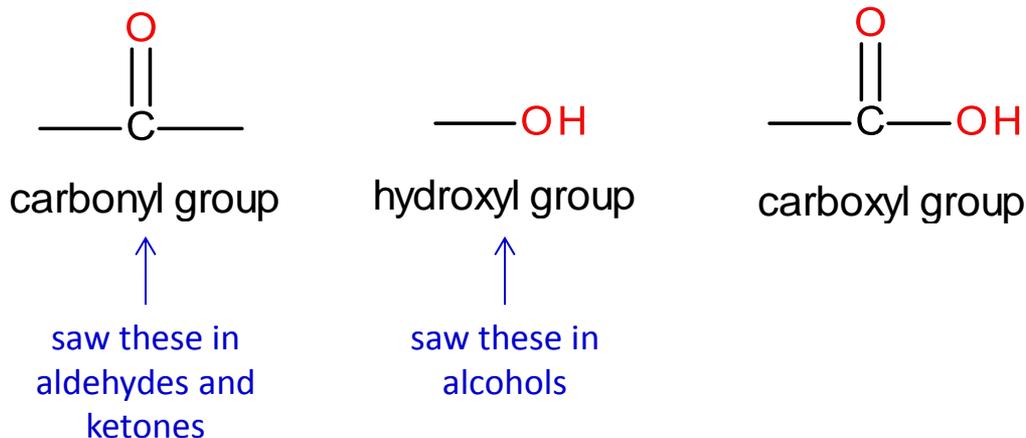


Carboxylic acids, esters, and other acid derivatives

Chapter 16

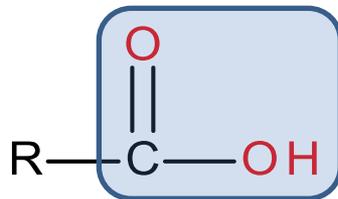
Structure of carboxylic acids and their derivatives

- The functional group present in a carboxylic acid is a combination of a carbonyl group and a hydroxyl group; however, the resulting **carboxyl group** (-COOH) possesses properties that are unlike those present in aldehydes/ketones and alcohols.

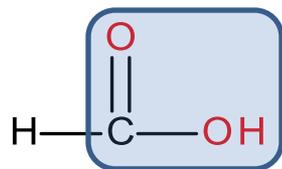


Structure of carboxylic acids and their derivatives

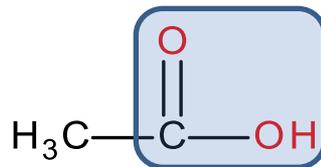
- Carboxylic acids have the following general formula:



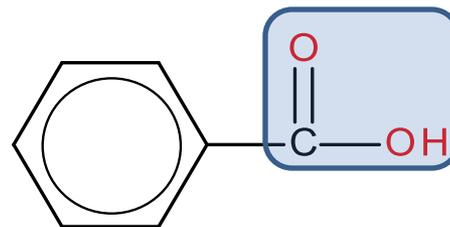
- Some simple carboxylic acids:



formic acid
IUPAC: methanoic acid



acetic acid
IUPAC: ethanoic acid

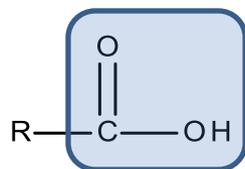


IUPAC: benzoic acid

- Since carbon can have only four bonds, there are no cyclic carboxylic acids (i.e. the carboxyl group cannot form part of a carbon ring)

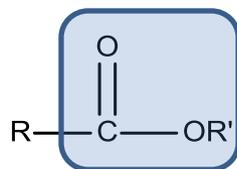
Structure of carboxylic acids and their derivatives

- The following molecules have a similar structure to carboxylic acids, and will be encountered in this chapter and the next.



