Course Chem 345 Lecturer Tellman

Day Monday Date 4-11-16

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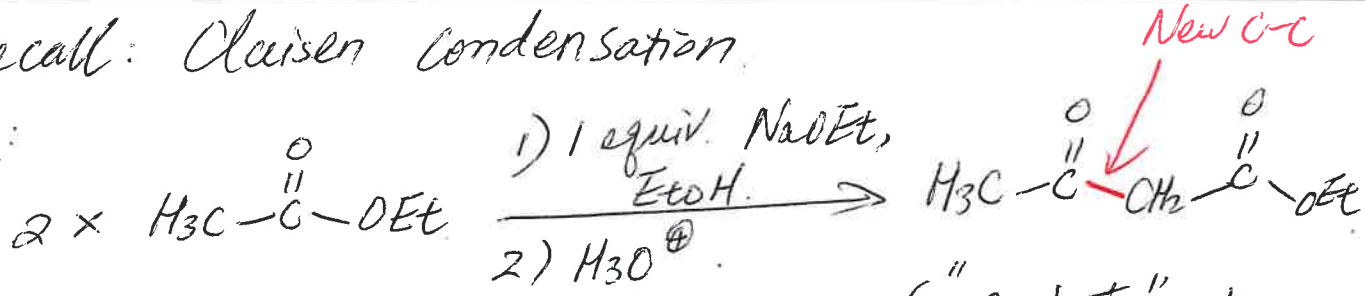
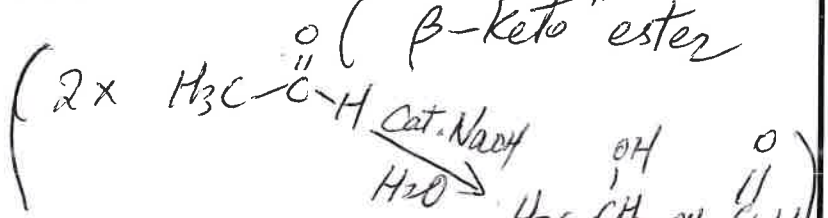
Recall: Claisen condensation

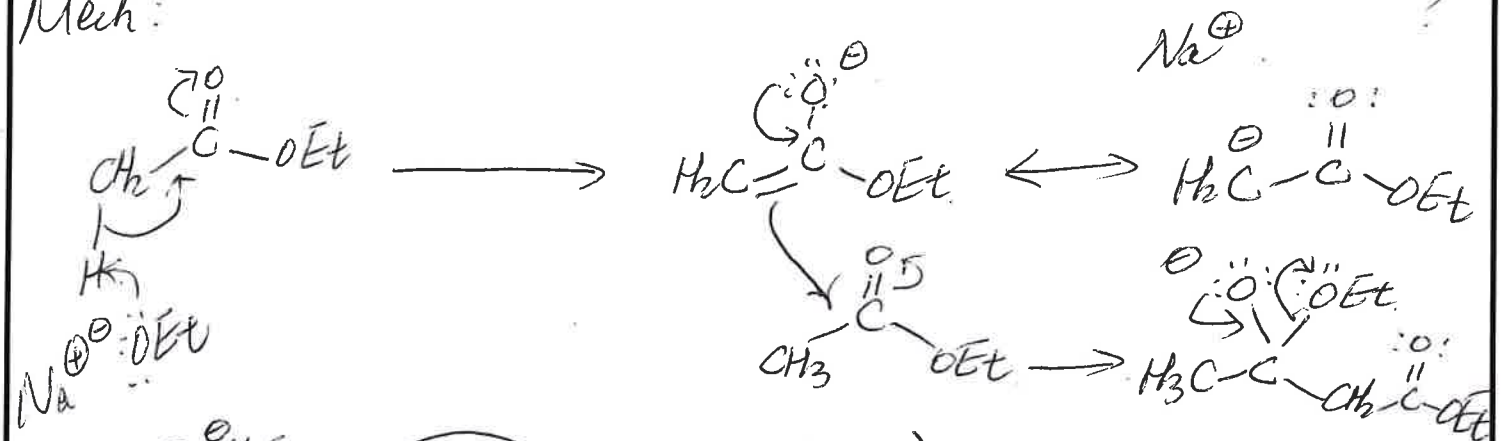
Ex:



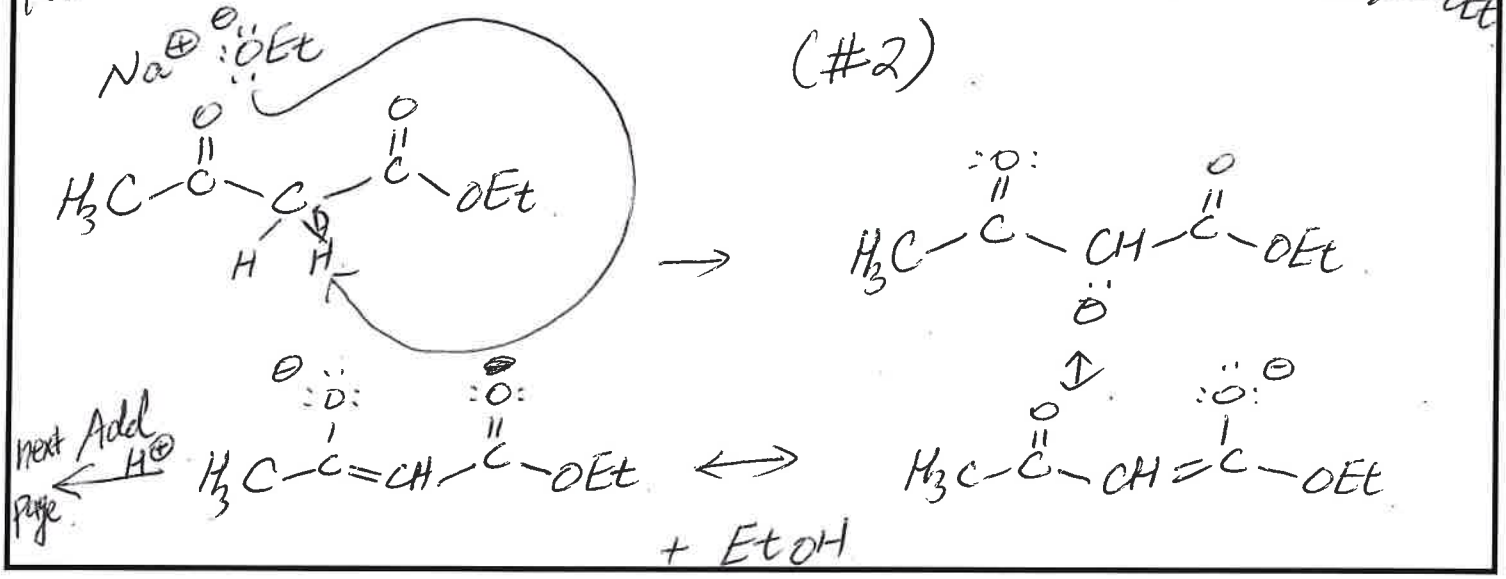

Compare/Contrast: Aldol




Mech:




(#2)



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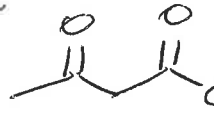
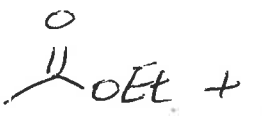
→ 

(final product)

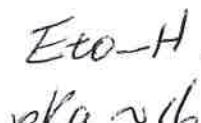
Comments

1) Note that every step is reversible. Also, β-keto ester product is less stable than 2 esters (SM)

~~  ~~ [  vs.  ]

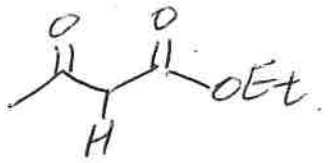
2) The final deprotonation of β-keto ester drives the condensation. This deprotonation is essentially irreversible.

pka Consideration:



pka ~16

vs.



pka ~11

3) Consequence — Claisen condensation does not occur if β-keto ester product lacks a highly acidic proton.

