

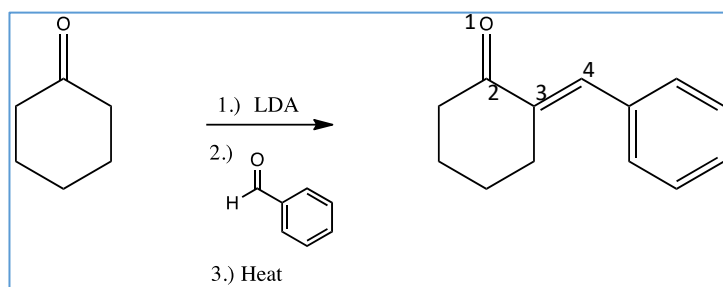
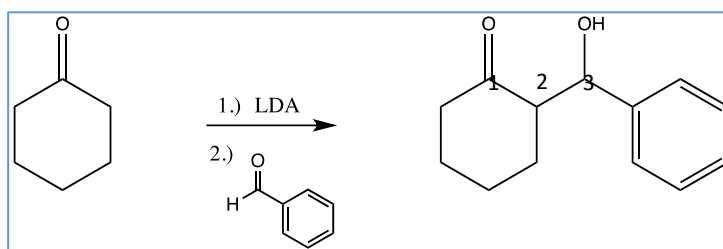
Enols, Enolates, and More #2: Practicing Aldol, Michael Add., & Robinson Rxns

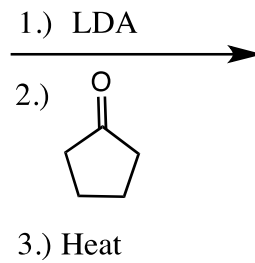
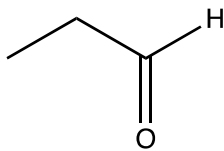
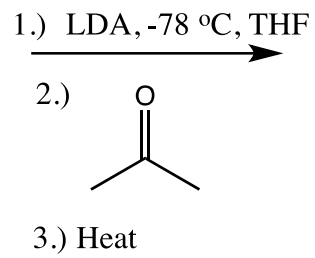
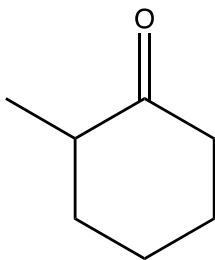
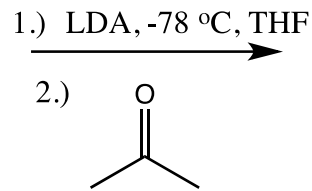
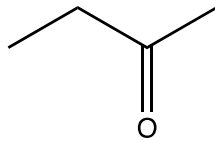
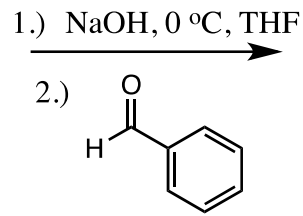
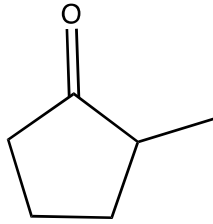
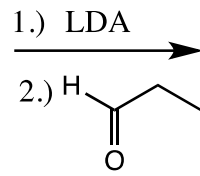
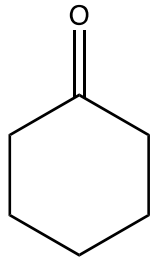
Yo, gang. Okay, so these 4 reactions (Aldol Rxn, Aldol Rxn with Condensation, Michael Addition, and Robinson Annulation) scared the hell out of me when I was going through O Chem 2. Yes, they are complex, and yes they are challenging. However, as long as you can remember the relationships we highlighted for each reaction and stick to your enol/enolate fundamentals, I guarantee you'll quickly nail these reactions down. I will say, like I did in the last video, these take practice to get good at—but so did a lot of other things in O Chem, and we've always made it through. So let's work hard, master these reactions, and charge onward 😊.

Let's step through each reaction, and I'll rehash all of the important aspects of each one as we go through them.

1.) Aldol Rxn (Basic Condition)

