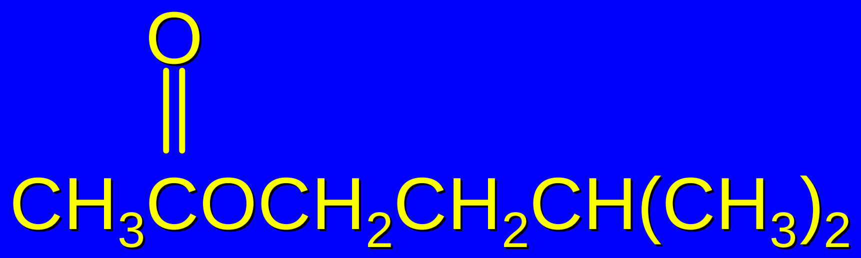
20.6

Sources of Esters

Esters are very common natural products



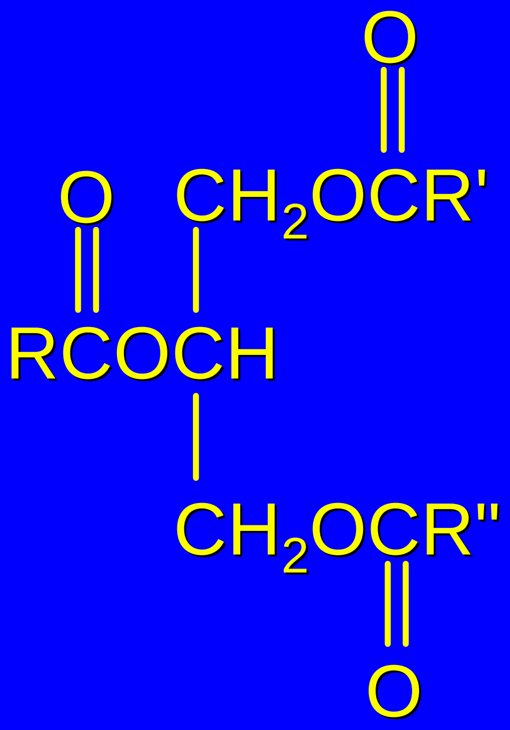
$$CH_3\overset{\overset{\displaystyle O}{\|}}{C}OCH_2CH_2CH(CH_3)_2$$

3-methylbutyl acetate

also called "isopentyl acetate" and "isoamyl acetate"

contributes to characteristic odor of bananas

Esters of Glycerol

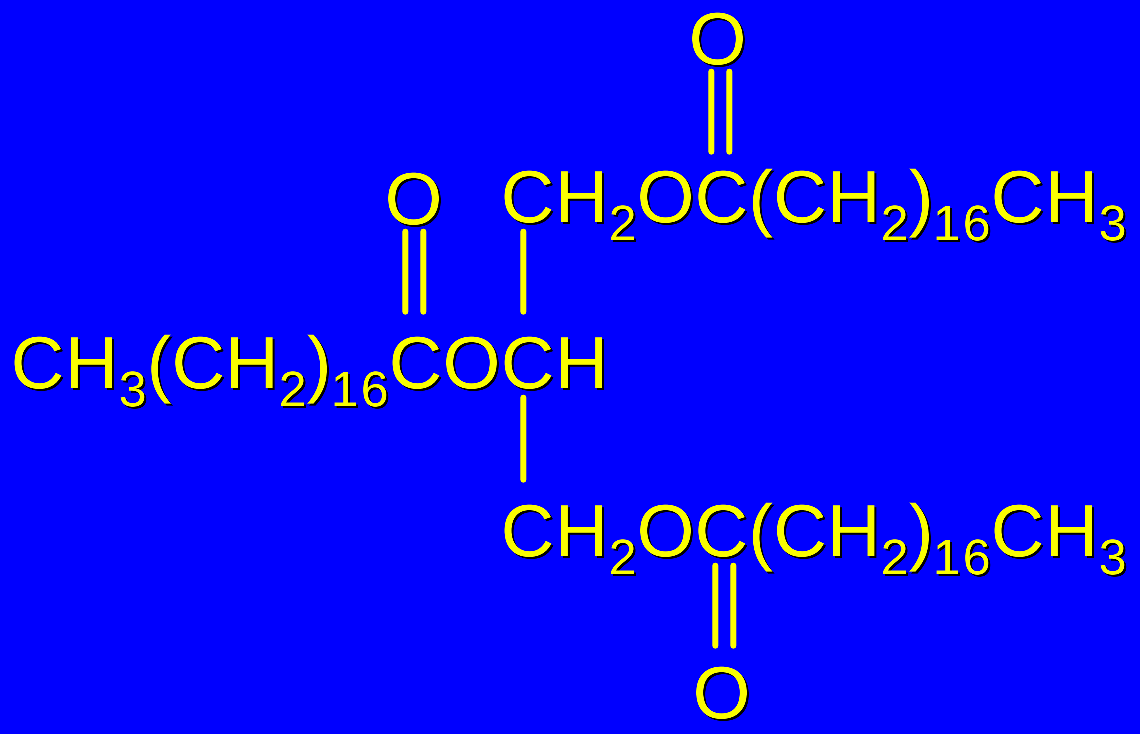


R, R', and R" can be the same or different

called "triacylglycerols," "glyceryl triesters," or "triglycerides"

fats and oils are mixtures of glyceryl triesters

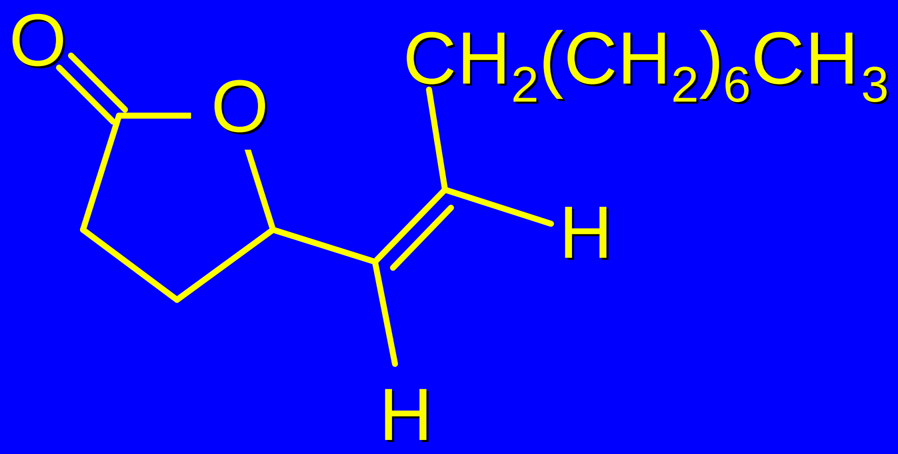
Esters of Glycerol



$$
\begin{array}{r@{}l}
 & CH_2O\overset{\overset{O}{\|}}{C}(CH_2)_{16}CH_3 \\
 & | \\
CH_3(CH_2)_{16}\overset{\overset{O}{\|}}{C}O & CH \\
 & | \\
 & CH_2O\underset{\underset{O}{\|}}{C}(CH_2)_{16}CH_3
\end{array}
$$

Tristearin: found in many animal and vegetable fats

Cyclic Esters (Lactones)



(Z)-5-Tetradecen-4-olide
(sex pheromone of female Japanese beetle)

Preparation of Esters

Fischer esterification (Sections 15.8 and 19.14)

from acyl chlorides (Sections 15.8 and 20.3)

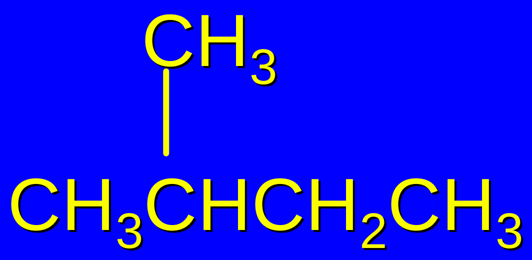
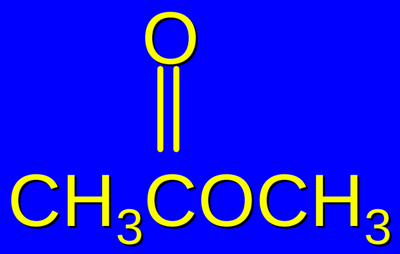
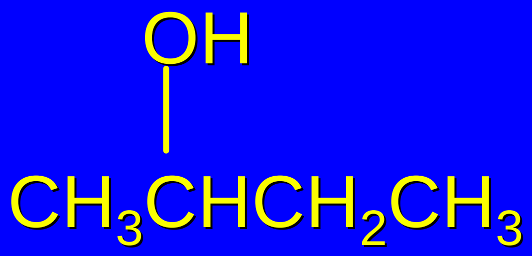
from carboxylic acid anhydrides (Sections 15.8 and 20.5)

Baeyer-Villiger oxidation of ketones (Section 17.16)

20.7

Physical Properties of Esters

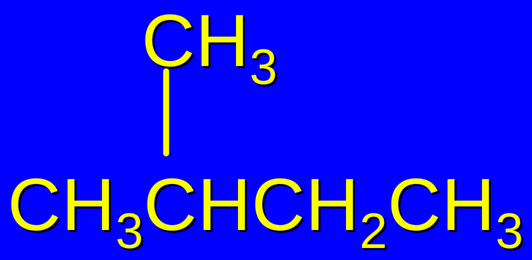
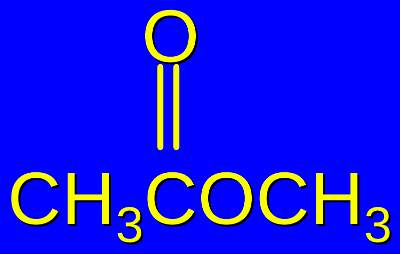
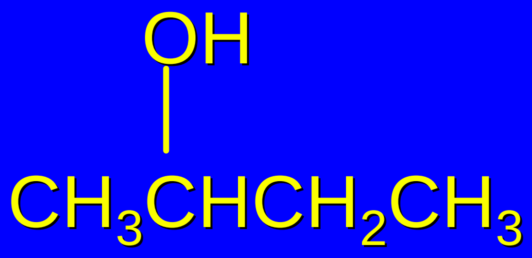
Boiling Points

	boiling point
 $CH_3\overset{\overset{CH_3}{\mid}}{C}HCH_2CH_3$	28°C
 $CH_3\overset{\overset{O}{\|}}{C}OCH_3$	57°C
 $CH_3\overset{\overset{OH}{\mid}}{C}HCH_2CH_3$	99°C

Esters have higher boiling points than alkanes because they are more polar.

Esters cannot form hydrogen bonds to other ester molecules, so have lower boiling points than alcohols.

Solubility in Water

	Solubility (g/100 g)
 $CH_3\overset{CH_3}{\overset{\vert}{C}}HCH_2CH_3$	~0
 $CH_3\overset{O}{\overset{\Vert}{C}}OCH_3$	33
 $CH_3\overset{OH}{\overset{\vert}{C}}HCH_2CH_3$	12.5

Esters can form hydrogen bonds to water, so low molecular weight esters have significant solubility in water.

Solubility decreases with increasing number of carbons.

20.8

Reactions of Esters: A Review and a Preview

Reactions of Esters

with Grignard reagents (Section 14.10)

reduction with $LiAlH_4$ (Section 15.3)

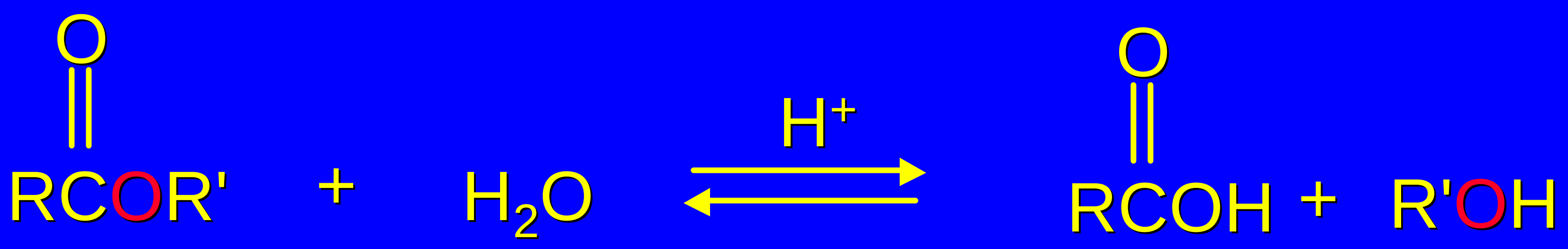
with ammonia and amines (Sections 20.13)

hydrolysis (Sections 20.9 and 20.10)

20.9
Acid-Catalyzed Ester Hydrolysis

Acid-Catalyzed Ester Hydrolysis

is the reverse of Fischer esterification



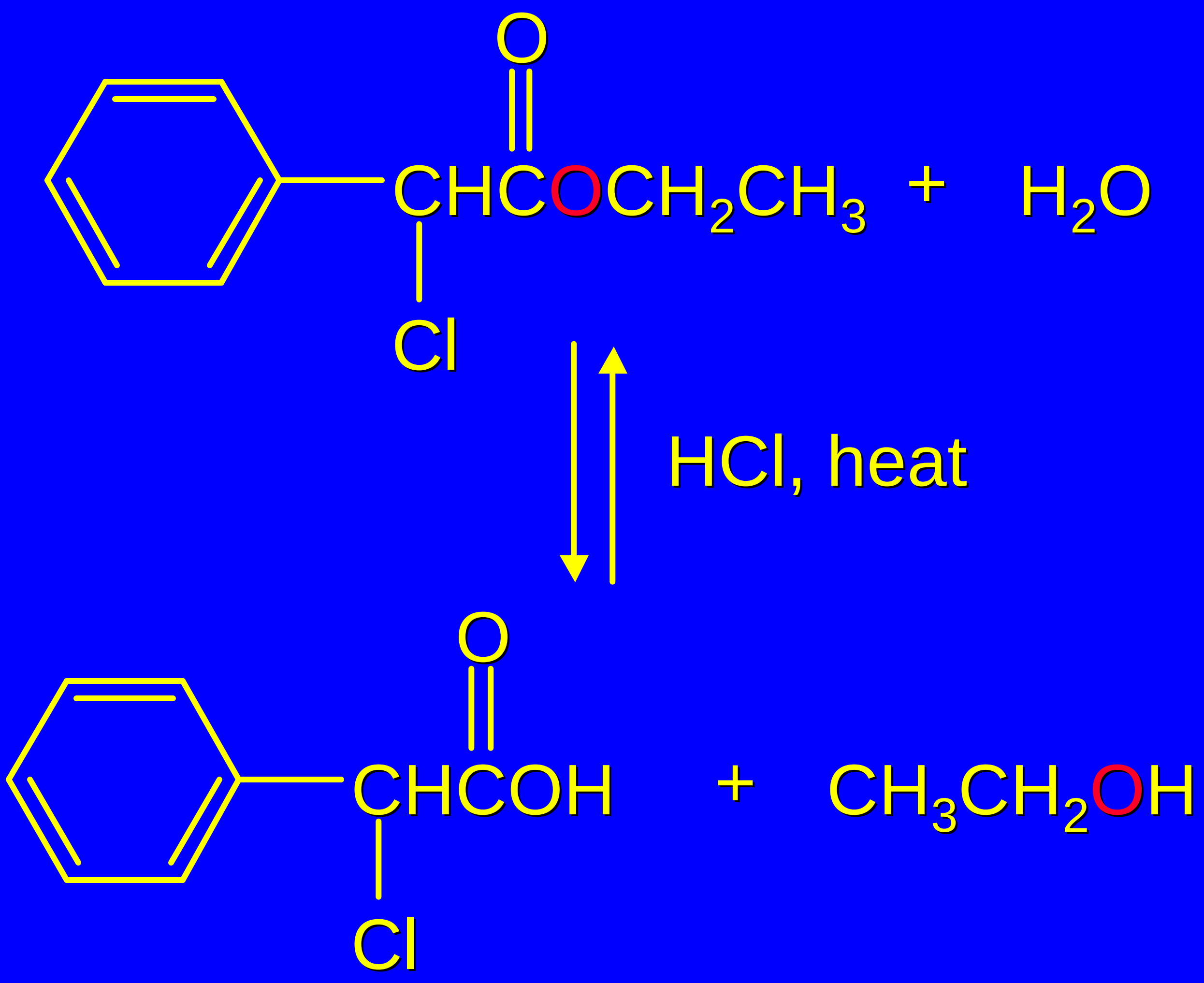
$$\mathrm{R}\overset{\overset{\mathrm{O}}{\|}}{\mathrm{C}}\mathrm{OR'} + \mathrm{H_2O} \overset{\mathrm{H^+}}{\rightleftharpoons} \mathrm{R}\overset{\overset{\mathrm{O}}{\|}}{\mathrm{C}}\mathrm{OH} + \mathrm{R'OH}$$

maximize conversion to ester by removing water

maximize ester hydrolysis by having large excess of water

equilibrium is closely balanced because carbonyl group of ester and of carboxylic acid are comparably stabilized

Example



HCl, heat

(80-82%)

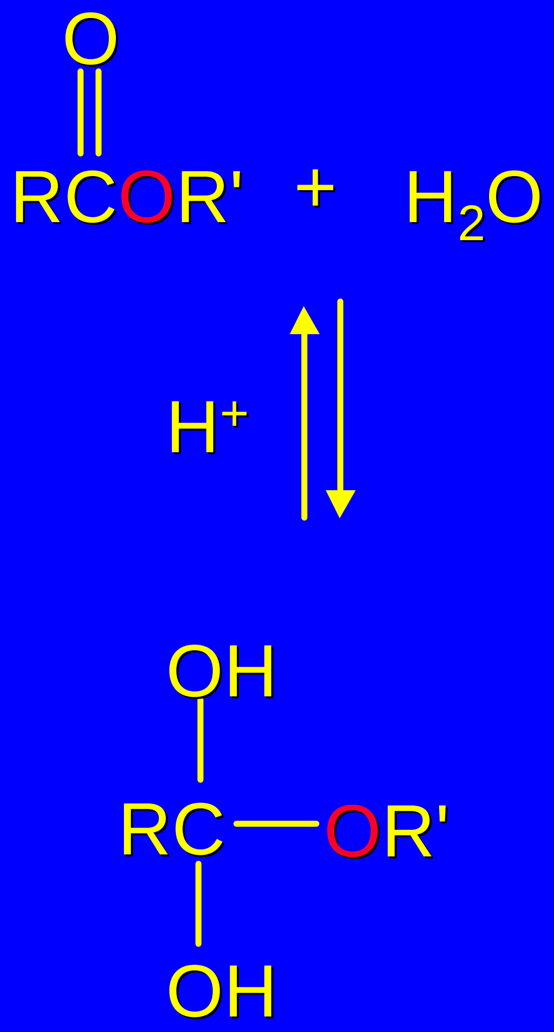
Mechanism of Acid-Catalyzed Ester Hydrolysis

Is the reverse of the mechanism for acid-catalyzed esterification.

