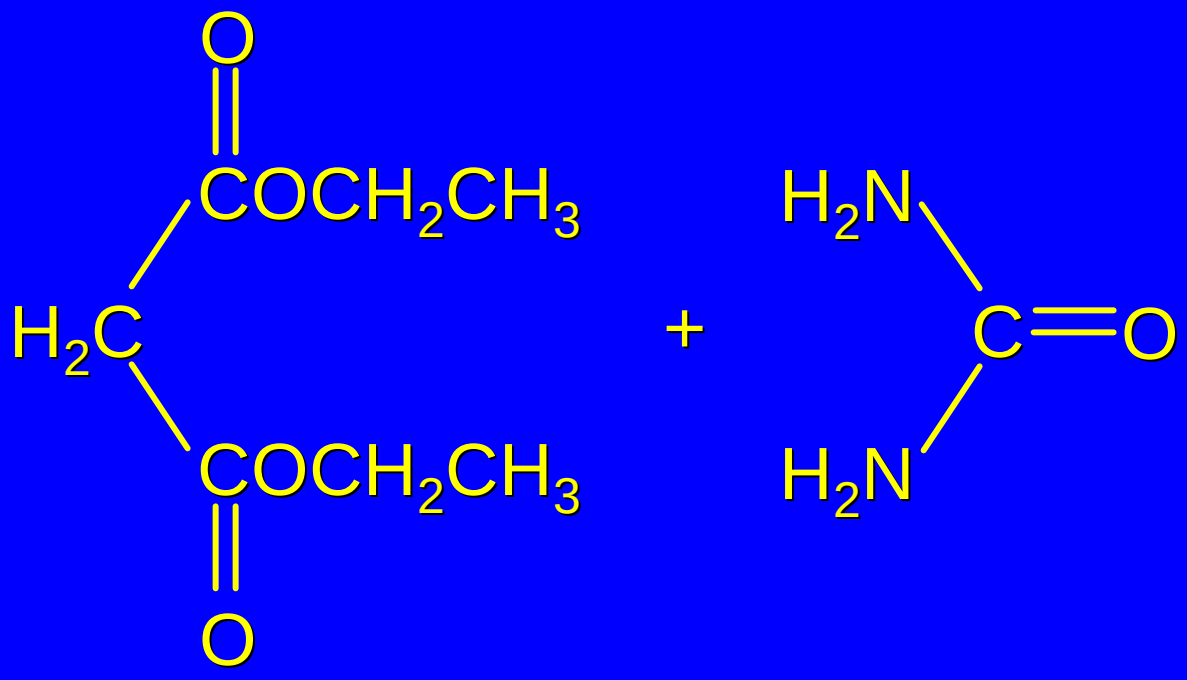
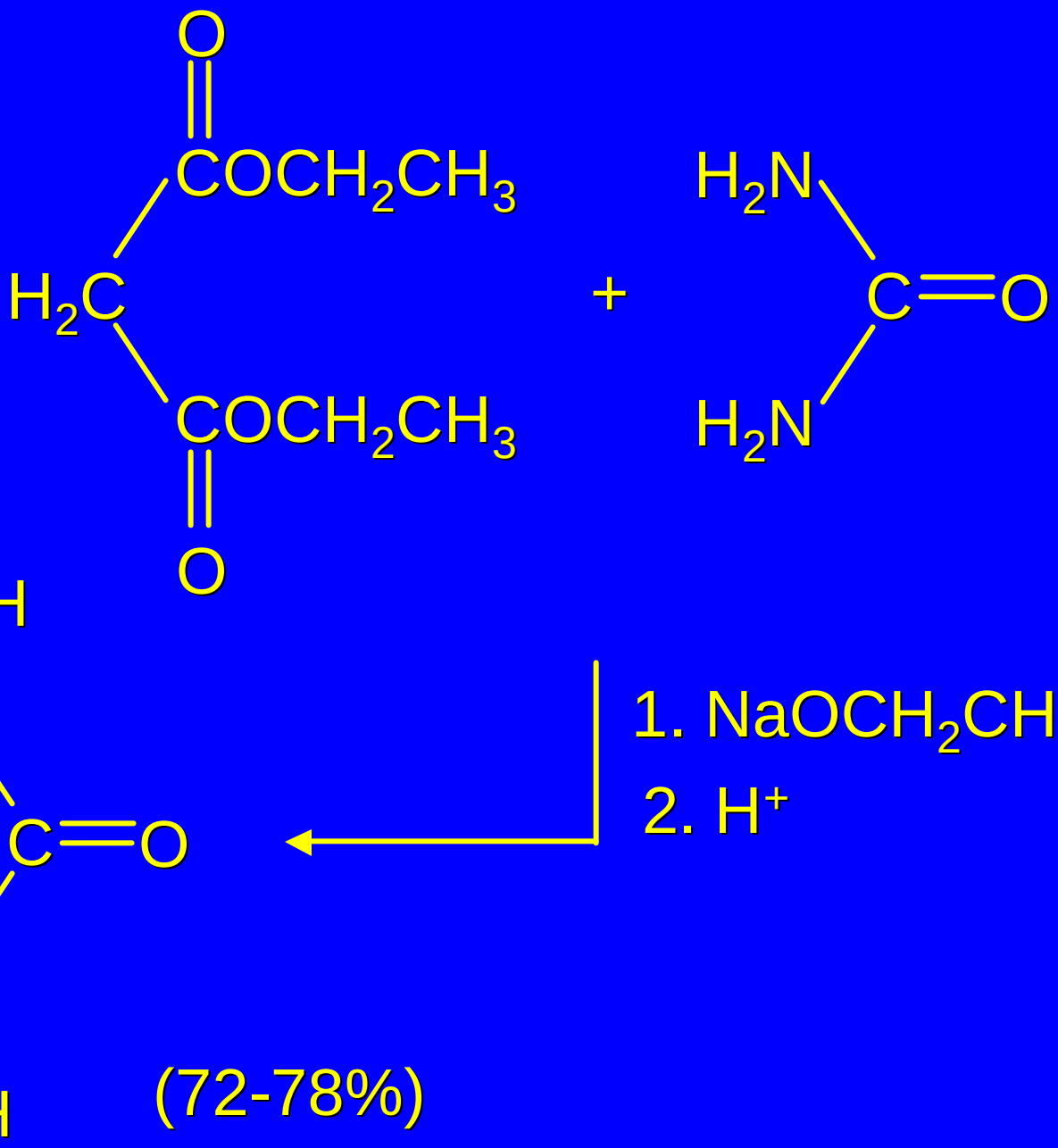
21.8

