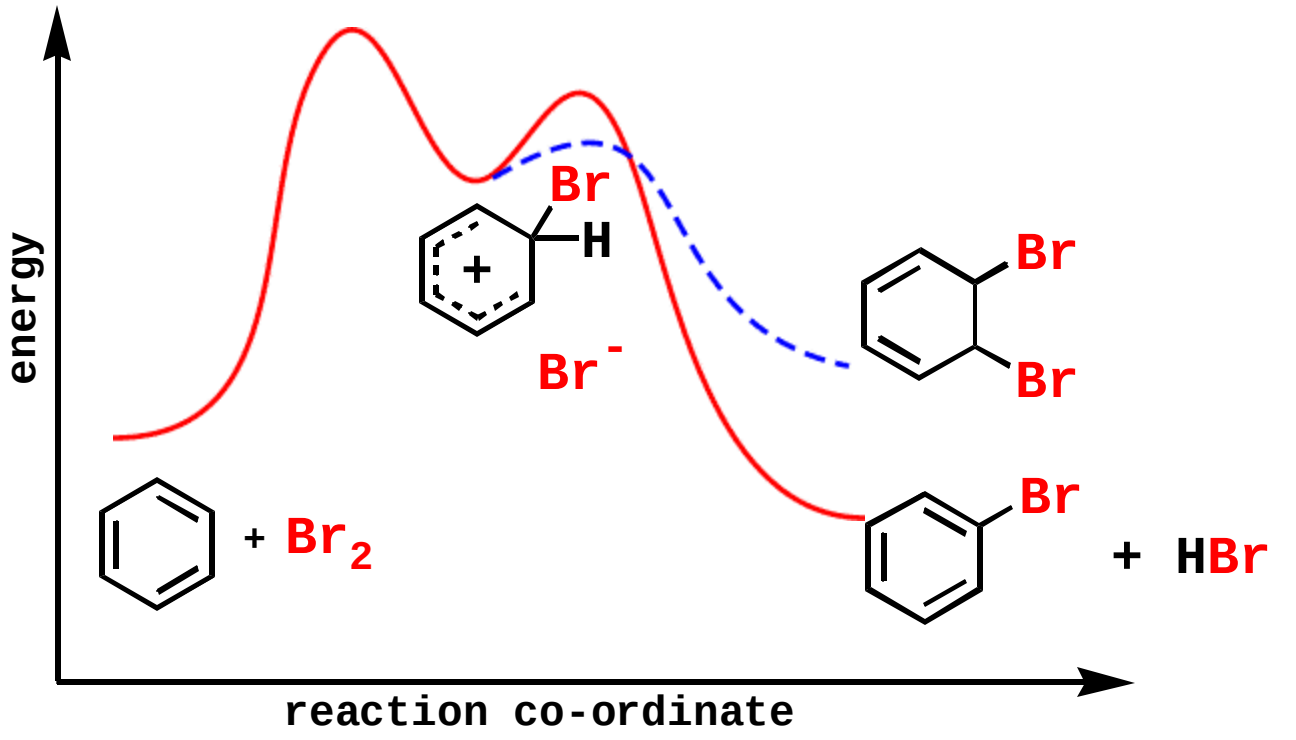
230 kJ/mol **206 kJ/mol** **<- $DH_{hydrogenation}$**



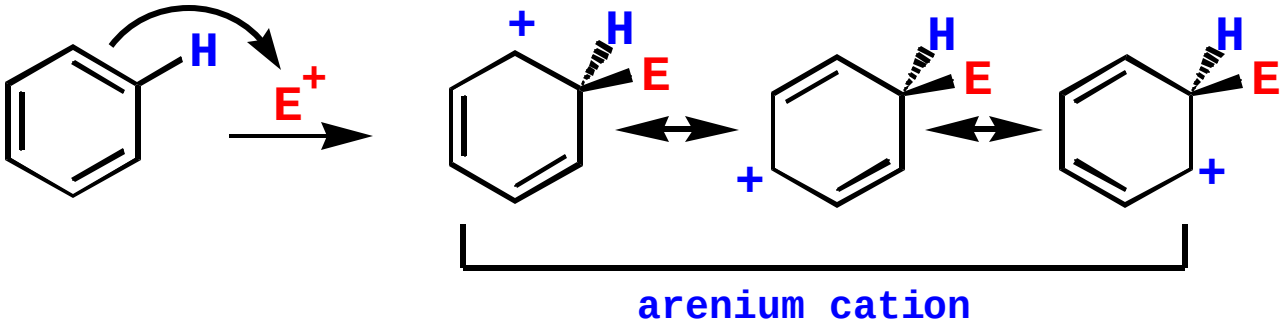
is ~24 kJ/mol less stable than benzene

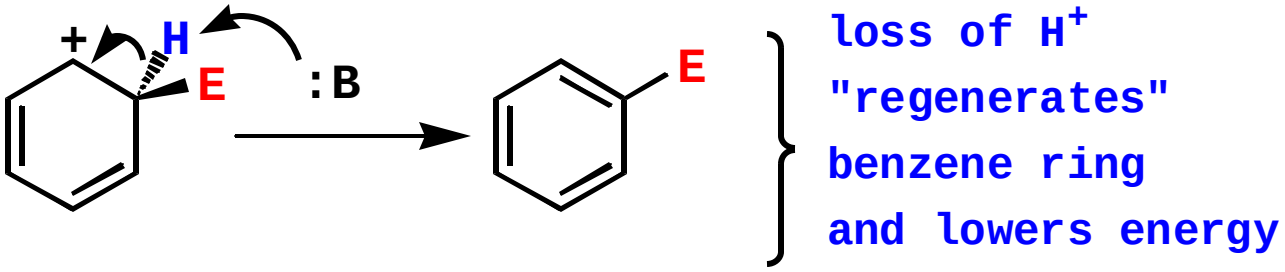
Reaction profiles for addition & substitution reactions…



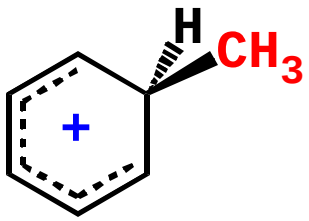


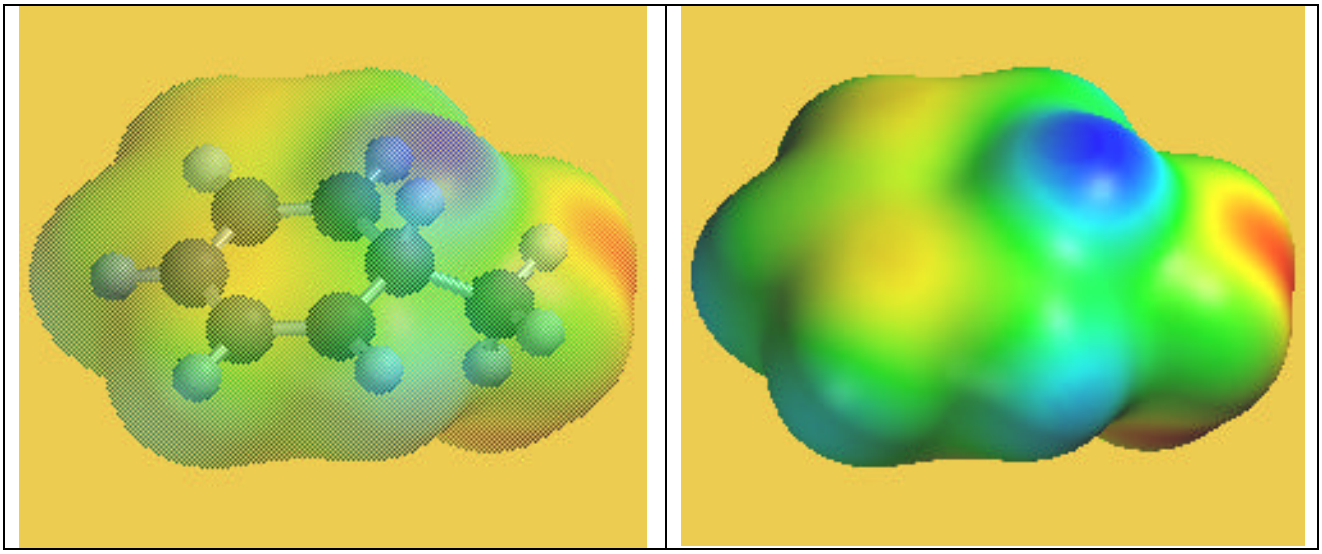
Typical substitution reaction…





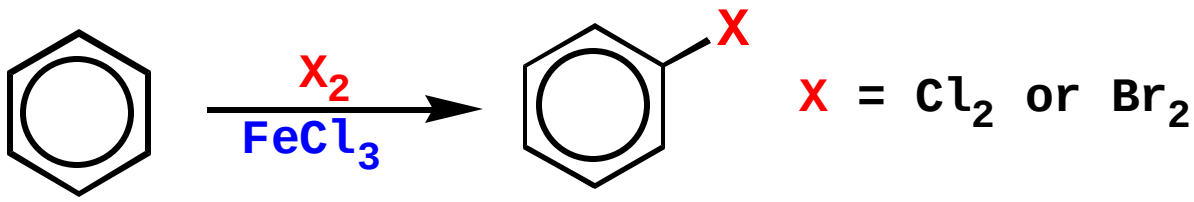
Resonance stabilized **arenium cation…**





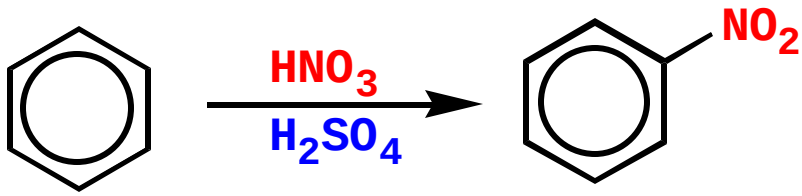
Types of electrophilic aromatic substitution rxns…

