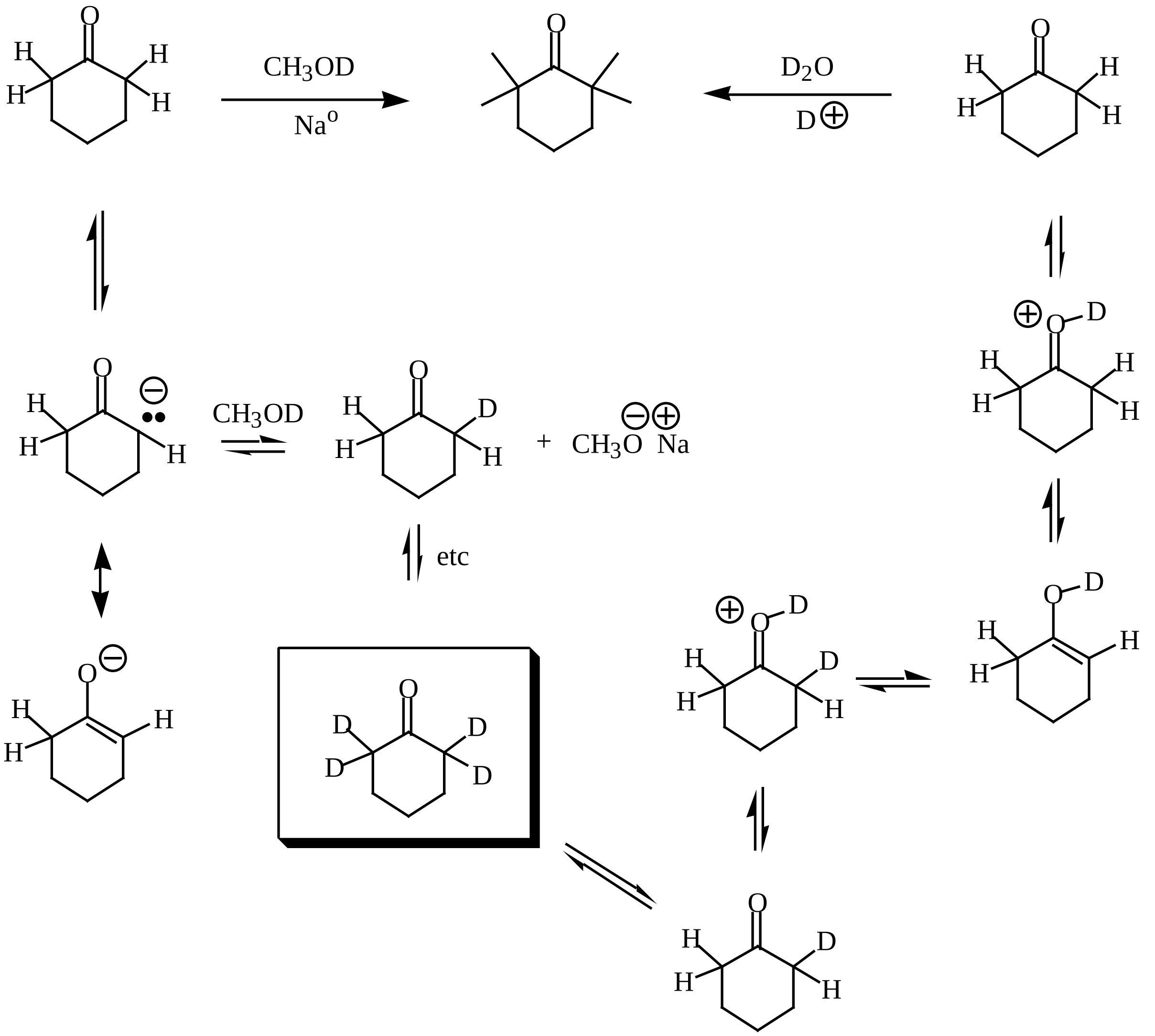
From last time: The carbonyl group can increase the acidity of the adjacent (alpha) C-H to pKa ca 20. There is an equilibration between the ketone (aldehyde) and enol, which strongly favors the ketone (aldehyde). Each is stable in the absence of acid or base, but these agents accelerate the establishment of equilibrium.

