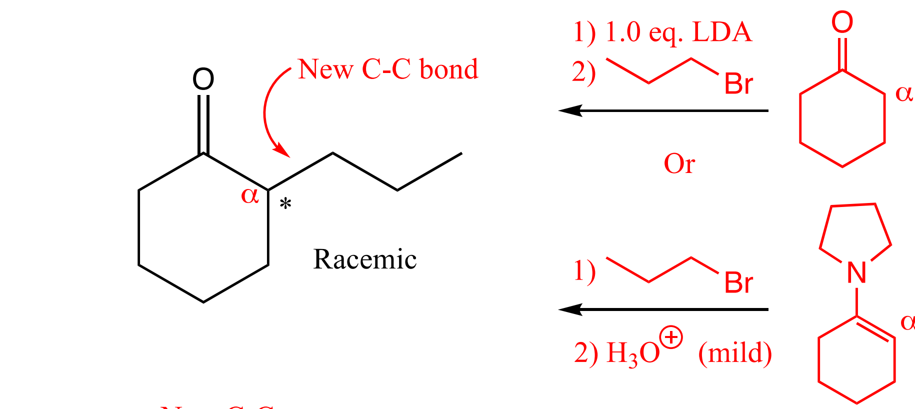
NAME (Print): ______________________________

SIGNATURE: ______________________________

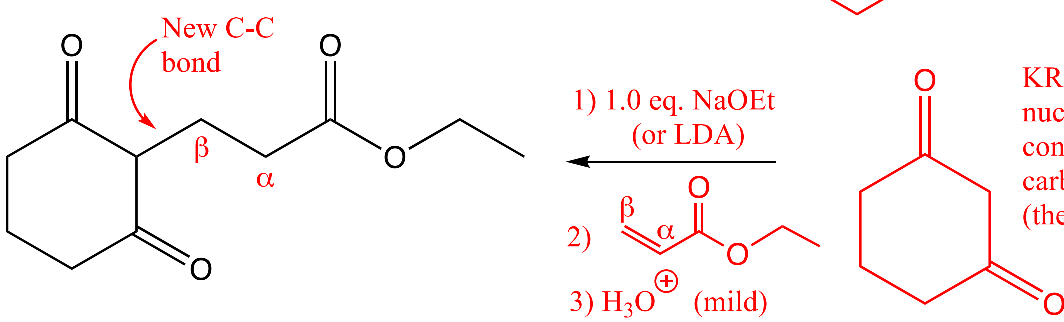
Chemistry 320N
Dr. Brent Iverson
9th Homework
April 2, 2025

Please print the first three letters of your last name in the three boxes

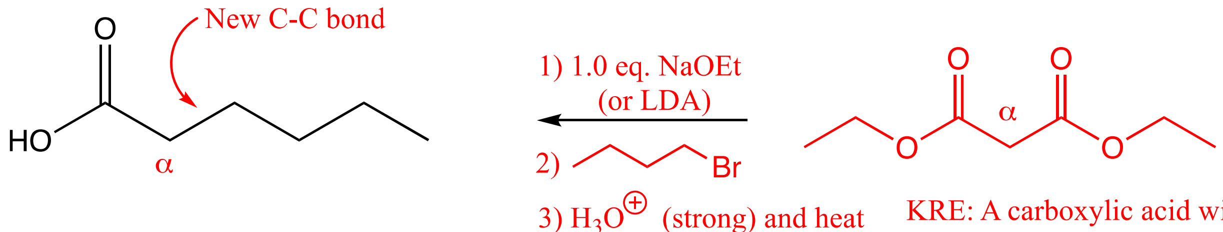
For the following three pages, a reaction product is given. Predict the starting materials and reagents needed to make each molecule. Note that some will take several steps. This problem is designed to test you ability to recognice KRE's in enolate and other types of reactions. Note this list exactly correlates to the structures presented in class as representative enolate products (Mechanism Sheet 33 on the course webstire under "Handouts")



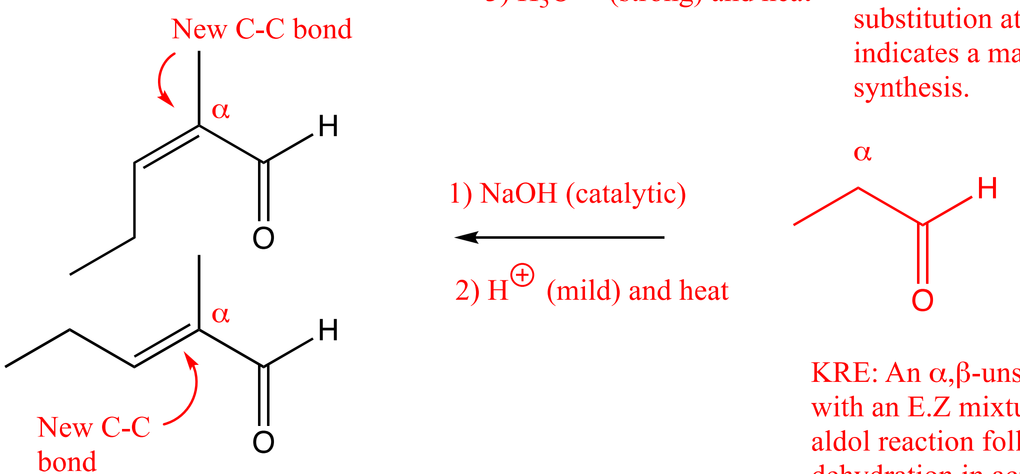
KRE: alkylated ketone deriving from either an enolate made with LDA or using an enamine