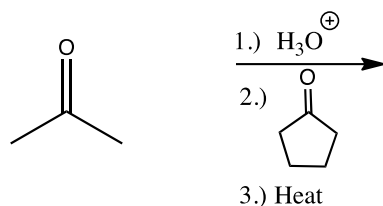
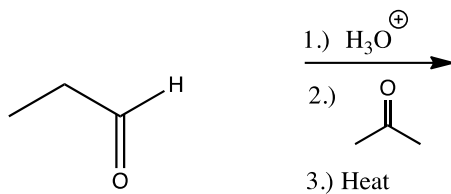
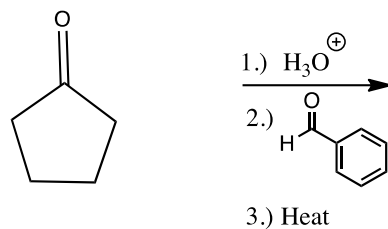
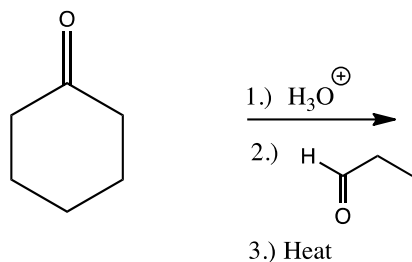
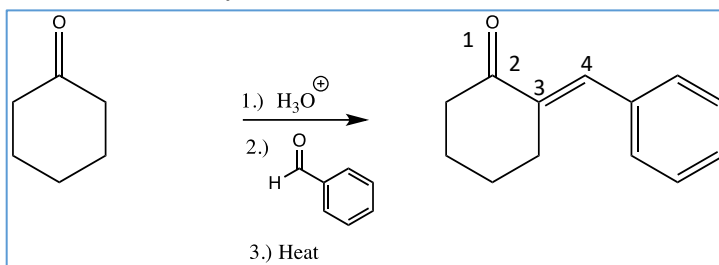
- If heat is added in, the aldol will proceed on to the condensation product. If no heat is added after forming the aldol, the reaction will stop at the aldol product.
- In any aldol product, you'll see a **1,3 hydroxy carbonyl relationship** AKA a carbonyl and an alcohol will be 3 carbons away from each other.
- **If heat is added in**, the $-OH$ will be driven off, and a double bond will be formed to form a 4-atom conjugated system with the double bond and the carbonyl (that's the relationship to look for). That's called an **enone**.
- This is in **basic conditions**, so we're working with enolates (remember when to form the Kinetic/Thermo enolate, if appropriate).





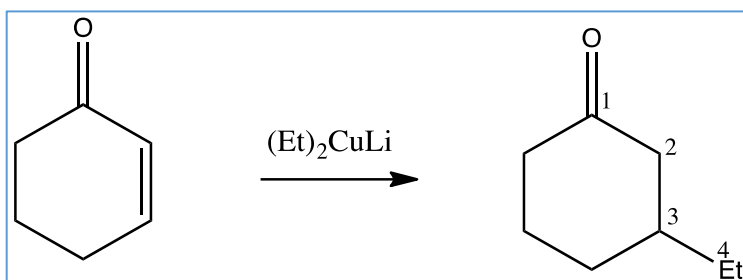
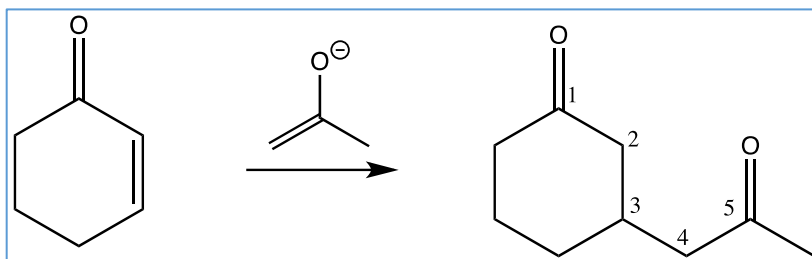
2.) Aldol Rxn with Condensation (Acidic Condition)

- This is performed in acidic environments, so **enols** are the nucleophile we're working with.
- Enols are less nucleophilic than enolates, so to make the reaction more favorable and drive it to completion, heat must be added in—the condensation product is **always** obtained.
- Remember the relationship the condensation product will have: We'll see an **enone**, a 4-atom conjugated system that includes the carbonyl and the 2 carbons in the double bond (exactly the same as an aldol condensation in basic conditions)

