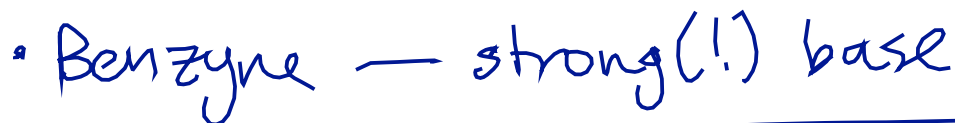
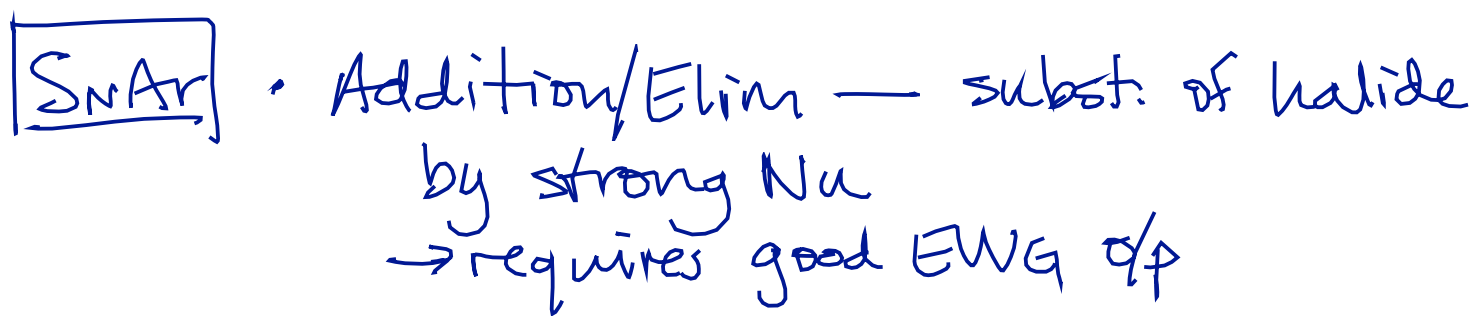
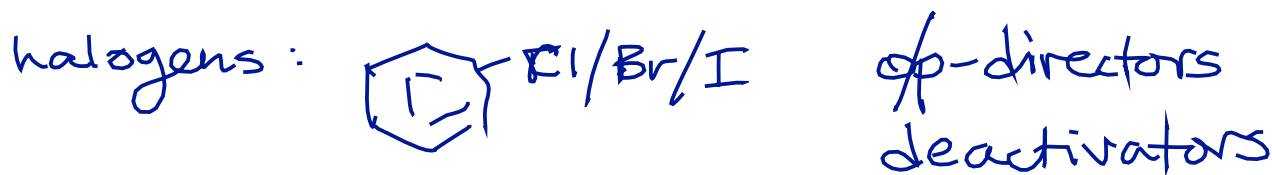
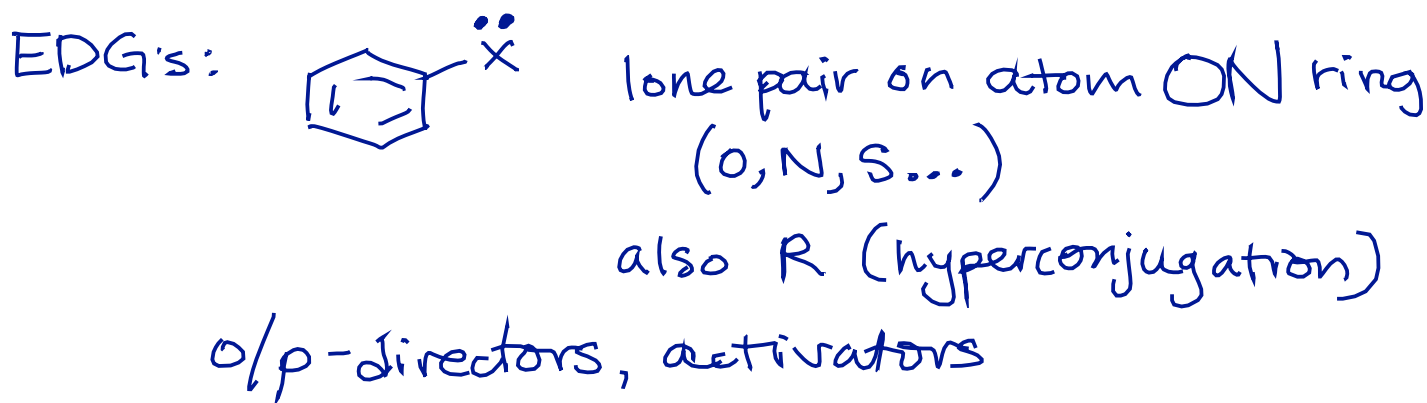
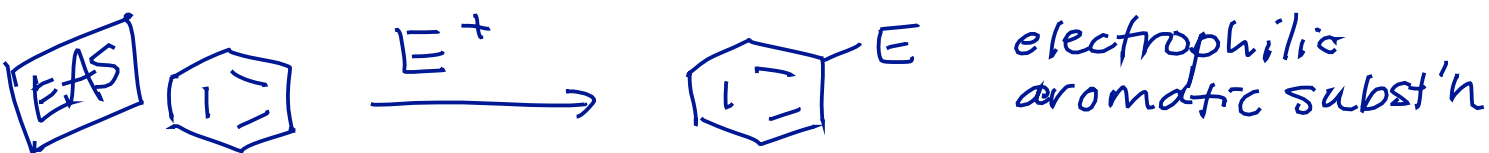
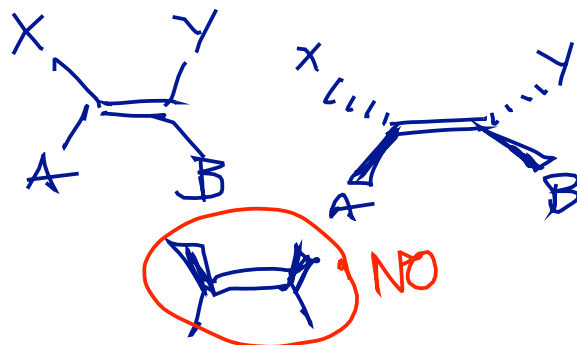
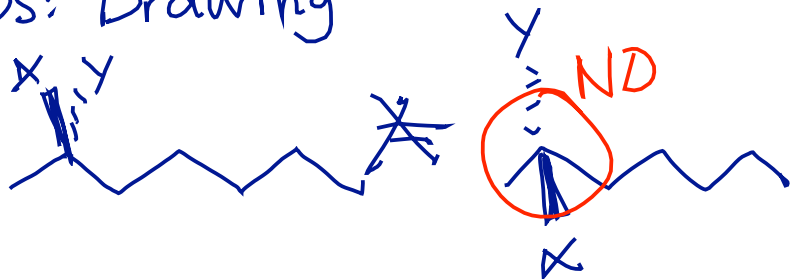


Recap:

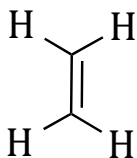


Tips: Drawing

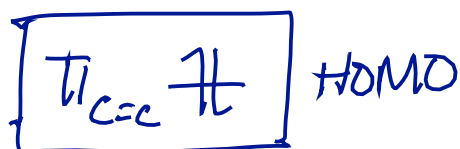


Molecular Orbitals of Aldehydes & Ketones

Draw molecular orbital diagrams for the following molecules and identify the HOMO and LUMO of each. In what ways are they similar; in what ways are they different?