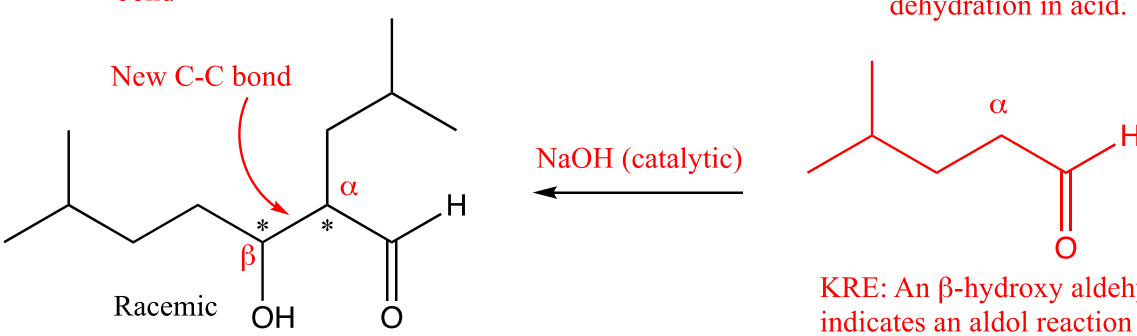
KRE: Reaction of a nucleophile (β-diketone) connected to the β-carbon of a carbonyl (the ester)



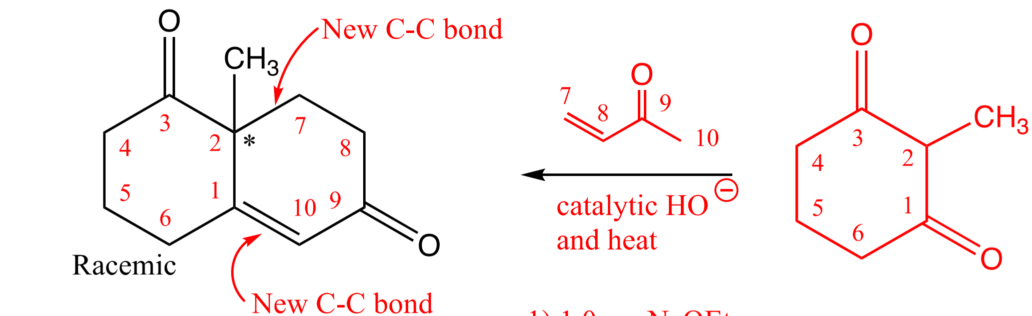
KRE: A carboxylic acid with substitution at the α-carbon indicates a malonic ester synthesis.



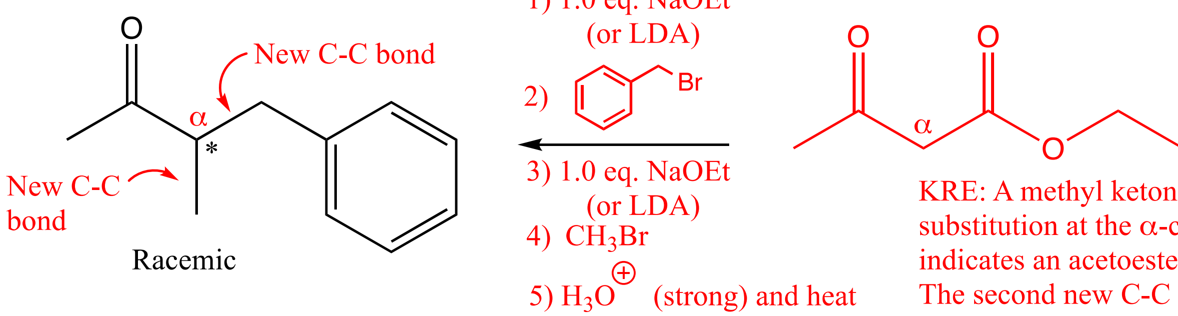
KRE: An α,β-unsaturated aldehyde with an E.Z mixture indicates an aldol reaction followed by dehydration in acid.



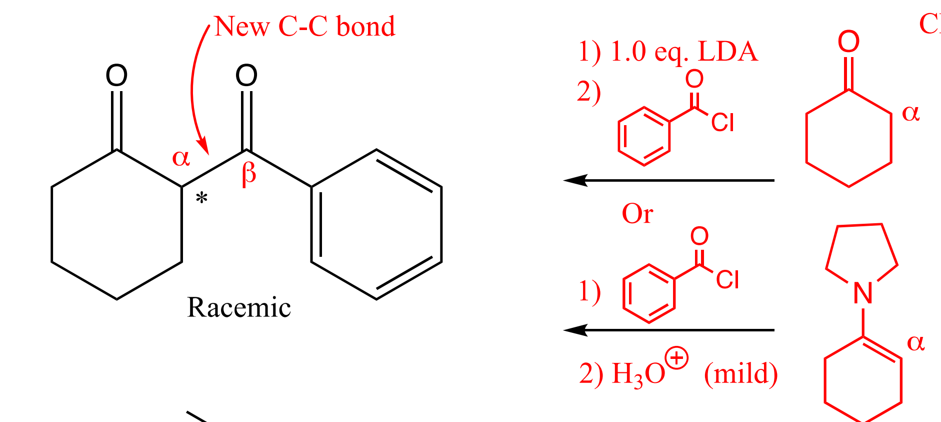
KRE: An β-hydroxy aldehyde with an indicates an aldol reaction with no dehydration.



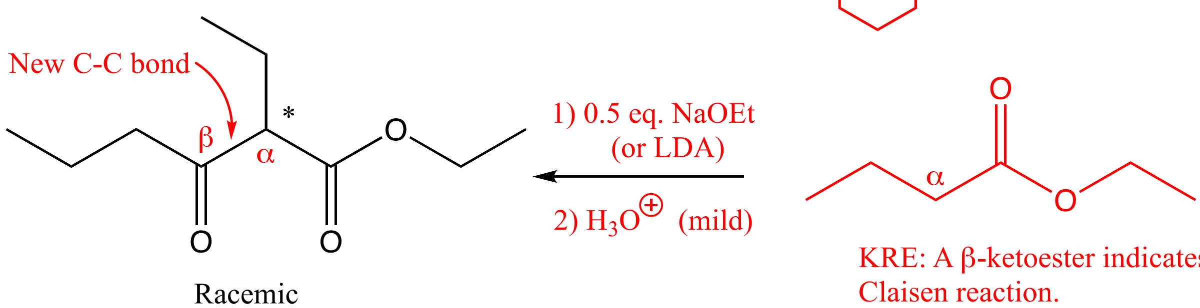
KRE: A new six-membered ring with two new C-C bonds and an α,β-unsaturated ketone indicates a Robinson reaction.



