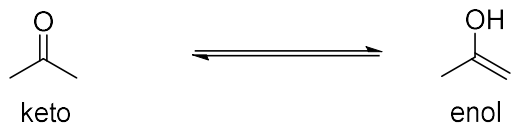
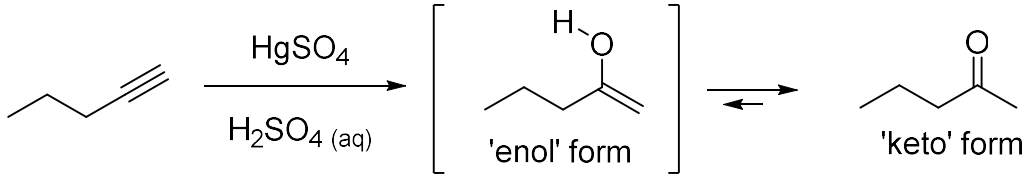
21.1 Intro to α-carbon chemistry: enols & enolates	**21.2** α-Halogenation	**21.3** Aldol Reactions

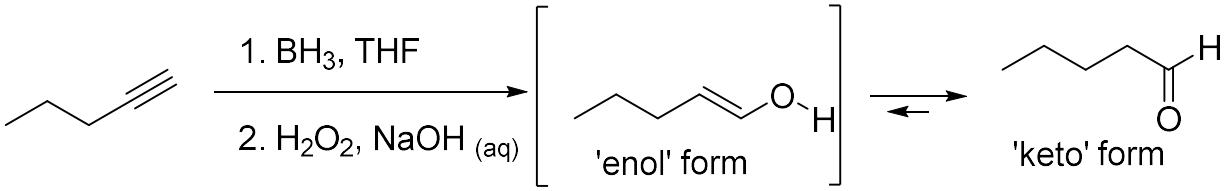
[21.1] Keto-Enol Tautomerization



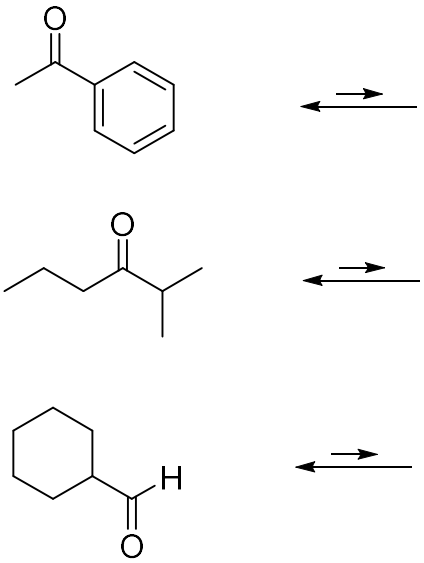
<u>Connecting prior knowledge from chapter 9 - alkyne hydration</u>…
- Markovnikov addition to alkynes



- *anti*-Markovnikov addition to alkynes

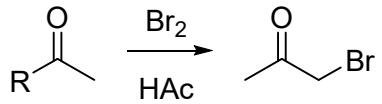


Draw the **enol form(s)** of each example below.