1. Halogenation…

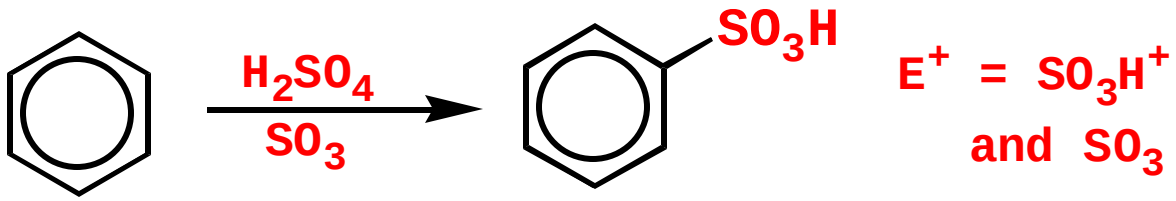


X = Cl_2 or Br_2

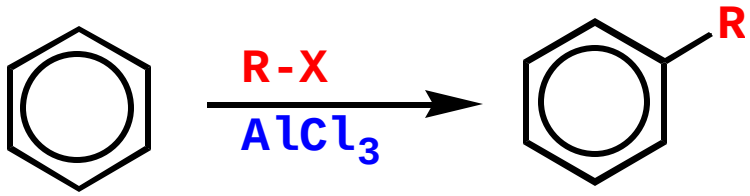
2. Nitration…



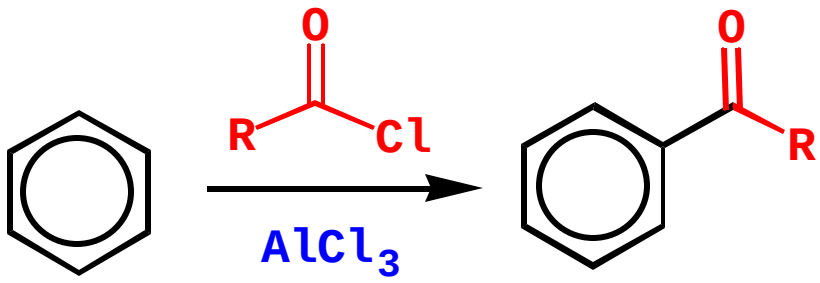
3. Sulfonation…



4. Friedel-Crafts alkylation…

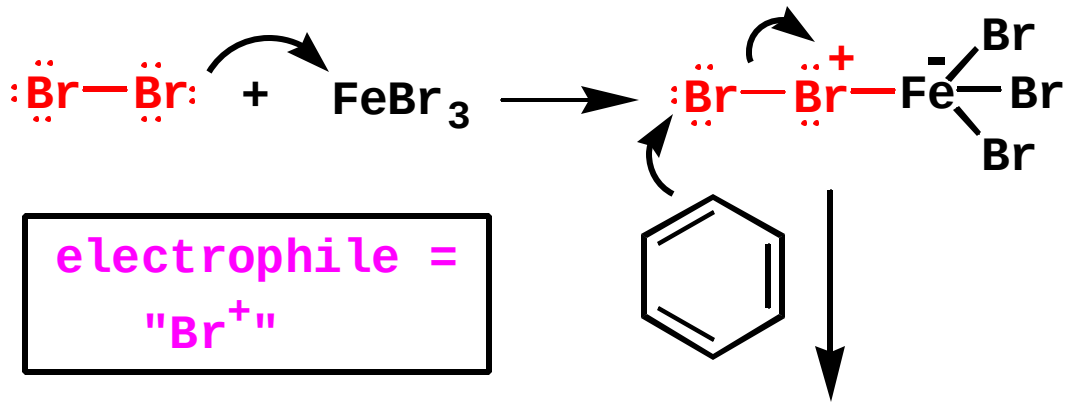


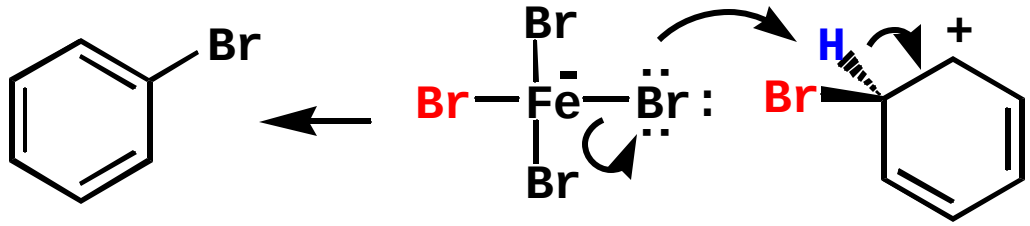
5. Friedel-Crafts acylation…



Mechanisms…

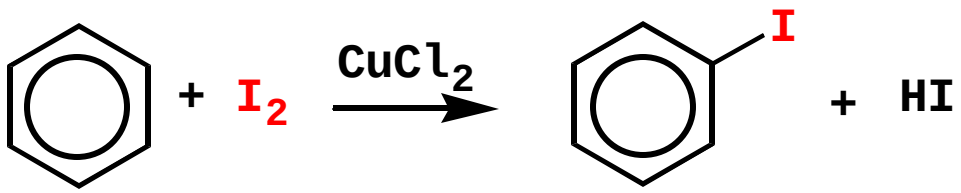
1. halogenation (Cl_2 and Br_2)





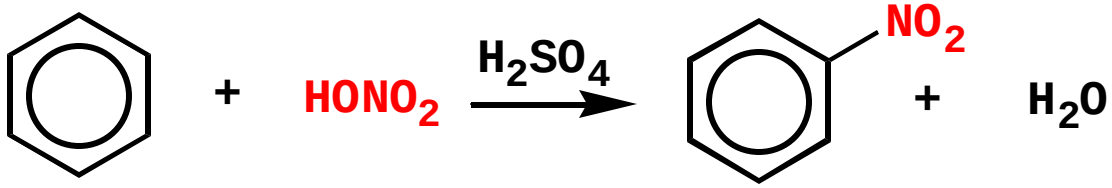
+ $FeBr_3$ + H-Br

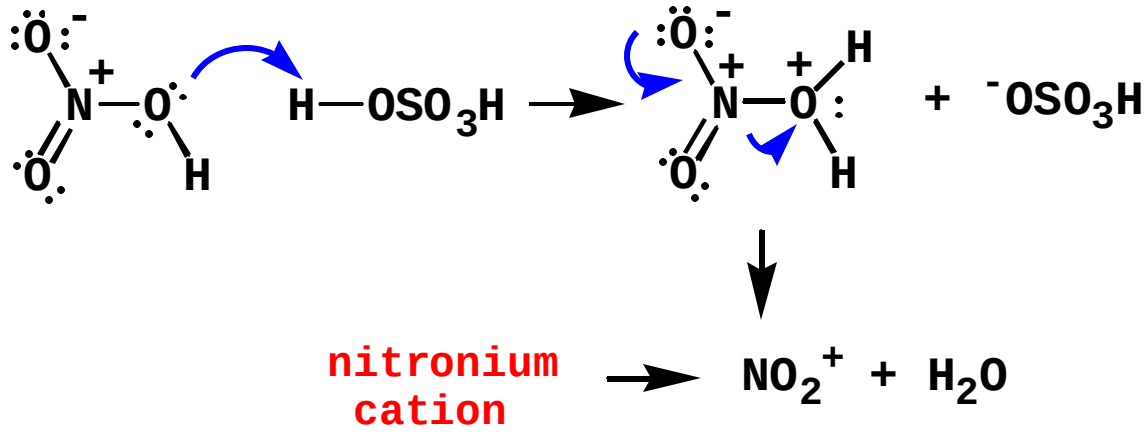
iodination is a bit different…



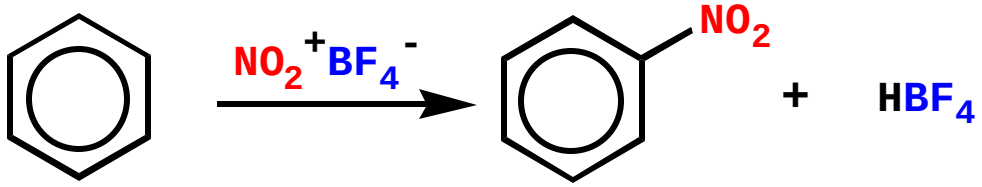
1/2 I_2 + Cu^{++} ⟶ "I^+" + Cu^+

2. Nitration…

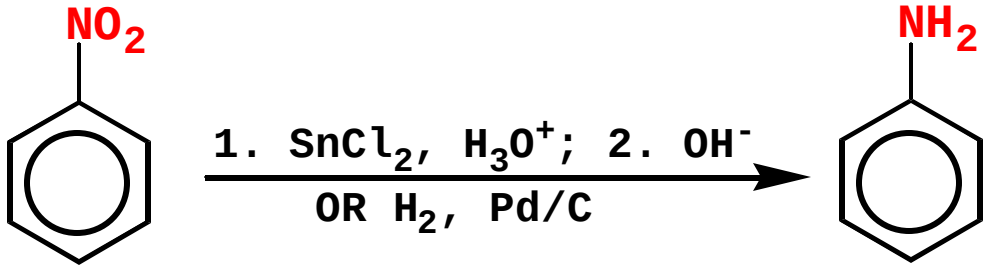




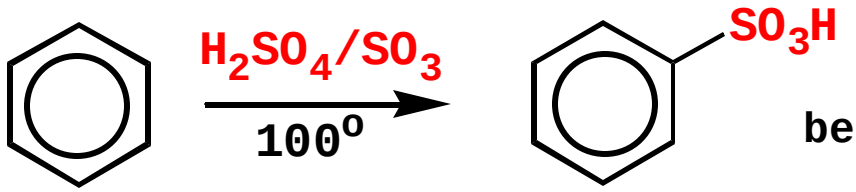
Alternative reagent is nitronium tetrafluoroborate…



There isn't a way to directly substitute $-NH_2$ and produce aniline, but NO_2 can be reduced to NH_2…



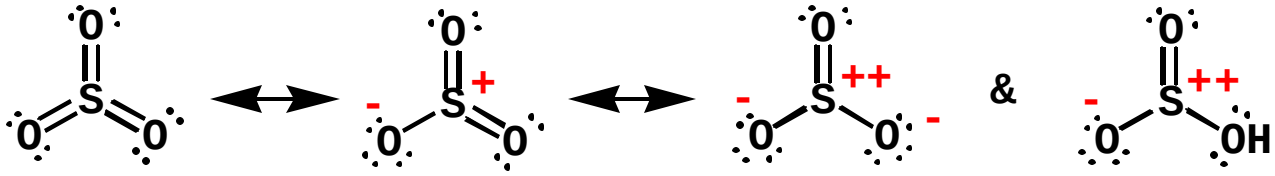
3. Sulfonation…



benzenesulfonic acid

fuming sulfuric acid (oleum) = $H_2SO_4 + SO_3$

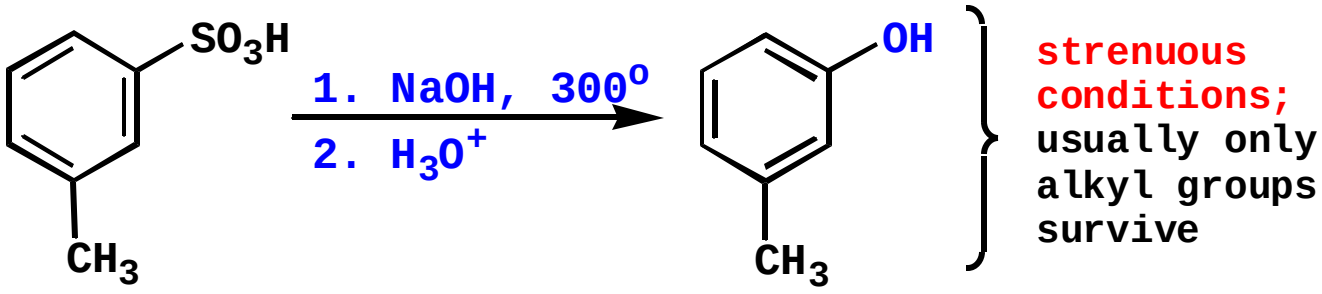
Mechanism -> both SO_3 and SO_3H+ are possible electrophiles -> how to they work?…



The reaction is reversible.

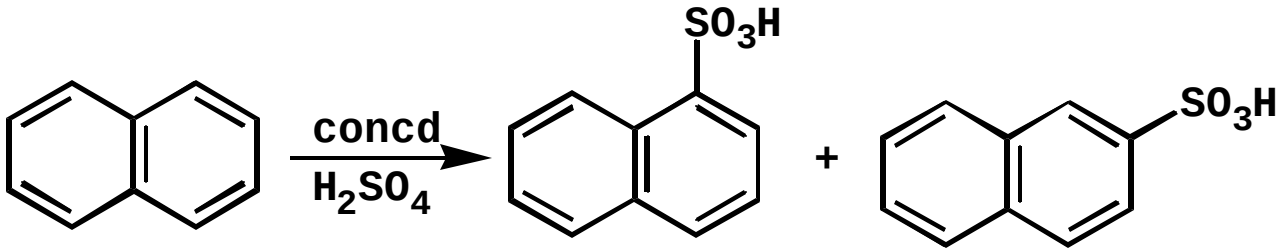
$Ar\text{-}SO_3H + H_2SO_4$, H_2O, D -> Ar-H.

