

Carbonyl “Self” Rxns

A/K Rxns (“Aldol”)

Ester Rxns (“Claisen”)

Michael & Robinson Rxns

Ref 17: 4 – 7; 9b ; 19: 1, 2, 9

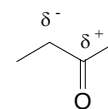
Prob 17: 7 – 9, 12, 13, 18, 19, 21, 26

19: 1-2

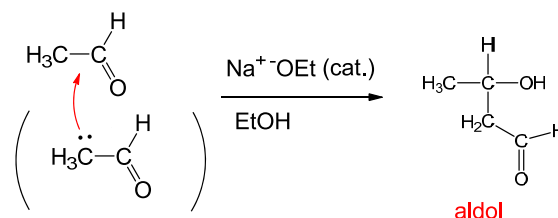
Adv Rdg 20: 1 – 6; 25: 4

General

- carbonyl C, electrophilic
 - α C, nucleophilic
- $\therefore$ 2 molecules can “self – react”

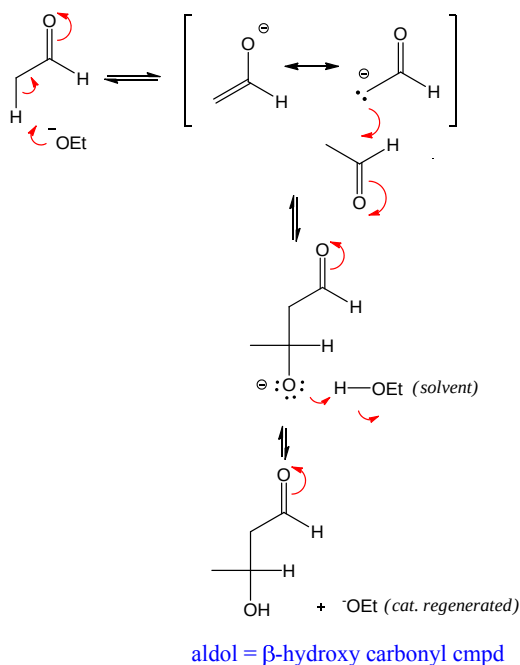


Ex.



- applies to A/K's

Mech.:



Comment: happens also under acidic conditions
(you can self-derive; I will skip)

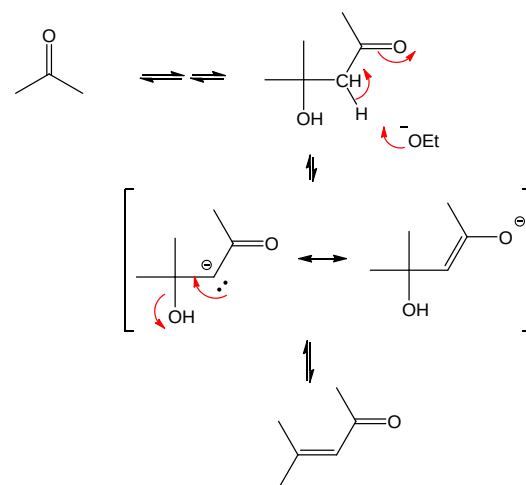
Dehydration = Condensation

(“enone formⁿ”)

aldol formation (C – C bond formⁿ)

often followed by loss of H₂O

Ex



α,β - unsaturated carbonyl cmpd = "enone"

Notes:

Generally

1.) aldehydes:

equilibrium aldol dimer $\rightleftharpoons$ aldehyde monomer

is in favor of dimer; aldol can be isolated;

can be driven to enone by extra heat, time ...

2.) ketones

equilibrium in favor of monomer;

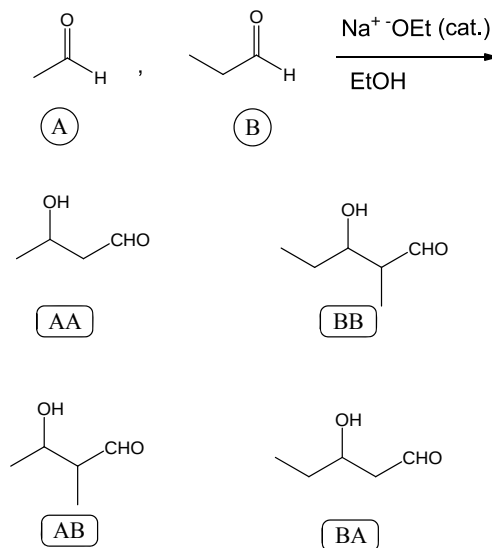
must driven to enone to make product

3.) “reverse aldol” (dimer $\rightarrow$ monomer)

