# Exam 3:

2013 mean 71

5-year mean 73

2014 · mean 77 median 80

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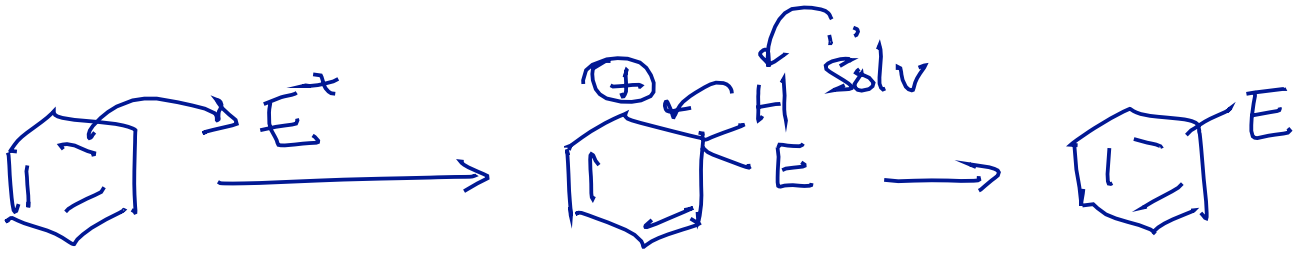
## Yesterday Recap:

Aromatic: cyclic, contiguous, planar arrays p orbs, $4n+2$

Antiaromatic = BAD, $4n$




$E^+$: $D^+$ ($D_2SO_4$)

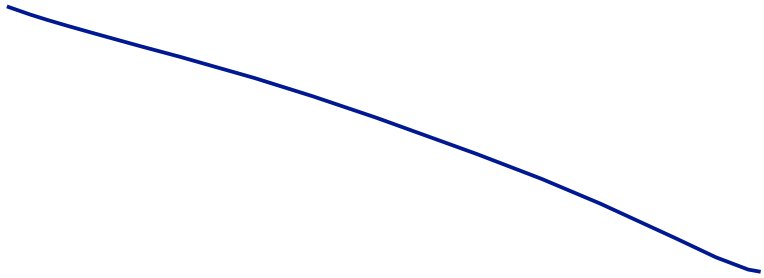
$Cl^+$ ($Cl_2$, $AlCl_3$)

$Br^+$ ($Br_2$, $FeBr_3$)

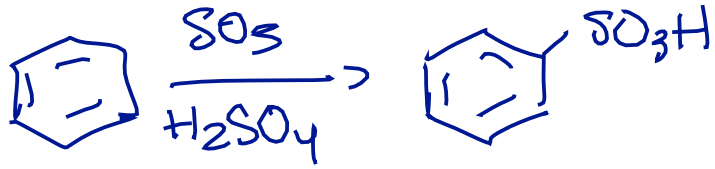
$NO_2^+$ ($HNO_3$, $H_2SO_3$)

# **Electrophilic Aromatic Substitution**: Nitration and Sulfonation

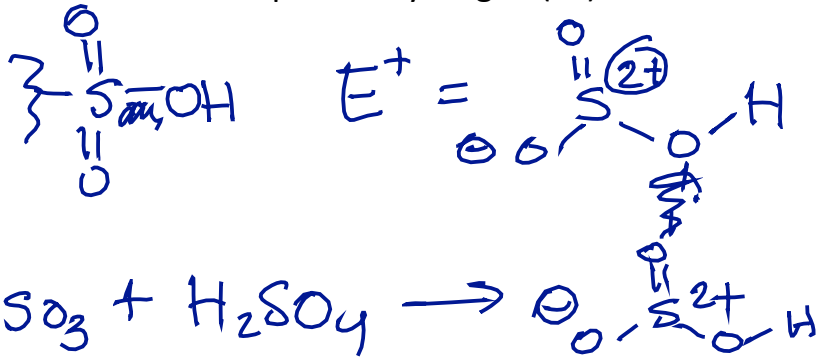
How can we replace a hydrogen ($H^+$) with a nitro group ($NO_2^+$)?

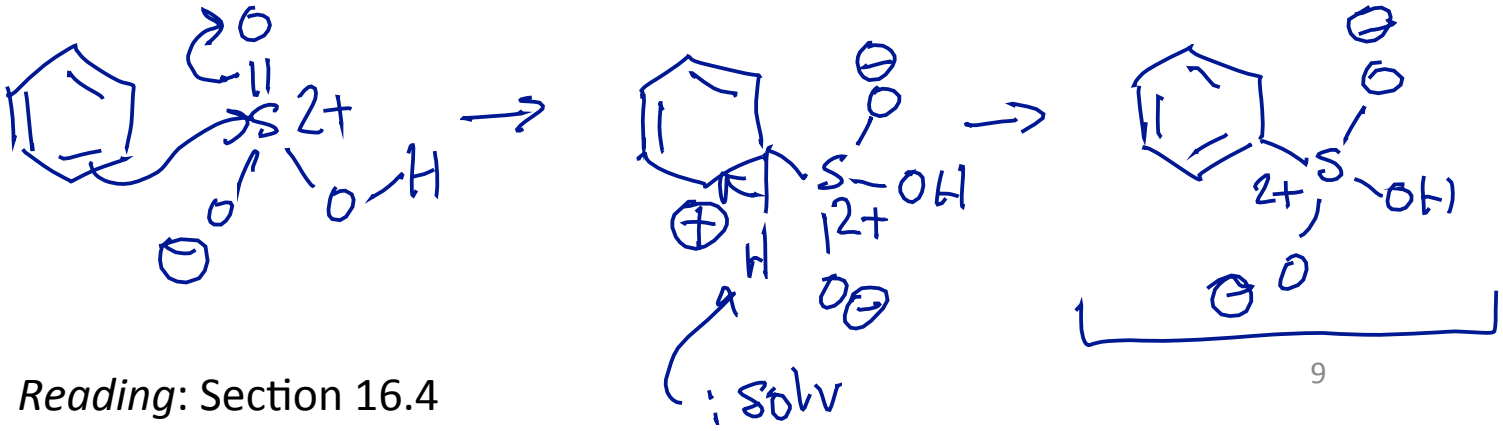


New Rxn:




How can we replace a hydrogen ($H^+$) with a sulfonic acid group ($SO_3H^+$)?

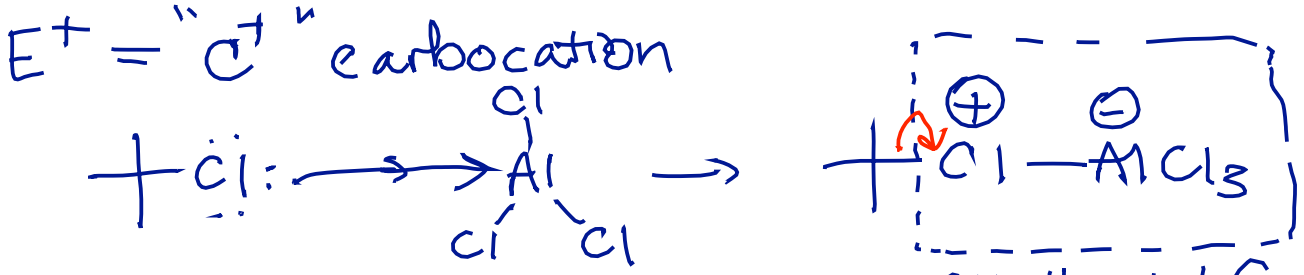


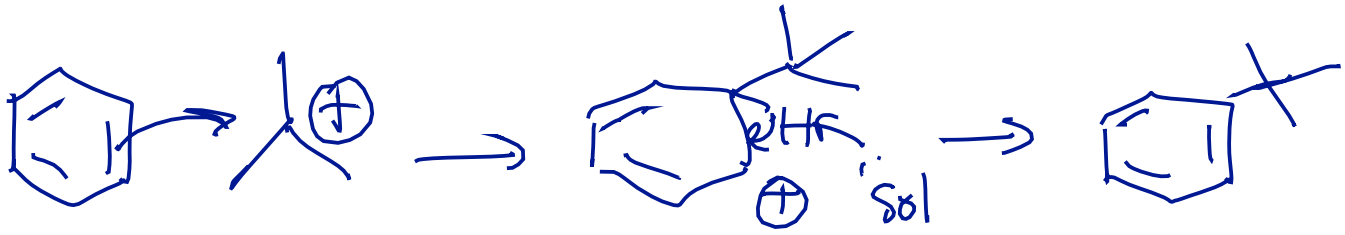




*Reading*: Section 16.4

# **Electrophilic Aromatic Substitution**: Alkylation

How can we replace a hydrogen ($H^+$) with an alkyl group ($R^+$, a carbocation)?
This reaction is known as *Friedel-Crafts Alkylation.*



Friedel-Crafts Alkylation

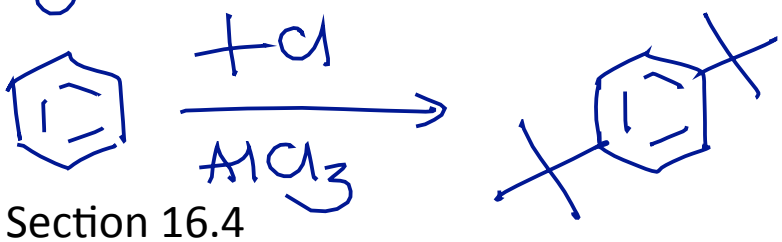
What are the significant problems with Friedel-Crafts alkylation?