SO_3H can be replaced with OH.



strenuous conditions; usually only alkyl groups survive

Sulfonation of naphthalene provides an example of a kinetic vs thermodynamic control reaction…

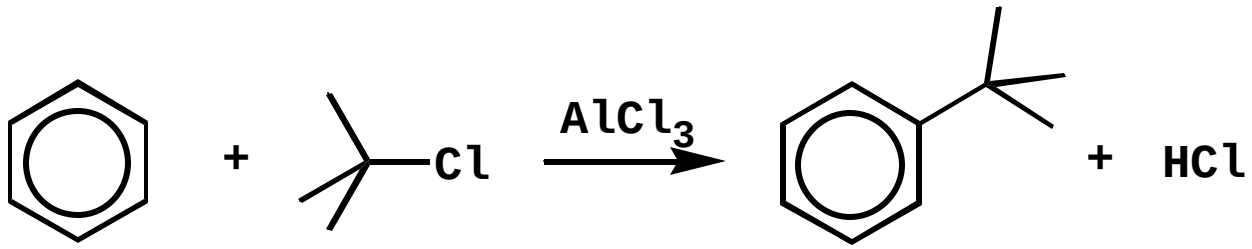


T = 0-40o -> 85% 15%

160o

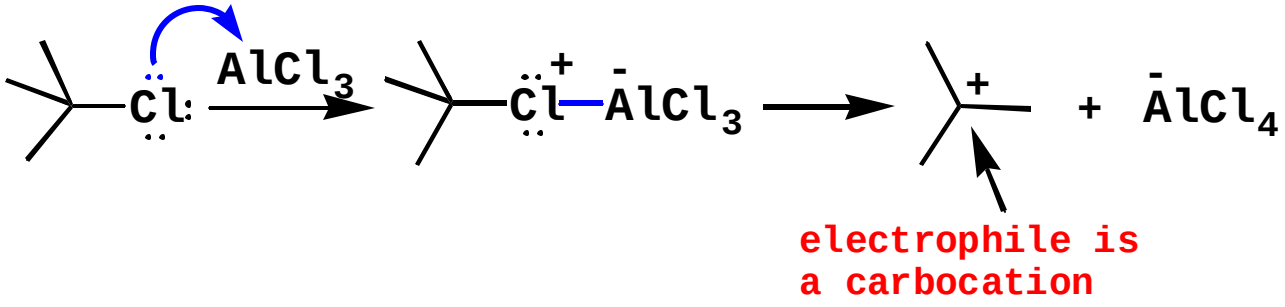
160o 15% 85%

4. Friedel-Crafts alkylation…



(excess)

Mechanism…

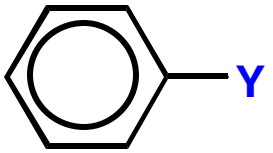


F-C limitations…

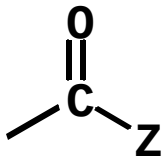
1. R-X must be C(sp^3)-X; C(sp^2)-X doesn't work

do not react with $AlCl_3$ to give electrophiles

2. no reaction if the aromatic ring contains strong electron withdrawing or amino substituents

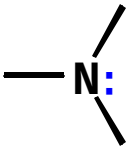


Y = $-NO_2$, $-SO_3H$, $-C\equiv N$



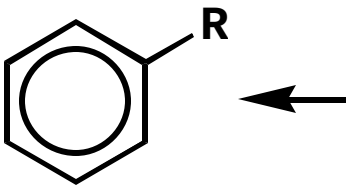
(Z = H, R, OH, OR)

N coordinates with $AlCl_3$

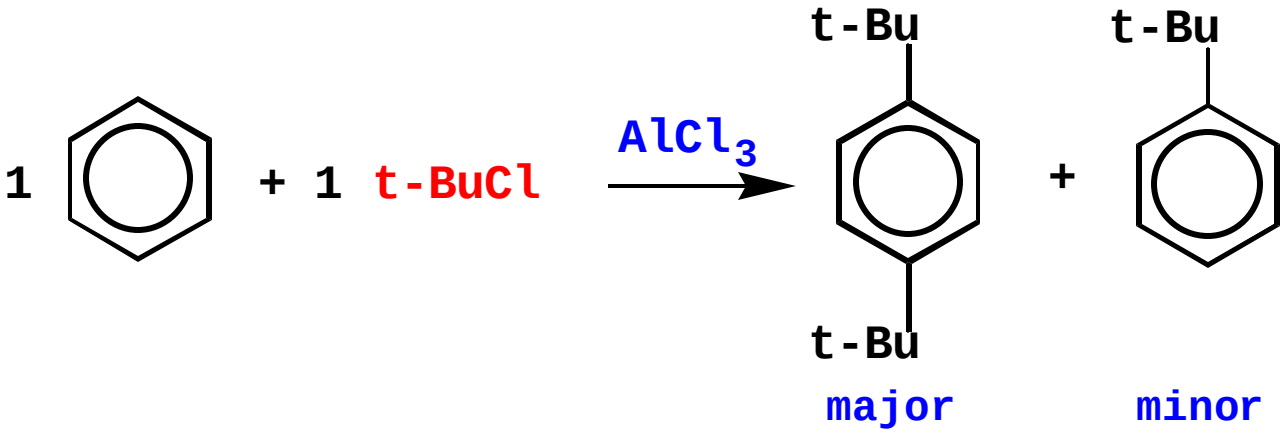


($-NH_2$, $-NHR$, $-NR_2$)

3. multiple substitution (alkyl groups activate the ring to EAS)…

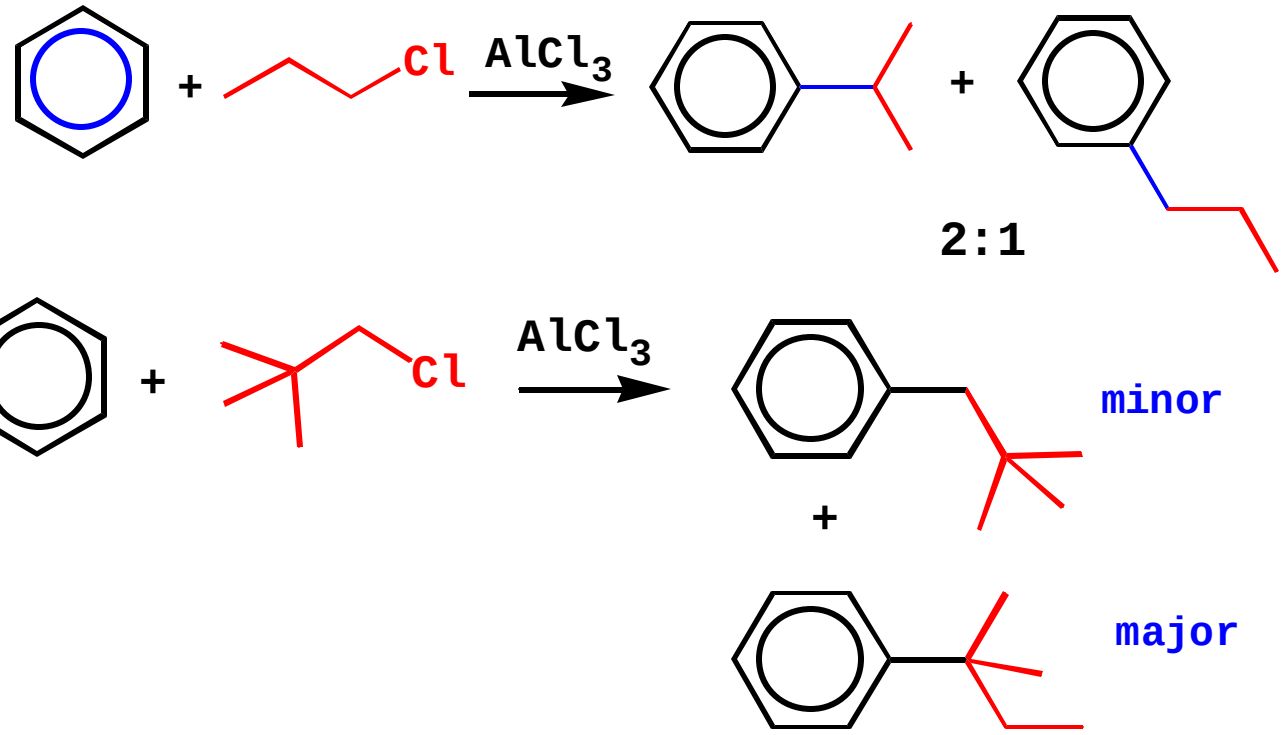


more reactive than benzene to EAS

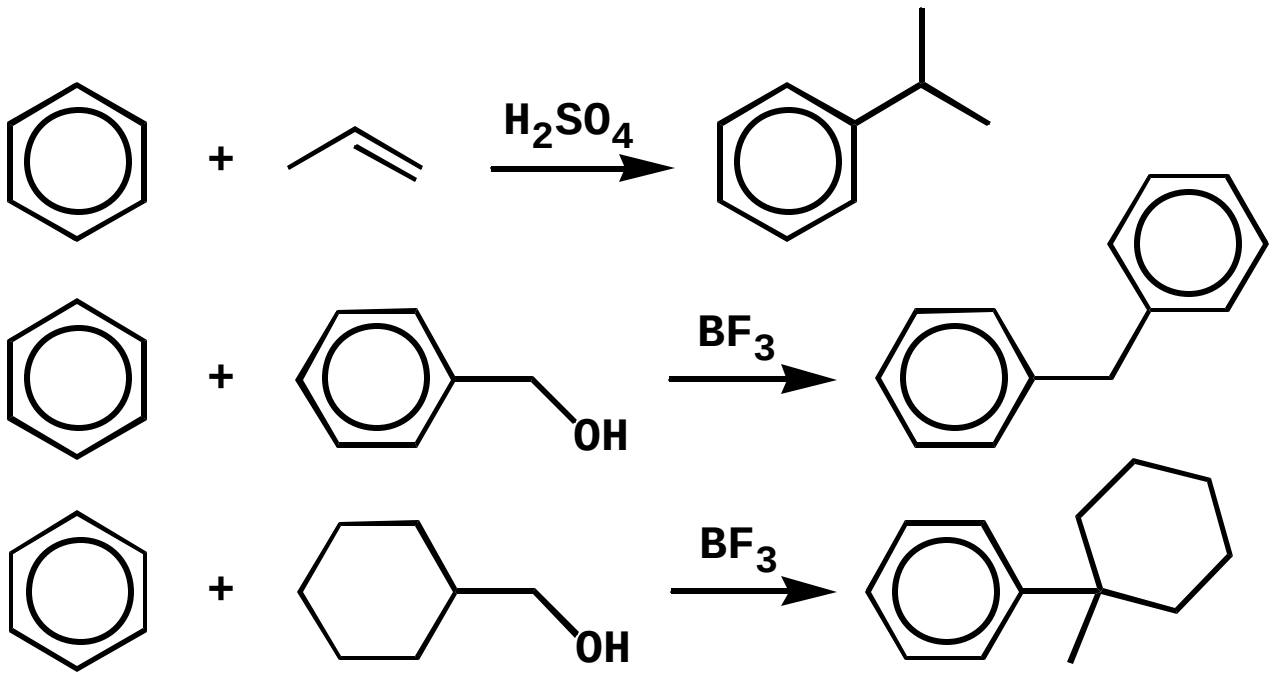


major minor

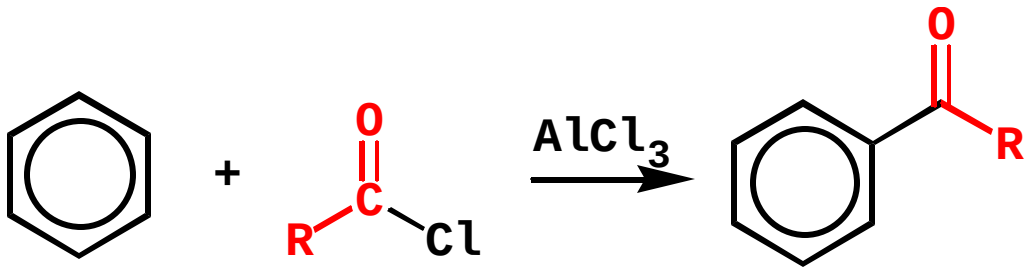
4. carbocation rearrangements…



alkenes and alcohols can also function as sources of carbocations ~ electrophiles