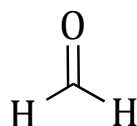


(σ^*)

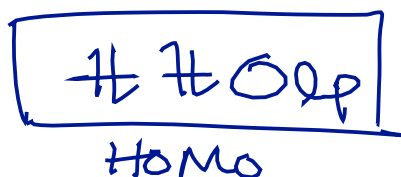
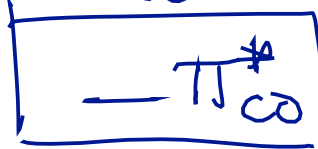


(σ -bonding)

alkenes are Nu:
(donor)



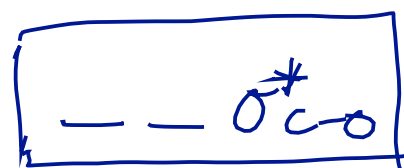
LUMO



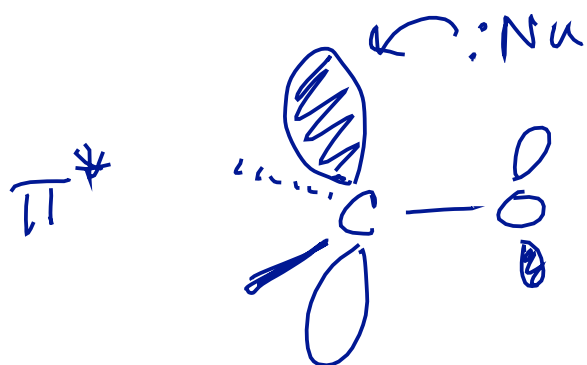
carbonyl \rightarrow
electrophiles



LUMO

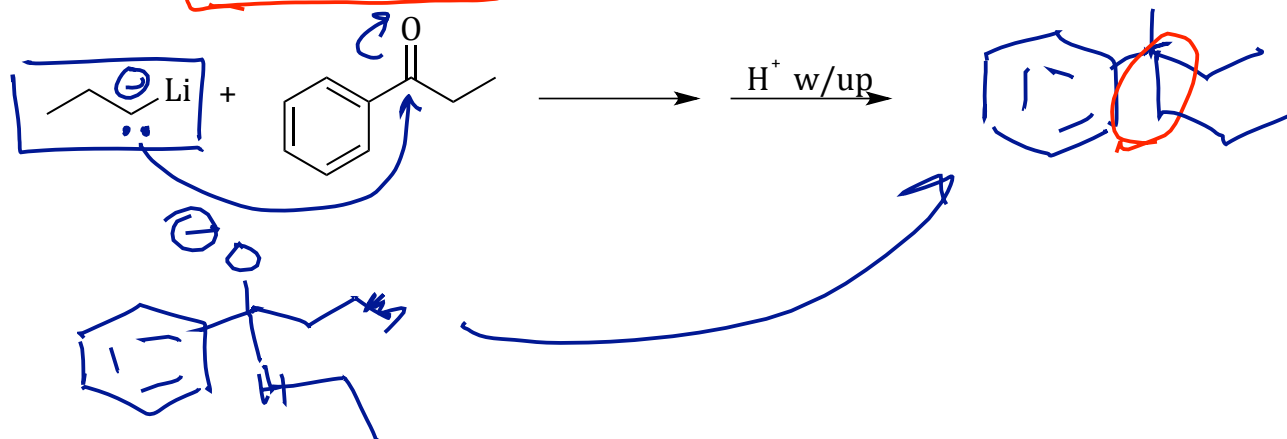
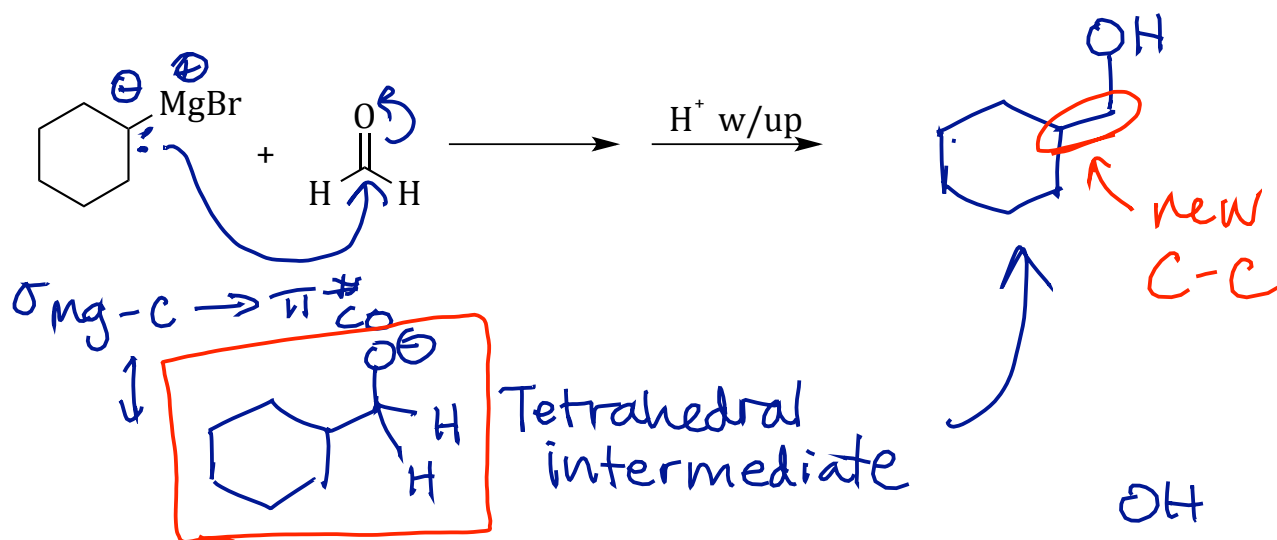
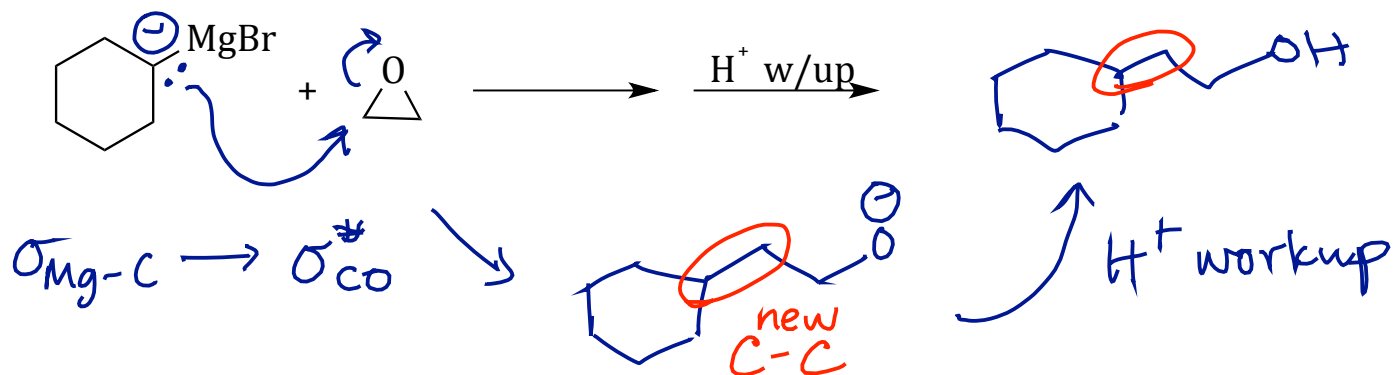


