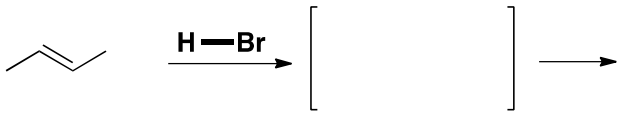
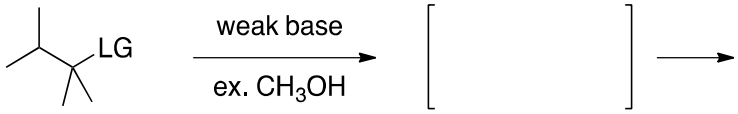
18.1 Electrophilic Aromatic Substitution Intro (EArS)	18.2 Halogenation	18.3 Sulfonation
18.4 Nitration	18.5 Friedel-Crafts Alkylation	18.6 Friedel-Crafts Acylation
18.7 Activating Groups	18.8 Deactivating Groups	18.9 Halogens: the Exception
18.10 EArS Directors	18.11 Multiple Substituents	18.12 Synthesis Strategies

Reaction Mechanisms from 8A…

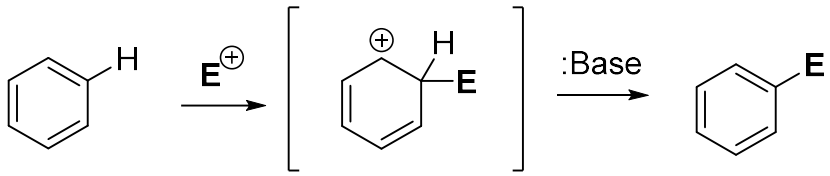
Chapter 8 – Electrophilic Addition to Alkenes

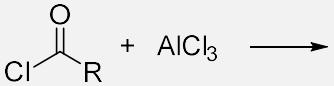
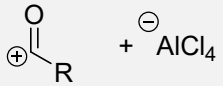


Chapter 6 – E1 = unimolecular elimination

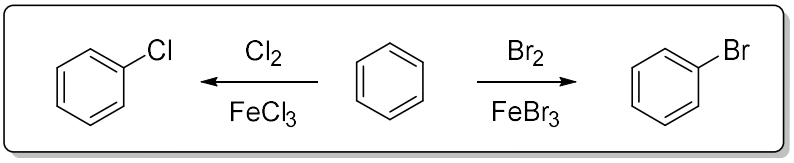


[18.1] Electrophilic Aromatic Substitution (EArS) of Benzene

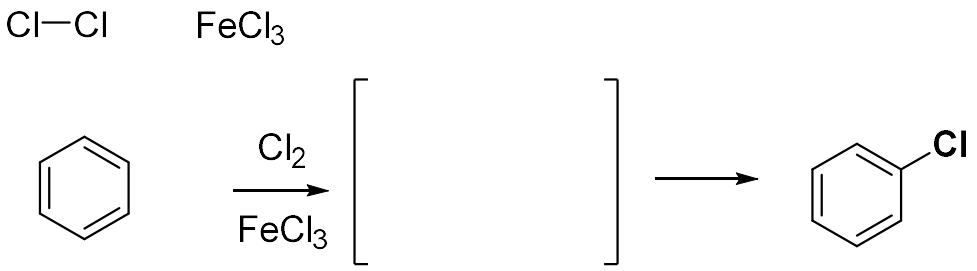


Reaction Type	"E" source + catalyst ⟶	$E^{\oplus}$ + Base
Chlorination	$Cl_2 + FeCl_3$ ⟶	$Cl^{\oplus} + FeCl_4^{\ominus}$
Bromination	$Br_2 + FeBr_3$ ⟶	$Br^{\oplus} + FeBr_4^{\ominus}$
Nitration	$HNO_3 + H_2SO_4$ ⟶	$NO_2^{\oplus} + H_2O$
Sulfonation	$SO_3 + H_2SO_4$ ⟶	$SO_3H + H_2O$
Alkylation	$RCl + AlCl_3$ ⟶	$R^{\oplus} + AlCl_4^{\ominus}$
Acylation		

