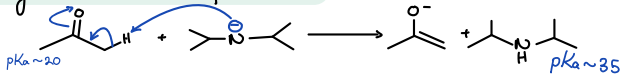
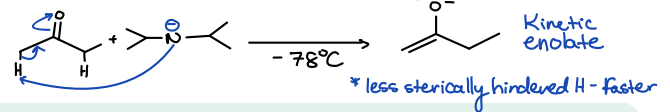


## Acidity of $\alpha$ -proton

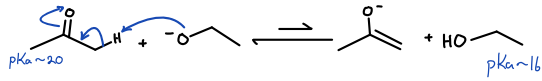
very stb: irreversible deprotonation



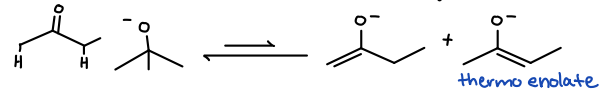
Irreversible Deprotonation  $\rightarrow$  Kinetic product



Alkoxide Base: Reversible deprotonation

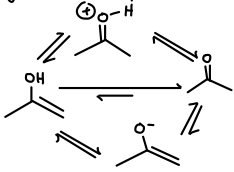


Reversible Deprotonation  $\rightarrow$  Thermodynamic product

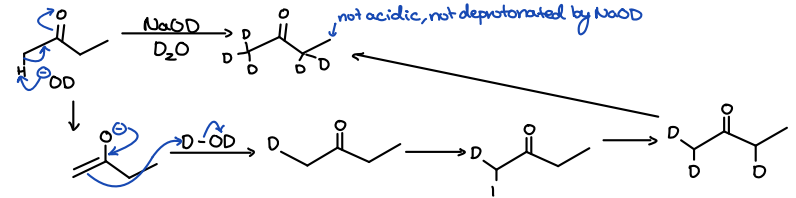


## Keto-Enol Equilibria

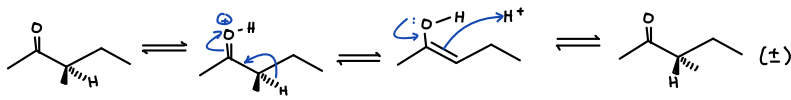
-tautomerization is always occurring under acidic or basic cond  
-eq. position depends on relative stability



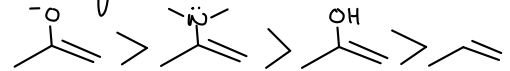
## Deuterium Exchange w/ deuterated solvents



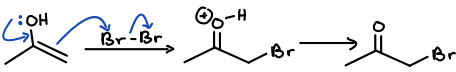
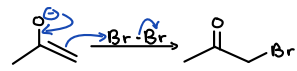
## Epimerization of $\alpha$ stereocenters



Nucleophilicity

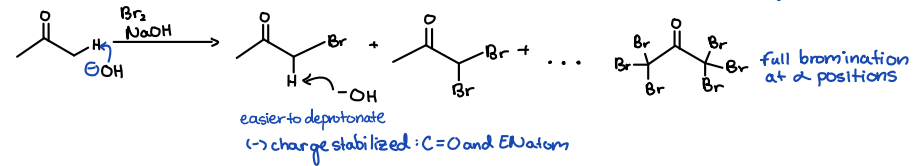


## Enol and Enolate Halogenation



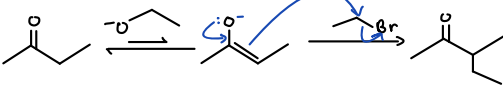
-avoid free  $C^+$  by lone pair coming down to make new pi bond

Stop at 1 eq w/ acidic cond, fully reacts in base

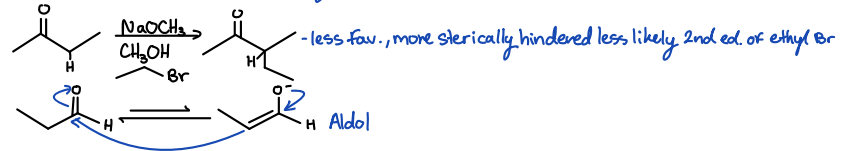


## Enolate Alkylation

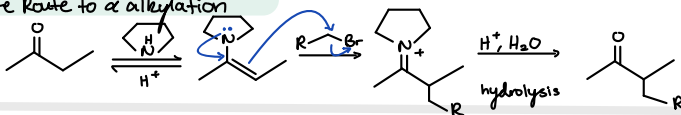
-create Kinetic and Thermo enolate, add primary halide  
 $\rightarrow$  doesn't work w/  $2^\circ$  haloalkanes — Elimination competitive



\* not as clean as might hope — mid-rxn proton transfers  
aldol rxn can compete especially for aldehydes



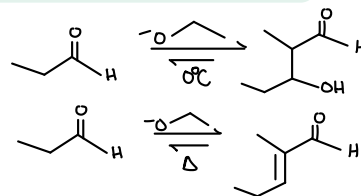
## Alternate Route to $\alpha$ alkylation



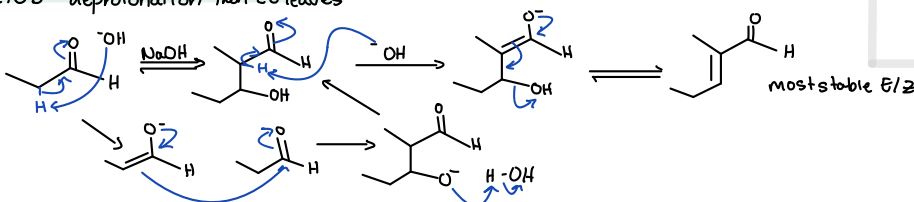
## Aldol Reaction

-treating aldehyde w/ base  $\rightarrow$  reversible formation of aldol  
-Ketones undergo aldol rxns but eq. favors starting material

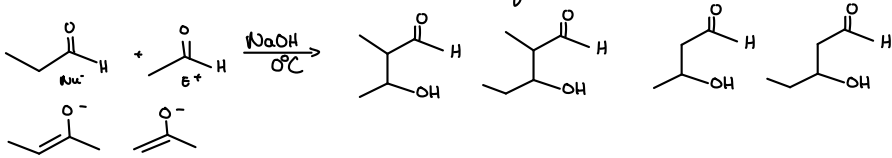
## Aldol addition at low T



## E1Cb - deprotonation then LG leaves

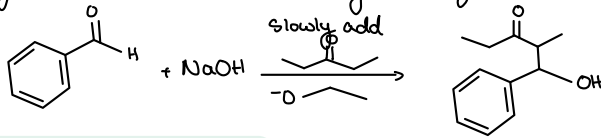


## Crossed Aldol Reactions — mix of 2 aldehydes → 4 possible additions



## Successful Crossed Aldol Reactions

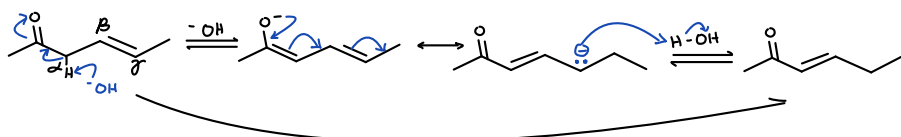
- 1) Aldehyde A has no  $\alpha$  Hs (only  $E^+$ )
- 2) Aldehyde or Ketone B is added slowly to Aldehyde A + base



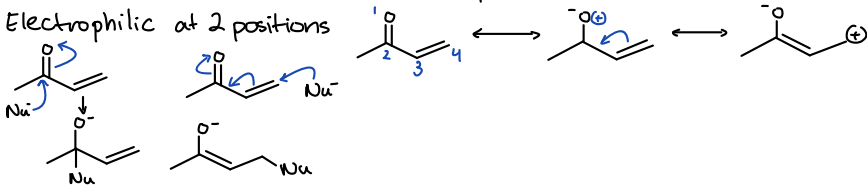
\* Intramolecular Aldol Reactions faster + more entropically fav.  
 ↳ if multiple products are possible only consider unstrained rings

## Alpha - Beta Unsaturated Carbonyls

- Conjugation is stabilizing
- $\beta$ - $\delta$  alkene will isomerize in acid or base

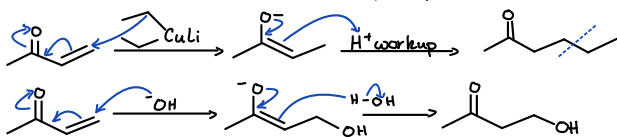


## Electrophilic at 2 positions



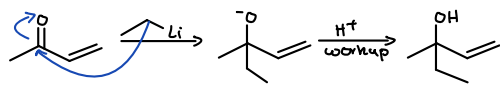
## 1,4 addition — $Nu^-$ that add reversibly

- $H_2O, OH^-, RO^-, ROH, RNH_2, R_2NH, RS^-, RSH, R_2CuLi, CN^-,$  enolates

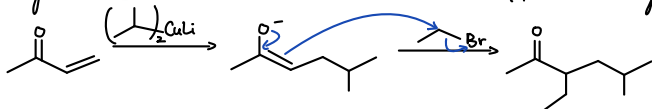


## 1,2 addition — $Nu^-$ that add irreversibly

- ↳  $LiAlH_4, H_2N-NHR, H_2N-OH, R-Li$  (inconsistent:  $NaBH_4, R-MgBr$ )

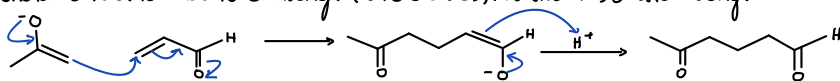


## Dialkylation — enolate intermediate can be trapped w/ alkyl halide



## Michael Addition

- ↳ enolates tend to add to carbonyl (is reversible), results in 1,5 dicarbonyl



## Robinson Annulation

- ↳ Michael addition + aldol condensation