1) Carbocations Rearrange

2) C+ must stable

∴ only usable for 3°, (2° if no rearrangements are possible

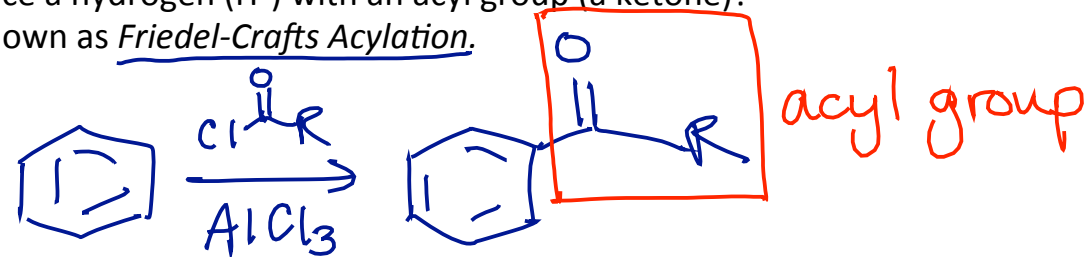
3) Overalkylation

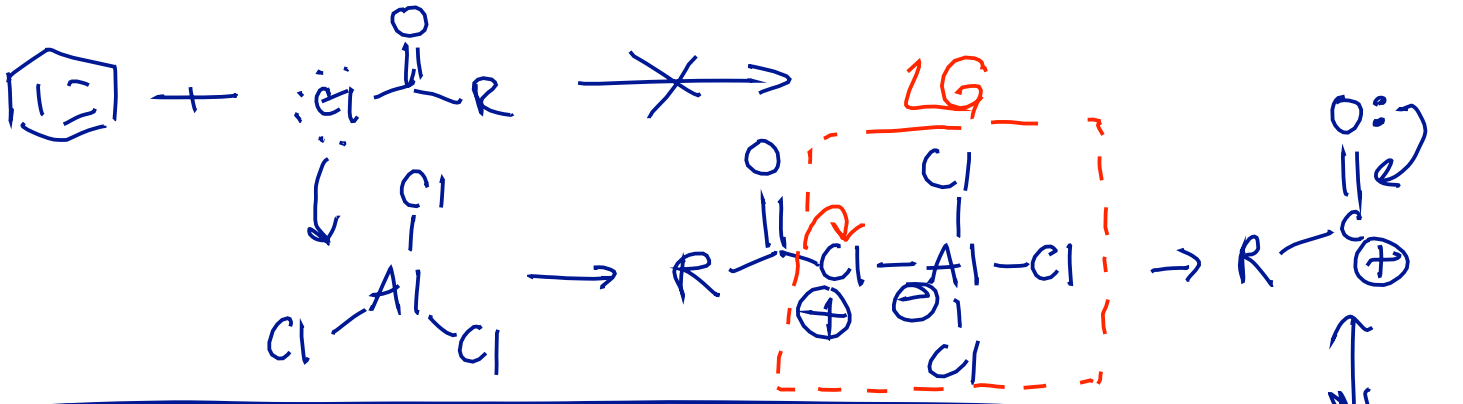



*Reading*: Section 16.4

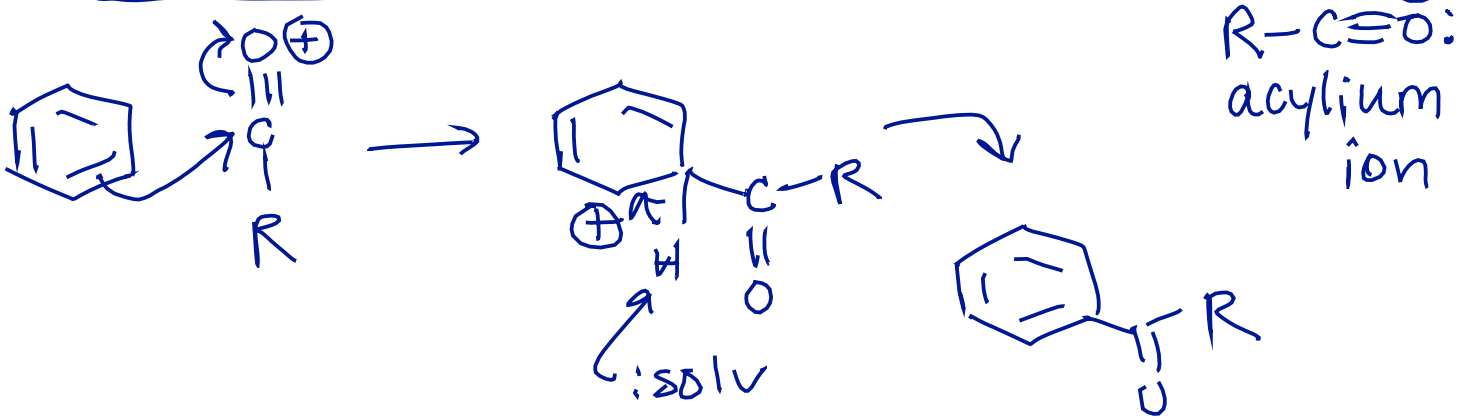
# **Electrophilic Aromatic Substitution**: Acylation

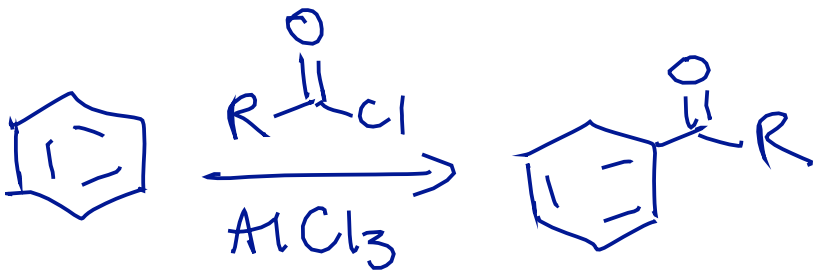
How can we replace a hydrogen ($H^+$) with an acyl group (a ketone)?
This reaction is known as *Friedel-Crafts Acylation*.



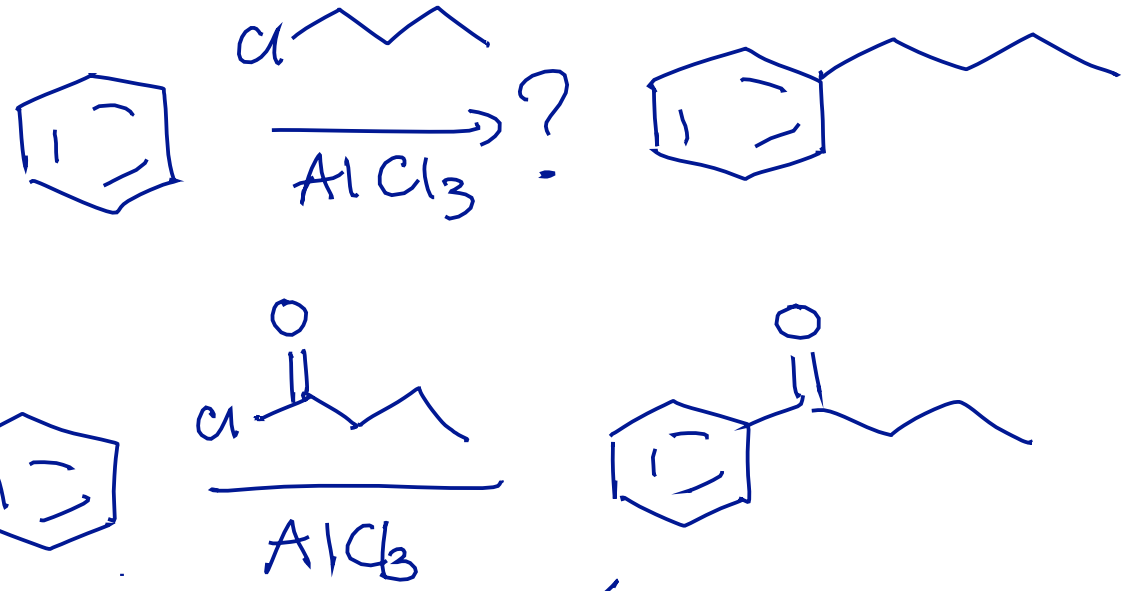

How can use *acylation* to avoid some of the problems of alkylation?

