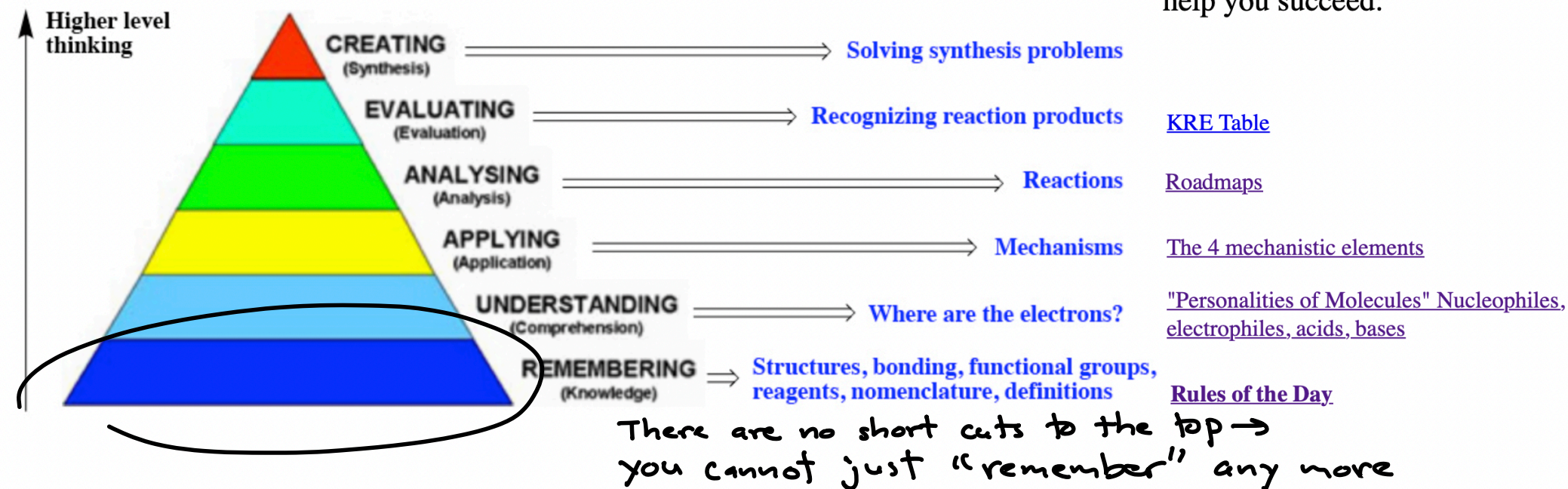


# Bloom's Taxonomy of Learning

# Organic Chemistry Analog

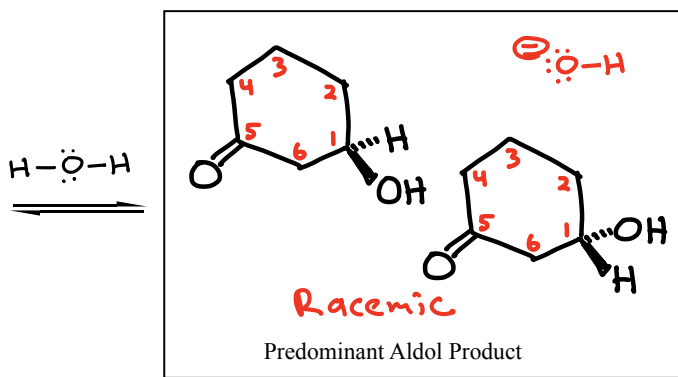
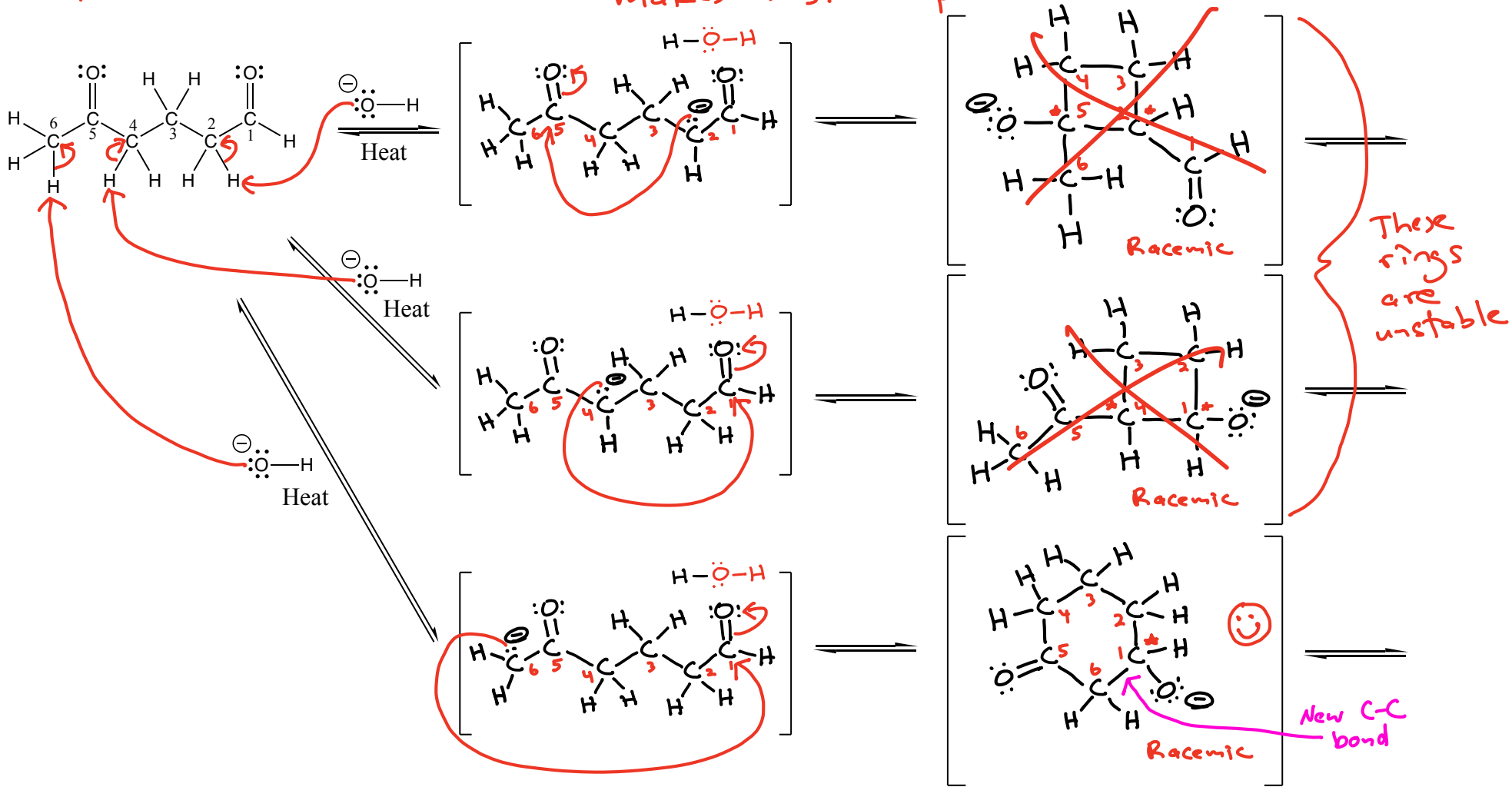
Tools we created to help you succeed:



Organic chemistry is difficult because it requires higher order thinking. According to Bloom's taxonomy of learning, the lowest level of learning involves pure memorization ("Remembering") As one moves up the pyramid to higher learning, understanding, applying, analysing, evaluating and creating are reached. I believe there are Organic chemistry analogs of all of these, culminating in synthesis which involves creativity along with all of the other levels of thinking. It is likely that many of you have never been challenged all the way to the top of the Bloom's taxonomy of learning pyramid before, explaining why this feels different and disorienting. DO NOT GIVE UP. As shown on the right, we have created tools to help you master each step up the ladder. On the above diagram you can click on the tools listed to go directly to them. Also, if you have any questions about how to study, [click here to read about the way I learned to study](#). I never earned a grade lower than an A after I started using this method during my own college career.