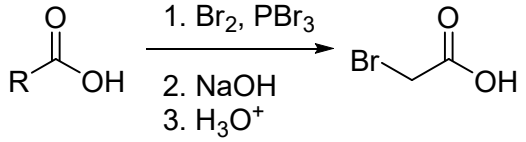


[21.2] α-Halogenation

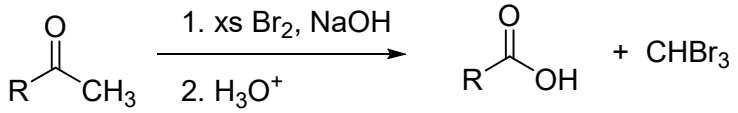
α-Bromination of Aldehydes & Ketones



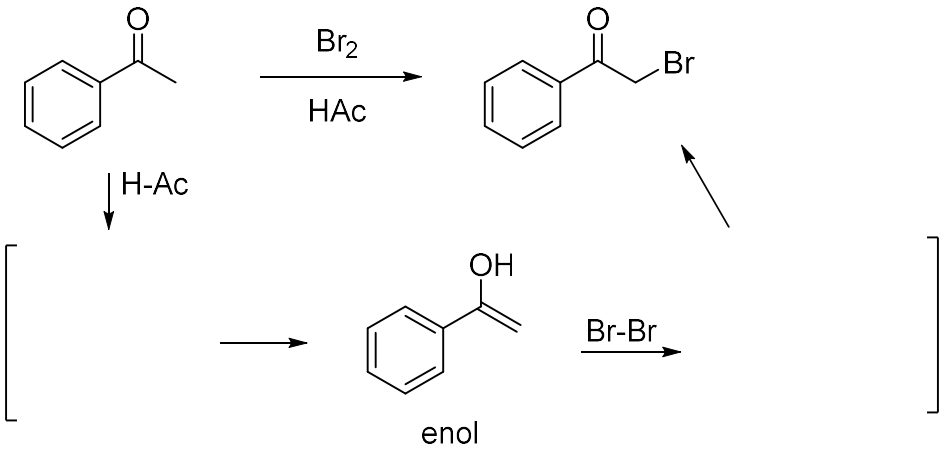
α-Bromination of Carboxylic Acids