Like the mechanism of esterification, it involves two stages:

1) formation of tetrahedral intermediate (3 steps)
2) dissociation of tetrahedral intermediate (3 steps)

First stage: formation of tetrahedral intermediate

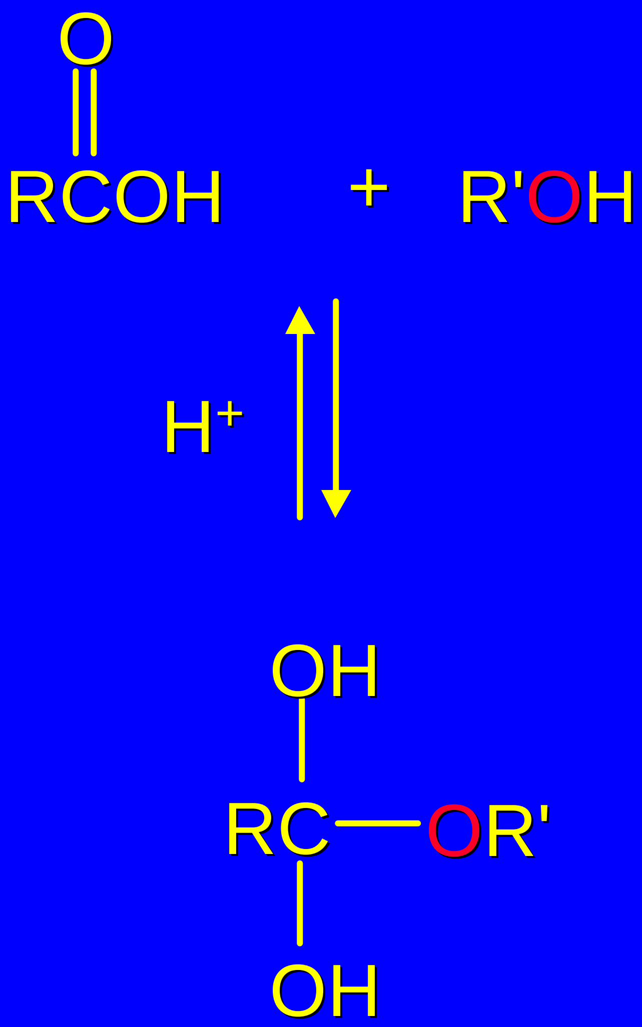


$$R\overset{\overset{\displaystyle O}{\|}}{C}OR' + H_2O \xrightleftharpoons{H^+} R\underset{\underset{\displaystyle OH}{|}}{\overset{\overset{\displaystyle OH}{|}}{C}}-OR'$$

water adds to the carbonyl group of the ester

this stage is analogous to the acid-catalyzed addition of water to a ketone

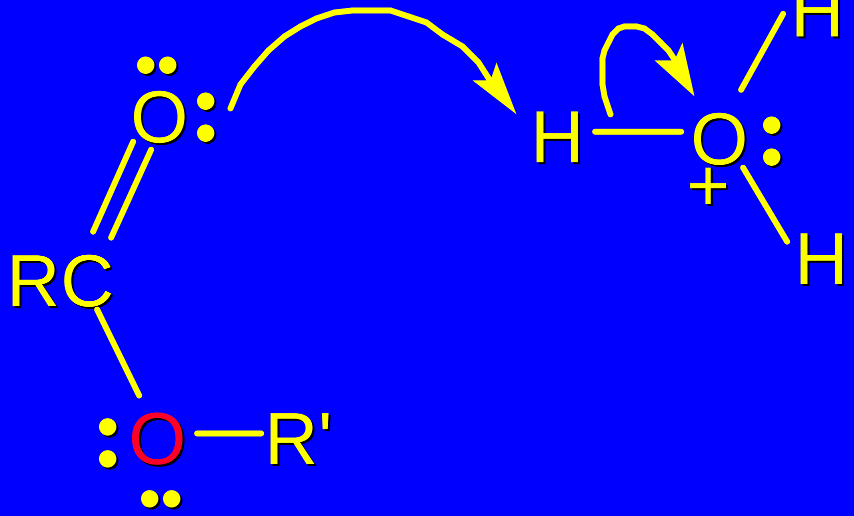
Second stage: cleavage of tetrahedral intermediate



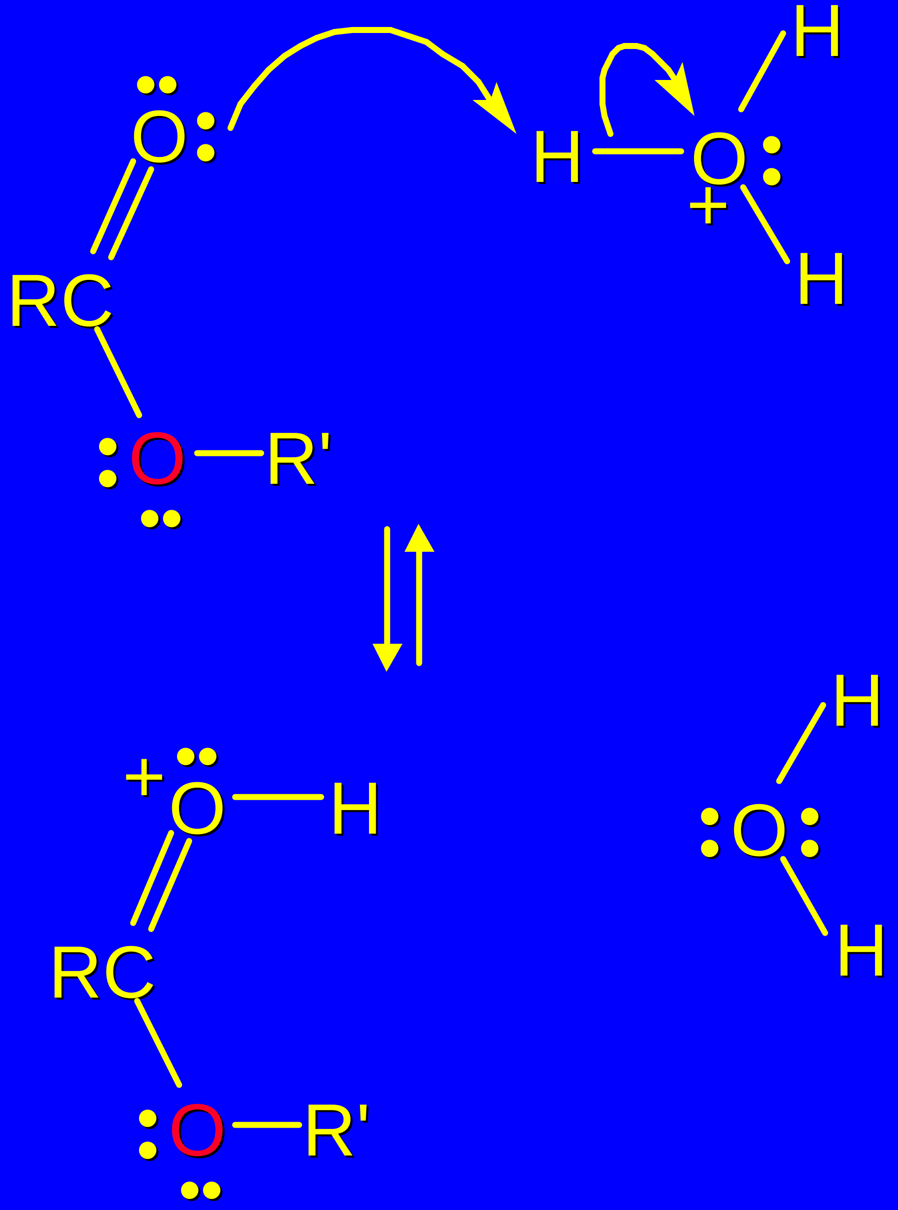
$$\mathrm{R\overset{\overset{O}{\|}}{C}OH} + \mathrm{R'OH} \quad \underset{H^+}{\rightleftharpoons} \quad \mathrm{R\underset{\underset{OH}{|}}{\overset{\overset{OH}{|}}{C}}\!-\!OR'}$$

Mechanism of formation of tetrahedral intermediate

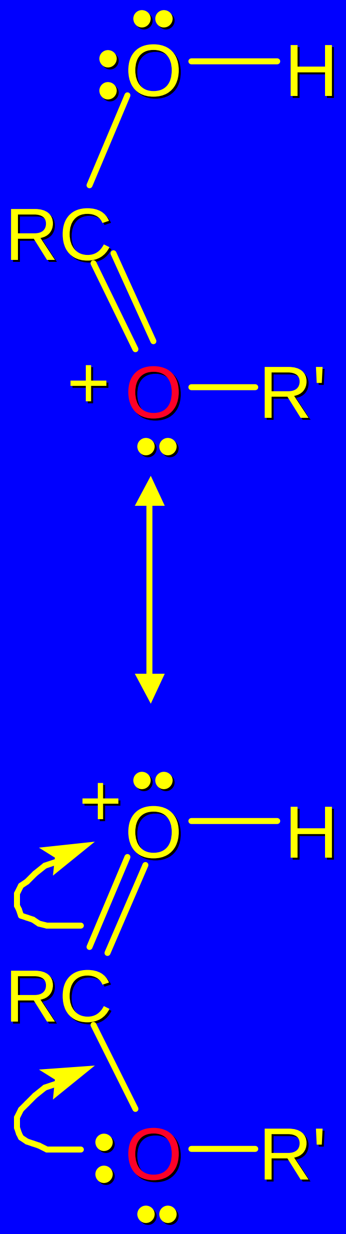
Step 1



Step 1

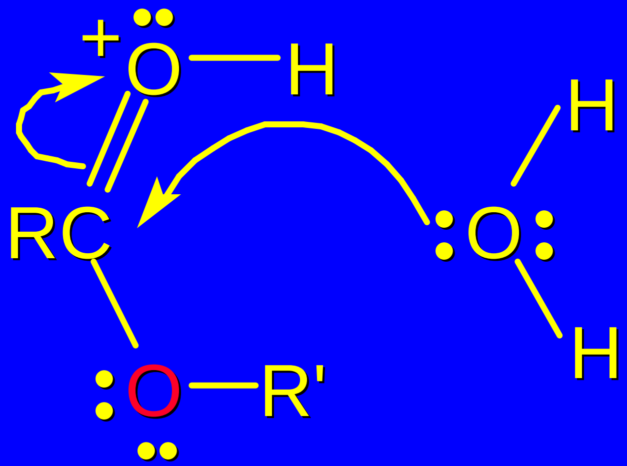


Step 1

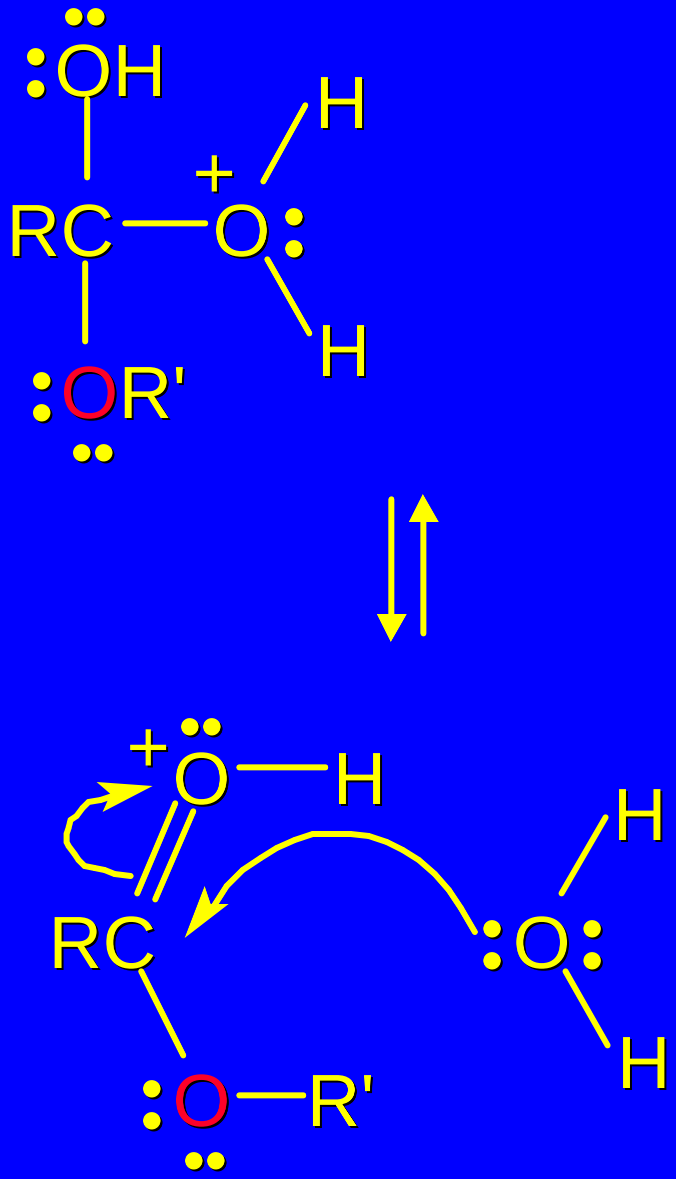


carbonyl oxygen is protonated because cation produced is stabilized by electron delocalization (resonance)