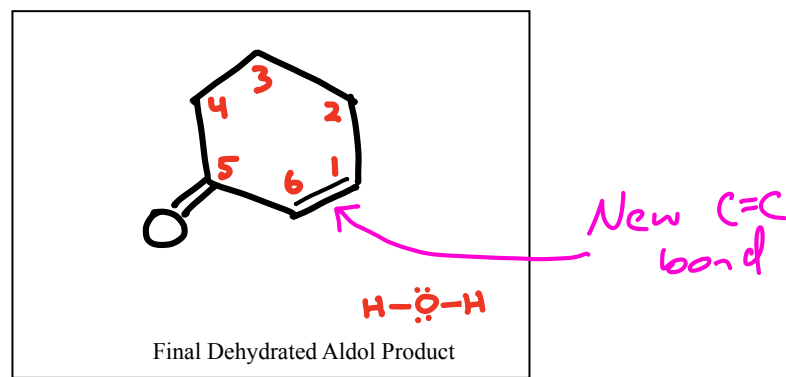
I understand that most of you are headed to the health professions, so you may be wondering if mastering synthesis problems will be important for you. I assert that it is. Solving a synthesis problem involves the detailed evaluation of a complex molecule while looking for KREs, then working backwards to the starting materials by analyzing possible reactions involved by thinking through your roadmaps, possibly applying your understanding of mechanism to make sure you predict the correct product for each reaction. This is the exact type of thinking you will need to diagnose a patient. A patient will present various complex combinations of symptoms, then you must evaluate which of these are important, then analyze, apply and understand how the patient got that way and how to get them back to their starting state (healthy) again. In other words, you will learn the "KREs of diagnosis" then work backwards to understand what happened to the originally healthy patient! Therefore, learning how to solve synthesis problems will teach you how to use higher level thinking skills, exactly the kind you will need to develop as a health care professional!

# Cyclic Aldol Reaction → 3 different enolates are possible, but only one makes a stable product

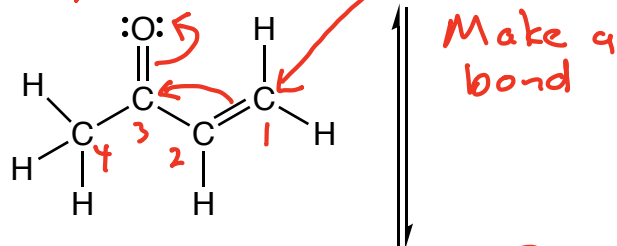
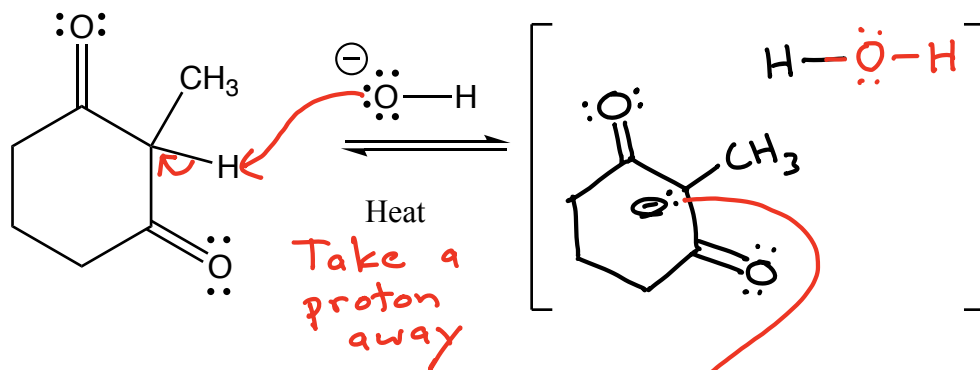


Dehydration

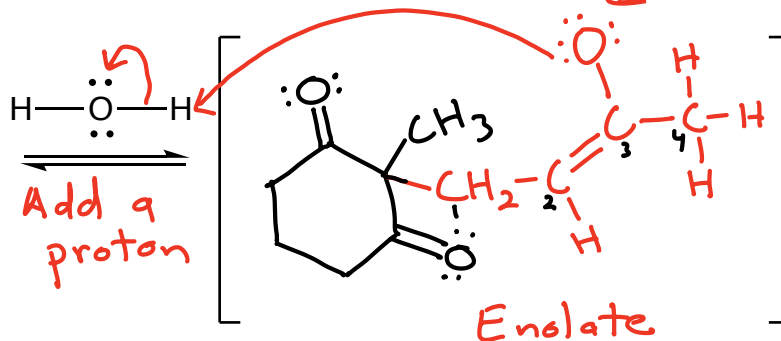
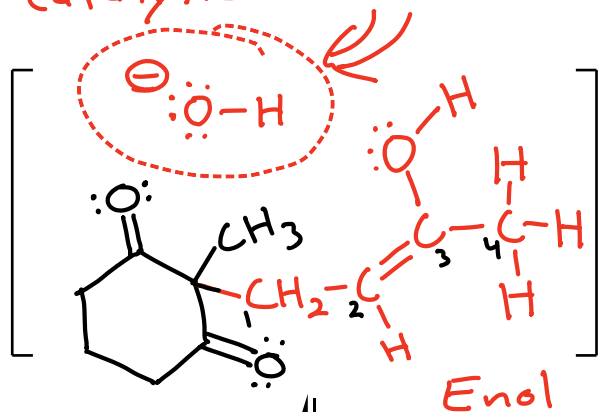
Spontaneous dehydration - Multiple steps You are not responsible for these