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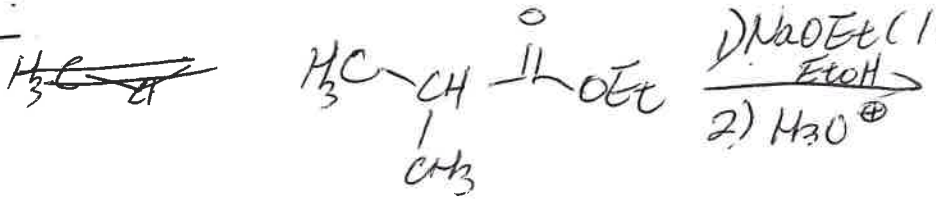
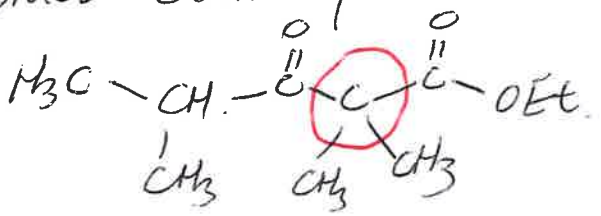
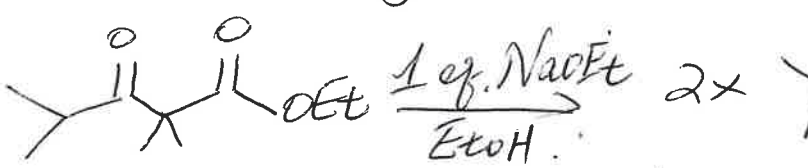



Consider Claisen product. We might envision:



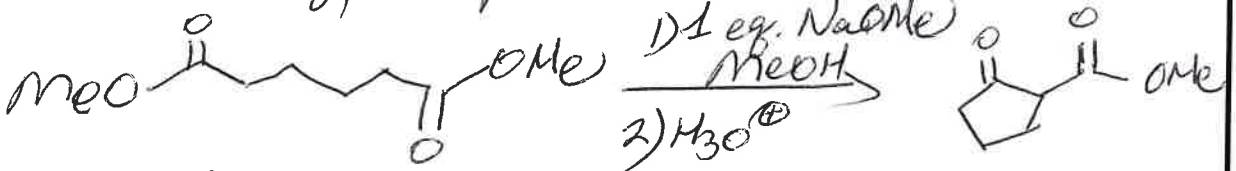
unstable under Rxn conditions

You draw out mech for "reverse Claisen",



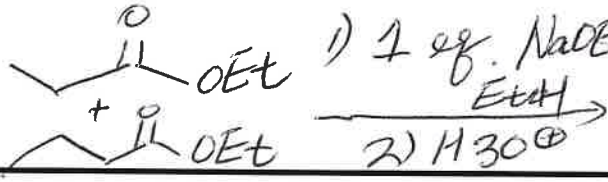

Intramolecular versions are good ways to generate 5- & 6-membered ring compounds.

Ex:




"Crossed claisen" → usually generates a product mixture ! (Not useful)

Ex:




4 products (you fill in)

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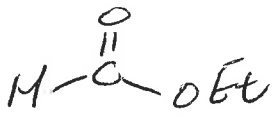
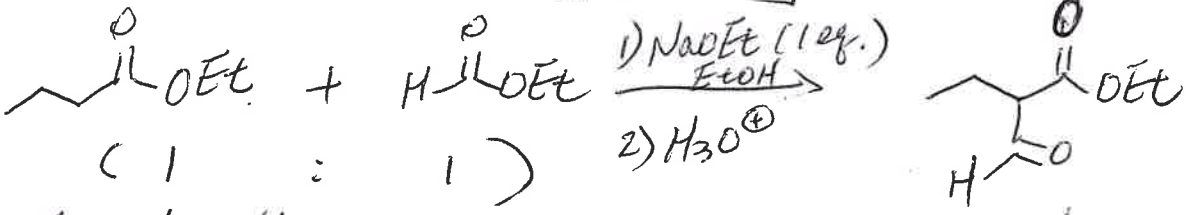
Special cases that allow single product from crossed Claisen...

1) One SM lacks α H's.