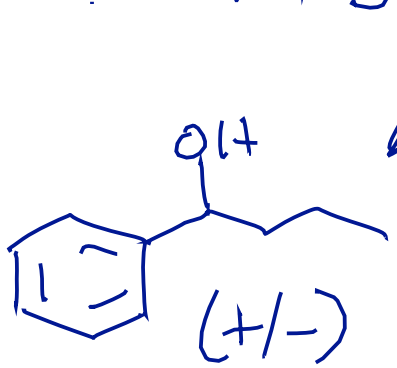


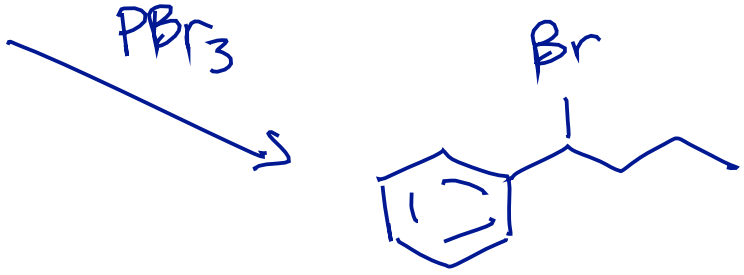



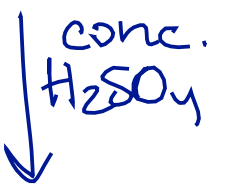
*Reading*: Section 16.4

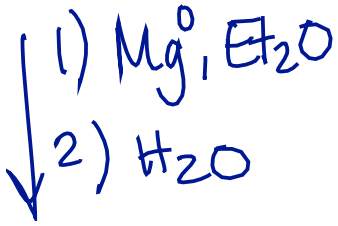
# Avoiding problems of FC Alkylation

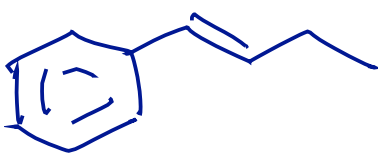


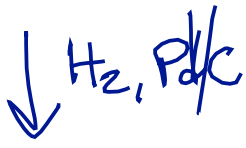



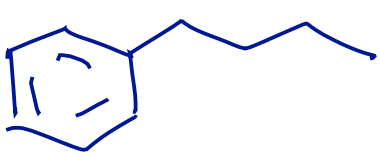



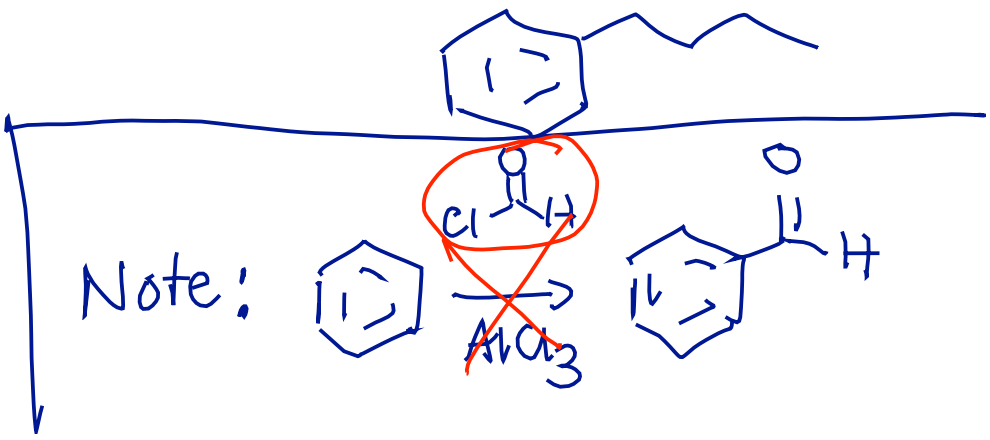





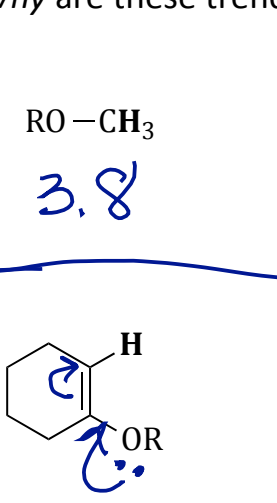





# Electron Donating & Withdrawing Groups

Match the chemical shifts with the highlighted protons in the compounds shown.
*Why* are these trends observed?

ppm
1.0
2.2
2.5
3.8
4.6
5.4
5.7
6.9




Cause deshielding: "Electron withdrawing group" EWG, inductive or resonance

Shielding: Electron donating groups EDG by resonance

*Reading*: Section 16.5

W = withdrawing, D donating

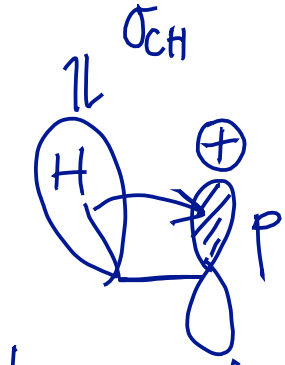


# Inductive vs. Resonance Effects

Complete the following table, indicating the relative magnitude of the various effects.

EDG, o/p-dir activators

| Functional Group | Inductive Effect | Resonance Effect |
|---|---|---|
| $-NMe_2$ | W | DDDD |
| $-OH$ | WW | DDD |
| $-CH_3$ | — | D |
| $-Cl$ | WW | D |
| $-C(=O)OEt$ | W | W |
| $-CN$ | W | W |
| $-N^+Me_3$ | W | — |
| $-NO_2$ | WW | WW |