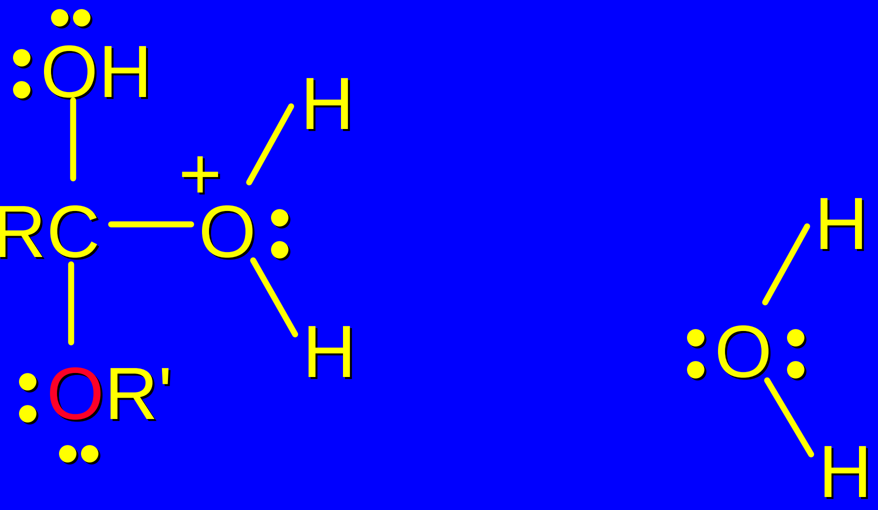
Step 2



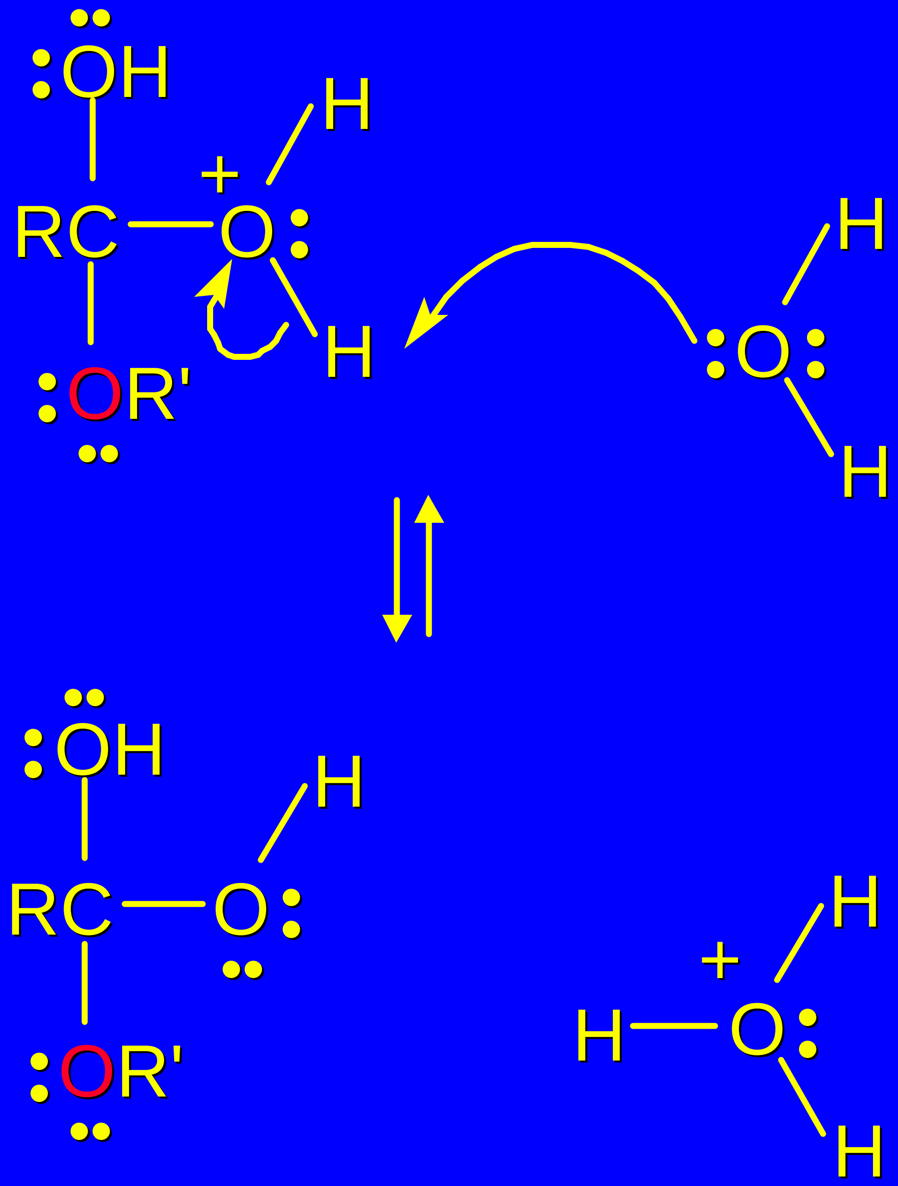
Step 2



Step 3

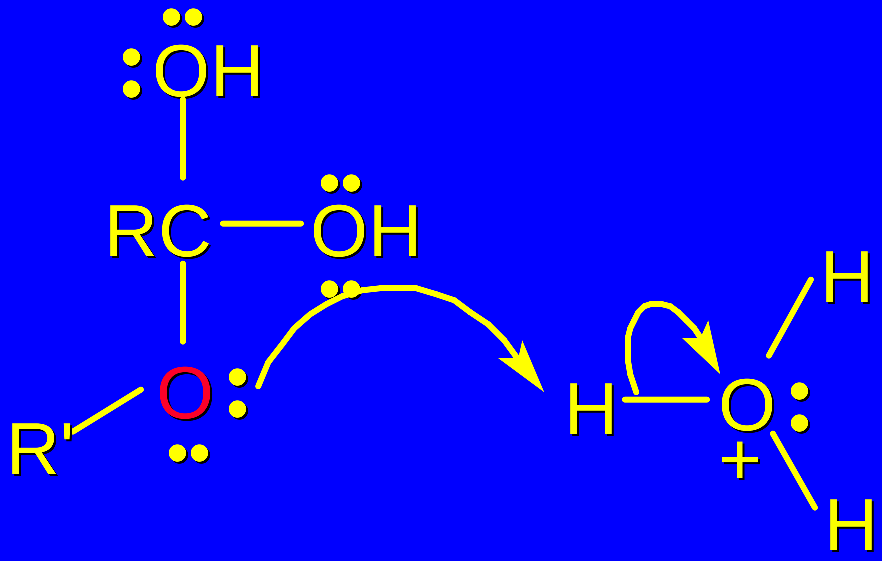


Step 3

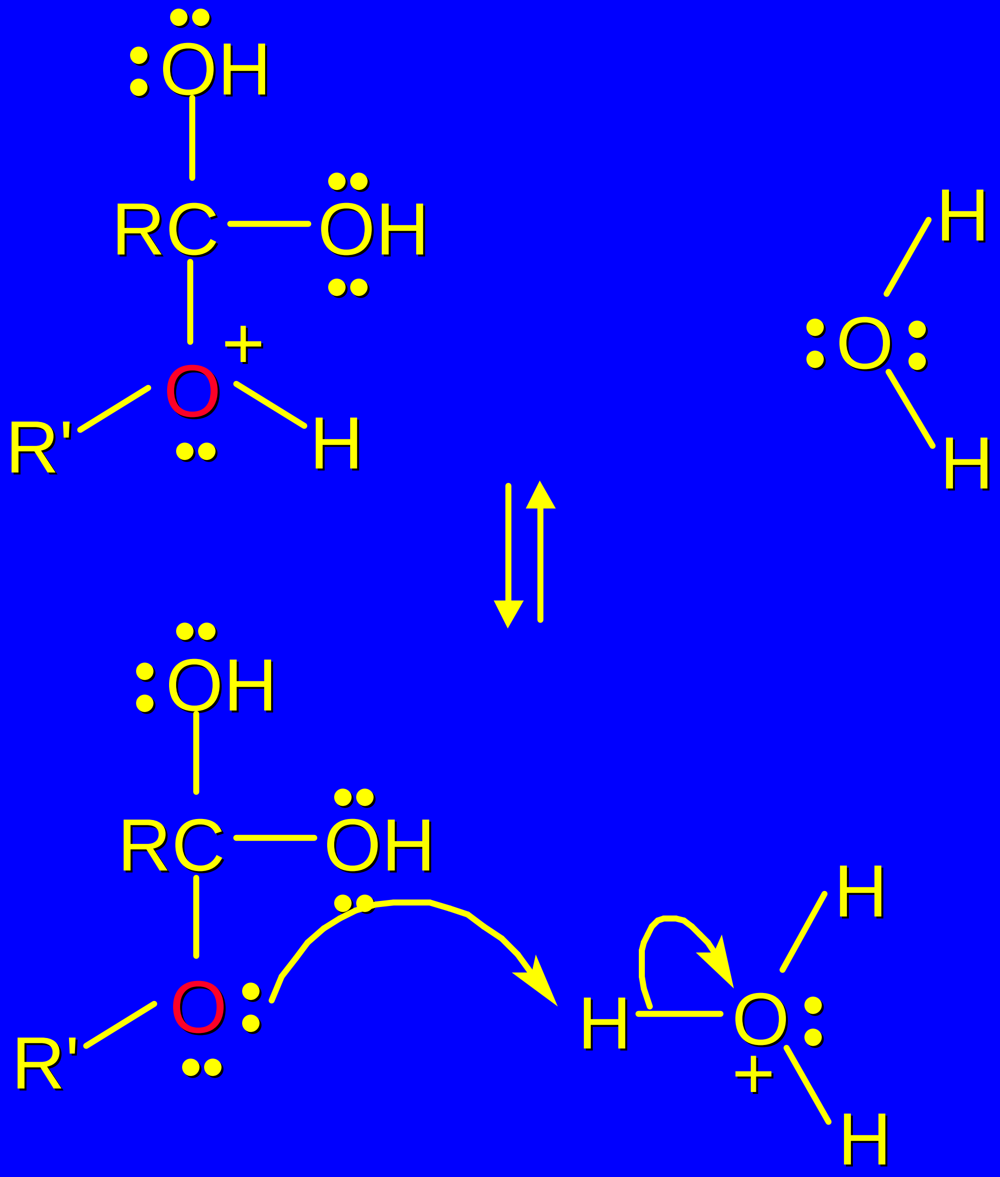


Cleavage of tetrahedral intermediate

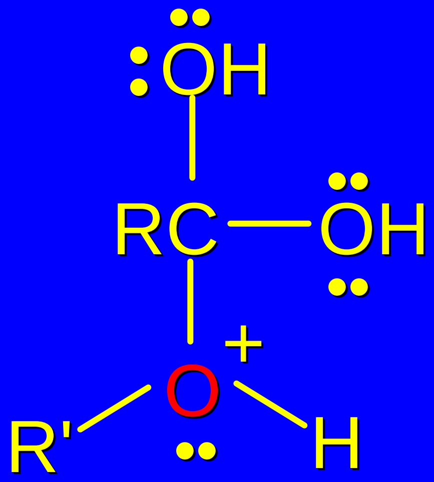
Step 4



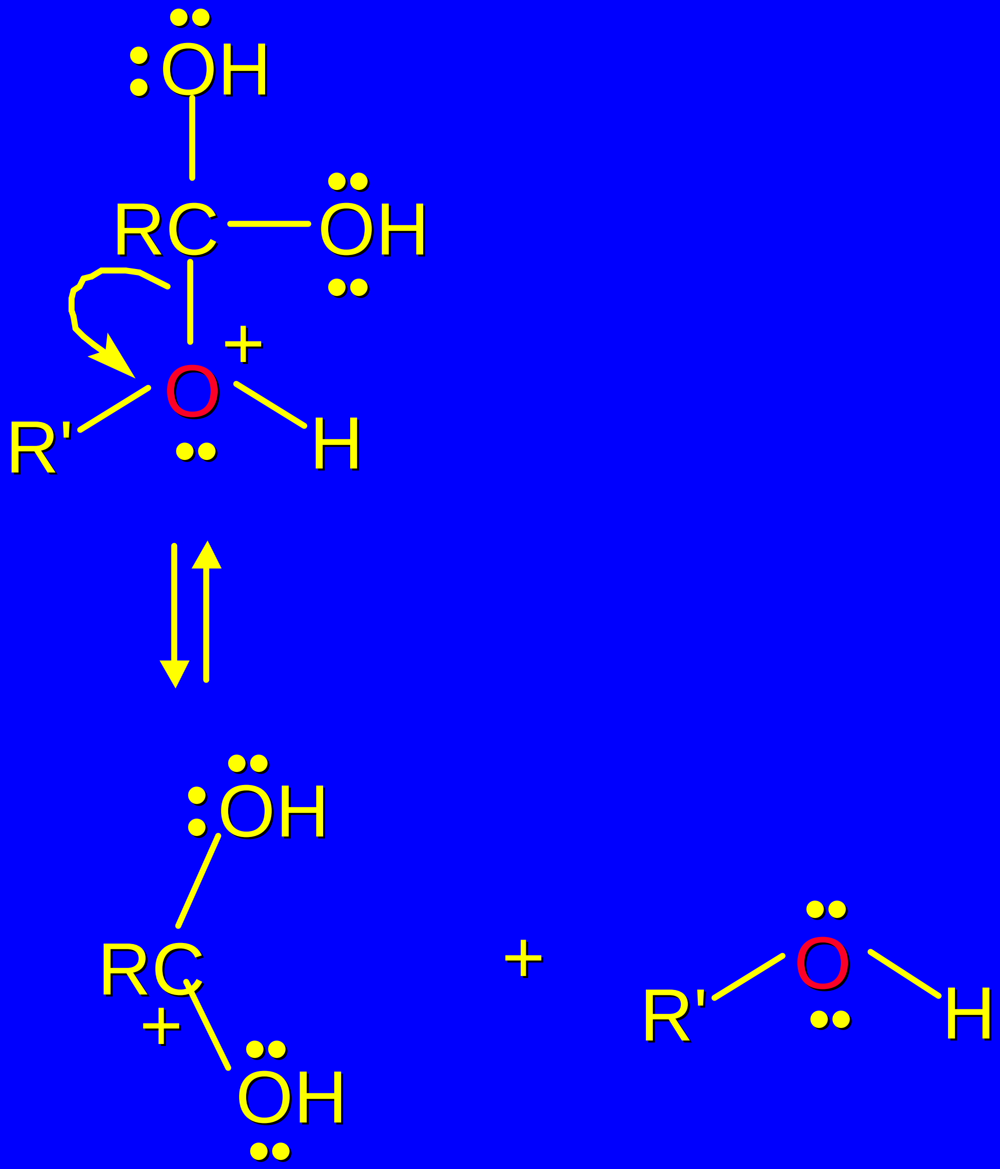
Step 4



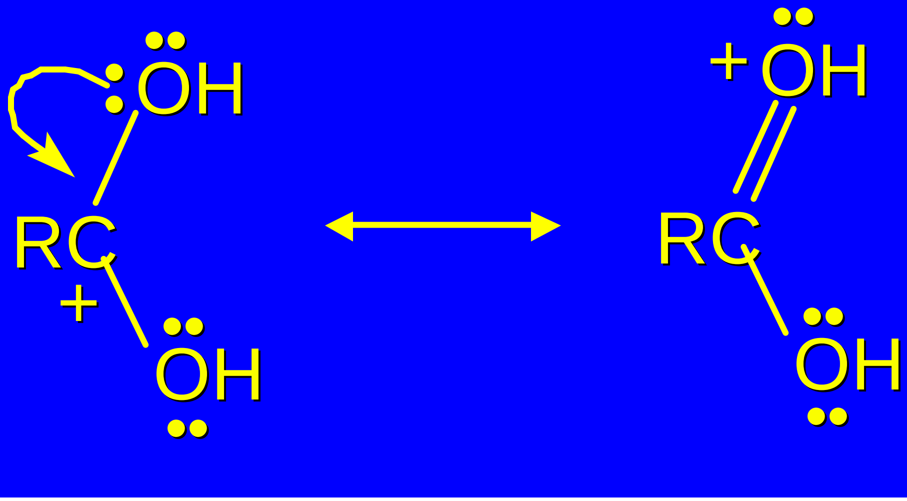
Step 5



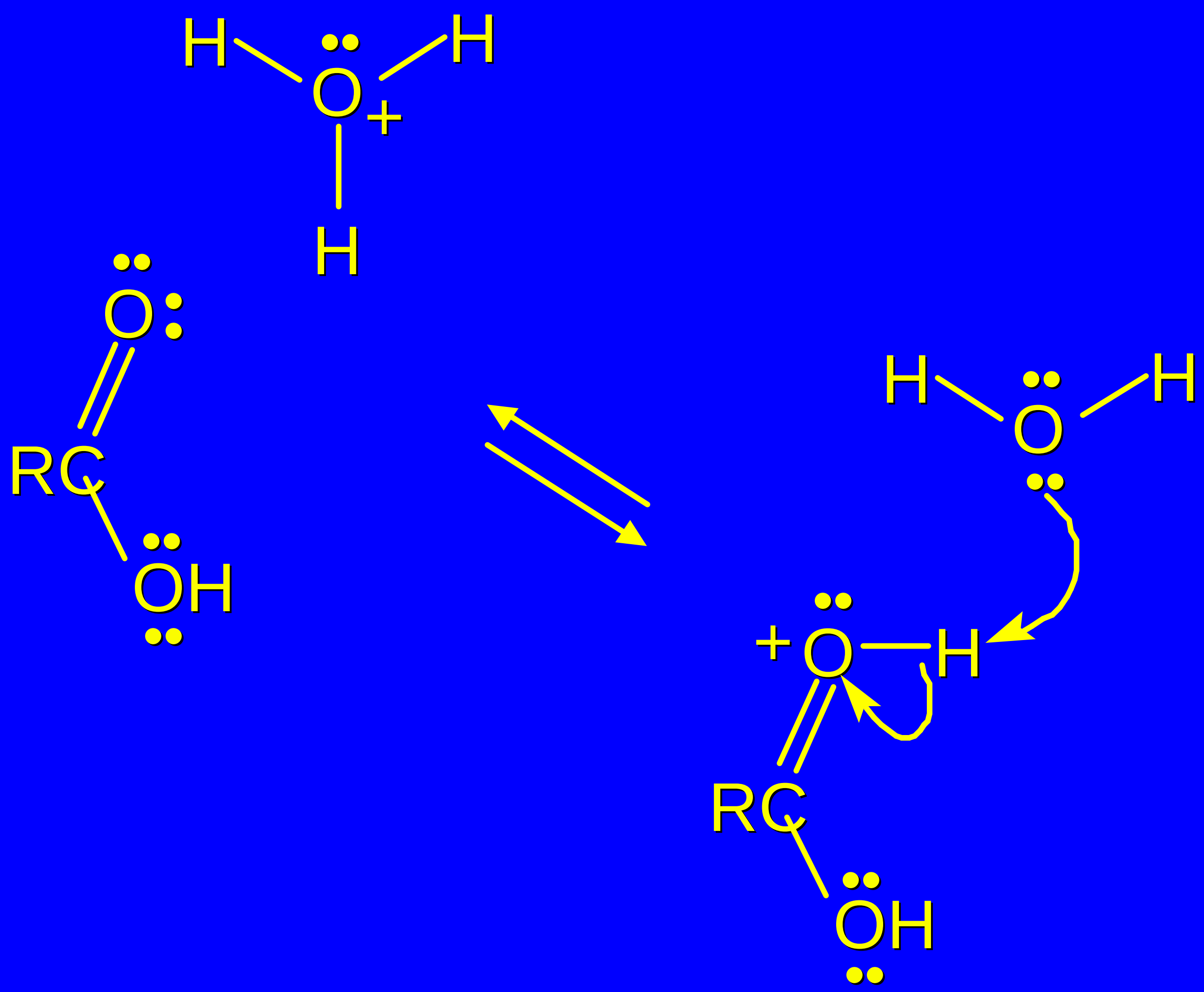
Step 5



Step 5



Step 6



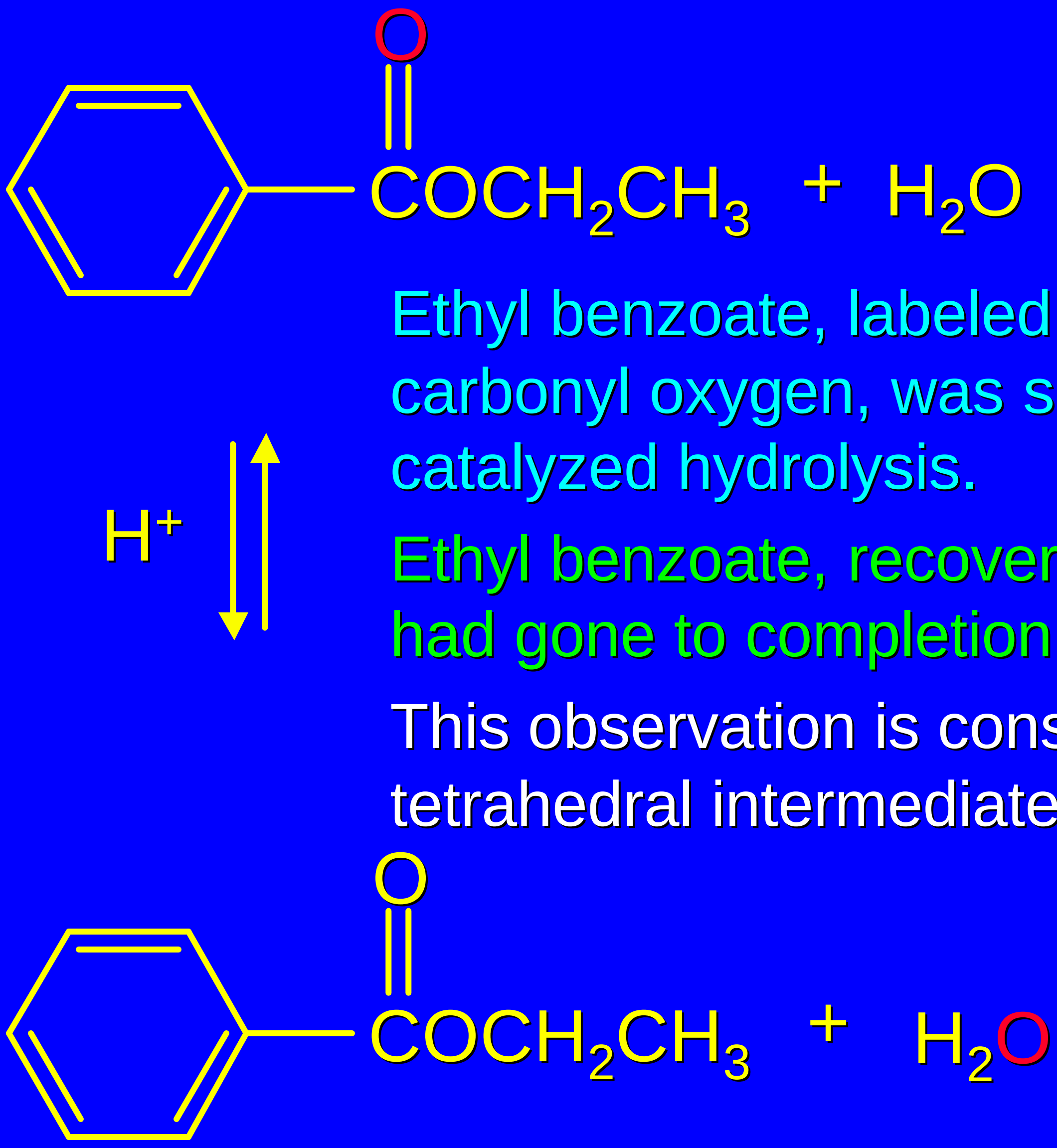
Key Features of Mechanism

Activation of carbonyl group by protonation of carbonyl oxygen

Nucleophilic addition of water to carbonyl group forms tetrahedral intermediate

Elimination of alcohol from tetrahedral intermediate restores carbonyl group

^{18}O Labeling Studies

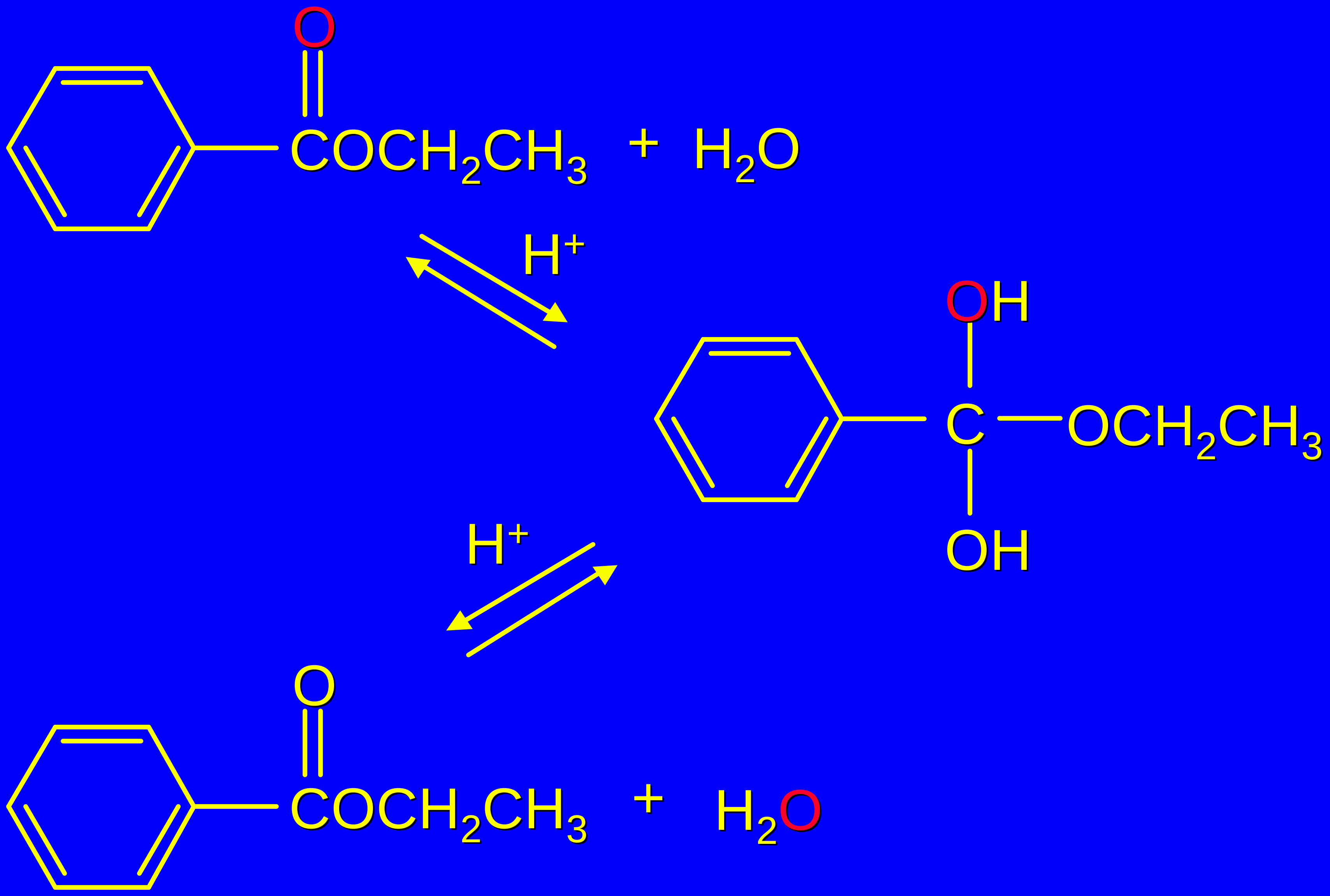


Ethyl benzoate, labeled with ^{18}O at the carbonyl oxygen, was subjected to acid-catalyzed hydrolysis.