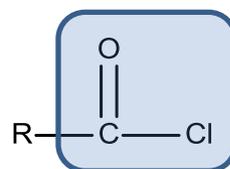
carboxylic acid

Ch-16



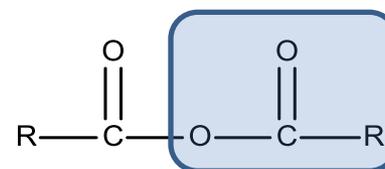
ester

Ch-16



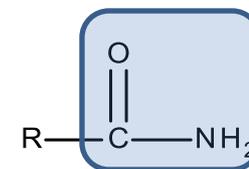
acid chloride

Ch-16



acid anhydride

Ch-16

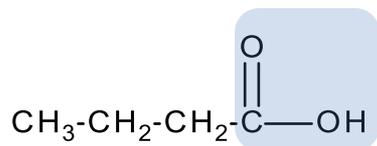


amide

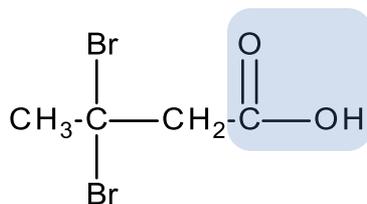
Ch-17

IUPAC nomenclature for carboxylic acids

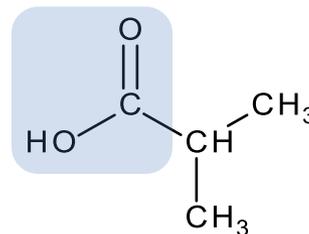
- For **naming** carboxylic acids:
 - Select the longest, continuous carbon chain that involves the carboxyl group. This is the parent chain and the -COOH carbon is designated as C #1.
 - Name the parent chain by dropping the “e” from the corresponding alkane name and changing to “oic acid”
 - Indicate the identity and location of substituents on the parent chain at the front of the carboxylic acid’s name



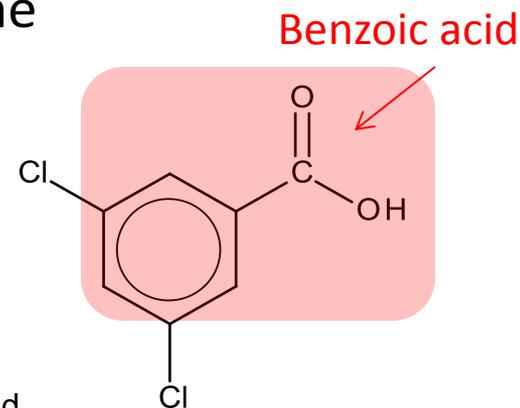
Butanoic acid



3,3-Dibromobutanoic acid



2-Methylpropanoic acid



3,5-Dichlorobenzoic acid

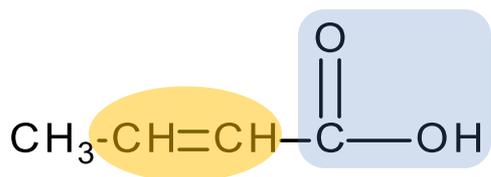
Common names for carboxylic acids

| Length of Carbon Chain | Structural Formula | Common Name ^a | IUPAC Name |
|-------------------------|--|--------------------------|----------------|
| C ₁ monoacid | H—COOH | formic acid | methanoic acid |
| C ₂ monoacid | CH ₃ —COOH | acetic acid | ethanoic acid |
| C ₃ monoacid | CH ₃ —CH ₂ —COOH | propionic acid | propanoic acid |
| C ₄ monoacid | CH ₃ —(CH ₂) ₂ —COOH | butyric acid | butanoic acid |
| C ₅ monoacid | CH ₃ —(CH ₂) ₃ —COOH | valeric acid | pentanoic acid |
| C ₆ monoacid | CH ₃ —(CH ₂) ₄ —COOH | caproic acid | hexanoic acid |

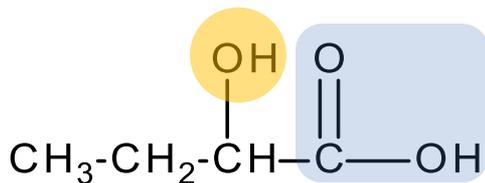
^aThe mnemonic “*Frogs are polite, being very courteous*” is helpful in remembering, in order, the first letters of the common names of these six simple saturated monocarboxylic acids.