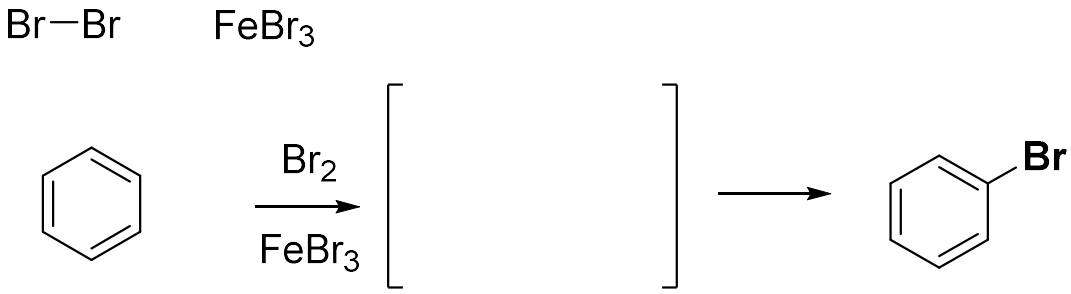
[18.2] Electrophilic Aromatic Substitution (EArS): Halogenation



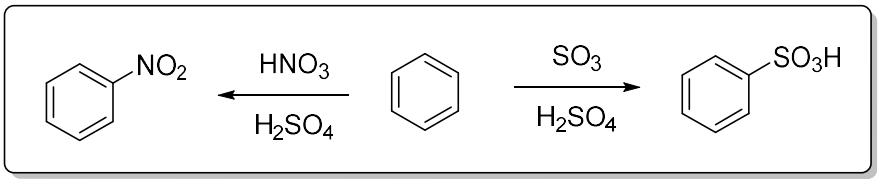
Chlorination mechanism



Bromination Mechanism



Electrophilic Aromatic Substitution (EArS): Addition of Heteroatoms (N & S)

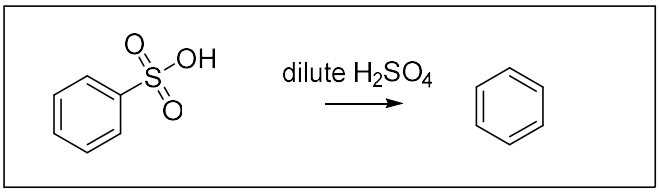


[18.3] Sulfonation with "Fuming" Sulfuric Acid (SO_3, H_2SO_4)

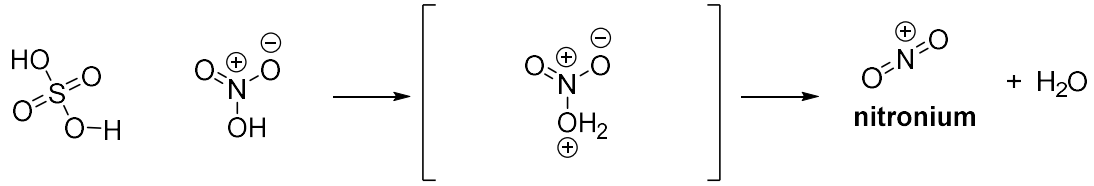
Mechanism

benzene sulfonic acid

Reversible reaction with dilute acid…



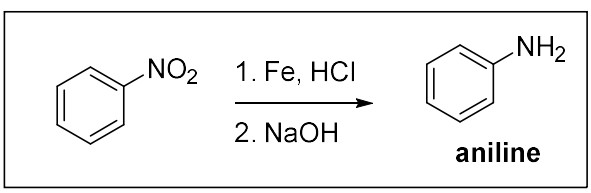
[18.4] Nitration with Nitric Acid in Sulfuric Acid (HNO_3, H_2SO_4)



