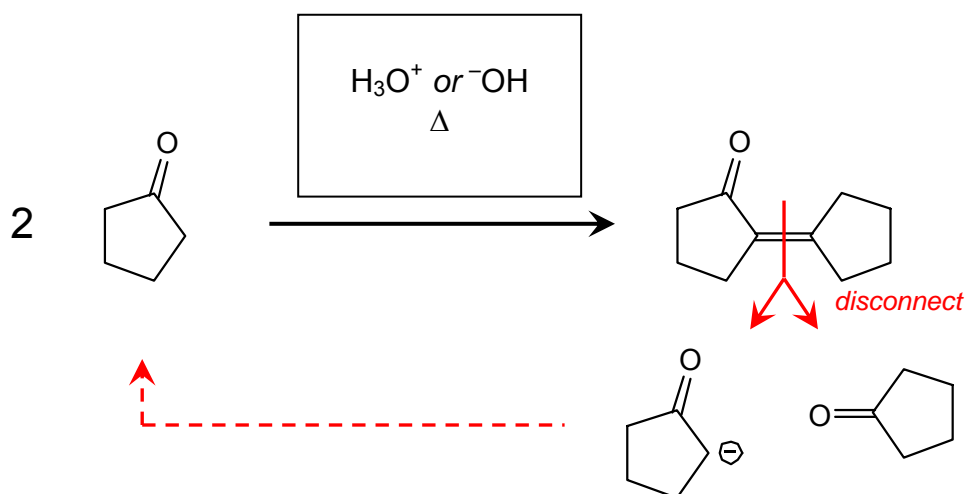
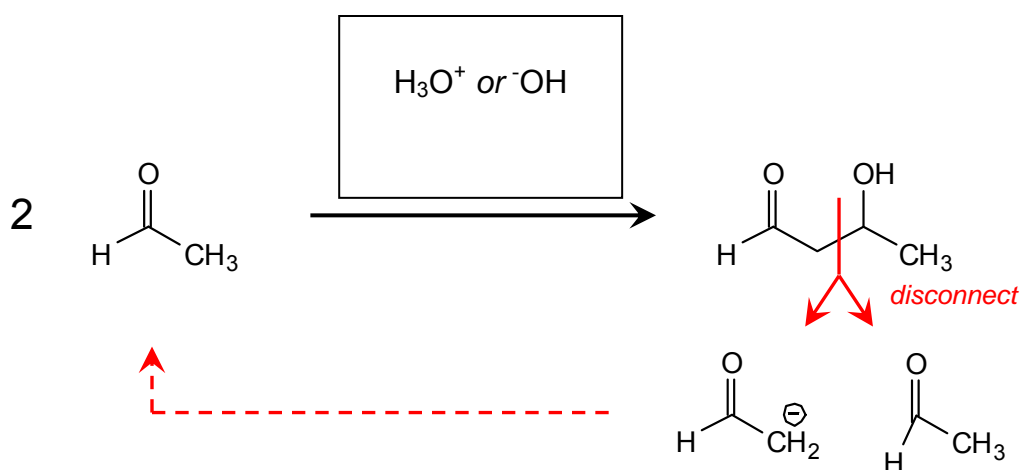


In-Class Exercise Solutions Planning Aldol Reactions

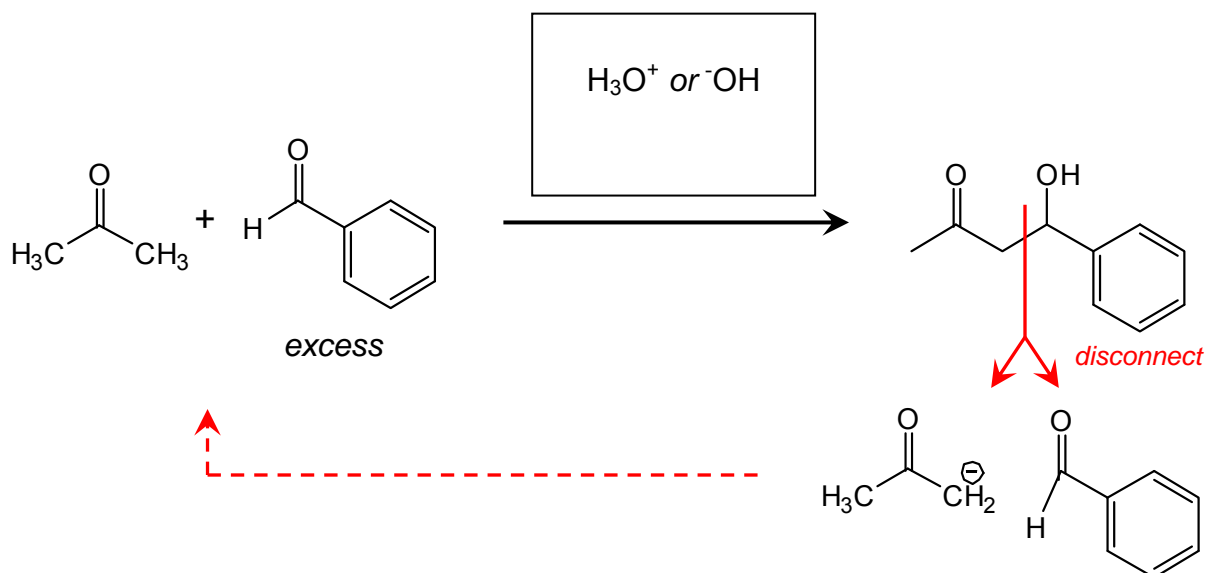
I think it was easiest to think of this problem “retrosynthetically”, by conceptually disconnecting bonds that would be made in the forward direction. The disconnection works as we talked about in lecture; β -hydroxyaldehydes/ketones disconnect at the C-C bond next to the alcohol, and α,β -unsaturated aldehydes/ketones disconnect at the double bond.