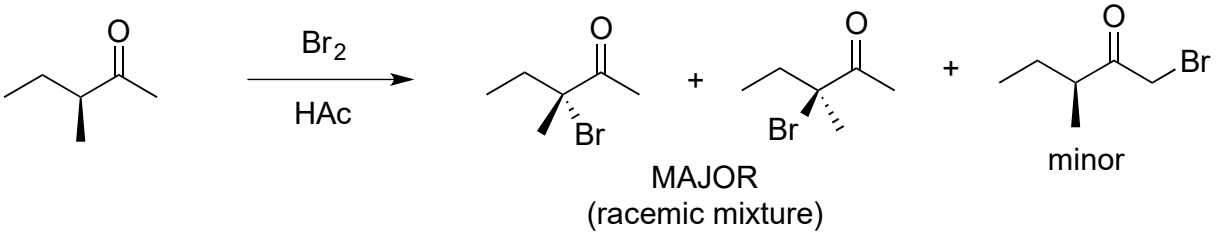
Haloform Reaction of Methyl Ketones



α-Halogenation of Aldehydes & Ketones

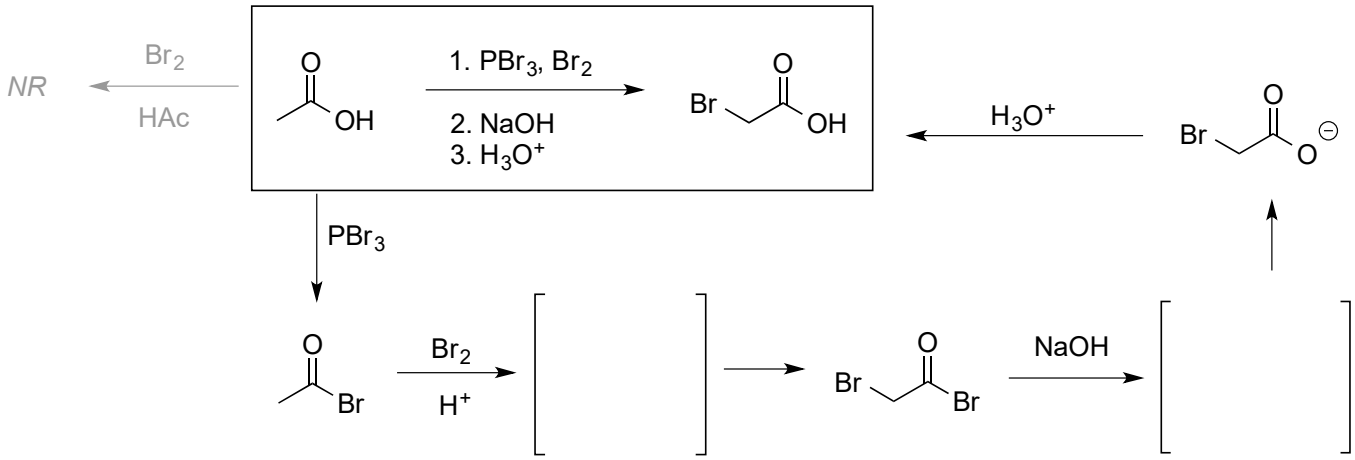


Explain this product mixture

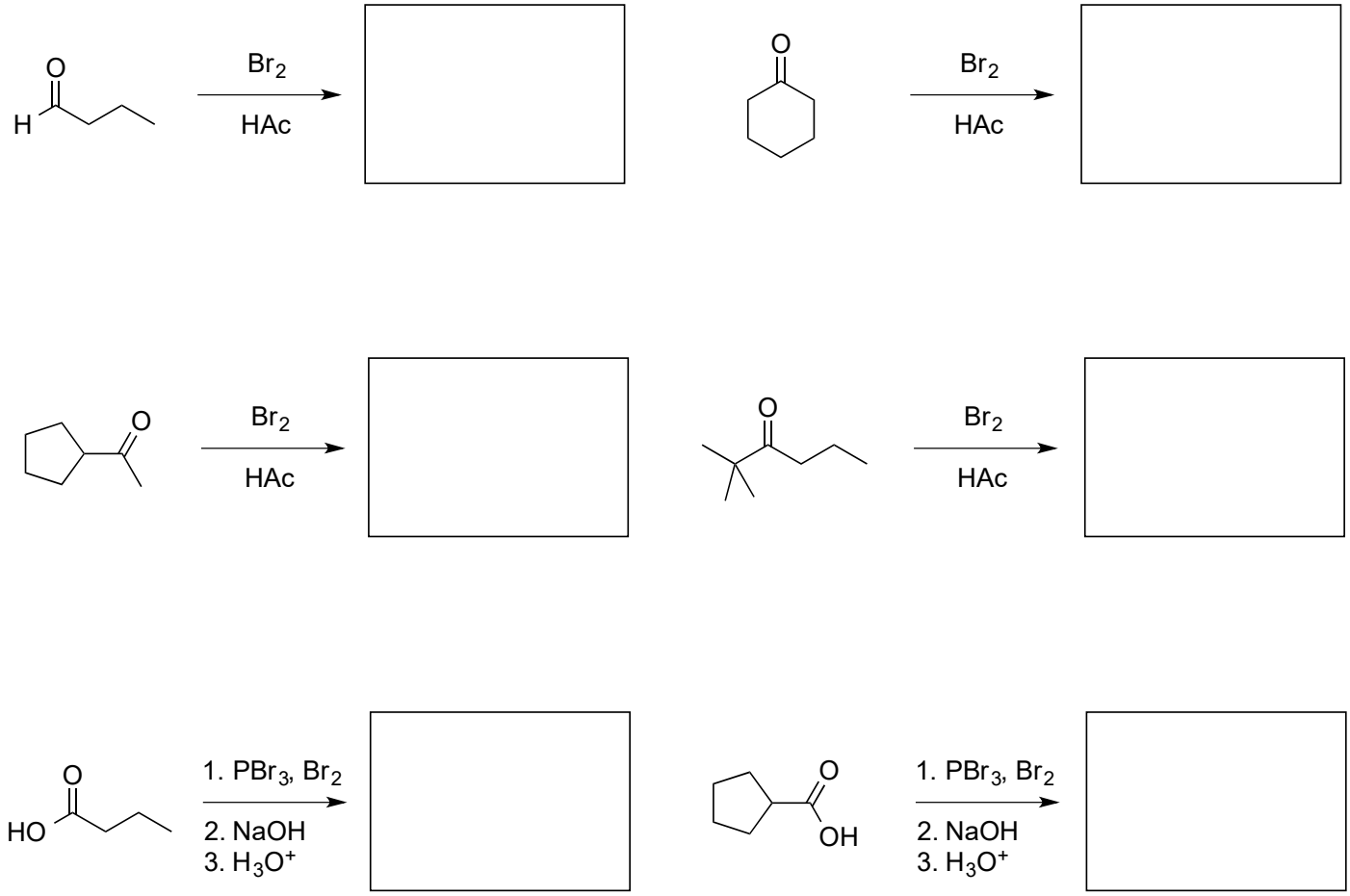


Why??