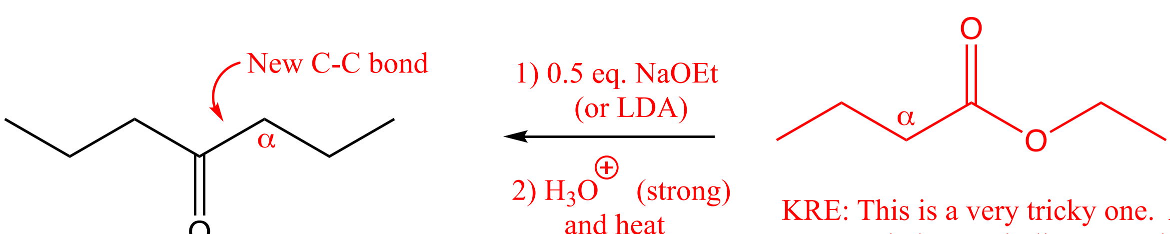
KRE: A methyl ketone with substitution at the α-carbon indicates an acetoester synthesis. The second new C-C bond indicates a second alkylation with CH_3Br



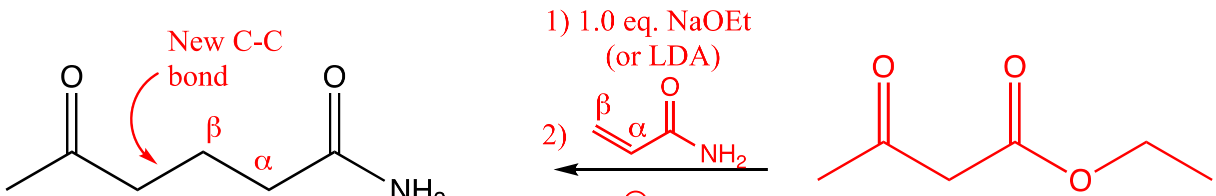
KRE: A β-diketone indicates reaction of an acid chloride with either an enolate made with LDA or using an enamine



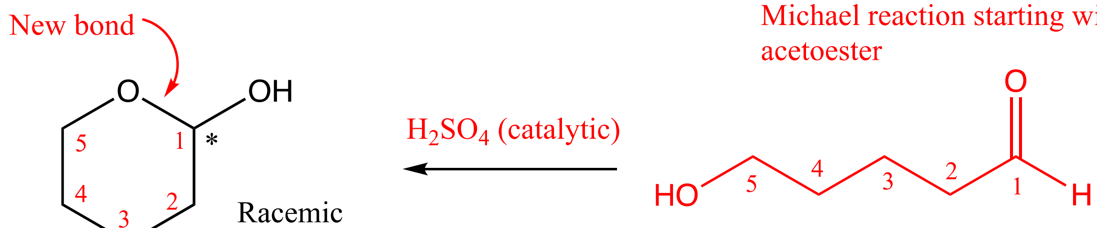
KRE: A β-ketoester indicates a Claisen reaction.



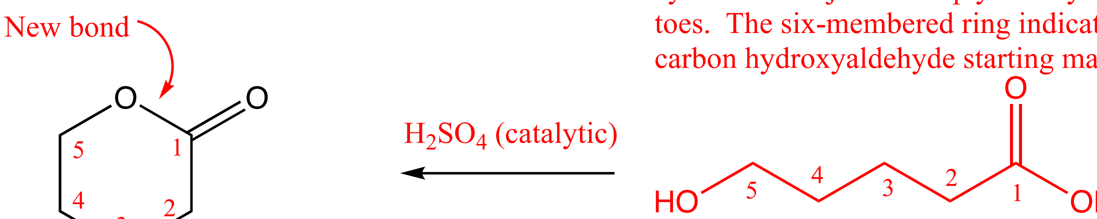
KRE: This is a very tricky one. A symmetric ketone indicates a Claisen reaction followed by ester hydrolysis and decarboxylation of the resulting β-keto ester.



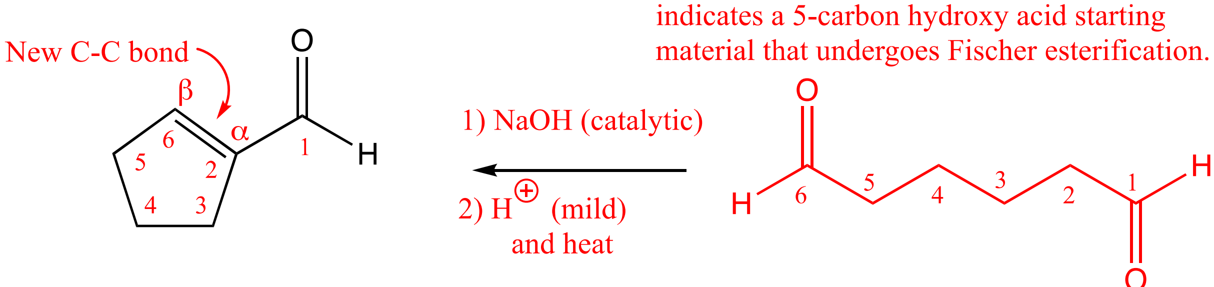
KRE: This is a nucleophile linked to the β-carbon of the amide. This is also a methyl ketone. Putting these together indicates a Michael reaction starting with acetoester



KRE: This is not an enolate reaction, it is a cyclic acetal...just to keep you on your toes. The six-membered ring indicates 5-carbon hydroxyaldehyde starting material.