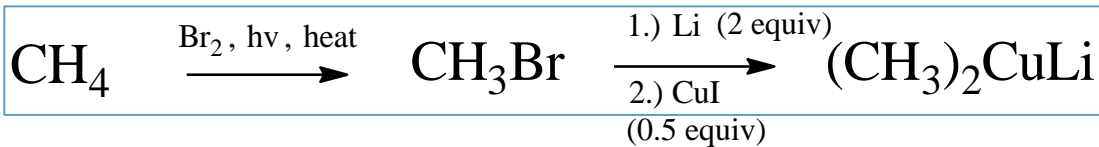


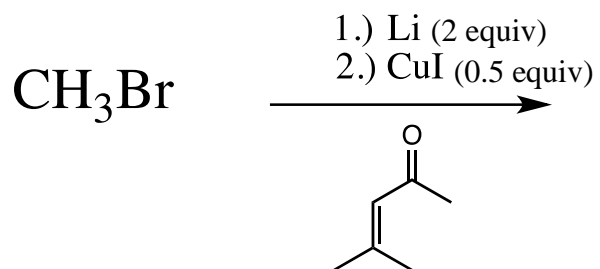
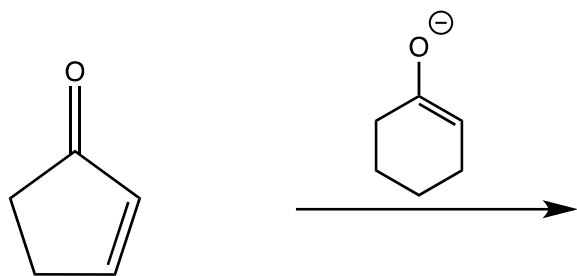
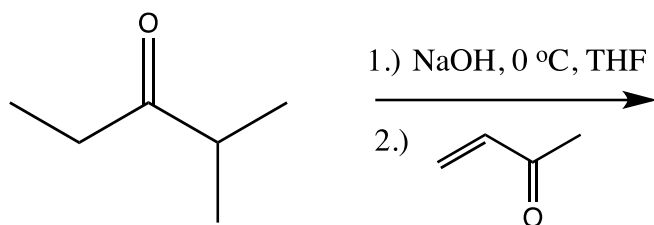
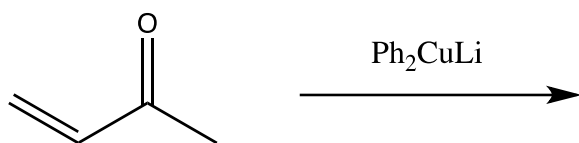
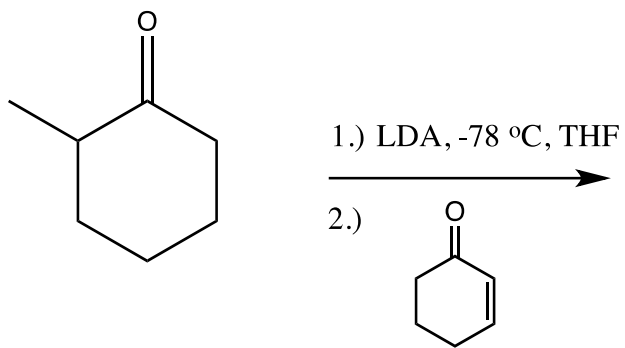
3.) Michael Addition

- In a Michael Addition, we are attacking the partially positive carbon in an **enone**. We know there is a partial positive charge on that carbon from resonance.
- We need a “soft” nucleophile (like an **enolate**, **enamine**, or a **cuprate**) to do a Michael Addition (attack in a 1,4 manner, right?). If we had something like a Grignard (a “hard” nucleophile), it would do a 1,2-addition and just attack the carbonyl carbon.
- Relationships to look for:
 - When an enolate/enamine attacks: You end up with a 1,5-dicarbonyl (2 carbonyls 5 carbons away from each other)
 - When a cuprate attacks: You have the original carbonyl still intact, and you’ve added some carbon piece attached to the partially positive carbon 4 atoms away from the carbonyl carbon



And remember, when making cuprates, you need twice as much organolithium than copper, whether that means $2 \text{ RLi} + \text{CuX}$ OR $\text{RLi} + 0.5 \text{ CuX}$

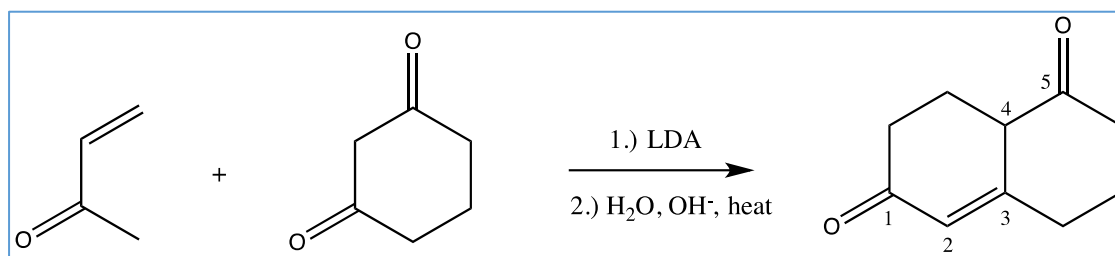




(Last one, give me just a little more effort/focus/hard work then we're done ☺)

4.) Robinson Annulation

- Believe it or not, a Robinson Annulation is nothing more than a Michael Addition, a small rearrangement, and then an intramolecular aldol condensation (in a basic environment).
- An annulation is a process **that creates a ring**, and in the Robinson Annulation a 6-membered ring is always made.
- You need to have an **enone** and something that has 1 or 2 carbonyls to become an **enolate** and attack the enone.
- There are 2 relationships you will see: The **1,5-dicarbonyl** (from the Michael Addition) and an **enone** (from the aldol condensation).
- Personally, I think it's best to arrange your pieces like I have them in the example below (people may not always be nice and give you them like they're shown below)



In my mind, there are 2 types of questions for a Robinson Annulation:

- 1.) You are given the enone and enolate precursor, and you have to predict the final Robinson product.
- 2.) You are given the final Robinson product, and you come up with the enone and enolate precursor that made that product.

Strategy for 2.)

- Like we talked about, find the enone and make a “cut” in the middle of the double bond.
- Locate the the carbonyl that is **not** a part of the enone, go to its alpha carbon closest to the enone and make a “cut” between that alpha carbon and the carbon its bonded to (not that one in the enone)

