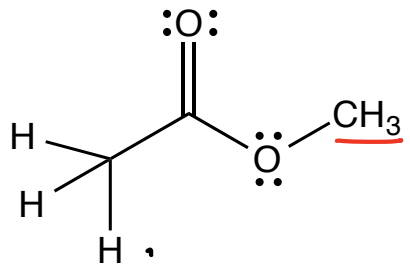
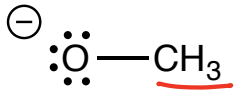
Claisen Condensation → "Aldol with Esters"

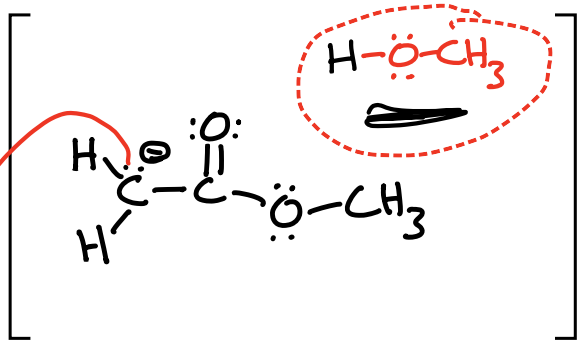


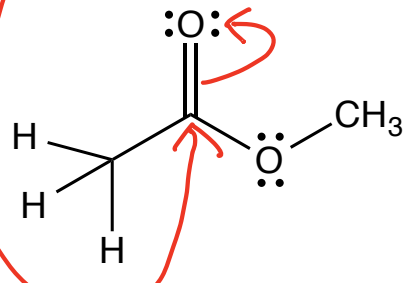


$NaOCH_3$

The R group of the base must match the ester!!

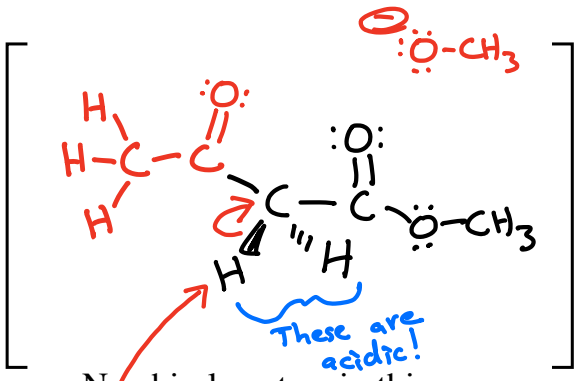
Take a proton away





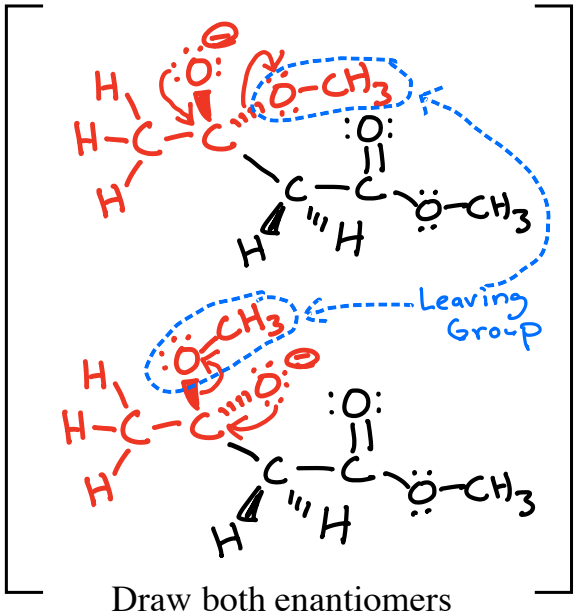
Make a bond

Mechanism B

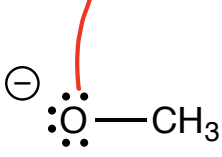


No chiral centers in this case

Break a bond



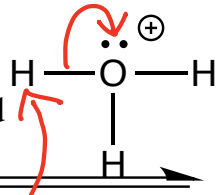
Draw both enantiomers



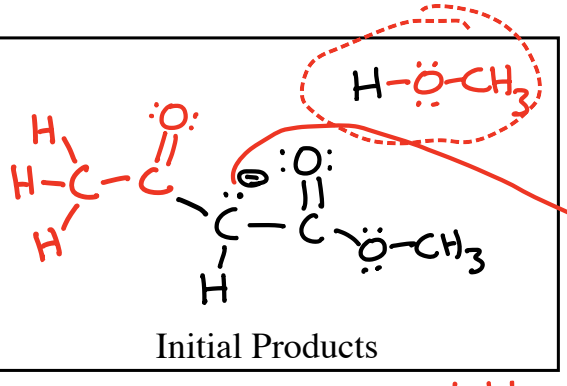
Take a proton away

(Chemist opens flask and adds a mild acid)