Barbiturates

Barbituric acid is made from diethyl malonate and urea

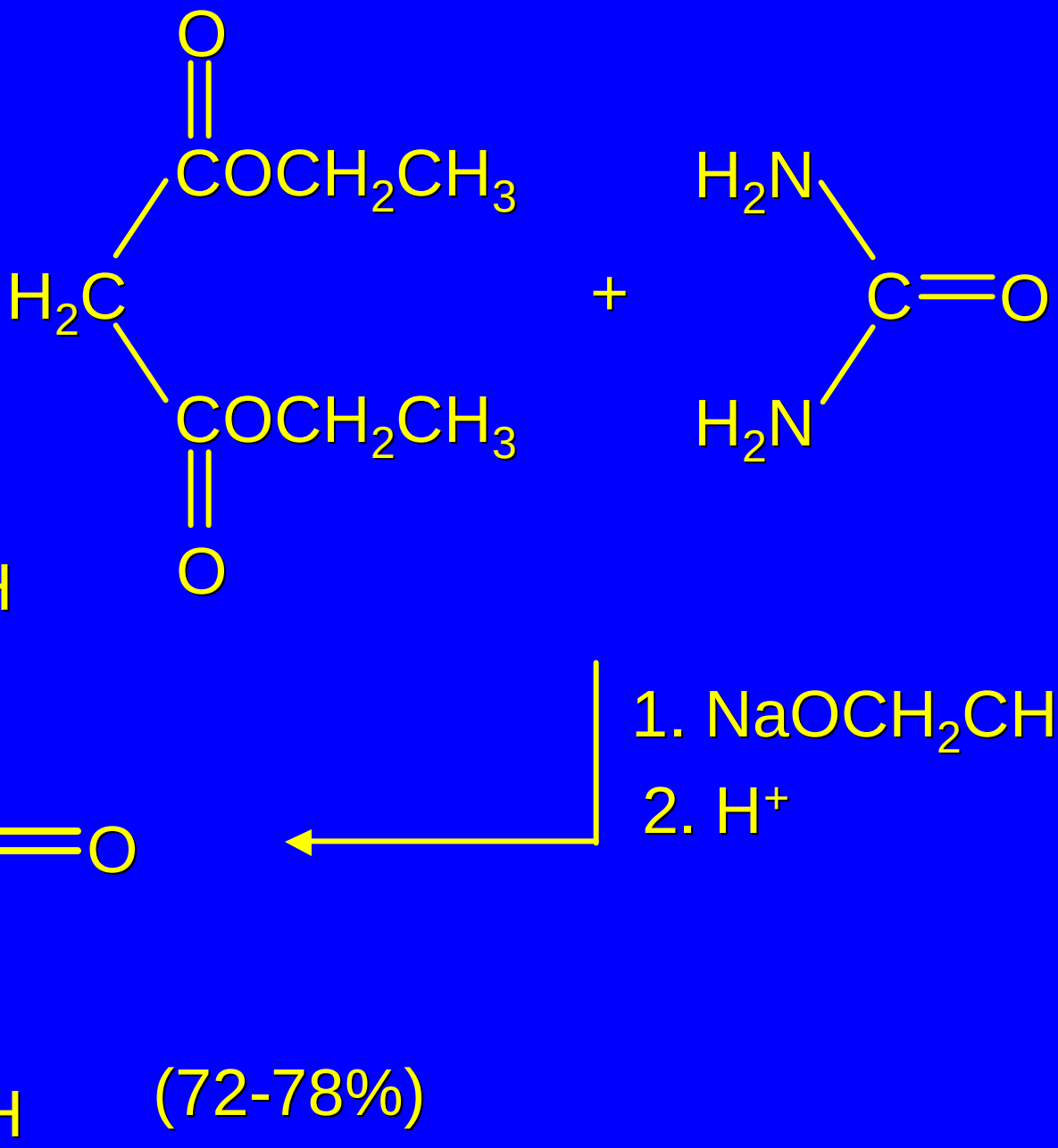


Barbituric acid is made from diethyl malonate and urea

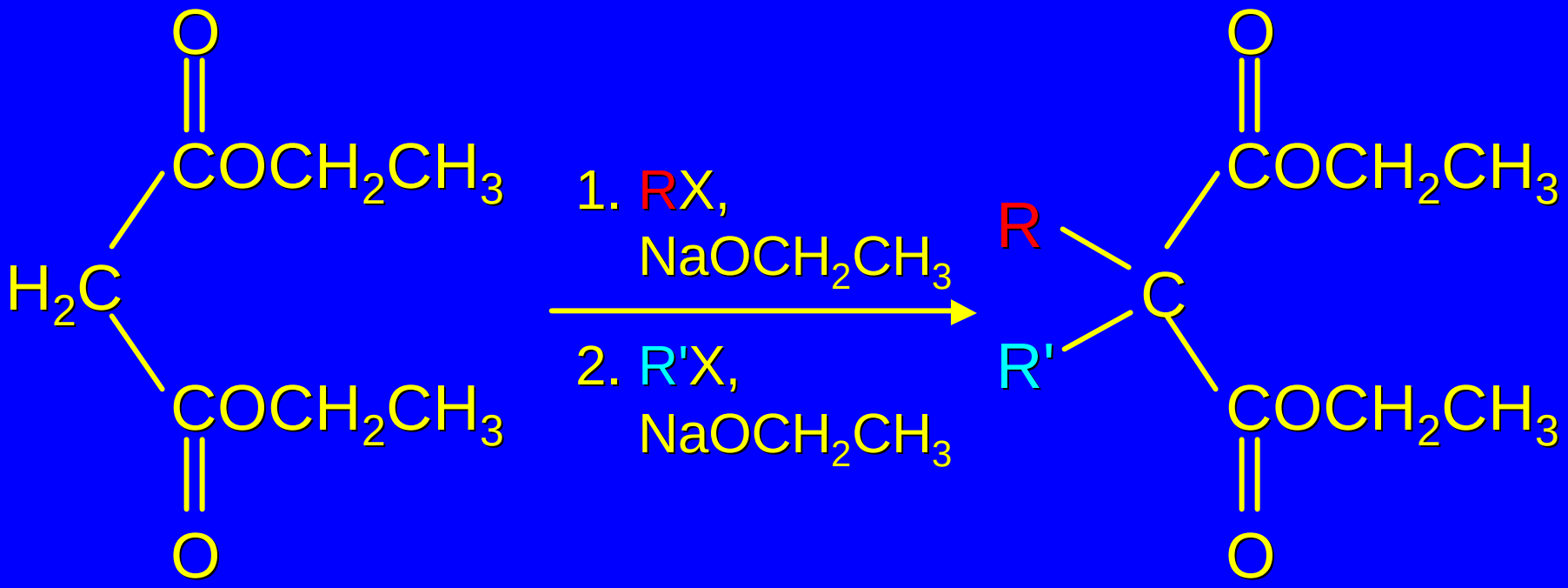


(72-78%)