Ethyl benzoate, recovered before the reaction had gone to completion, had lost its ^{18}O label.

This observation is consistent with a tetrahedral intermediate.

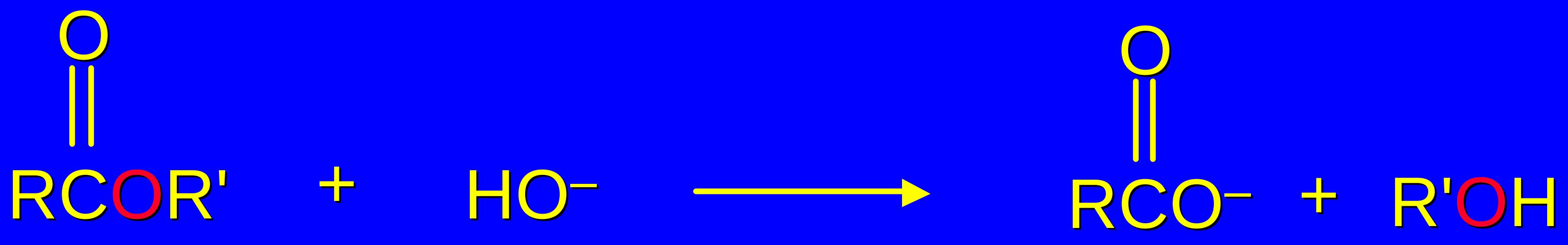
^{18}O Labeling Studies



20.10

Ester Hydrolysis in Base: Saponification

Ester Hydrolysis in Aqueous Base



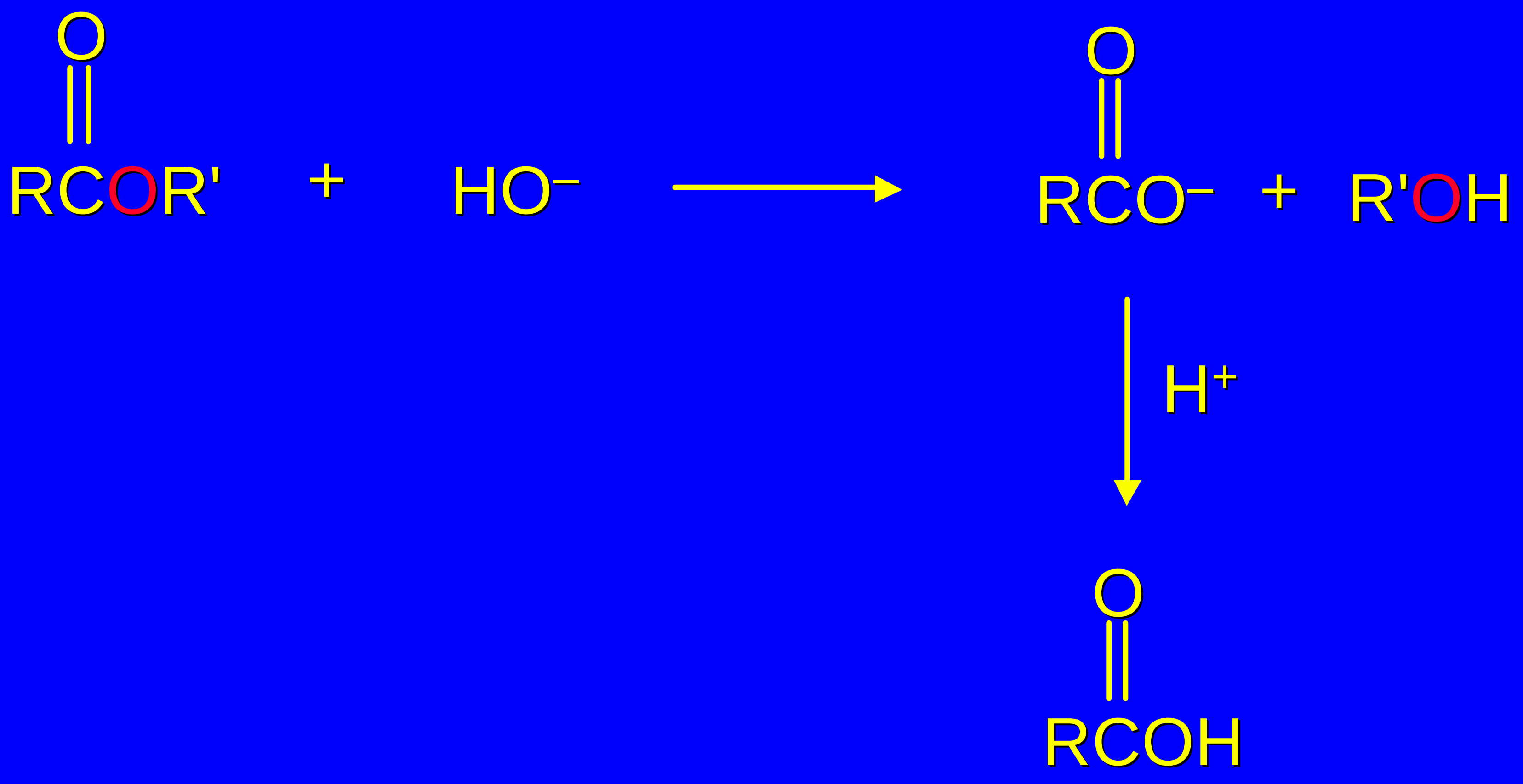
$$R\overset{\overset{O}{\|}}{C}OR' + HO^{-} \longrightarrow R\overset{\overset{O}{\|}}{C}O^{-} + R'OH$$

is called *saponification*

is irreversible, because of strong stabilization of carboxylate ion

if carboxylic acid is desired product, saponification is followed by a separate acidification step (simply a pH adjustment)

Ester Hydrolysis in Aqueous Base

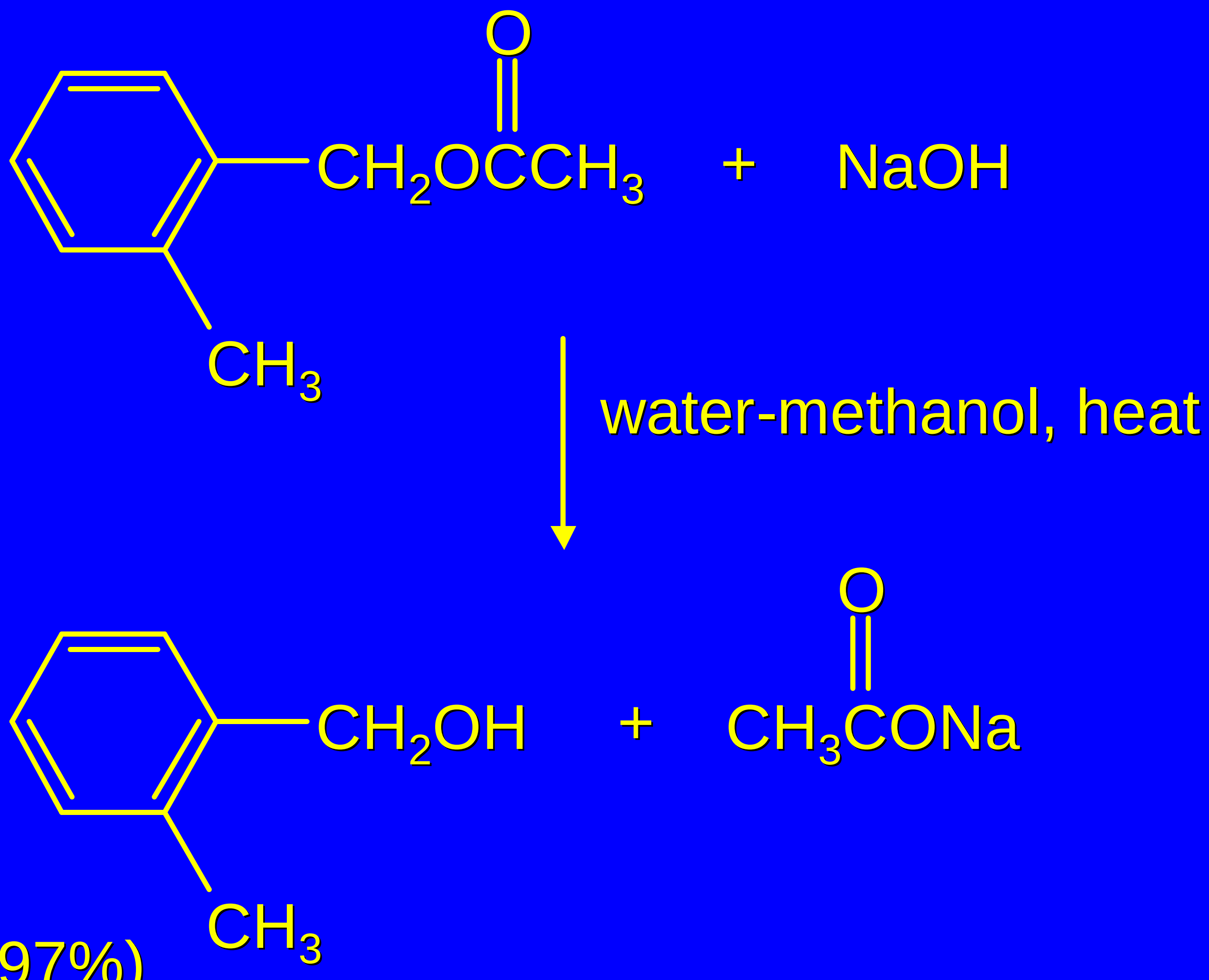


$$R\overset{\overset{\displaystyle O}{\|}}{C}OR' \quad + \quad HO^- \longrightarrow R\overset{\overset{\displaystyle O}{\|}}{C}O^- \quad + \quad R'OH$$