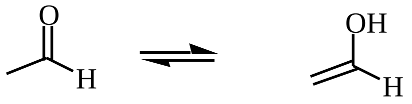


Consequences:

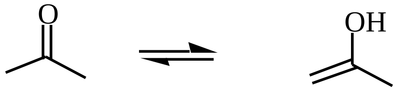
racemization via
enolization

Bromination of ketones

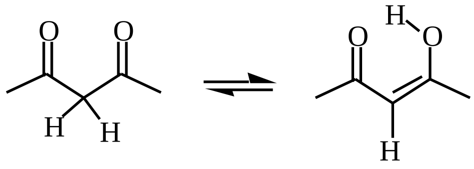
Enol stability relative to the ketone (aldehyde):



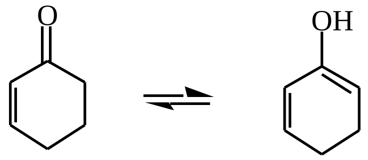
5×10^{-6}



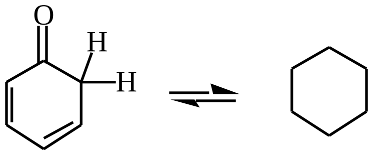
6×10^{-8}



3.2



10^{-5}



Enol and Enolate nucleophiles in addition to ketones and aldehydes:

In base:

an "aldol"

In acid:

an "aldol"

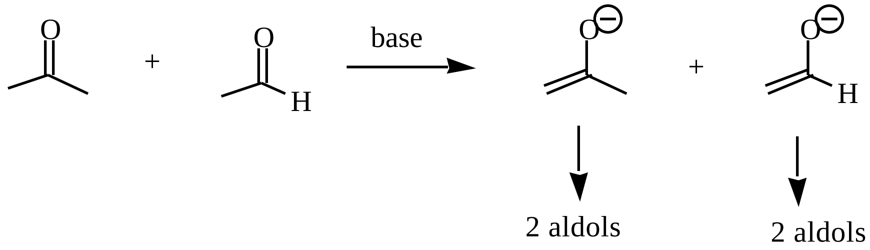
These reactions are typically reversible: write the mechanism backwards.

And, as usual, the equilibrium for ketones is less favorable.

Need a trick to drive the equilibrium: fig 18.63 Soxhlet Extractor

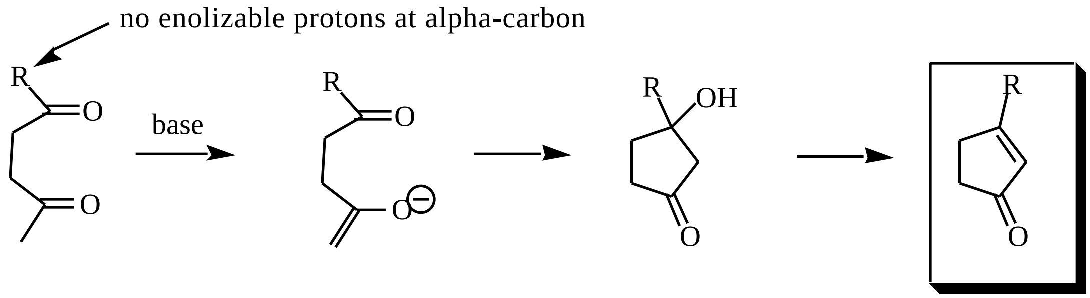
Ketones, in acid:

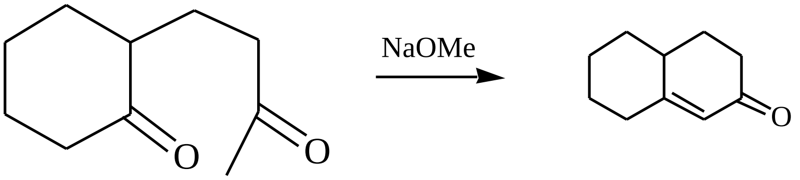
Problem: Crossed Aldol reactions give mixtures



