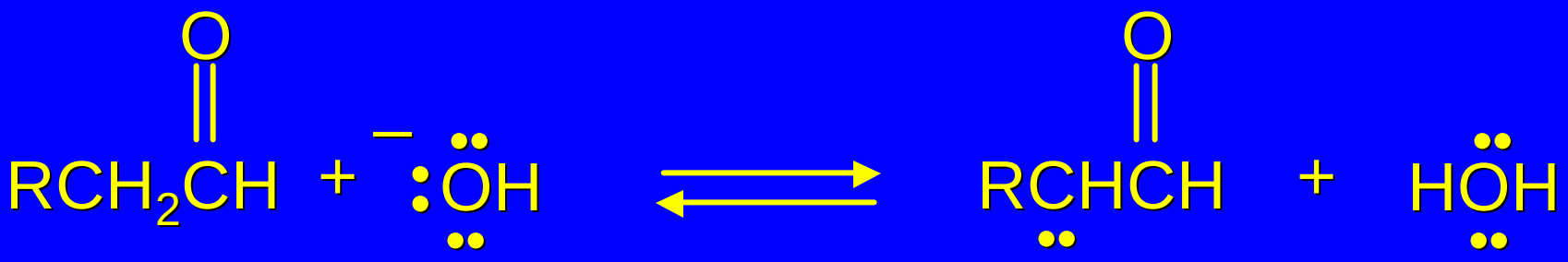
18.9

The Aldol Condensation

Some thoughts...



pK_a = 16-20

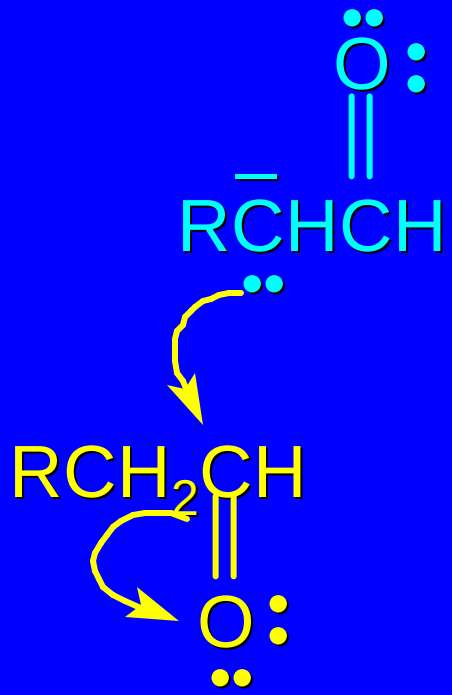
pK_a = 16

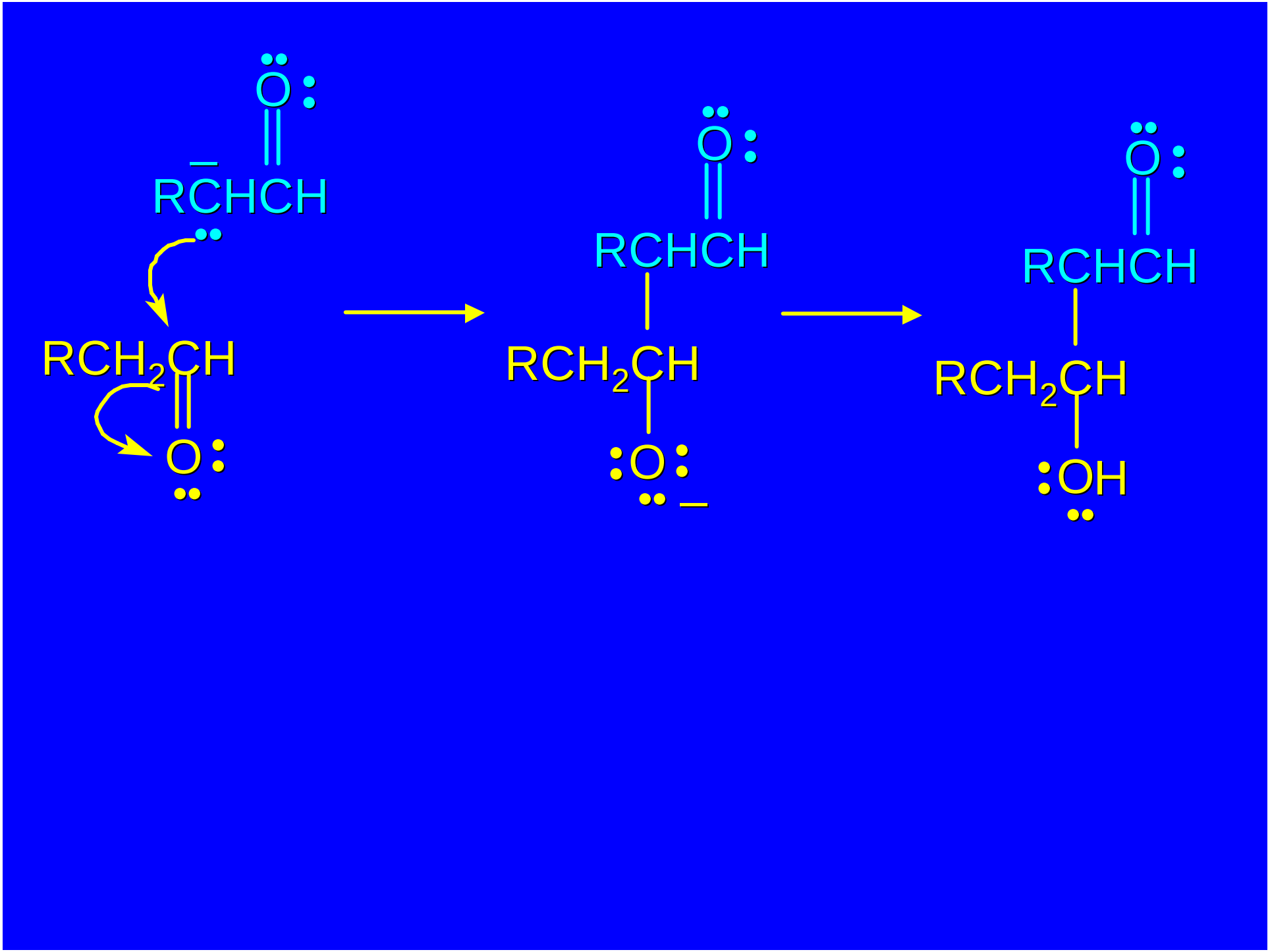
A basic solution contains comparable amounts of the aldehyde and its enolate.

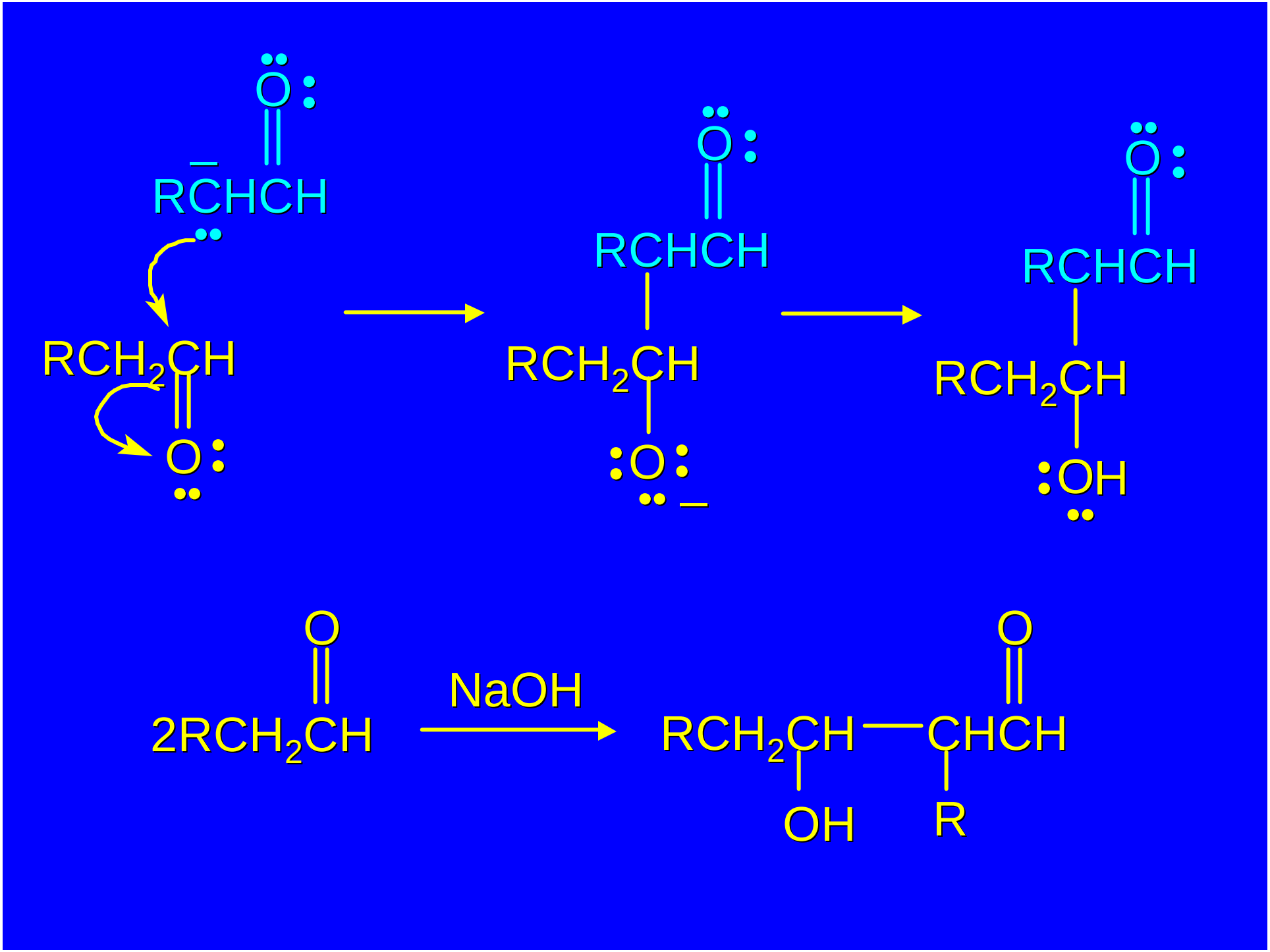
Aldehydes undergo nucleophilic addition.