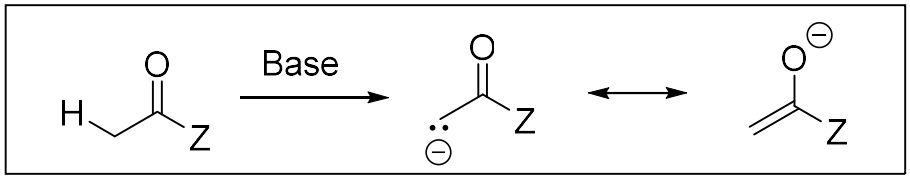
[21.2] Hell-Volhardt-Zelinski (HVZ) Reaction: α-Halogenation of Carboxylic Acids



Mono-bromination (acidic) examples…

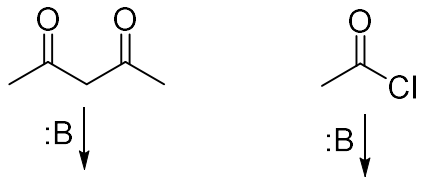


[21.1] Enolate Ion: Conjugate Base of Carbonyl Compounds

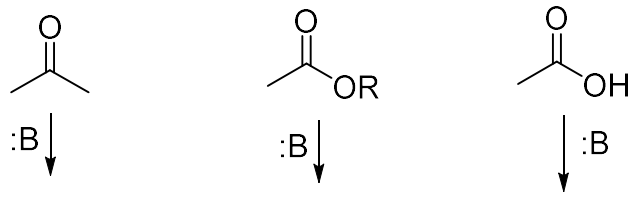


*Draw the **conjugate base** of each, then rationalize relative acidity at the **alpha-carbon***

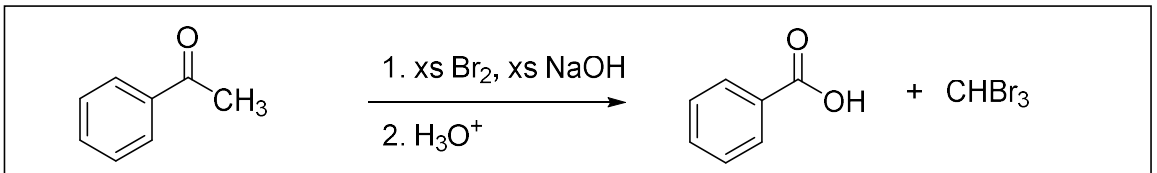
pKa 10

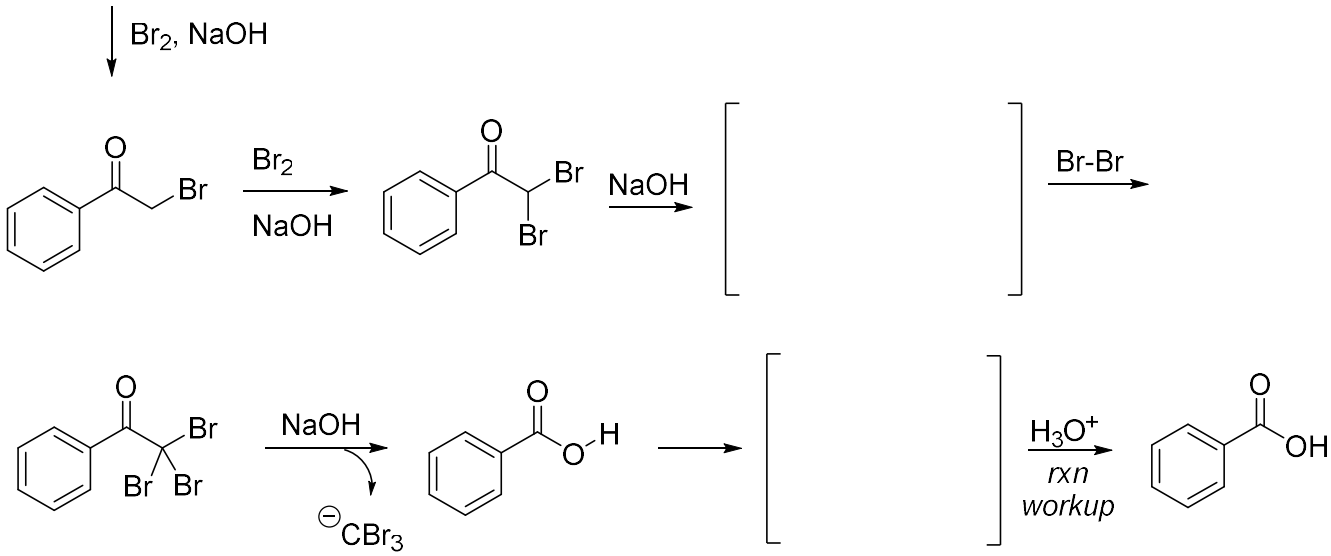


pKa 19

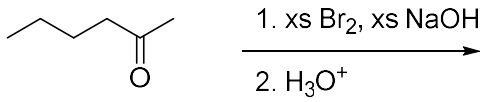


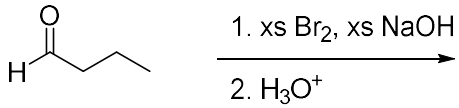
[21.2] Haloform Reaction – Methyl Ketones only