may be possible given appropriate experimental conditions

Mixed (“Crossed”) Aldol

- between 2 different A/K cmpds;
- usually gives mixtures



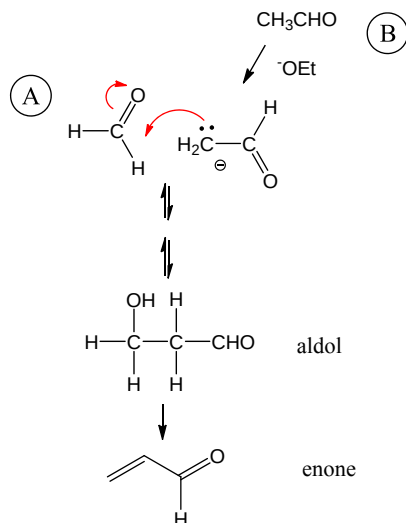
mixtures of aldols; “USELESS”

mixed ...

- can be successful, if

1.) **B** can form enolate (“enolizable”);**A** cannot (normally, has no α H), but has reactive carbonyl C

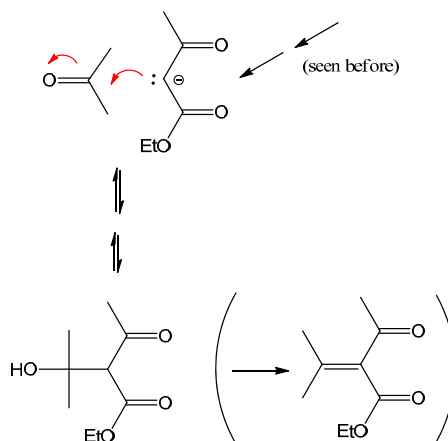
Ex.



mixed ...

2.) **B** is doubly activated (malonic ester, etc. ...);**A** is normal (“mono carbonyl”)

Ex.

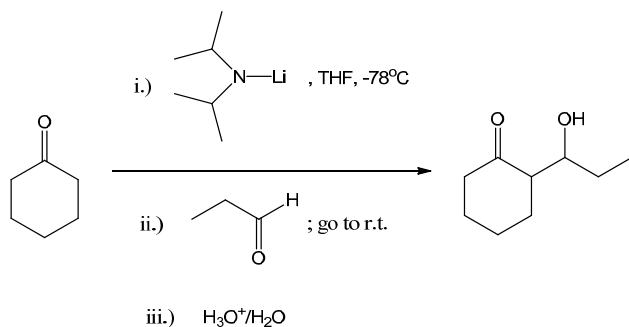


mixed ...

3.) use LDA methodology

- i.) produce enolate of one A/K with LDA at -78°C (fast, quantitatively, irreversibly)
- ii.) mix w/ 2nd A/K and allow to warm to r.t.
- iii.) work up w/ H_3O^+

Ex.



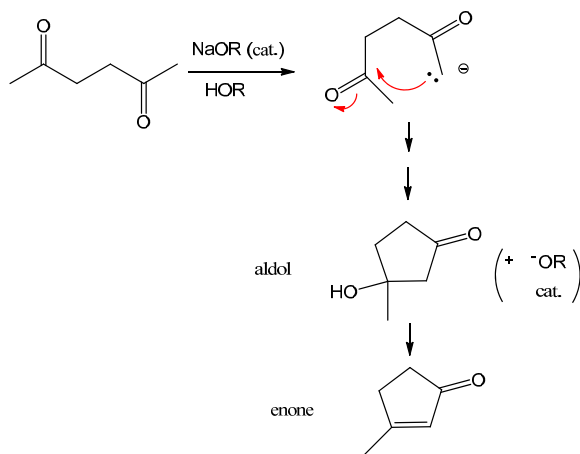
Intramolecular Aldol

can occur when 2 A/K carbonyls are present in one molecule;
esp.

A.) 1,4 dicarbonyl $\rightarrow$ cyclopentane derivativeb.) 1,5 dicarbonyl $\rightarrow$ cyclohexane derivative

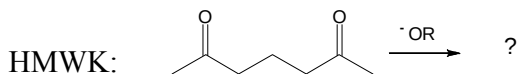
intramolecular ...

Ex.