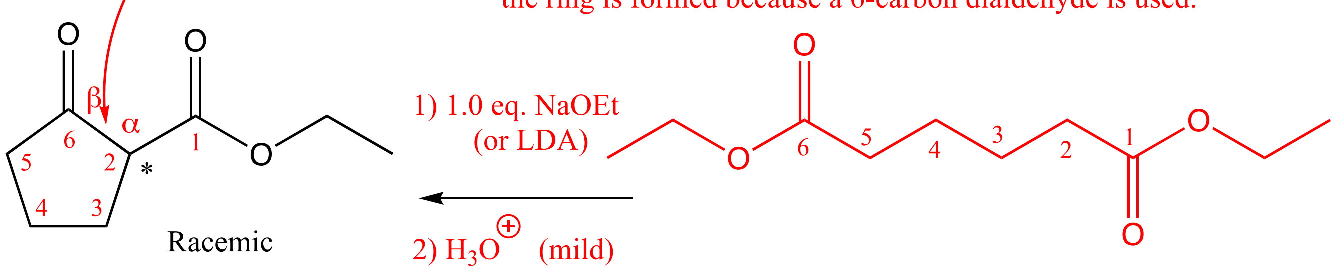


KRE: This is also not an enolate reaction, it is a lactone (cyclic ester). The six-membered ring indicates a 5-carbon hydroxy acid starting material that undergoes Fischer esterification.



KRE: This is an α,β-unsaturated aldehyde that indicates an aldol reaction followed by dehydration. In this case the ring is formed because a 6-carbon dialdehyde is used.

New C-C bond

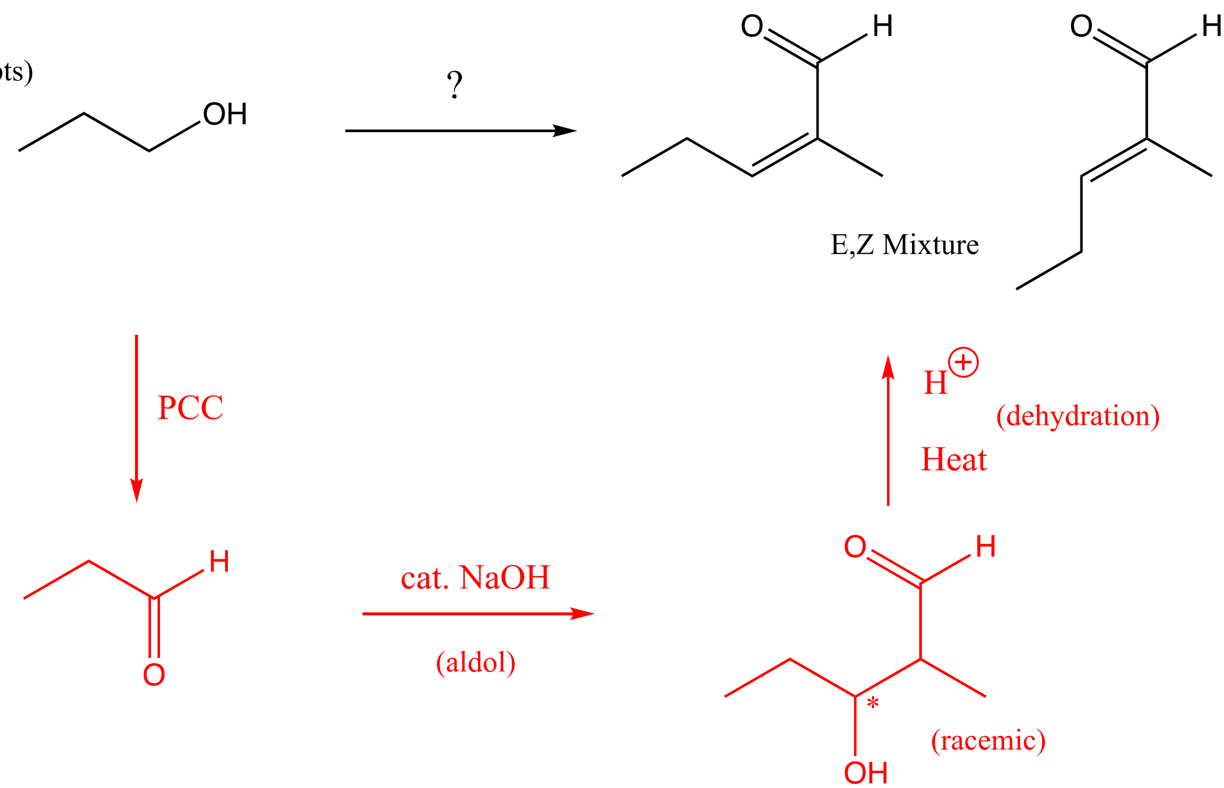


KRE: This is a cyclic β-ketoester that indicates a Dieckmann reaction starting with a 6-carbon diester. Notice that Dieckman reactions require 1.0 equivalent of base.

These are enolate synthesis problems. In each case, all of the carbons of the products must come from the listed starting materials. You may use any reagents we have discussed this semester or last semester. Show all molecules synthesized along the way. For each step, you will only get full credit if the product you list is the major product of that transformation. Remember to work backwards, count carbons, and make sure you know your KRE's.