Polyfunctional carboxylic acids

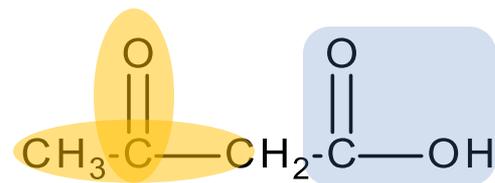
- Carboxylic acids that contain other functional groups besides the $-\text{COOH}$ group are called **polyfunctional** carboxylic acids. Some examples are shown below:



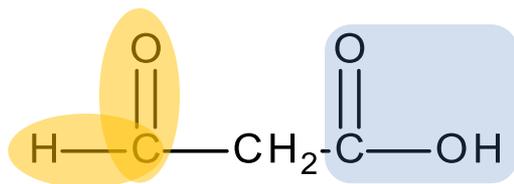
an unsaturated acid



a hydroxy acid

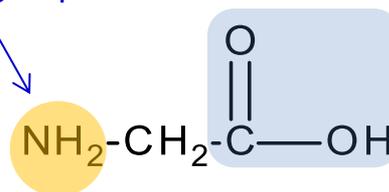


a keto acid



an aldo acid

amine group

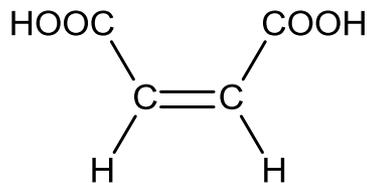


an amino acid

Polyfunctional carboxylic acids

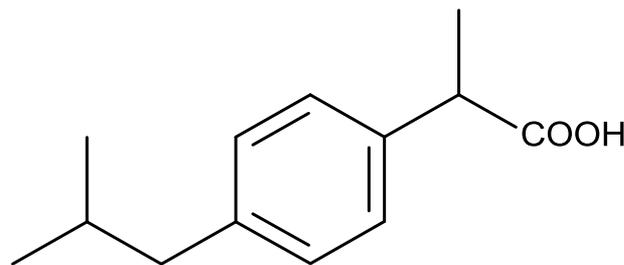
Unsaturated acids

- Unsaturated acids possess a unit of unsaturation (double/triple C-C bond) in the structure. Three common unsaturated acids are shown:

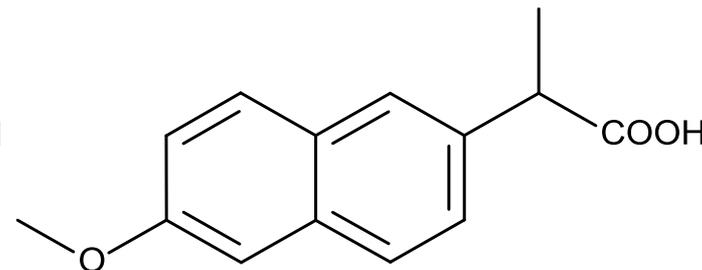


maleic acid

IUPAC: cis-Butenedioic acid



Ibuprofen

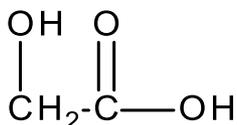


Naproxen

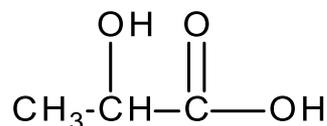
Polyfunctional carboxylic acids

Hydroxy acids

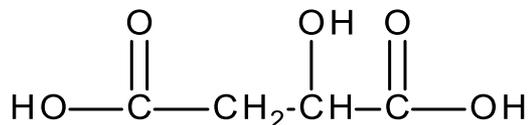
- Four of the simplest hydroxy acids:



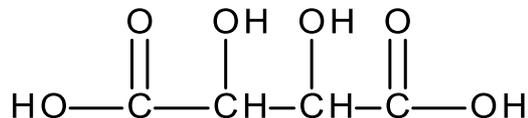
glycolic acid
hydroxyacetic acid
IUPAC: 2-Hydroxyethanoic acid