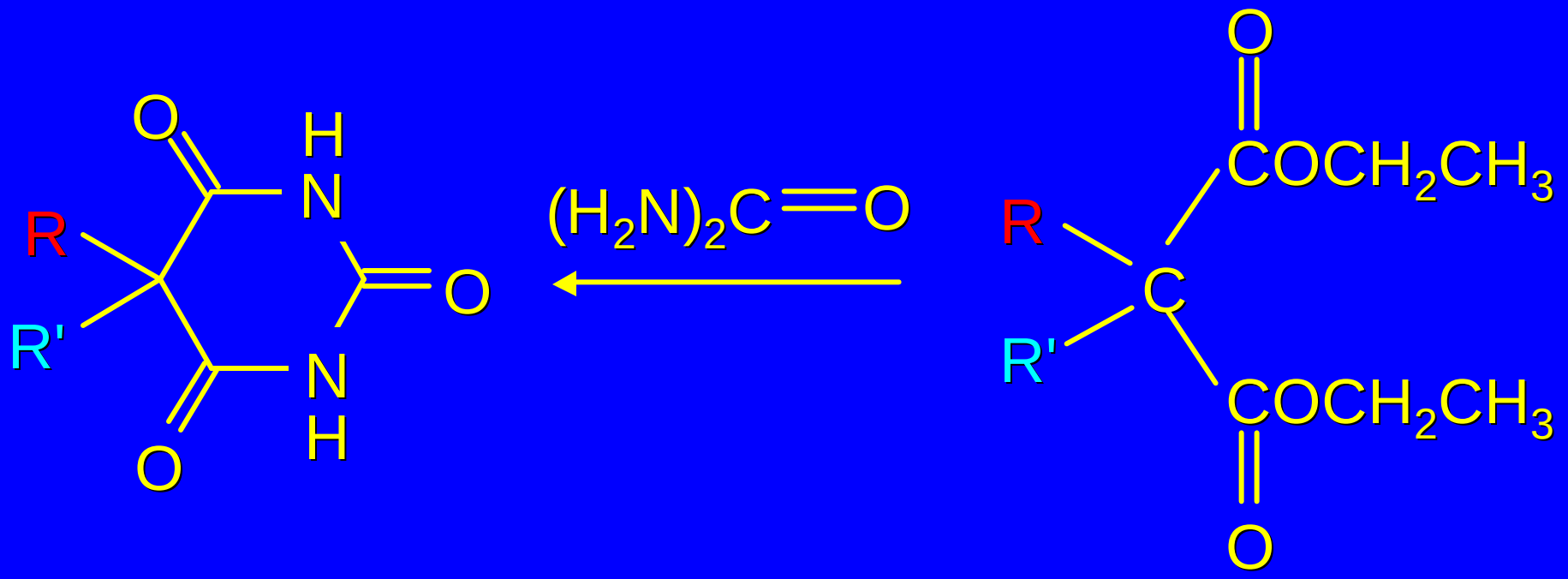
Barbituric acid is made from diethyl malonate and urea



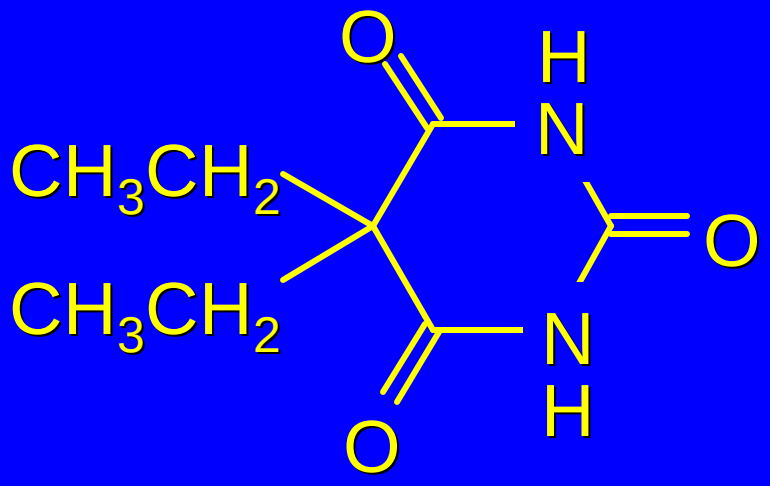
Substituted derivatives of barbituric acid are made from alkylated derivatives of diethyl malonate