N.B.:

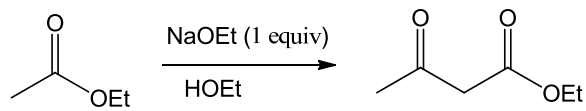
rxn essentially “one-way” due to cyclization



Claisen Rxn

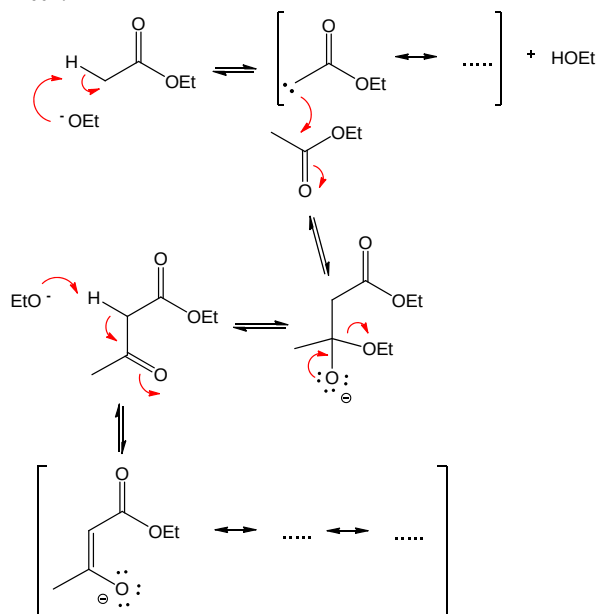
- between 2 ester molecules
- w/ 1 equiv. of base
- “enolate” reacts “keto”,
in typical “nucleophilic acyl substitution” fashion,
going through “tetrahedral intermediate”

Ex., overall rxn



Claisen ...

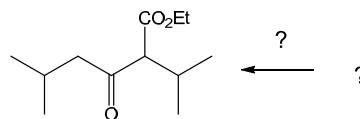
Mech.



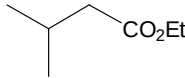
N.B.:
 final step irreversible;
 consumes 1 equiv. of base;
 drives rxn "one-way";
 need to acidic work-up to get product: β -ketoester

Claisen

Practice as HMWK; incl. mechanism



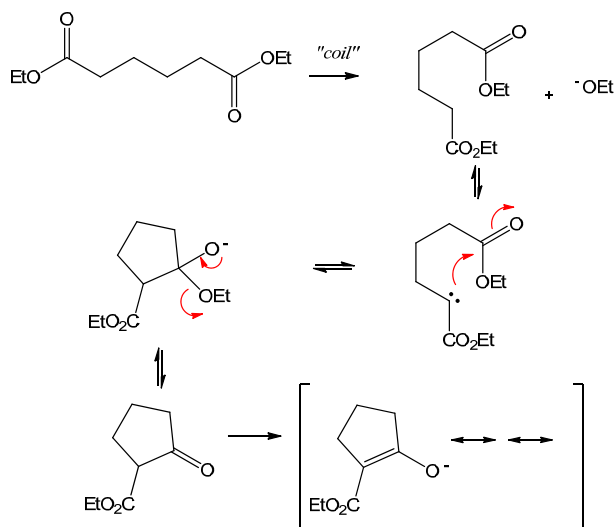
Ans.

use  as starting material and repeat the mechanism from the previous page

Dieckman Rxn

($\equiv$ Intramolecular Claisen)

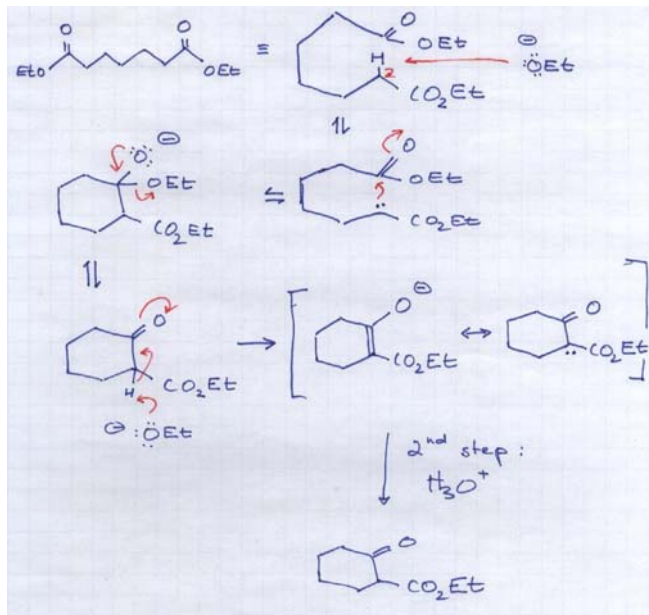
esp.: 1,6 & 1,7 diesters give ring systems;
 5C-ring 6C-ring



acidic work-up: β -ketoester

HMWK: cyclyze 1,7 diester; w/ mech.