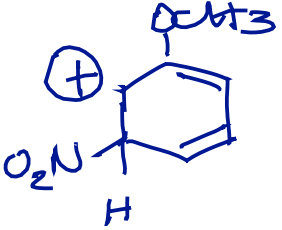



hyperconjugation

deactivators o/p directs



*Reading*: Section 16.5

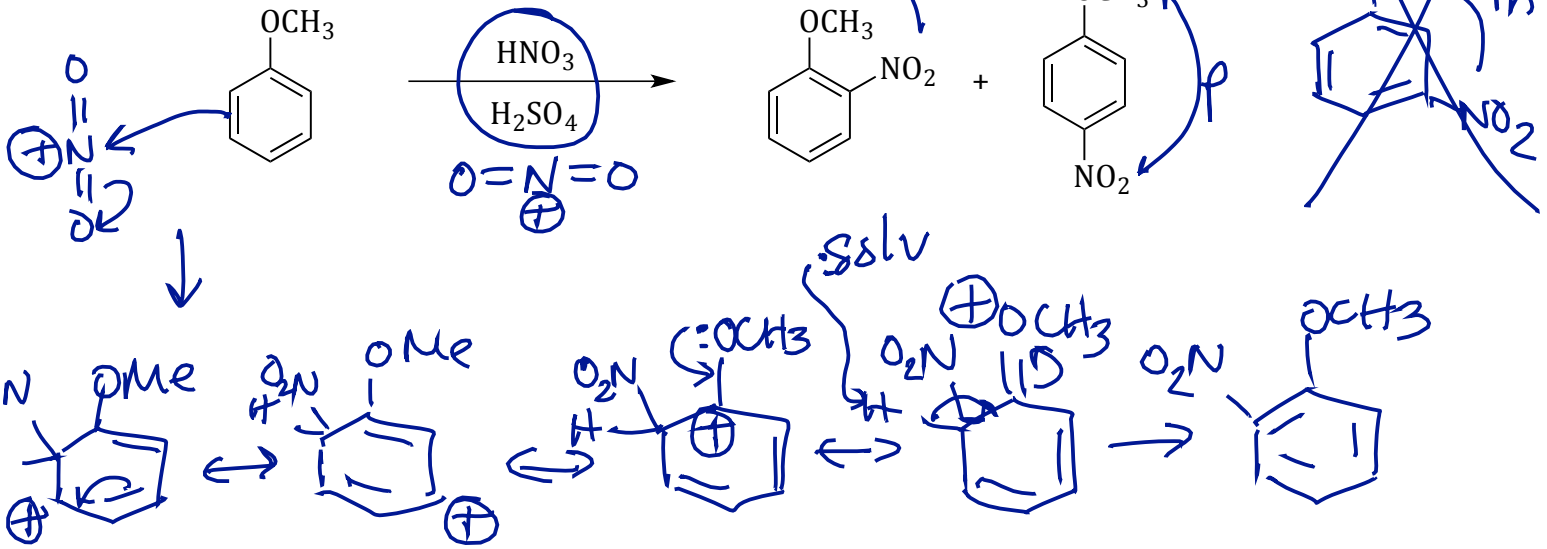



↔ no full octet res. structures, so NO rxn

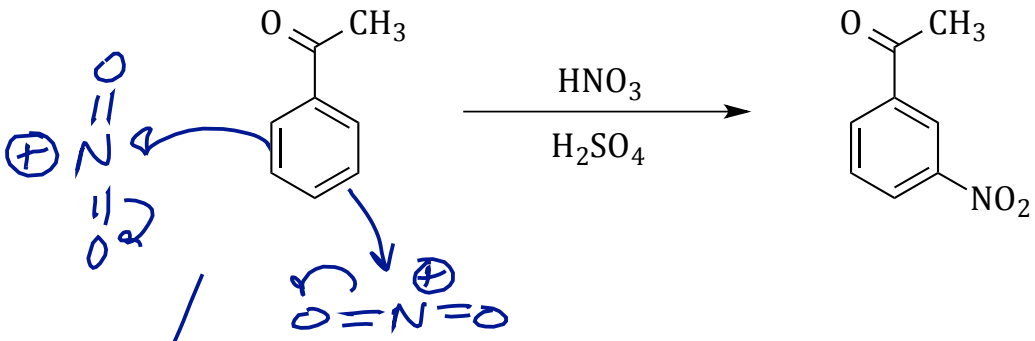


# Electrophilic Aromatic Substitution: Directing Effects ("Regioselectivity")

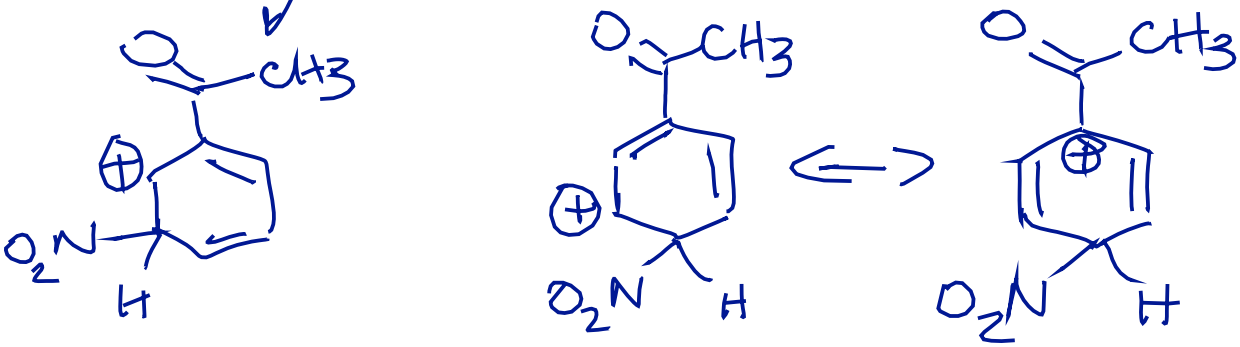
When anisole is nitrated, the *ortho* and *para* products predominate. Why?




When acetophenone is nitrated, the *meta* product predominates. Why?




EWGs destabilize ⊕ charge



*Reading*: Section 16.5

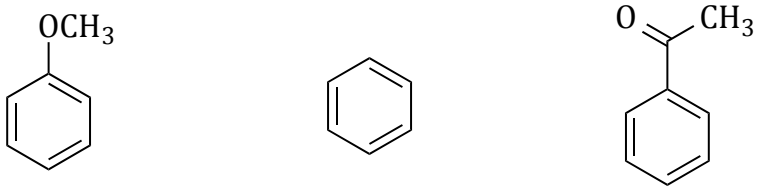
EWGs → direct "meta"

EDGs → direct ortho/para




# Electrophilic Aromatic Substitution:
## Activating Effects

Explain the observed trend in the *rate* of nitration of the following compounds:




| Relative rate of reaction with $HNO_3/H_2SO_4$: | *fast* | *normal* | *slow* |
|---|---|---|---|

Energy of HOMO of Nu: What's the E HOMO here?

EDG: raise E HOMO → better nucleophiles → faster

EWG: lower HOMO → poorer nucleophiles → slower rxns

In general, *ortho/para*-directing groups are *activating*, while *meta*-directing groups are *deactivating*. Why?

EDG: o/p-directing, activating

EWG: m-directing, deactivating

However, *halogen* substituents are *deactivating*, but are *o/p*-directors. Why?

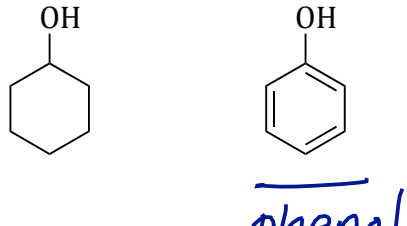
EW by induction → deactivators

ED by resonance → o/p directors

*Reading*: Section 16.5

# **Application of Substituent Effects**: The Acidity of Phenols

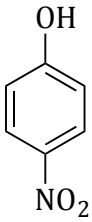
Explain the observed trends in the p$K_a$ values of the following compounds:

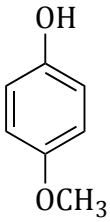




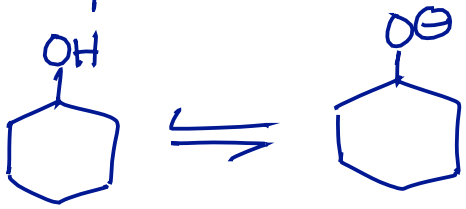


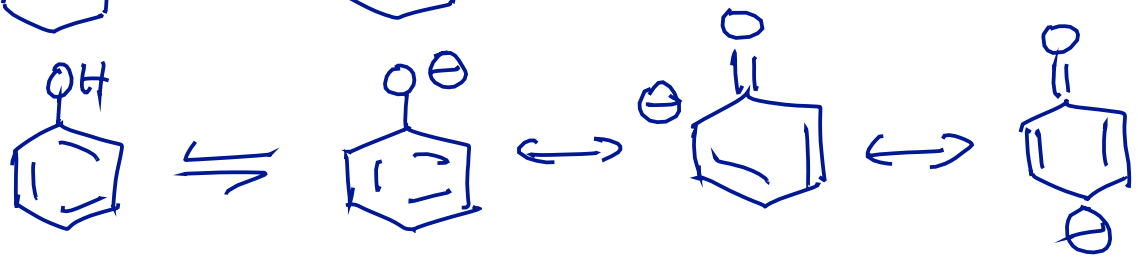
phenol

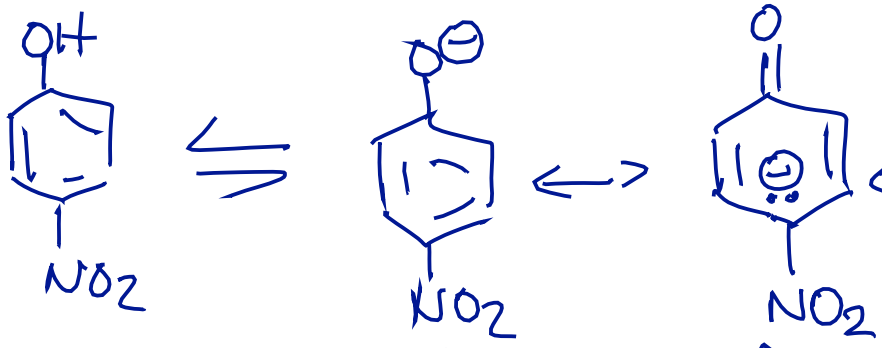


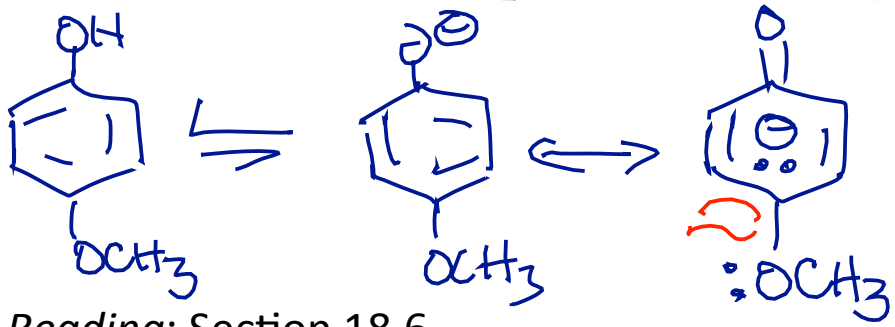

pKa: 16.5 9.9 7.1 10.2




good stabilizing resonance str.