Enolate ions are nucleophiles.

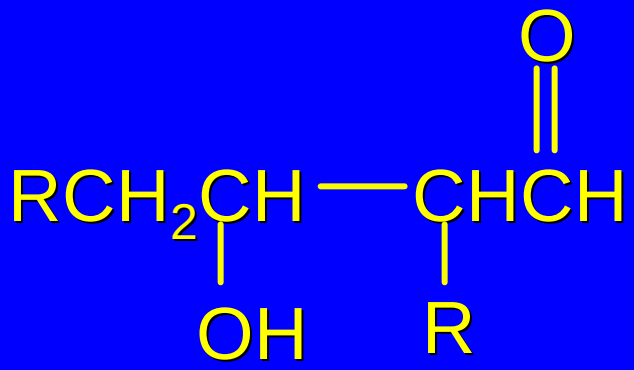
What about nucleophilic addition of enolate to aldehyde?


O
RCHCH
RCH2CH
O


O
RCHCH
RCH2CH
O
RCHCH
RCH2CH
O
RCHCH
RCH2CH
OH

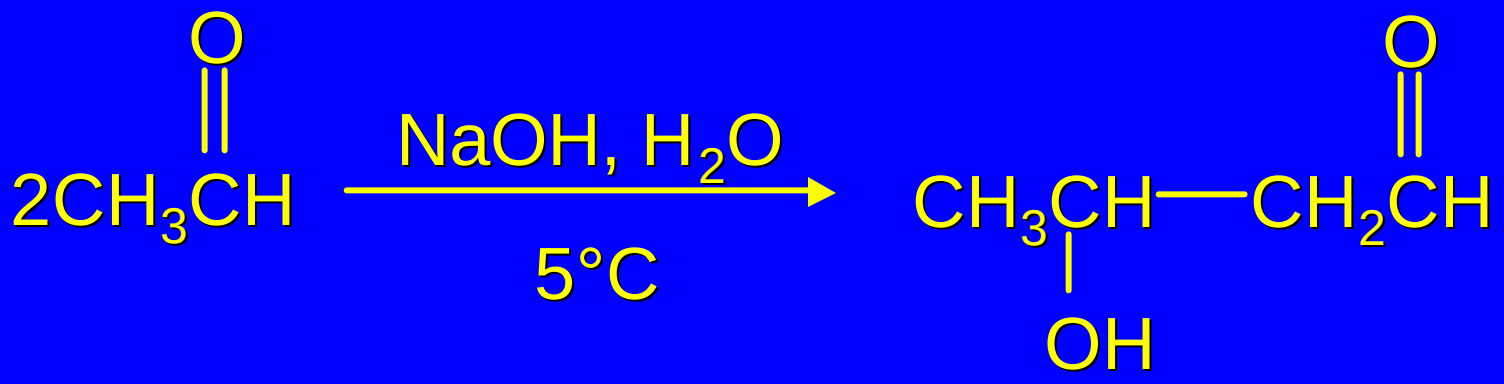

RCHCH
RCH2CH
RCHCH
RCH2CH
RCHCH
RCH2CH
OH
2RCH2CH
NaOH
RCH2CH
CHCH
OH
R

Aldol Addition



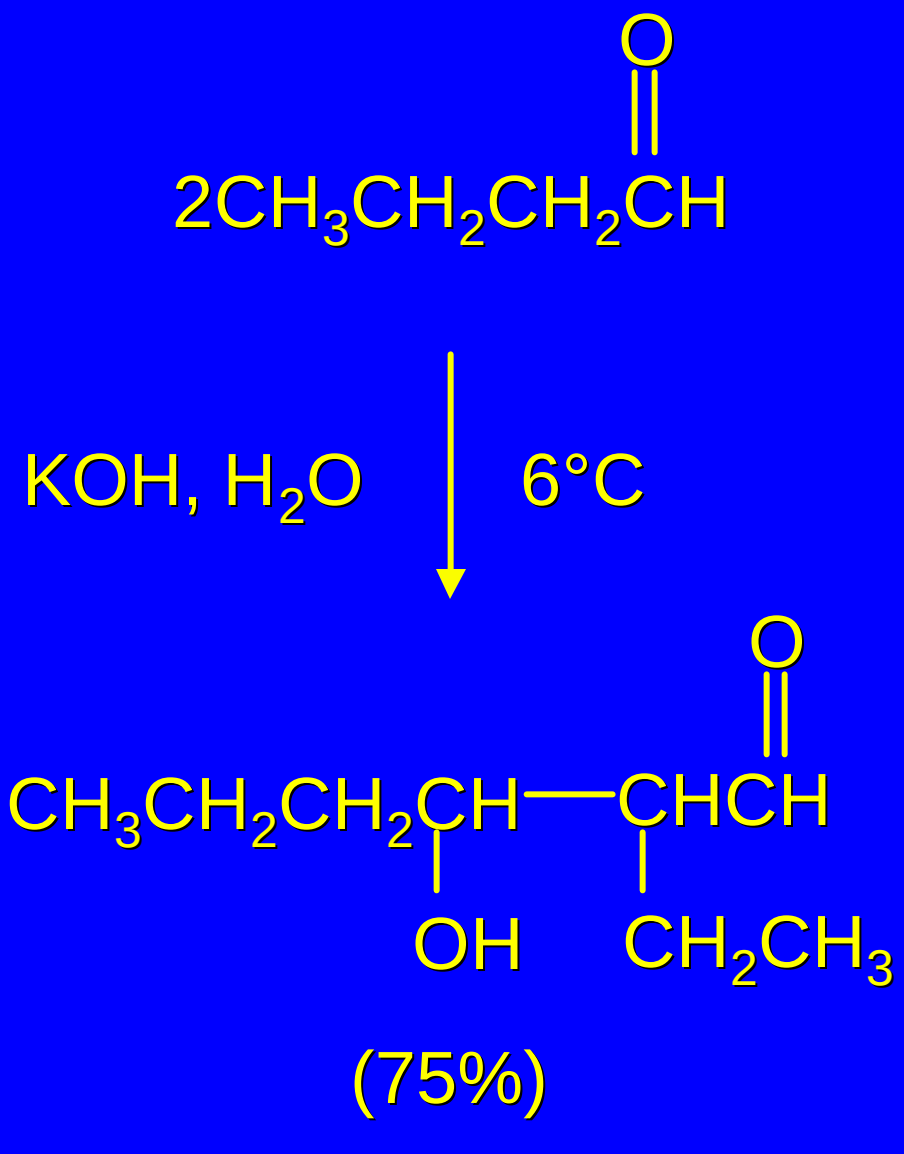
product is called an "aldol" because it is both an aldehyde and an alcohol

Aldol Addition of Acetaldehyde



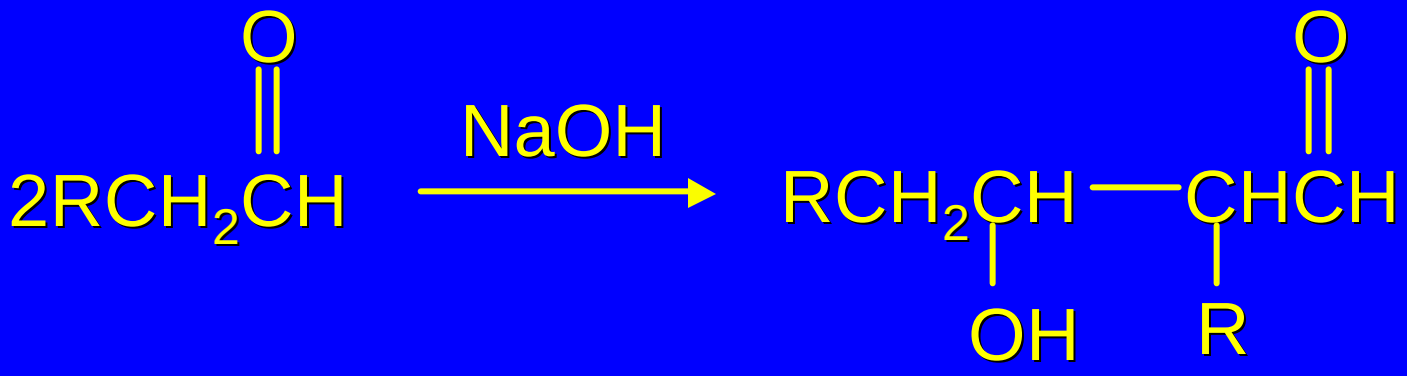
Acetaldol
(50%)