# Robinson Annulation Part 1 - Michael Reaction Steps

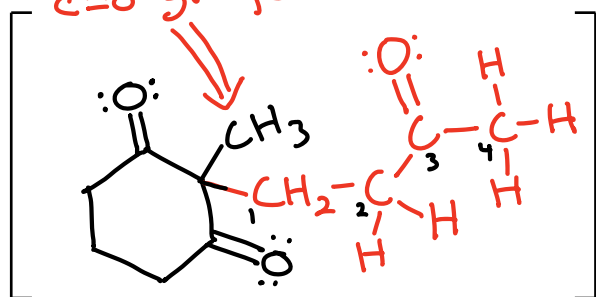


This step is catalytic in  $\text{OH}^-$



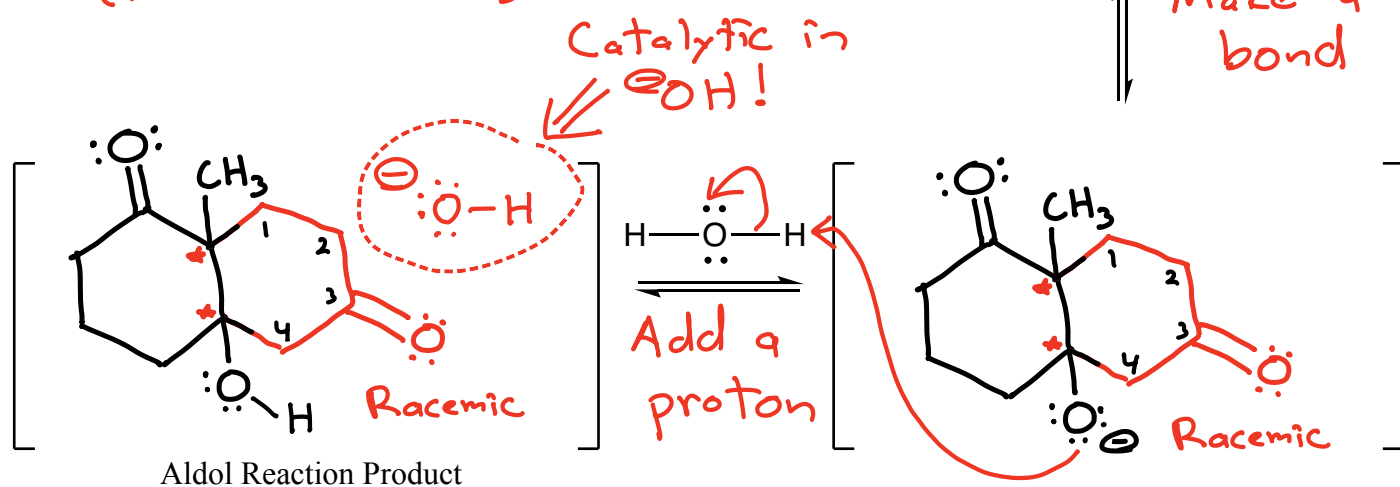
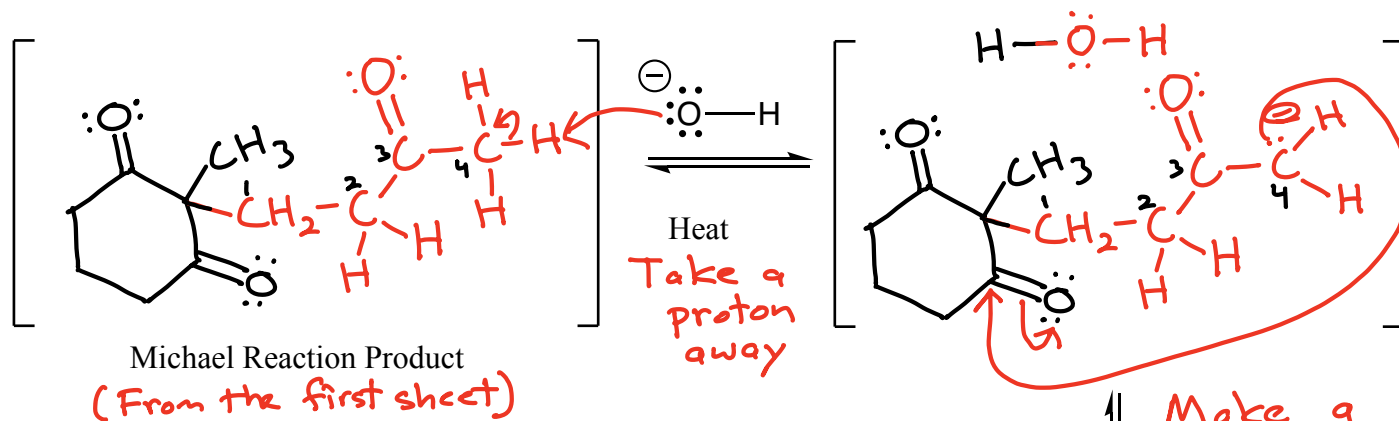
This methyl (not H!) group prevents deprotonation between the  $\text{C}=\text{O}$  groups

Tautomerization

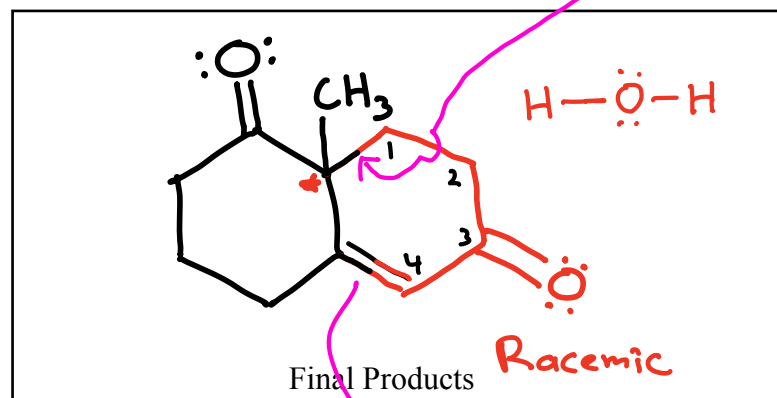


Michael Reaction Product

## Robinson Annulation Part 2 - Aldol and Dehydration Steps



Spontaneous  
 dehydration - multiple steps  
 You are not responsible for  
 these

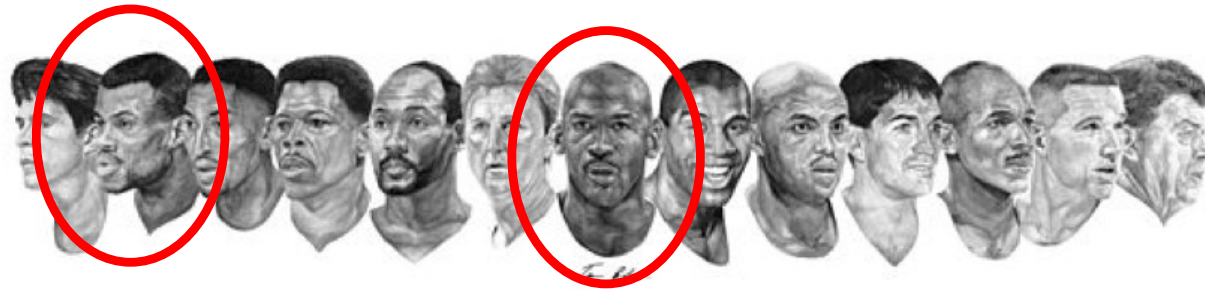


New C=C  
bond

# File: Dream Team Basketball 1992 Olympic Games Barcelona.jpg

From Wikipedia, the free encyclopedia

[File](#) [File history](#) [File usage](#)



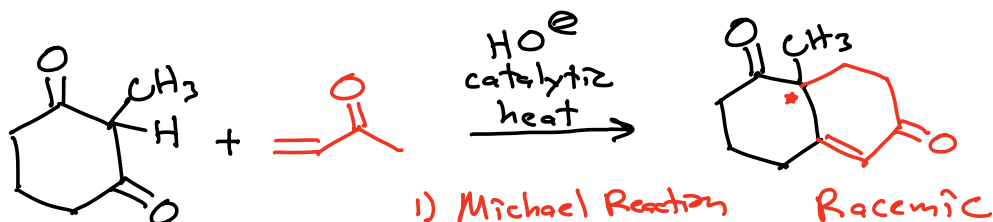
Michael

Robinson

Iverson

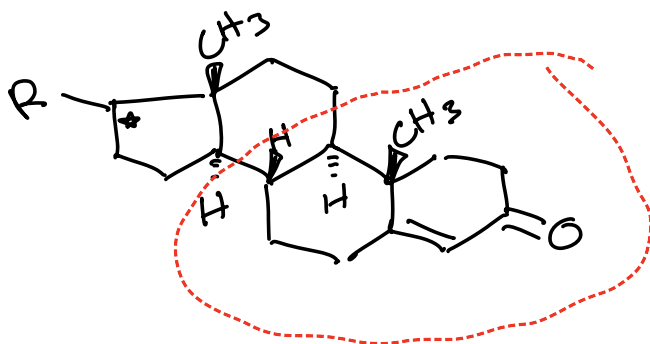


This is the only Robinson annulation reaction you will see on exams



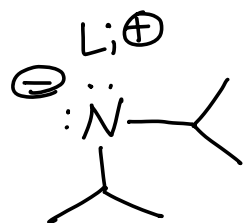
- 1) Michael Reaction
- 2) Aldol Reaction
- 3) Dehydration

AKA "Dream Team"  
of reactions that  
happen in a cascade



The Robinson annulation can be used to assemble complex molecules like this steroid

The wicked strong base that changes things



Lithium Diisopropylamide  
"LDA"



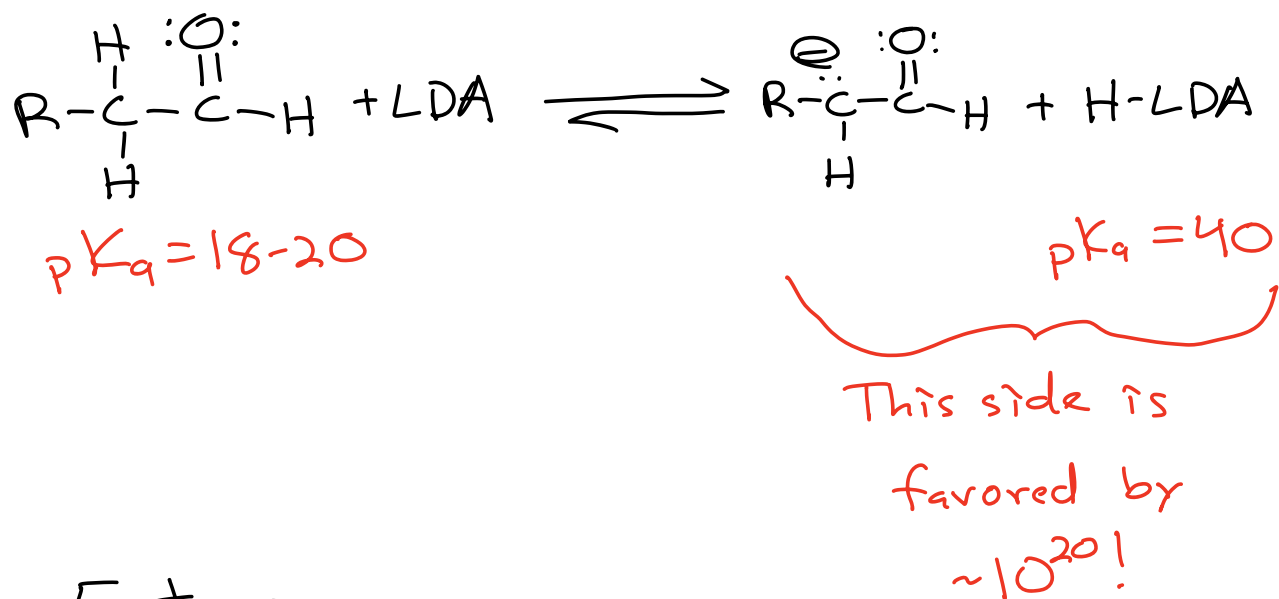
$pK_a \approx 40$

"H-LDA"

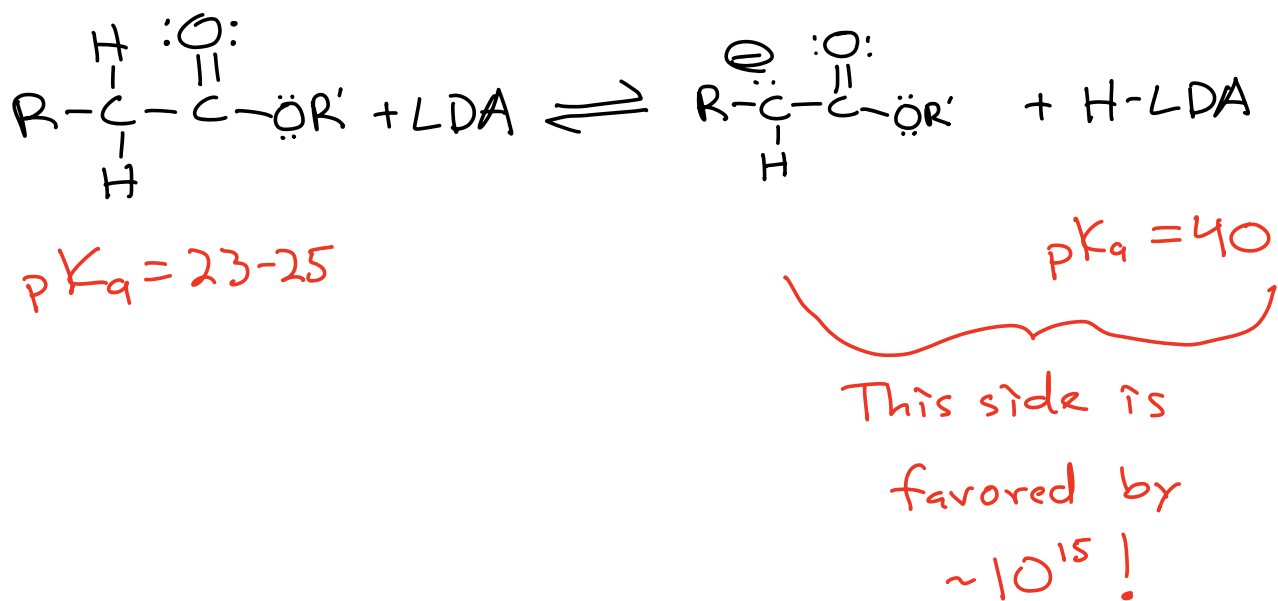
Not a nucleophile  
because of the two  
isopropyl groups

LDA will quantitatively  
deprotonate aldehydes, ketones  
and esters to make enolates!

## Aldehydes



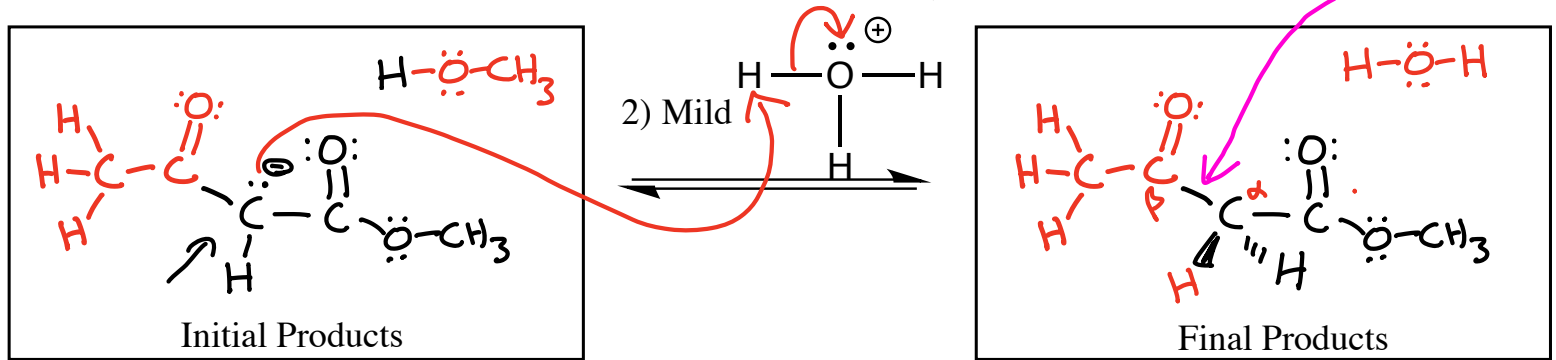
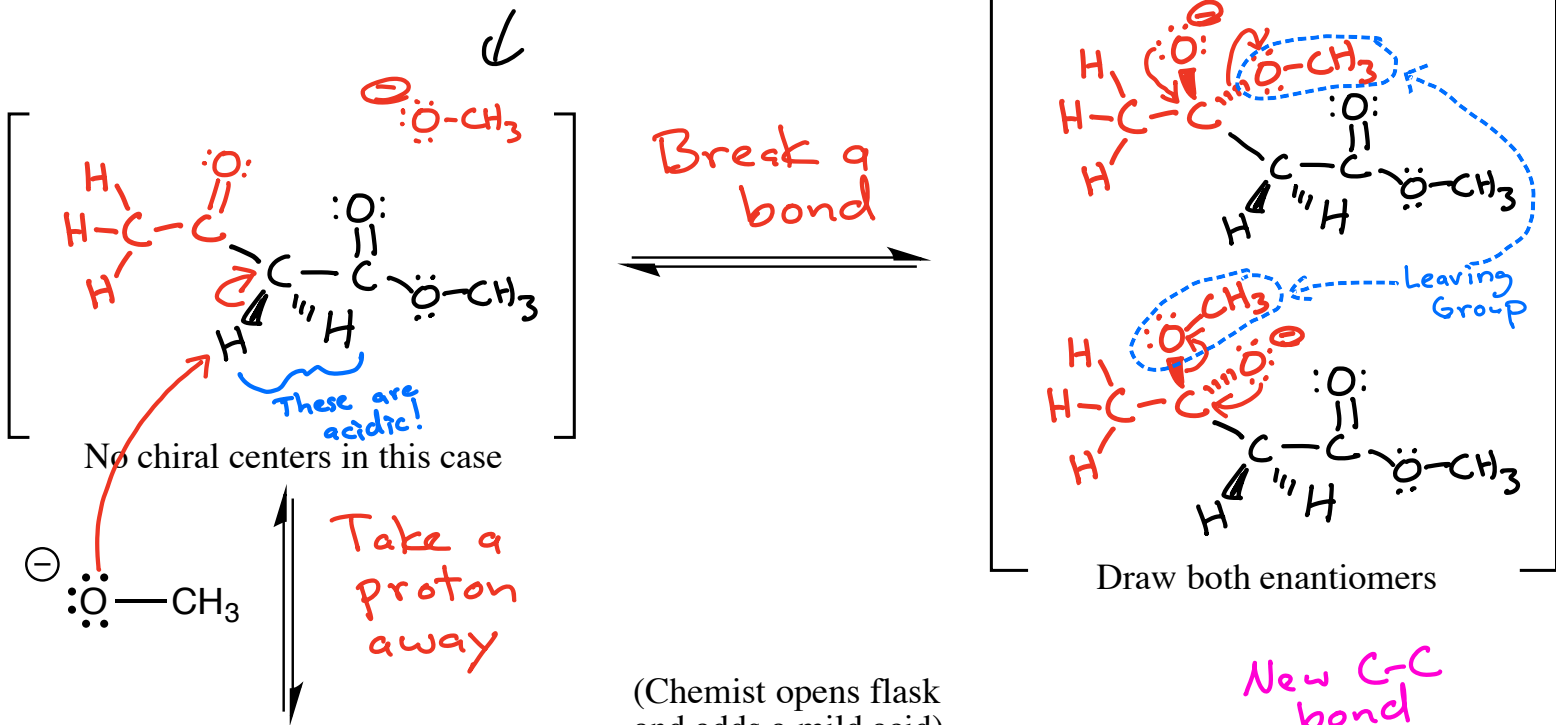
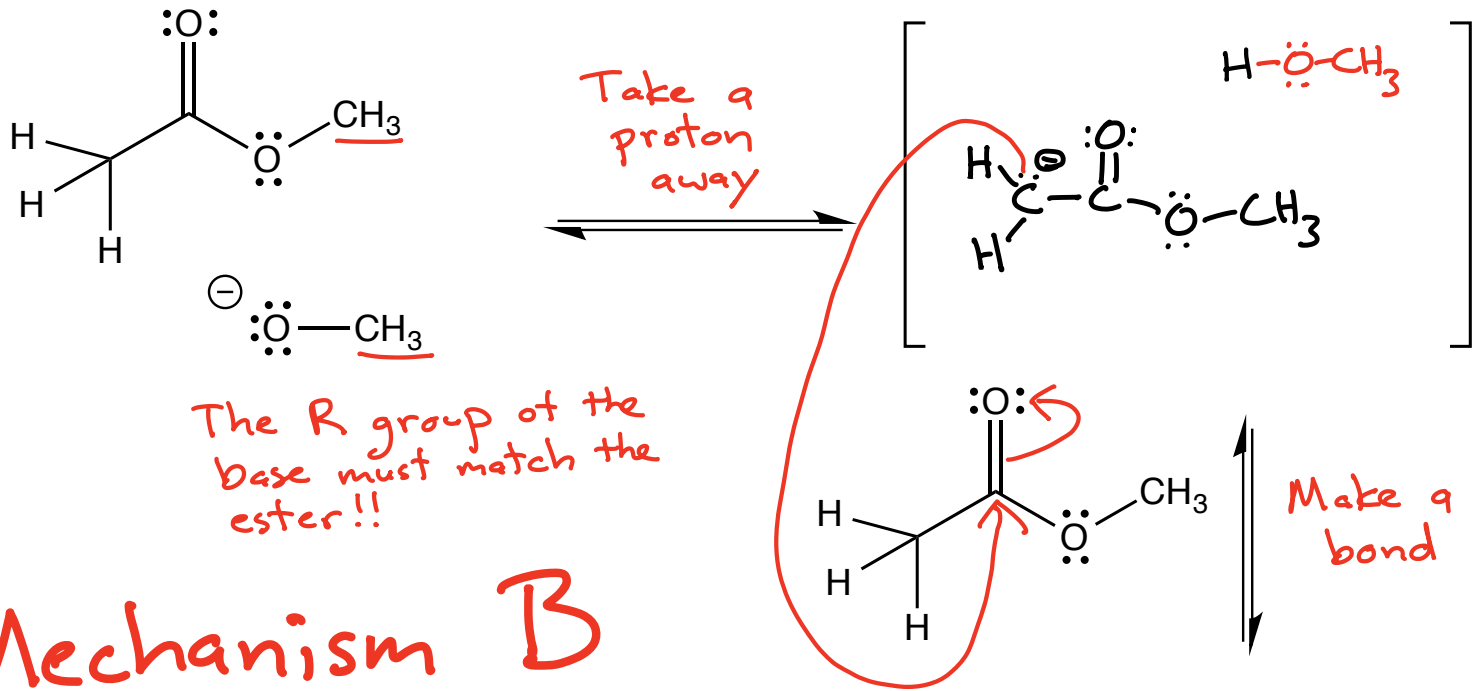
## Esters





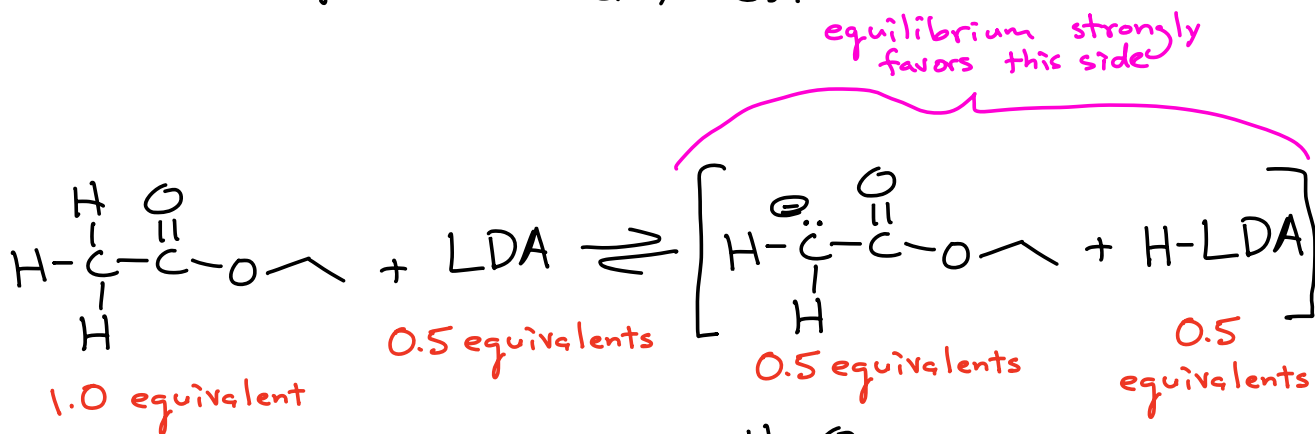


# Claisen Condensation → "Aldol with Esters"

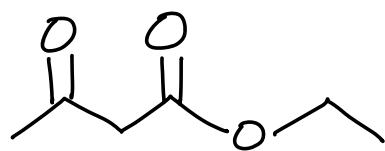
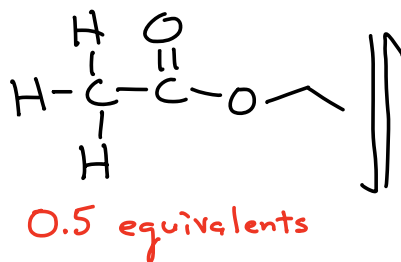


This is a much more stable anion compared to  $\ominus\text{OCH}_3$ , providing a strong driving force (motive) for the Claisen condensation reaction

What if we use 0.5 equivalents of LDA with an ester?

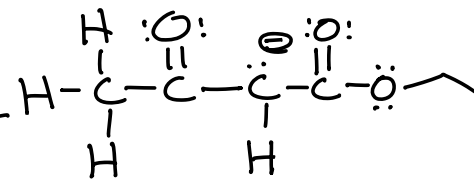


Amount of ester left over after 0.5 equivalents of enolate is made



0.5 equivalents

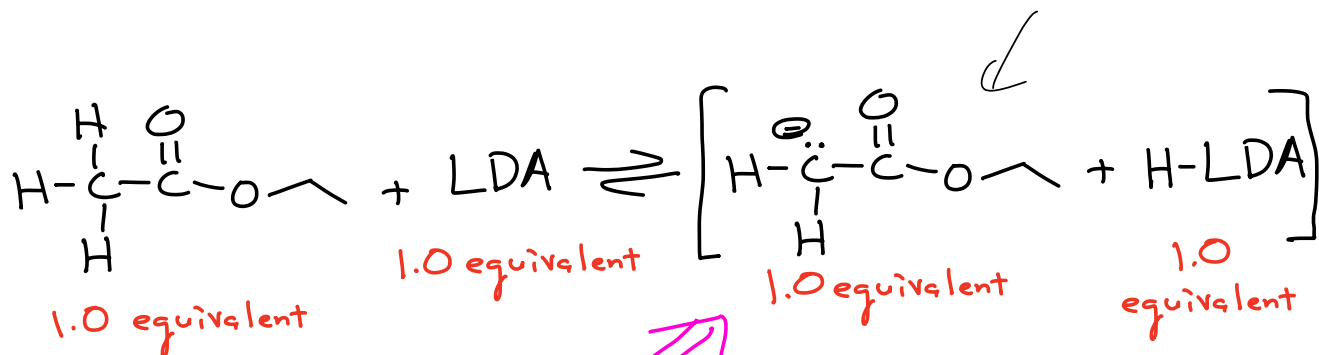
2) HCl/H<sub>2</sub>O  
mild



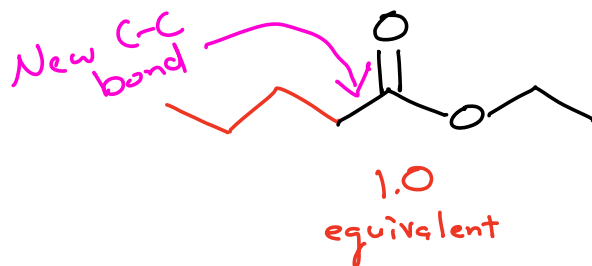
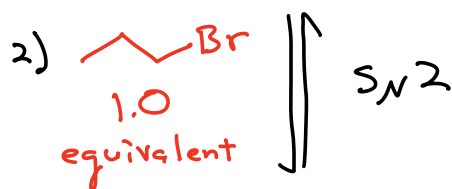
0.5 equivalents

(There are 2 ester molecules used for each product molecule so there can only be half the number of product molecules compared to starting ester molecules)

What if we use 1.0 equivalent of LDA with an ester?

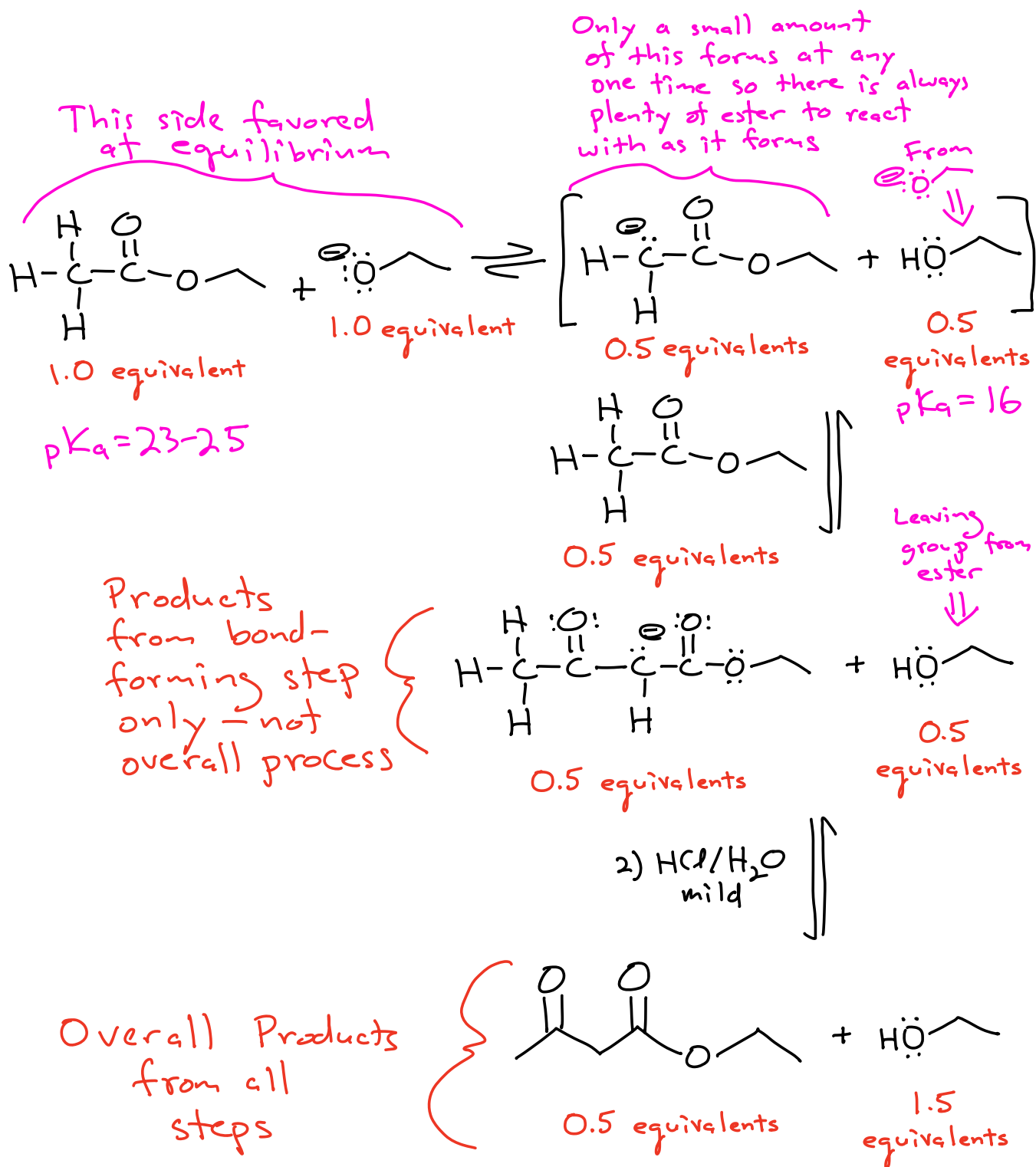


The enolate forms quantitatively so there is no ester left to react with!

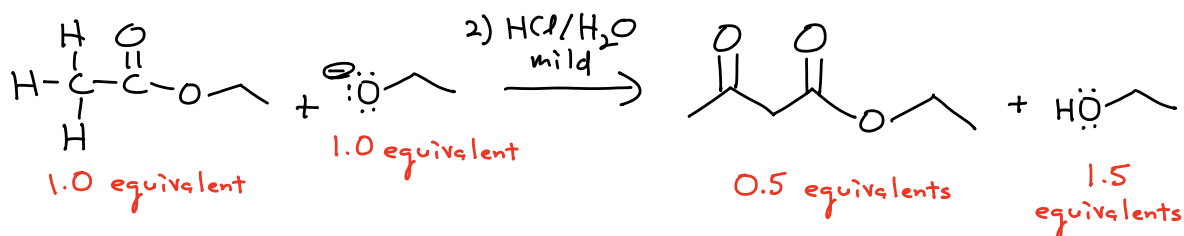


All of the starting ester molecules end up as the same number of product molecules with a new C-C bond!

What if we use 1.0 equivalent of  $\text{CH}_3\text{CH}_2\text{O}^-$  with an ester?



## Overall Reaction

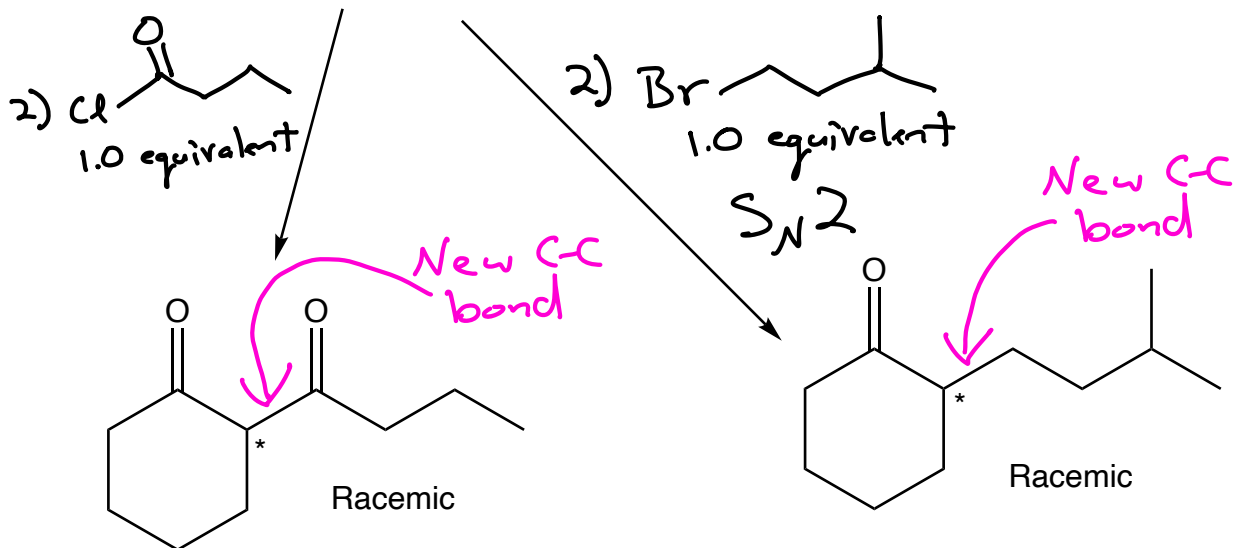
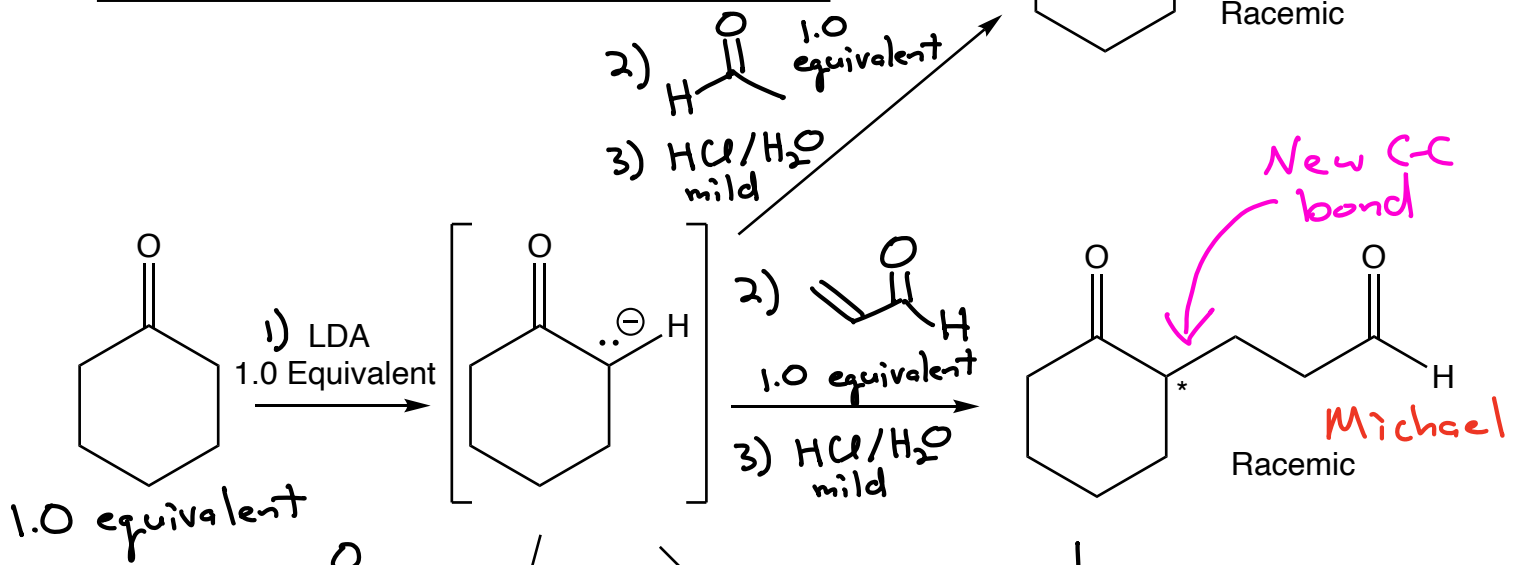
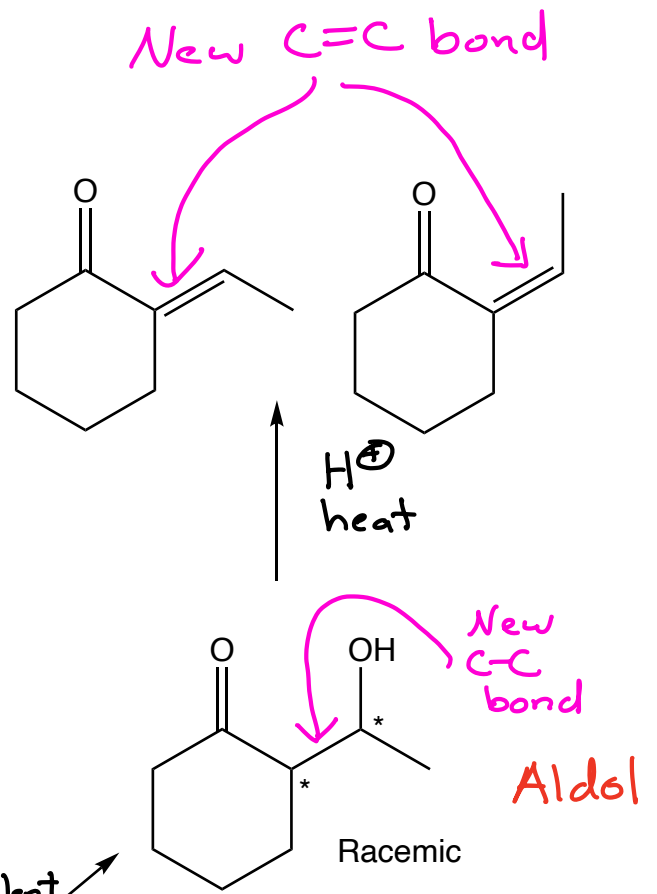
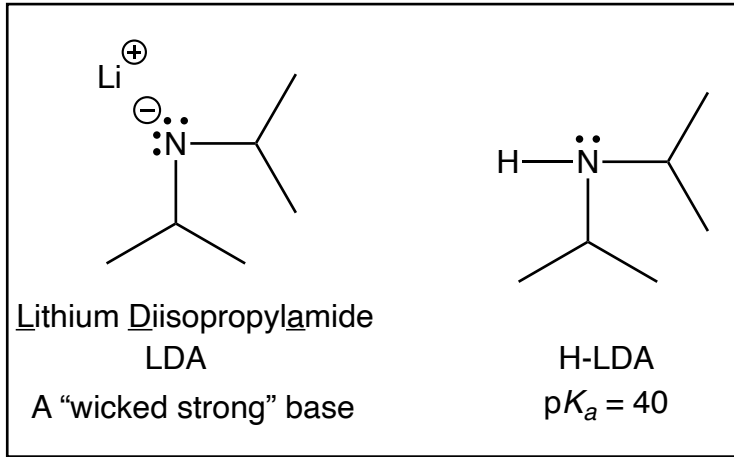


0.5 equivalents comes from first step, formation of the enolate

0.5 equivalents comes from second step, loss of  $\ominus\text{O}^-$  leaving group from ester (see mechanism)

0.5 equivalents is left over from original  $\ominus\text{O}^-$  that was not used

Note: Considerable detail was added to the preceding four pages compared to what I wrote in lecture — I wanted to capture more of the key points for you to study



**$\beta$ -Substituted  
aldehydes,  
nitriles, ketones,  
or esters**

**$\alpha,\beta$ -Unsaturated, nitriles,  
ketones, or esters**

**$\beta$ -Keto esters**

**$\alpha,\beta$ -Unsaturated aldehydes**

**Acid Chlorides**

**$\beta$ -Hydroxy aldehydes**

**Aldehydes**

**Ketones**

**Carboxylic esters**

**$\beta$ -Ketoaldehyde**

**$\beta$ -Diketone**

**Carboxylic acids**

**Substituted aldehyde**

**Substituted ketone**

**$\beta$ -Diester**