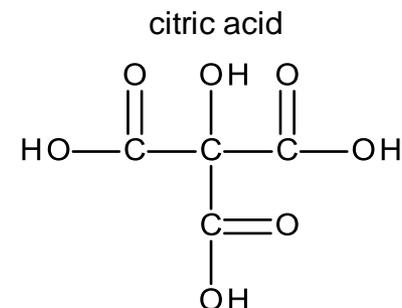
lactic acid
 α -hydroxypropionic acid
IUPAC: 2-Hydroxypropanoic acid



malic acid
hydroxysuccinic acid
IUPAC: Hydroxybutanedioic acid



tartartic acid
 α, β -dihydroxysuccinic acid
IUPAC: 2,3-Dihydroxybutanedioic acid



* don't memorize these names

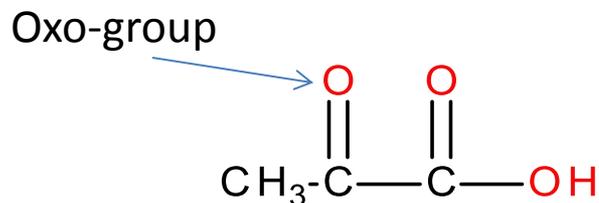
Polyfunctional carboxylic acids

Keto acids

- For keto acids, a carbonyl group is present as part of a carbon chain that involves a carboxylic acid group:



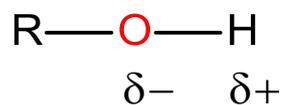
For IUPAC naming of this structure, the O-atom of the carbonyl group is treated as an “oxo” substituent and the molecule is called 2-oxopropanoic acid



* don't memorize these names

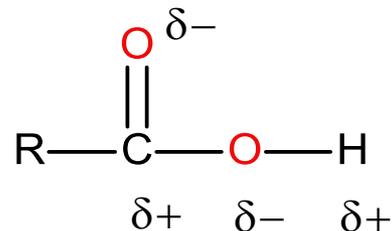
Physical properties of carboxylic acids

- Carboxylic acids are the most polar functional group we have seen so far. The presence of the carbonyl group next to the OH causes the O-H bond to be even more polar.



alcohols

$\text{pK}_a \sim 16-19$



carboxylic acids

$\text{pK}_a \sim 4-10$

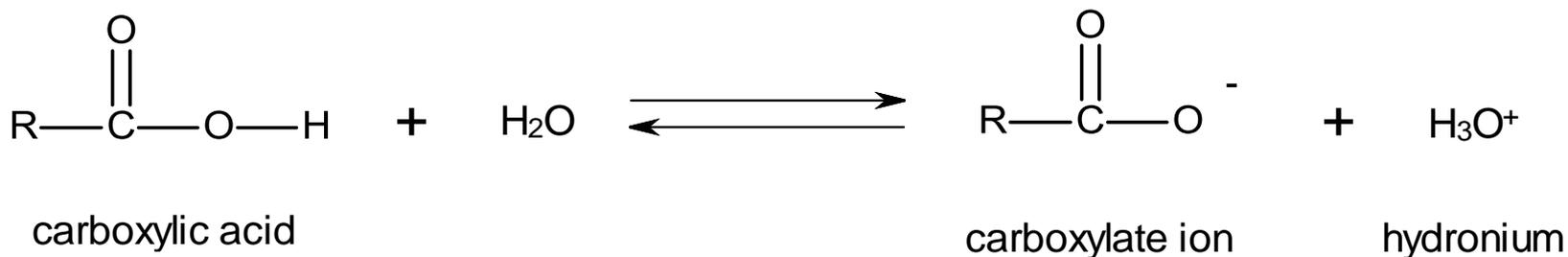
This is why -COOH groups are considered to be acidic, while -OH groups are not.

