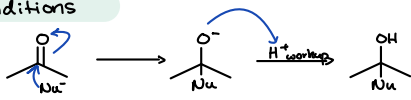
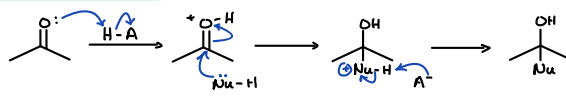


General Nu⁻ addition
Basic Conditions



Acidic Conditions



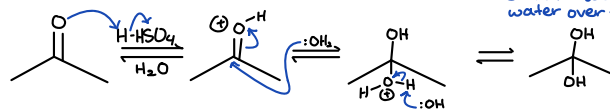
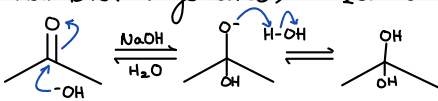
- Strong Bases add irreversibly to C=O
↳ Hydride reagents and Organometallics
- Moderate and weak Bases add reversibly to carbonyls under acidic and basic conditions
↳ OH⁻, OR⁻, RNH₂, R₂NH, H₂O, ROH
↳ equilibrium can often be shifted w/ Le Chatlier's

* single addition not that stable. Tough to isolate intermediates because over time they will decompose and lose water, alcohol, or the amine added.

Summary

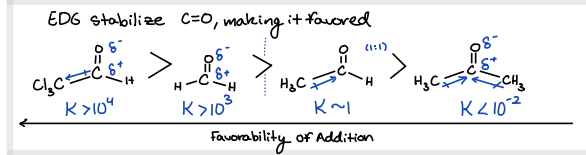
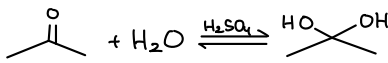
<chem>C=O</chem>	$\xrightleftharpoons[\text{Acid or Base}]{\text{H}_2\text{O}}$	<chem>C(OH)2</chem> Geminal diol (hydrate)
<chem>C=O</chem>	$\xrightleftharpoons[\text{Acid or Base}]{\text{ROH}}$	<chem>C(OH)(OR)</chem> Hemiacetal
<chem>C=O</chem>	$\xrightleftharpoons[\text{Acid}]{\text{RNH}_2}$	<chem>C(OH)(NHR)</chem> Hemiaminal
<chem>C=O</chem>	$\xrightleftharpoons[\text{Acid}]{\text{R}_2\text{NH}}$	<chem>C(OH)(NR2)</chem> Hemiaminal
<chem>C=O</chem>	$\xrightleftharpoons[\text{Acid Only}]{\text{ROH, -H}_2\text{O}}$	<chem>C(OR)2</chem> Acetal
<chem>C=O</chem>	$\xrightleftharpoons[\text{Acid}]{-\text{H}_2\text{O}}$	<chem>C=NR</chem> Imine
<chem>C-H</chem>	$\xrightleftharpoons[\text{Acid}]{-\text{H}_2\text{O}}$	<chem>C=C-NR2</chem> Enamine

Geminal Diols (Hydrates) - H₂O/-OH



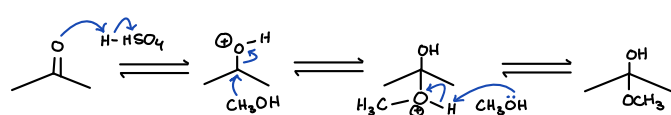
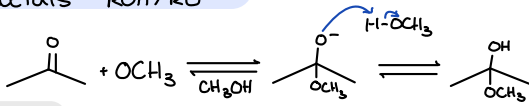
* even if we remove acid or base, will still lose water over time

Hydrates in equilibrium w/ C=O

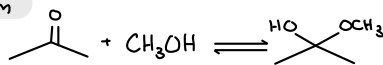


* tough to isolate hydrates even when fav. equil.

Hemiacetals - ROH/RO⁻



Equilibrium

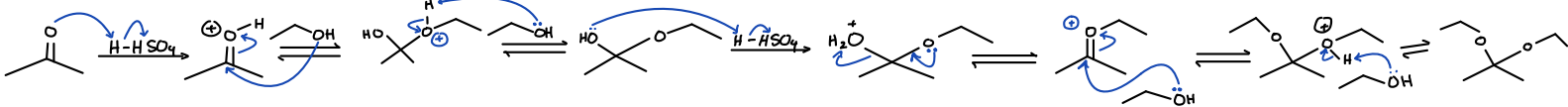
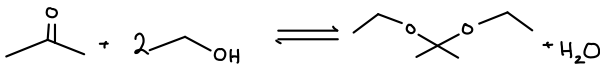


Hemiacetals can be isolated only w/ fav. equil.