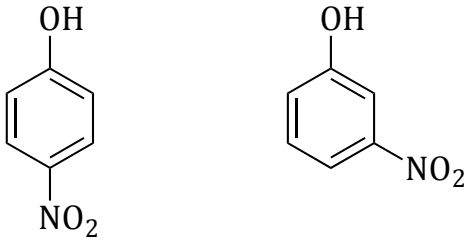

destabilizing

*Reading*: Section 18.6

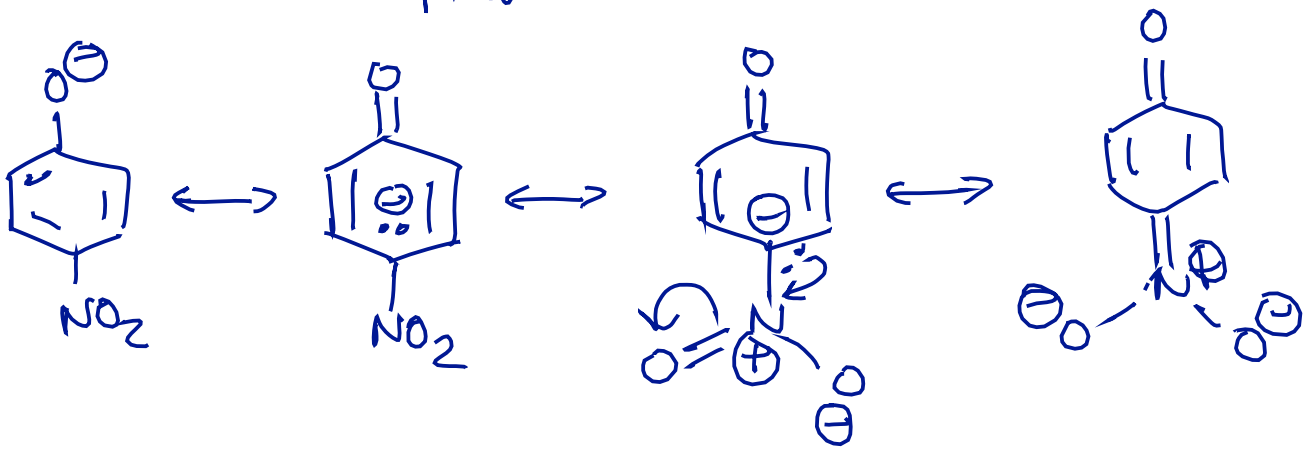
# **Application of Substituent Effects**: The Acidity of Phenols, cont.

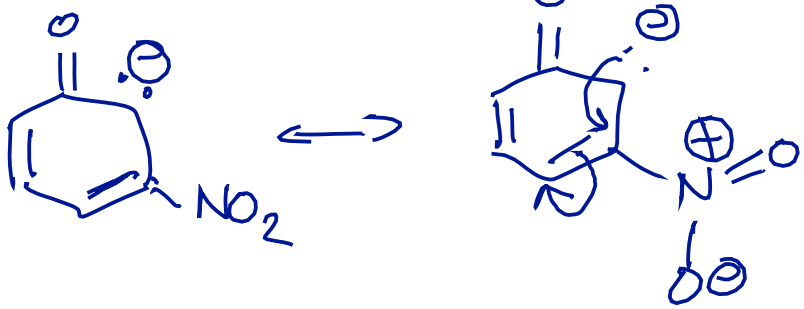
Explain the observed trends in the p$K_a$ values of the following compounds:

EWG is farther away but stronger effect




pKa: 7.1 8.4



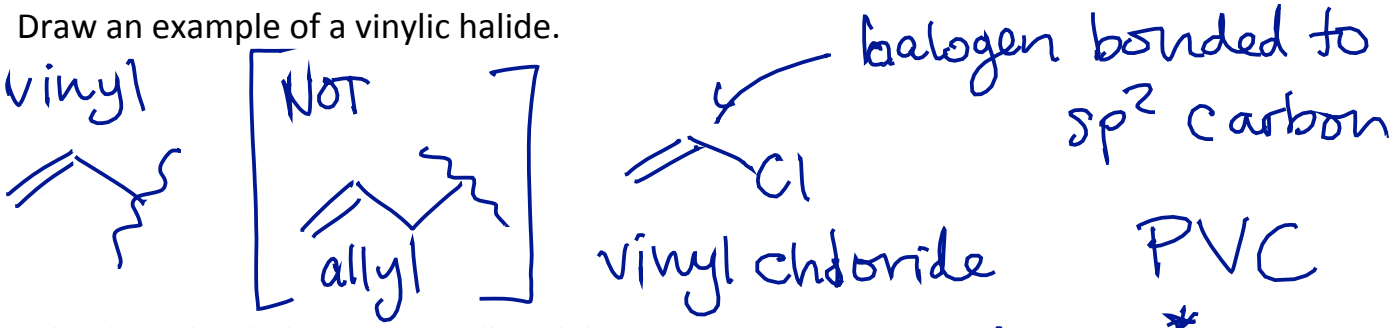

No way to delocalize ⊖ onto $NO_2$ by resonance



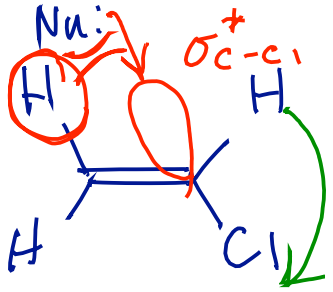
*Reading*: Section 18.6

# Reactivity of Vinylic Halides

Draw an example of a vinylic halide.




Why does that halide *not* usually exhibit $S_N2$ reactivity?

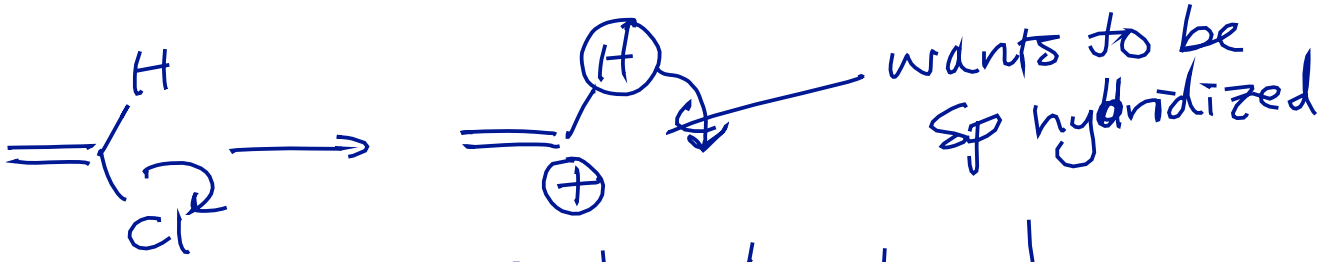



Nu lp → $\sigma^*_{C-Cl}$

* backside attack blocked

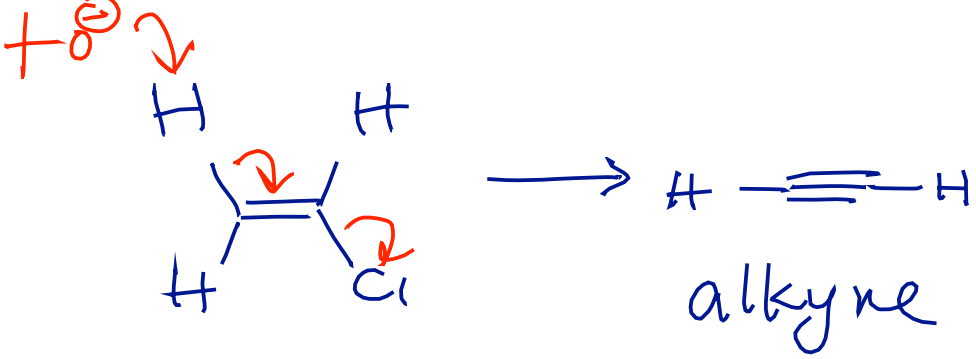
* inversion requires tons of E at $sp^2$ carbon

Why does that halide *not* usually exhibit $S_N1$ or E1 reactivity?




no vinyl carbocations!

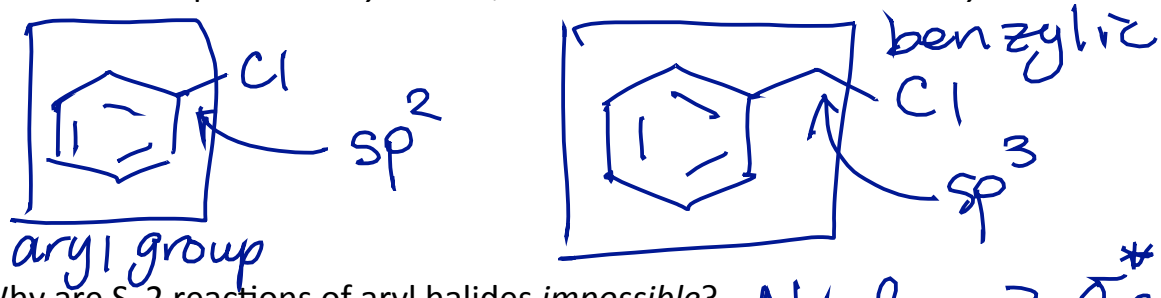
What product would be formed from an E2 reaction of that halide?