Substituted derivatives of barbituric acid are made from alkylated derivatives of diethyl malonate

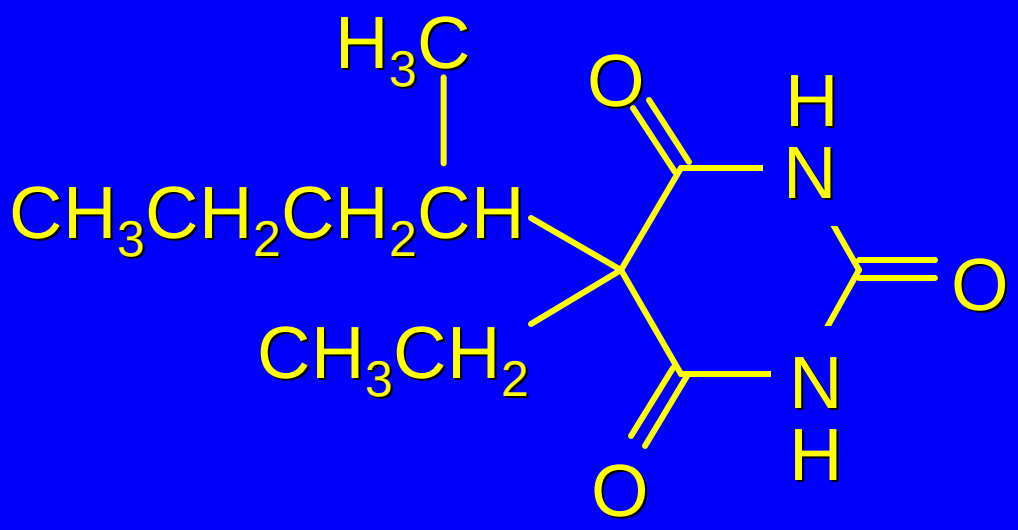


Examples



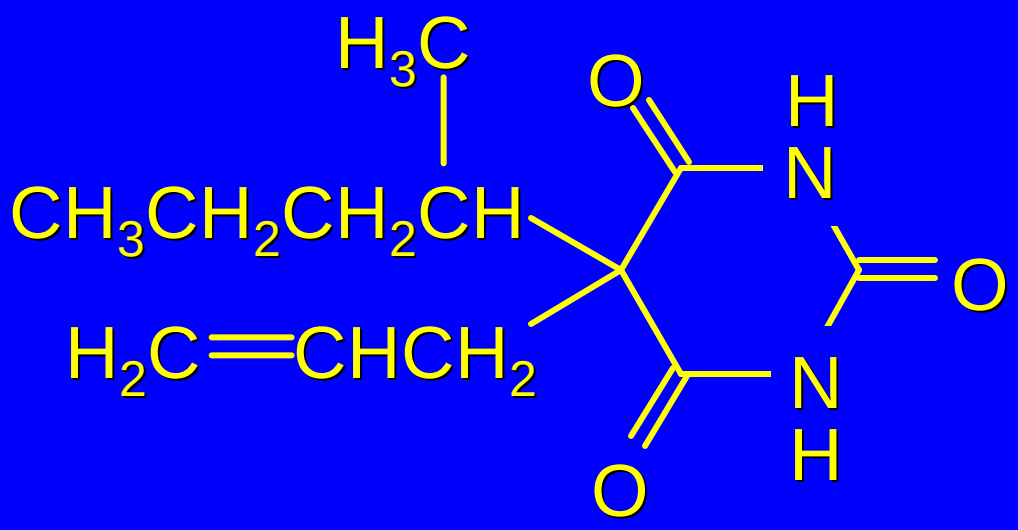
5,5-Diethylbarbituric acid
(barbital; Veronal)

Examples



5-Ethyl-5-(1-methylbutyl)barbituric acid
(pentobarbital; Nembutal)