ring strain
weak C-O
bonds \therefore
electrophile



Irreversible Addition to Aldehydes & Ketones: Organometallic Reagents

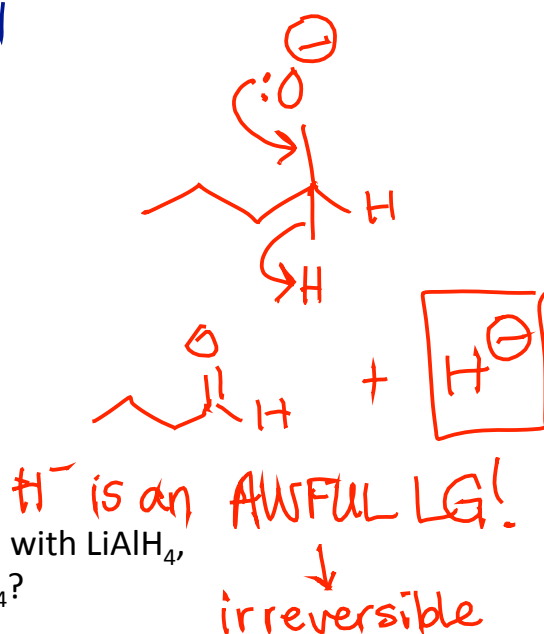
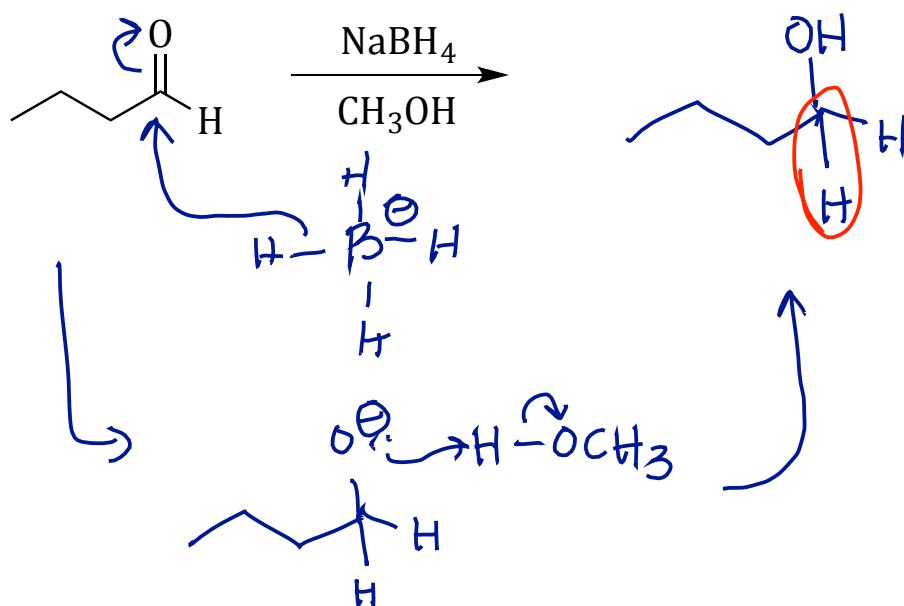
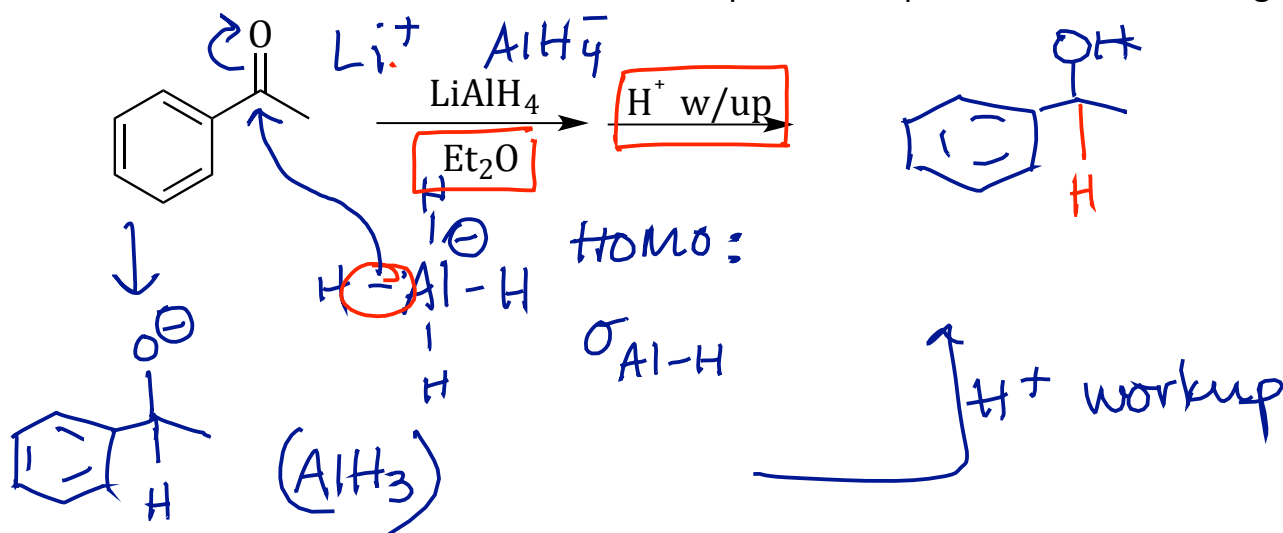
Provide a curved-arrow mechanism and predict the product of the following reactions:



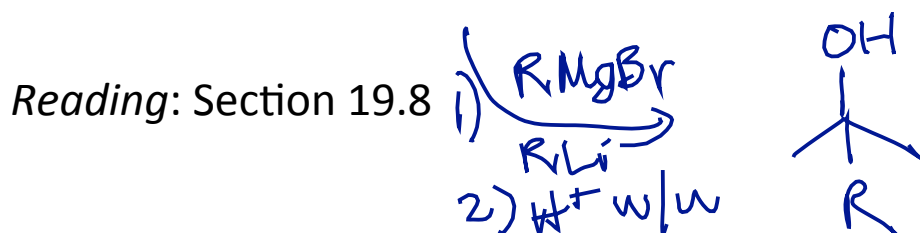
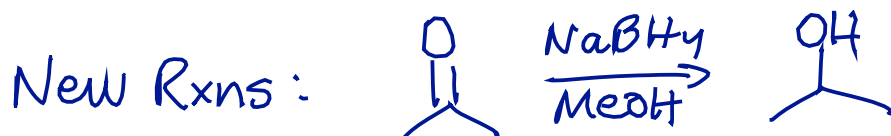
Fate #1: protonation

Irreversible Addition to Aldehydes & Ketones: Hydride Reducing Reagents

Provide a curved-arrow mechanism and predict the product of the following reactions:



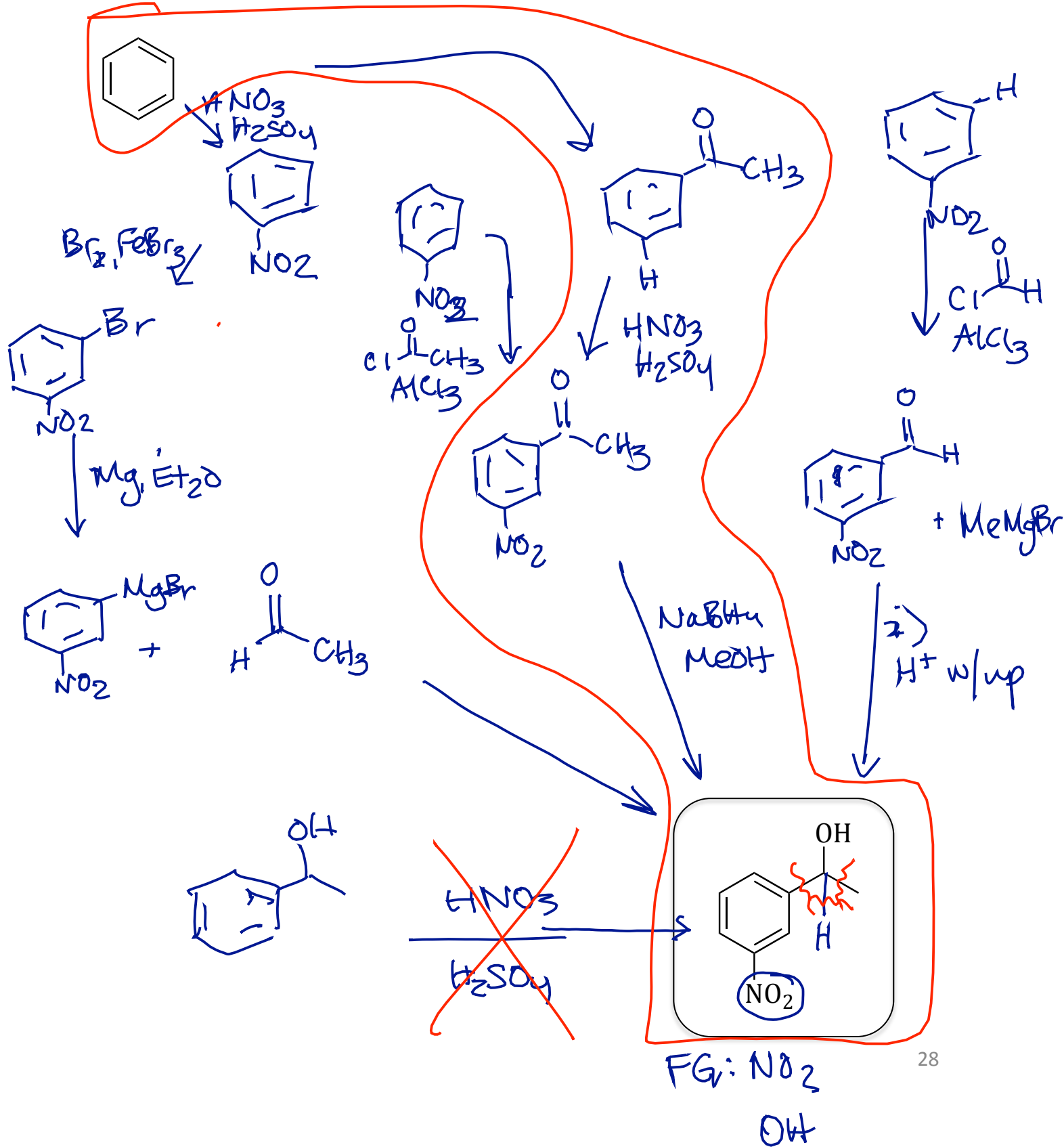
Why is acid work-up required for reduction with LiAlH_4 , but not for reduction with NaBH_4 ?