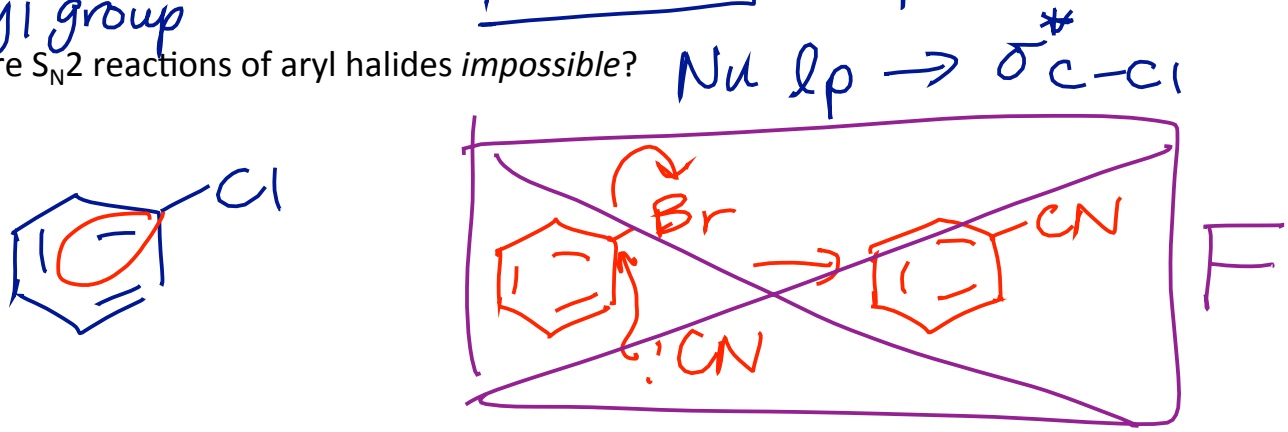

*Reading*: Section 18.1-18.3

# Reactivity of Aryl Halides

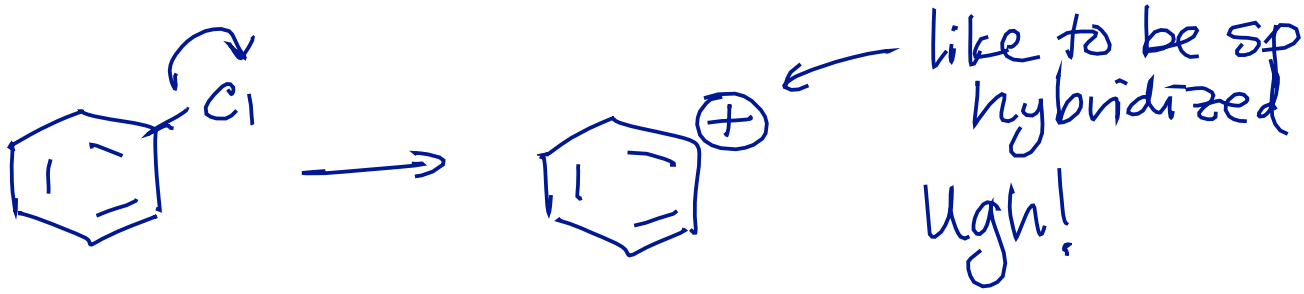
Draw an example of an *aryl* halide; how is it different from a *benzylic* halide?



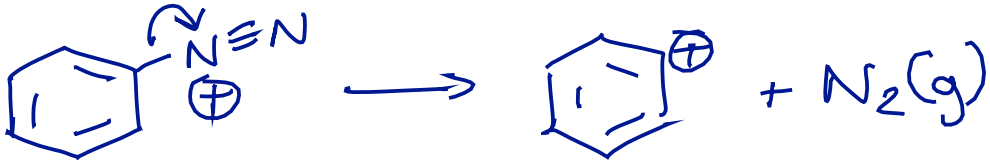

Why are $S_N2$ reactions of aryl halides *impossible*?

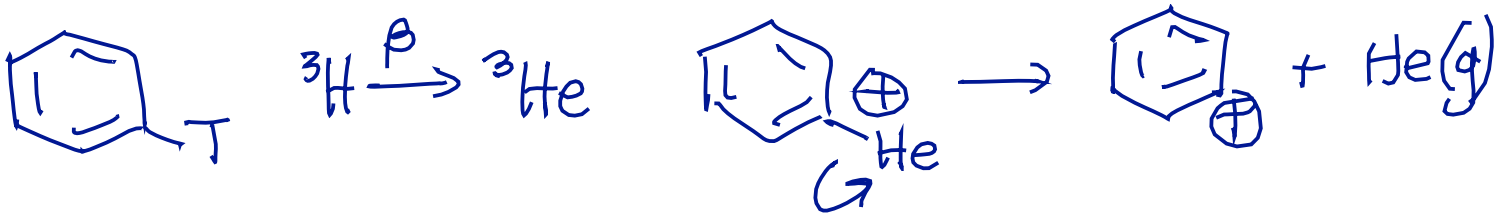



Why are $S_N1$ reactions of aryl halides (very nearly) *impossible*?




Are there *any* leaving groups that can provide $S_N1$ reactivity by forming an aryl cation?



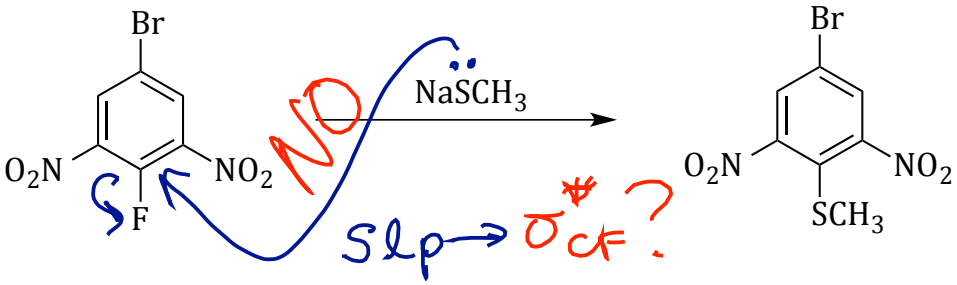




*Reading*: Section 18.1-18.3

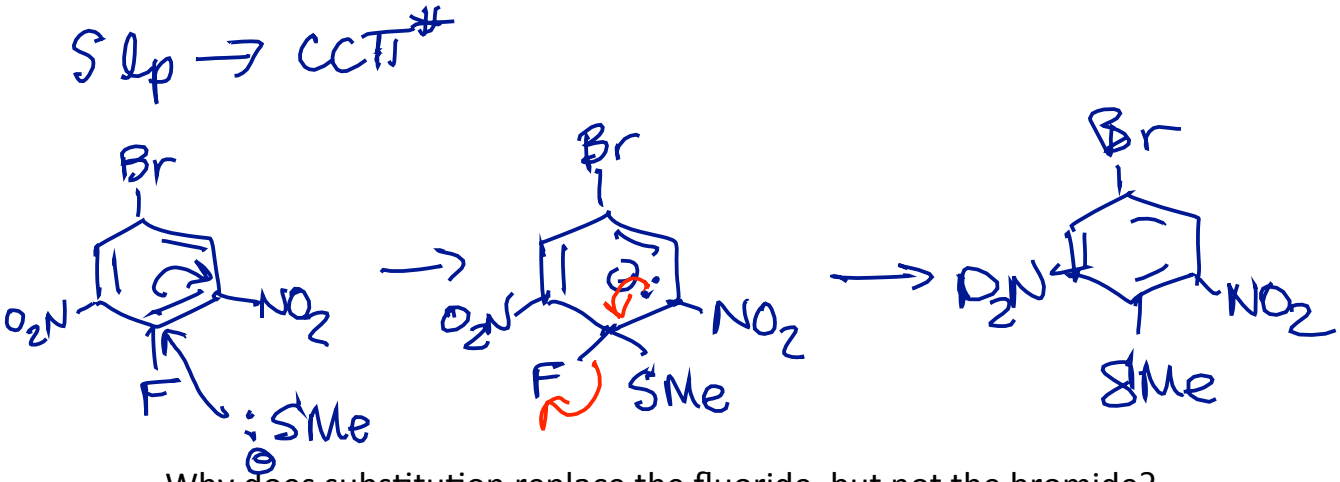
# **Nucleophilic Aromatic Substitution**: Addition-Elimination

When an *aryl halide* has *nitro groups* in *o/p* positions, then nucleophilic substitution can take place **IF** you have a good nucleophile. This reaction is referred to as "*Nucleophilic aromatic substitution* ($S_NAr$) *by the addition-elimination mechanism*."