Aldol Addition of Butanal

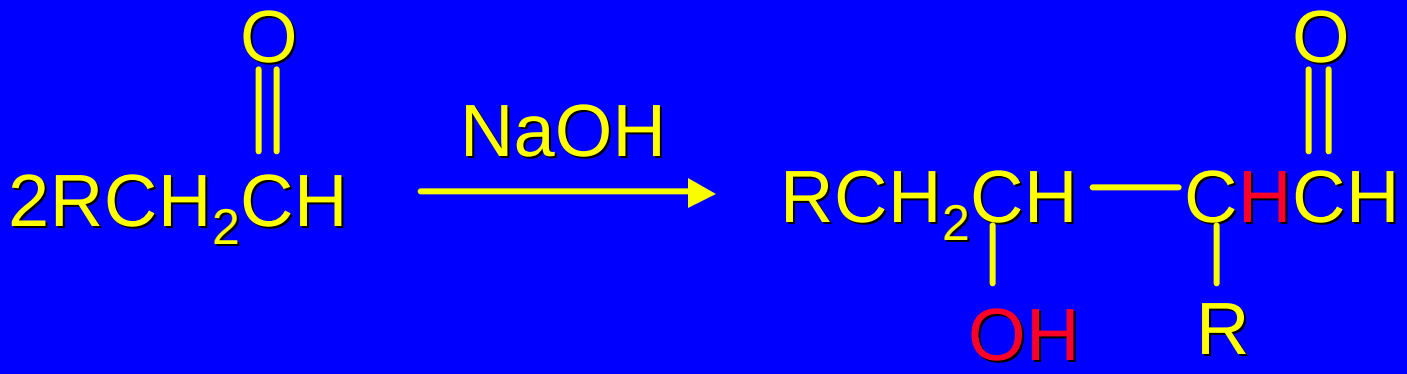


(75%)

