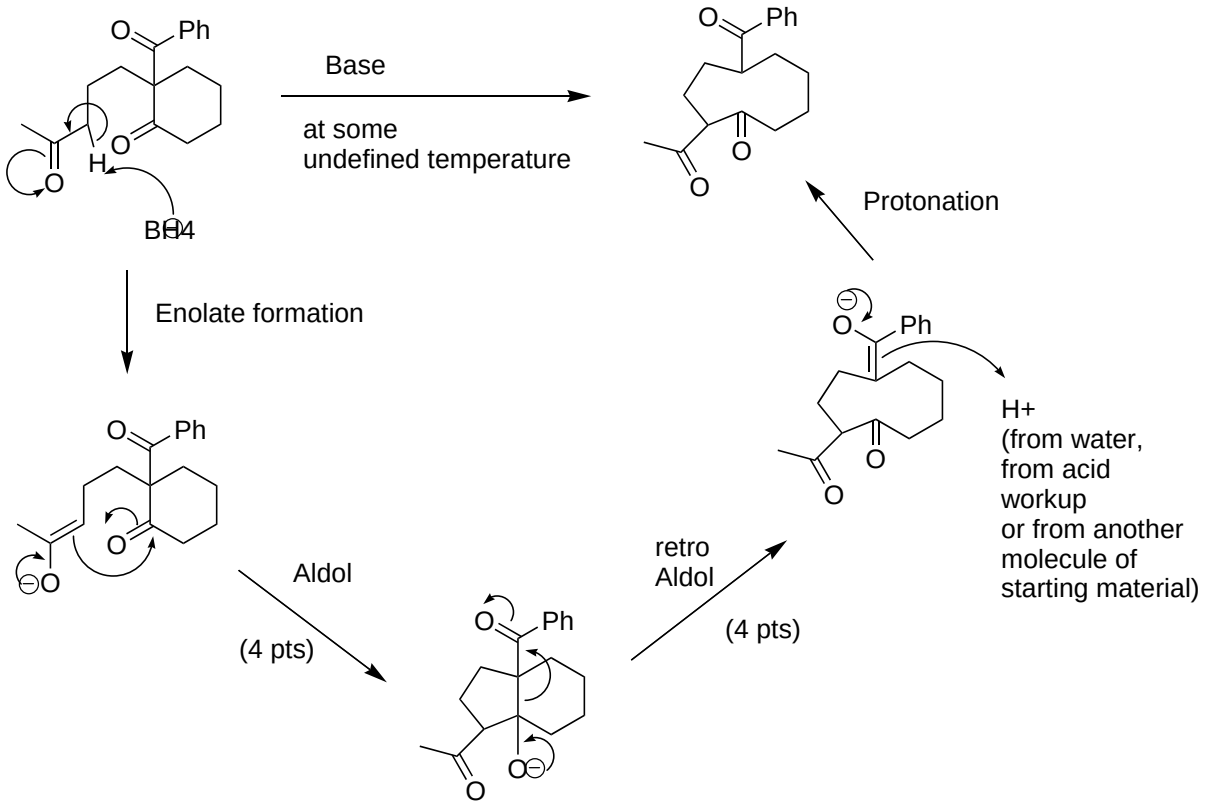
Quiz 5 Name:

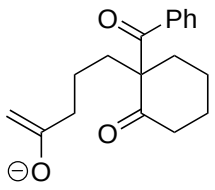
1. (8 pts) The following reaction involves an intramolecular aldol reaction followed by a retro aldol reaction. Show the detailed mechanism of each step.



2. (4 pts) The nature of the base AND the conditions of the reaction in question #1 are critical to obtaining the product shown. What base is necessary to get the product? At what temperature should the reaction be run to maximize the formation of the product? Explain your answers.

We want to form the thermodynamic (more substituted) enolate, so **higher temperatures (2 pts)** AND **equilibrating base (alkoxide base or hydroxide) (2 pts)** in protic solvent (H_2O, ROH) is necessary.

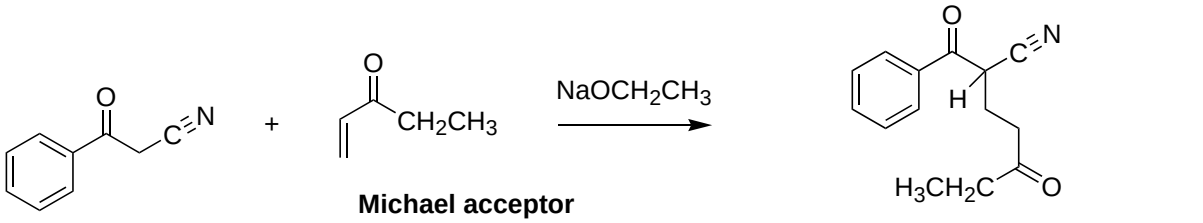
If LDA at low temperatures is used, then the predominant enolate will be



which is the kinetic enolate. Cyclization of this enolate will give you the 7-membered ring prior to the retro aldol step. Try it out to see for yourself.

(problem 3 on back)

3. (4 pts each) Predict the **major** product of the following reactions, and then make as complete an argument as you can to support your choice of normal (1,2) versus conjugate (1,4) addition.



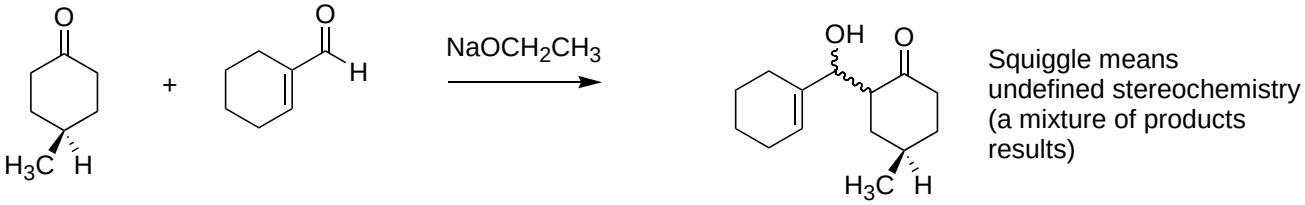
Enolate donor

Michael acceptor

Conjugate addition is major

Why 1,4 addition? 1) Enolate stabilized by resonance with the aromatic ring and the cyano group. 2) Michael acceptor has more steric blockage around the carbonyl (2 position) rather than the terminal position of the double bond (4 position).

A number of you might be wondering why the Michael acceptor does not form an enolate. Remember that the base will react first with the lowest pKa hydrogens, which are those on the enolate donor (pKa ~10) rather than the pKa ~20 on the Michael acceptor.



Squiggle means undefined stereochemistry (a mixture of products results)

Enolate donor

Aldol acceptor (electrophile)

Normal addition product is major

Why 1,2 addition? 1) Enolate is NOT stabilized by resonance. 2) Acceptor is most sterically hindered around the 4 position (the termination of the double bond) rather than around the carbonyl (aldehydes are not significantly sterically hindered.

Technically if you have the ketone reacting with itself you are incorrect because the ketone will form an enolate and then react with the less hindered acceptor, which is the aldehyde (as we've discussed in class). However I gave credit for this answer -- I was really looking for the 1,2-addition answer.