(7 pts)

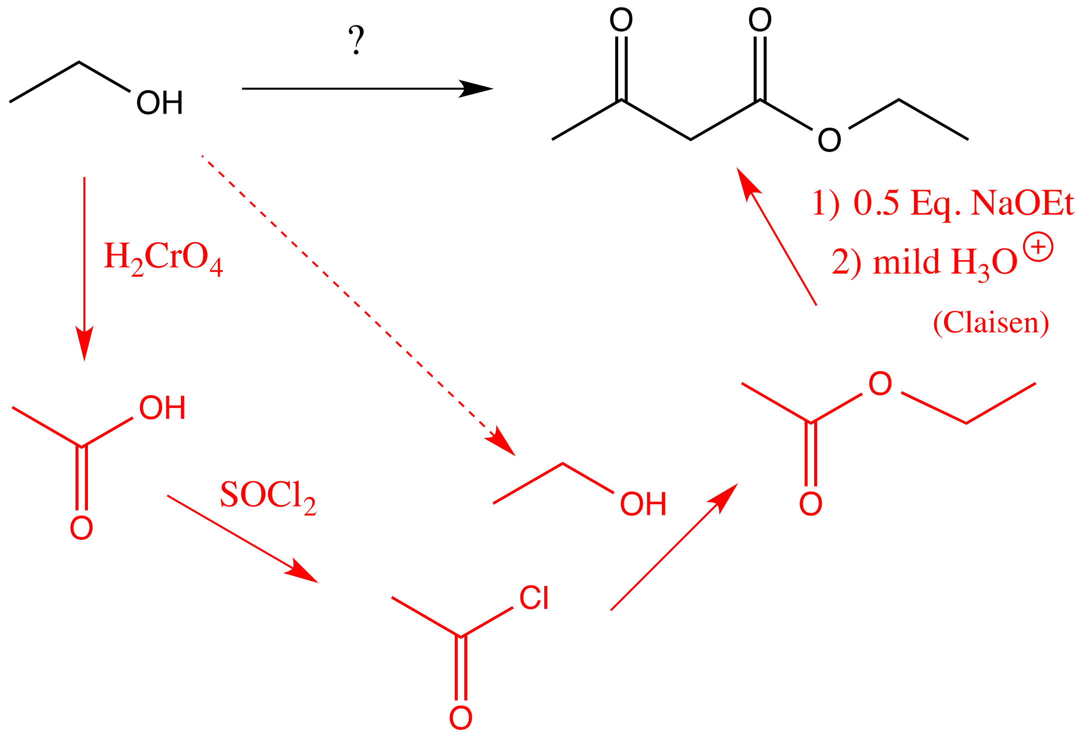
A)



The key recognition element is the α,β-unsaturated aldehyde, which indicates an aldol followed by dehydration.

(10 pts)

B)

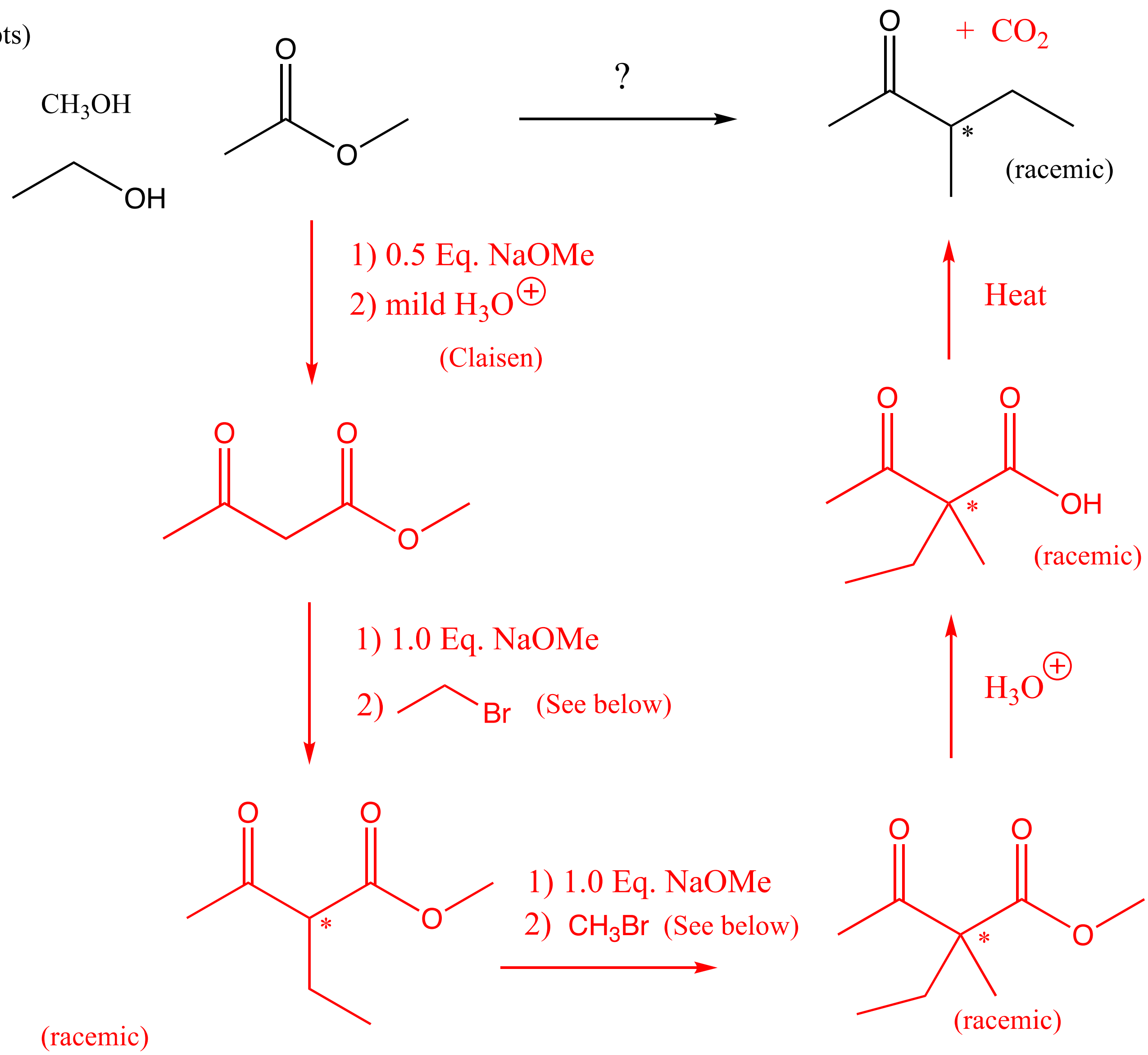


The key recognition element is the β-keto ester product indicating a Claisen as the last step.