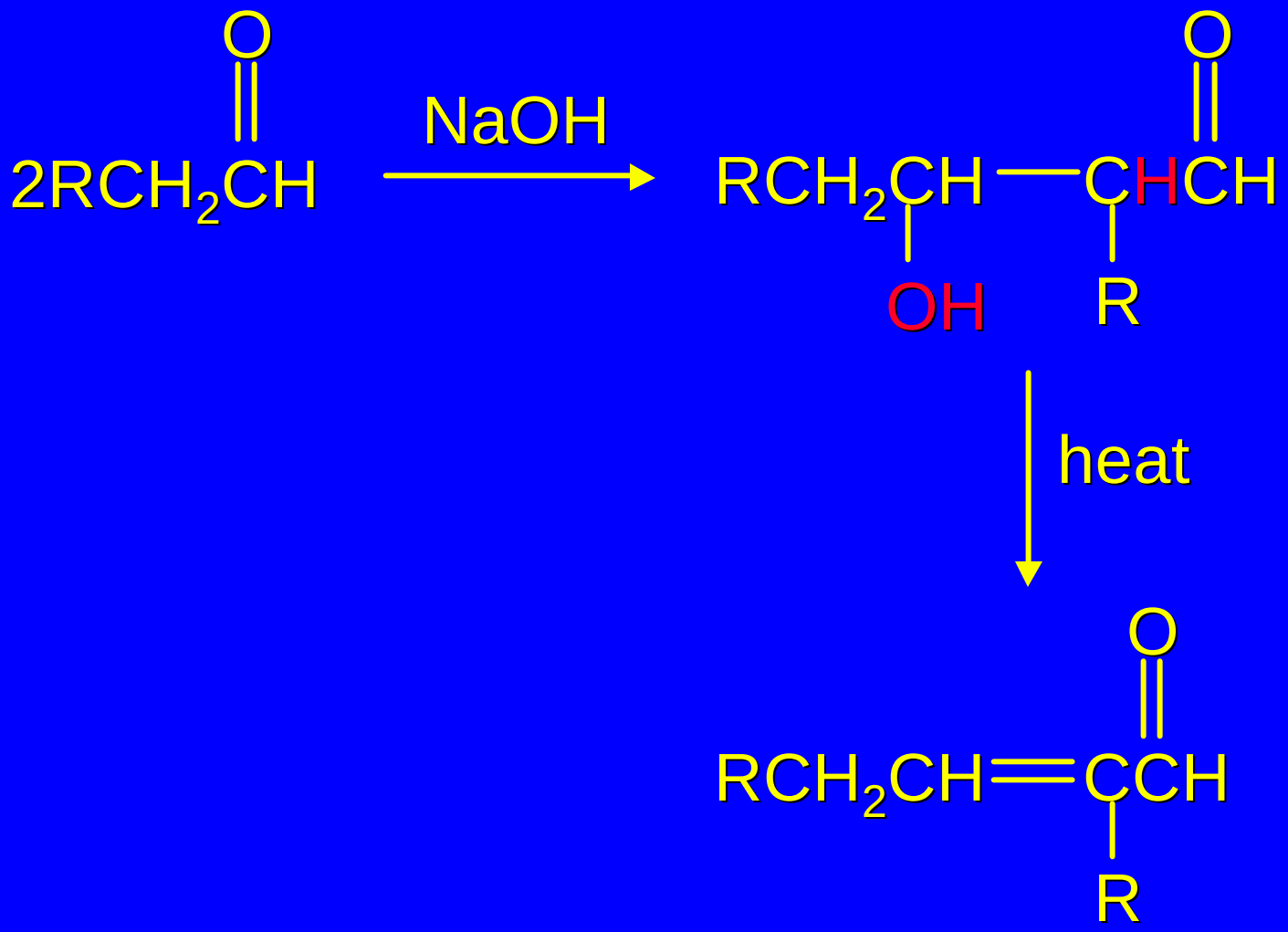
Aldol Condensation



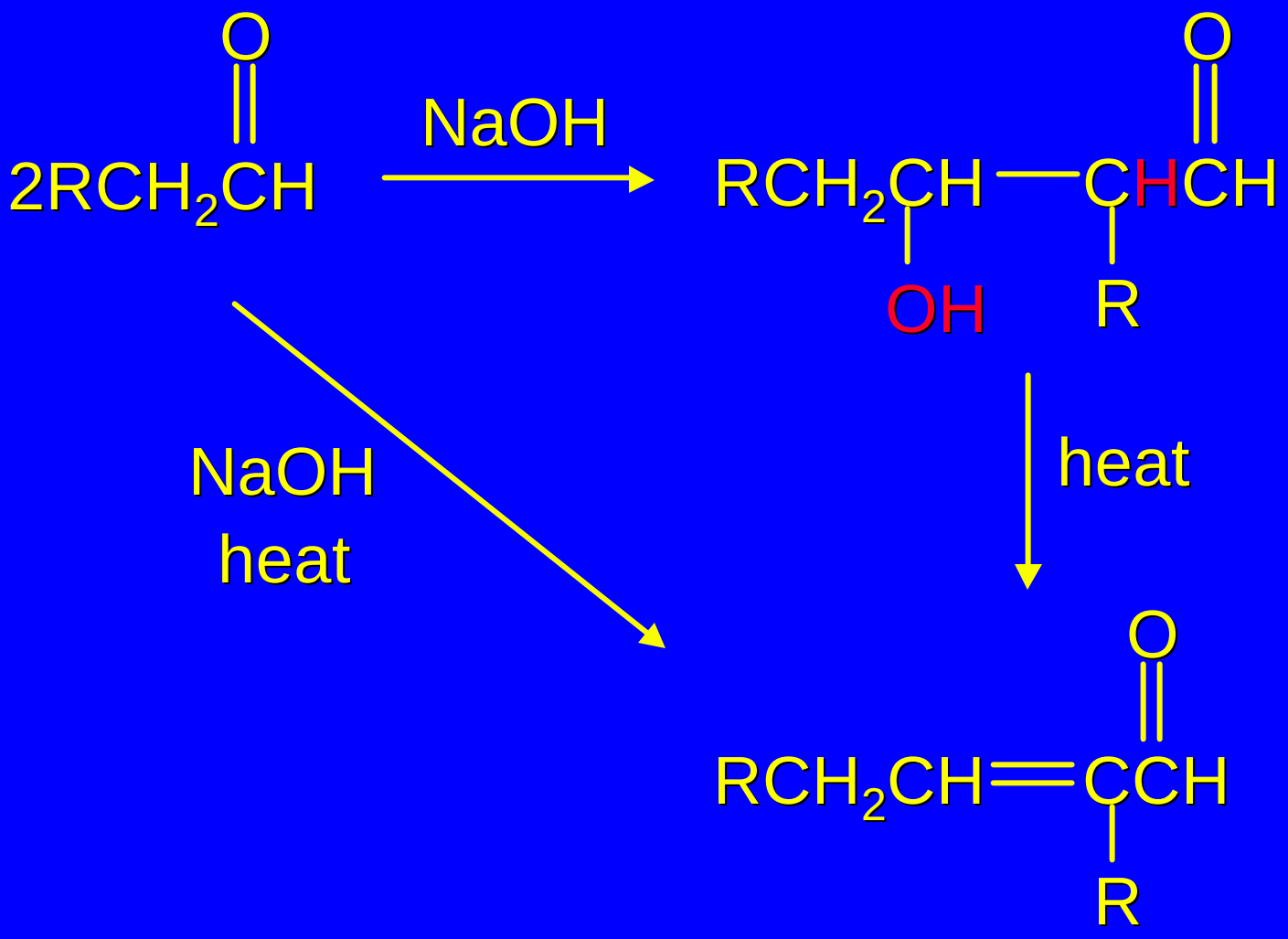
Aldol Condensation



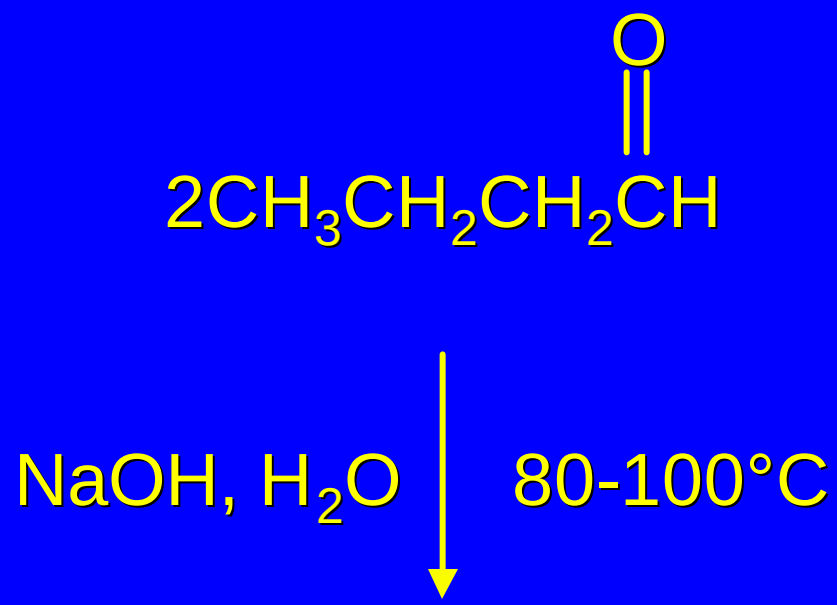
Aldol Condensation



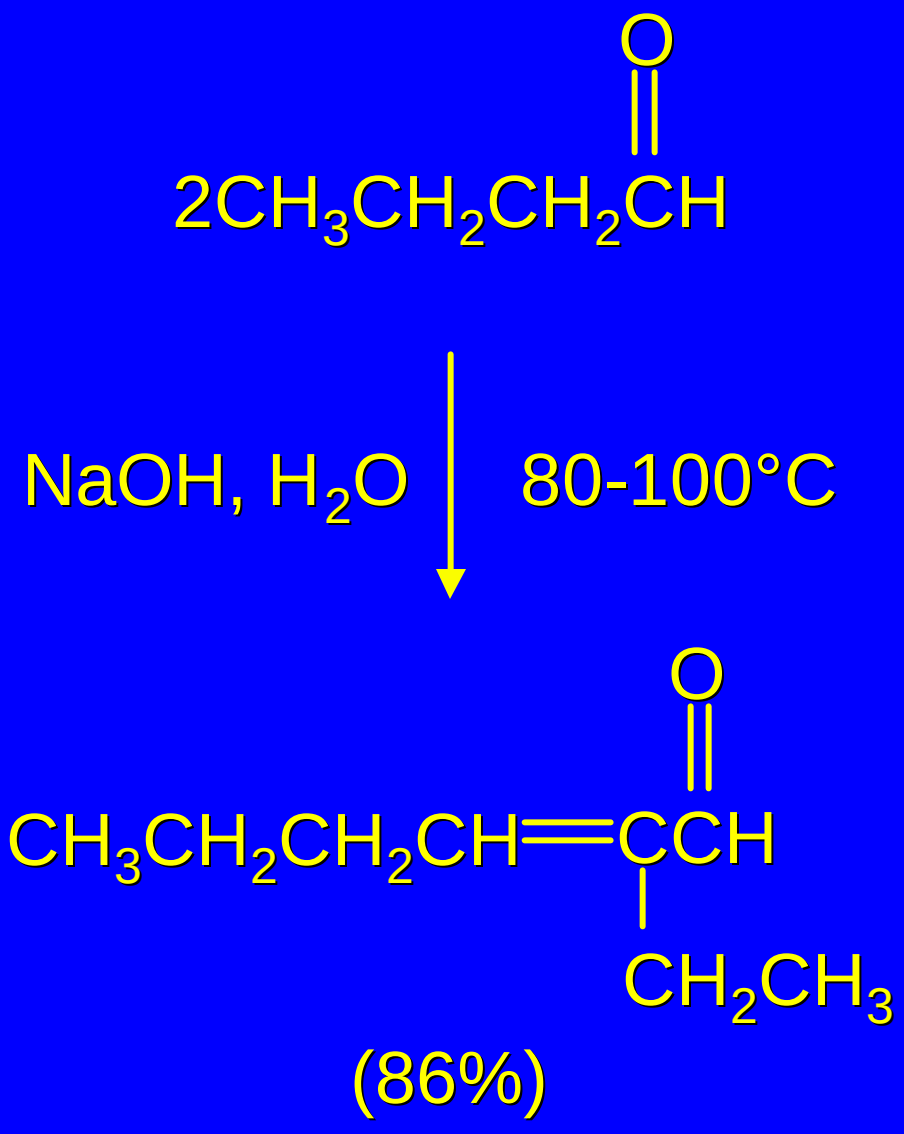
Aldol Condensation



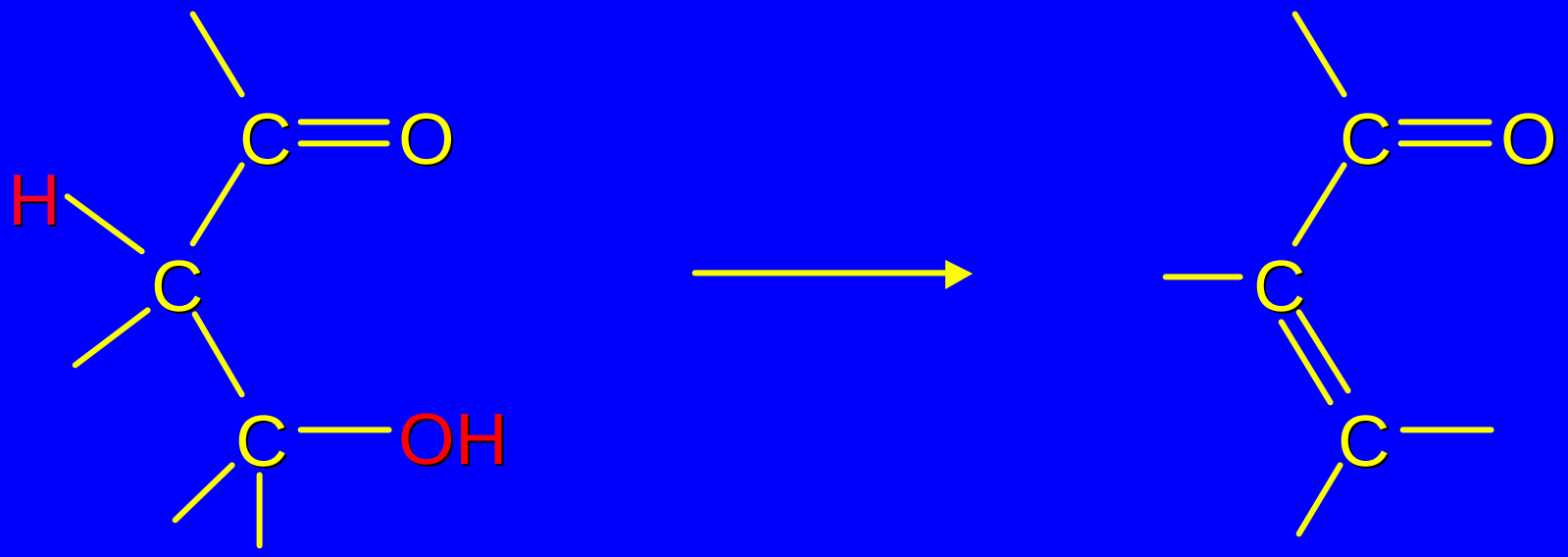
Aldol Condensation of Butanal



Aldol Condensation of Butanal

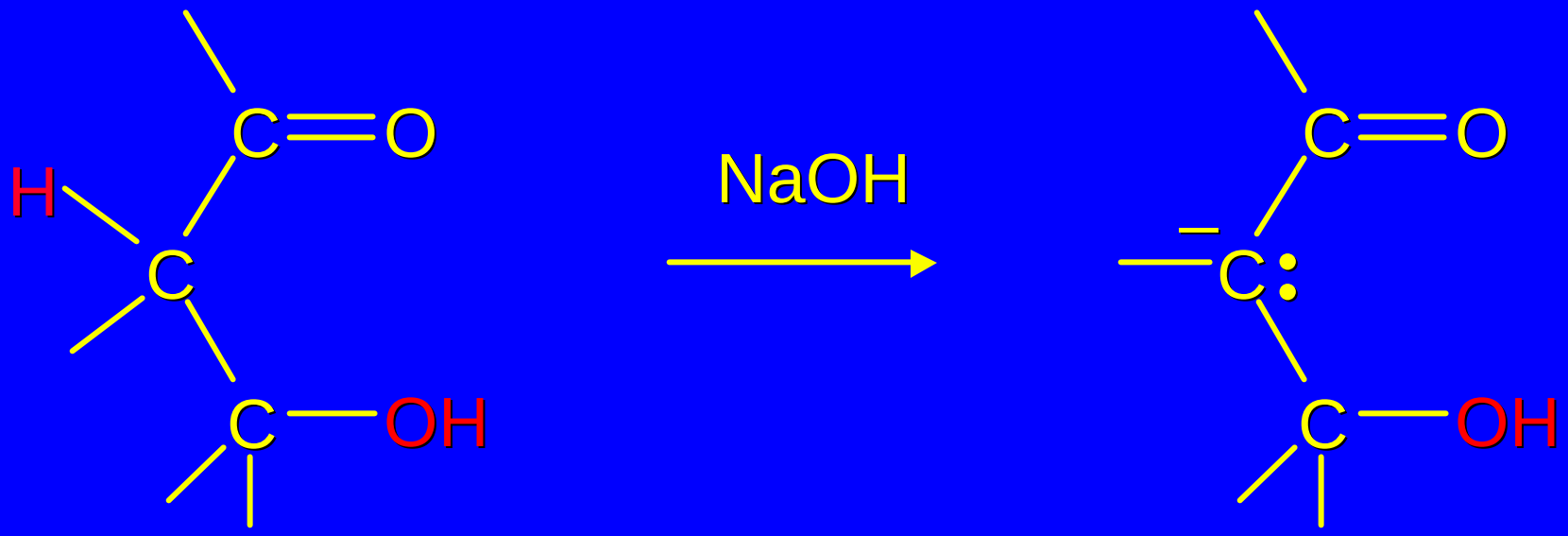