Examples

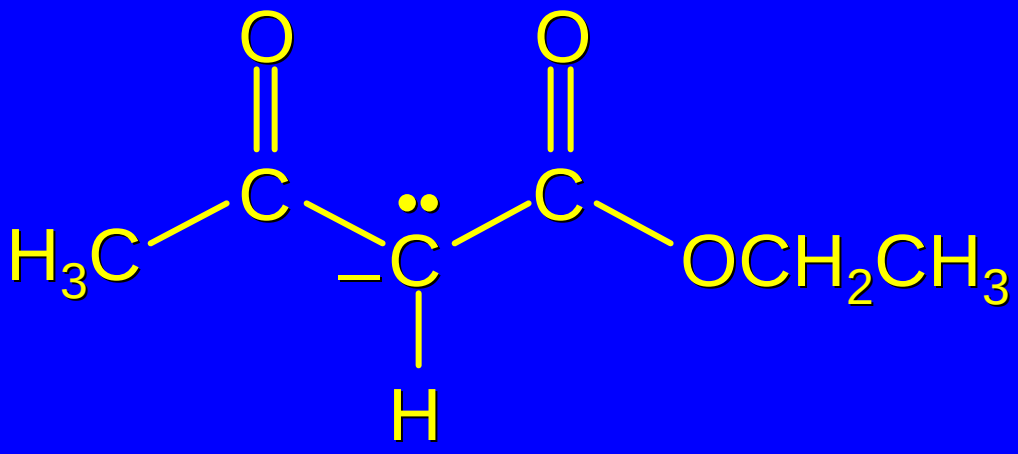


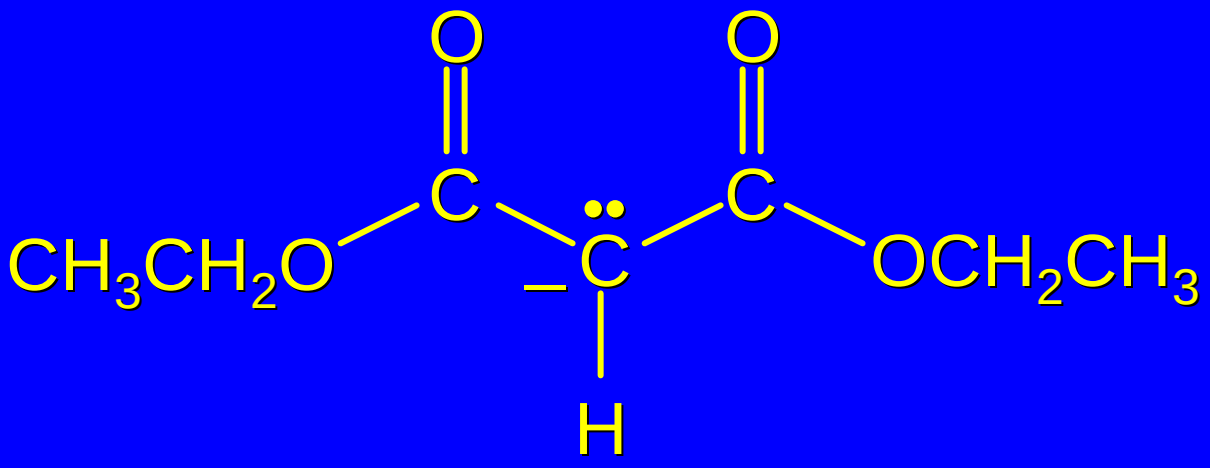
5-Allyl-5-(1-methylbutyl)barbituric acid
(secobarbital; Seconal)

21.9

Michael Additions of Stabilized Anions

Stabilized Anions

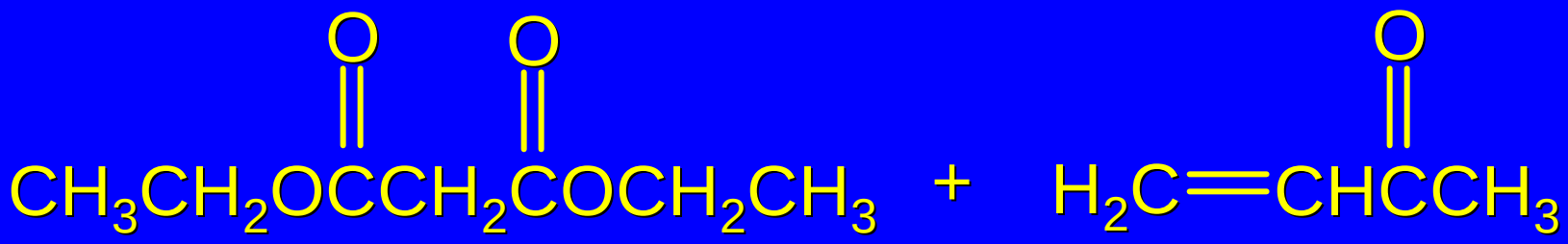




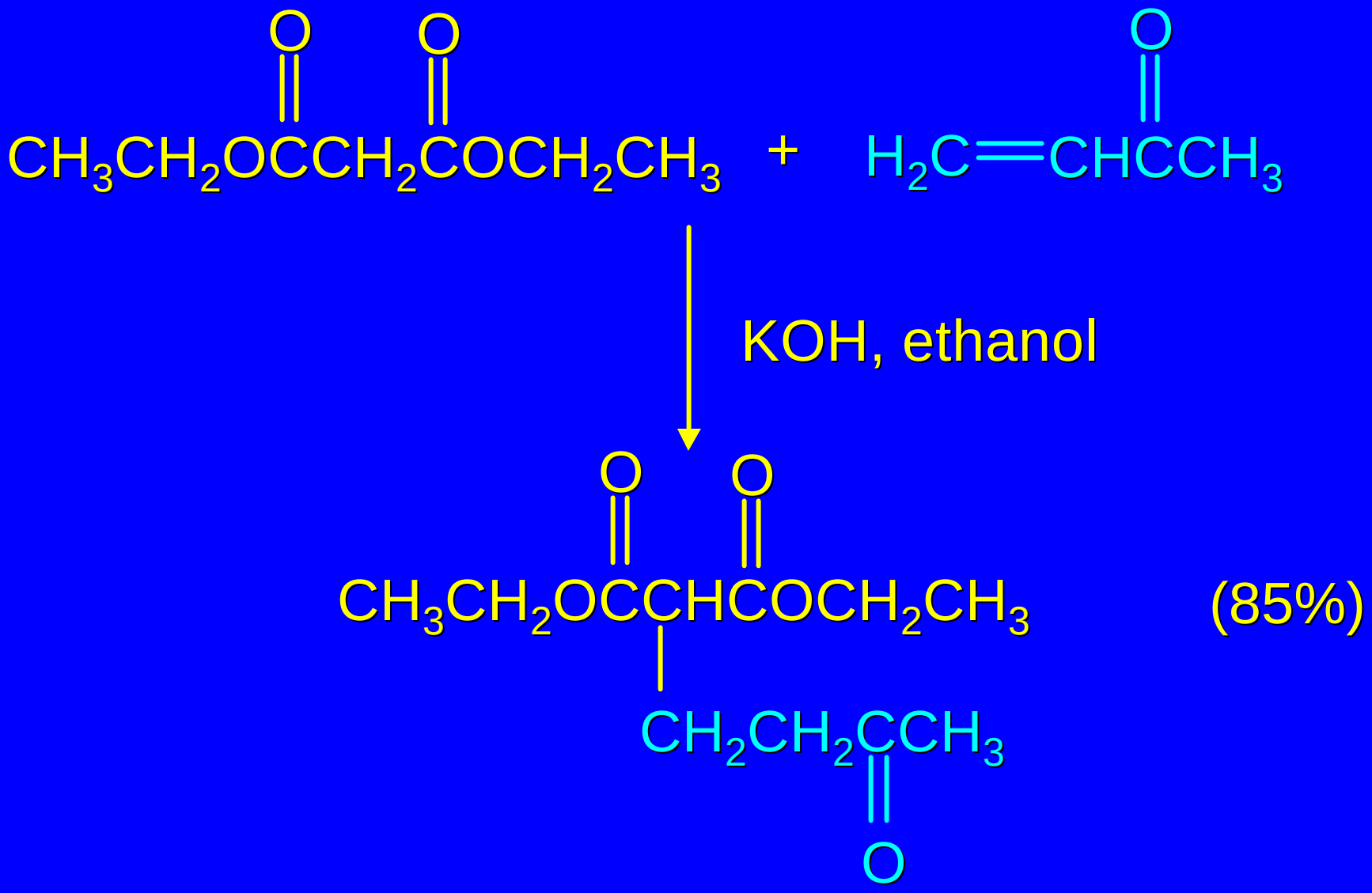
The anions derived by deprotonation of β-keto esters and diethyl malonate are weak bases.