Special solutions, each with limitations:

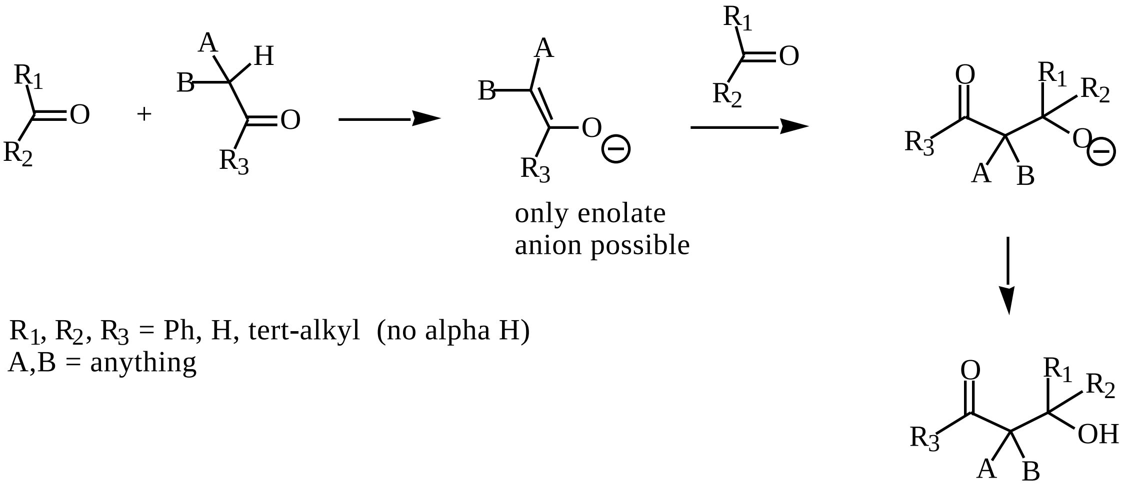
1. Make intramolecular favorable for five- and six-membered rings.


no enolizable protons at alpha-carbon

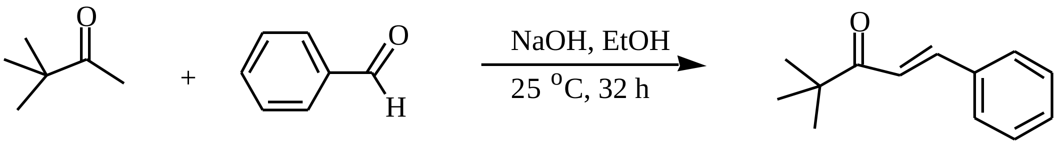


2. Crossed Aldol (intermolecular): Ideal--one ketone with no enolizable C-H
another ketone with less reactive C=O

Original: Claisen-Schmidt (ketone with aldehyde)