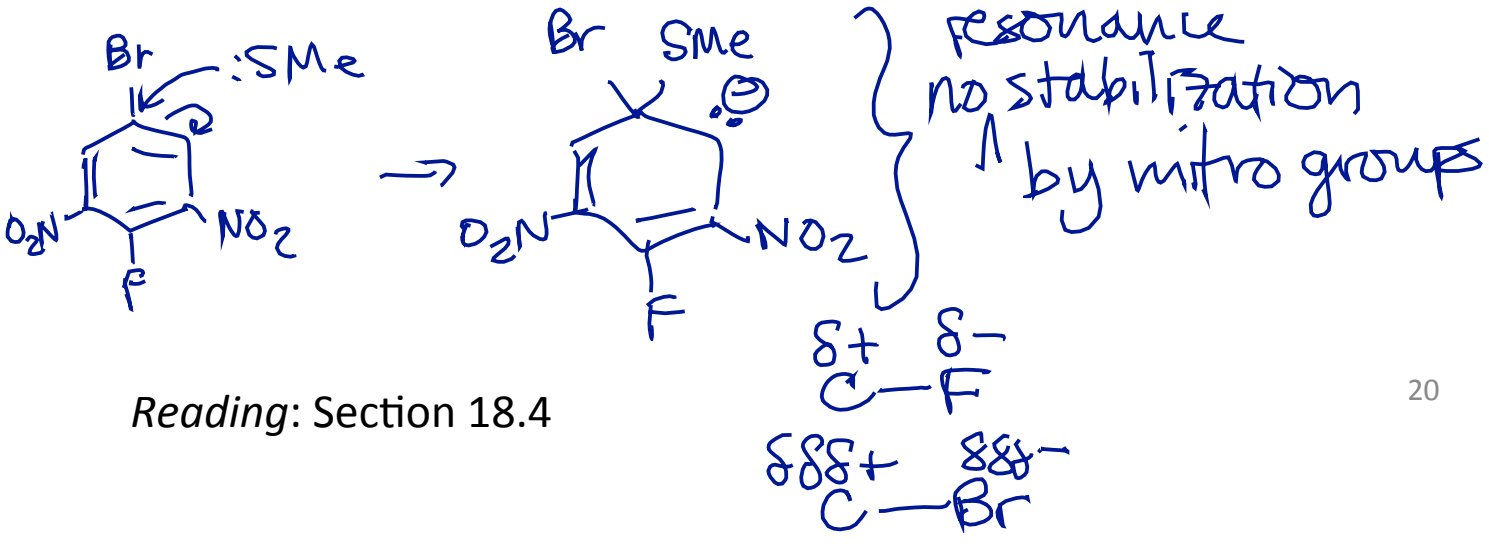
Consider the following reaction:




Provide a complete curved-arrow mechanism for this transformation.




Why does substitution replace the fluoride, but not the bromide?

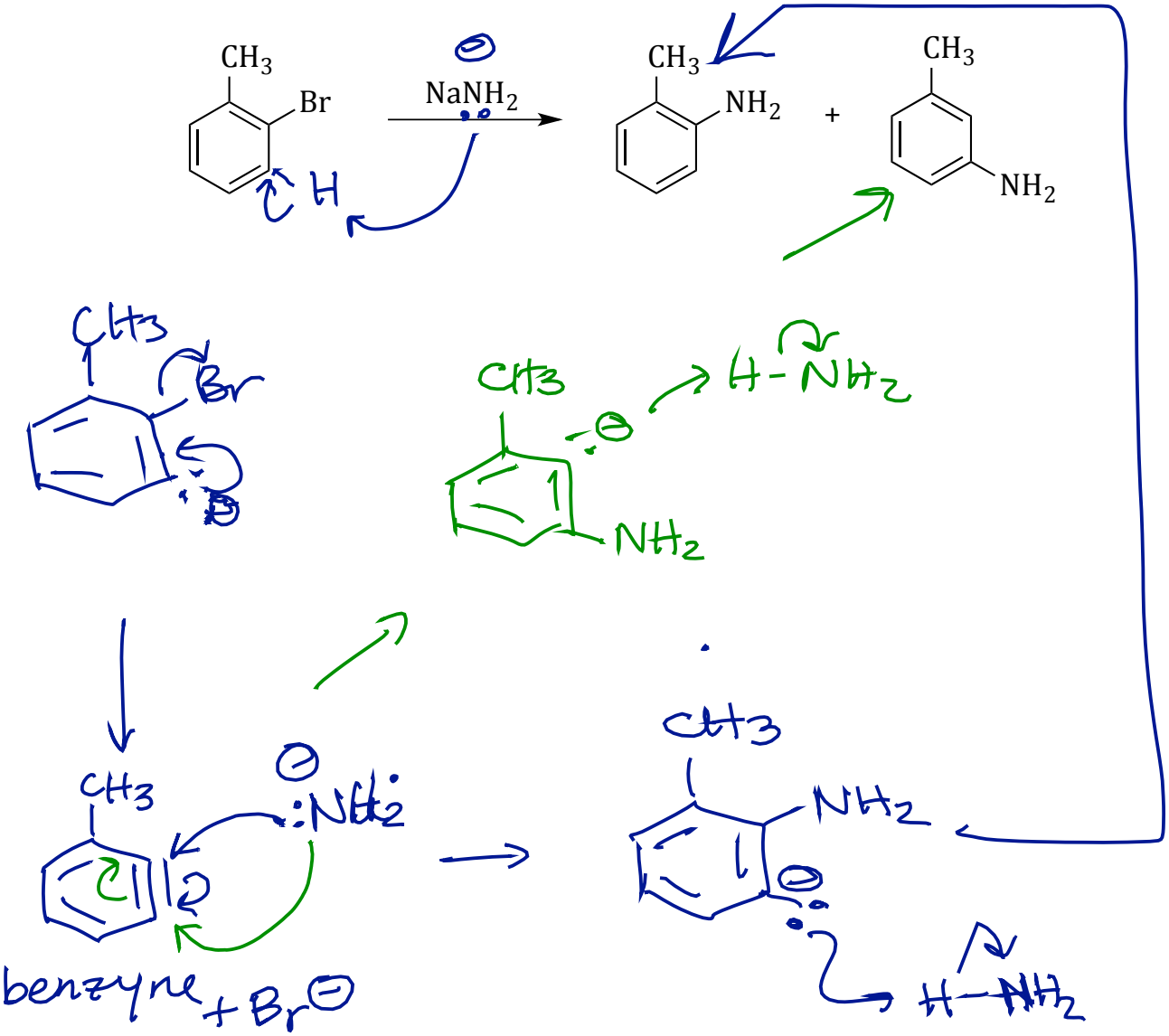



*Reading*: Section 18.4

# **Nucleophilic Aromatic Substitution**: Elimination-Addition ("The Benzyne Mechanism")

When an *aryl halide* does **not** have EWGs in *o/p* positions, and it is treated with a ***very*** strong base, then nucleophilic substitution can take place via an intermediate known as a *benzyne*. Substitution by this mechanism is referred to as "*Nucleophilic aromatic substitution* ($S_NAr$) *by the elimination-addition mechanism*."

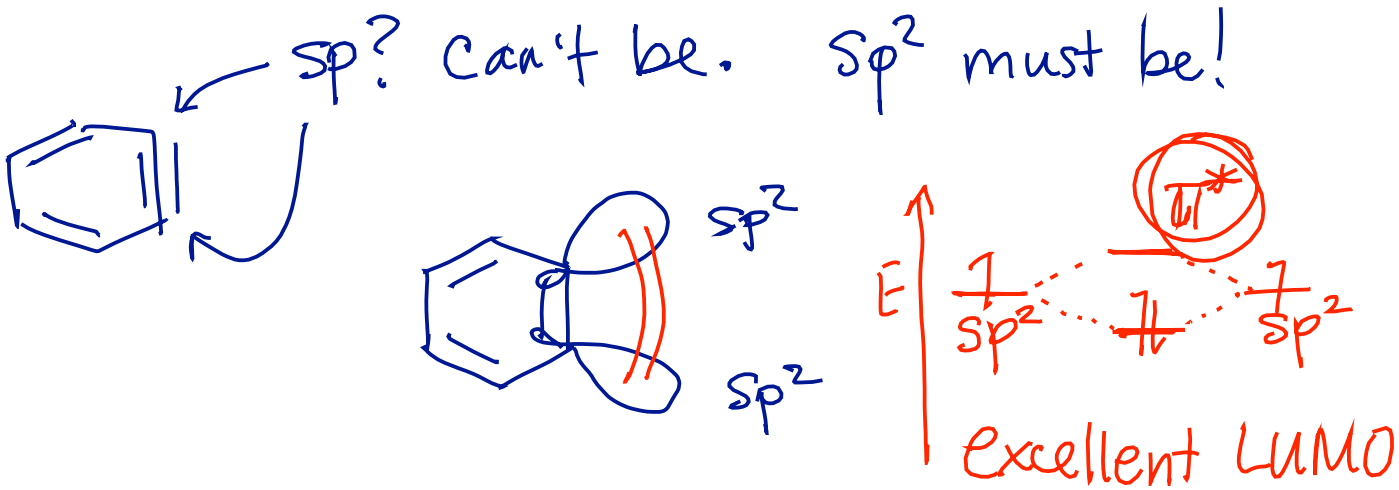
Provide a curved-arrow mechanism for the following reaction; this mechanism *must* account for why a *mixture* of products is formed!