Weak bases react with α,β-unsaturated carbonyl compounds by conjugate addition.

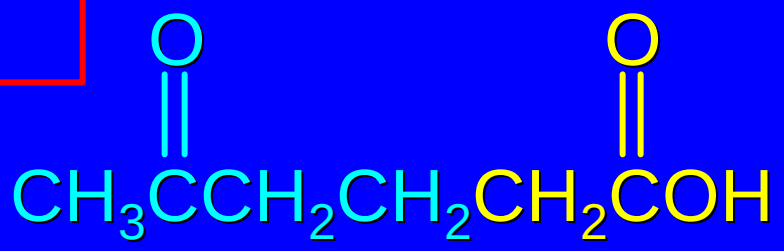
Example



Example

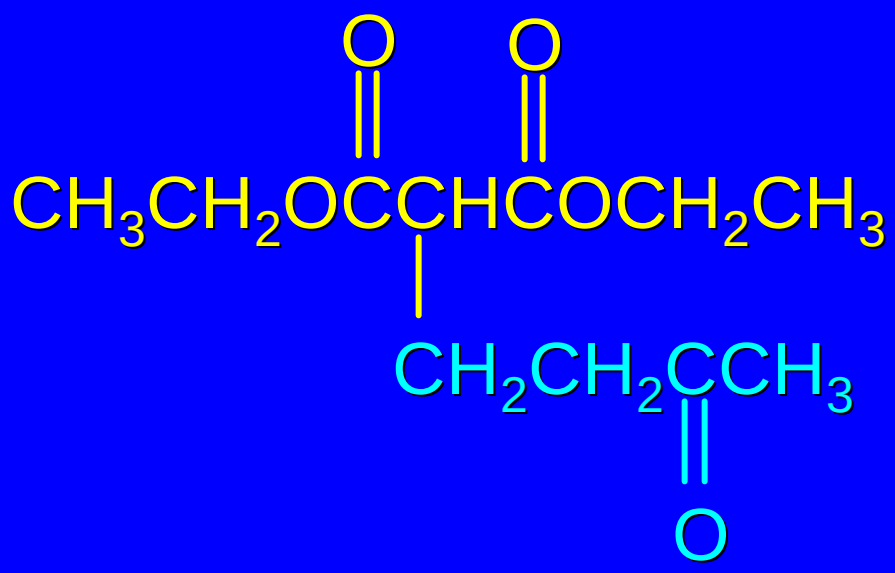

CH3CH2OCCH2COCH2CH3
+
H2C=CHCCH3
KOH, ethanol
CH3CH2OCCHCOCH2CH3
CH2CH2CCH3
(85%)

Example



(42%)

1. KOH, ethanol-water
2. H^+
3. heat



21.10
α-Deprotonation of Carbonyl Compounds by Lithium Dialkylamides

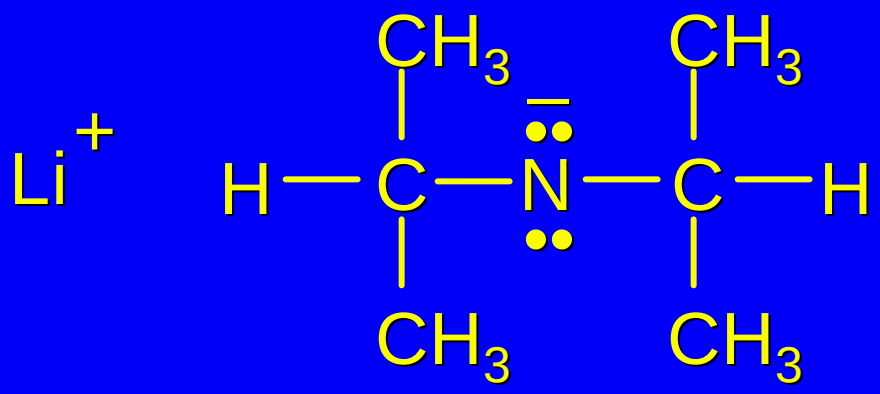
Deprotonation of Simple Esters

Ethyl acetoacetate (pKa ~11) and diethyl malonate (pKa ~13) are completely deprotonated by alkoxide bases.

Simple esters (such as ethyl acetate) are not completely deprotonated, the enolate reacts with the original ester, and Claisen condensation occurs.

Are there bases strong enough to completely deprotonate simple esters, giving ester enolates quantitatively?