Reading: Section 19.8

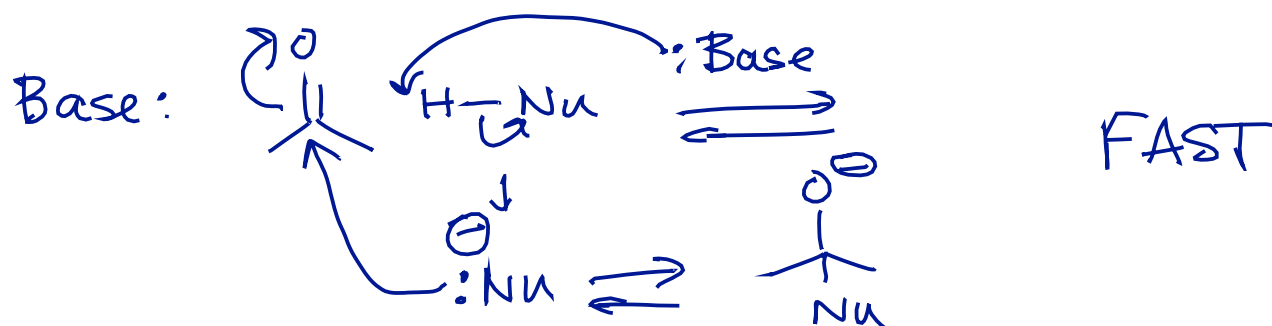
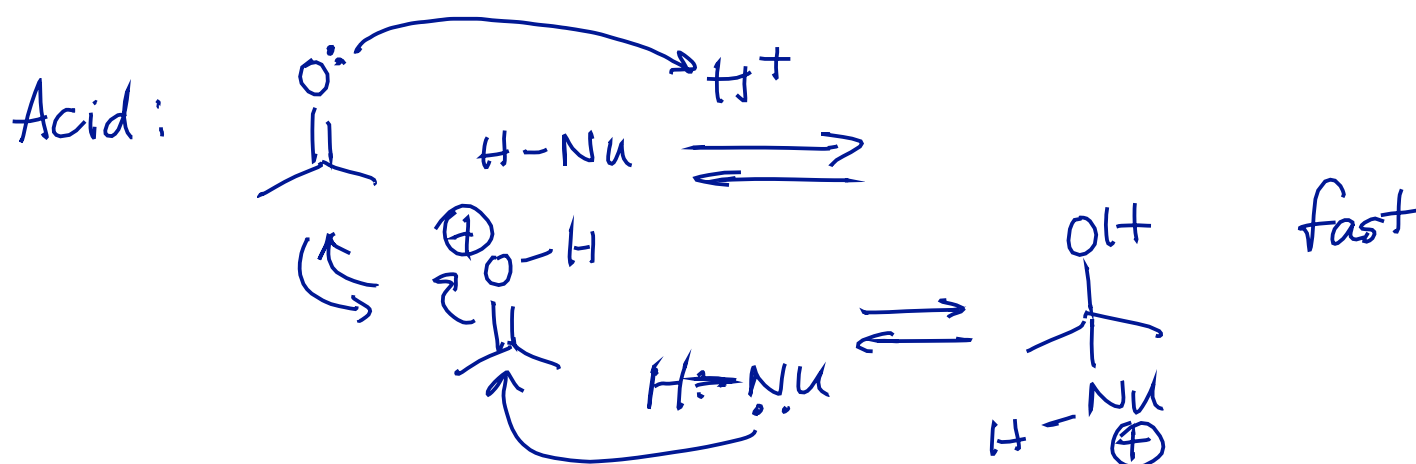
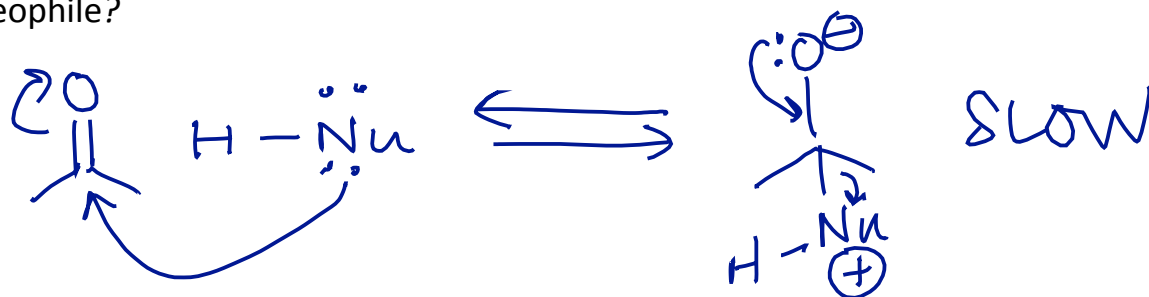
Putting it Together: Synthesis

Starting from *benzene*, provide a synthesis of the following compound:



Reversible Addition to Carbonyls: pH-Dependence

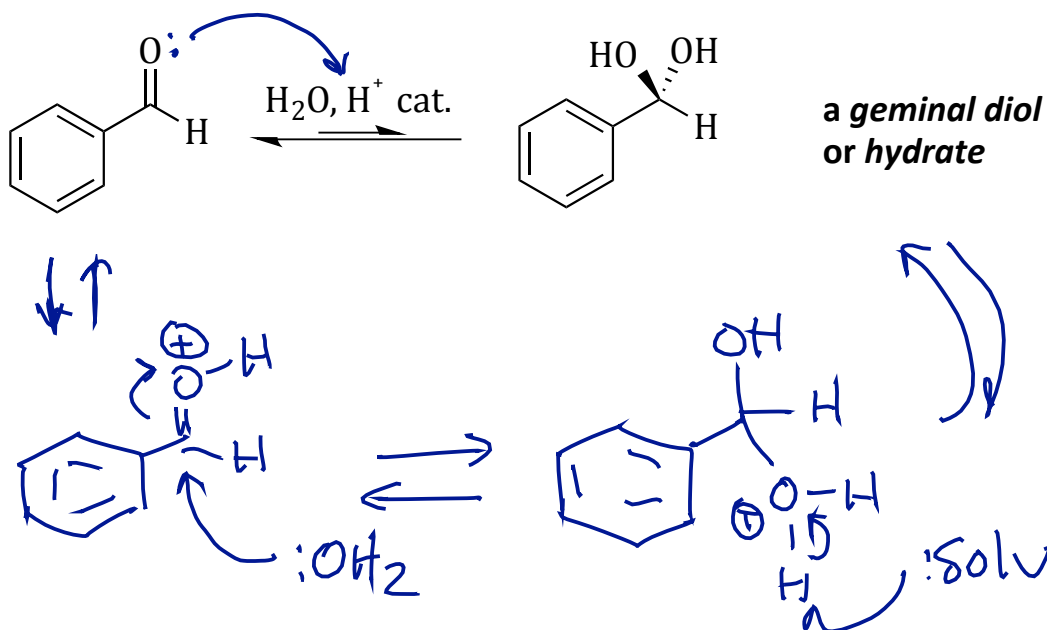
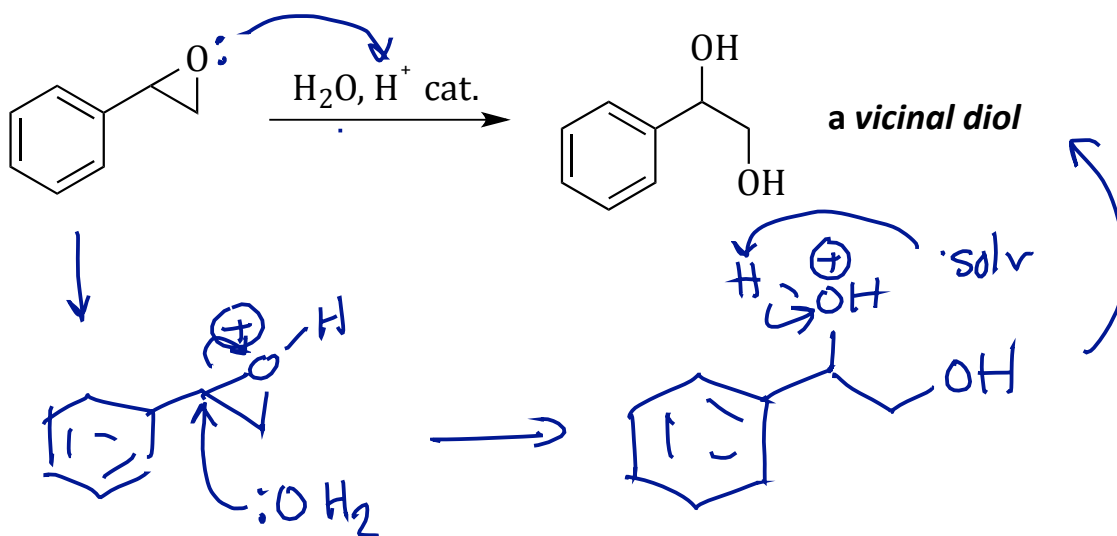
Hydride reducing agents and organometallic reagents are both examples of *excellent*, strong nucleophiles. What happens if we treat a carbonyl compound with a *weaker* nucleophile?