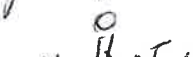

(formate ester)

or


"carbonate ester"
[C(+4)]

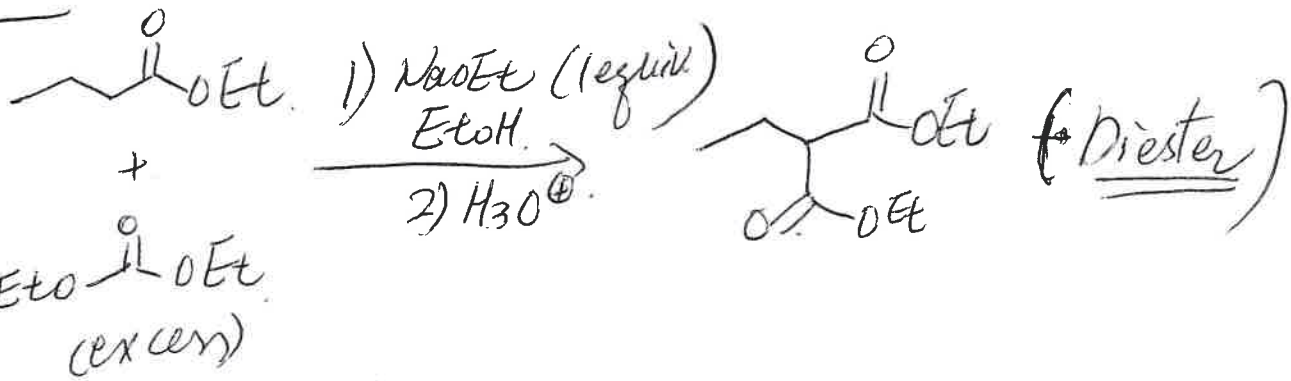
Thus, 
(1 : 1)

Origin of selectivity:

(i)  cannot form an enolate (can't be the nucleophile)

(ii)  much poorer electrophile than  (steric effect)

Ex #2


(+ Diester)

2) Ketone + ester ----> Diketone

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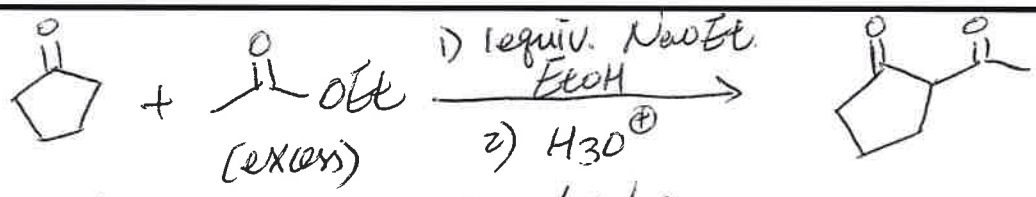
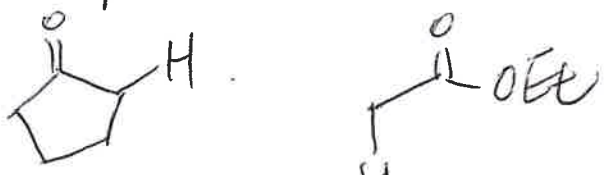
Ex: 


Origin of Selectivity (multiple)

(i) Recall that Ketone Self-aldol is unfavorable

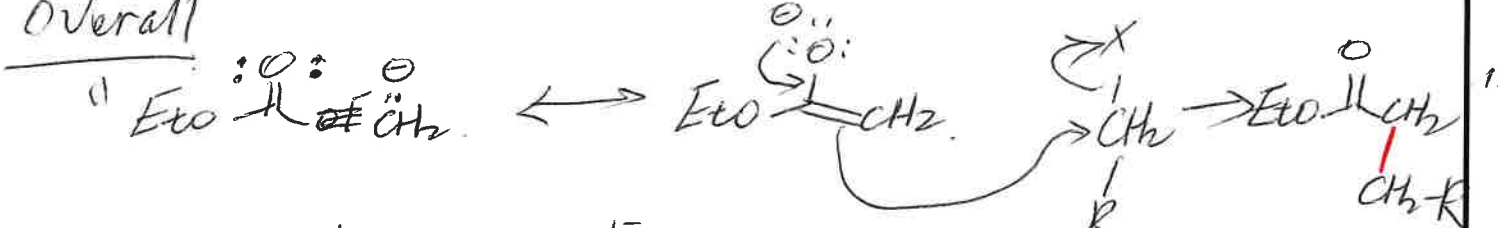
(ii) pka considerations suggest that ketone enolate will be major nucleophile.




See § 22.6 D — Synthetic perspective on Claisen condensations.

$S_N2$ Rxns of enolates — introduce alkyl groups α to C=O.

Overall



Worry about competing Claisen condensation