$$\Big\downarrow \, H^+$$

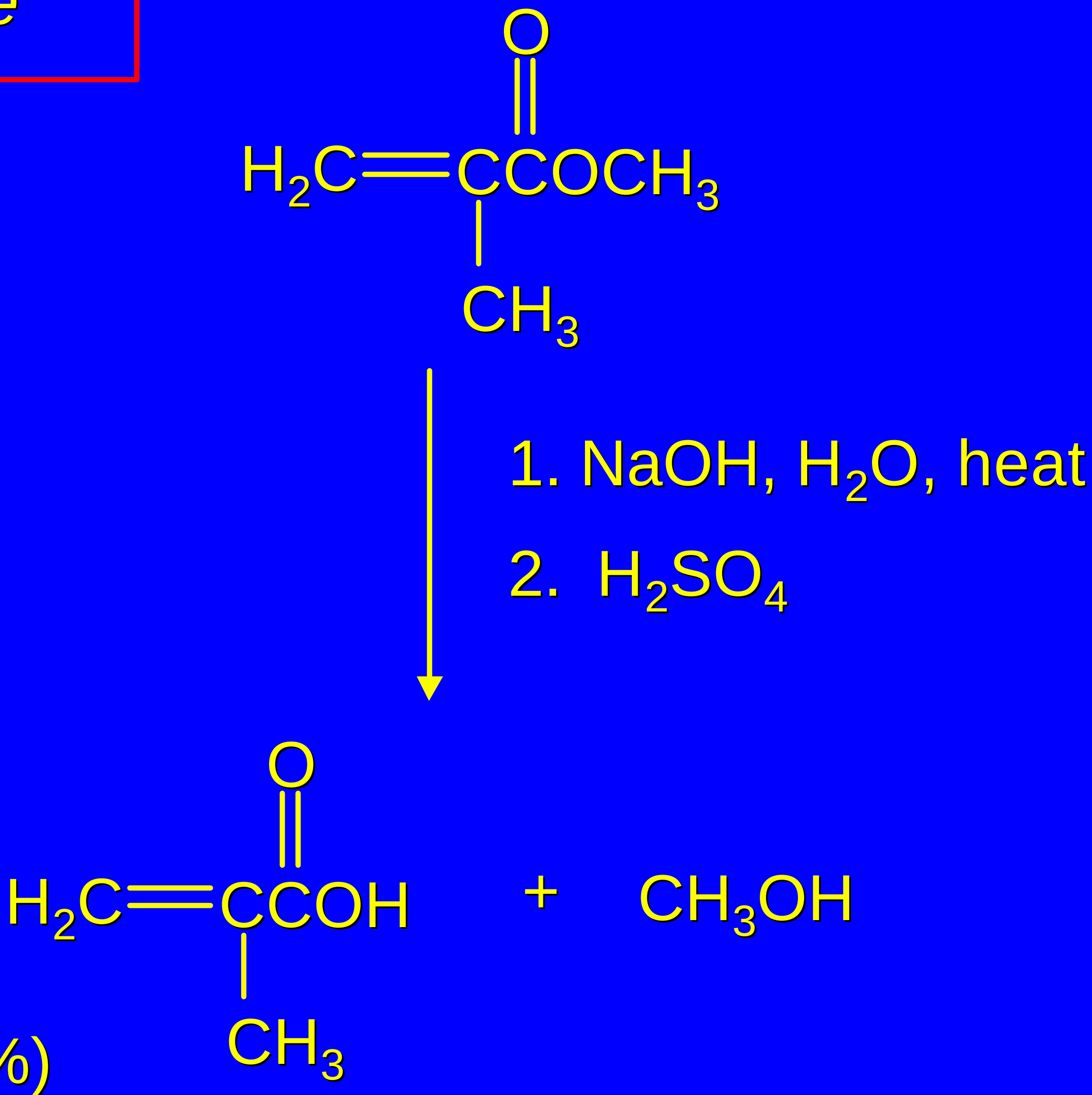
$$R\overset{\overset{\displaystyle O}{\|}}{C}OH$$

Example



(95-97%)

Example



$$\mathrm{H_2C{=}\underset{\underset{CH_3}{|}}{C}\overset{\overset{O}{\|}}{C}OCH_3}$$

1. NaOH, H_2O, heat

2. H_2SO_4

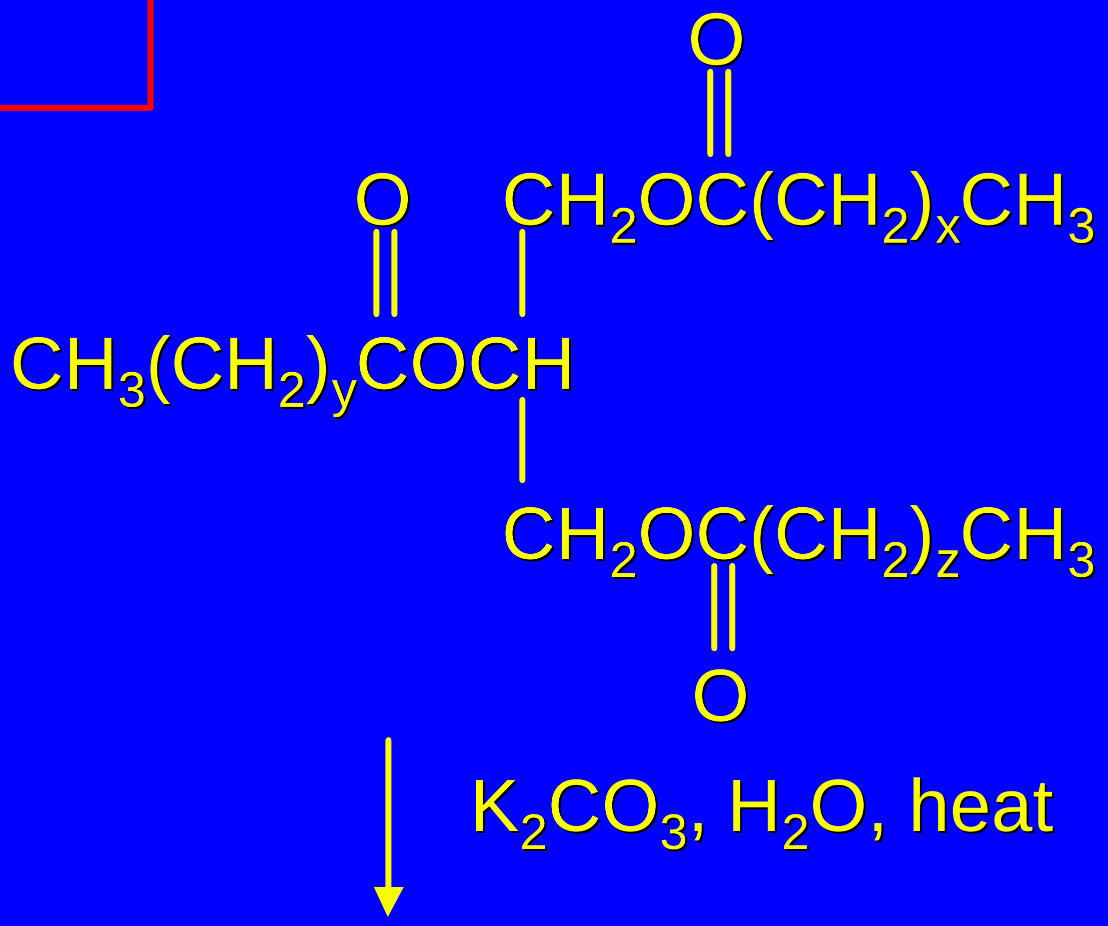
$$\mathrm{H_2C{=}\underset{\underset{CH_3}{|}}{C}\overset{\overset{O}{\|}}{C}OH} \quad + \quad \mathrm{CH_3OH}$$

(87%)

Soap-Making

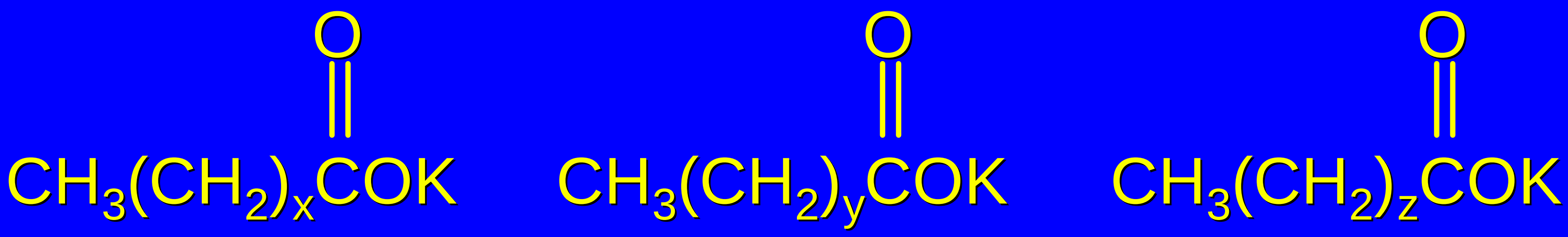
Basic hydrolysis of the glyceryl triesters (from fats and oils) gives salts of long-chain carboxylic acids.

These salts are soaps.



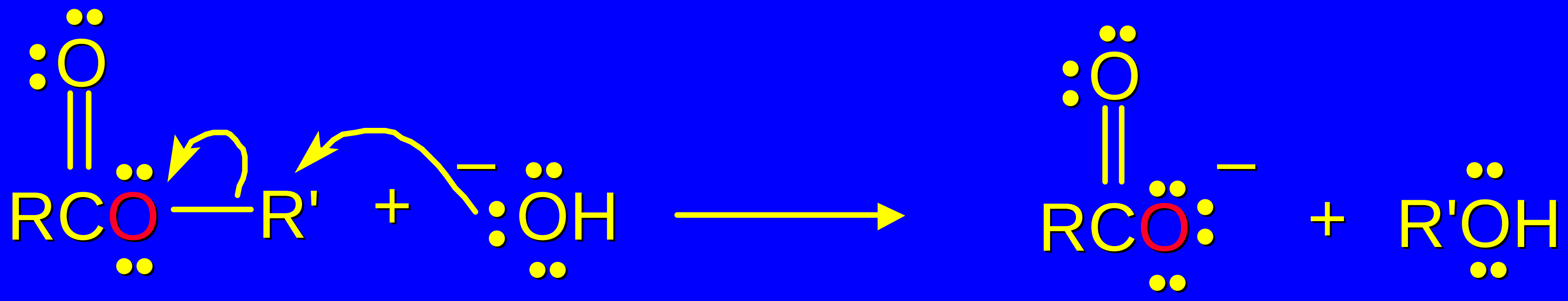
$$\begin{array}{rl} & CH_2O\overset{\overset{O}{\|}}{C}(CH_2)_xCH_3 \\ & | \\ CH_3(CH_2)_y\overset{\overset{O}{\|}}{C}OCH & \\ & | \\ & CH_2O\underset{\underset{O}{\|}}{C}(CH_2)_zCH_3 \end{array}$$

K_2CO_3, H_2O, heat



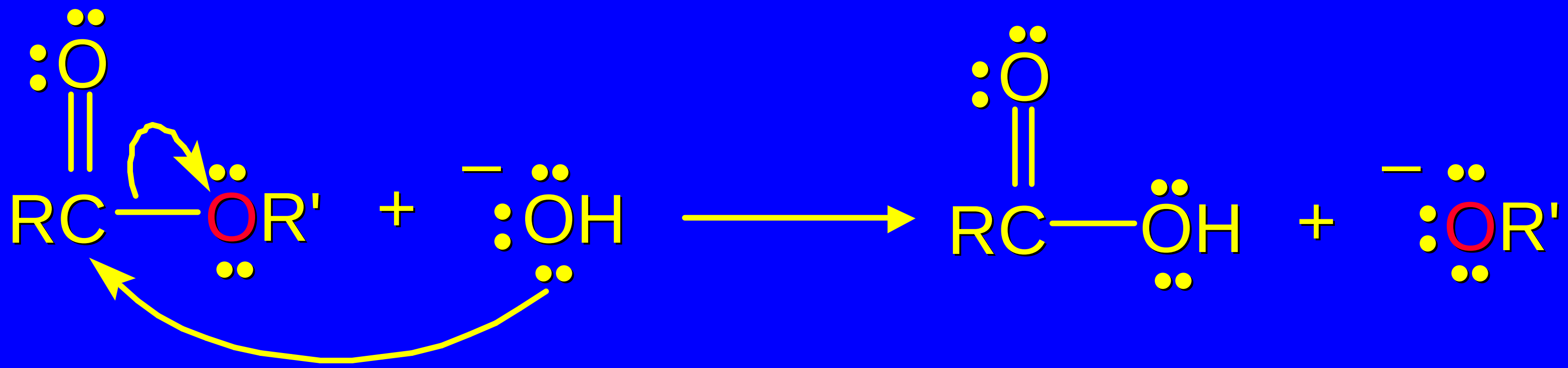
$$CH_3(CH_2)_x\overset{\overset{O}{\|}}{C}OK \qquad CH_3(CH_2)_y\overset{\overset{O}{\|}}{C}OK \qquad CH_3(CH_2)_z\overset{\overset{O}{\|}}{C}OK$$

Which bond is broken when esters are hydrolyzed in base?



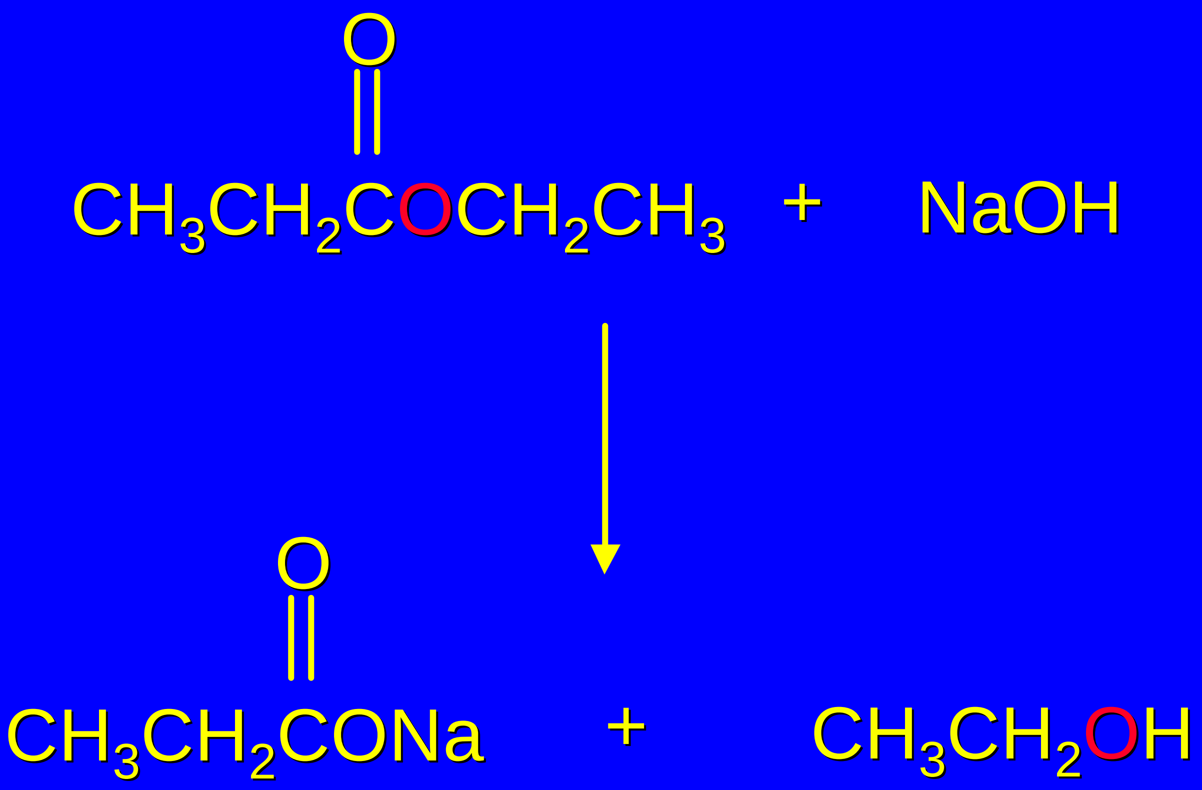
One possibility is an S_N2 attack by hydroxide on the alkyl group of the ester (alkyl-oxygen cleavage). Carboxylate is the leaving group.

Which bond is broken when esters are hydrolyzed in base?



A second possibility is nucleophilic acyl substitution (acyl-oxygen cleavage).