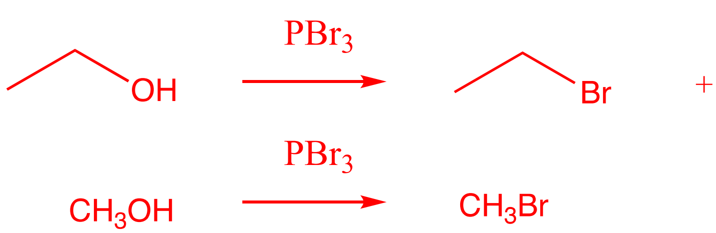
Alternatively, the ethyl ester could have been made from a reaction of ethanol with sufuric acid directly, avoiding the acid chloride intermediate.

(19 pts)

C)

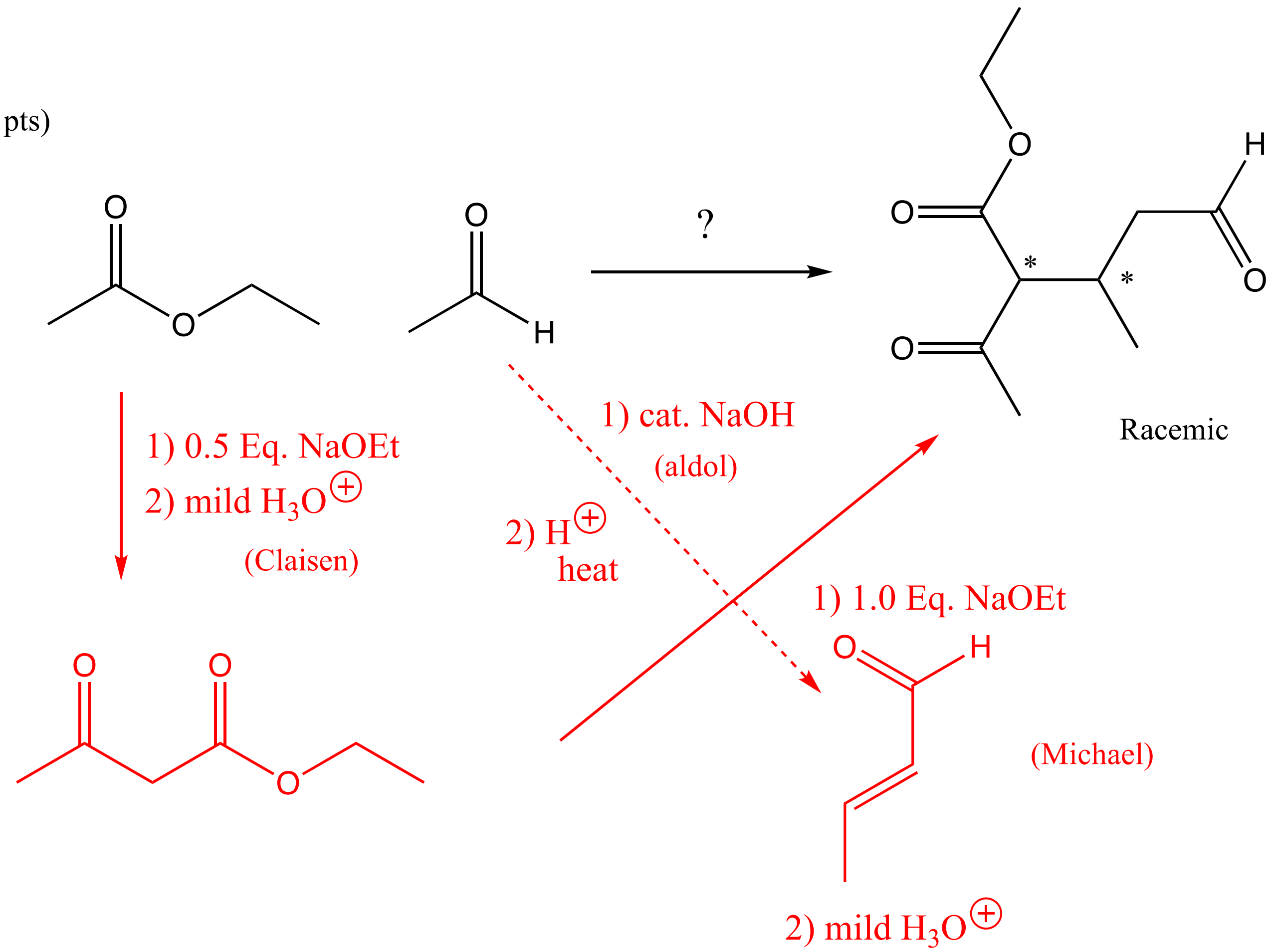


Following the initial Claisen, this is just an aceto ester synthesis. The key recognition element in the product is the substituted methyl ketone. The ethyl bromide and methyl bromide are made according to the scheme below:



(7 pts)