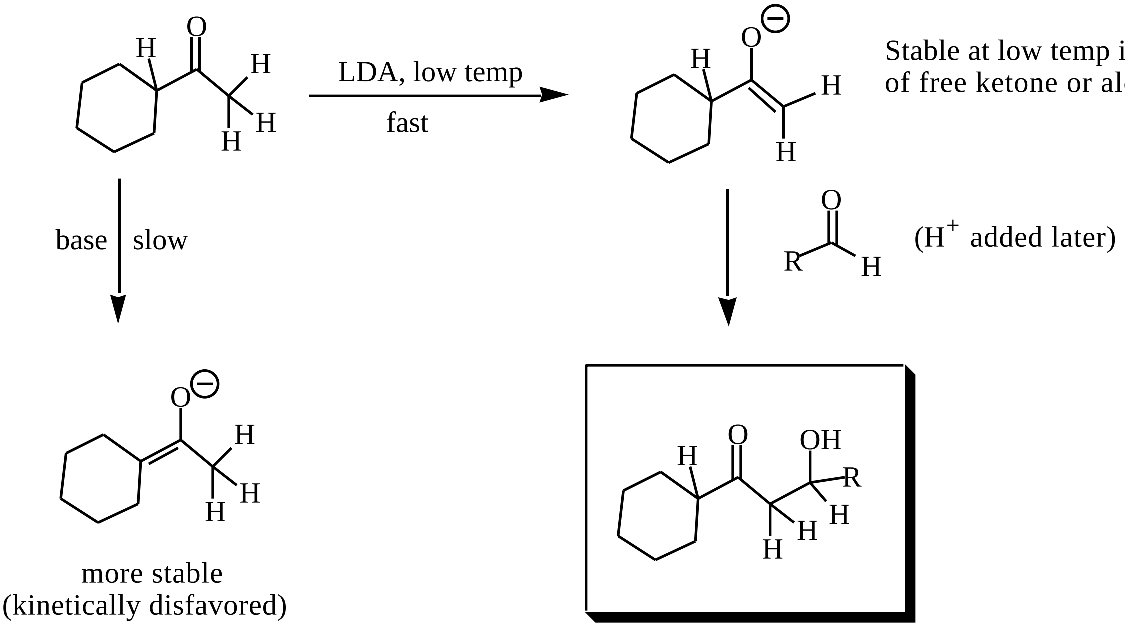

only enolate anion possible

e.g., R_1, R_2, R_3 = Ph, H, tert-alkyl (no alpha H)
A,B = anything



Mechanism: p 914

Modern: Selective generation of the enolate anion, add other carbonyl component.

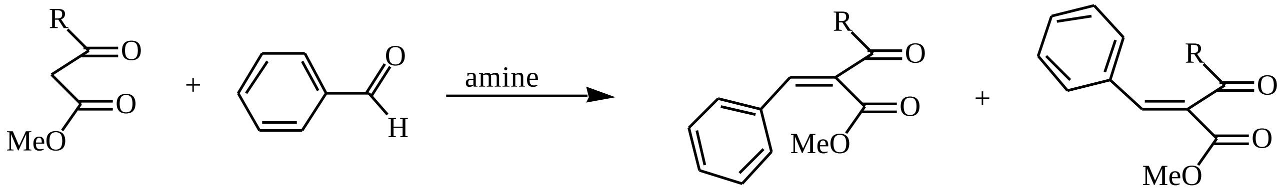


Stable at low temp in absence of free ketone or aldehyde

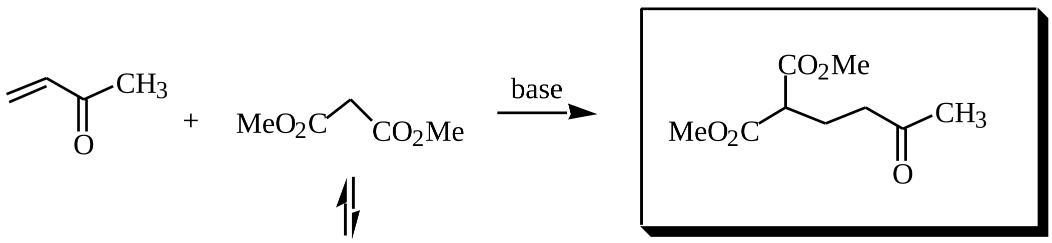
more stable
(kinetically disfavored)

Classics:

Very stabilized carbanion in one component: Knoevenagel Condensation



"Conjugate Addition" The Michael Reaction



Reversible addition of stabilized anion → most stable product favored at equilibrium