HMWK Answer

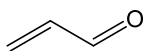


Michael Addition

General Background

Terminology

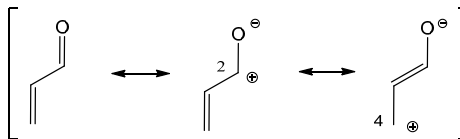
" α,β unsaturated carbonyl" = "conjugated carbonyl" = "enone"



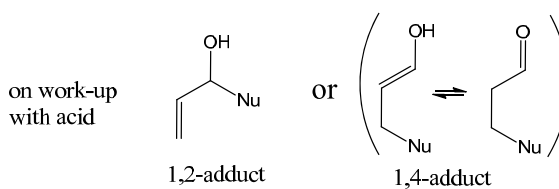
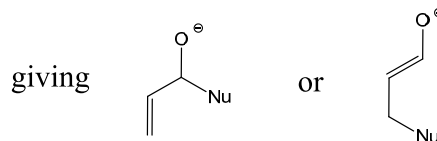
(somewhat reminiscent of 1,3 dienes;
but in the 1st step of 1,3- dienes electrophiles are added;
while enones are attacked by nucleophiles)

general ...

resonance structures of enones



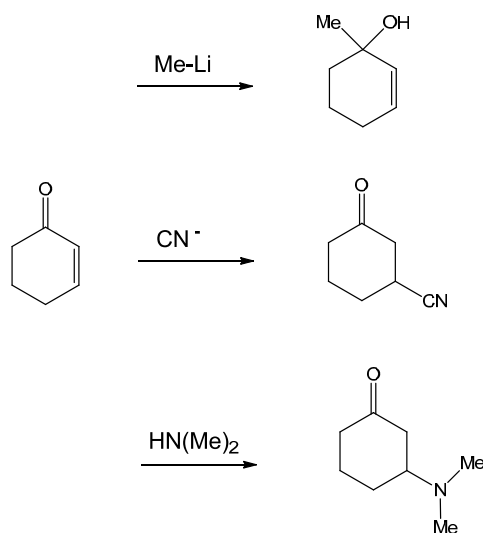
Nu: can attack at posⁿ 2) or posⁿ 4); giving



general ...

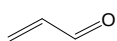
- attack at posⁿ 2) requires less activation energy (E_a)
= kinetic product
- attack at posⁿ 4) require more E_a , but product is more stable (carbonyl group is regenerated)
= thermodynamic product
- aggressive, strong Nu's (e.g., LiAlH_4 , R-Li form 1,2 product irreversibly: *kinetic product*
- mild, weak nucleophiles (amines, CN^- , **enolates**) can also form 1,2 adduct, but can equilibrate to the 1,4 adduct: *thermodynamic product* giving mostly 1,4 adduct, if allowing sufficient time.

Practice



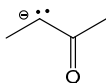
Michael Addⁿ w/ Enolates

Michael Acceptor



conj. carbonyl:
A/K, ester, ...

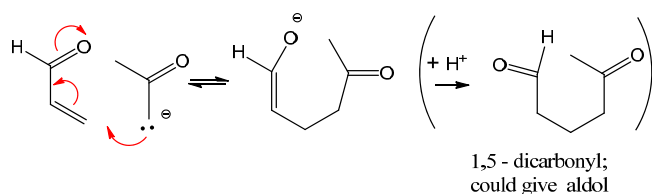
Michael Donor



mono or 1,3 di
carbonyl cmpds

rxn conditions: 1.) NaOH(cat.)/THF/H₂O, or
2.) NaOEt(cat.)/EtOH

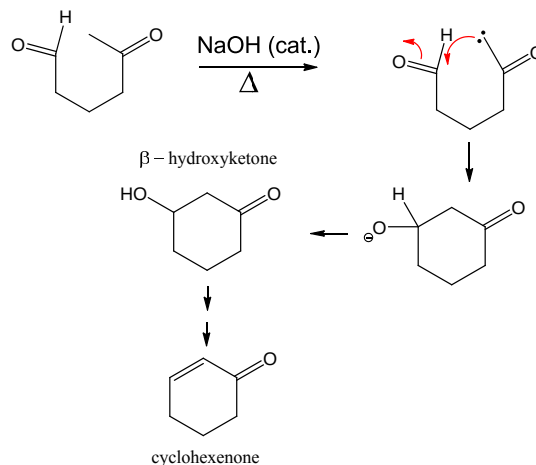
Simple Ex.



Robinson Rxn

= combination of Michael & internal aldol rxn;
need increase in temp.

Ex. cont^d:



Note: other aldols could form,
but all these rxns are equil. rxns;
and the cyclohexenone is the most stable !!

Practice: Retrosynthetic Analysis