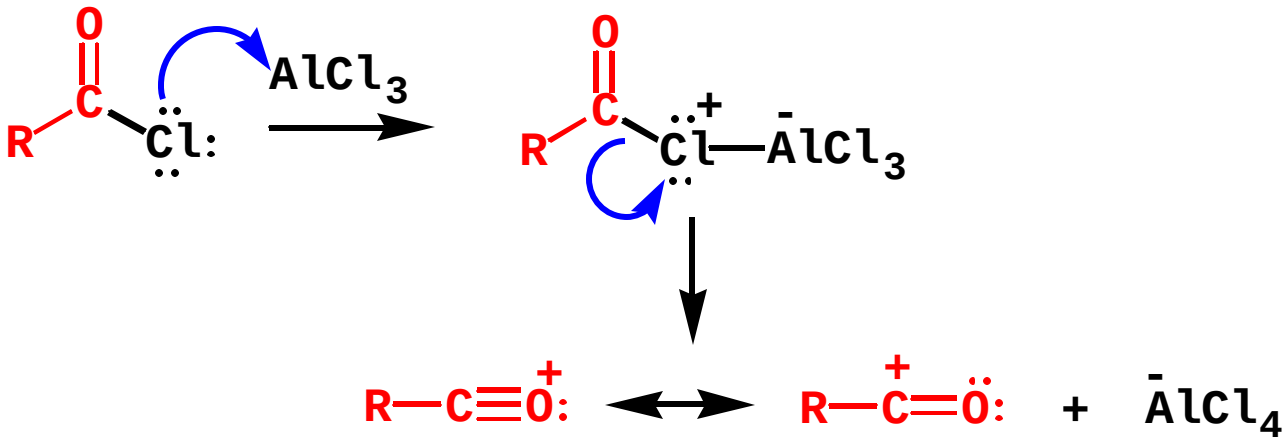


5. Friedel-Crafts acylation…

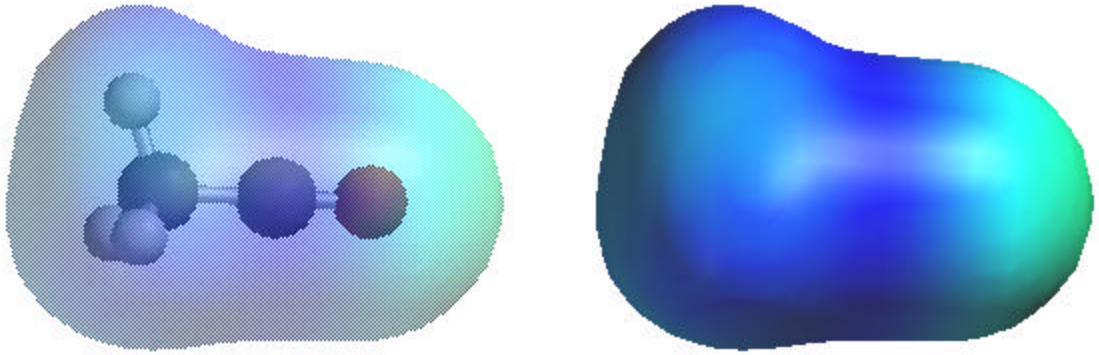


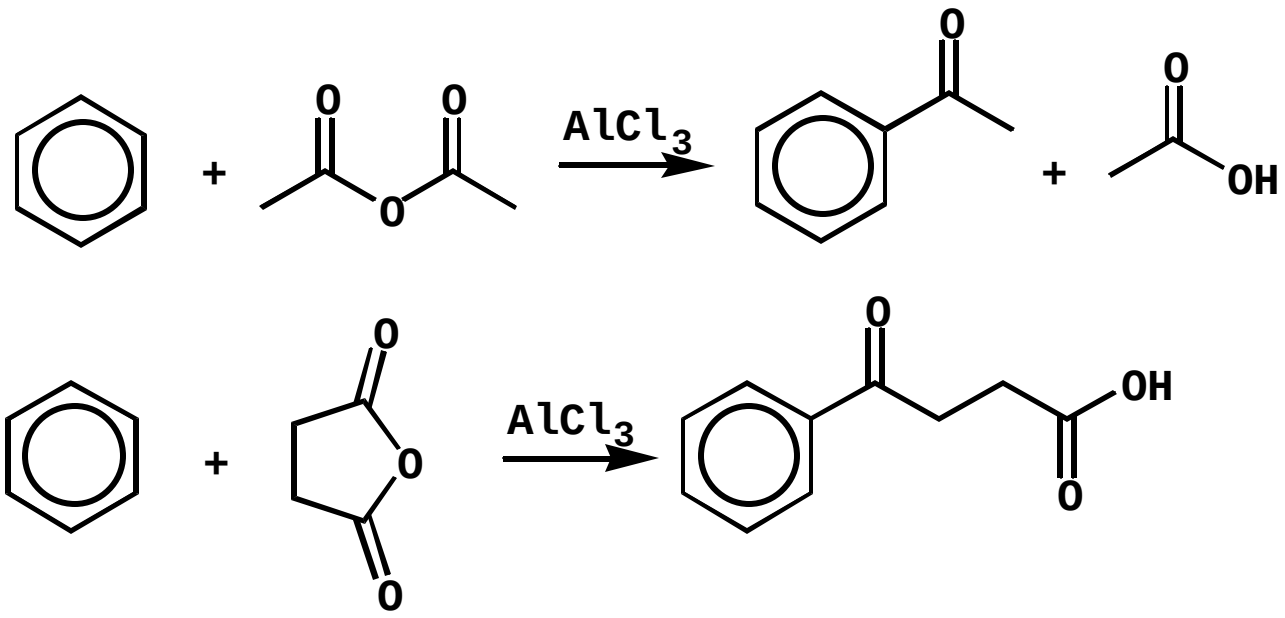
advantages over alkylation -> no rearrangement and product is less reactive than benzene.

mechanism…

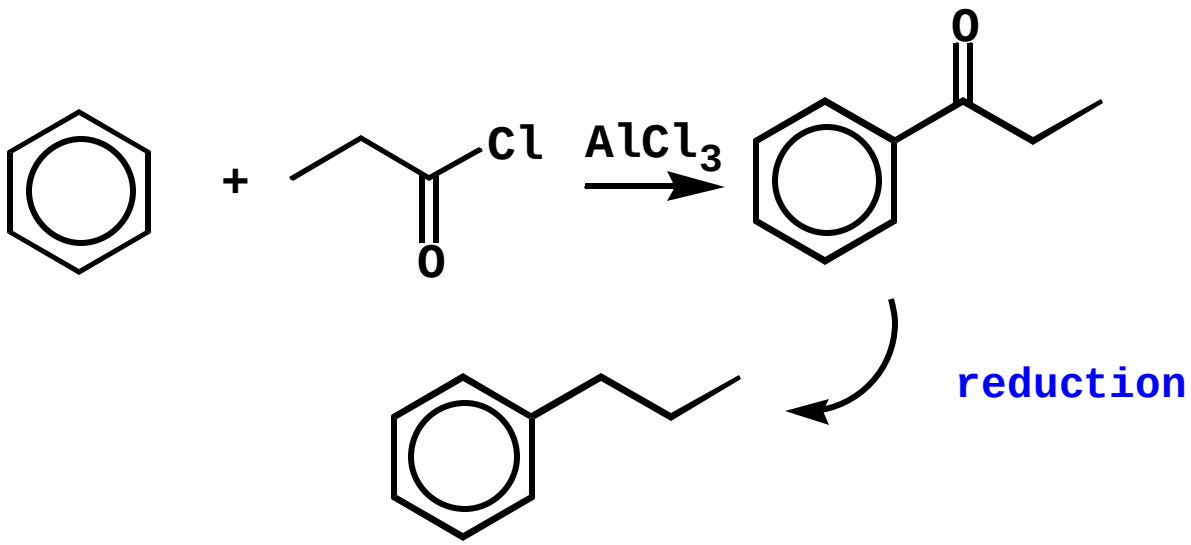


acyl/acylium cation





*Reduction of aryl ketones…



possible reduction methods:

1. H_2, Pd/C (does not work for Ar-C(=O)-Ar)
2. Clemenson -> Zn-Hg/HCl
3. Wolff-Kishner -> NH_2NH_2, OH^-, DMSO, D

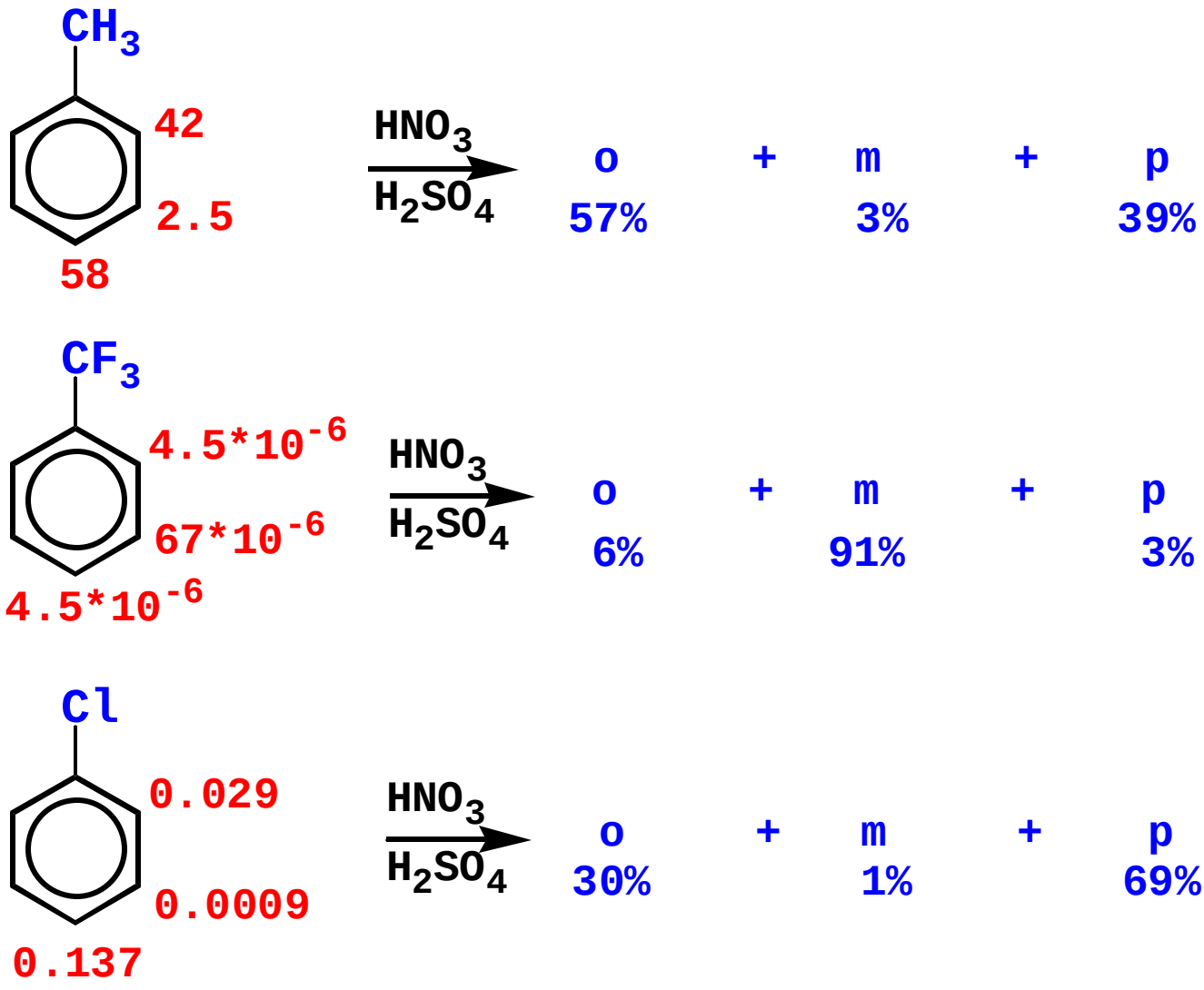
**Substituent effects…

How does an aromatic ring substituent influence EAS reactivity and regiospecificity for a new electrophile?

Some examples…

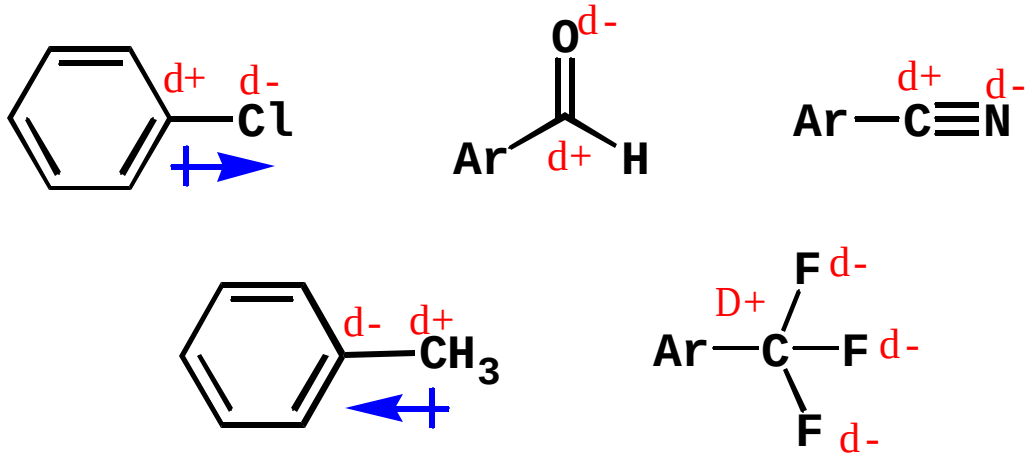
RED = relative position reactivity

BLUE = %'s of o, m, p-products

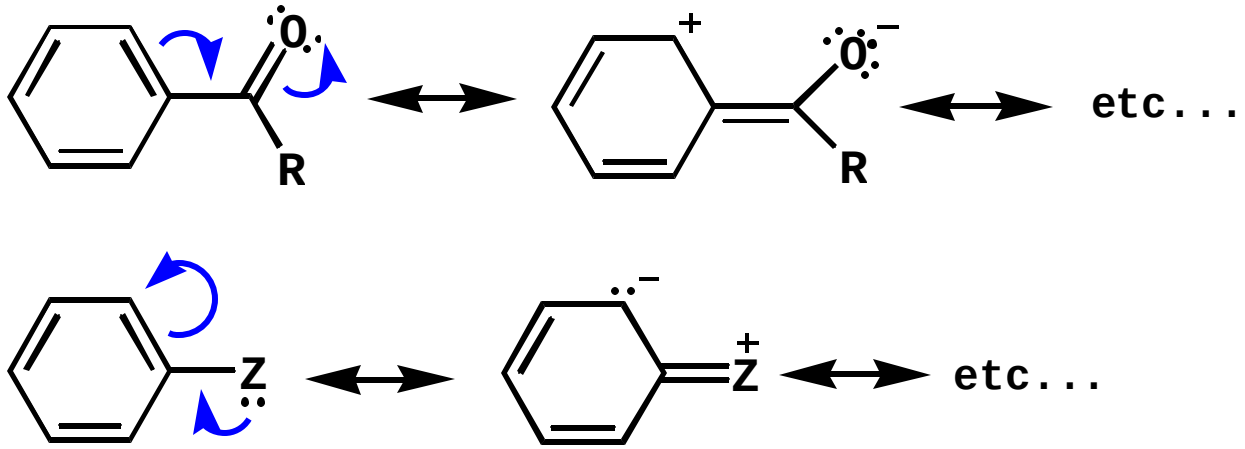


A substituent can influence the electron density in an arene by both inductive and resonance effects.