2) Mild

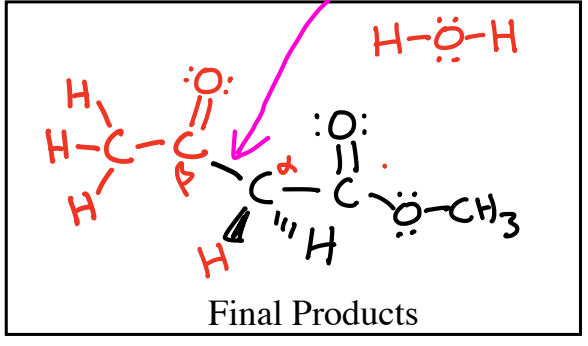


(H-Cl)



Initial Products

New C-C bond



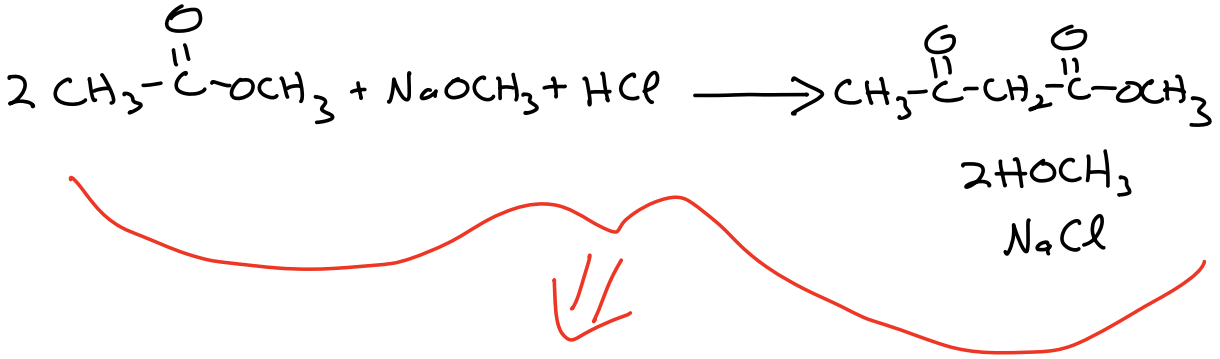
Final Products

This is a much more stable anion compared to $^{\ominus}OCH_3$, providing a strong driving force (motive) for the Claisen condensation reaction

KRE → A β-keto ester with a new C-C bond between the α and β carbons

Before we add acid → the last step drives the reaction because we make a relatively stable anion.

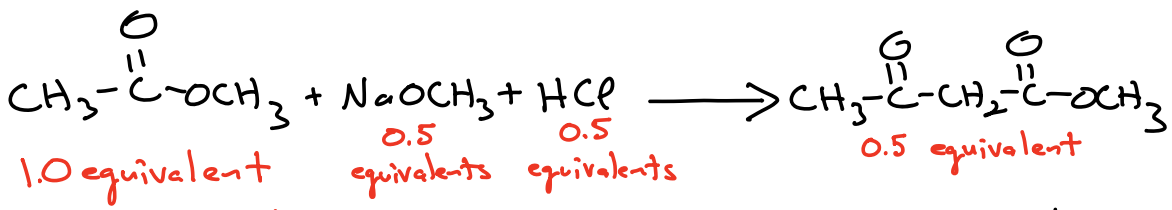
Balanced Equation for the Overall Process



This is the balanced equation that is explained by the mechanism

With the balanced equation in hand we can set up a reaction properly in the lab because we know how much of each reactant is needed → For this we use the notation of "equivalents"

Notation we use for the lab and therefore synthesis and "box" problems on the exams