Starting materials:

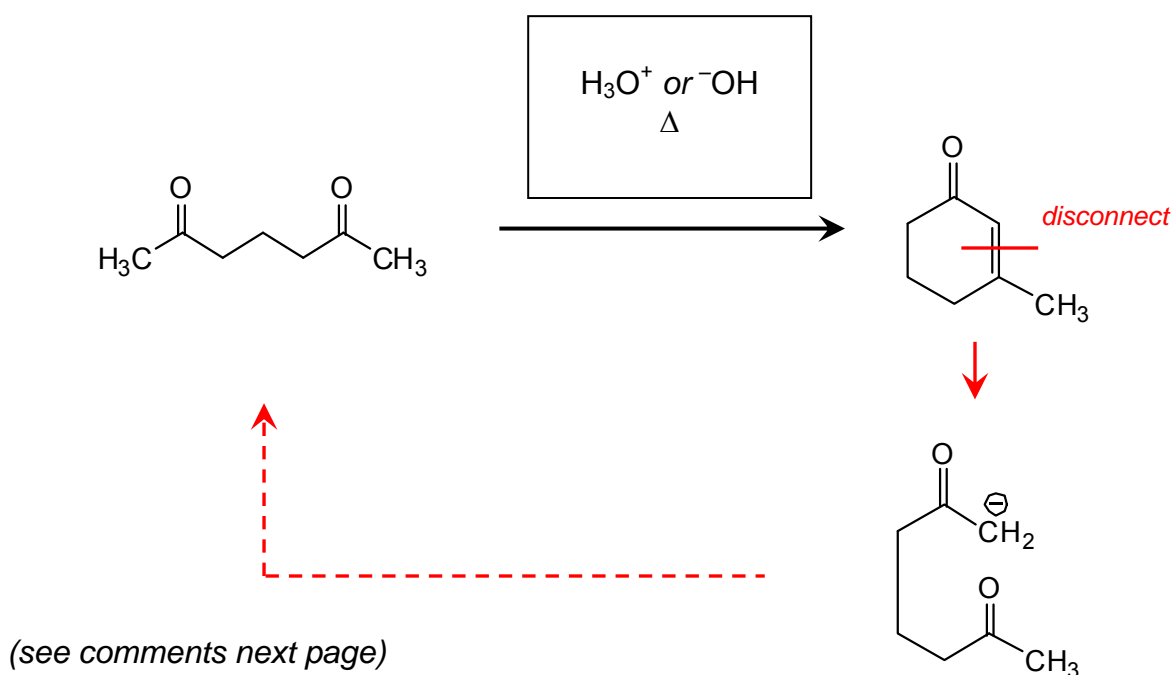
Reaction conditions:



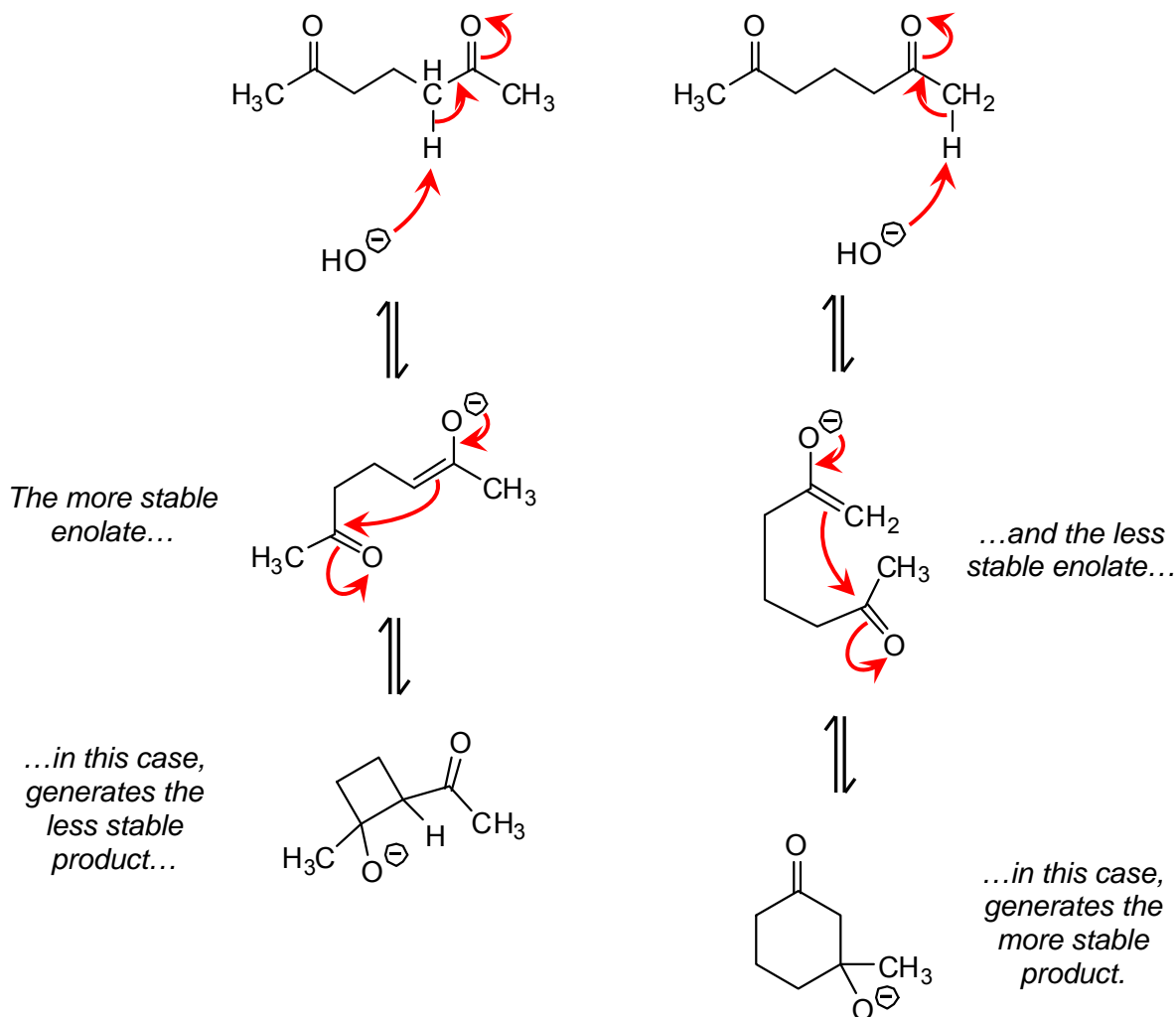
We need the heat in the second reaction, but not the first, to convert an aldol intermediate into the α,β -unsaturated ketone product.



This one is different than the previous two, in that it is a crossed aldol condensation—it involves two different starting material molecules. When considering cross-condensations, we have to be careful that they yield only the desired product, and that in the intended reaction of enolate 1 and carbonyl 2, we don't also get products from enolate 2 and carbonyl 1, or enolate 1 and carbonyl 1, or enolate 2 and carbonyl 2. Here, only the first molecule has enolizable protons, so we don't have to worry about an enolate from the second molecule. But we still have to worry about acetone enolate reacting with another molecule of acetone. To solve this, we use benzaldehyde in excess. That way, if acetone enolate reacts with the first molecule it sees, that molecule will always be benzaldehyde.



The disconnection drawn on the previous page raises an interesting question: how can this be a reliable synthesis when it goes through the less stable, less substituted enolate? Wouldn't a base more likely remove a $-\text{CH}_2-$ proton than a $-\text{CH}_3$ proton?



In this case, the more stable, 2° enolate would generate a strained cyclobutane aldol product—and let's face it, that's not gonna happen. So, while that enolate is certainly created under equilibrium conditions, only the less stable enolate proceeds to product.