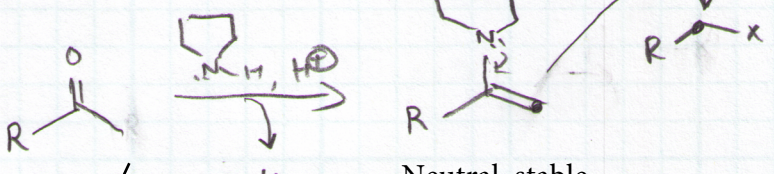
Workaround. Form an enamine w/ pyrrolidine 

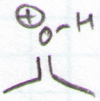
① No LDA ∴ no need for kinetic control
No E2 competition
No overalkylation

2° amine



ketone: R = alkyl
aldehyde: H

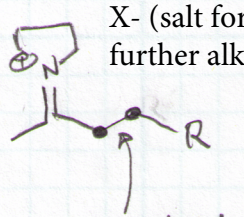
protonated α-carbon

via 

this 'kick starts' the process

Neutral, stable enamine by loss of H w pKa of 9.5

X- (salt formed) reduces further alkylation

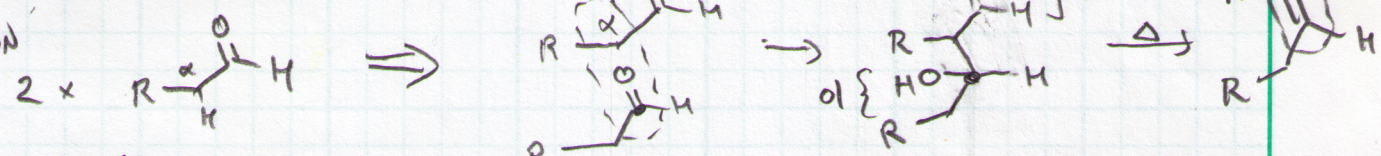


new bond

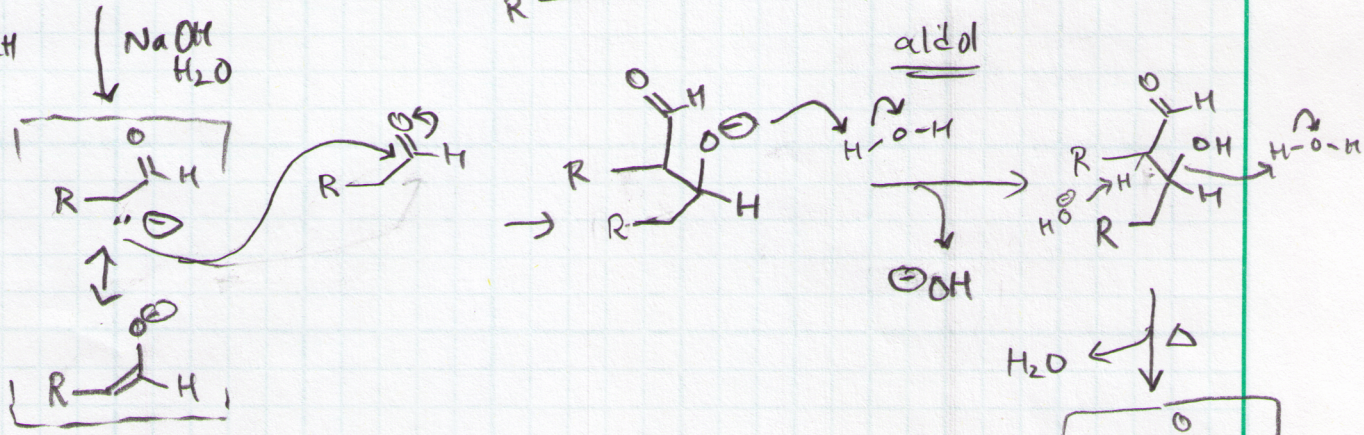
C=N+ is a strong, stable bond after alkylation that forms a salt with the Leaving Group
X=halogen, OTs, etc

Aldol condensations

self condensation

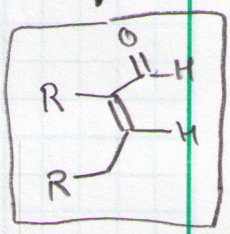


MECH



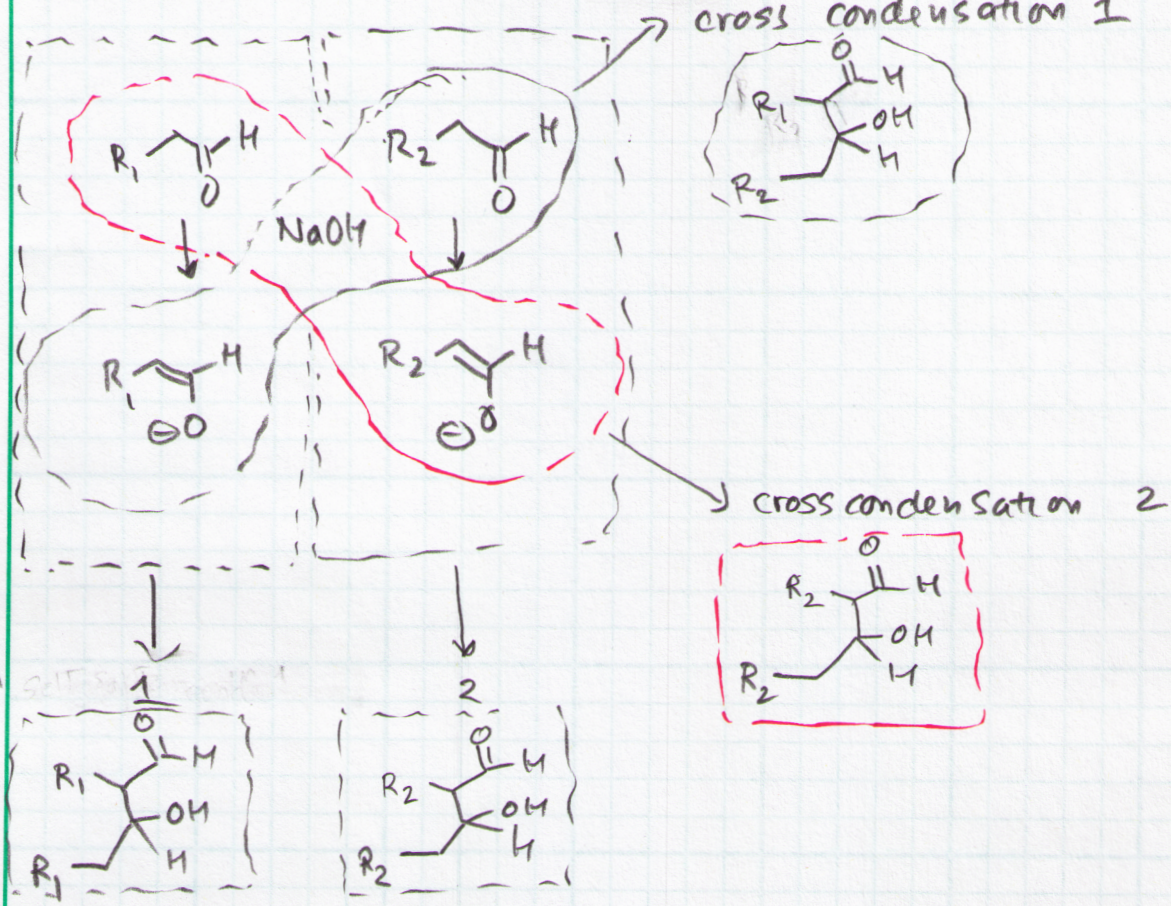
aldol

After heat Δ



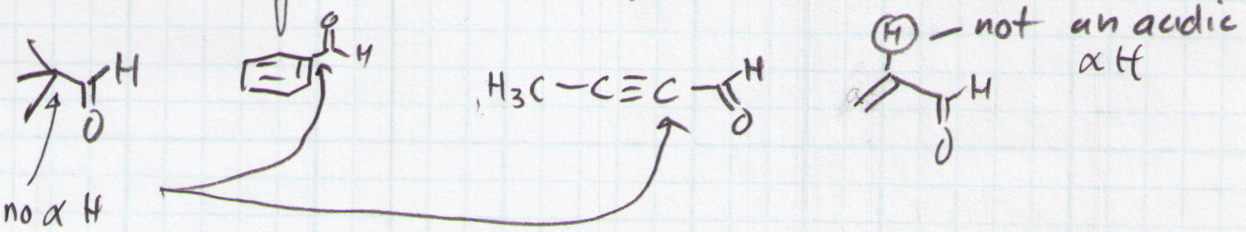
These steps are ALL reversible, so the final heat treatment helps drive the reaction to the α/β-unsaturated carbonyl

Cross or Mixed Condensation

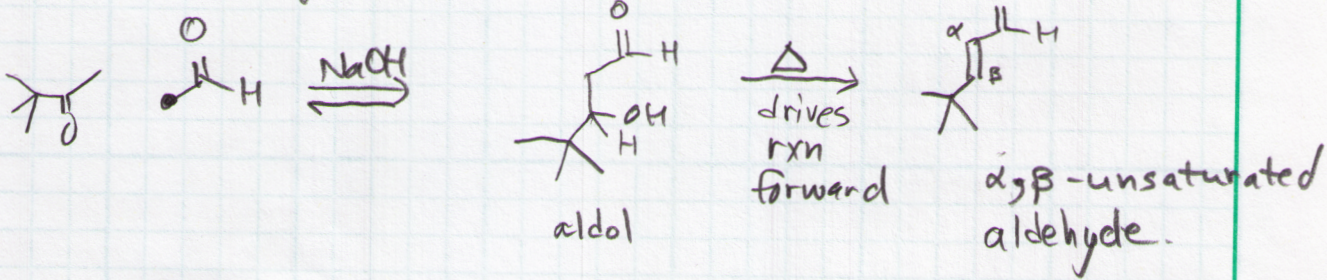


Cannot control mixture. So what has to be done. LIMITS!

Use one aldehyde that does not have α-Hs!



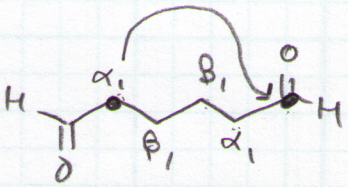
... and use aldehyde that contains α-H



We are now familiar with (self and cross) aldol condensations

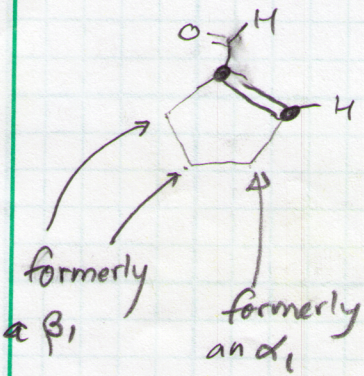
(see page 18-12 of these notes)

These reactions were <u>inter</u>molecular, i.e, between two different aldehyde molecules. But what if the condensation occurred <u>intra</u>molecularly within the same molecule? A cyclic cpd results.

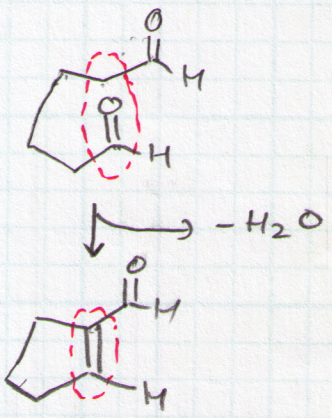


Molecule is symmetrical ∴ numbering is the same left and right

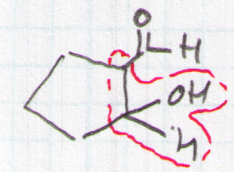
NaOH
H_2O, Δ



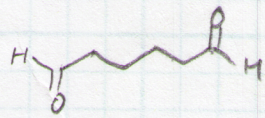
recall setup



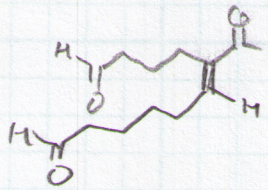
via



Why does intramolecular aldol condensat^n out compete <u>inter</u>molecular?



× 2 $\xrightarrow[\text{NaOH}]{\Delta}$



× 1

Entropically ordered
ΔS° is negative

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