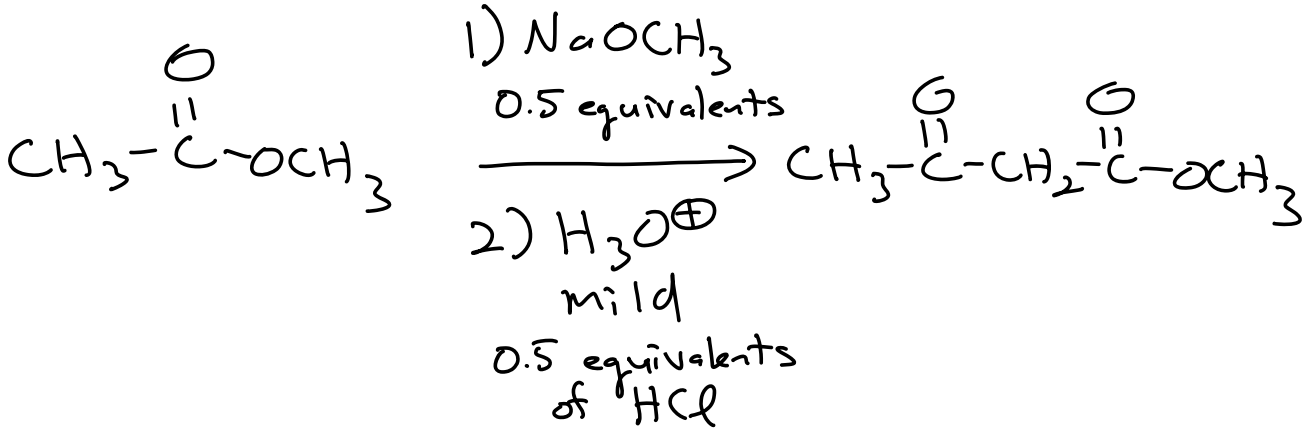


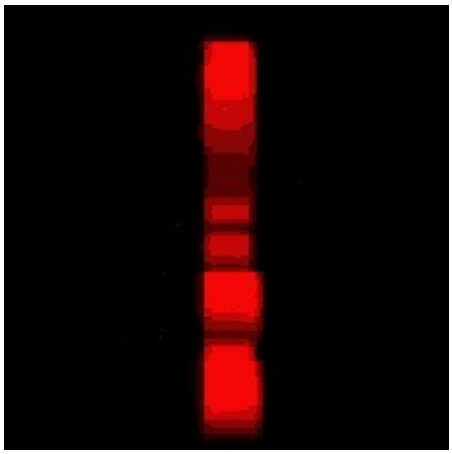
Defined as 1.0 equivalent as the important carbon containing starting material