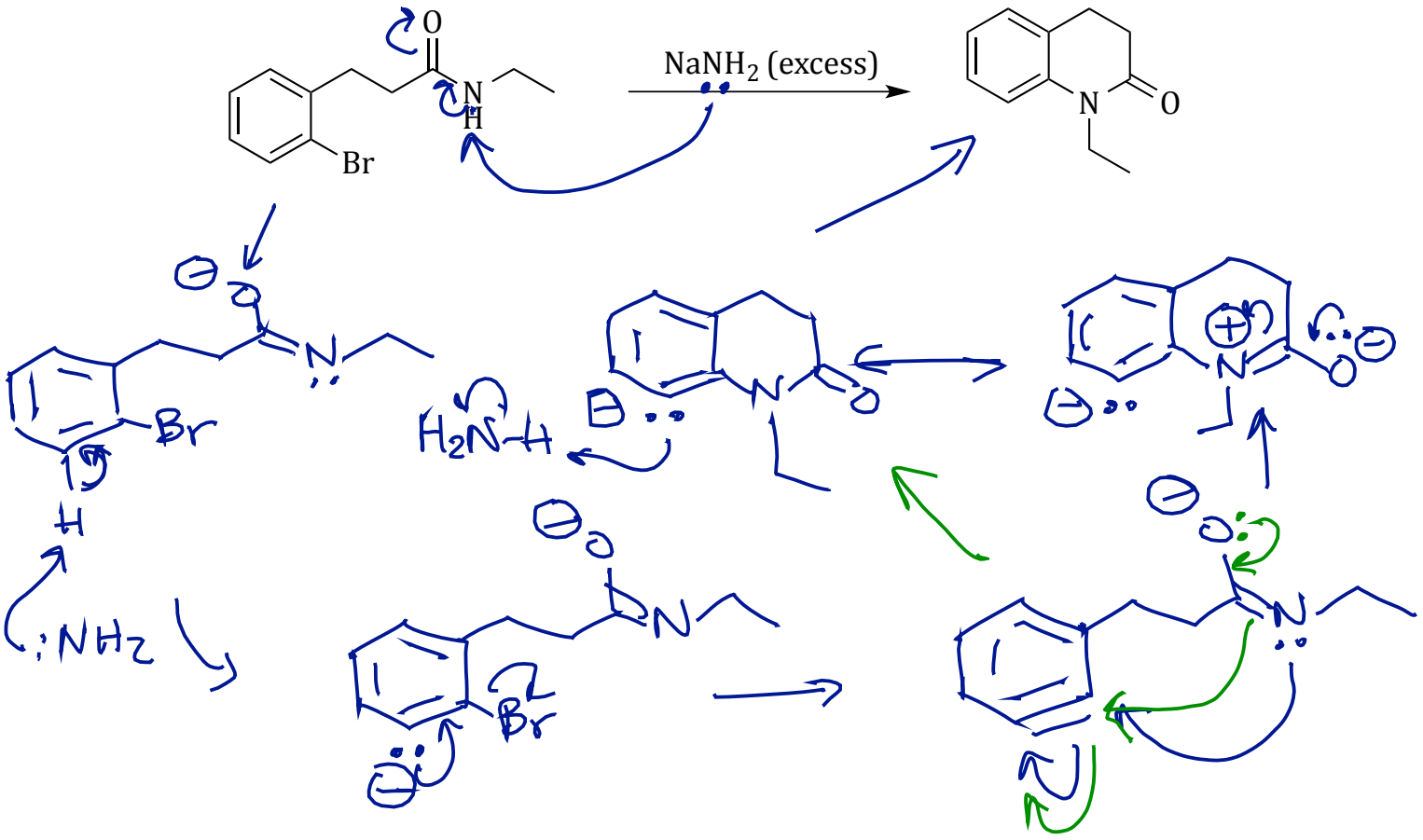

*Reading*: Section 18.5

# Structure and Reactivity of Benzyne

Benzyne is a very unstable species. How can we think about bonding in benzynes?




Provide a complete curved-arrow mechanism for the following transformation:



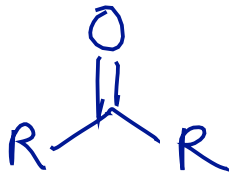

*Reading*: Section 18.5

carbonyl: C=O
↑ carbonyl carbon

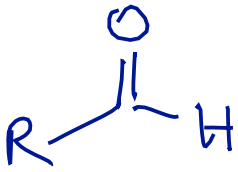


# **Electrophilic π-Bonds**: Carbonyl Chemistry

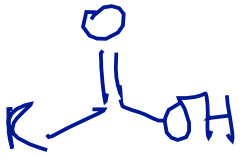
What functional groups contain a carbonyl group?



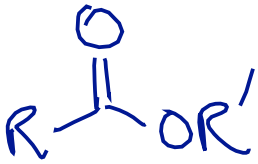
ketones



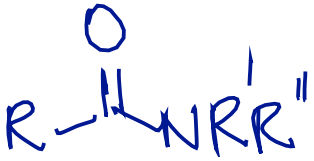
aldehyde



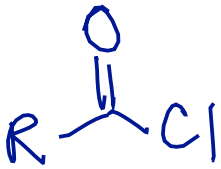
carboxylic acid



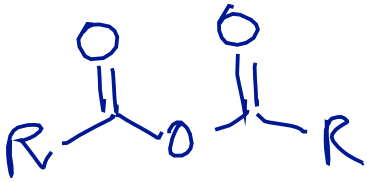
ester



amide



acid chloride

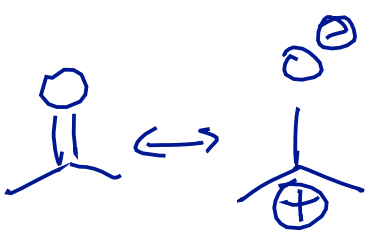


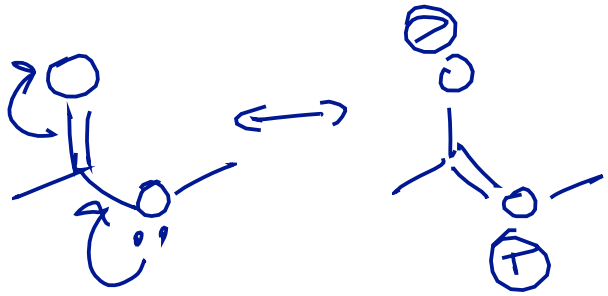
acid anhydride

What distinguishes some carbonyl-containing compounds from others?

1) # of bonds to heteroatoms (not H, C)

2) Resonance structures



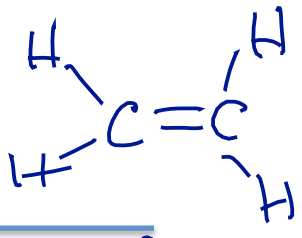


*Reading*: Section 19.1 & 19.4

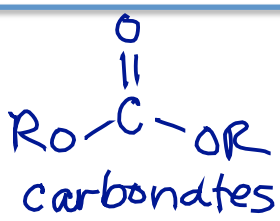
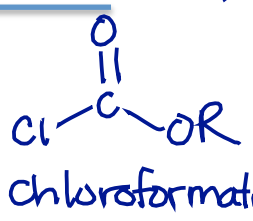
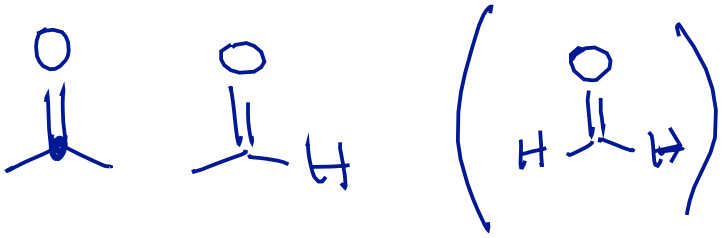
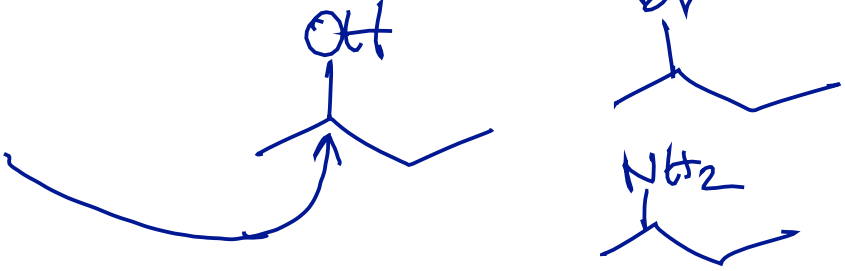
ox state: hypothetical charge

Week 4 +8 ← $OsO_4$ ← −2 July 15, 2014

# Oxidation Levels in Organic Chemistry



of carbon atoms

| # of bonds to e⁻-neg atoms | Oxidation "level" | Examples |
|---|---|---|
| 4 | *carbon dioxide* | O=C=O  carbonates  chloroformates |
| 3 | *carboxylic acid* |  ureas carb. acids, esters, amides, acid chlorides, anhydrides |
| 2 | *ketone* |  |
| 1 | *alcohol* |  |
| 0 | *alkane* |  |