Acidity of carboxylic acids

| Acid | K_a | Percent Ionization (0.100 M Solution) |
|-----------|----------------------|--|
| Formic | 1.8×10^{-4} | 4.2% |
| Acetic | 1.8×10^{-5} | 1.3% |
| Propionic | 1.3×10^{-5} | 1.2% |
| Butyric | 1.5×10^{-5} | 1.2% |
| Valeric | 1.5×10^{-5} | 1.2% |
| Caproic | 1.4×10^{-5} | 1.2% |

Acidity of carboxylic acids

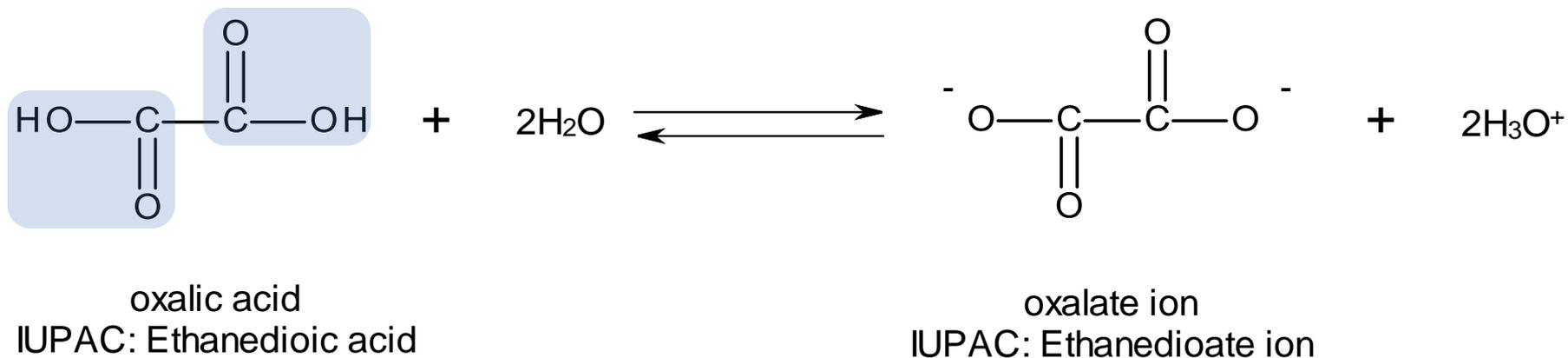
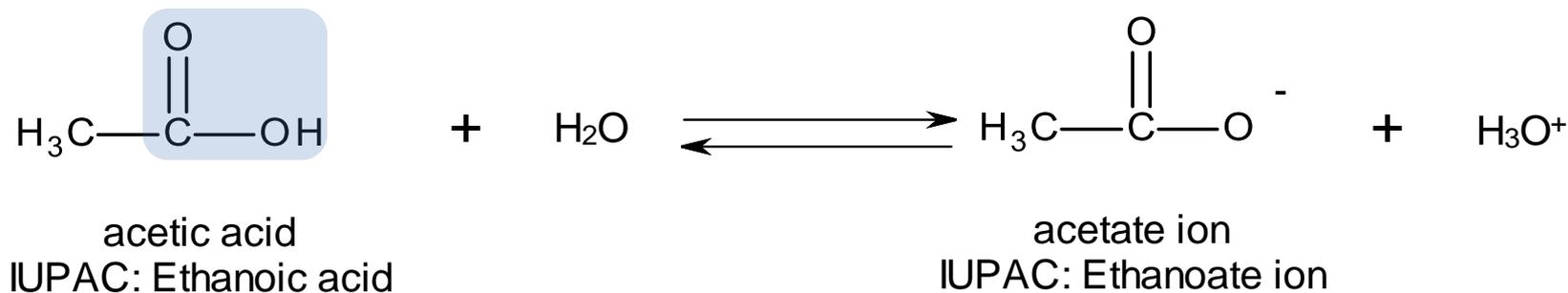
- When carboxylic acids are placed in water, they undergo deprotonation as discussed in Ch-10:



Remember from Ch-10:



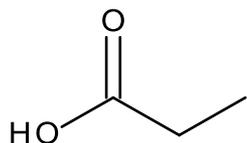
Acidity of carboxylic acids



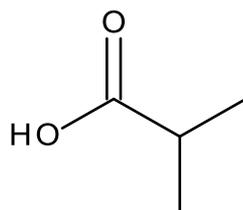
Conjugate bases of carboxylic acid

- The name of the de-protonated carboxylic acid (i.e. the conjugate base) is obtained from the name of the carboxylic acid.
- Remove the “-ic acid” part of the acid’s name and replace with “-ate”