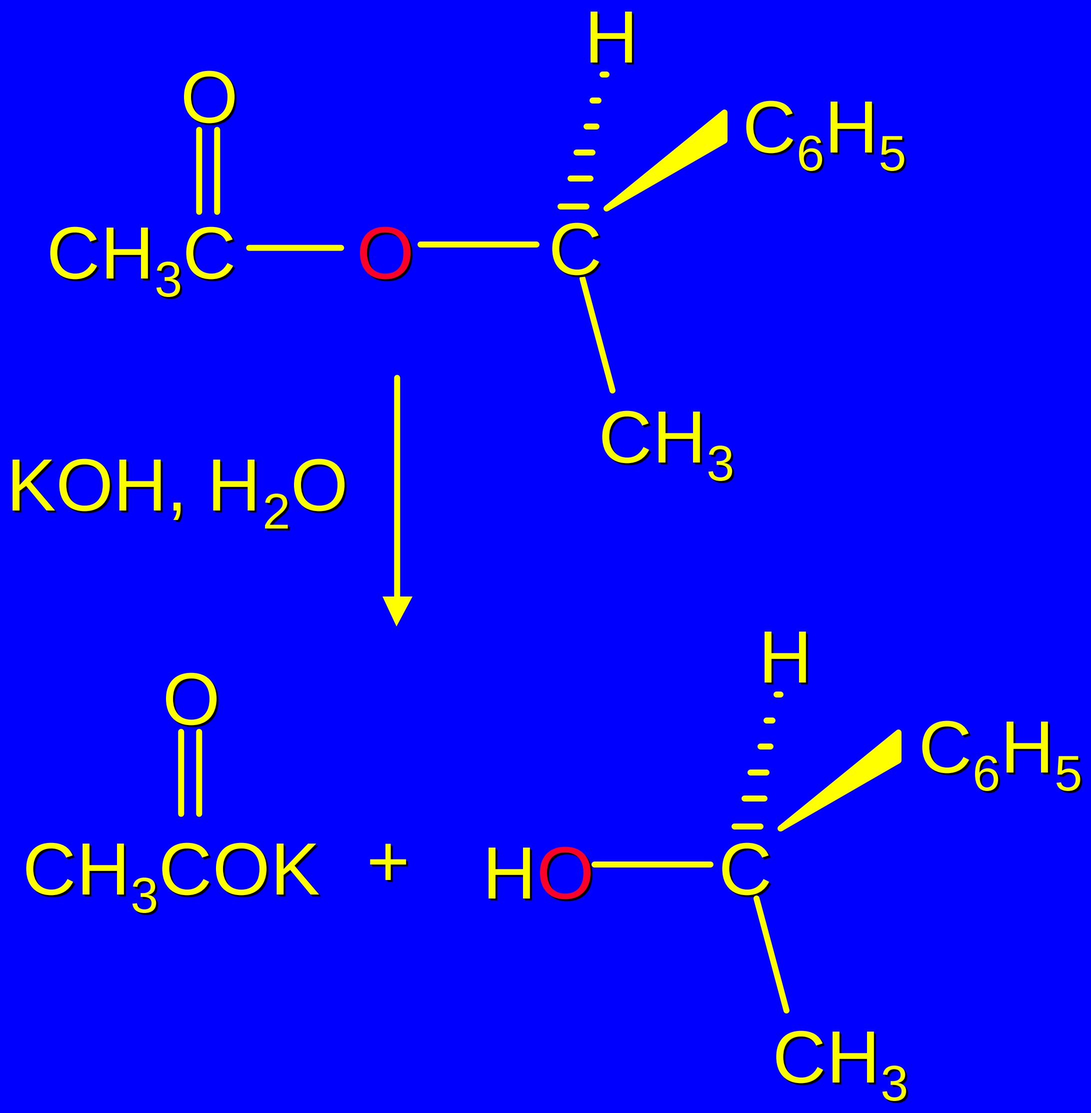
^{18}O Labeling gives the answer



$$\mathrm{CH_3CH_2\overset{\overset{O}{\|}}{C}OCH_2CH_3 + NaOH \longrightarrow CH_3CH_2\overset{\overset{O}{\|}}{C}ONa + CH_3CH_2OH}$$

^{18}O retained in alcohol, not carboxylate; therefore nucleophilic acyl substitution (acyl-oxygen cleavage).

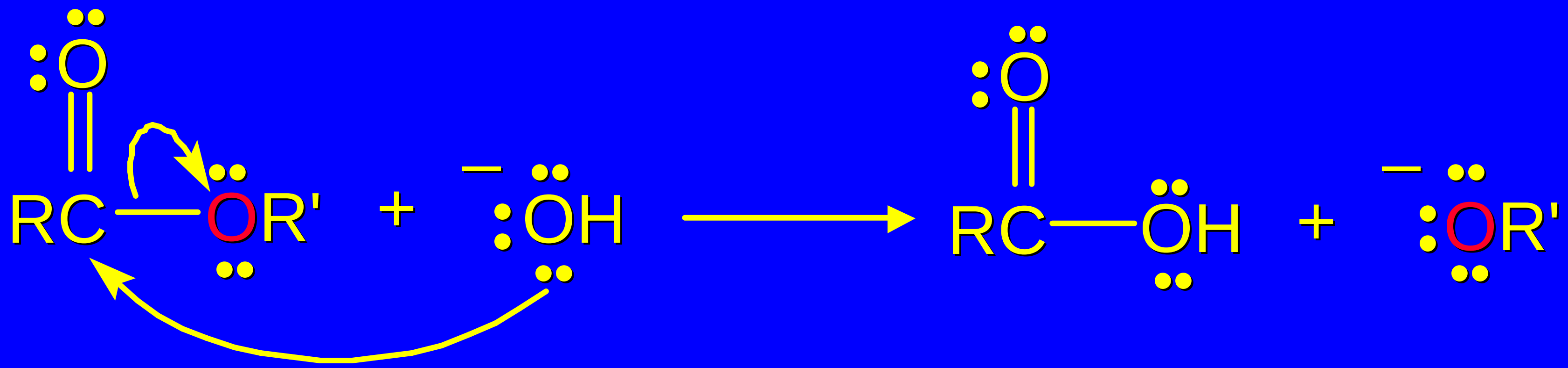
Stereochemistry gives the same answer



alcohol has same configuration at stereogenic center as ester; therefore, nucleophilic acyl substitution (acyl-oxygen cleavage)

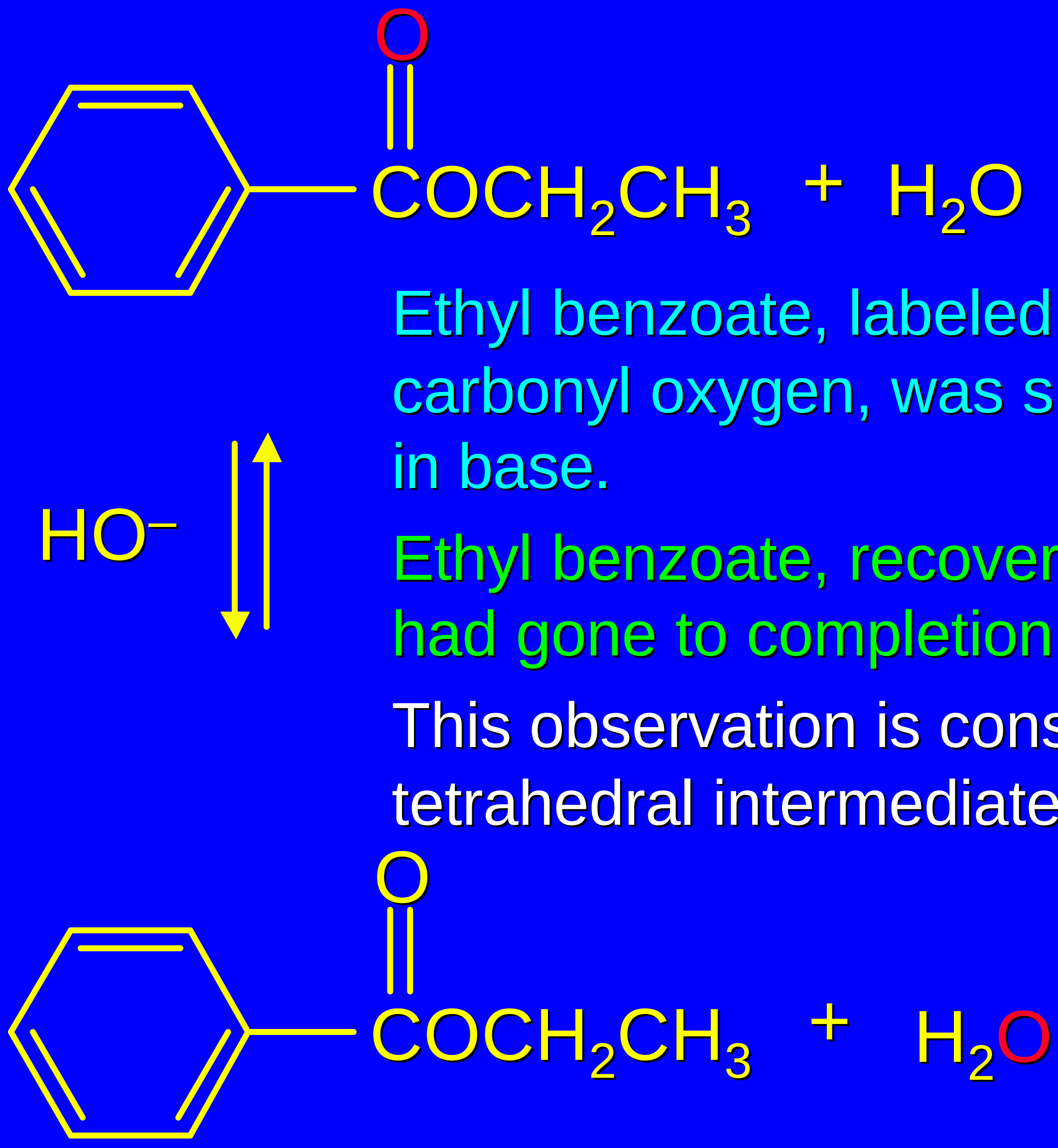
not S_N2

Does it proceed via a tetrahedral intermediate?



Does nucleophilic acyl substitution proceed in a single step, or is a tetrahedral intermediate involved?

^{18}O Labeling Studies

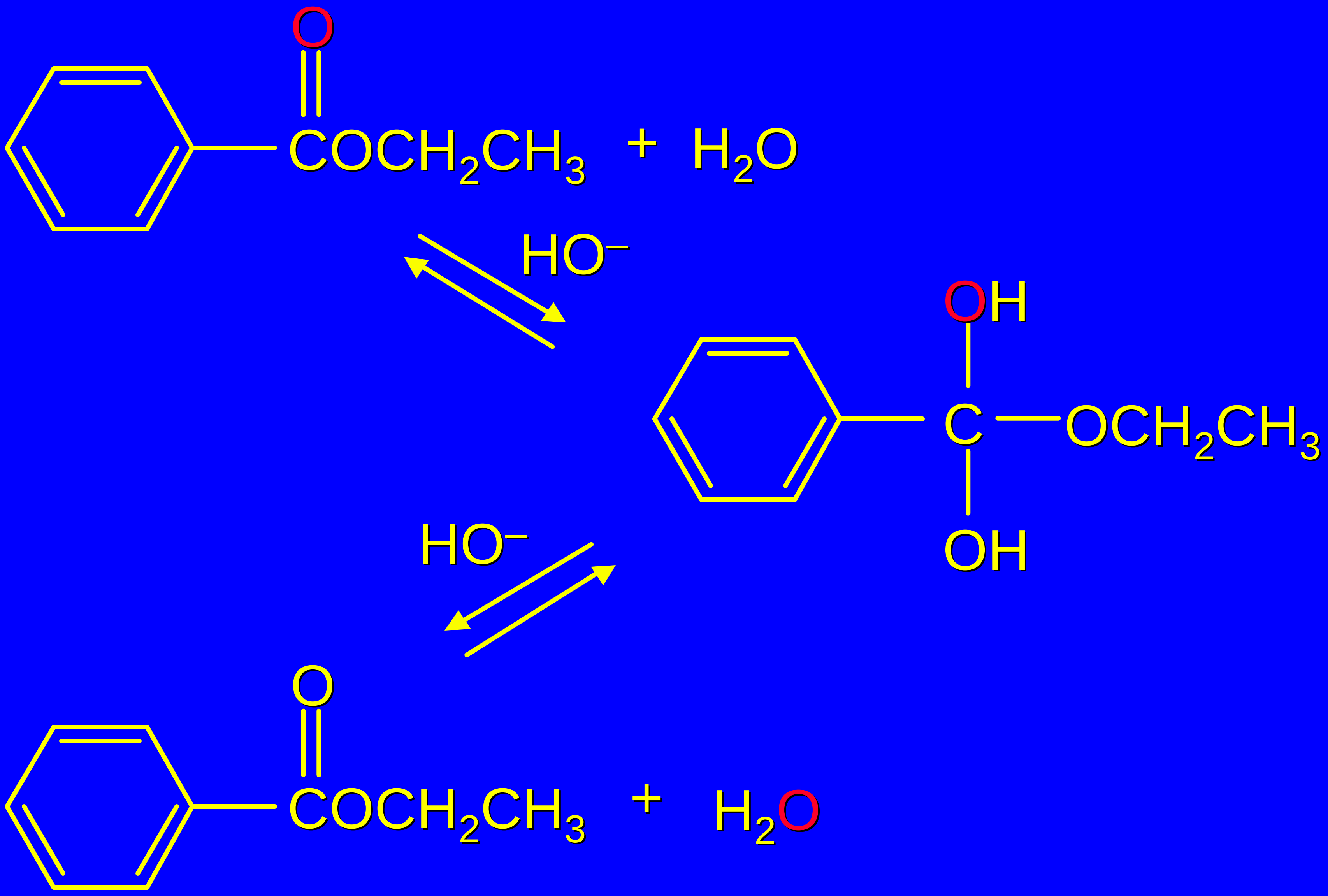


Ethyl benzoate, labeled with ^{18}O at the carbonyl oxygen, was subjected to hydrolysis in base.

Ethyl benzoate, recovered before the reaction had gone to completion, had lost its ^{18}O label.

This observation is consistent with a tetrahedral intermediate.

^{18}O Labeling Studies

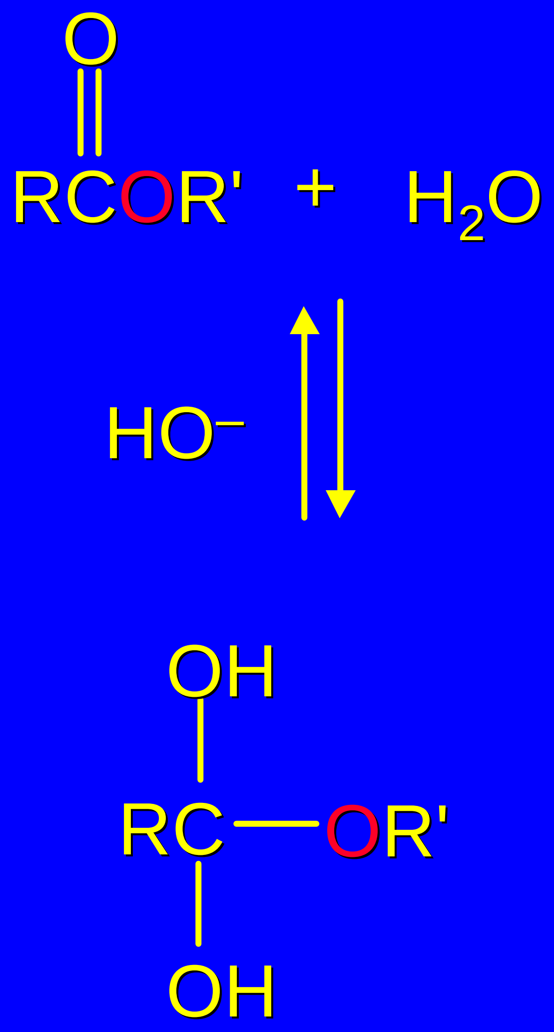


Mechanism of Ester Hydrolysis in Base

Involves two stages:

1) formation of tetrahedral intermediate
2) dissociation of tetrahedral intermediate

First stage: formation of tetrahedral intermediate

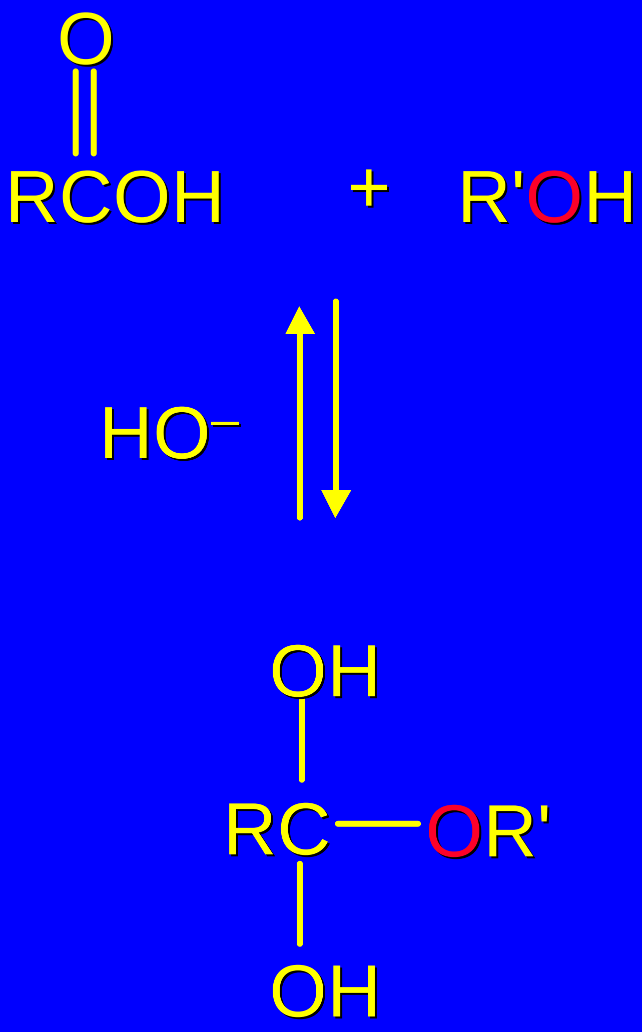


$$\overset{\overset{\Large O}{\|}}{\mathrm{RCOR'}} + H_2O \;\underset{}{\overset{HO^-}{\rightleftharpoons}}\; \mathrm{RC}\underset{\mathrm{OH}}{\overset{\mathrm{OH}}{|}}\!\!-\!\mathrm{OR'}$$

water adds to the carbonyl group of the ester

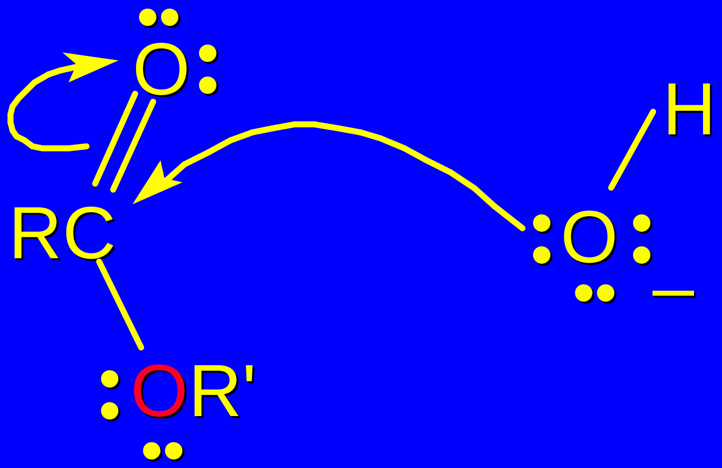
this stage is analogous to the base-catalyzed addition of water to a ketone