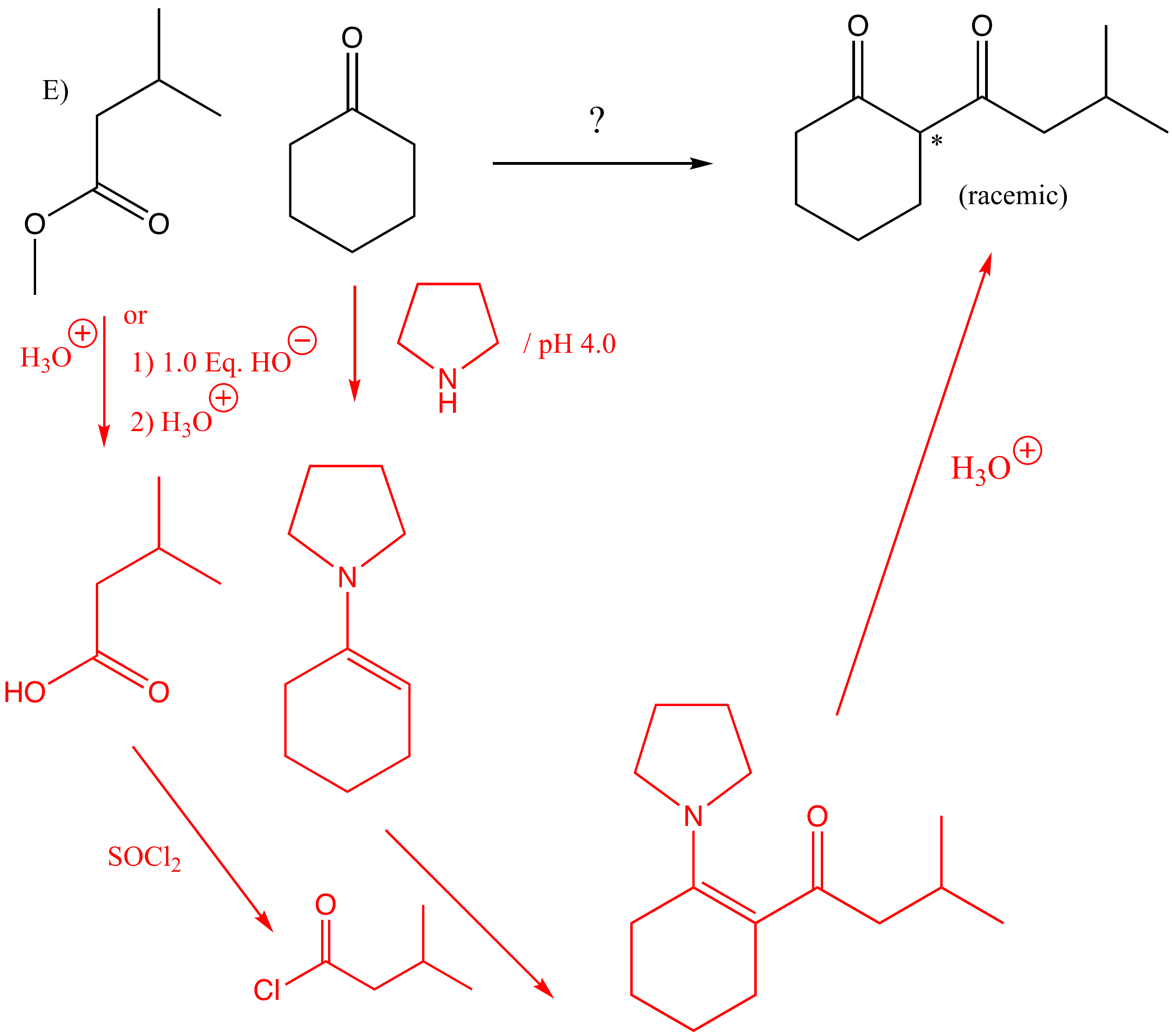
D)



The key recognition element is as the product of a Michael reaction between acetoacetic ester and the α,β-unsaturated aldehyde shown. These can be produced by a Claisen and aldol, respectively. This problem demonstrates how multiple reactions can be put together in powerful ways to create very complex molecules from simple starting materials.

(16 pts)

E)