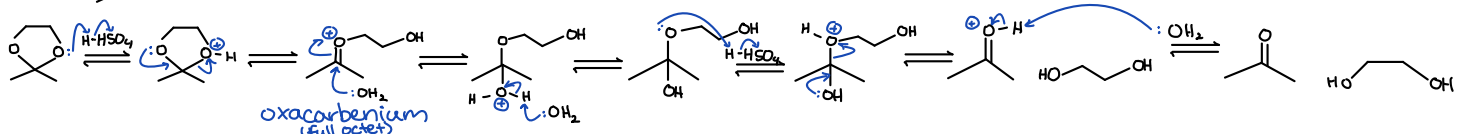
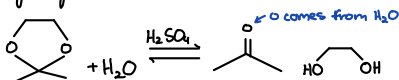
↳ certain aldehydes, 5 mem or 6 mem cyclic hemiacetals



Acetals - ROH

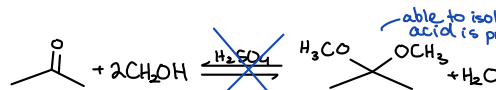


Acetal Hydrolysis - Reverse Mechanism



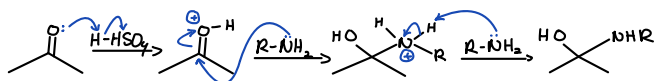
* Equilibrium only when conditions are acidic

- carbonyl or acetal can be favored w/ different conditions
↳ once acid quenched, no more interconversion possible

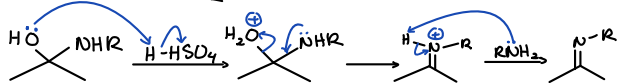


able to isolate acetal bc it can only react when acid is present

Hemiaminal Formation - RNH₂

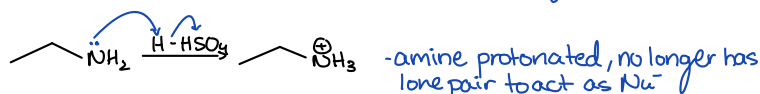


Imine Formation - RNH₂

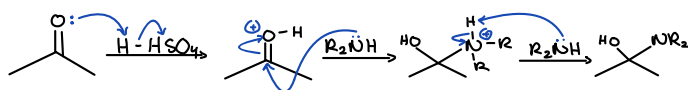


Imine / Enamine Formation best in Mild Acid

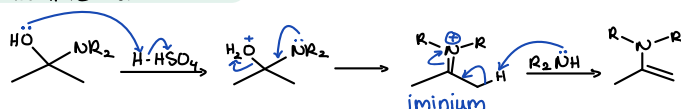
- imines and enamines can form under neutral conditions, but slower
- very concentrated SA shuts down rxn pH ~ 4-5 optimal



Hemiaminal Formation - R₂NH

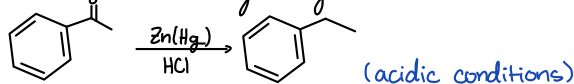


Enamine Formation

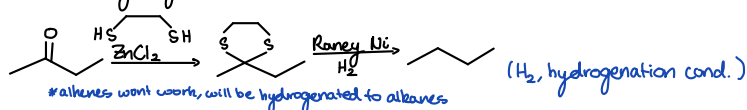


Carbonyl Deoxygenation

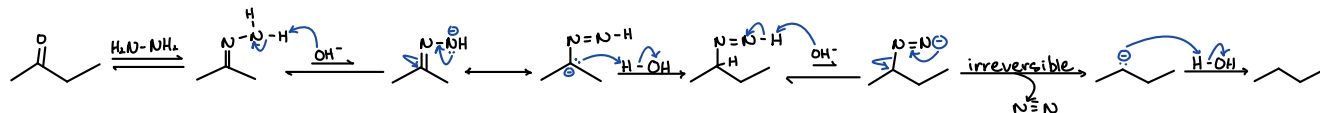
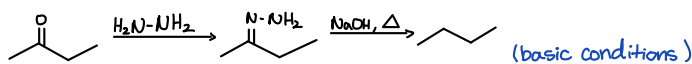
Clemmensen Reduction (benzylic only)