Second stage: cleavage of tetrahedral intermediate

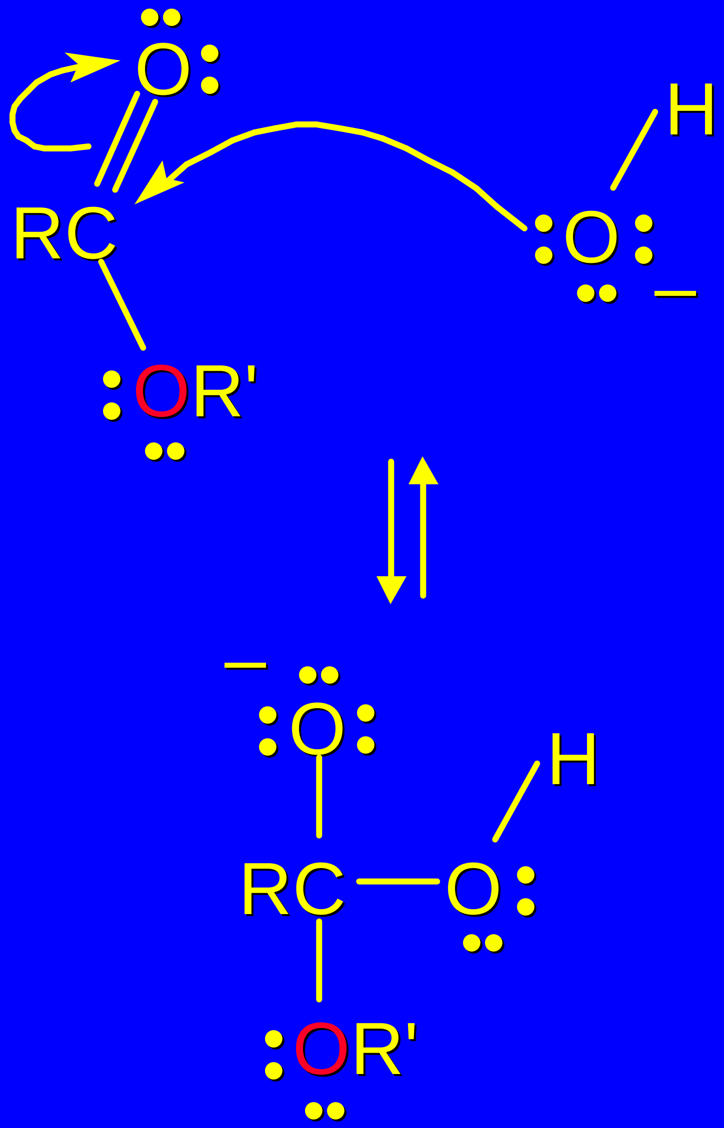


Mechanism of formation of tetrahedral intermediate

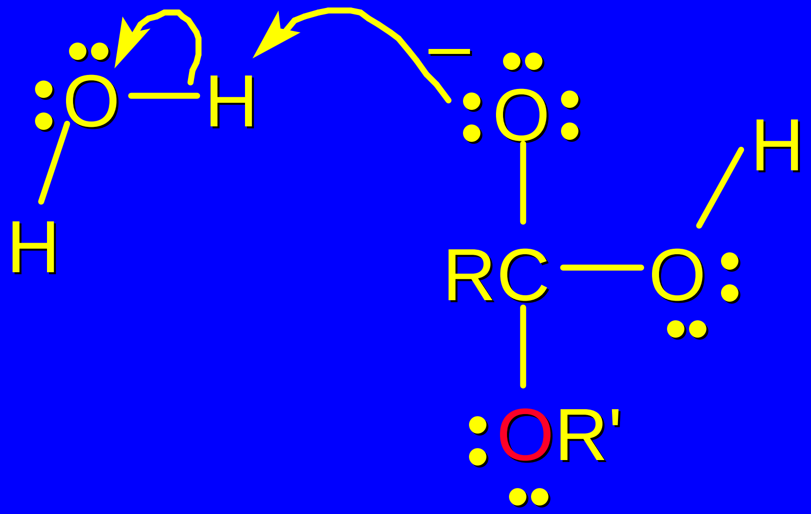
Step 1



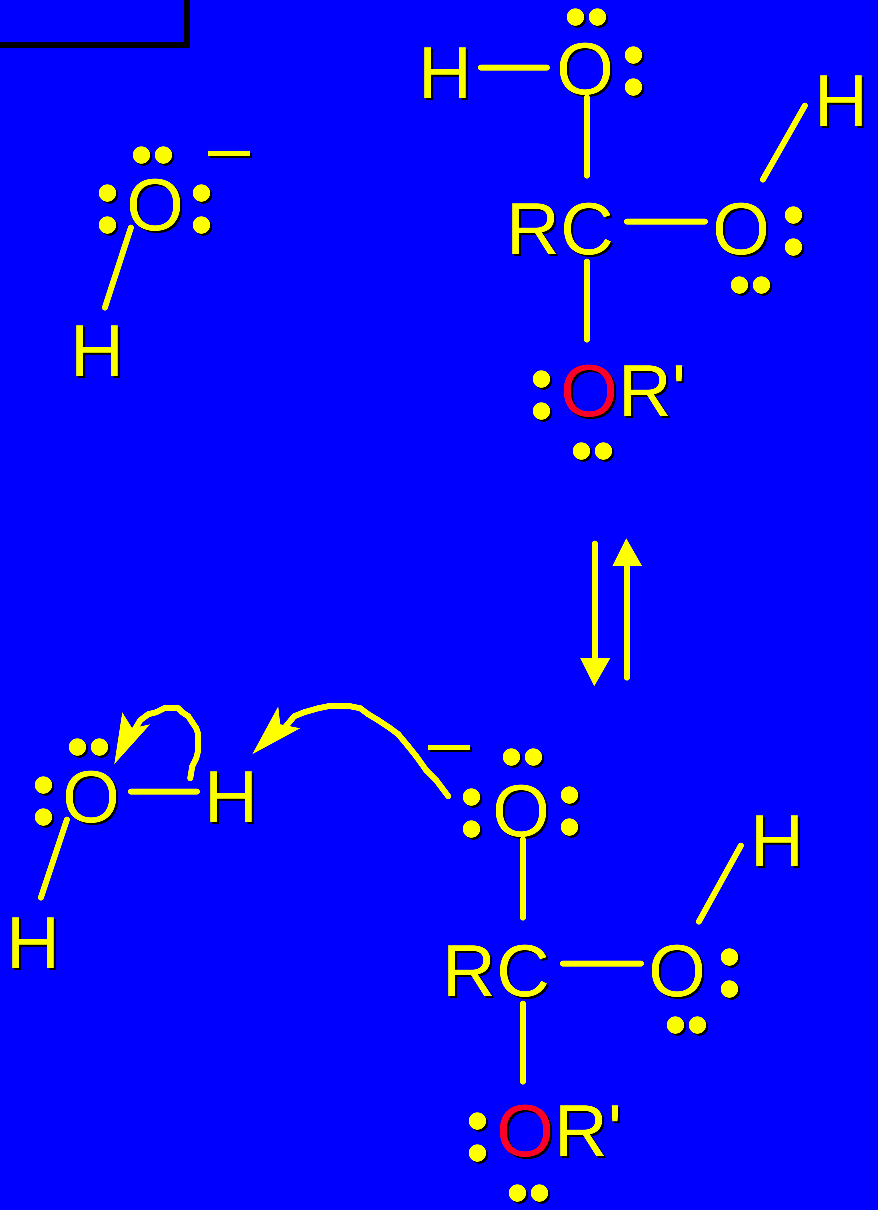
Step 1



Step 2

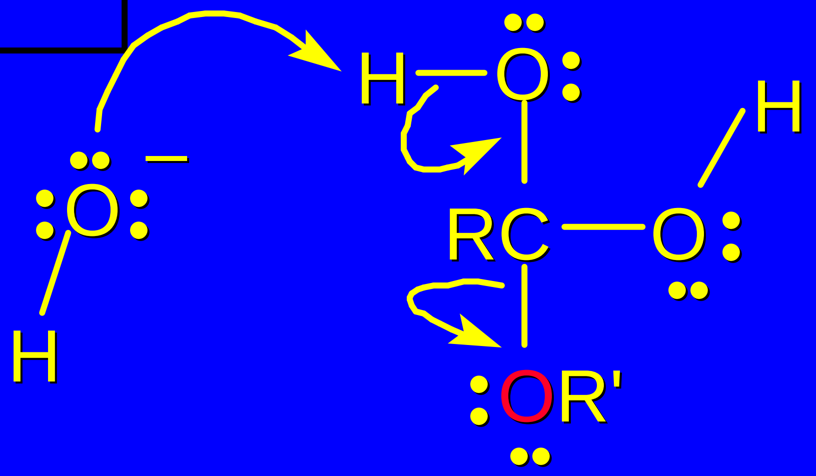


Step 2

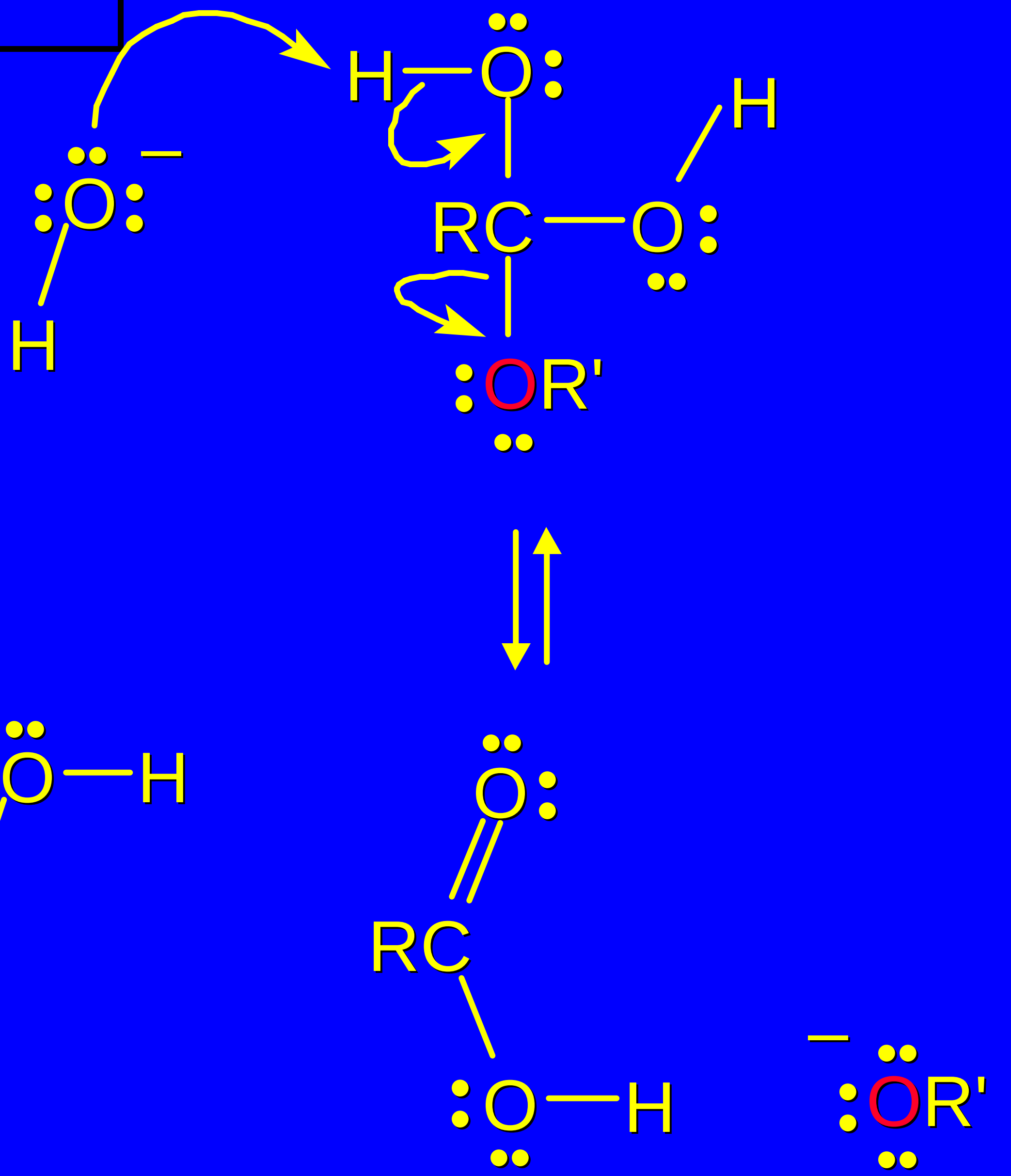


Dissociation of tetrahedral intermediate

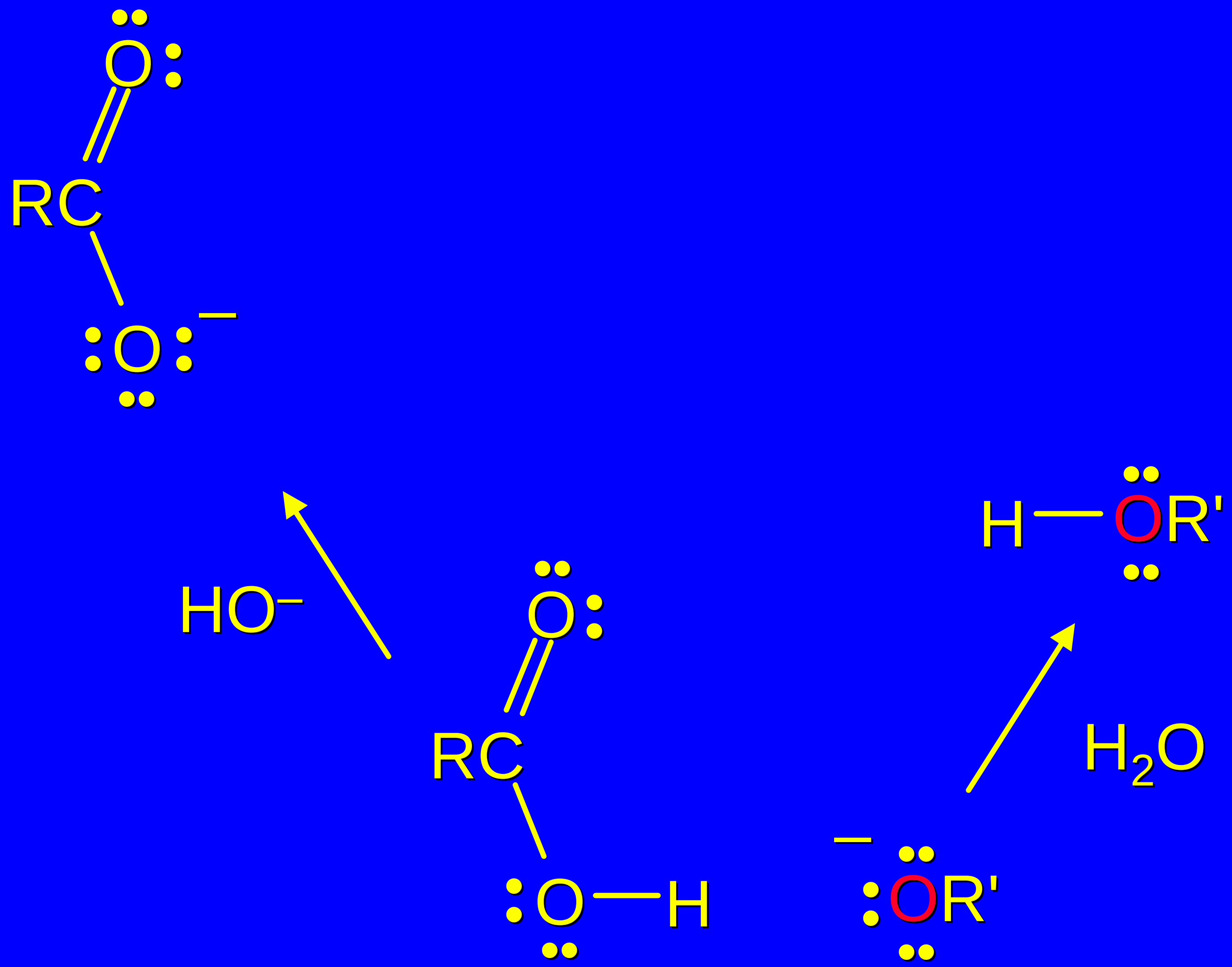
Step 3



Step 3



Step 4



Key Features of Mechanism

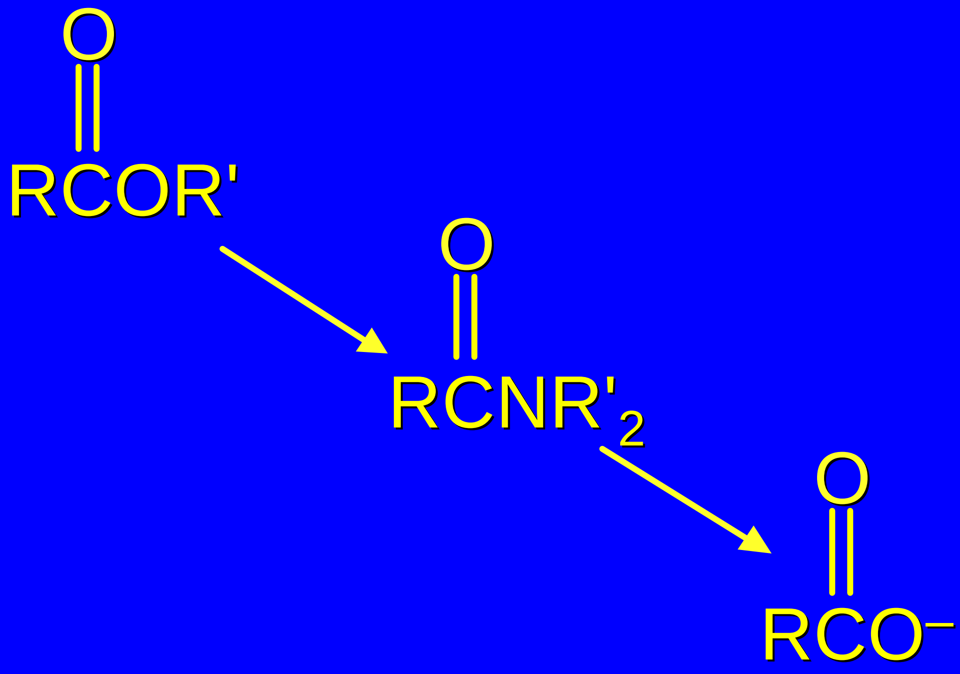
Nucleophilic addition of hydroxide ion to carbonyl group in first step

