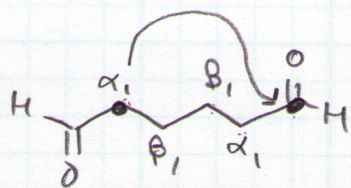
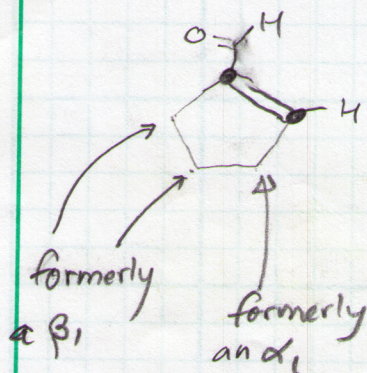
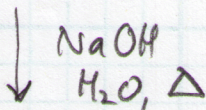


We are now familiar with self and cross aldol condensations
(see page 18-12 of these notes)

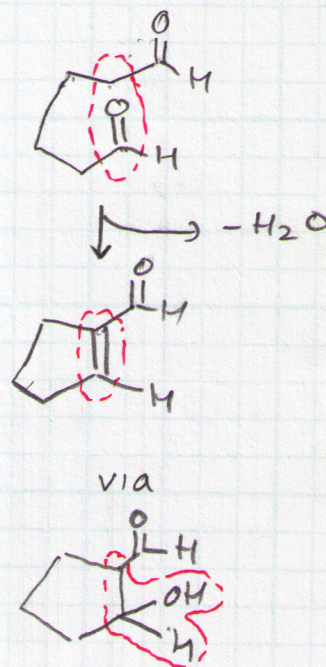
These reactions were intermolecular, i.e., between two different aldehyde molecules. But what if the condensation occurred intramolecularly within the same molecule?
A cyclic cpd results.



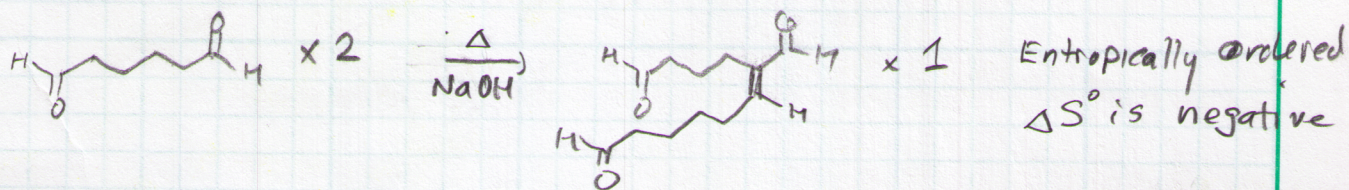
Molecule is symmetrical $\therefore$ numbering is the same left and right



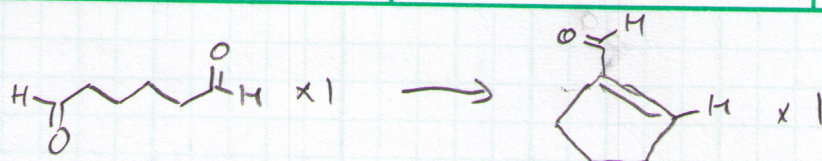
recall setup



Why does intramolecular aldol condensatⁿ out compete inter molecular?



$\Delta G^\circ = \Delta H^\circ - T\Delta S^\circ$ if $\Delta S < 0$ then ΔG° become less favorable
 i.e., it becomes less negative

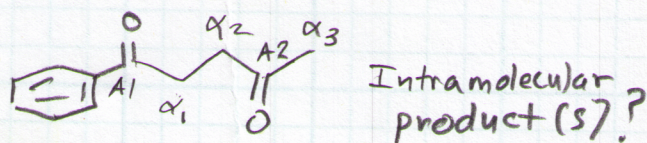


$$\Delta S^\circ \approx 0$$

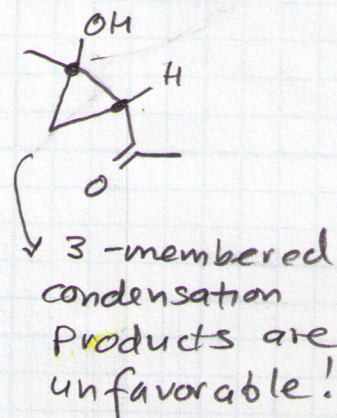
$$\Delta G^\circ = \Delta H^\circ - T \underbrace{\Delta S^\circ}_{\emptyset}$$

unimolecular $\rightarrow$ unimol.
conversion cause ΔS° to
not affect ΔG°

Aldol condensations also occur analogously w/ ketones.
The α -H is acidic, too!