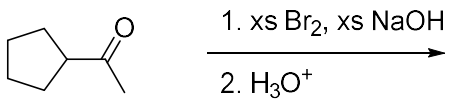


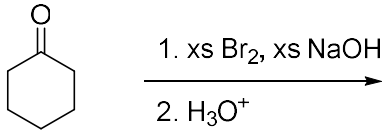


Which compounds will undergo the haloform reaction?



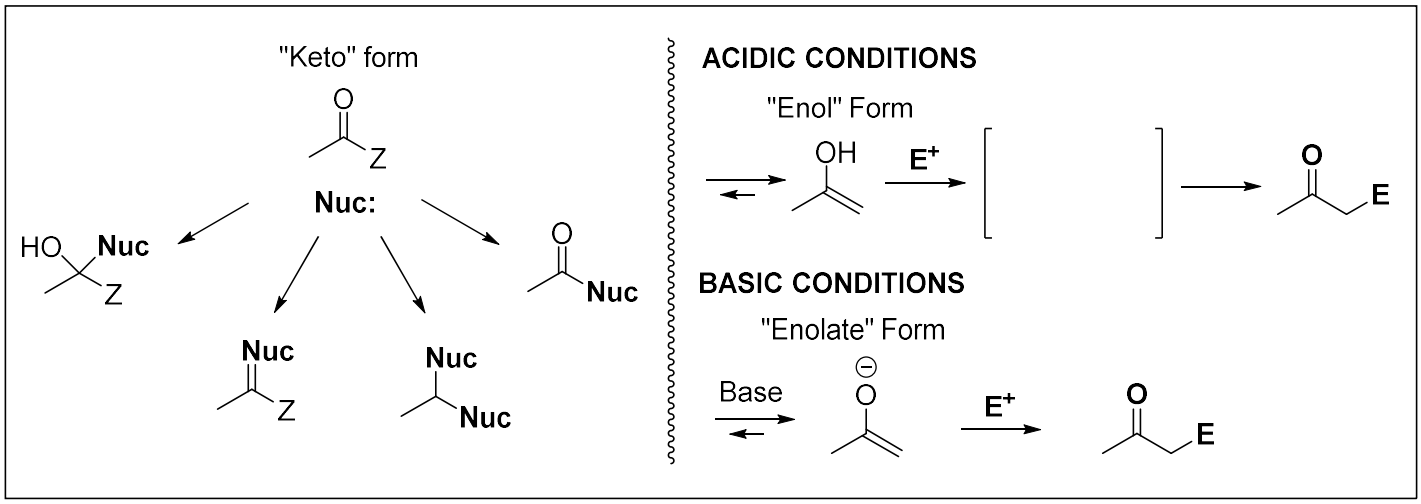




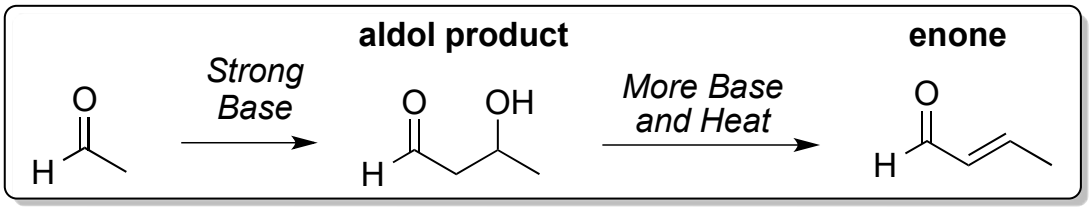


<u>Nucleophilic Addition to Carbonyl C</u> vs. **<u>Carbonyl α-Substitution</u>**