1. inductive effects -> essentially caused by polarization of the Ar-Z bond…



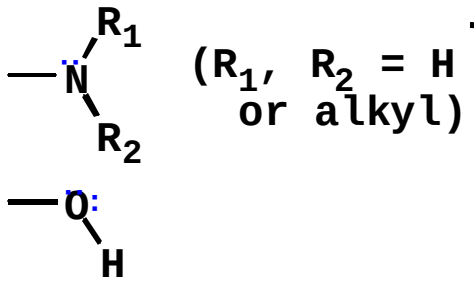
2. resonance effects…



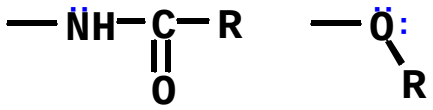
Substituents can have both resonance and inductive effects -> generally, resonance more important than inductive effects in determining regiospecificity

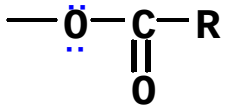
Common Substituents in EAS Reactions

Very strongly activating...



Strongly activating...





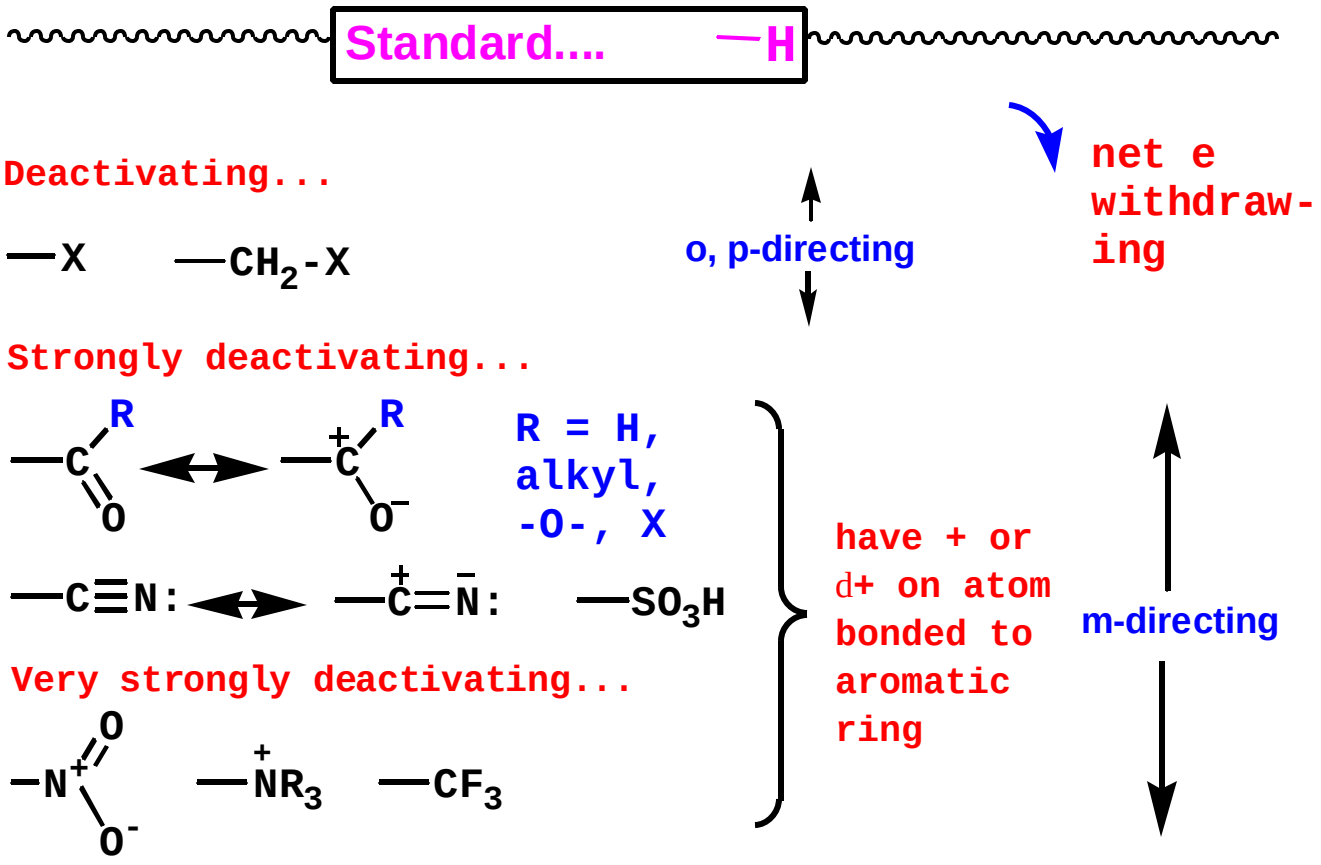
all have unshared e-pairs on the atom bonded to aromatic ring

o, p-directing

Activating...

net e donating

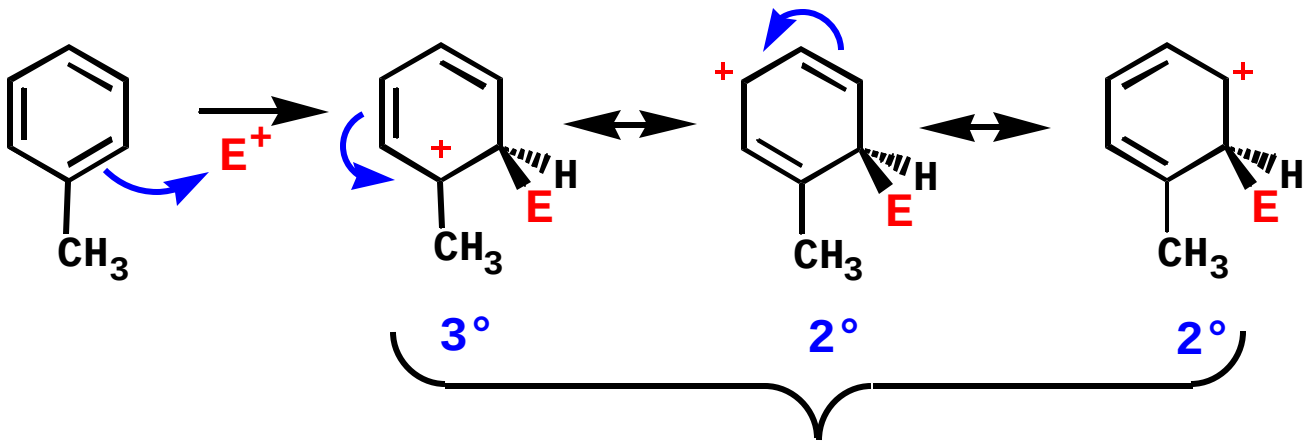
Standard.... —H


Standard.... —H
net e withdraw-ing
Deactivating...
—X —CH2-X
o, p-directing
Strongly deactivating...
R = H, alkyl, -O-, X
—C≡N: —SO3H
have + or d+ on atom bonded to aromatic ring
m-directing
Very strongly deactivating...
—NR3 —CF3

Substituents effects -> explained…

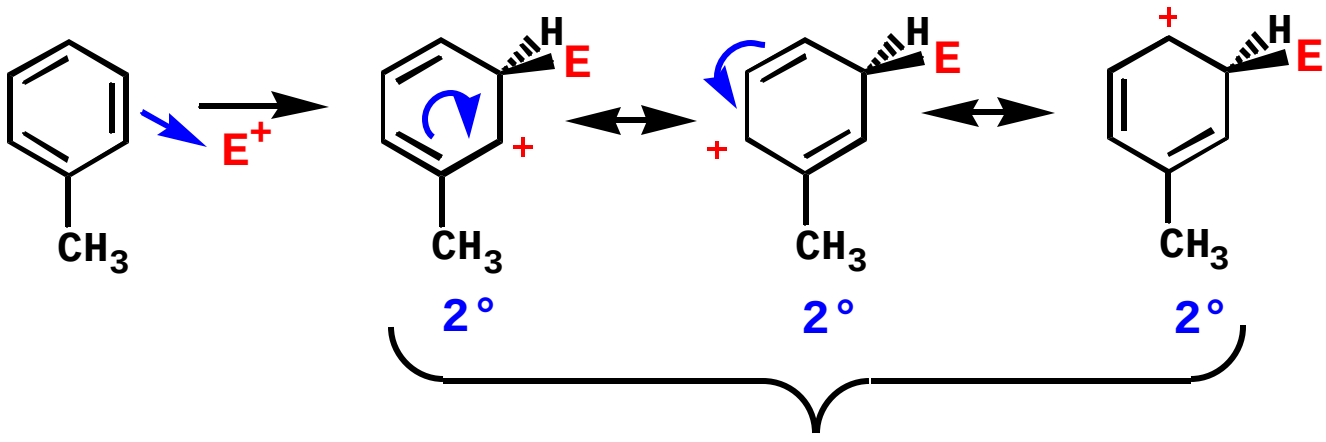
KEY FACTOR -> stabilization of the intermediate arenium cation

case # 1: o, p-directing substituent and o-substitution…



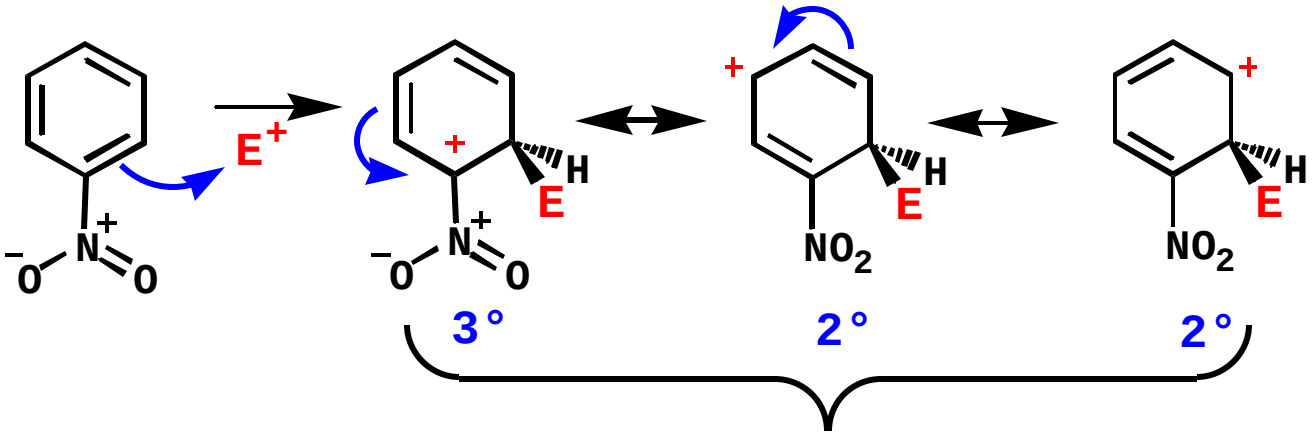
*resonance structures for arenium cation arising from o-addn;
*p-addn also gives one 3° & two 2°