Lithium diisopropylamide

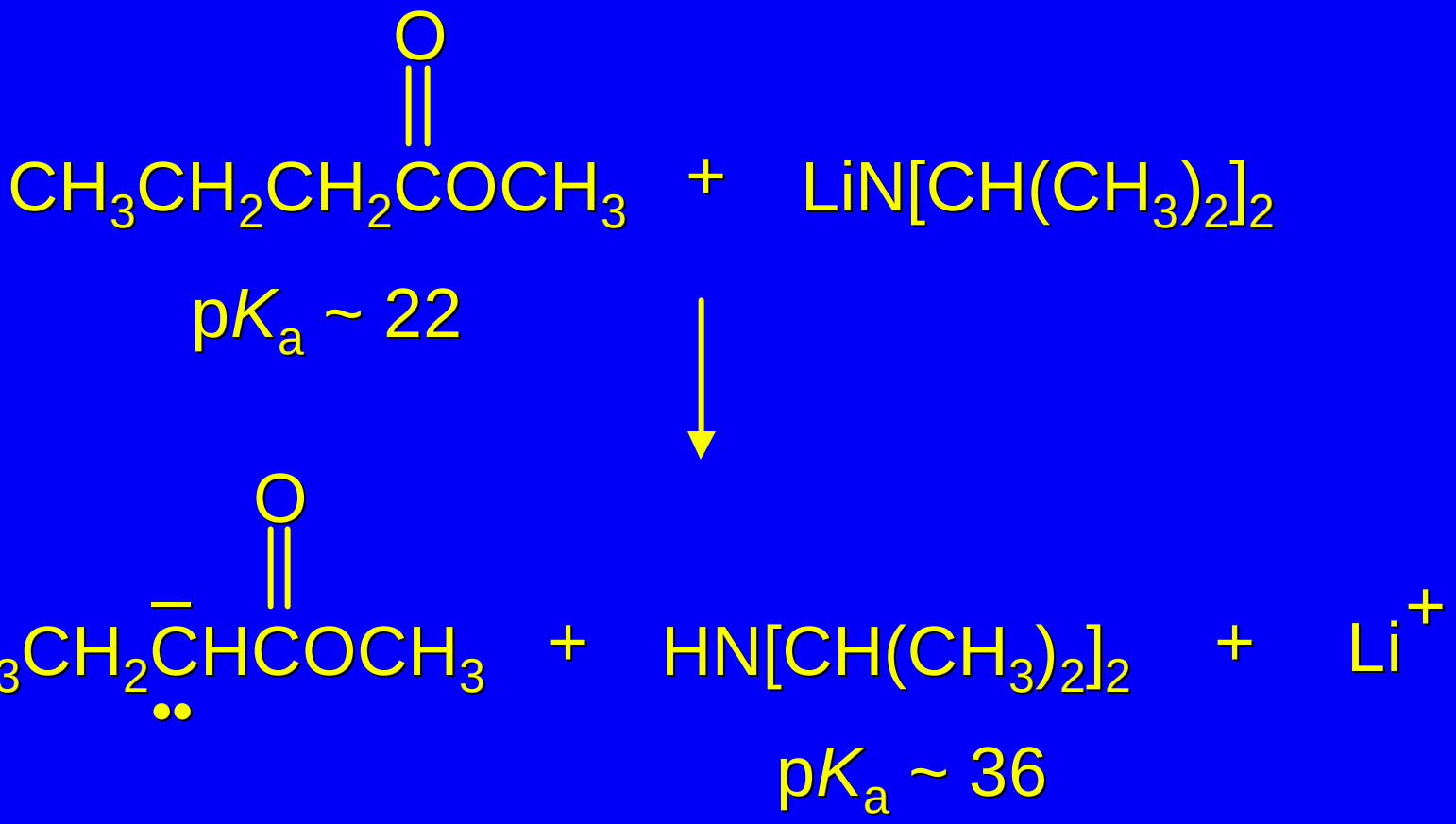


Lithium dialkylamides are strong bases (just as $NaNH_2$ is a very strong base).

Lithium diisopropylamide is a strong base, but because it is sterically hindered, does not add to carbonyl groups.

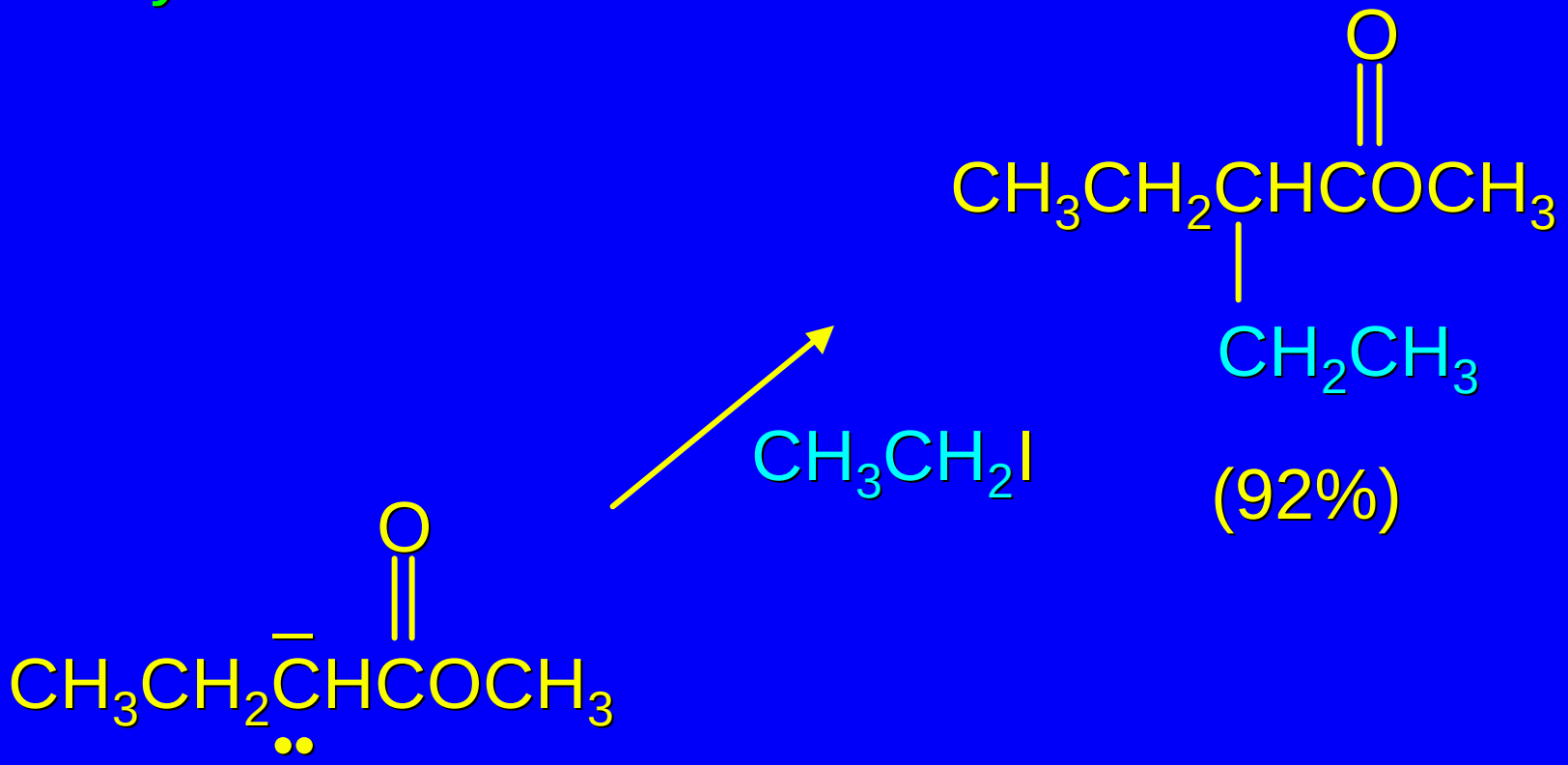
Lithium diisopropylamide (LDA)

Lithium diisopropylamide converts simple esters to the corresponding enolate.



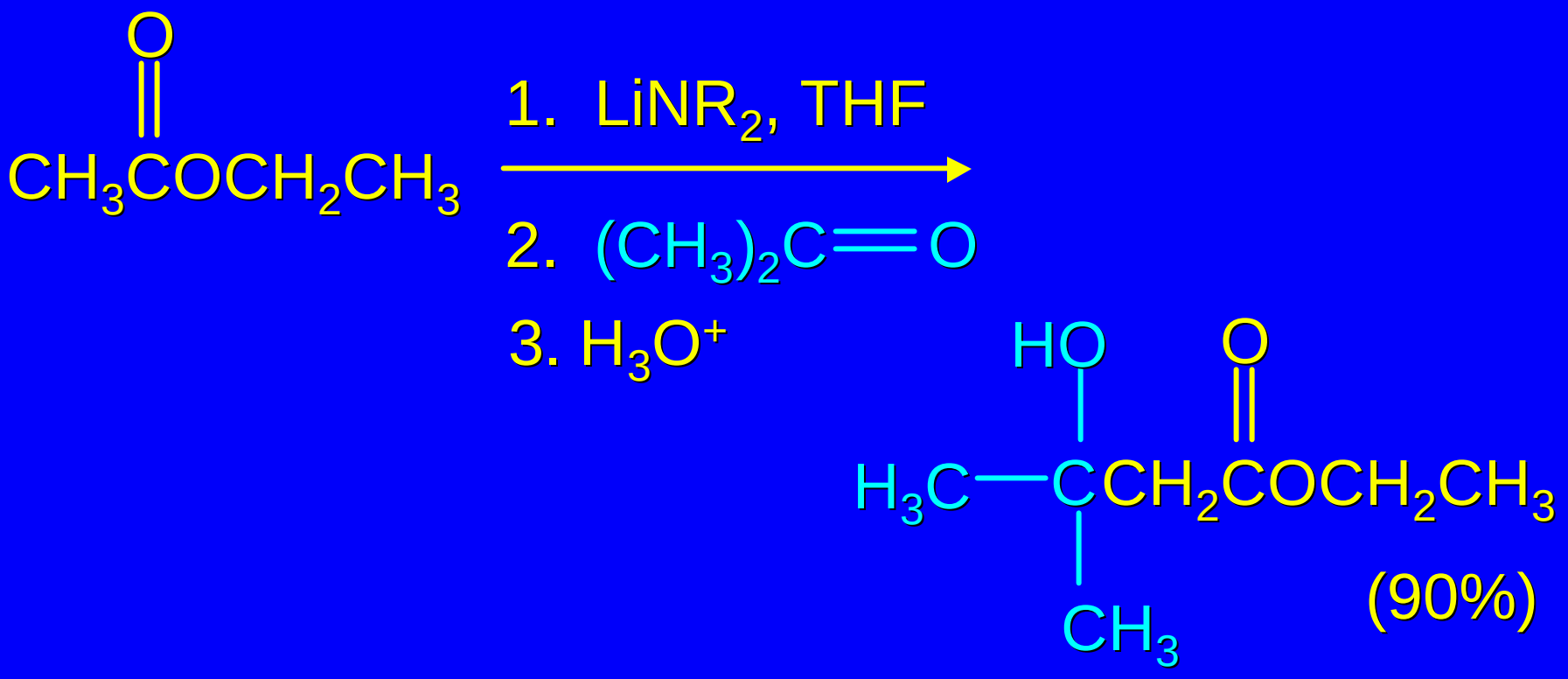
Lithium diisopropylamide (LDA)

Enolates generated from esters and LDA can be alkylated.



Aldol addition of ester enolates

Ester enolates undergo aldol addition to aldehydes and ketones.



Ketone Enolates

Lithium diisopropylamide converts ketones quantitatively to their enolates.