Chapters 12, 19, 20 — Chapter 21



[21.3] Aldol Reaction

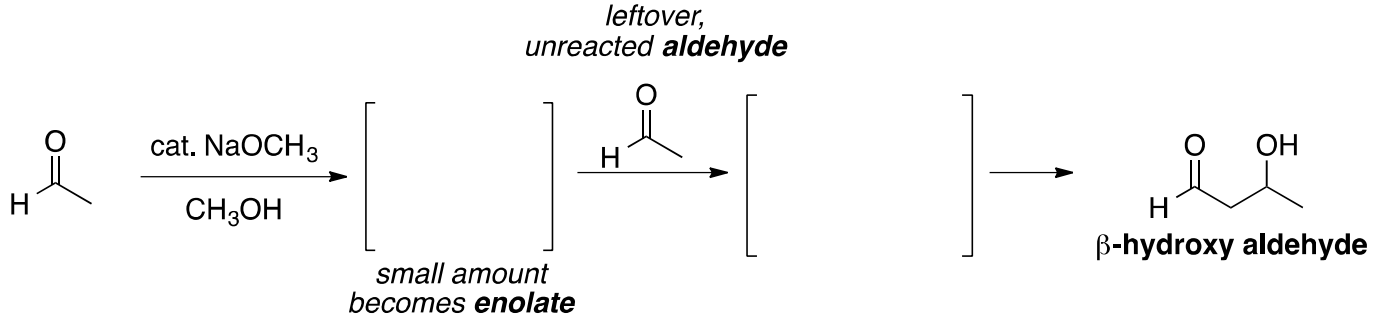


Self-Aldol Reaction

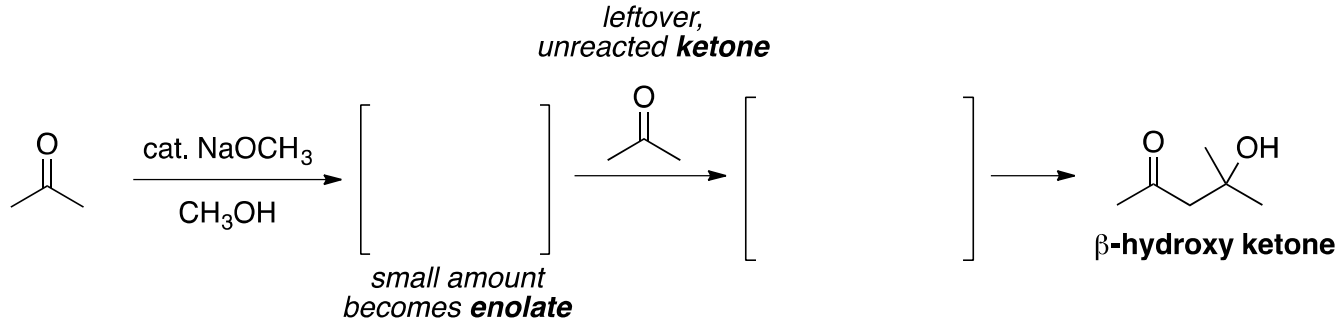
Aldehyde or ketone reacts with its own **enolate** to form a ***β*–hydroxy aldehyde or ketone**

* **Catalytic (small) amount of base** used at room temperature

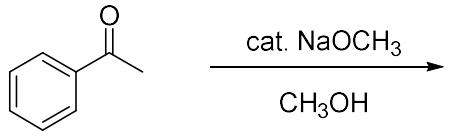
- Self-Aldol of Aldehyde



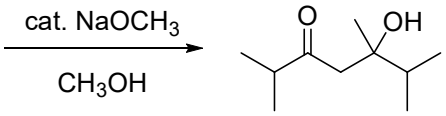
- Self-Aldol of Ketone



Predict the product:



Draw the structure of the aldehyde or ketone that would undergo self-aldol to give the following product:

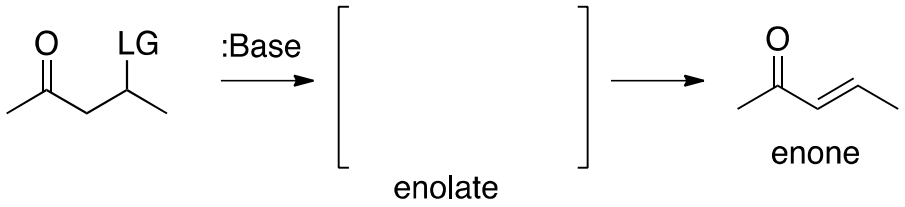


Self-Aldol with Condensation

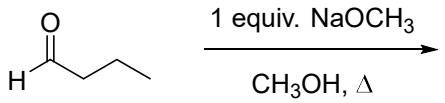
Aldol reaction followed by dehydration

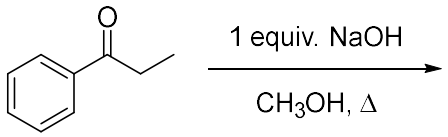
* Requires a **full equivalent of base and/or heat** to promote dehydration

E1cB Mechanism = Unimolecular Elimination with Conjugate Base
- Two-step elimination with enolate intermediate
- Specific to β–substituted aldehydes & ketones

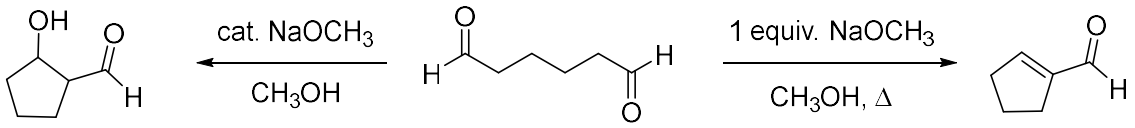


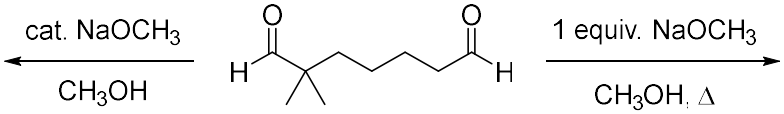
Full Aldol + Dehydration Reactions



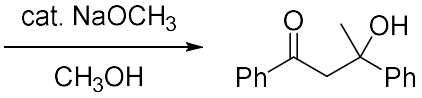


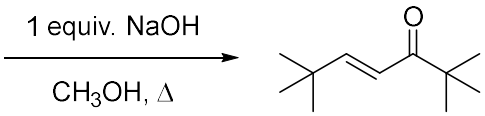
- Intramolecular Aldol Reactions – number those carbons!





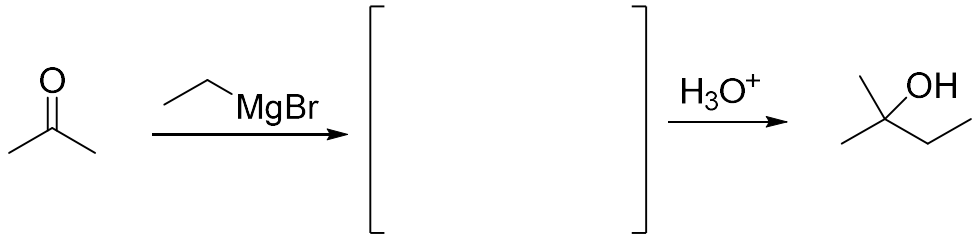
- Determine the missing aldehyde or ketone:





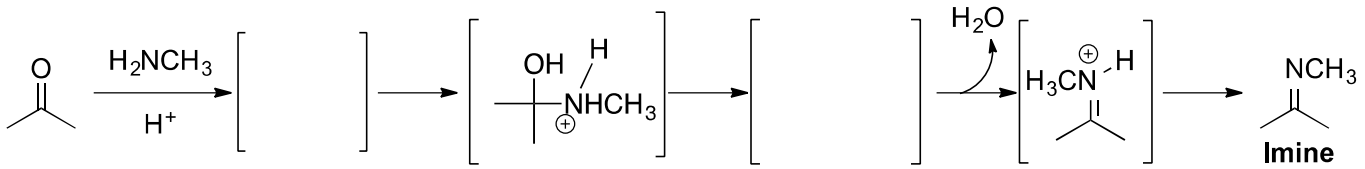
OVERVIEW: The Four Carbonyl Mechanisms

1. Nucleophilic Addition (Nuc Add'n) – Chapter 19
Ex: Grignard Addition



See also: Addition of Alcohol (1 mol), Hydrides, & HCN to aldehydes & ketones
Also also the 2nd half of acetal mechanism