Acid catalysts make an *electrophile more electrophilic*;
base catalysts make a *nucleophile more nucleophilic*.

Reversible Addition to Carbonyls: Acidic Conditions

Provide complete curved-arrow mechanisms for the following reactions:

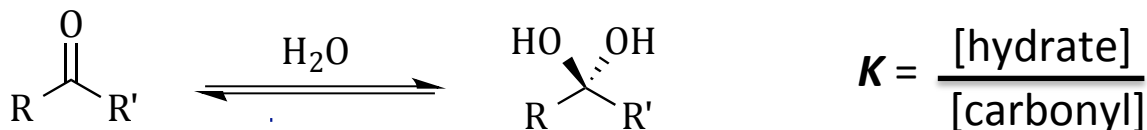


Why is the hydration of an aldehyde or ketone *reversible*?

all steps are reversible
(incoming nucleophile
good leaving group)

Reversible Addition to Carbonyls: Hydration Equilibria

Explain the observed ranking of equilibrium constants for carbonyl hydration:

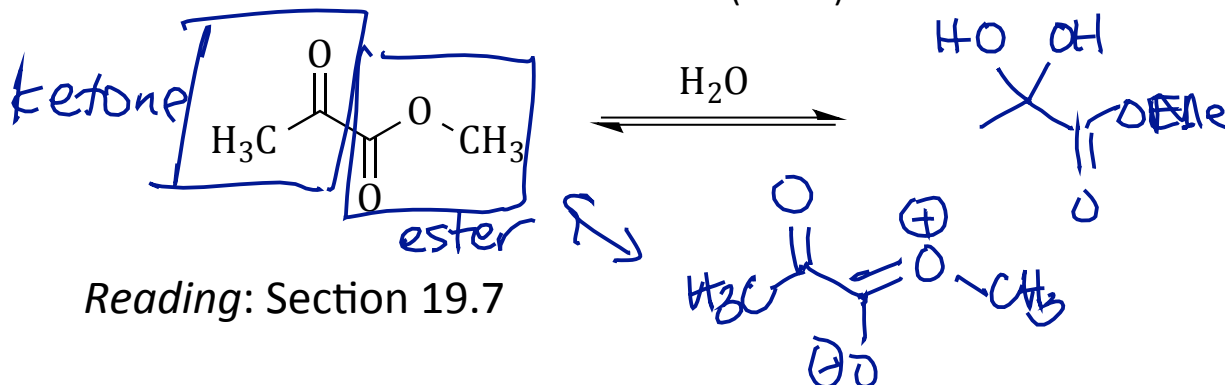


Carbonyl compound	relative K
<chem>FC(F)(F)C(=O)C(F)(F)F</chem>	1×10^6
<chem>FC(F)(F)C=O</chem>	3×10^4
<chem>C=O</chem>	2×10^3
<chem>CC=O</chem>	1
<chem>CC(=O)C</chem>	1×10^{-3}
<chem>CC(=O)c1ccccc1</chem>	9×10^{-6}

Handwritten notes:

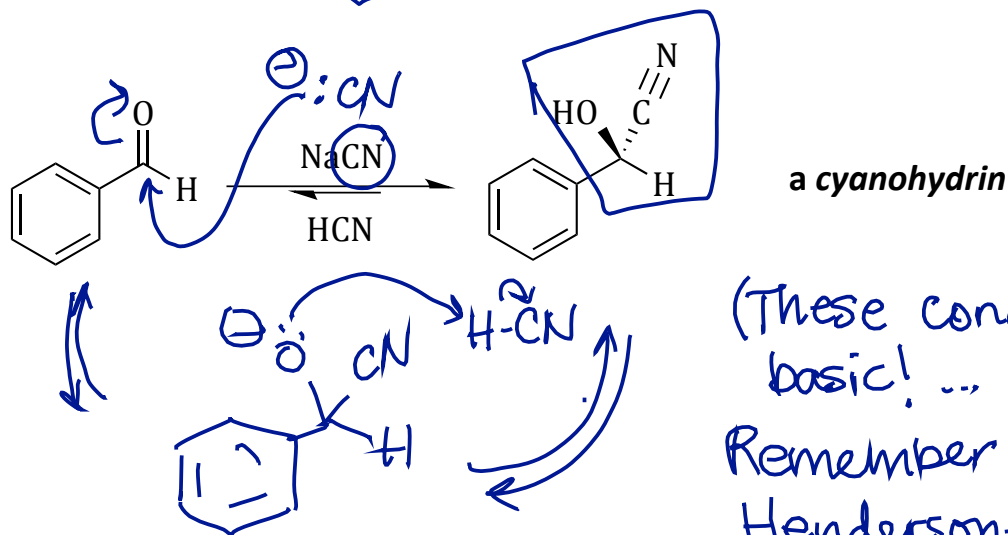
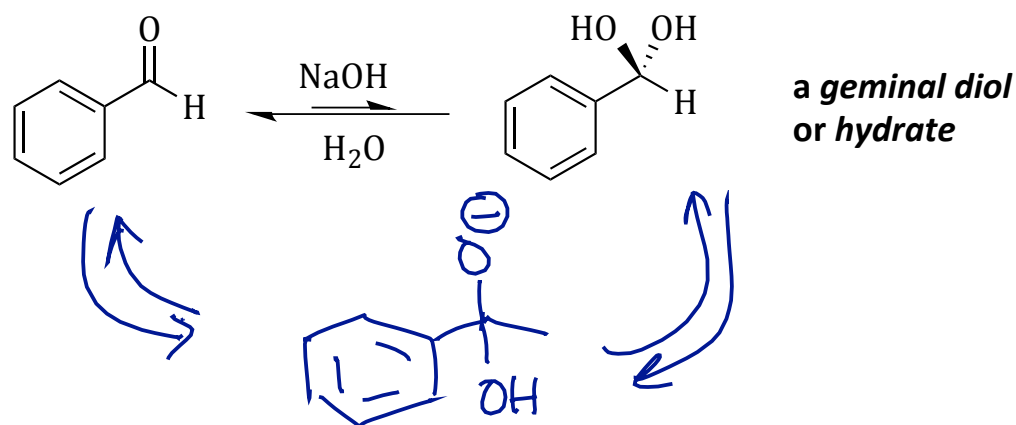
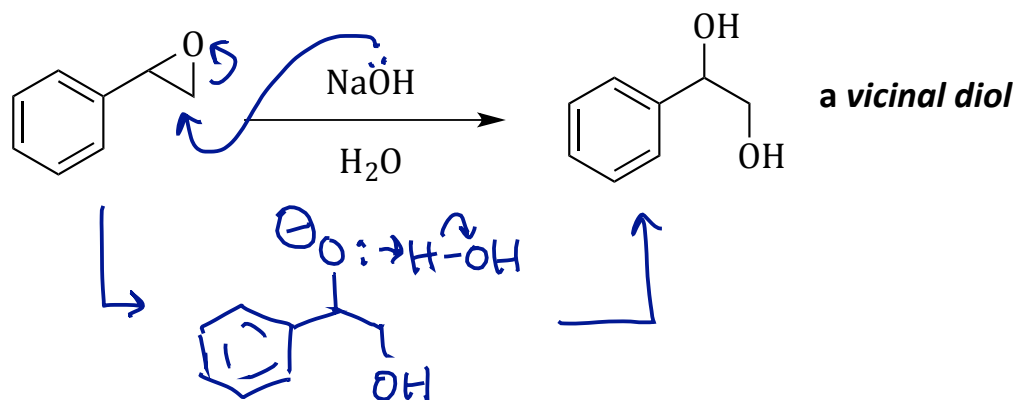
- big \therefore favor hydrate** (for 10^6 to 10^3)
- EWGs destabilize $\text{C}=\text{O}$ \therefore more electrophilic** (for 10^6 to 10^3)
- small, favor carbonyl** (for 10^{-3} to 10^{-6})
- EDG stabilizes $\text{C}=\text{O}$ \therefore less electrophilic** (for 10^{-3} to 10^{-6})
- no hyperconj. from H** (for $\text{H}_3\text{C}-\text{C}=\text{O}$)

The following compound has two carbonyl groups. Which one will become hydrated under aqueous conditions? Explain why $K_{\text{rel}} = 0.8$, i.e. significantly larger than for most unsubstituted ketones such as acetone (above).