NOTE

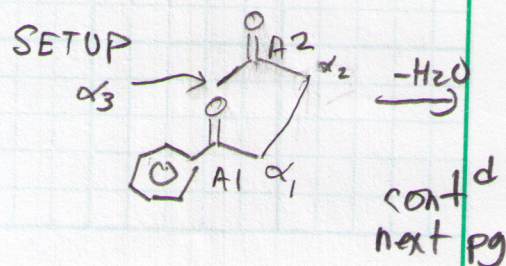


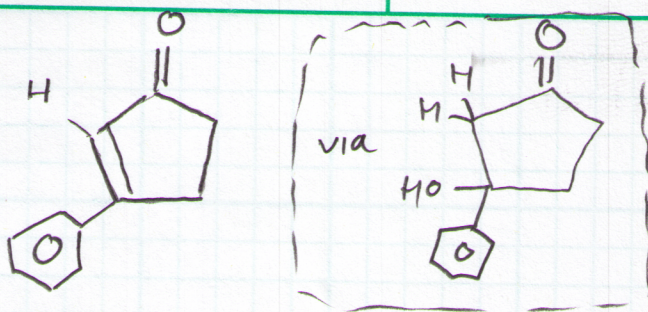
- ① ID α -C
- ② Do α C have α H?
- ③ when α H is removed to form enolate is a ring > 4 atoms formed?
- ④ Yes, then that is a valid condensatⁿ product.

Above: α_1 C condenses with A2
that yields 3-atom ring $\Rightarrow$ NOT FAVORABLE

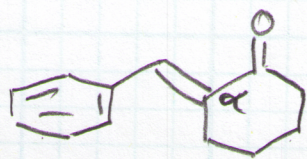
α_2 C condenses with A1
also yields 3-atom ring $\Rightarrow$ NOT FAVORABLE

α_3 condenses with A1
yields 5-atom ring!



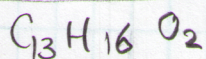
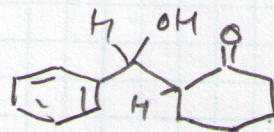
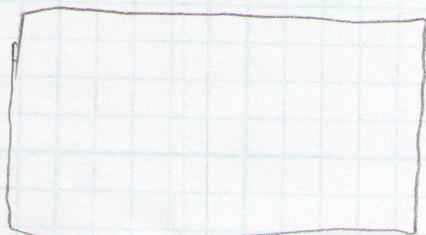


what aldehydes and/or keto compound(s) are used to make



WORK BACKWARDS

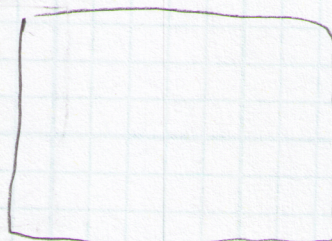
⇓ THIS CAME FROM?



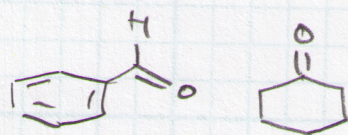
⇓ THIS CAME FROM?

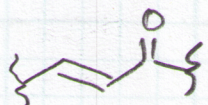


Aldehyde or
ketone 1

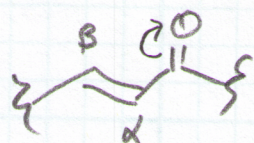


aldehyde or
ketone ?

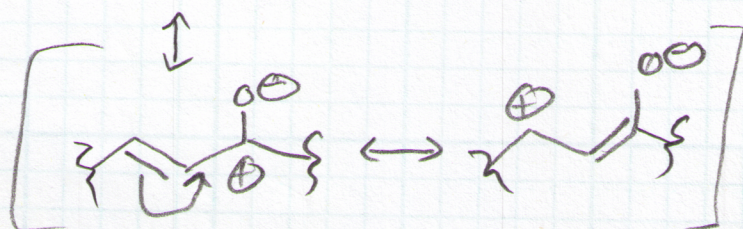


We have been making  condensation products after treatment of aldehydes + ketones with NaOH, Δ .

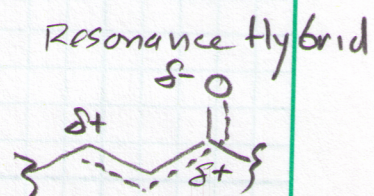
These



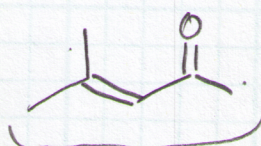
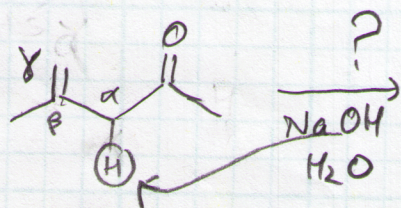
are α, β -unsaturated aldehy and Ketones



Resonance forms



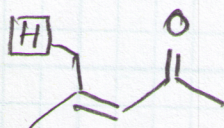
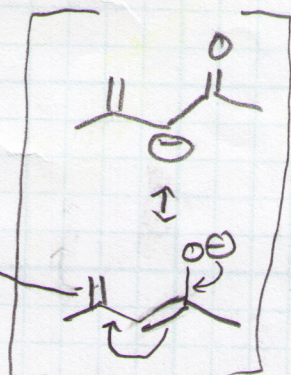
The $C=C$ is conjugated with the $C=O$ and thus resonance stabilization results.