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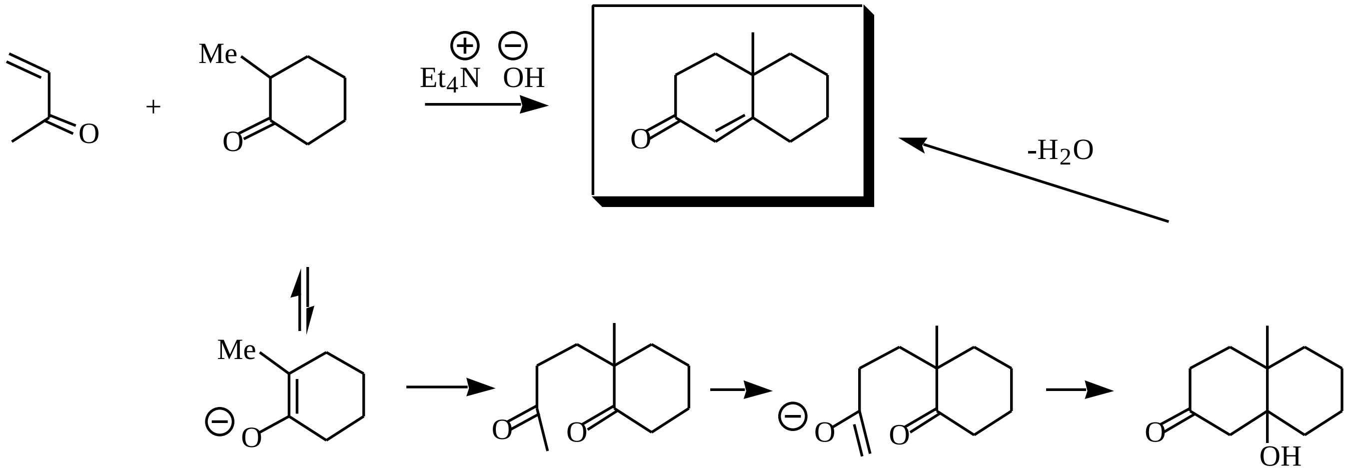
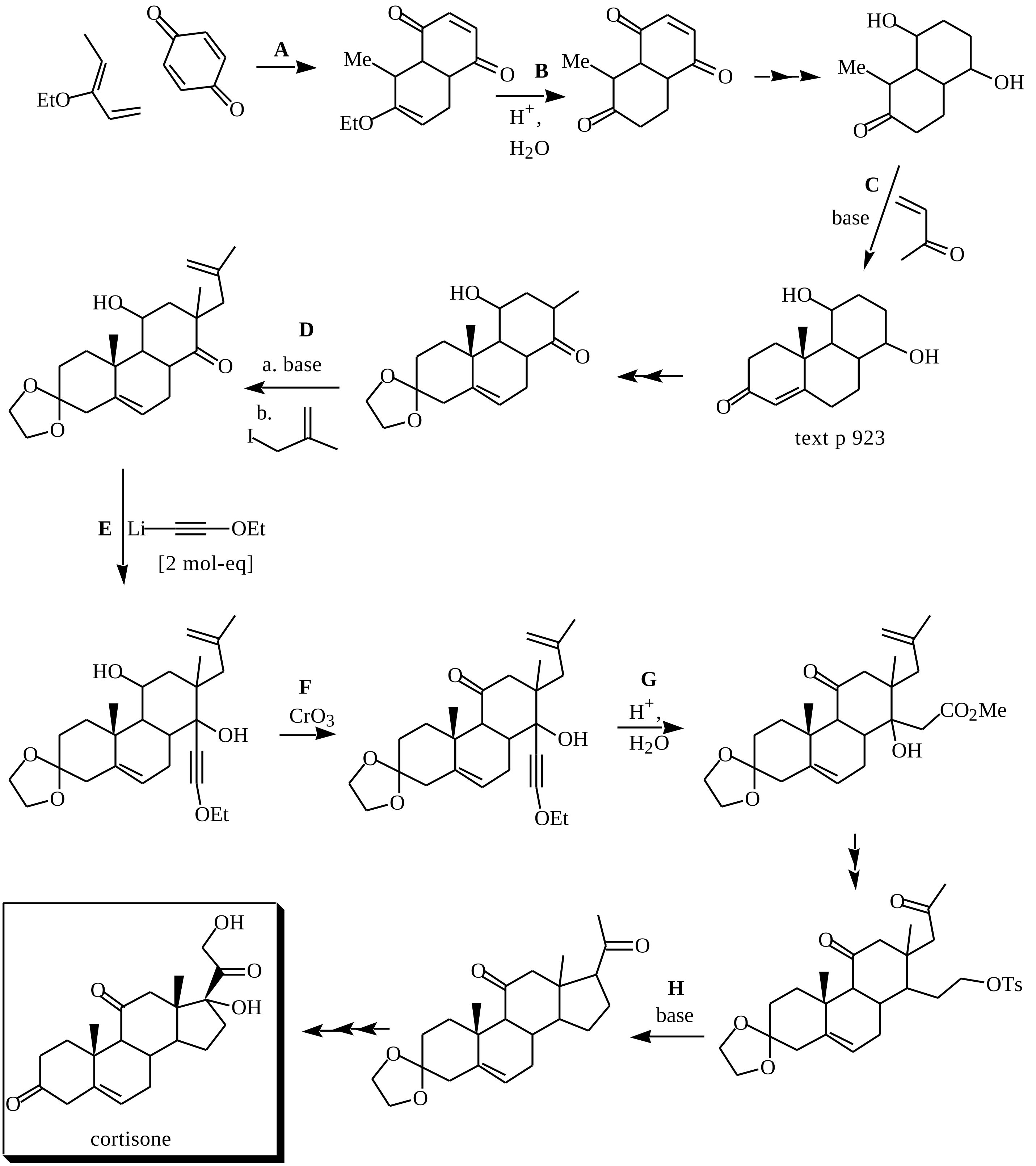
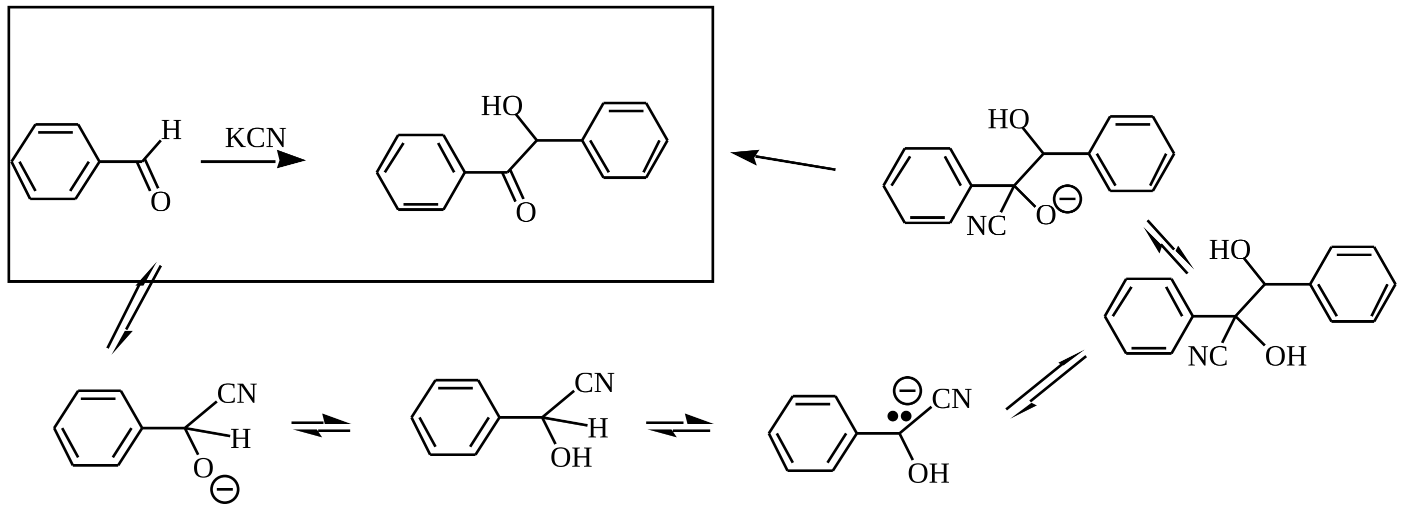
Combination condensation reactions:



Sarett's Cortisone synthesis:



The Benzoin reaction and Vitamin B1 [thiamine] Very old:



Role of CN: Add to C=O; favor deprotonation of alpha H

Nature's analog of CN: Thiamine pKa 12.7