Reversible Addition to Carbonyls: Basic Conditions

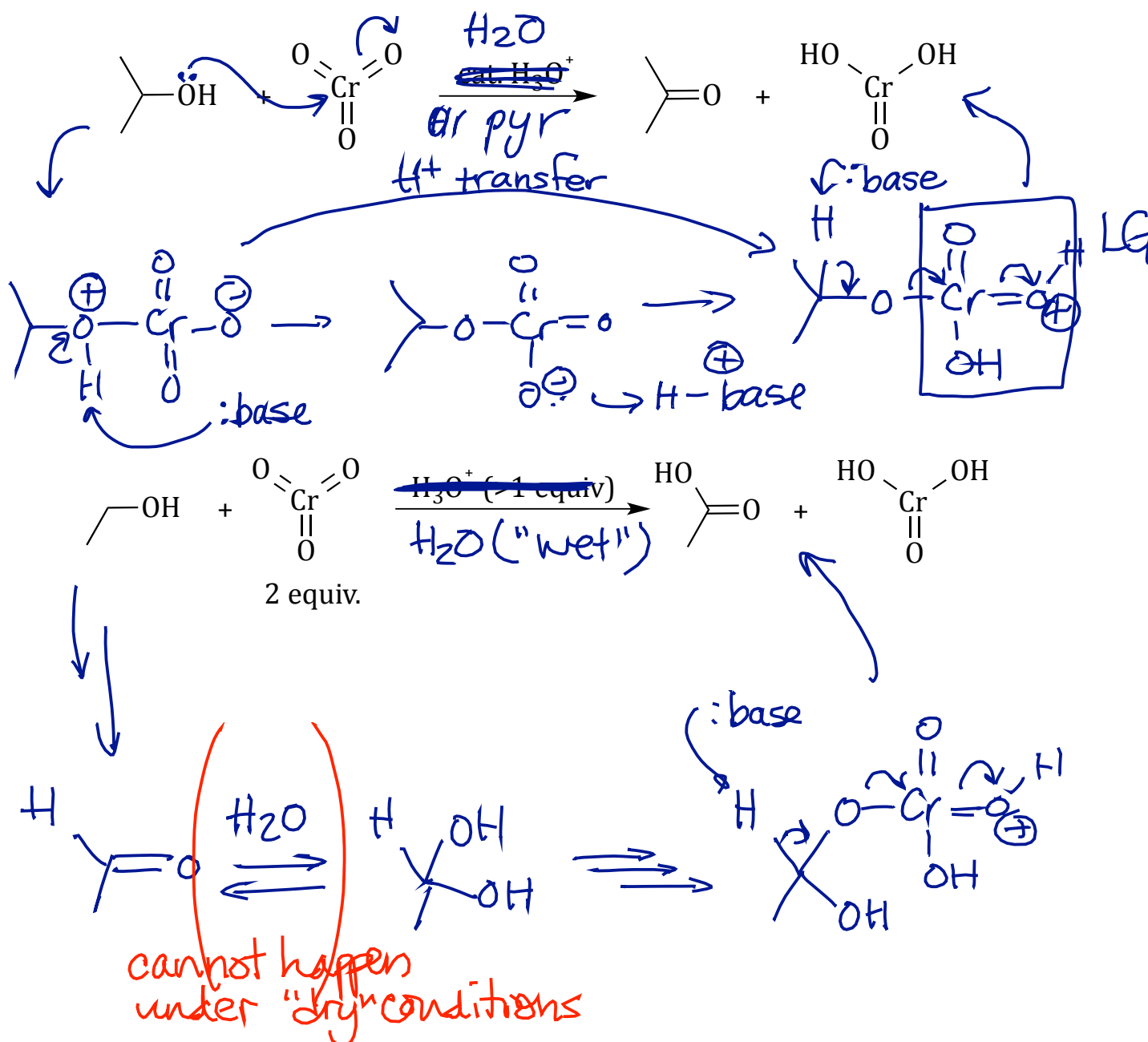
Provide complete curved-arrow mechanisms for the following reactions:



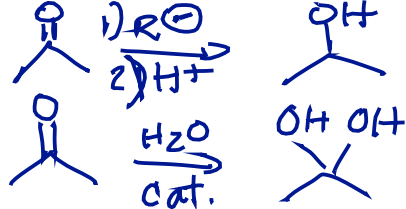
(These conditions are basic! ... It's a buffer. Remember Henderson-Hasselbalch?)

Going Backward: Oxidation of Alcohols

Provide curved-arrow mechanisms for each of the following oxidation reactions.



Why are wet & dry condⁿs diff.

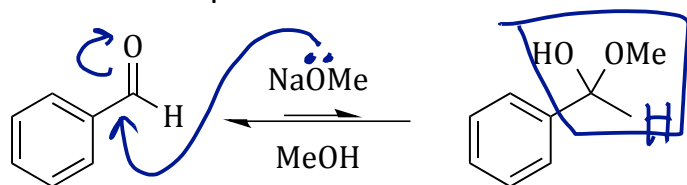


$R-OH$ as Nuc.

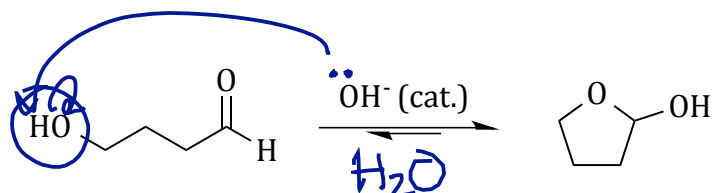
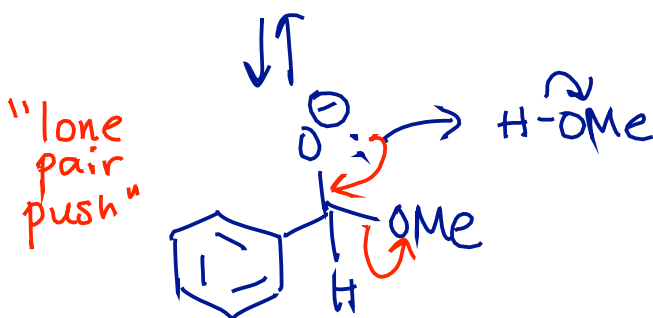
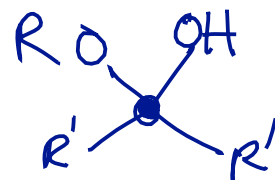
July 16, 2014

Reversible Addition to Carbonyls: Hemiacetals

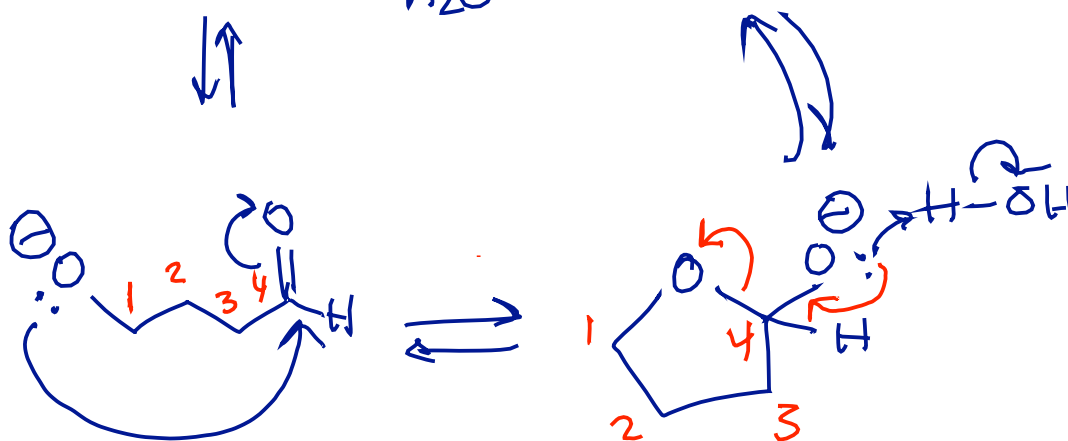
Provide a complete curved-arrow mechanism for each of the following reactions:



a hemiacetal



a cyclic hemiacetal



Monosaccharides (glucose, fructose, etc.) all exist naturally as hemiacetals; we'll discuss more later...