$HOCH_3$
1.0 equivalent

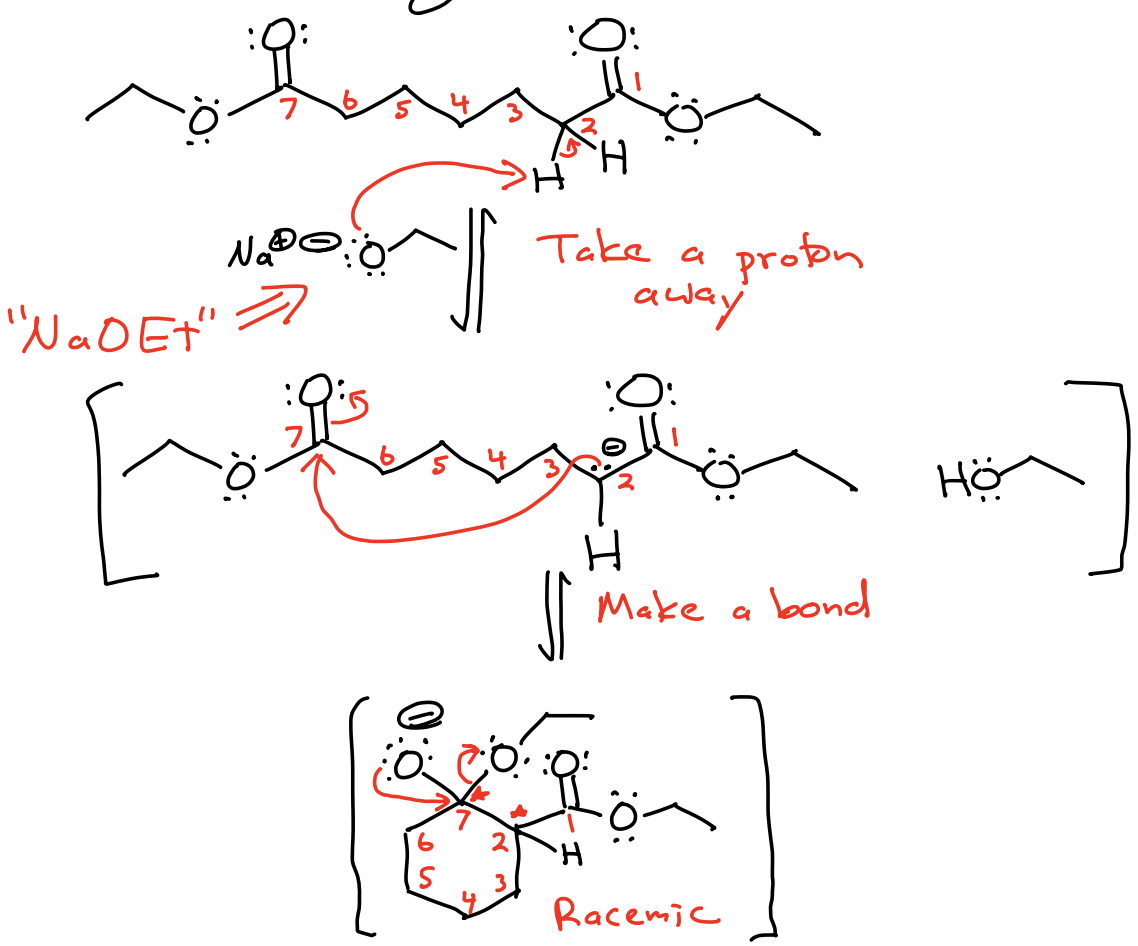
NaCl
0.5 equivalent

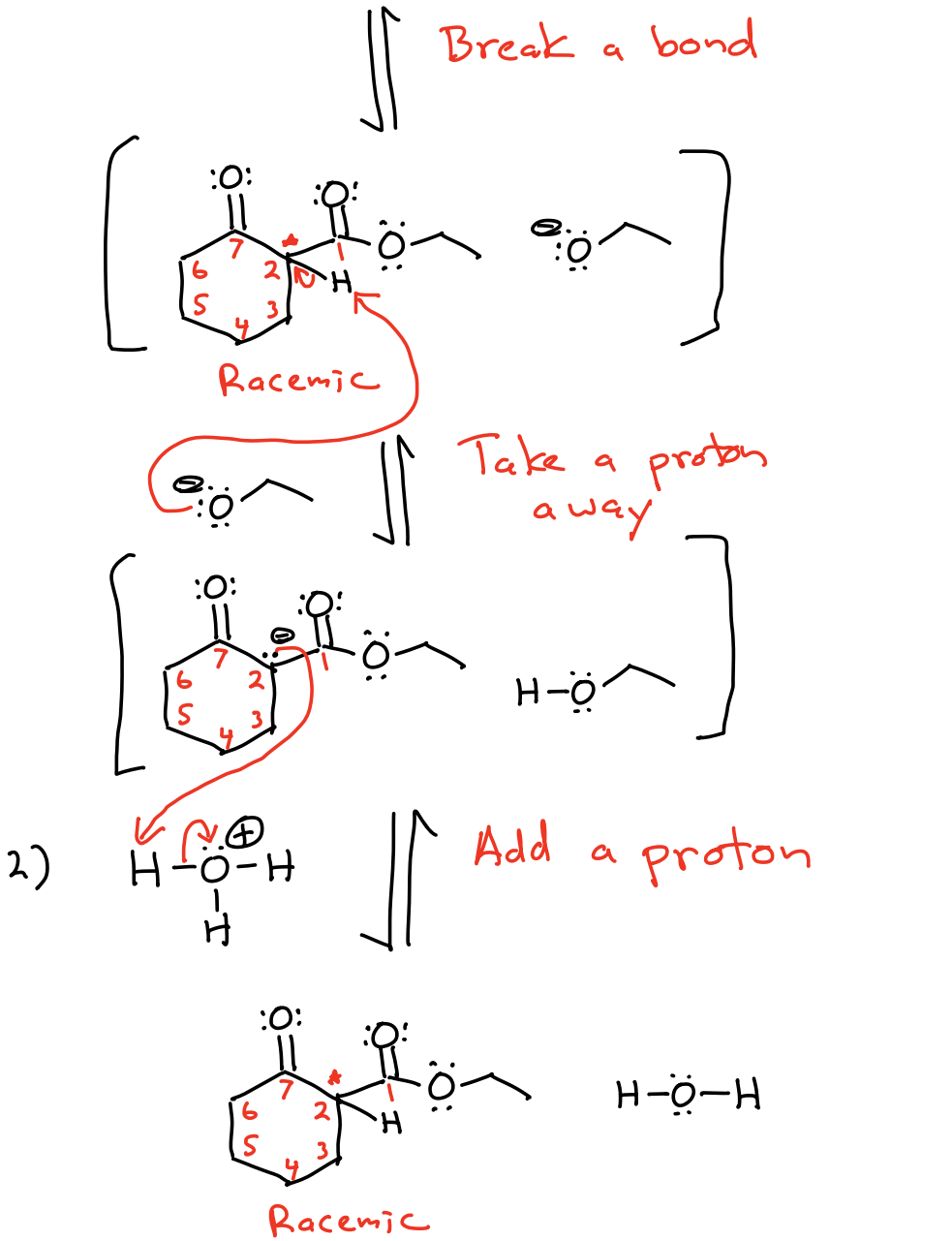
Example of using equivalents



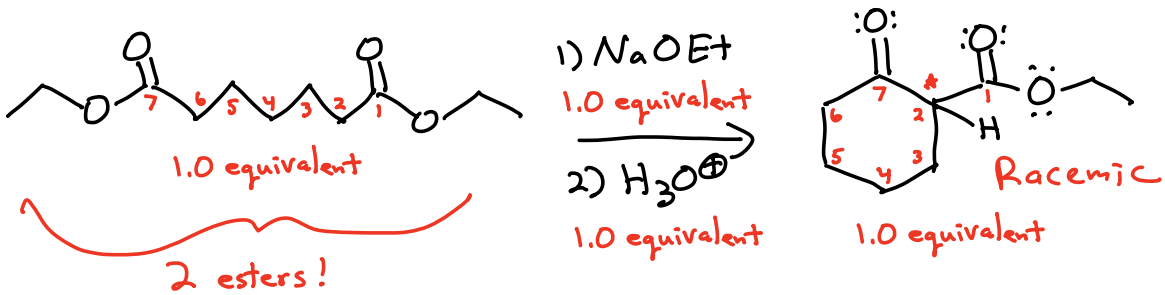


The Dieckmann Condensation → Using a Claisen to make a ring.