Tetrahedral intermediate formed in first stage

Hydroxide-induced dissociation of tetrahedral intermediate in second stage

20.11
Reactions of Esters with Ammonia and Amines

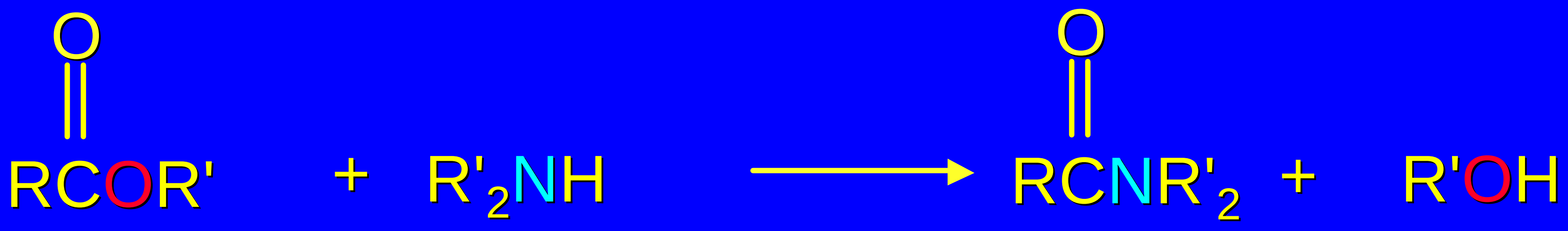
Reactions of Esters



$$R\overset{\overset{O}{\|}}{C}OR' \longrightarrow R\overset{\overset{O}{\|}}{C}NR'_2 \longrightarrow R\overset{\overset{O}{\|}}{C}O^-$$

Reactions of Esters

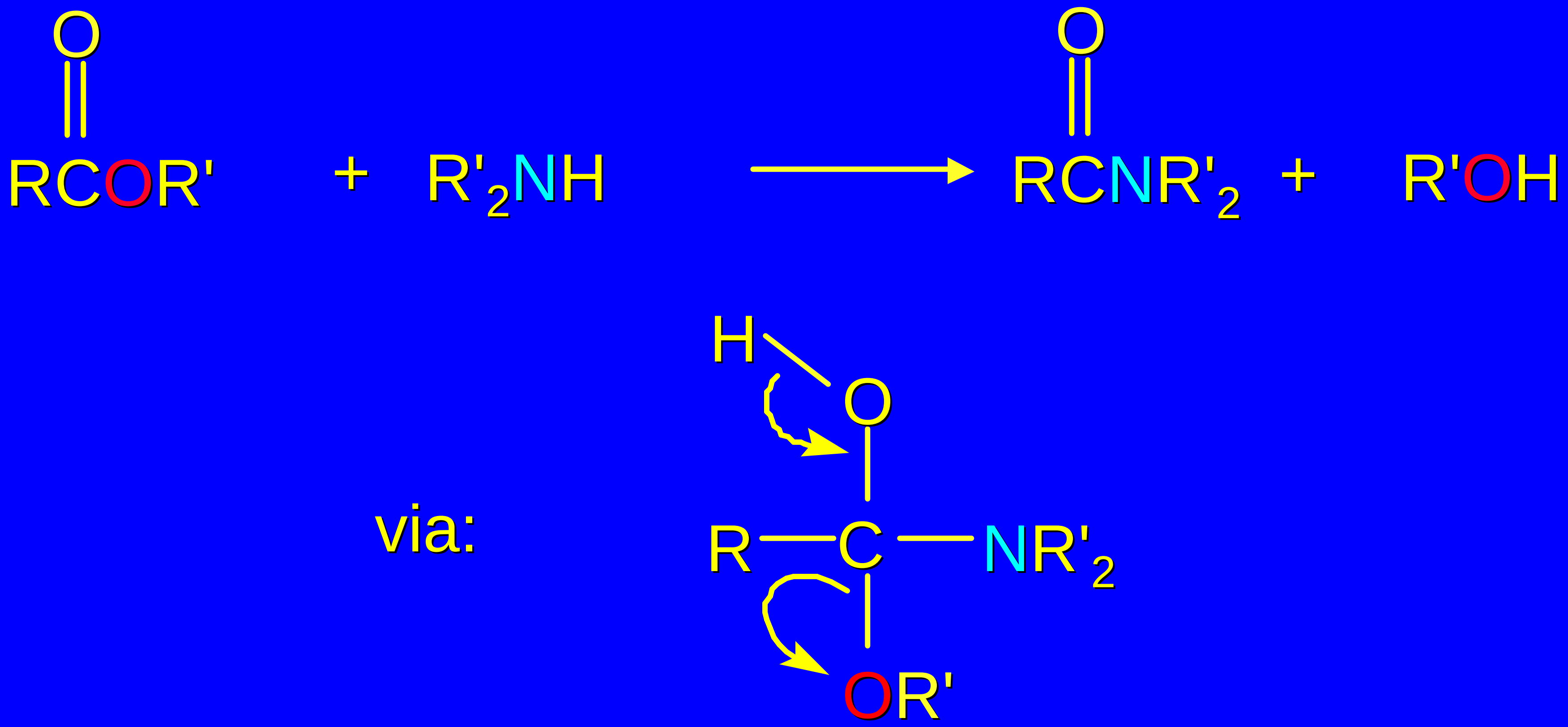
Esters react with ammonia and amines to give amides:



$$\mathrm{R}\overset{\overset{\displaystyle\mathrm{O}}{\|}}{\mathrm{C}}\mathrm{OR'} \quad + \quad \mathrm{R'_2NH} \longrightarrow \mathrm{R}\overset{\overset{\displaystyle\mathrm{O}}{\|}}{\mathrm{C}}\mathrm{NR'_2} \quad + \quad \mathrm{R'OH}$$

Reactions of Esters

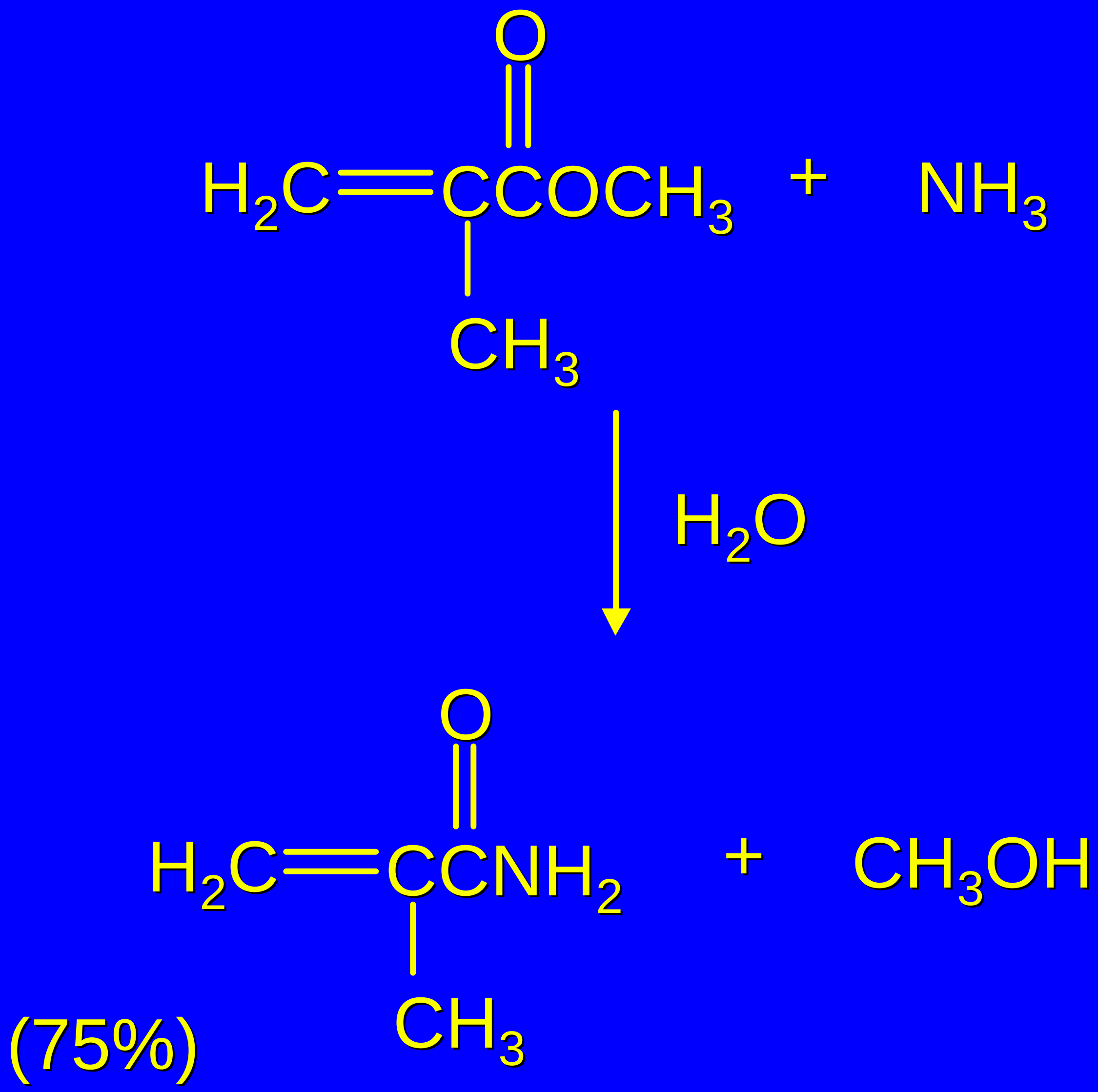
Esters react with ammonia and amines to give amides:



$$R\overset{\overset{O}{\|}}{C}OR' \quad + \quad R'_2NH \longrightarrow R\overset{\overset{O}{\|}}{C}NR'_2 \quad + \quad R'OH$$

via:

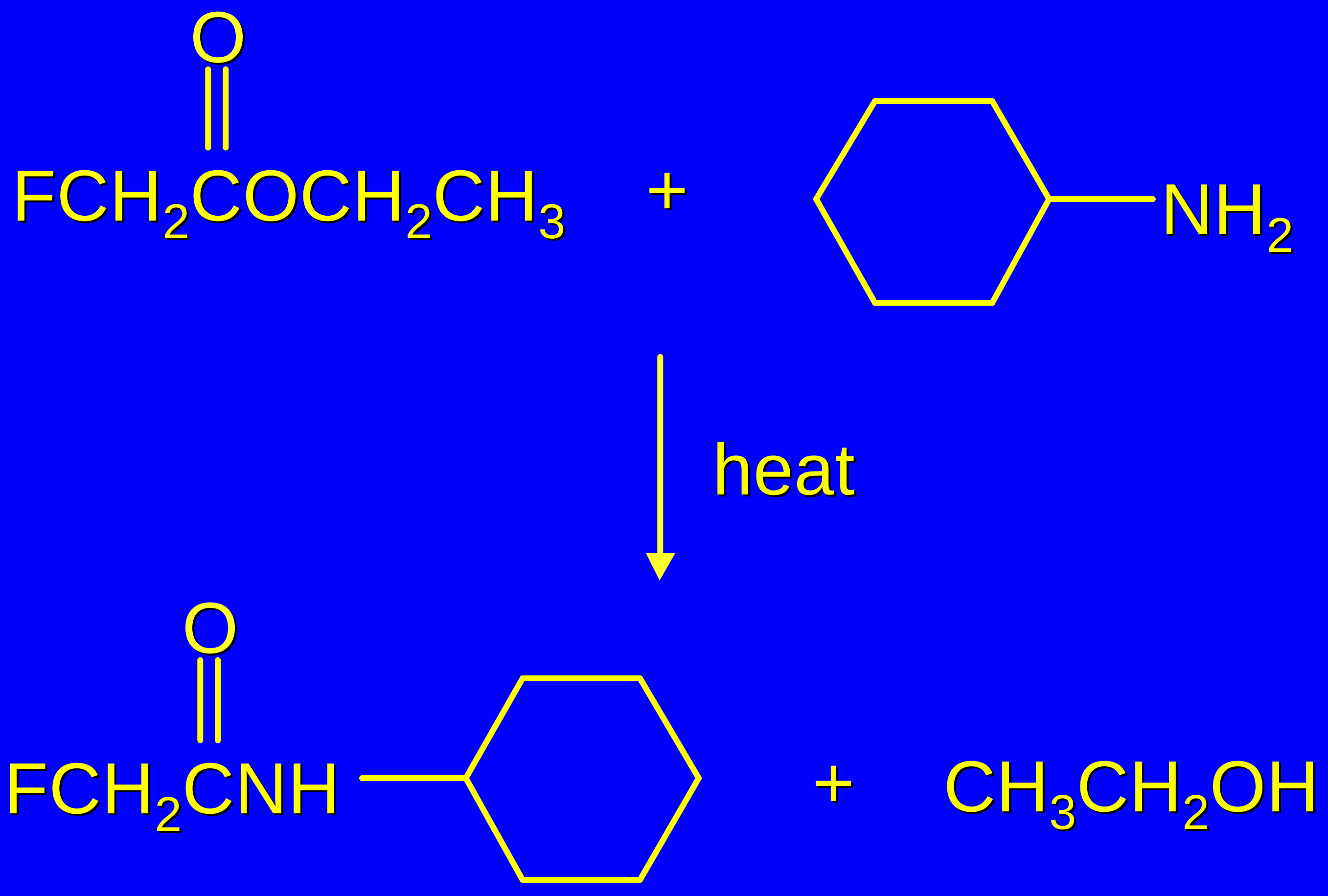
Example



$$H_2C{=}\underset{CH_3}{\overset{}{C}}\overset{O}{\overset{\|}{C}}OCH_3 + NH_3 \xrightarrow{H_2O} H_2C{=}\underset{CH_3}{\overset{}{C}}\overset{O}{\overset{\|}{C}}NH_2 + CH_3OH$$

(75%)

Example

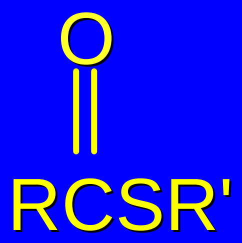


(61%)

20.12
Thioesters

Thioesters

Thioesters are compounds of the type:



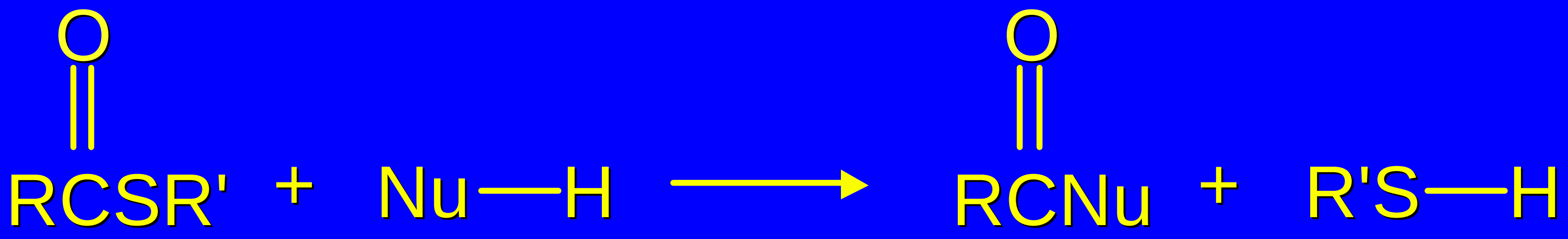
$$\overset{\overset{\displaystyle O}{\|}}{RCSR'}$$

Thioesters are intermediate in reactivity between anhydrides and esters.

Thioester carbonyl group is less stabilized than oxygen analog because C—S bond is longer than C—O bond which reduces overlap of lone pair orbital and C=O π orbital

Thioesters

Many biological nucleophilic acyl substitutions involve thioesters.



$$R\overset{\overset{\displaystyle O}{\|}}{C}SR' + Nu{-}H \longrightarrow R\overset{\overset{\displaystyle O}{\|}}{C}Nu + R'S{-}H$$

via: