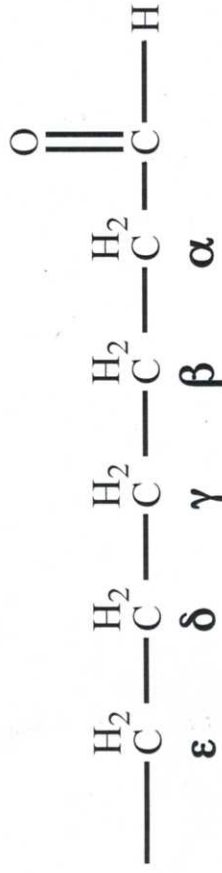


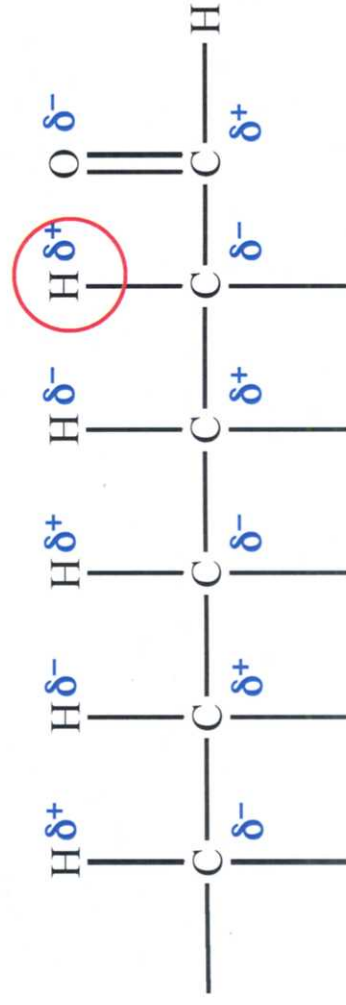
Reactions at the alpha (α) carbon

alpha carbon is the carbon adjacent to the carbonyl carbon.
beta is the next one etc



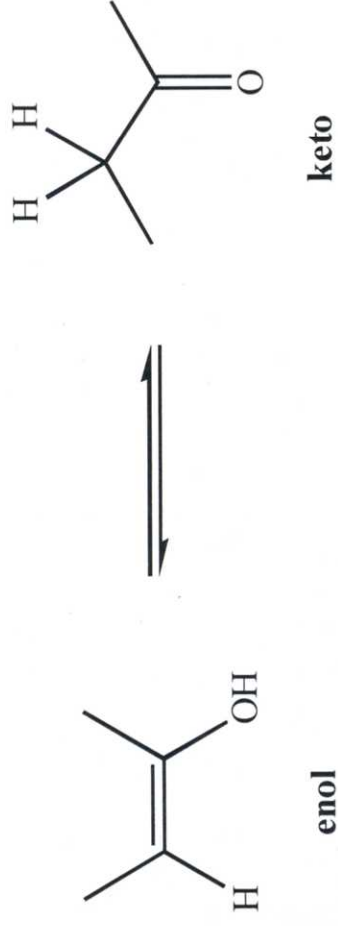
the hydrogen attached to the carbon at that position has the same name
hydrogen attached to carbonyl carbon is called the aldehyde hydrogen
or formyl H (not alpha hydrogen).

Due to polarization of carbonyl, charges (stabilization thereof) alternate

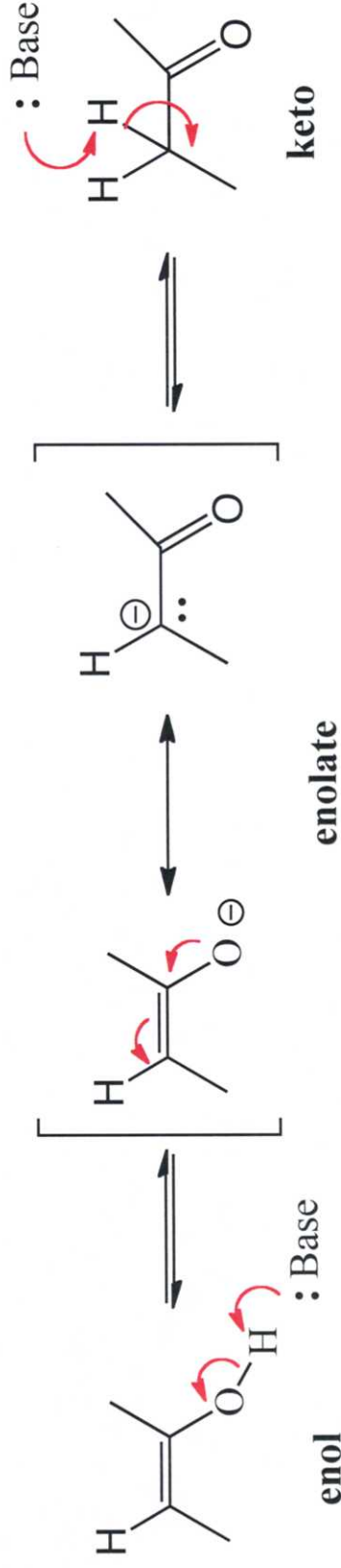


α -hydrogens are acidic
($\text{pK}_a \sim 20$)

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Review: **tautomers** (rapidly interconverting structural isomers)



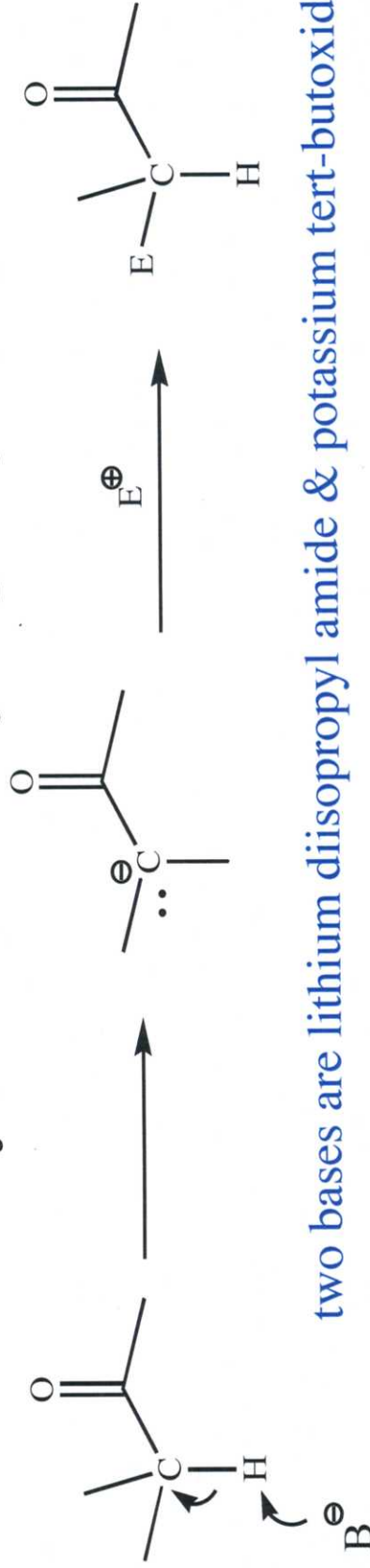
Enolates are the conjugate bases of enols obtained by deprotonation



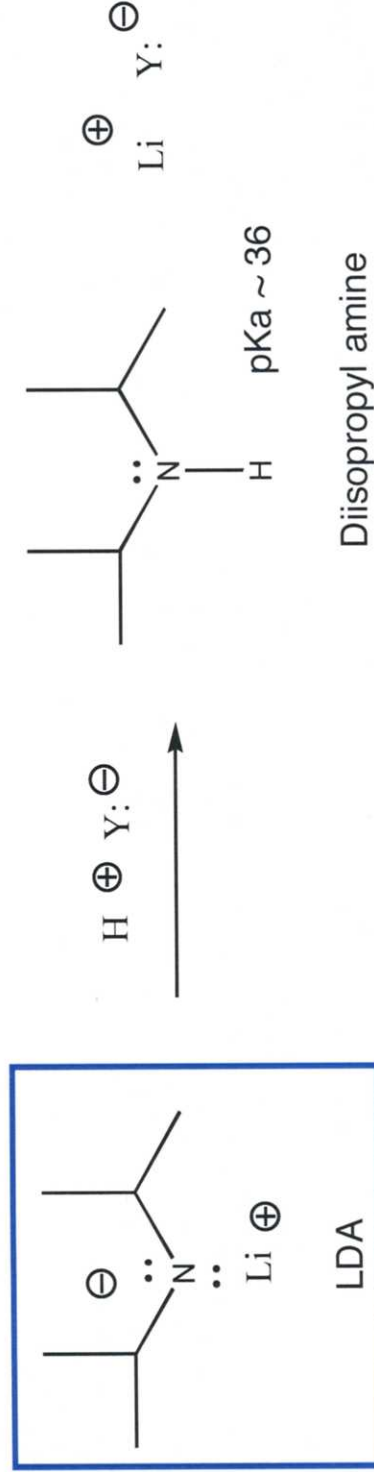
the two **enolate** structures are **resonance forms**

as they are **anionic, enolates are nucleophiles**
(for this course they react on carbon not oxygen)

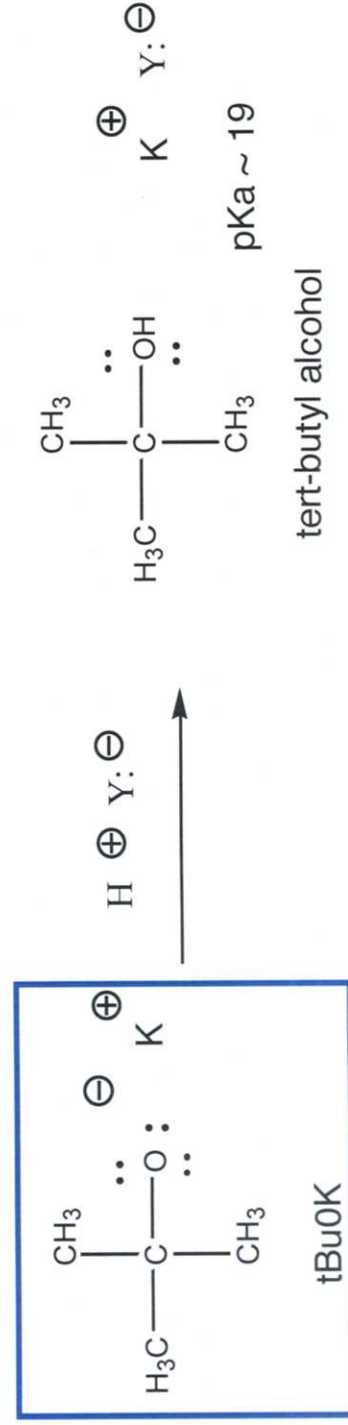
Enolates made by removal of α -hydrogen by strong base



two bases are lithium diisopropyl amide & potassium tert-butoxide



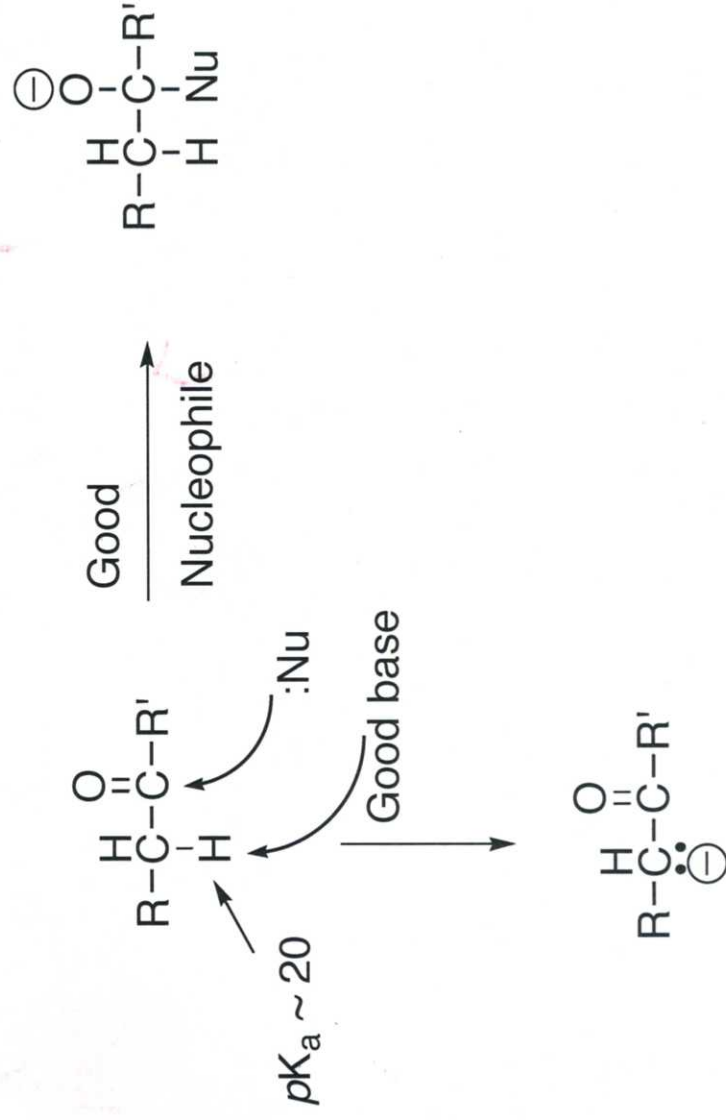
LDA and KOtBu are hindered and therefore poor nucleophiles



Reactions of ketones & aldehydes: Nucleophiles vs Bases

a good **nucleophile** attacks the carbonyl group to form a tetrahedral intermediate

a good **base** deprotonates the alpha hydrogen



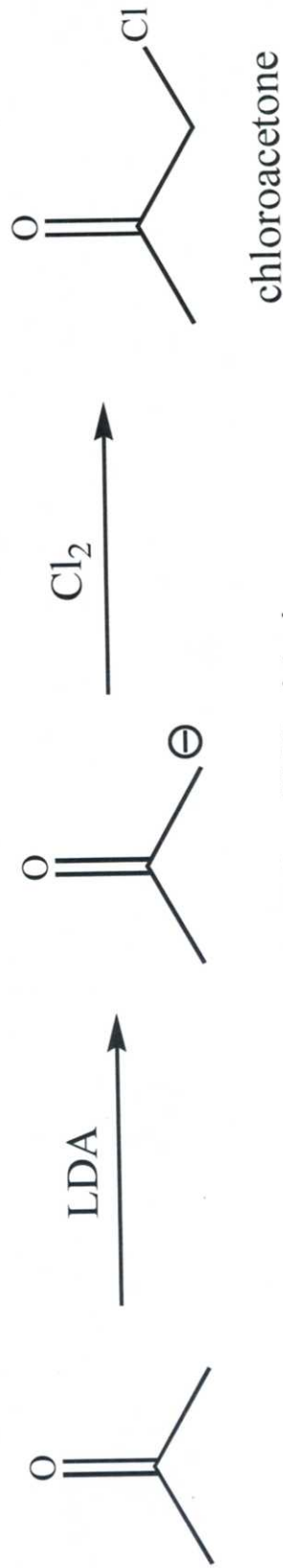
Good bases (that are not nucleophiles) are usually hindered

Reactions of Enolates with Electrophiles



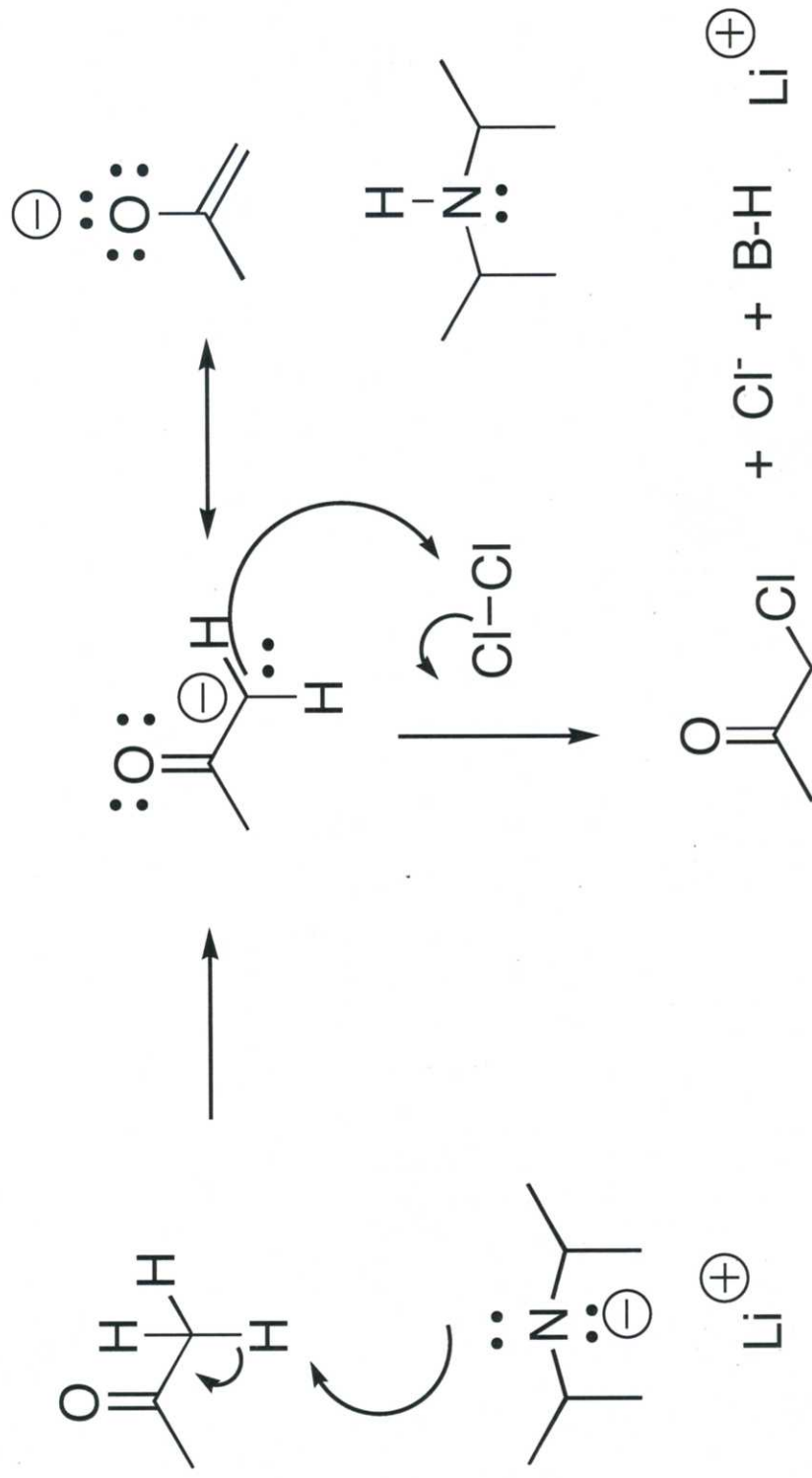
Example - halogenation

chloroacetone is tear gas



http://www.kewego.com/video/iLyROoaffM9_.html

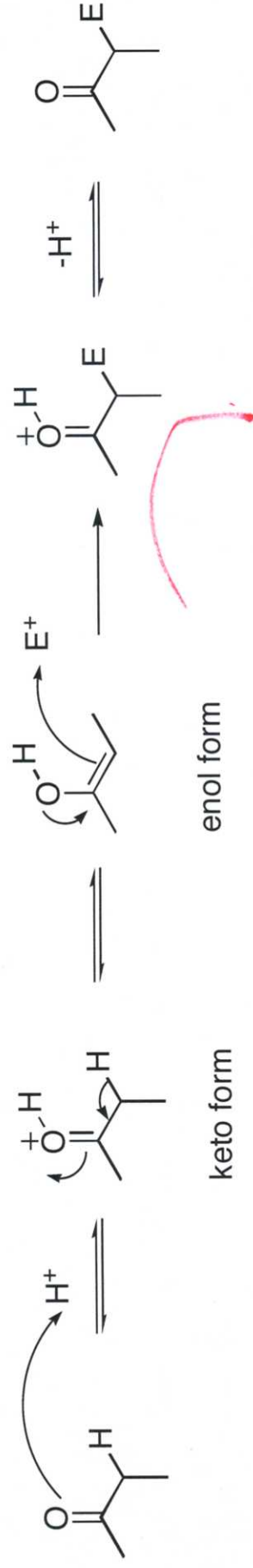
Halogenation mechanism



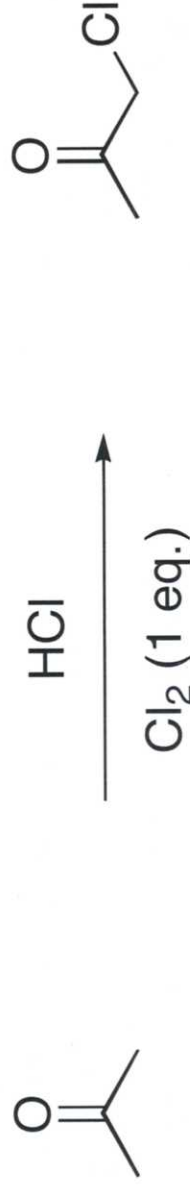
addition of chlorine makes the alpha hydrogens of the product (chloroacetone) more acidic due to the electron withdrawing effect of the chlorine. Side reactions, including multiple chlorinations are possible

Enol Formation (Under acidic conditions)

Enols behave as nucleophiles and react with electrophiles in much the same way as enolates (except **acid conditions**)

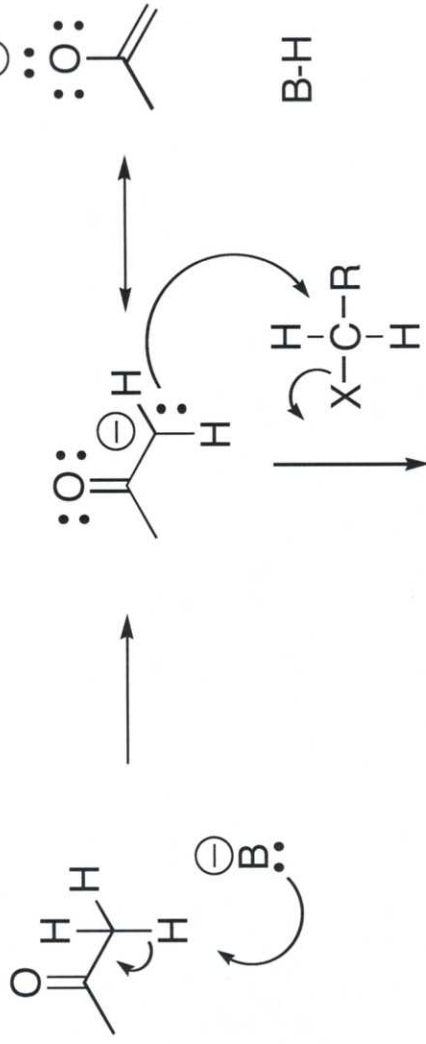


Example - halogenation



Enolate Alkylation Reactions

Electrophile is R^+ from alkyl halide RX (best if primary, 3° fails)



(S)-4-methylheptan-3-one

Example - alkylation make

ant alarm pheromone

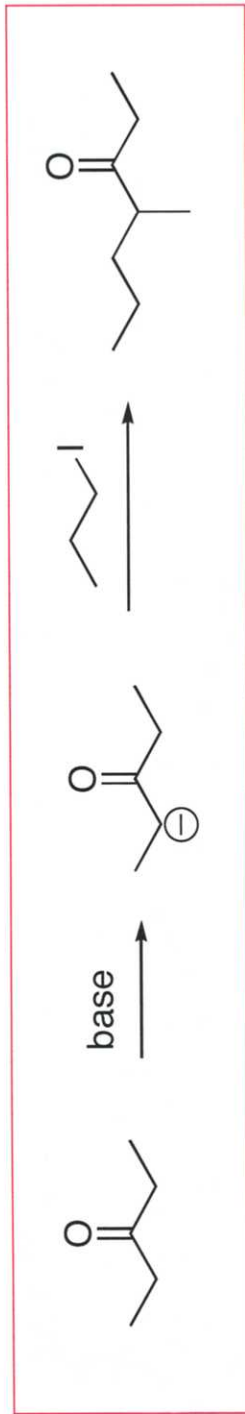
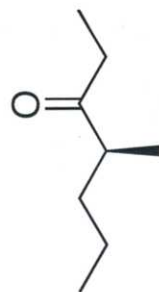
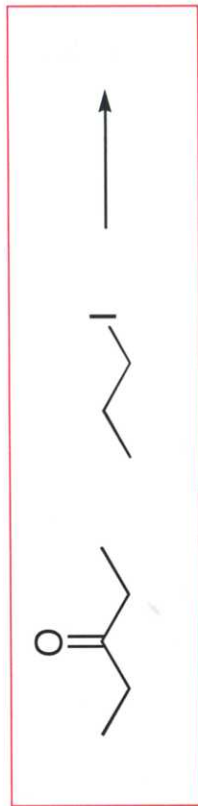


Best route ?

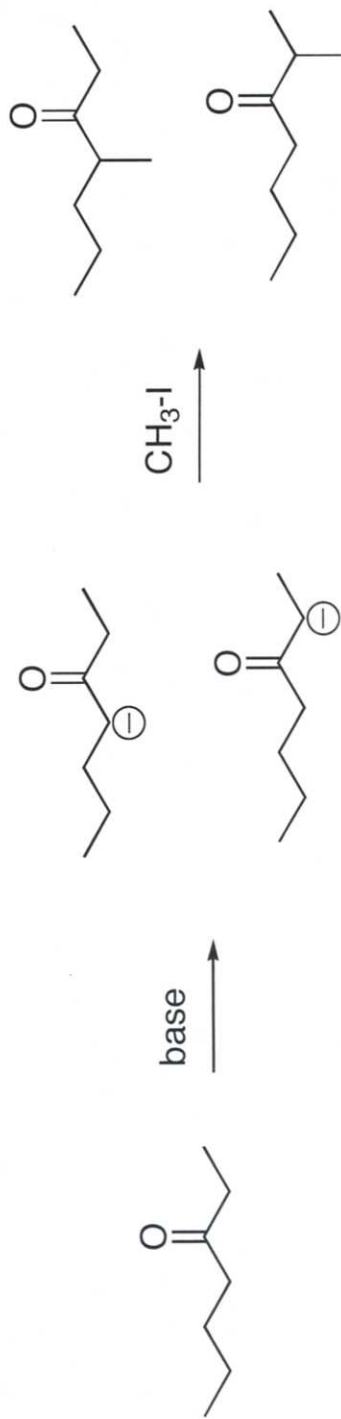


Enolate Alkylation Reactions

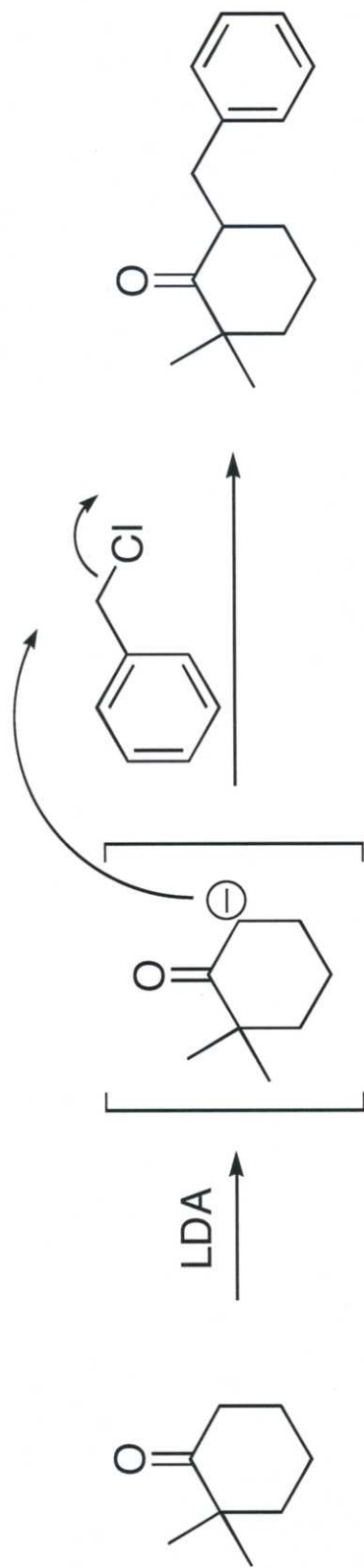
Best route



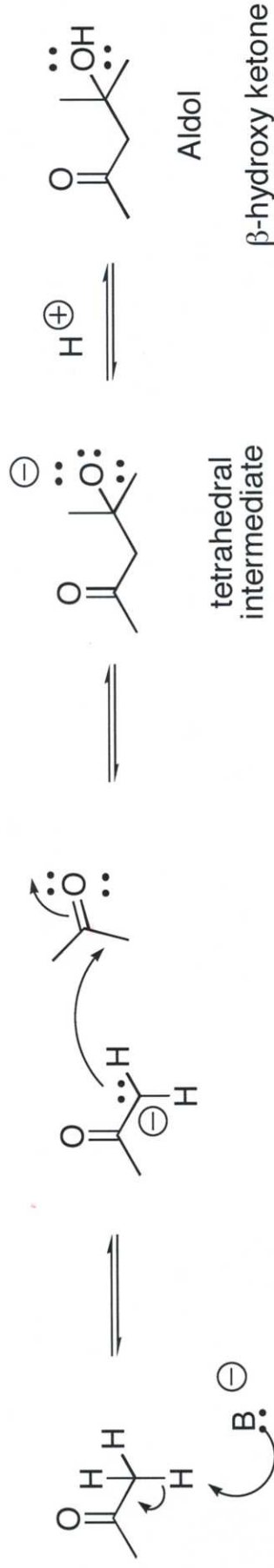
methylation gives undesired side reaction



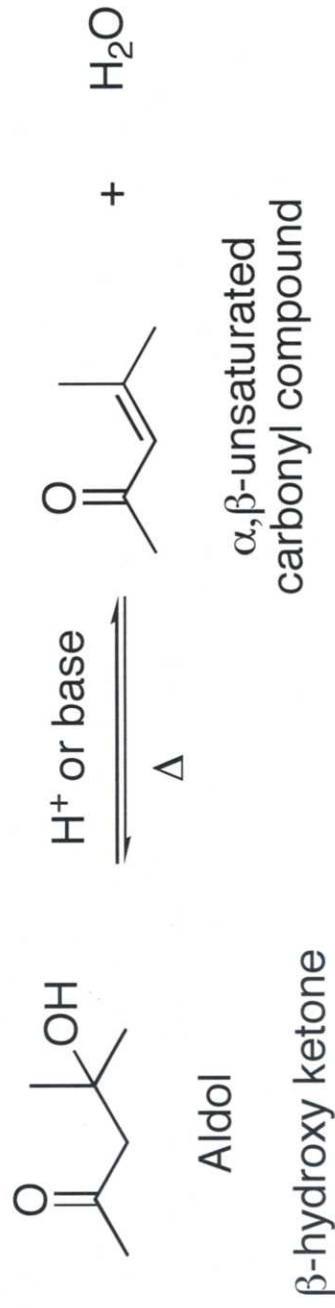
Enolate Alkylation Reaction - example



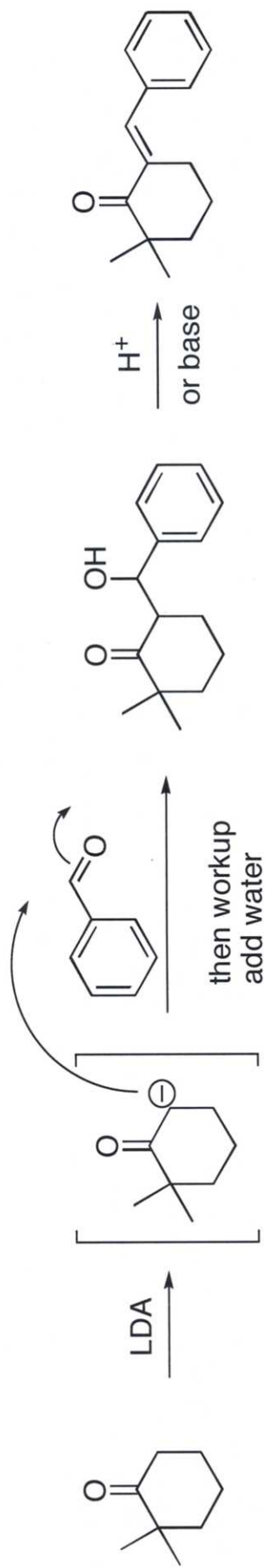
Aldol Formation



The β -hydroxy ketones and β -hydroxy aldehydes formed in the aldol process can easily be dehydrated ($-\text{H}_2\text{O}$) to yield conjugated enones called α,β -unsaturated carbonyl compounds with the application of heat with acid or base



Aldol Formation with Dehydration - example

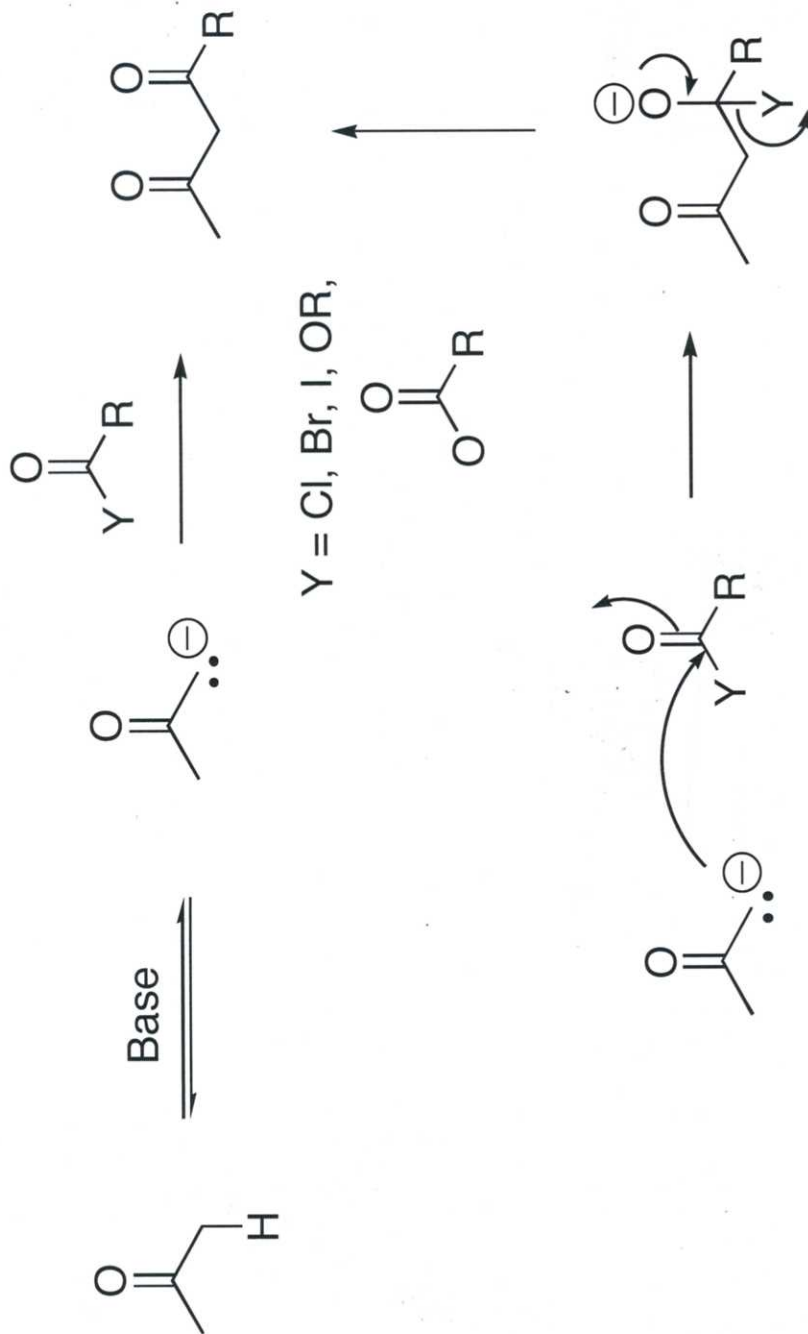


aldol condensation of 2,2-dimethylcyclohexanone with benzaldehyde

hard to stop at aldol stage - dehydrates readily - Why ?

forms extended conjugated system when it dehydrates

Acylation (addition of an acyl group)



Example