Dehydration of Aldol Addition Product



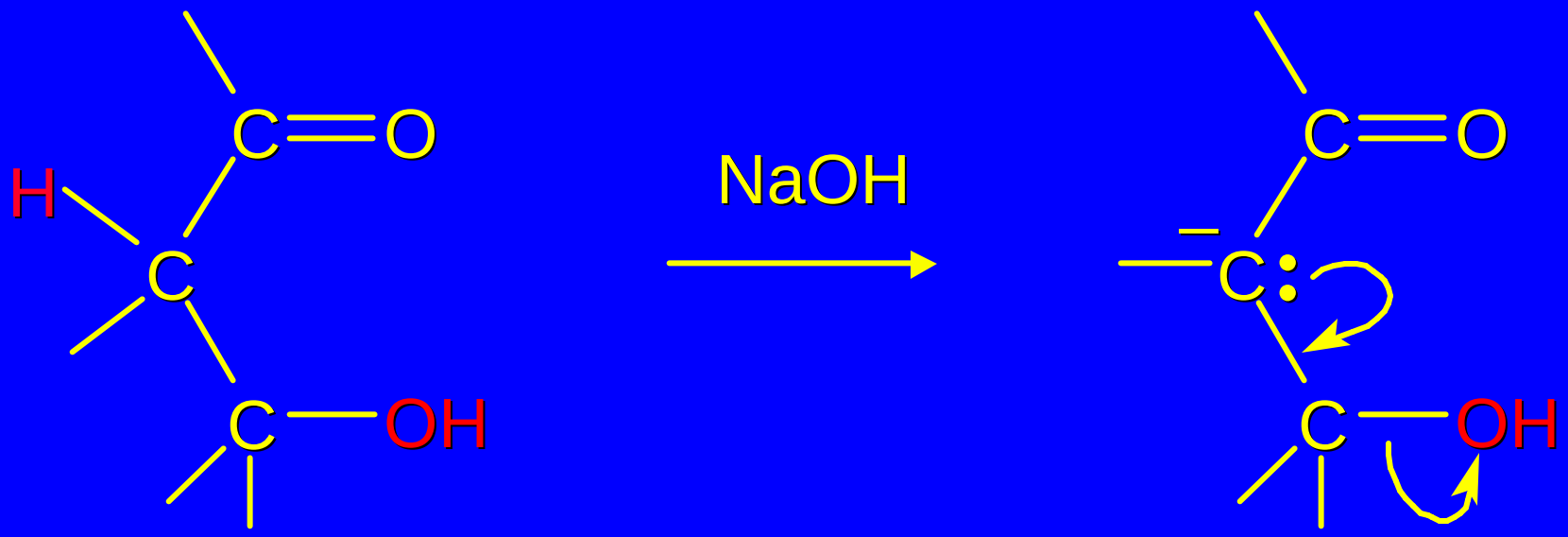
dehydration of *b*-hydroxy aldehyde can be catalyzed by either acids or bases

Dehydration of Aldol Addition Product



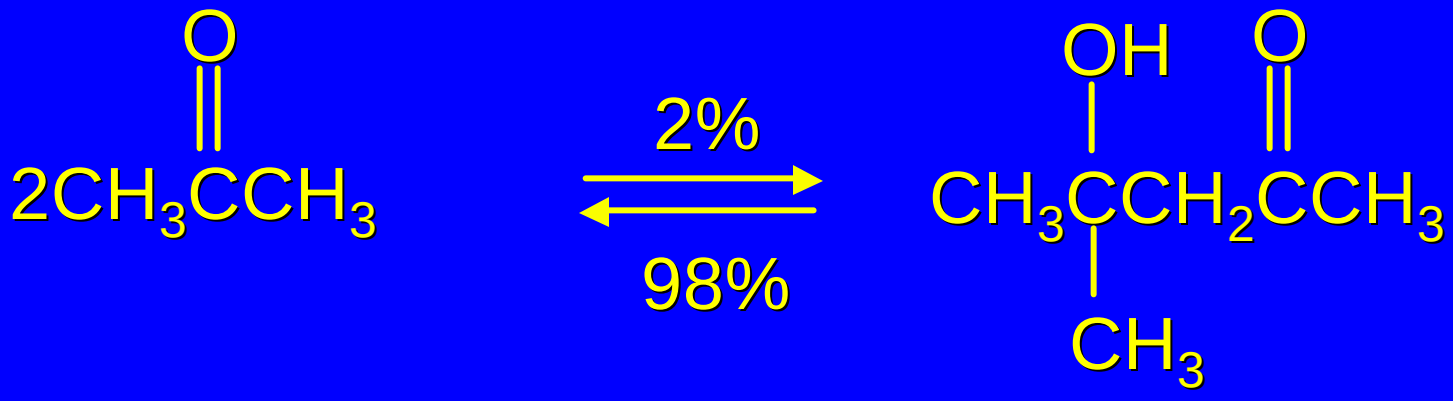
in base, the enolate is formed

Dehydration of Aldol Addition Product



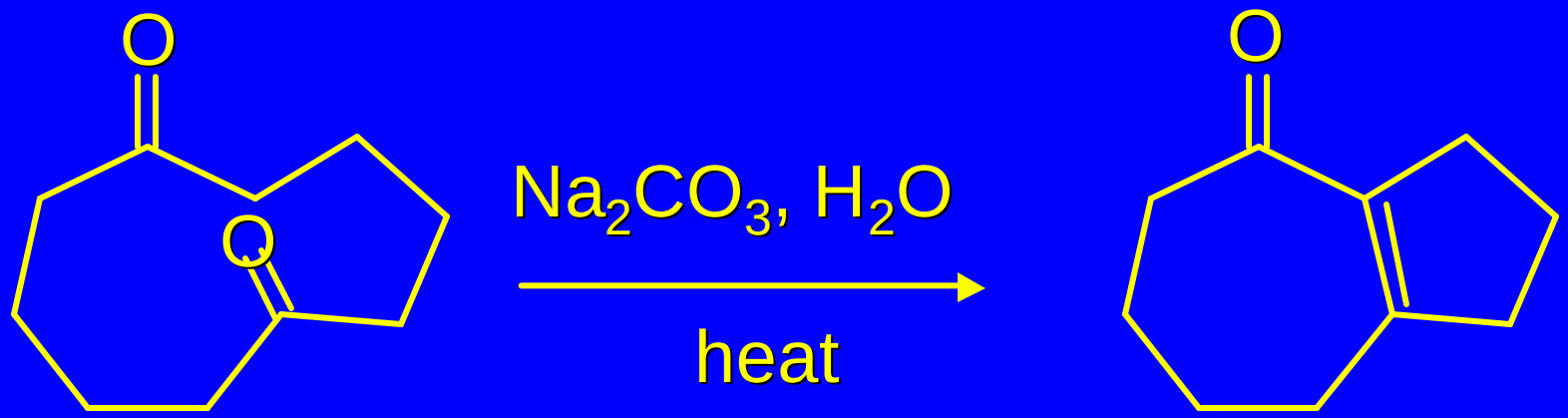
the enolate loses hydroxide to form the
α,β-unsaturated aldehyde

Aldol reactions of ketones



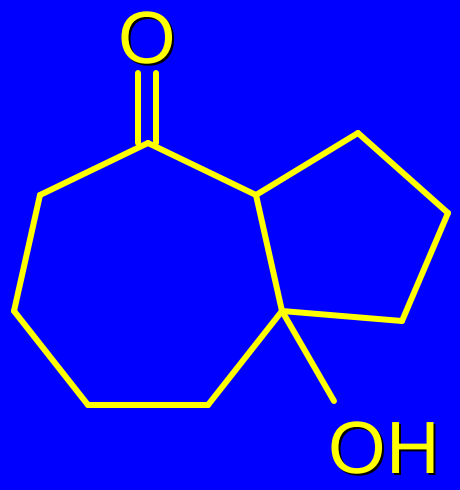
the equilibrium constant for aldol addition reactions of ketones is usually unfavorable

Intramolecular Aldol Condensation

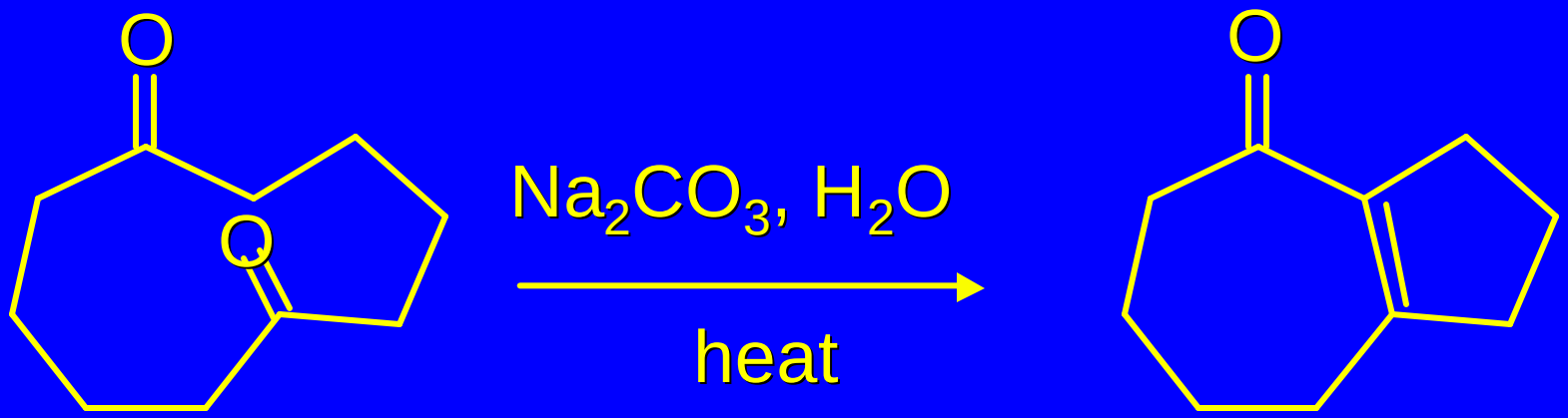


(96%)

via:



Intramolecular Aldol Condensation



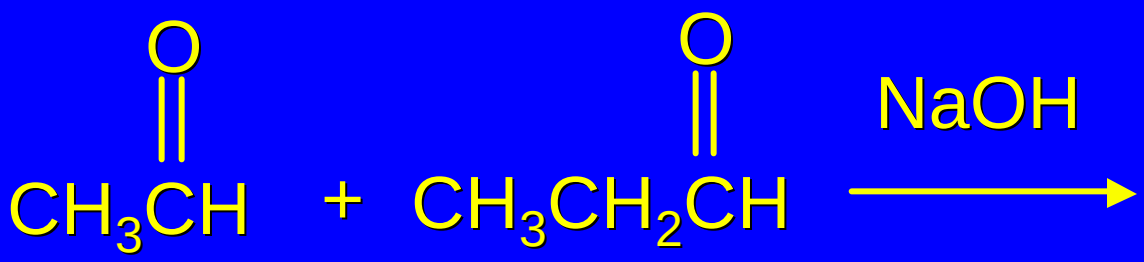
(96%)

even ketones give good yields of aldol condensation products when the reaction is intramolecular

18.10

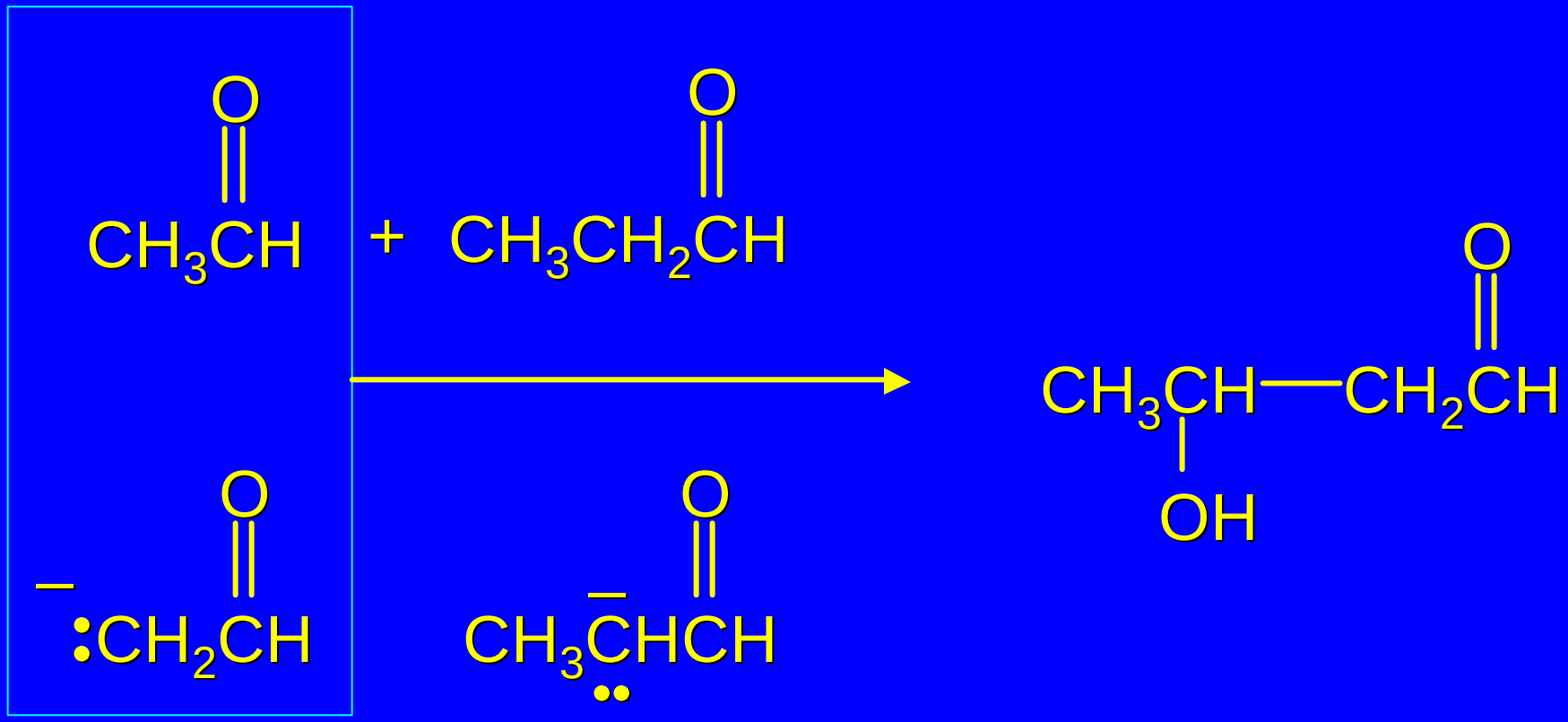
Mixed Aldol Condensations

What is the product?

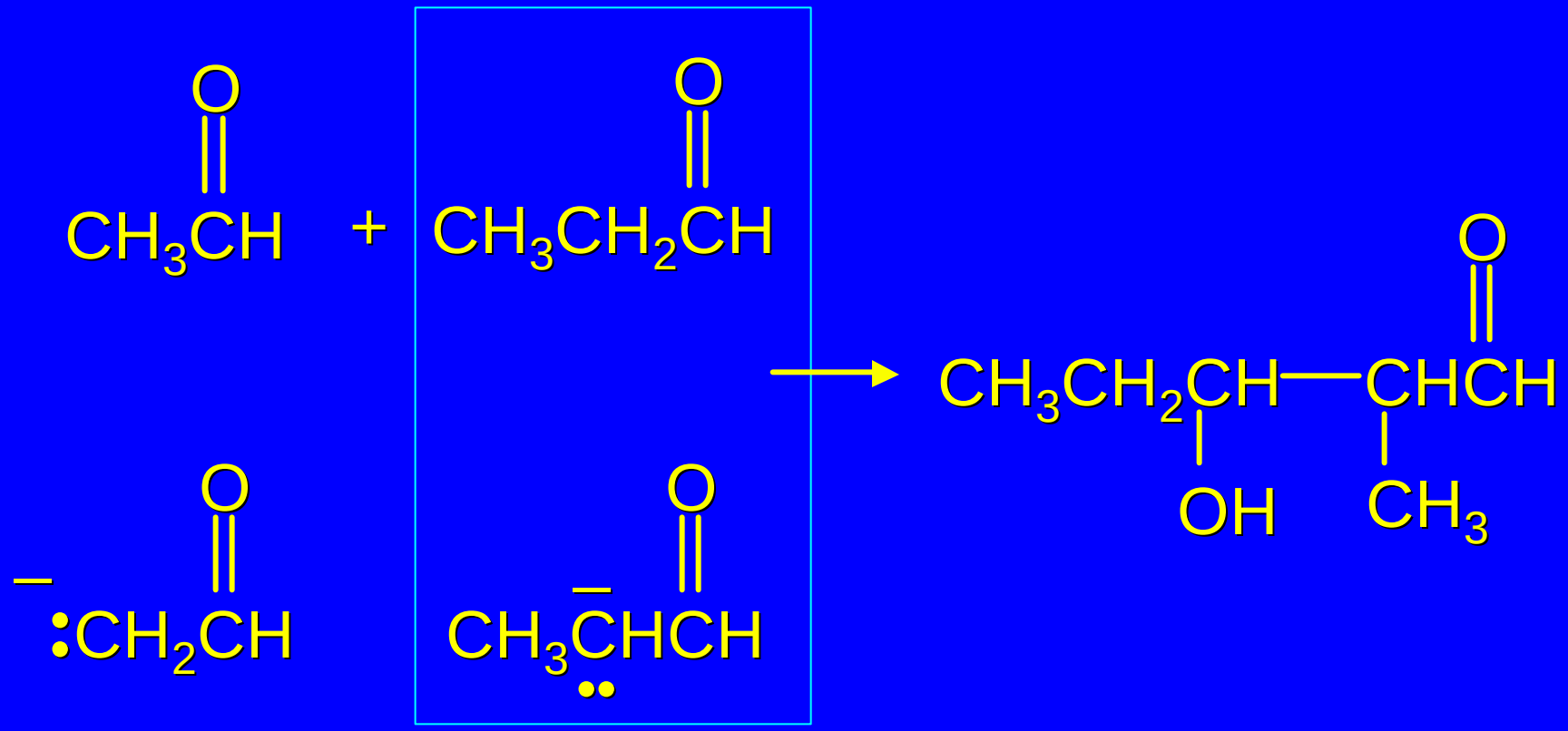


There are 4 possibilities because the reaction mixture contains the two aldehydes plus the enolate of each aldehyde.

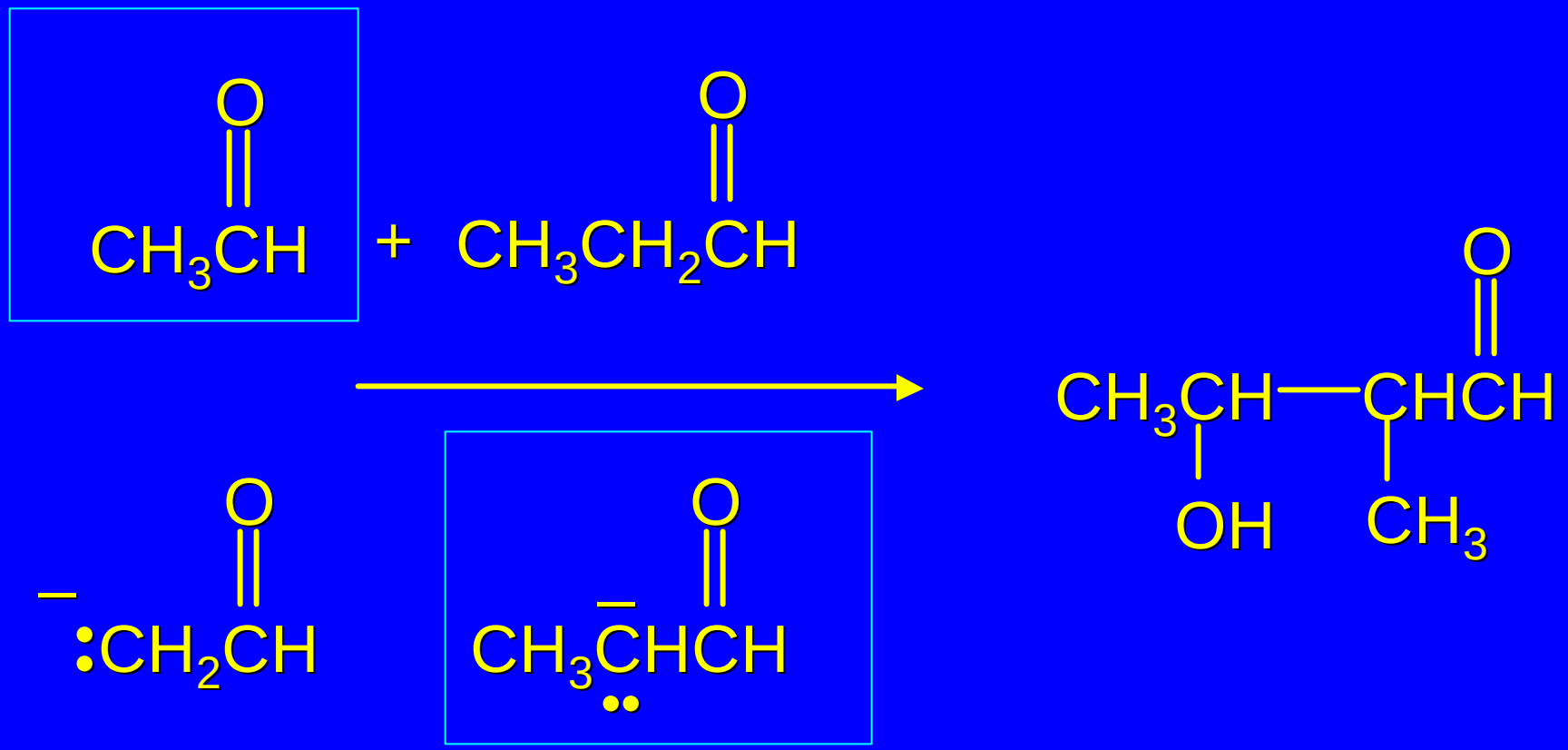
What is the product?



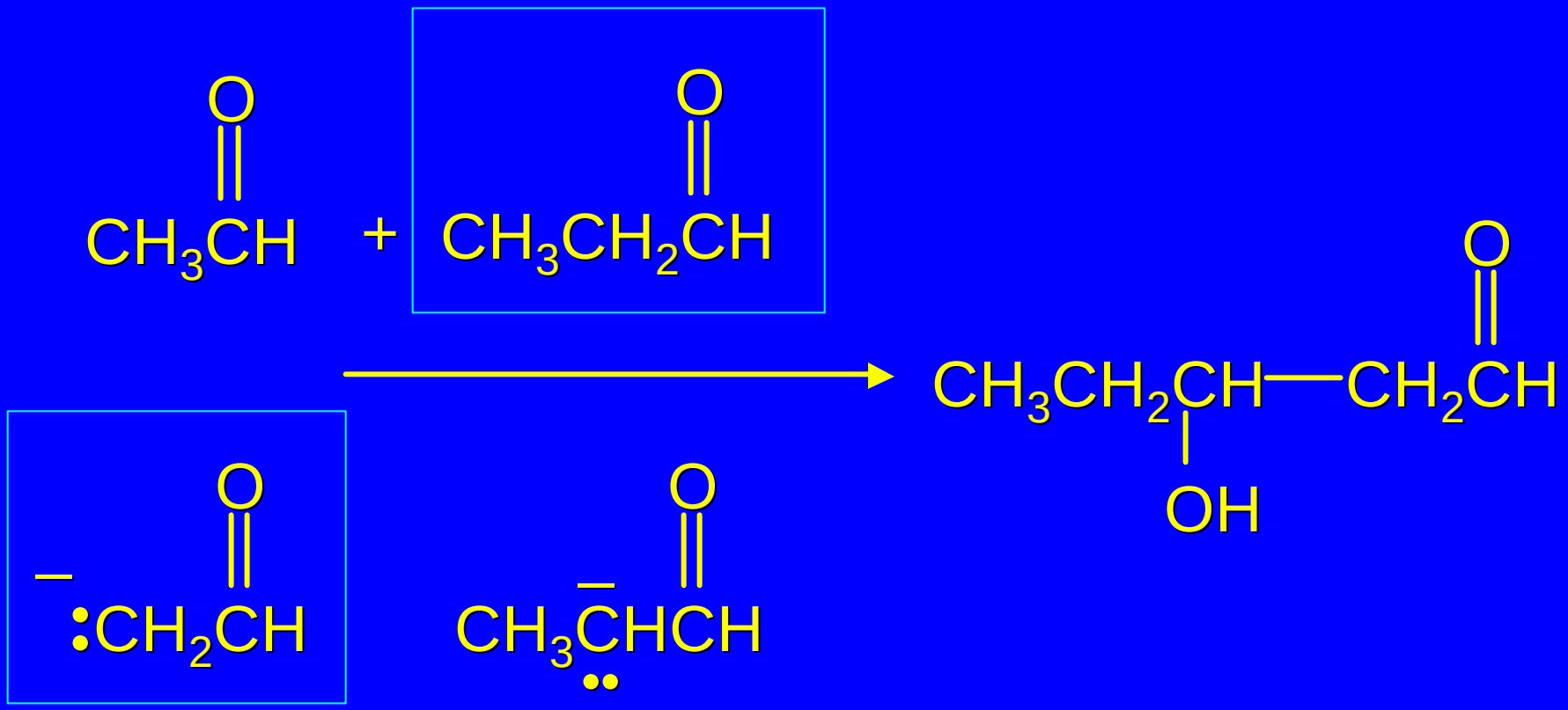
What is the product?



What is the product?



What is the product?



In order to effectively carry out a mixed aldol condensation:

need to minimize reaction possibilities

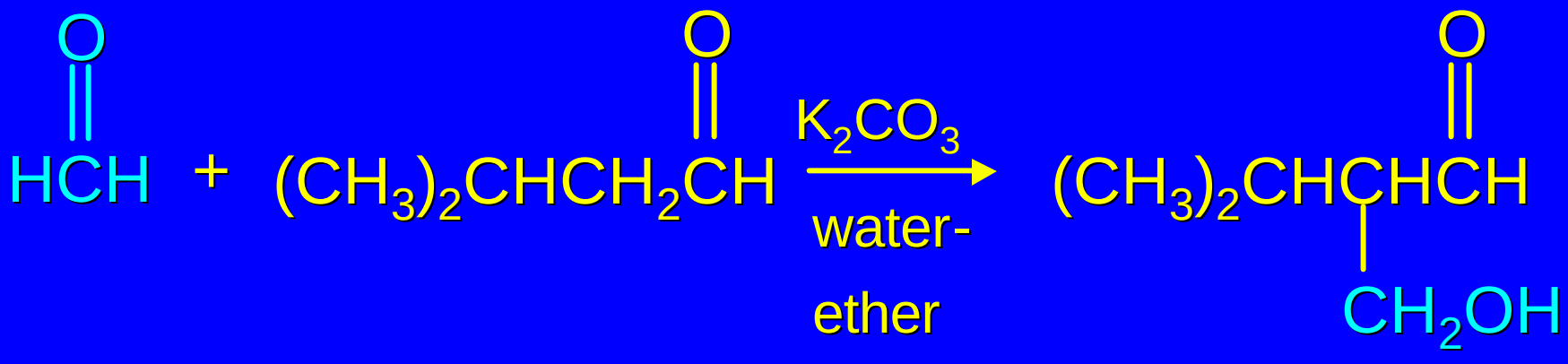
usually by choosing one component that cannot form an enolate

Formaldehyde

formaldehyde cannot form an enolate

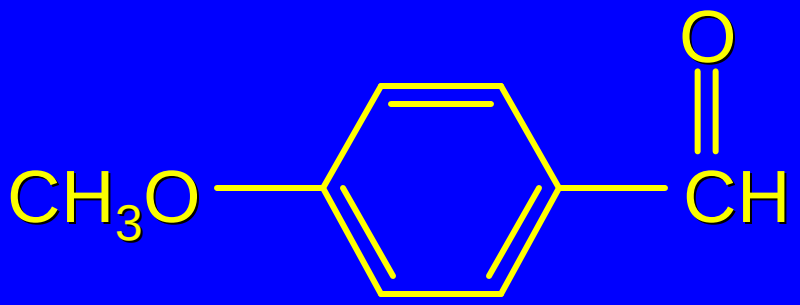
formaldehyde is extremely reactive toward nucleophilic addition

Formaldehyde



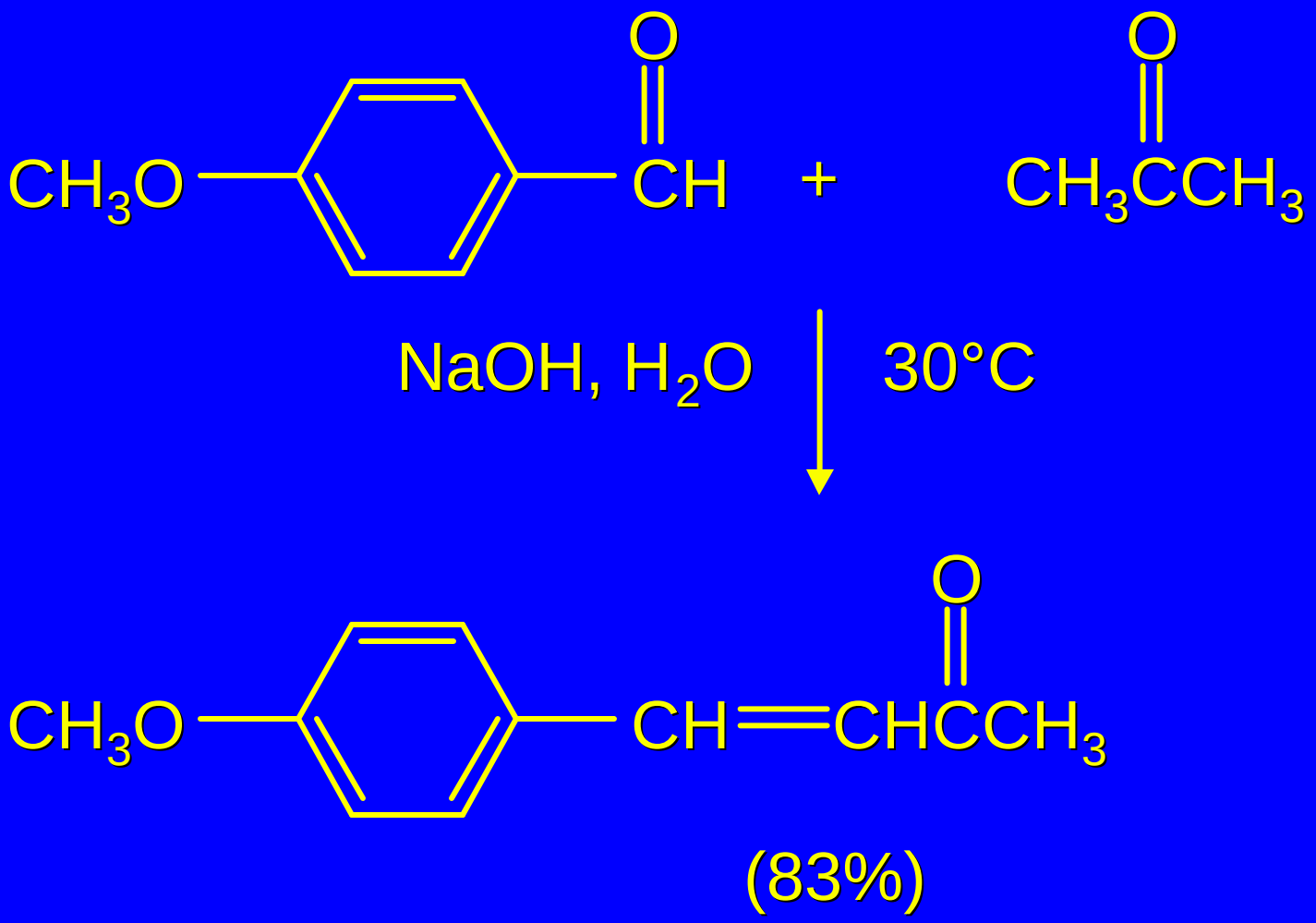
(52%)

Aromatic Aldehydes



aromatic aldehydes cannot form an enolate

Aromatic Aldehydes



(83%)