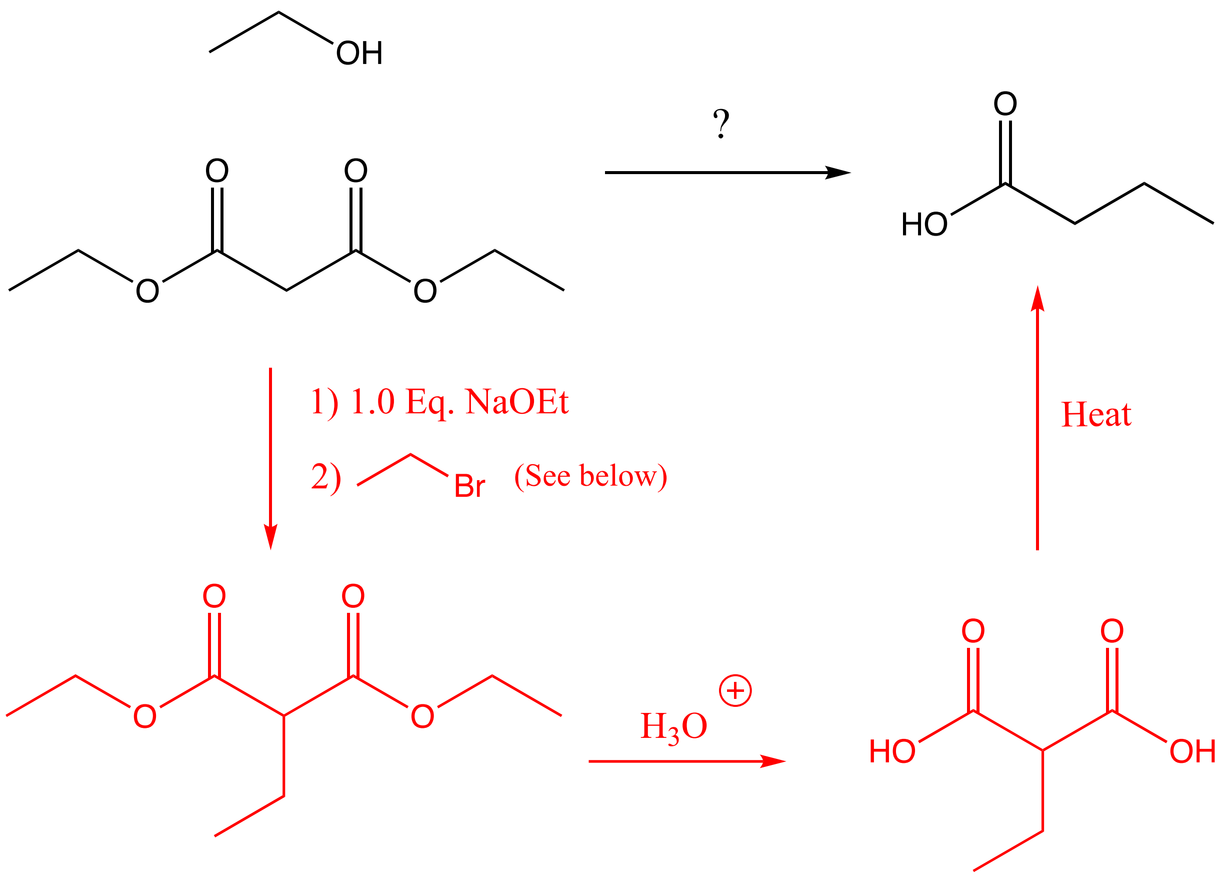


The key recognition element here is that there was an acylation via the enamine. The acid chloride is made from the starting ester via hydrolysis to the carboxylic acid followed by reaction with $SOCl_2$.

Note that the above could have also been accomplished using a directed enolate reaction in which the enolate of the ketone is created by addition of 1.0 Eq. of LDA, followed by treatment with the ester in a reaction that follows mechanism B.

(10 pts)

F)

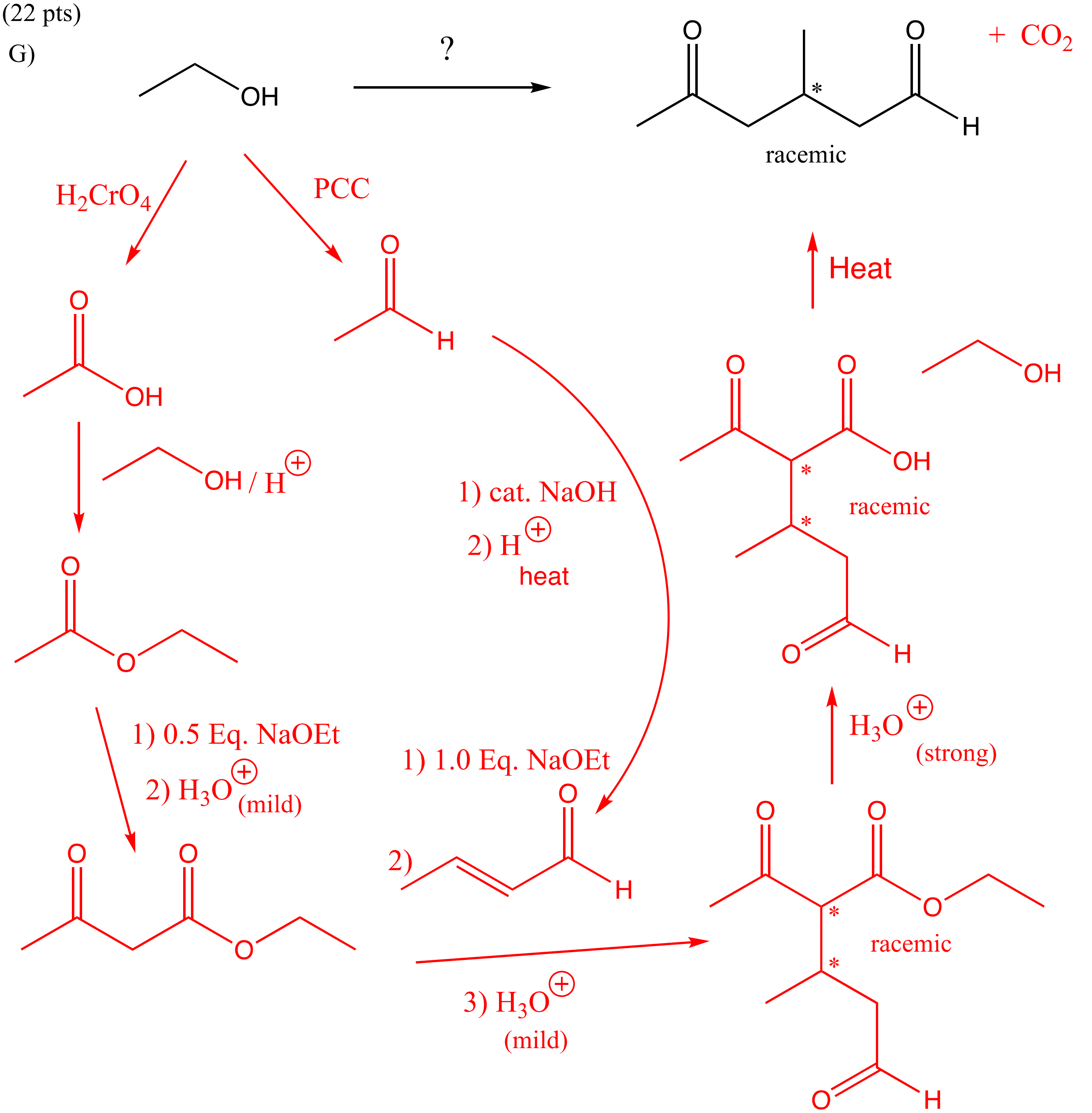


This can be tough to spot, but it is just a reduction following a malonic ester synthesis. The key recognition element in the product is the alkylation pattern with the alcohol on the terminal carbon, indicating reduction of a carboxylic acid. The ethyl bromide is made according to the scheme below:

The KRE might be very difficult to spot here. Hint: A substantial portion of this one comes from ones you have done earlier in this homework set. Look at problems B) and D).

(22 pts)

G)



This is also just plain hard. The methyl ketone is the key recognition element that indicates an acetoester synthesis. The aldehyde substituted at the β-carbon indicates a Michael reaction. Both the α,β-unsautrated aldehyde and acetoester can be derived from ethanol via an aldol and Claisen reaction, respectively. If you got this, I am VERY impressed!