nitronium

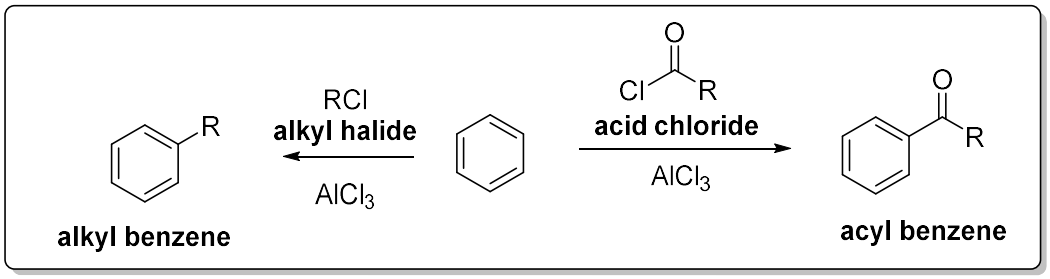
nitrobenzene

Reduction reaction…

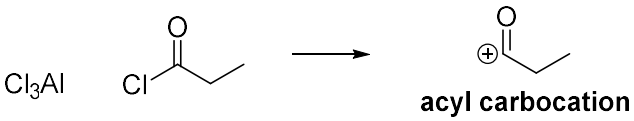


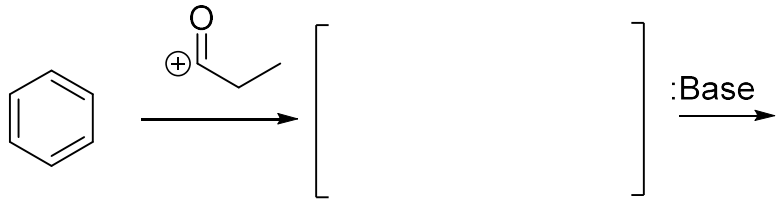
aniline

Friedel-Crafts (FC) Reactions (Rxns) ***How to Add C's to Benzene***

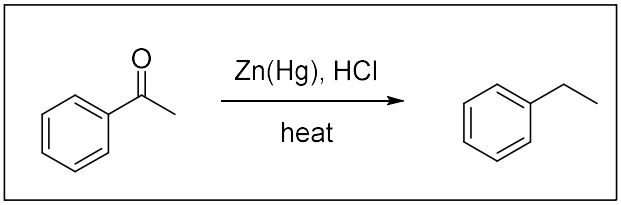


[18.6] FC Acylation Mechanism

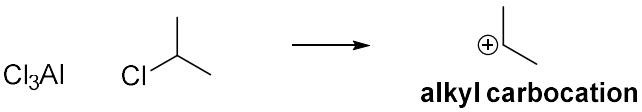


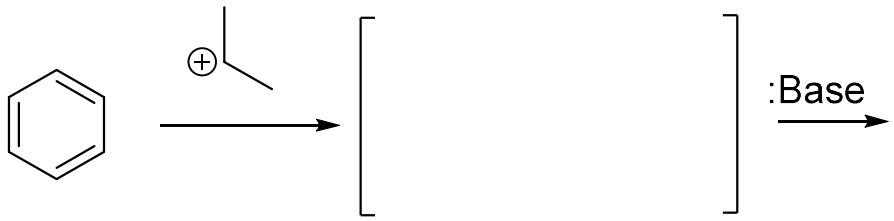


Aryl ketone reduction…

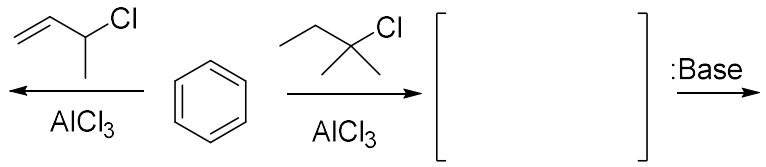


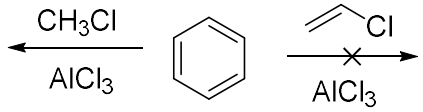