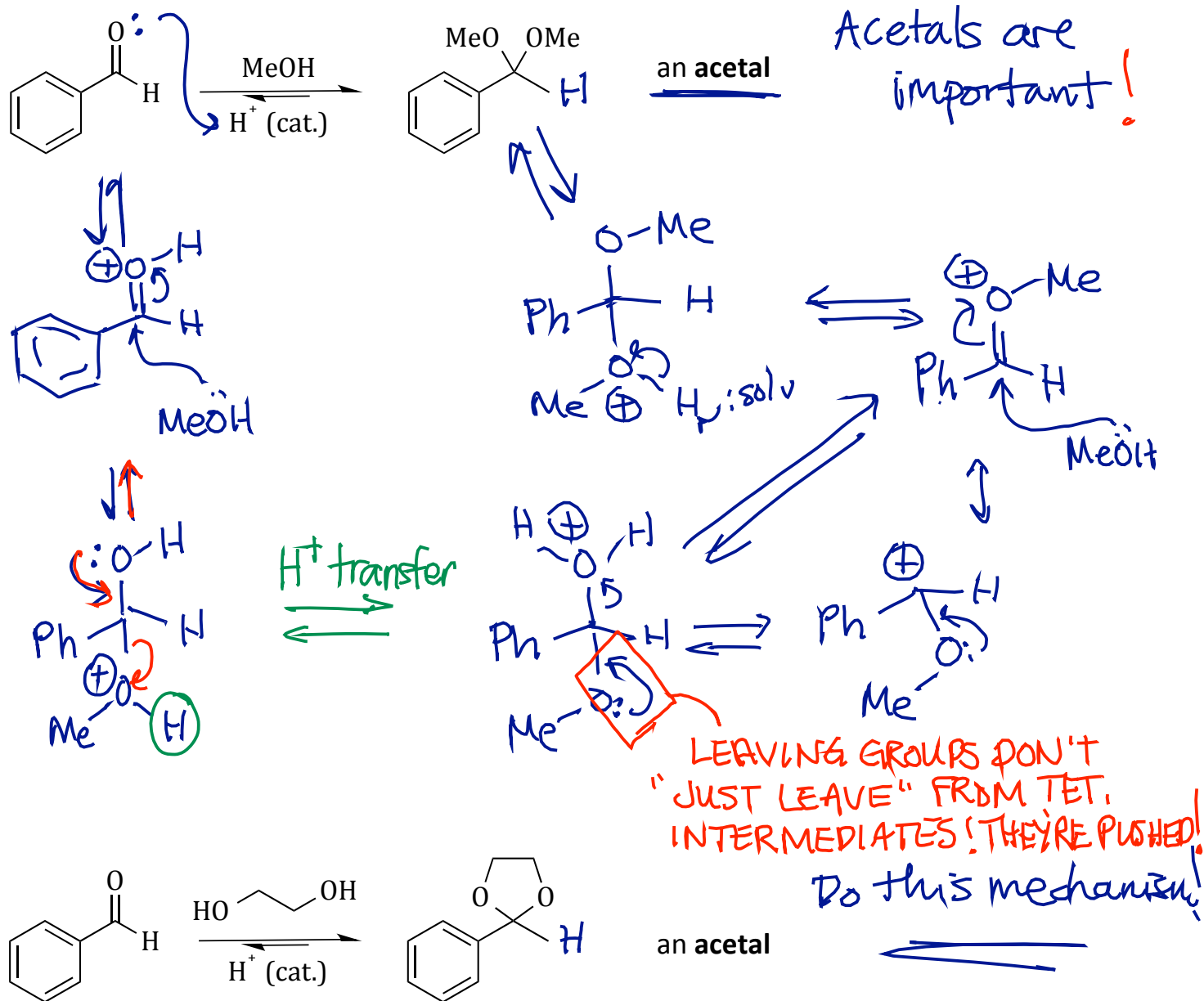
R-OH = Nuc:

Week 4

July 16, 2014

Reversible Addition to Carbonyls: Acetals

Provide a complete curved-arrow mechanism for each of the following reactions:



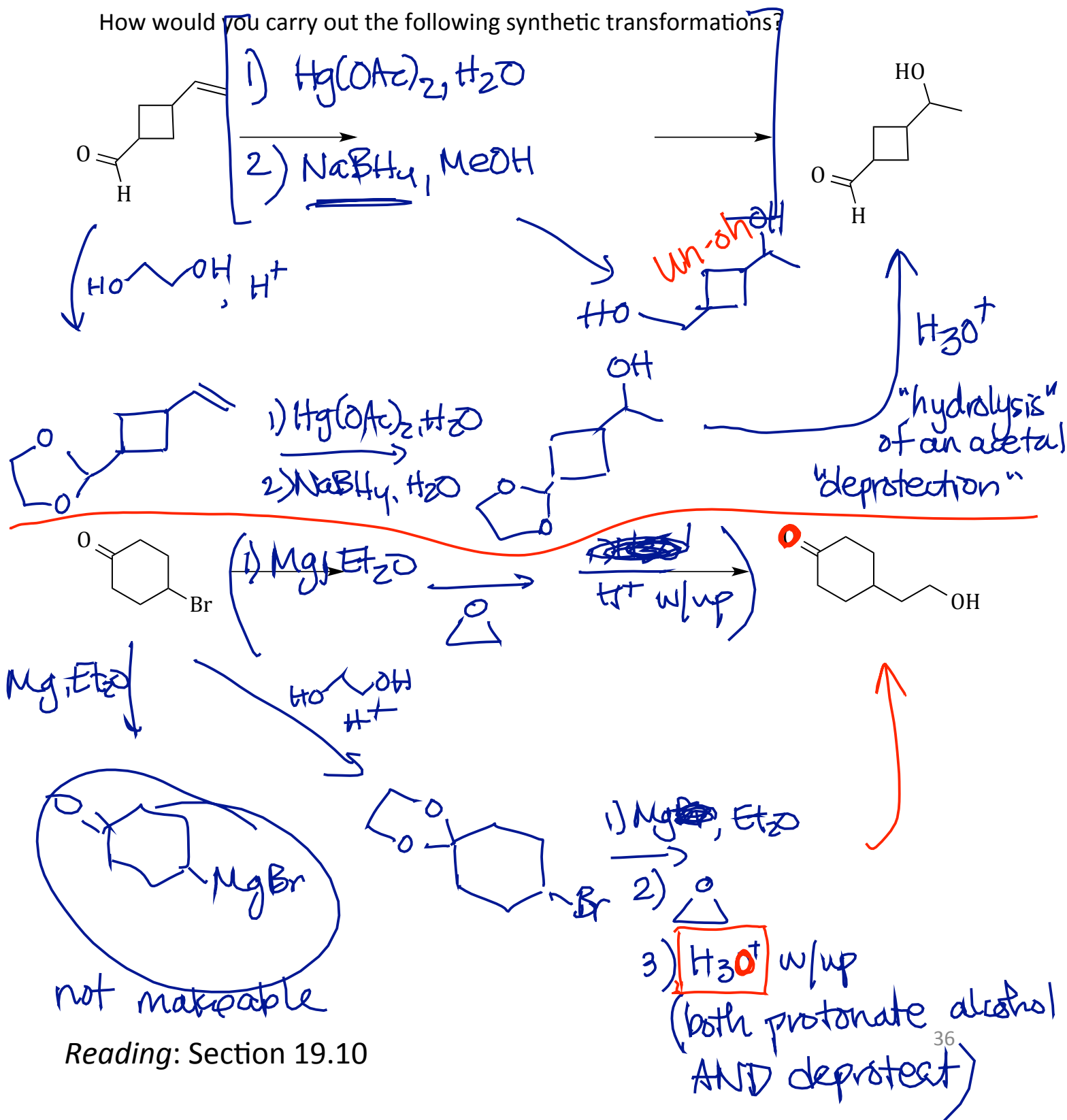
Acetals → make them under acidic conditions,

Reading: Section 19.10

STABLE to basic
conditions

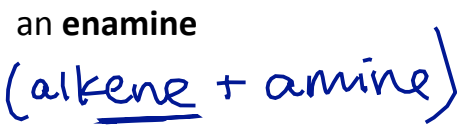
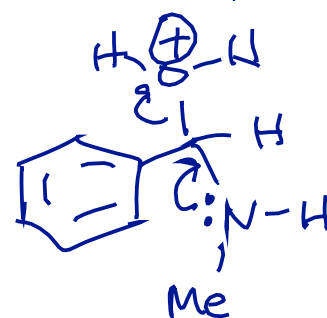
Reversible Addition to Carbonyls: Acetals as Protecting Groups

How would you carry out the following synthetic transformations?