case # 2: o, p-directing substituent and m-substitution…



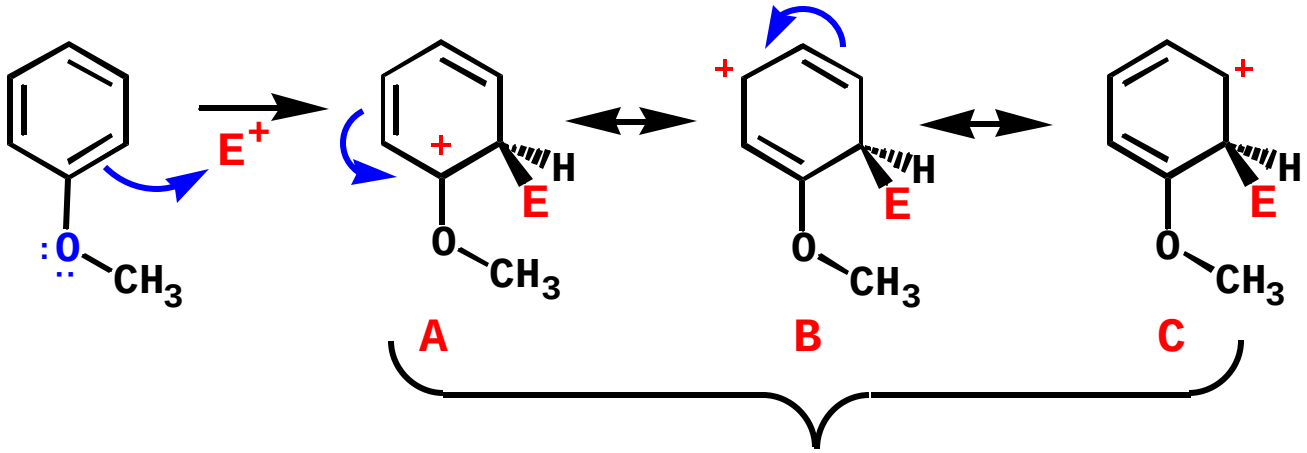
*resonance structures for arenium cation arising from m-addn;
*all three structures are 2°

case # 3: m-directing substituent and o-substitution…



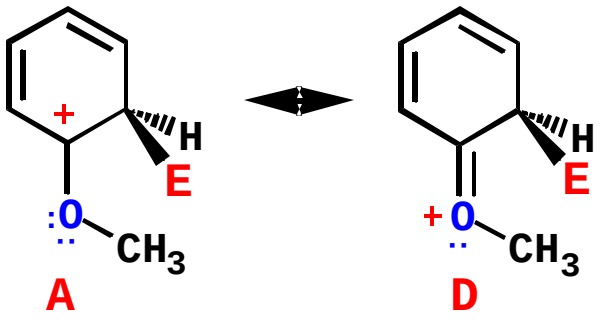
*resonance structures for arenium cation arising from o-addn;
*p-addn also gives one 3° & two 2°;
*3° structure is very high energy (+ charges on adjacent atoms) & makes a very small contribution to resonance hydrid

case # 4: o, p-directing substituent with unshared e-pairs on atom bonded to aromatic ring...



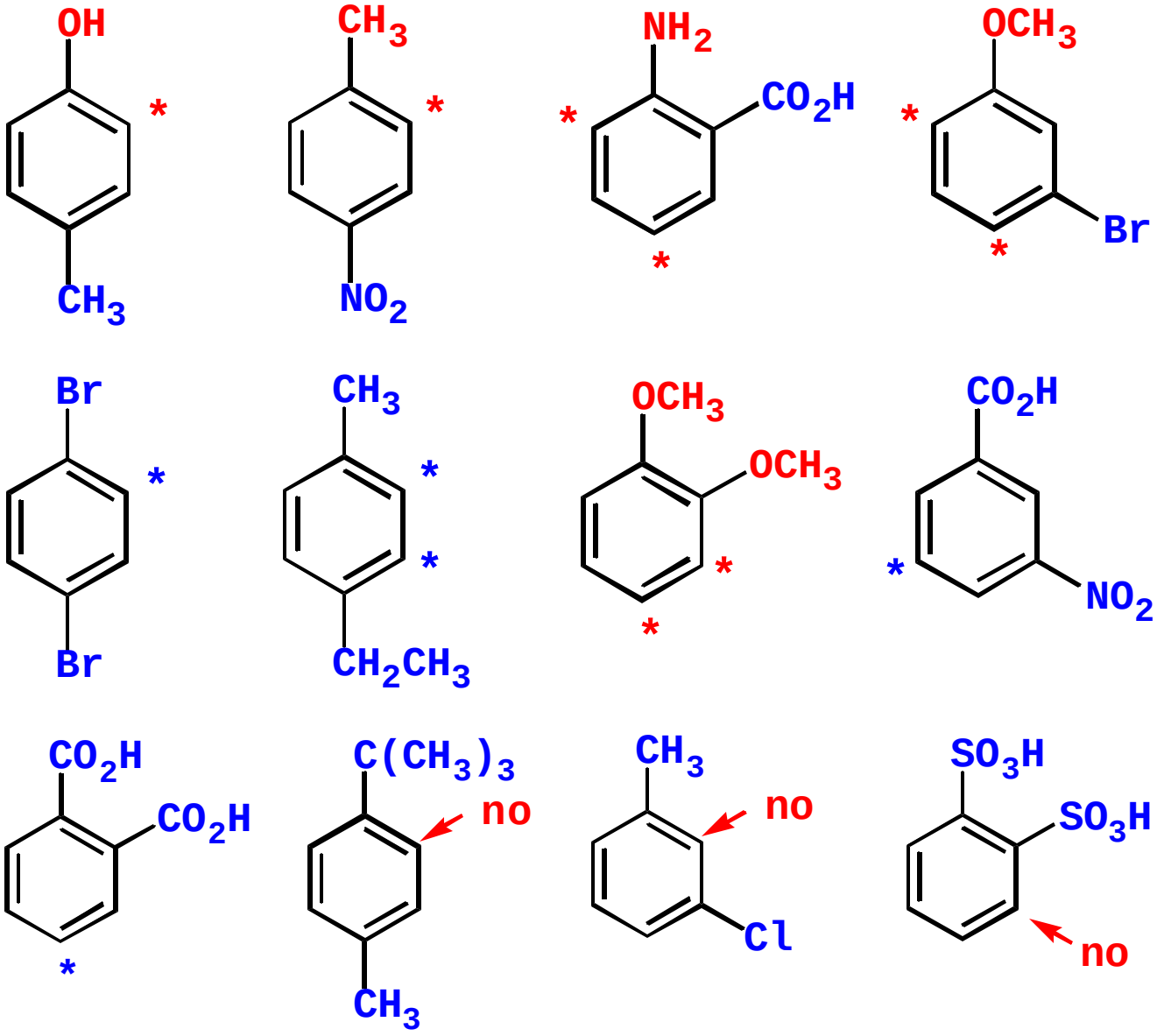
*resonance structures for arenium cation arising from o-addn;
*p-addn also gives one 3° & two 2°;
*these 3 structures (A - C) are essentially identical to those written for toluene

Important -> one more resonance structure (D) can be written if the bonded atom has an unshared e-pair; delocalization of the + charge is now over 4 atoms (3 C's in ring & external hetero atom)

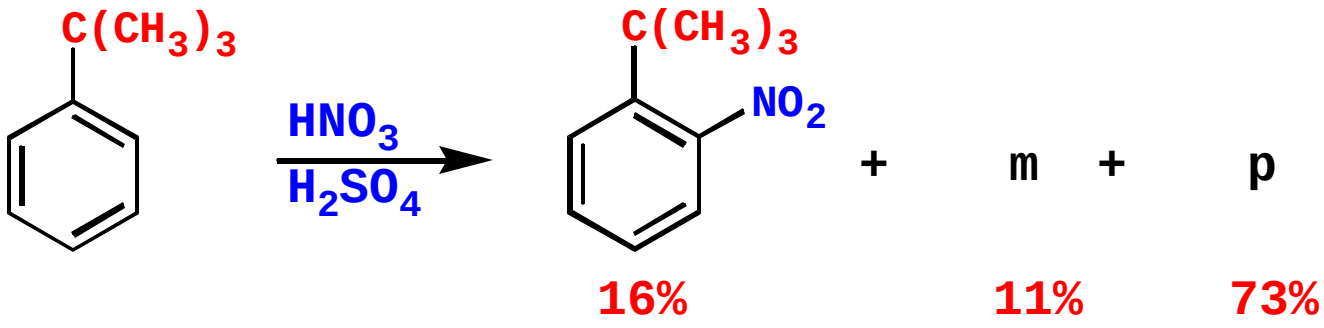


Substitution of disubstituted benzenes -> additivity of effects

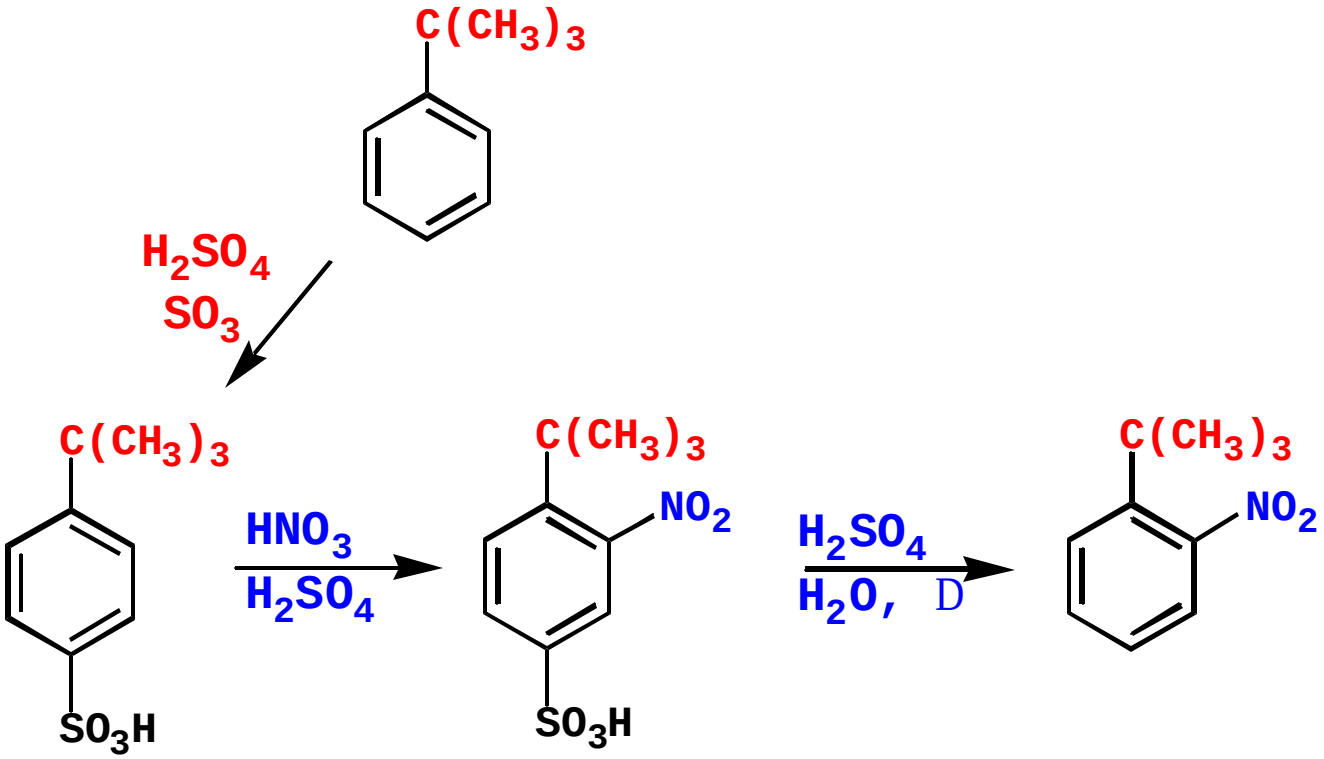
most powerful activator controls position of attack; steric factors of secondary importance



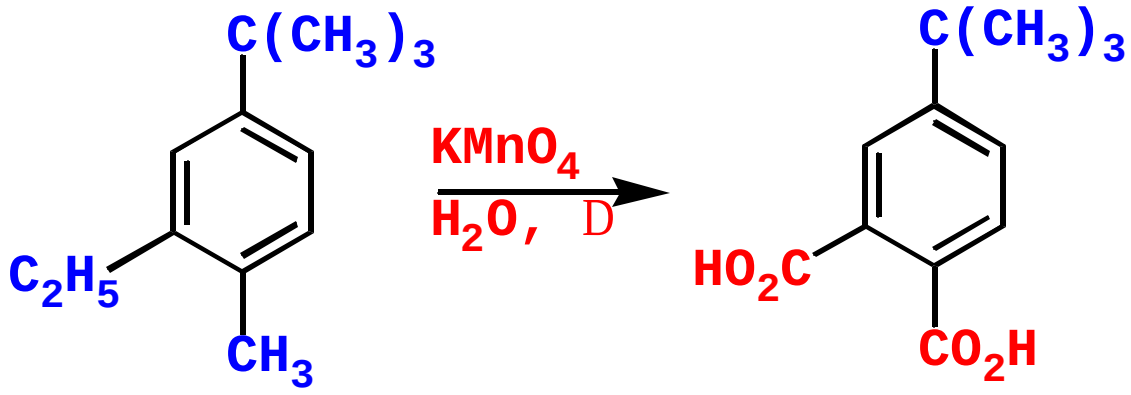
An example of the utility of reversible sulfonation…



How can the yield of *ortho* be increased?

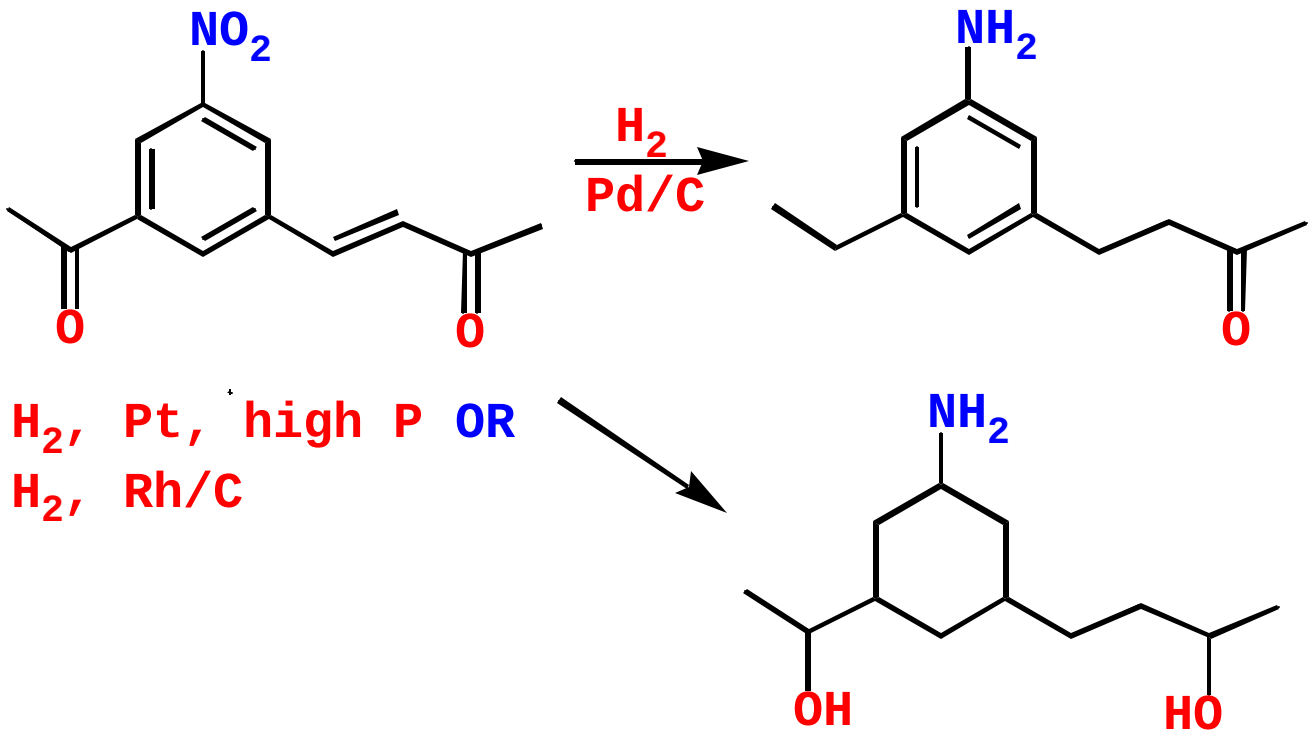


Side chain oxidation -> despite "unsaturation," arenes are resistant to strong oxidizing agents such as $KMnO_4$ and $Na_2Cr_2O_7$.

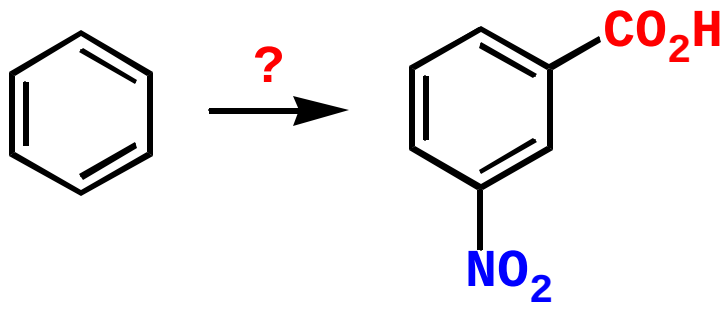


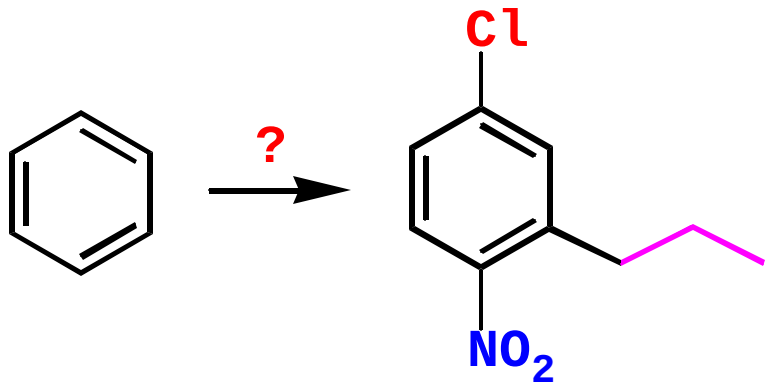
Note: side chain oxidation requires a-C to be bonded to at least one H or O

Reductions -> arenes are resistant to reduction

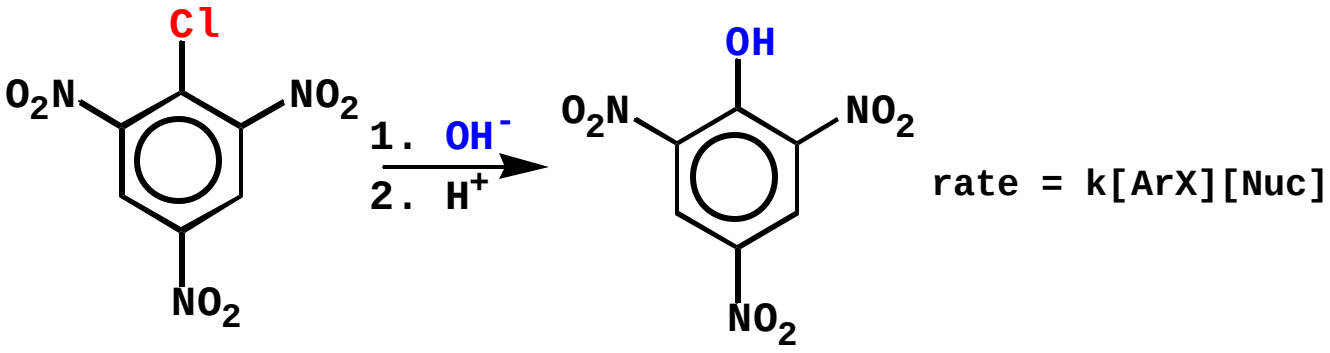


Some synthetic examples…



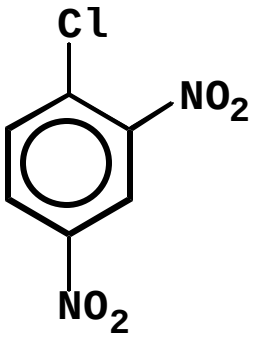


Nucleophilic aromatic substitution…

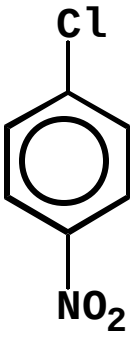


rate = k[ArX][Nuc]

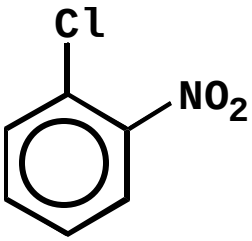
Relative reactivities to $NaOCH_3$, CH_3OH, 50°…



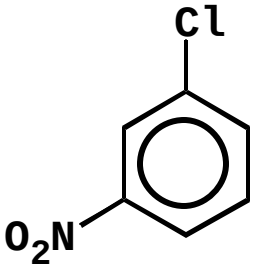
115,000



3.4



1.0



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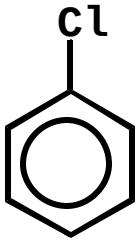
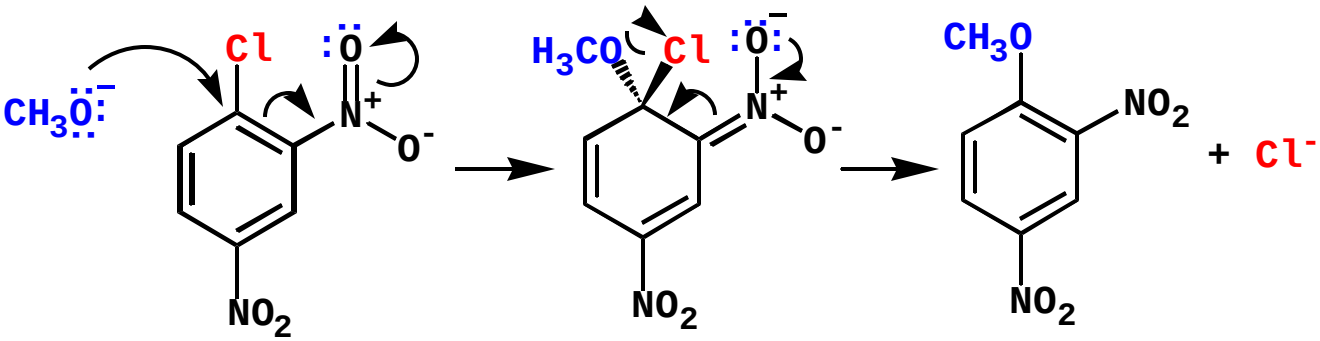
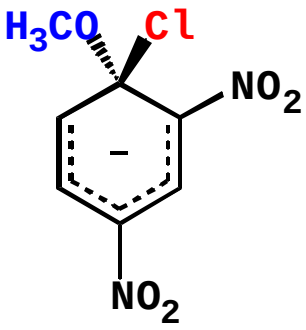


0

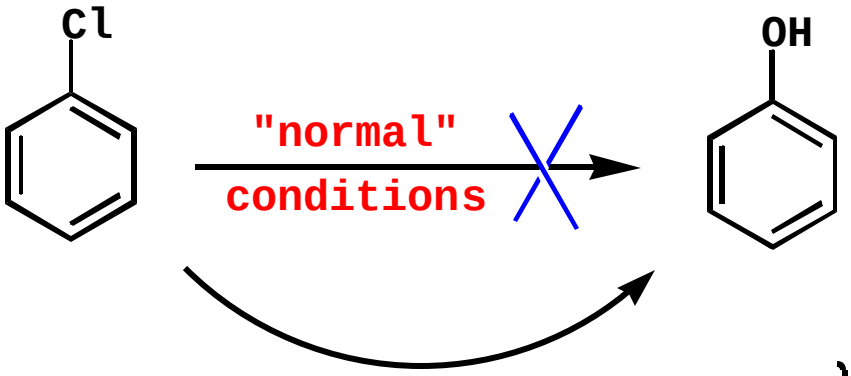
Mechanism…must have o or p-NO_2 to soak up – charge