[18.5] FC Alkylation





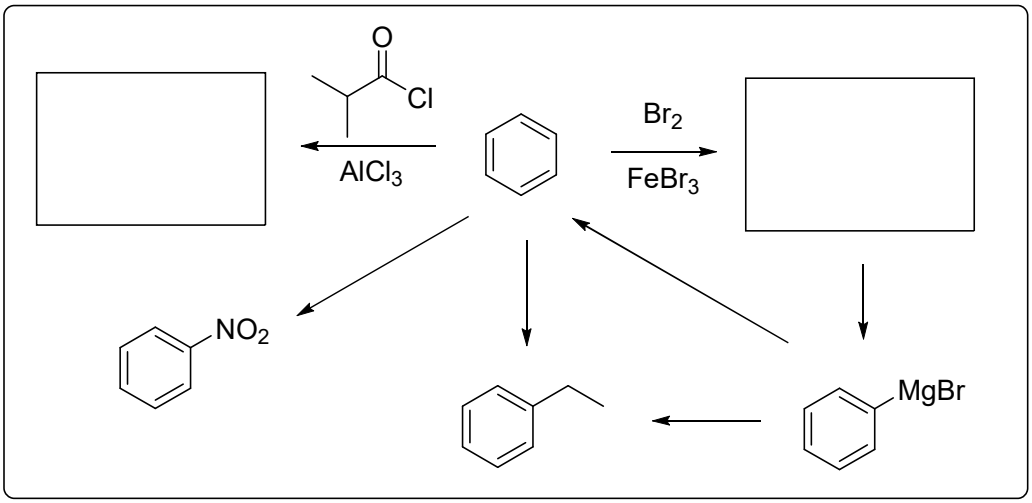
Simple FC Alkylations without carbocation rearrangements (RRGT)



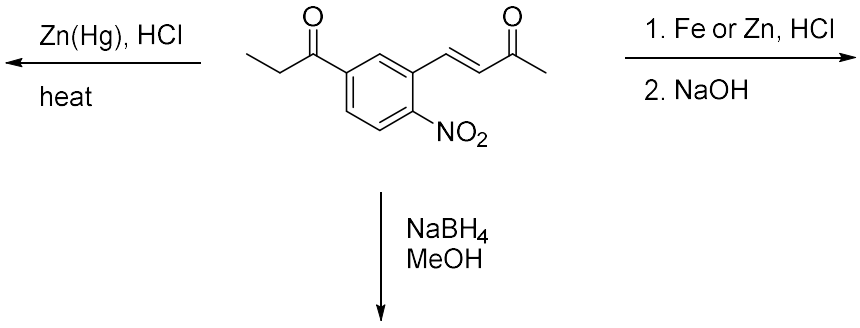


Monosubstitution with EArS Reaction Puzzle / Summary

fill in the boxes and add missing reagents over blank arrows



Chemoselectivity Puzzle



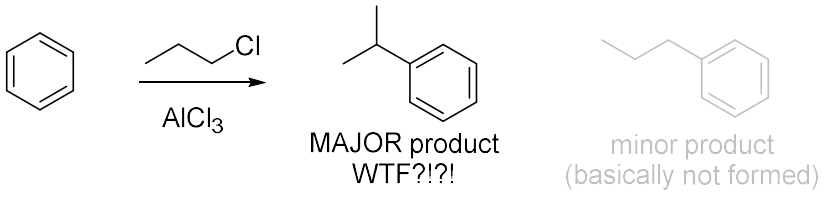
Carbocation Rearrangements (C^+ RRGTs) in FC Alkylations

- Is there a more substituted carbon next to the alkyl halide?

NO: substitution happens without rearrangement 😊

YES: Alkyl C^+ rearranges to more substituted C before adding to the ring

Hydride Shift



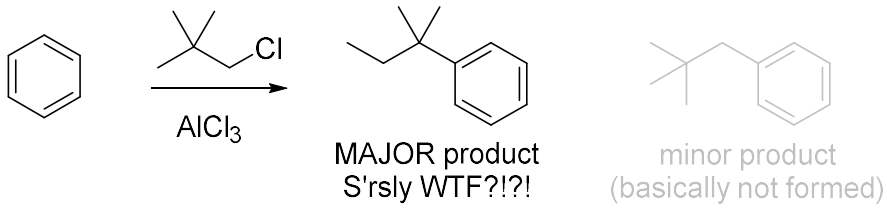
How to handle this…

1. Deep breath / Don't panic!

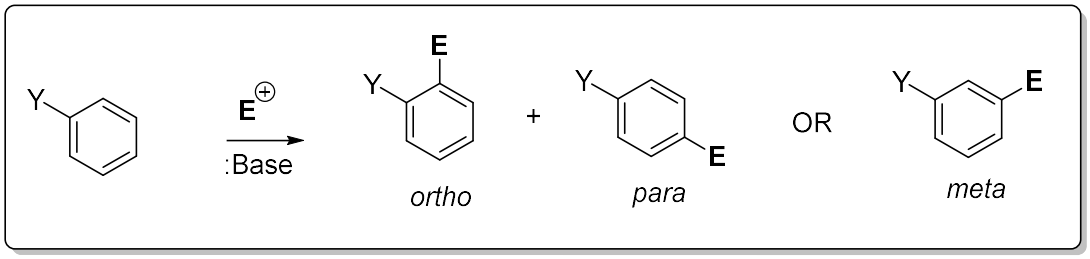
2. Start the mechanism as usual

3. Draw C^+ leading to major product (work backwards)

Alkyl Shift …when a quaternary C is next-door



[18.7-18.10] EArS Substituent Effects



How do these groups effect the rates and substitution pattern in a 2nd EArS rxn?

1. **Activators** make certain positions on the ring more nucleophilic

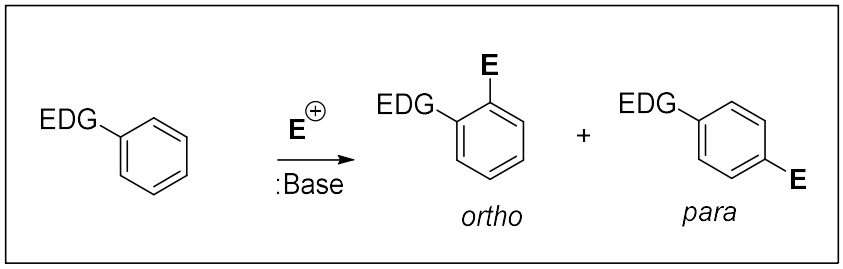
2. C^+ intermediate more stabilized in certain **positions relative to EWG or EDG**

EWG = electron withdrawing group **EDG** = electron donating group

Substituent Effects on EArS Reactions

***ortho/para* activators**	***ortho/para* deactivator**	***meta*-deactivators**
- EDG's - strong by resonance - weak by EN *Ex. OH, NH_2, R groups*	- *Halides only* - weak EWG	- EWG's (not X) - strong by resonance - weak by EN *Ex. NO_2, SO_3H, C(O)R*

EDG's are *Ortho / Para* **Activators**

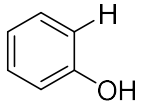


Strong EDG (Resonance)

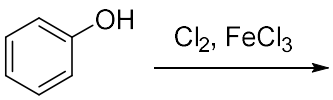
- Atom attached to ring has lp

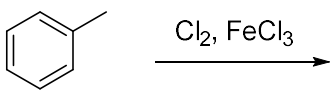
Weak EDG (inductive effect)

- Alkyl groups

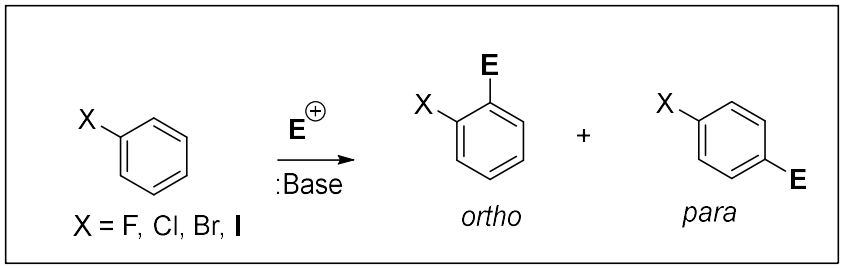


phenol



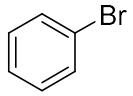


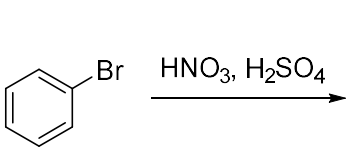
Halides are *Ortho / Para* Deactivators

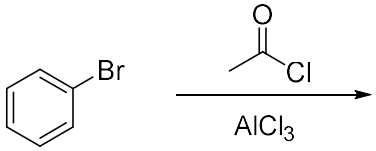


EWG (Electronegativity, EN) = deactivator

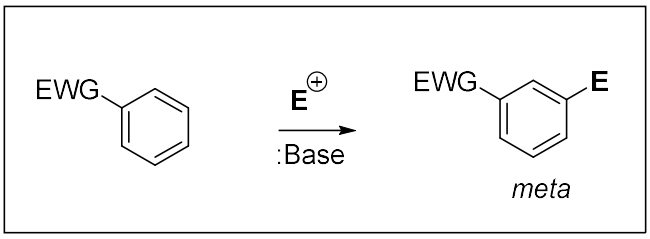
* **EDG (Resonance) = *ortho / para* directors**





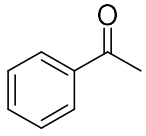


EWG's are *Meta*-Deactivators

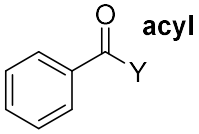


StrongEWG (Resonance)

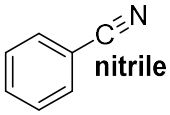
carbonyl or similar group attached to ring



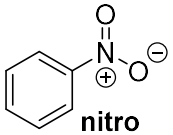
acetophenone



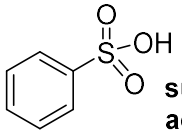
acyl



nitrile



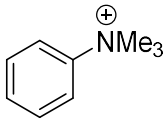
nitro



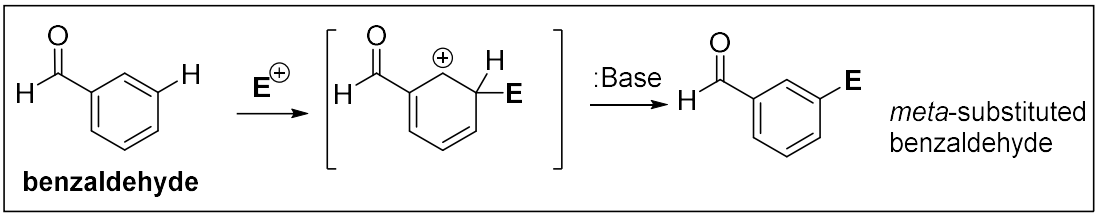
sulfonic acid

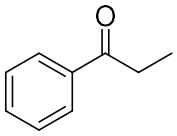
Weak EWG (Induction)

Ammonium groups

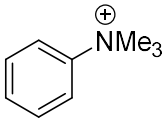


EWG's stabilize C^+ intmd if substitution occurs meta





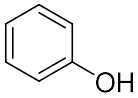
HNO_3, H_2SO_4



Cl_2, $FeCl_3$

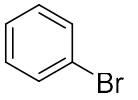
EArS Limitation: Friedel-Crafts reactions don't work with strong EWG(s) on the ring

EDG's are great!



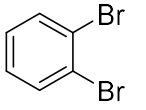
CH_3Cl, $AlCl_3$

Can have 1 halide (weak deactivator) on the ring

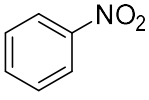


CH_3Cl, $AlCl_3$

No Reaction (NR) with 2+ halides or other EWG



CH_3Cl, $AlCl_3$ NR



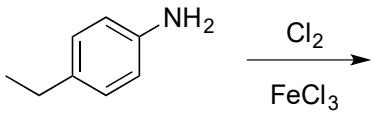
CH_3Cl, $AlCl_3$ NR

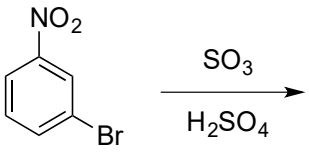
Trisubstituted Benzenes

Strong o/p act	weak o/p act	weak o/p deact	weak m-deact	strong m-deact
- OH	$-CH_3$	-Cl	$-{}^{+}NR_3$	$-NO_2$

EArS on Disubstituted Benzene:

Position of 3rd substituent dictated by the **strongest activator** (or weakest deactivator)

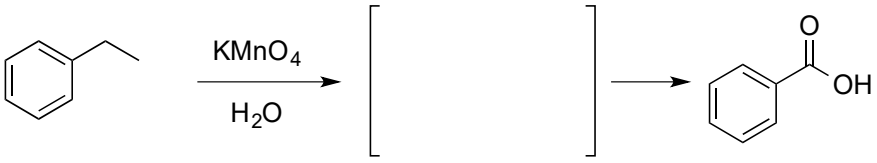




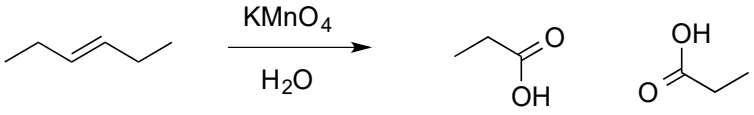
Chapter 18 Review of Reactions

Chapter 17 Review (?): REACTIONS AT THE BENZYLIC POSITION

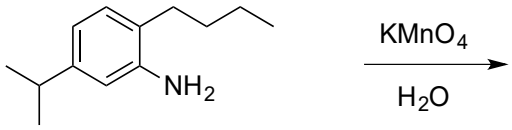
Oxidative Cleavage of Alkyl Benzenes

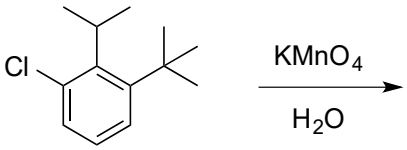


Recall from Chapter 8...



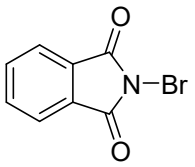
Oxidative Cleavage cont'd





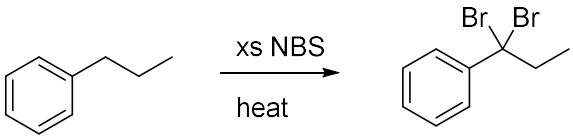
2. Benzylic Bromination

Da brominator:



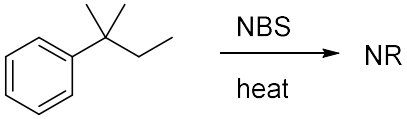
N-bromosuccinimide (NBS)

What if there's an excess of NBS?

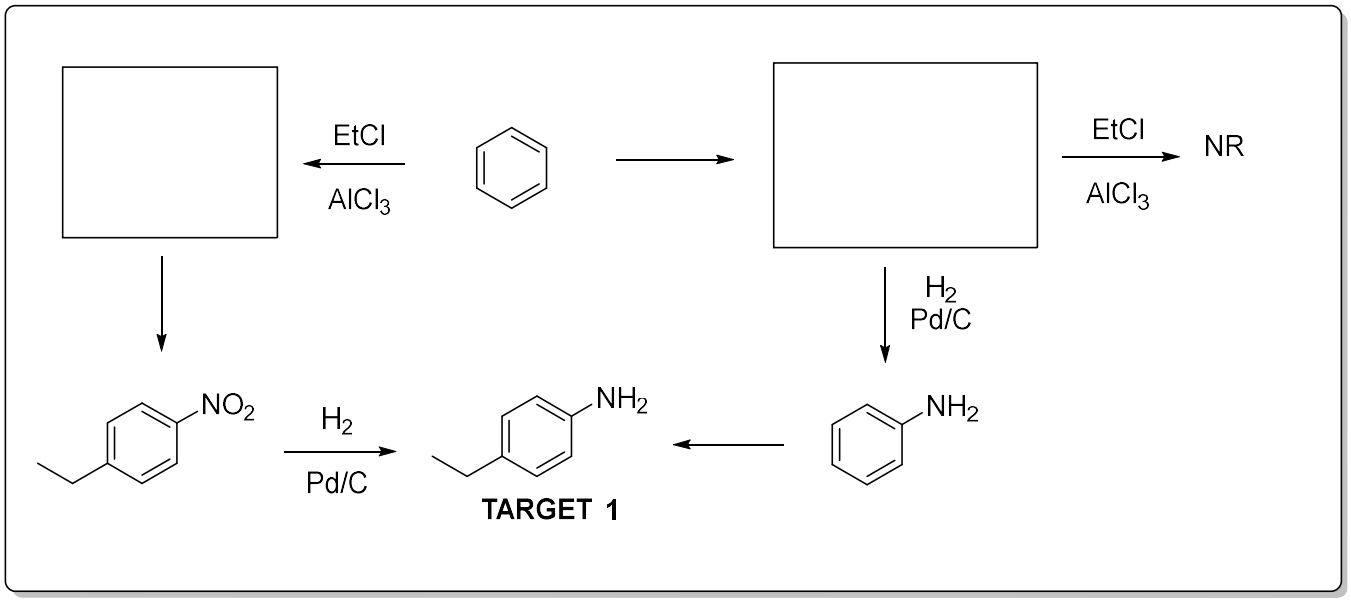


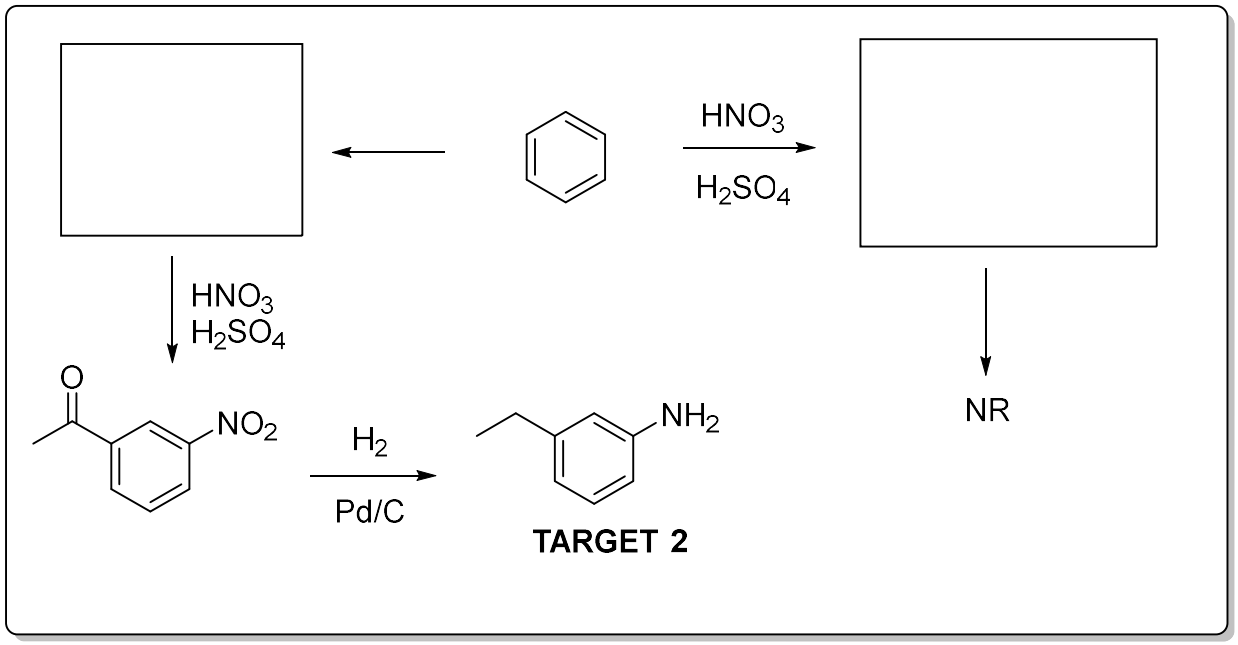
What about toluene?

Limitation: benzylic H's are required



Reaction Puzzles: Disubstitution with EArS





POLYSUBSTITUTED BENZENES…Strategery!

Chapter 18 Mega-Puzzle