H^+ - solv
 H^+ \oplus Me
 ctions.

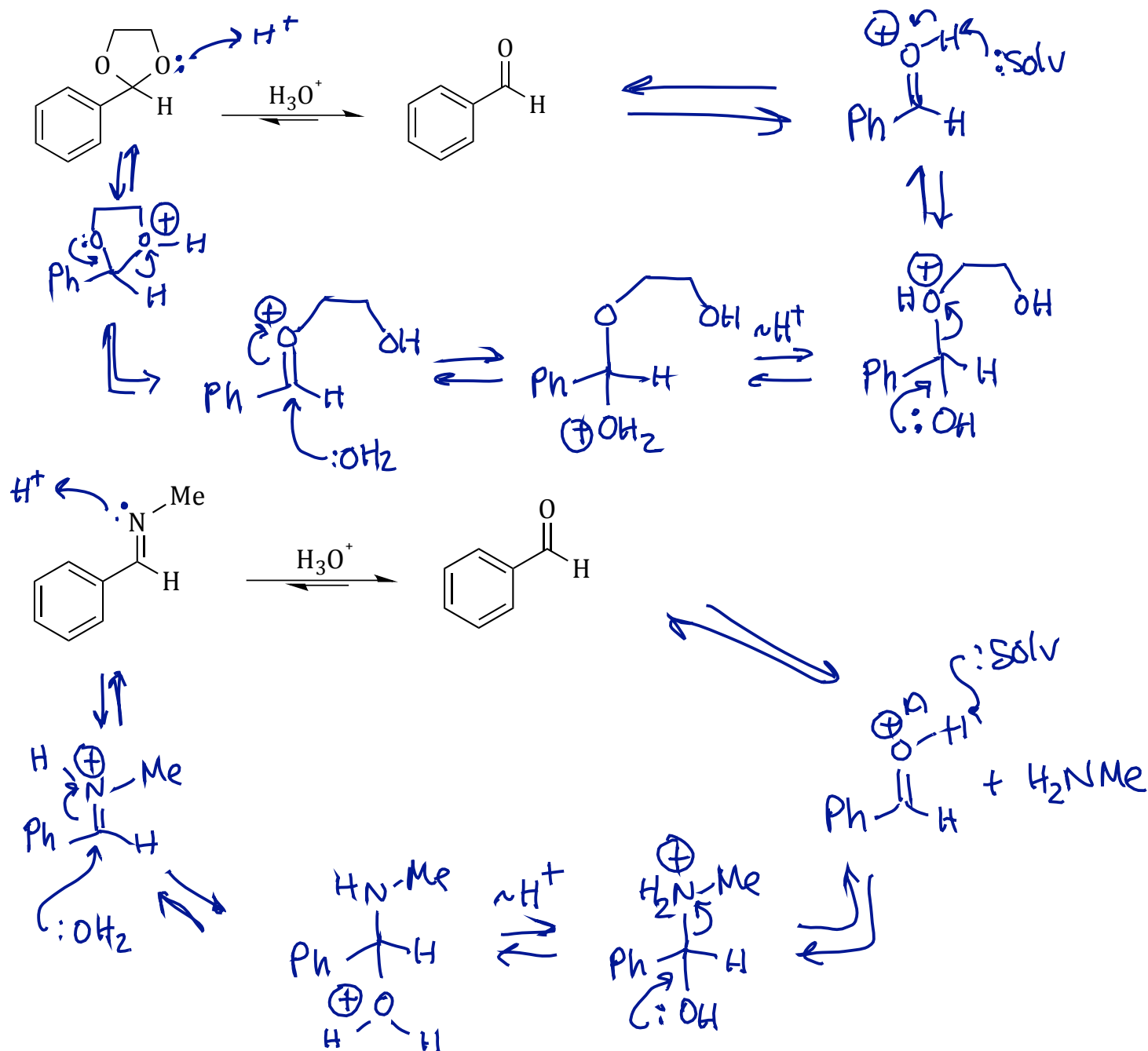
↑↓



Why pH 5? mildly acidic
acidic enough to \oplus some carbonyl
but leaves some amine unprotonated

Reversible Addition to Carbonyls: Hydrolysis of Acetals, Iminium Ions, & Enamines

The hydrolysis of acetals & imines is simply the reverse of their formation! Provide a complete curved-arrow mechanism for each of the following reactions.



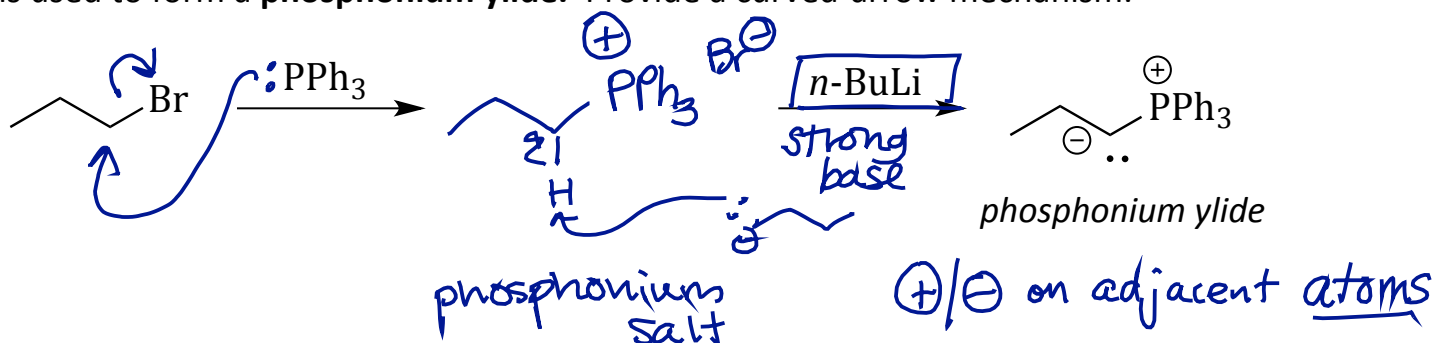
pronounced "Vittig" 1979

Week 4

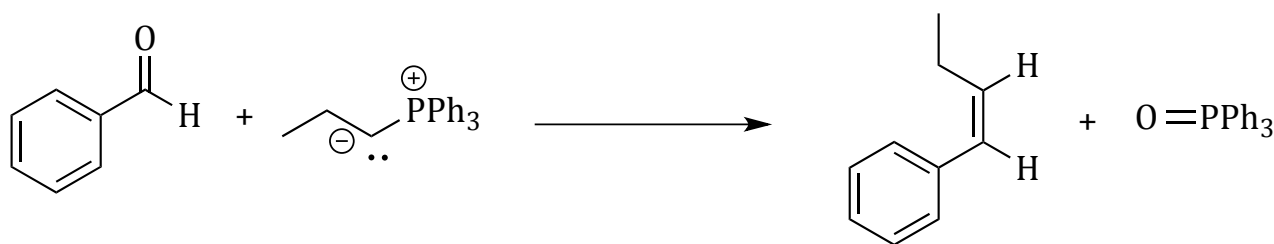
July 16, 2014

The Wittig Reaction: Synthesizing Alkenes from Carbonyls

The Wittig reaction is a remarkably useful synthesis of alkenes. First, an alkyl halide is used to form a **phosphonium ylide**. Provide a curved-arrow mechanism.



Then the phosphonium ylide is added to an aldehyde or ketone to yield a new carbon-carbon **double** bond! Provide a mechanism.



** The Wittig reaction tends to give *cis* alkenes when there is a choice. **

Reading: Section 19.13