Thioacetal Hydrogenation

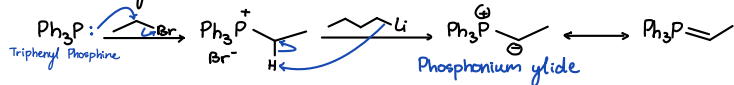


Wolff-Kishner Reaction



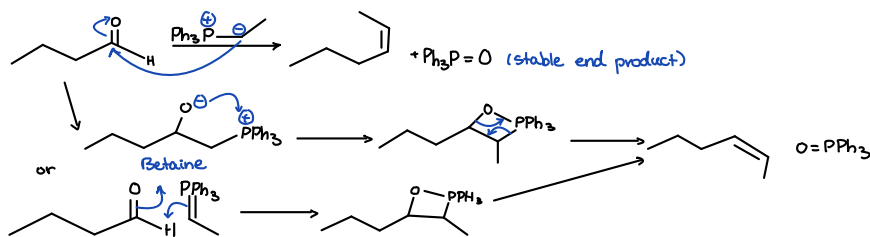
Wittig Reaction

Preparation of reagent

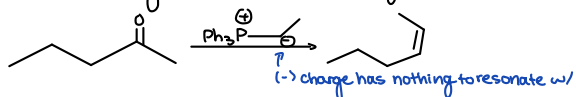


* (+) charge on phosphorus makes adjacent protons a little acidic

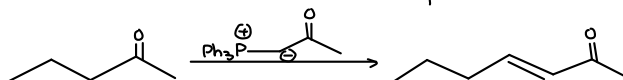
Reaction



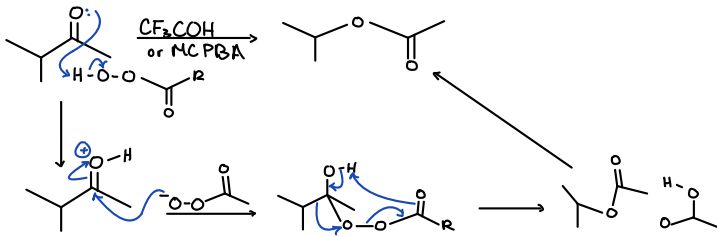
Stereoselectivity — unstabilized ylide → cis product



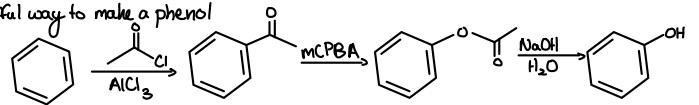
Resonance stabilized → trans prod.



Baeyer-Villiger Reaction

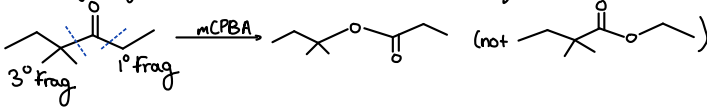


* Useful way to make a phenol



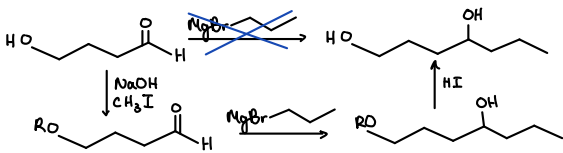
Regioselectivity

Migratory aptitudes: $H > 3^\circ > 2^\circ > Ph > 1^\circ > methyl$



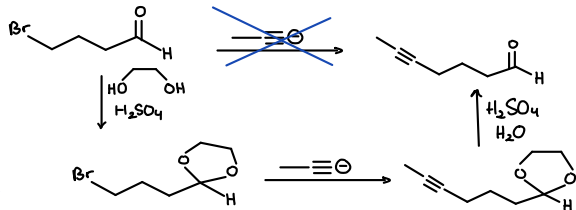
Protecting Groups

Alcohol \rightarrow Ether



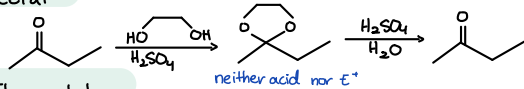
- Grignards not compatible w/ free OH groups, H on O is acidic enough to be taken by SB like an organometallic — won't get addition, just deprotonation

Carbonyl \rightarrow acetal



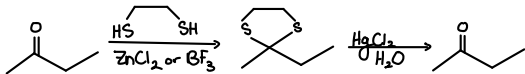
* αE^- in mole. alkynyl ion will add to either $C=O$ or Br. no good selectivity

Acetal



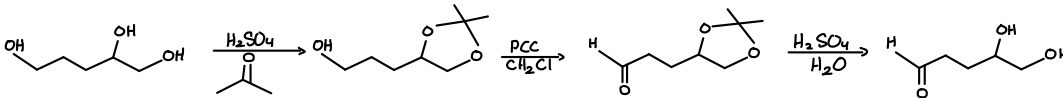
protects against: SB and Strong Nu^-

Thioacetal

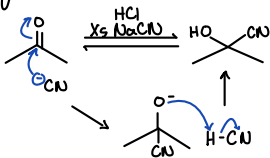


protects against: SB, strong Nu^- , moderate acid

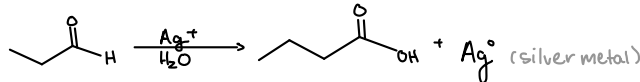
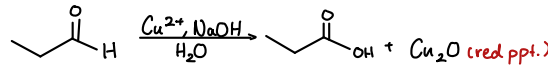
Acetals also protect diols



Cyanohydrin Formation

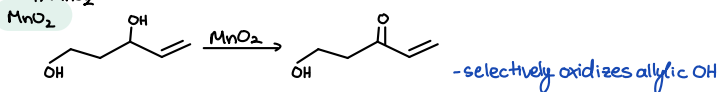


Tests for Aldehydes



Review: Methods for Synthesizing Aldehydes/Ketones

- 1) Alcohol Oxidation: CrO_3, H_2SO_4, H_2O
- 2) PCC
- 3) Ozonolysis
- 4) MnO_2
- 5) Hydration of Alkynes
- 6) Friedel Crafts Acylation



Hydration of Alkynes