2. Nuc Add'n with Dehydration – Chapter 19
Ex: Imine Formation



See also: first half of acetal mechanism

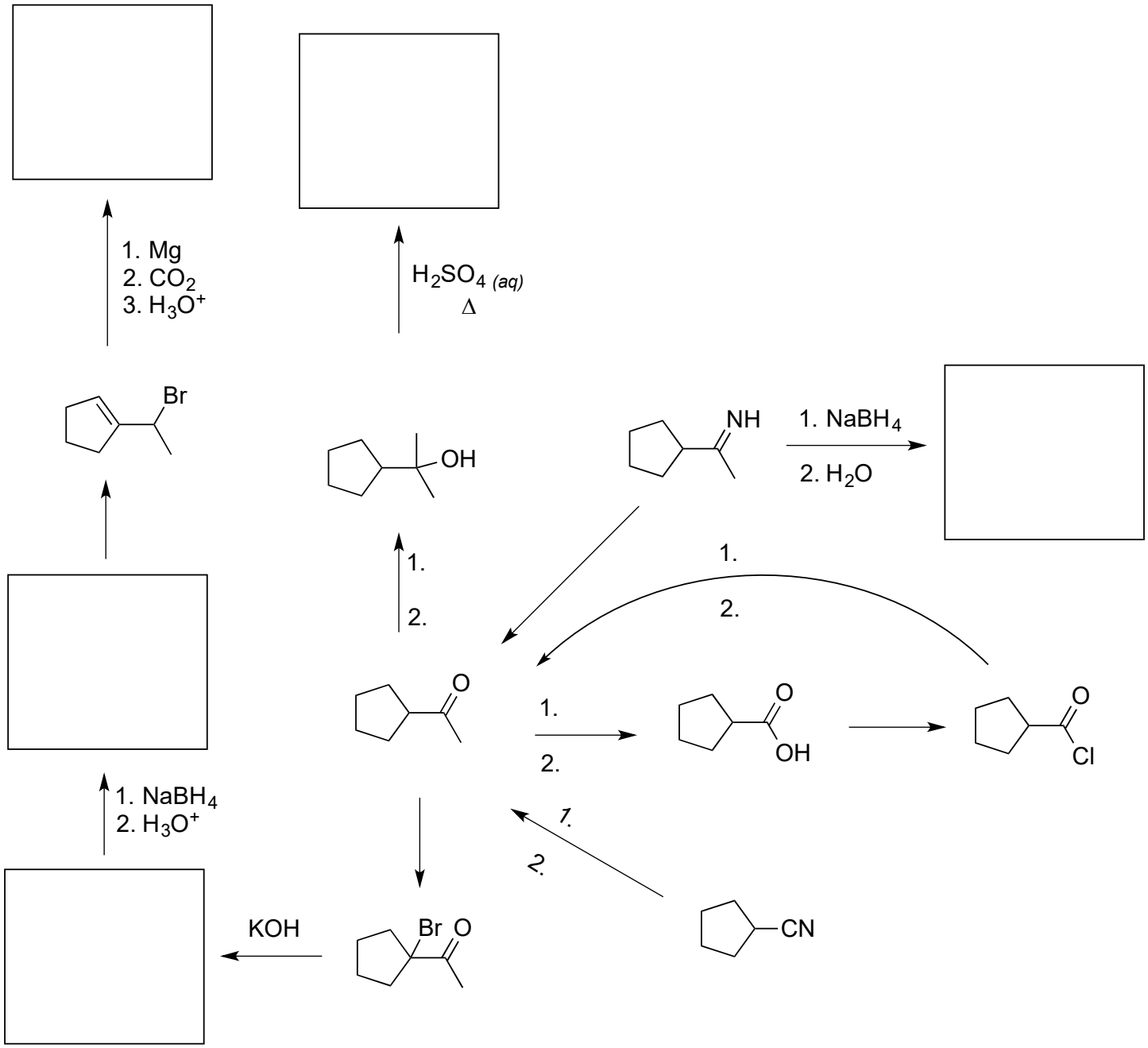
3. Nucleophilic Acyl Substitution (NAS) – Chapter 20
Ex: Hydrolysis of Acid Chlorides

See also: most Chapter 20 reactions!

4. α-Substitution – Chapter 21
Ex: Basic Bromination of Ketones

See also: acidic bromination, haloform, HVZ reaction

Reaction Mega-Puzzle!!



All-Carbonyl-Inclusive Reaction Puzzle