Meisenheimer complex

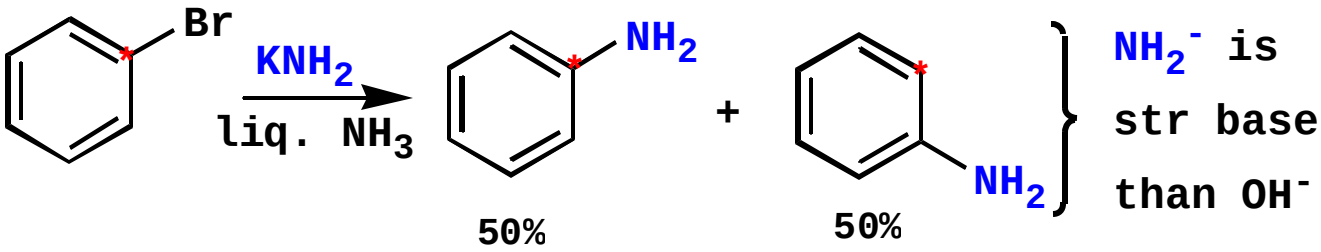
Benzyne…

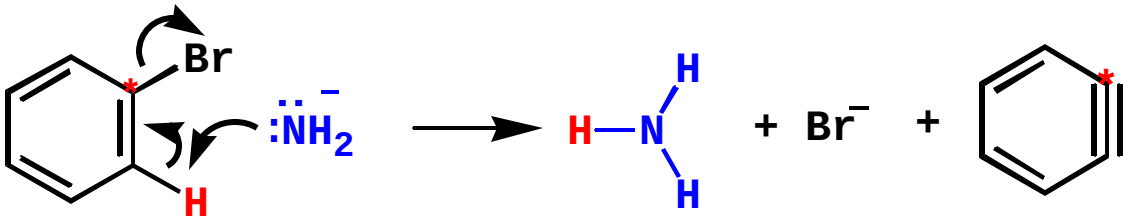


1. NaOH, H_2O, 340°, 2500 psi
2. H^+

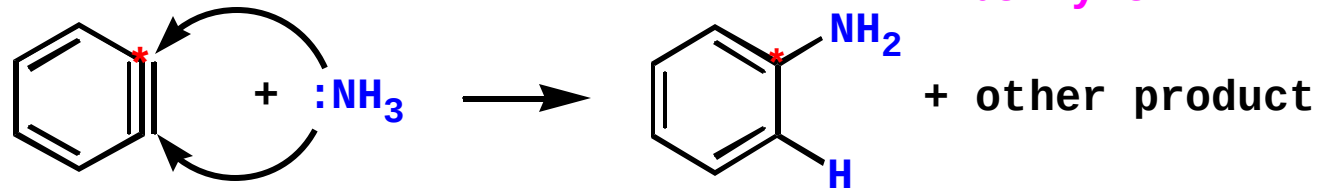
} chemical "hammer" OR ????

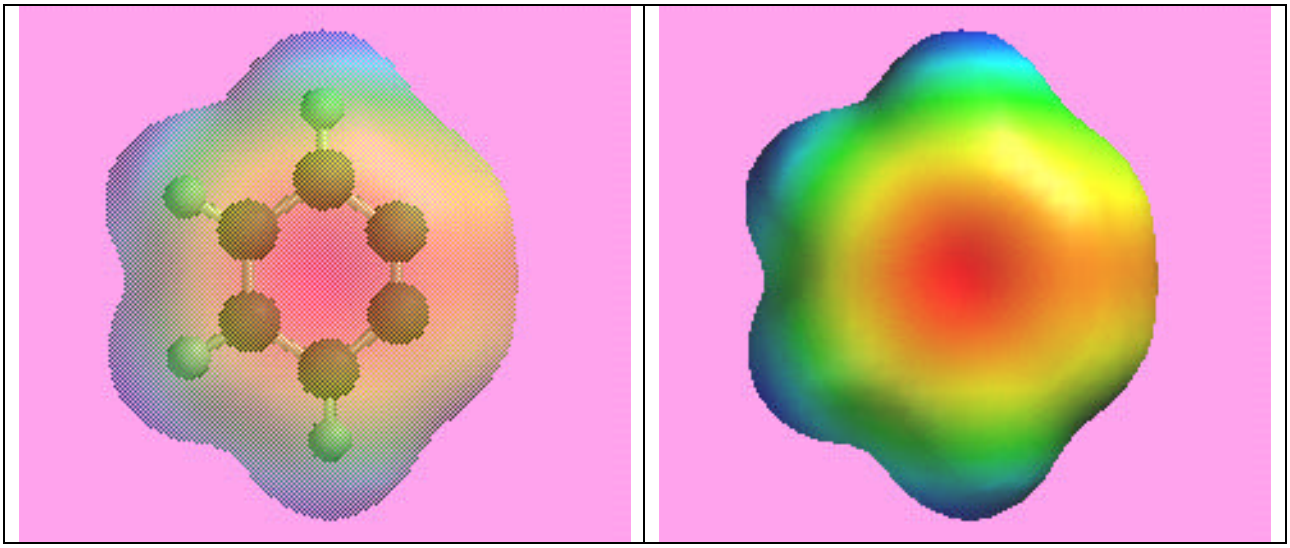
Not an example of aromatic nucleophilic substn…

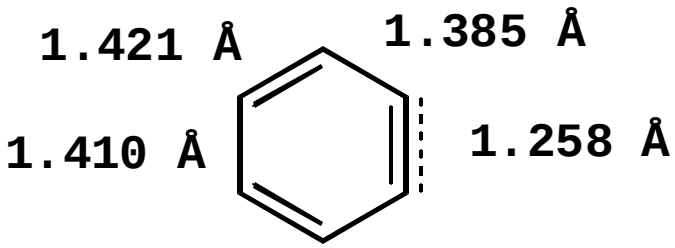


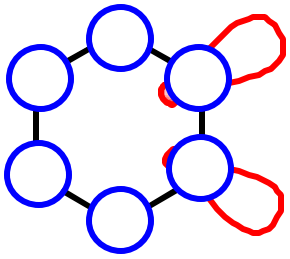


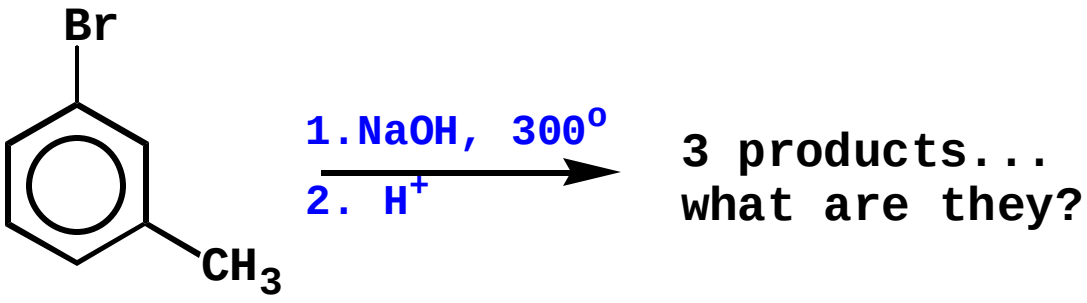
benzyne

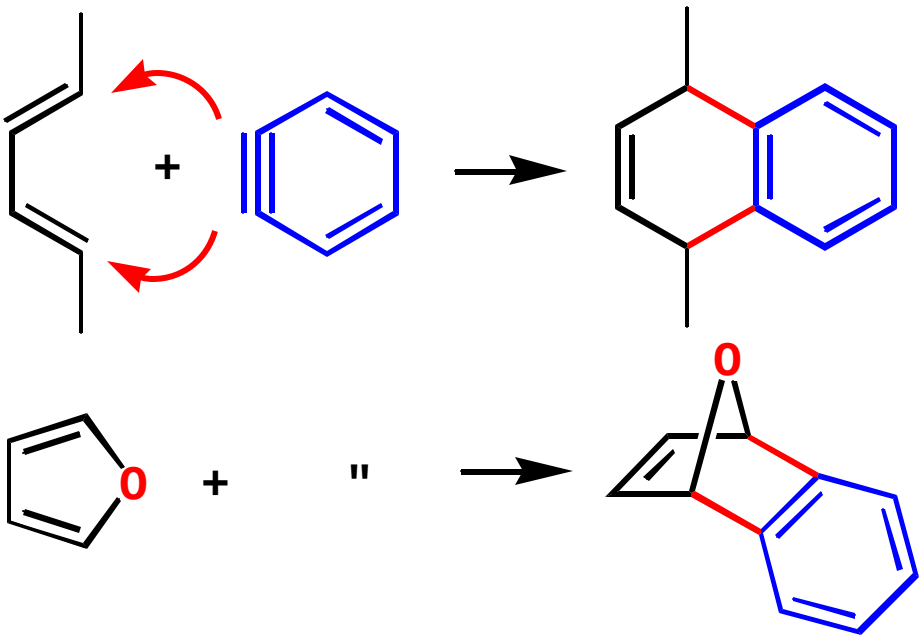


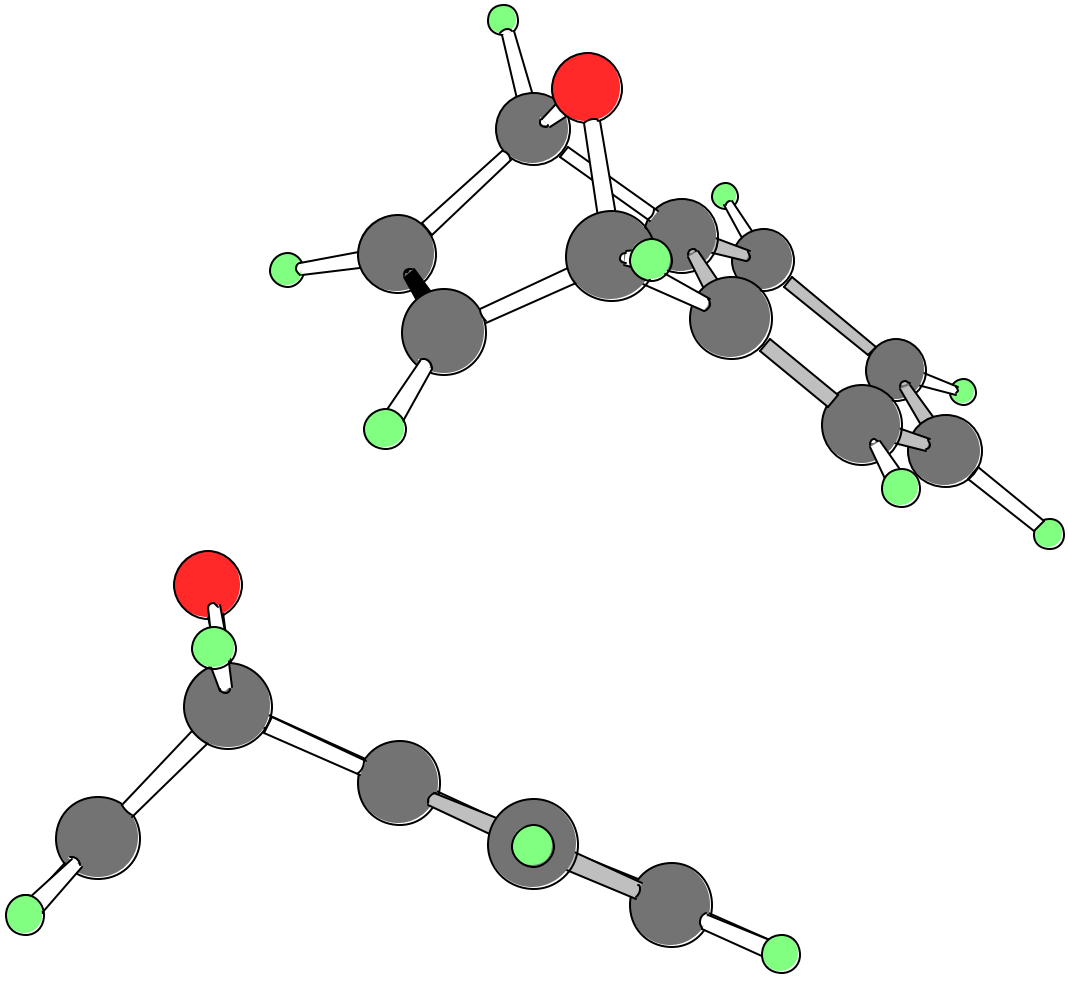



1.421 Å
1.385 Å
1.410 Å
1.258 Å




Br
CH3
1.NaOH, 300°
2. H+
3 products...
what are they?


+
O
+
"
O



Benzylic bromination…