Overall Process

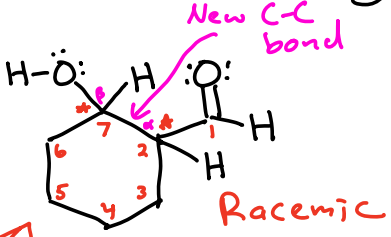


Cyclic aldol reactions are analogous

1.0 equivalent

2 aldehydes

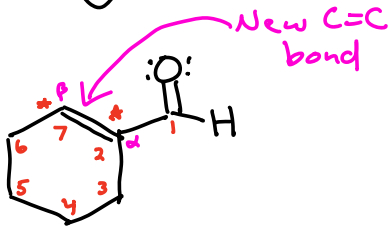
H-Ö: (catalytic)



1.0 equivalent

$H^{\oplus}$
heat

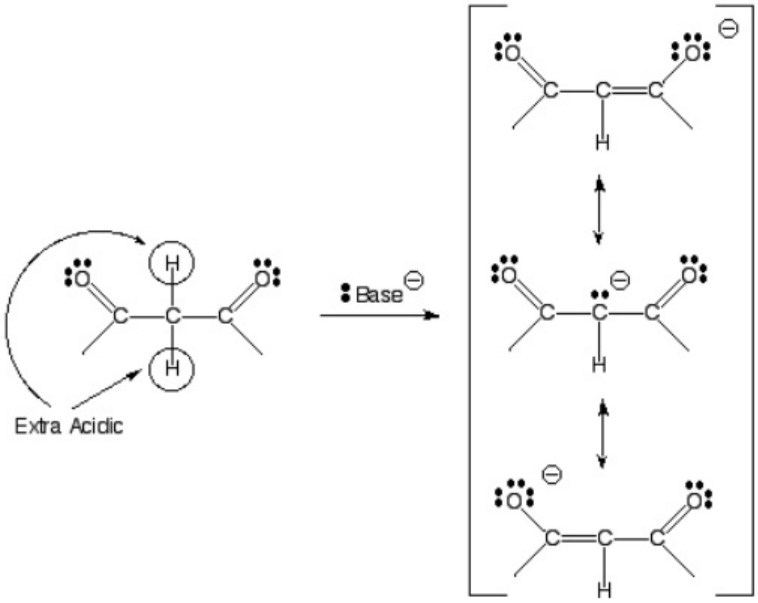
KRE → A β-hydroxy aldehyde with a new C-C bond between the α and β carbons

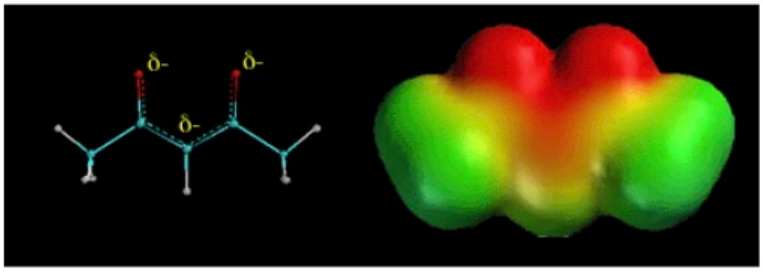


1.0 equivalent

KRE → An α-β unsaturated aldehyde with a new C=C bond between the α and β carbons

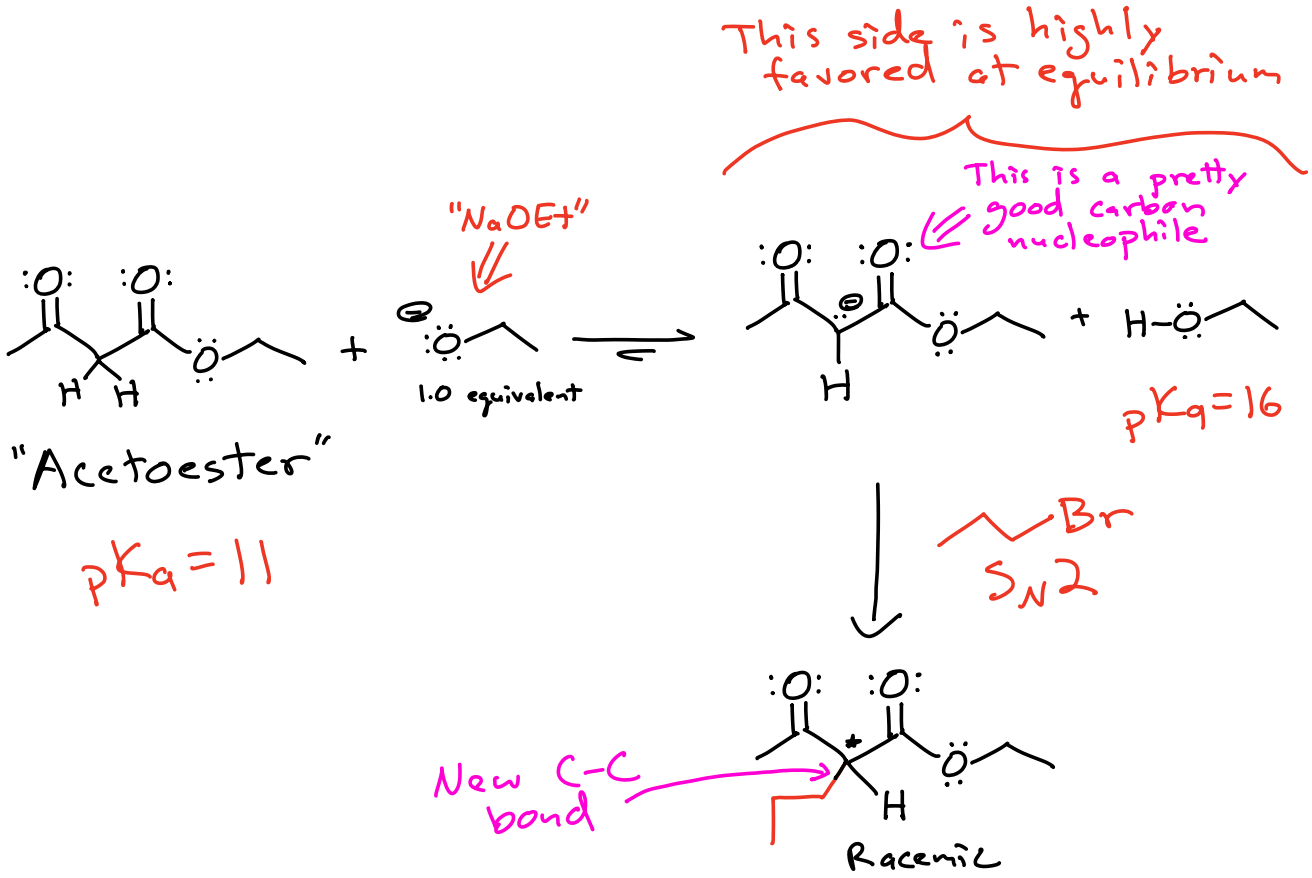
Beta-dicarbonyls have alpha-hydrogens that are extra acidic



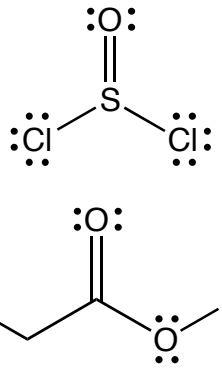


The C-H hydrogen atoms between two carbonyl groups are aven more acidic than normal a hydrogens because the resulting anion is double resonance stabilized. The above electrostatic potential surface shows how the negative charge (red color) is spread over all three atoms as predicted by the three resonance contributing structures.

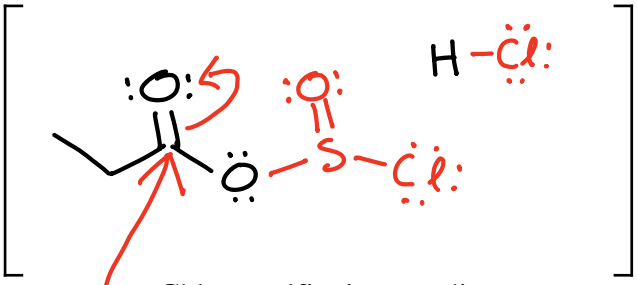
Acetoester Synthesis



Reaction with Thionyl Chloride

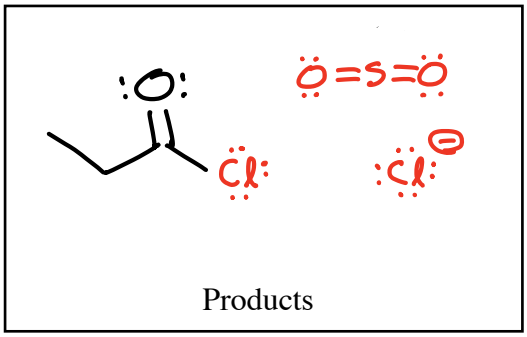


Several Steps

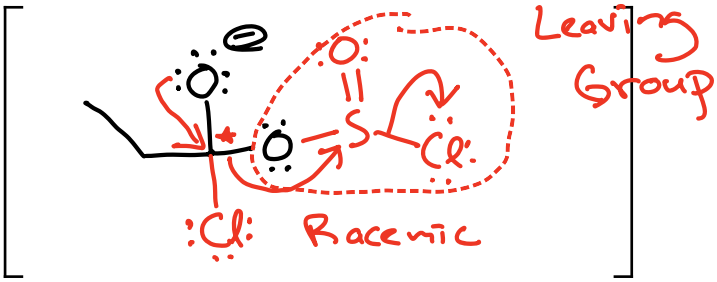


KRE → An acid chloride

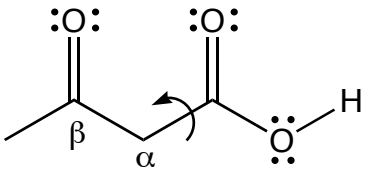
Make a bond



Break a Bond

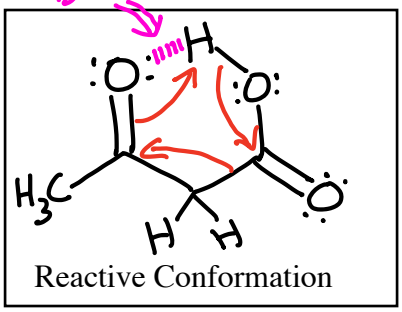


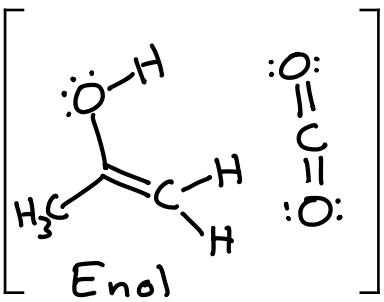
Decarboxylation of a β-Keto Acid

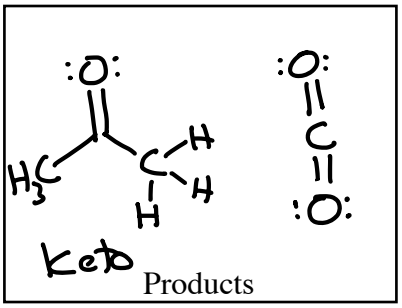


Bond rotates to give a more stable conformation

Hydrogen Bond

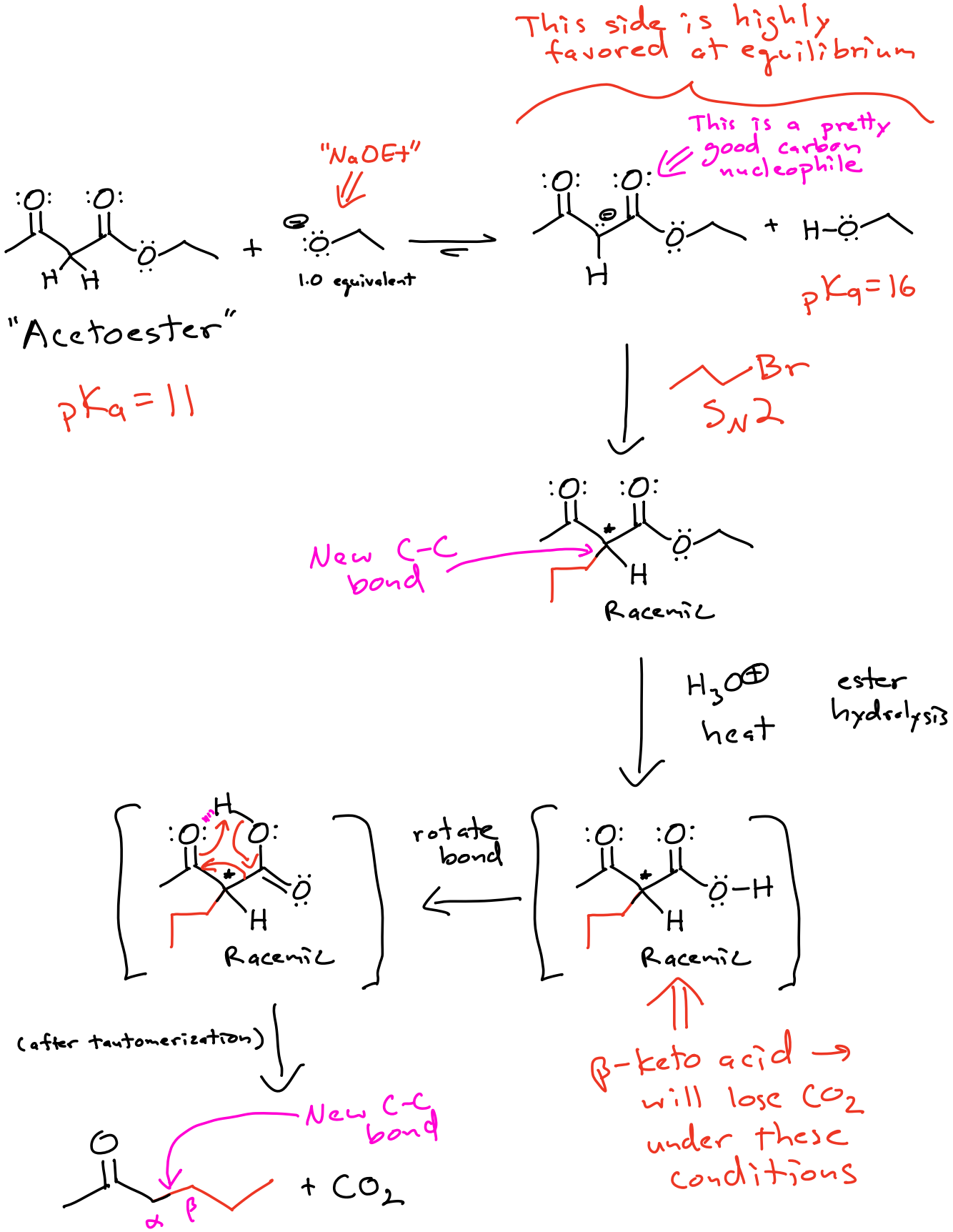




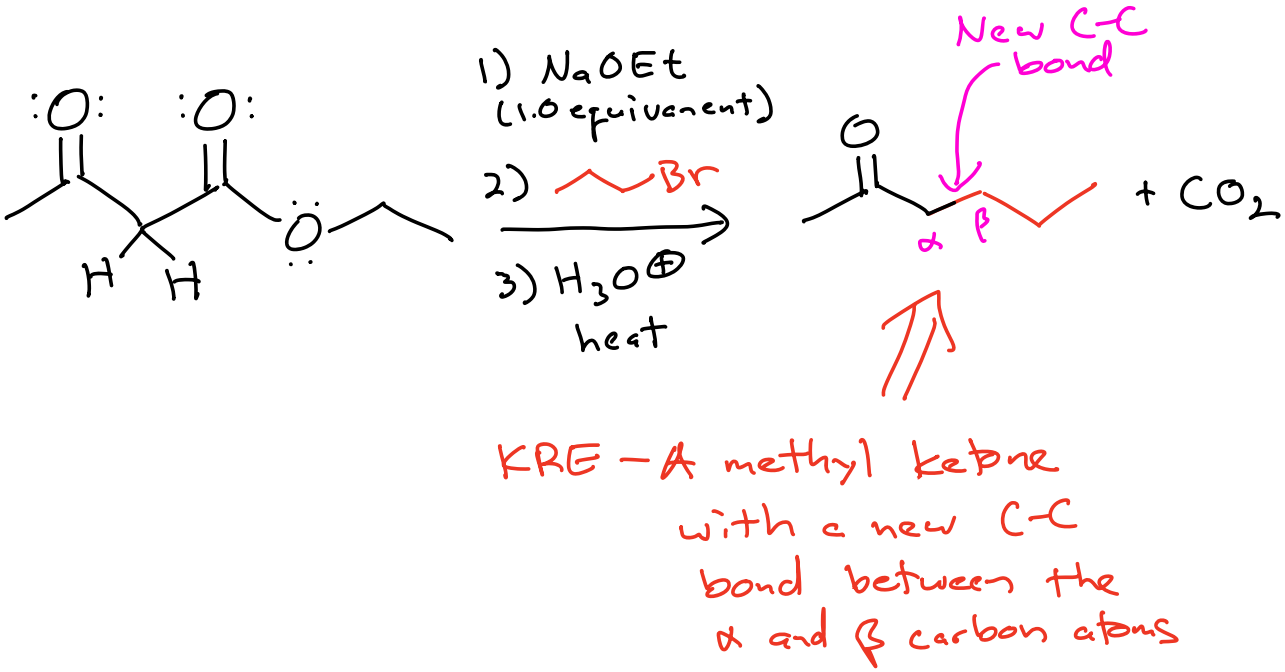


6-Membered Ring
6 "Pi" Electrons
} VERY STABLE
"Aromatic"

C–C Bond Breaks!


This side is highly favored at equilibrium
This is a pretty good carbon nucleophile
"NaOEt"
1.0 equivalent
"Acetoester"
pKa = 11
pKa = 16
Br
SN2
New C-C bond
Racemic
H3O⊕
heat
ester hydrolysis
rotate bond
Racemic
Racemic
(after tautomerization)
New C-C bond
+ CO2
α
β
β-keto acid → will lose CO2 under these conditions

Acetoester Synthesis Summary



KRE - A methyl ketone with a new C-C bond between the α and β carbon atoms

Enamine Formation