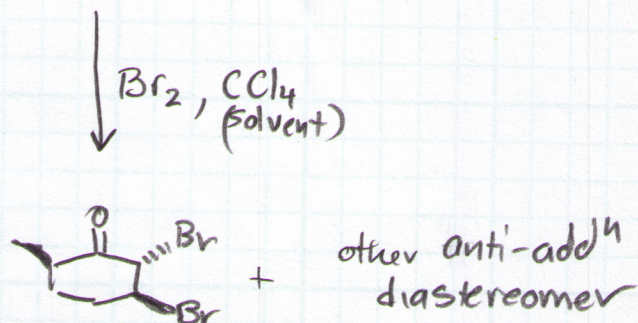
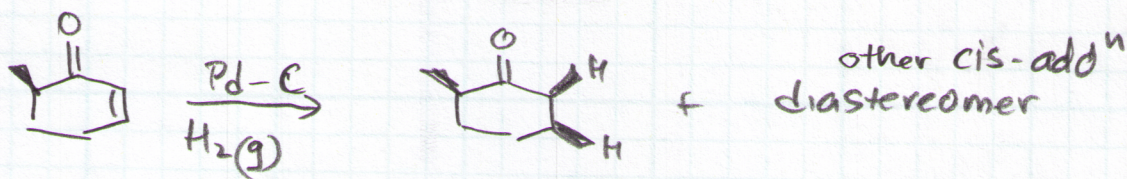
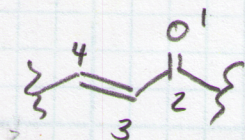


conjugated
 $C=C$

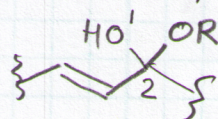
Mechanism

SAME



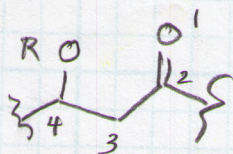
CEM 351 RXNS w/ $C=C$ Back to α,β -unsaturated carbonyl cpds.

we have seen 1,2-addition rxns when acetals, hemiacetals/aminals were formed

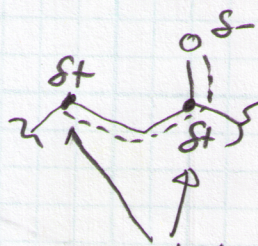


1,2-addition
w/ acid or base
catalysis

but can also undergo 1,4-addition reactions

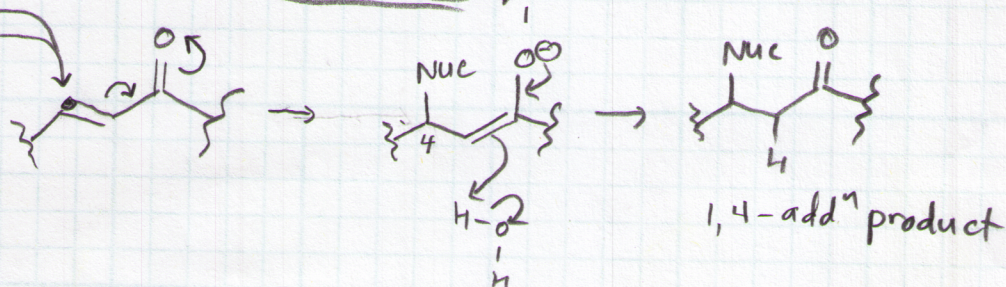


resonance
hybrid

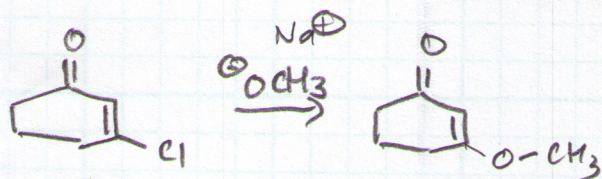


electrophilic centers

Mechanism (Michael Addition)

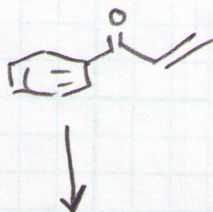


show the mechanism of the following

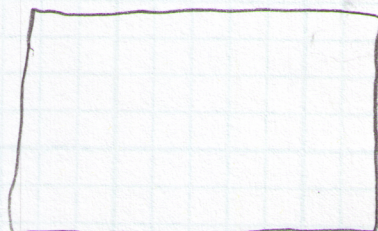


Hint: start with a conjugate (1,4)-addition

show the mechanism



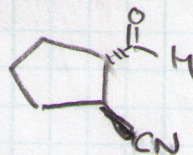
MECHANISM?



conjugate addⁿ product

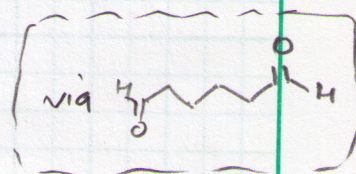
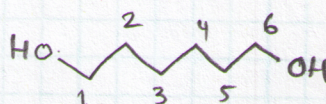
Let's work backwards

Product



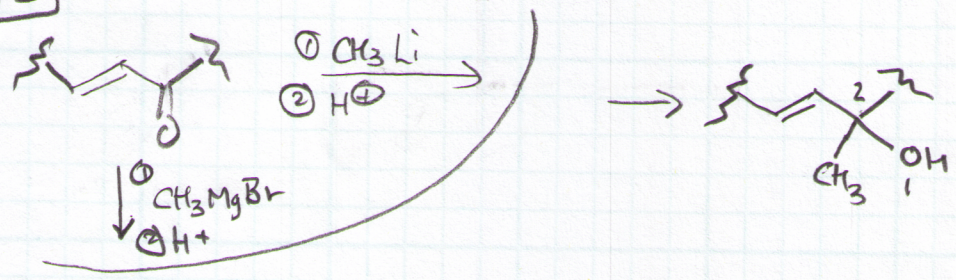
back to

Reactant



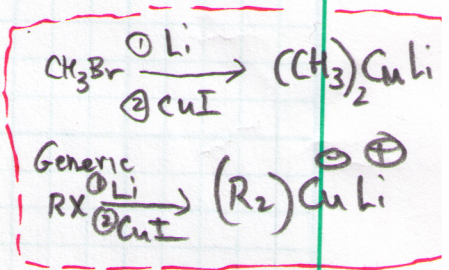
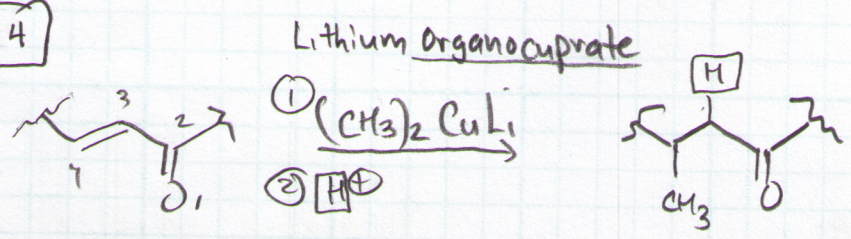
1,2 vs 1,4-addⁿ with Organometallic Reagents

1,2



strongly electroneg
C=O rxn at
higher δ^+
C-O center
 δ^+ δ^-

1,4



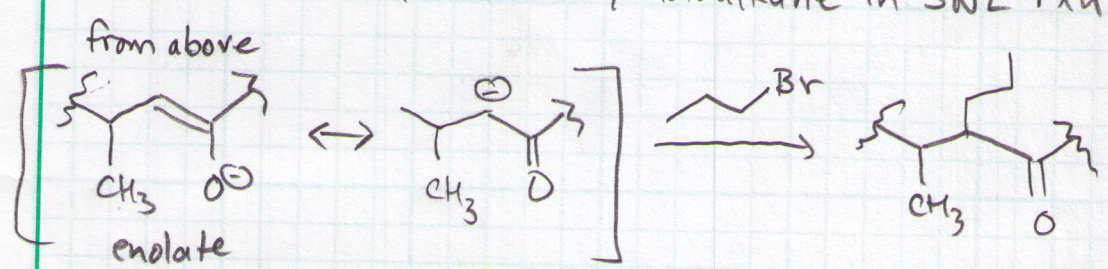
H3C-Cu-CH3
 Li^+
 HOMO of δ^-CH_3
 closer in E
 to LUMO of $C=C$

NOTE (-) charge is borne by Cu^+ and δ^-CH_3

$\therefore$ (-) charge on CH_3 is reduced compared to that in Grignard and CH3Li

Li^+ $\ominus CH_3$
 highly reactive
 HOMO closer in E
 to LUMO of $C=O$

NOTE: Before H^+ is added in 2nd step, enolate can react w/ haloalkane in S_N2 rxn



Interesting processes to add C-C bonds to carbonyl compds

why trans?