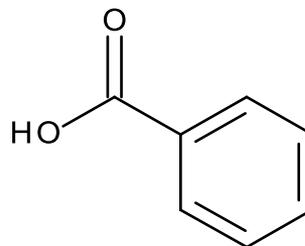
acid



propanoic acid

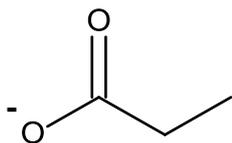


2-methylpropanoic acid

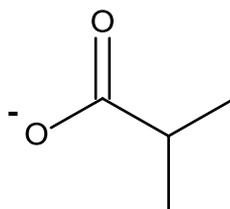


benzoic acid

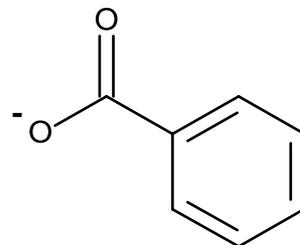
base



propanoate ion



2-methylpropanoate ion

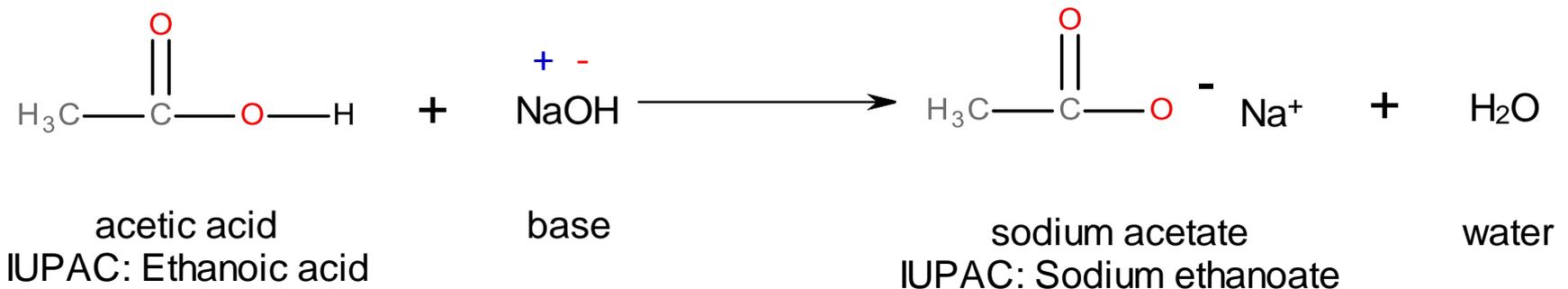
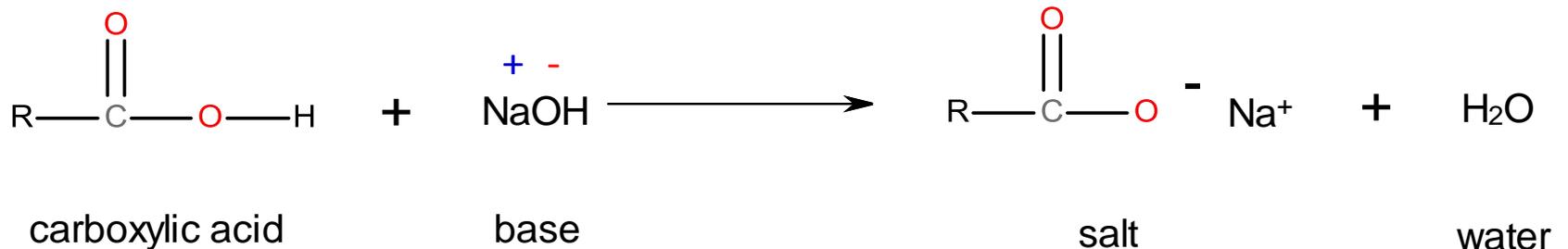


benzoate ion

Carboxylic acid salts

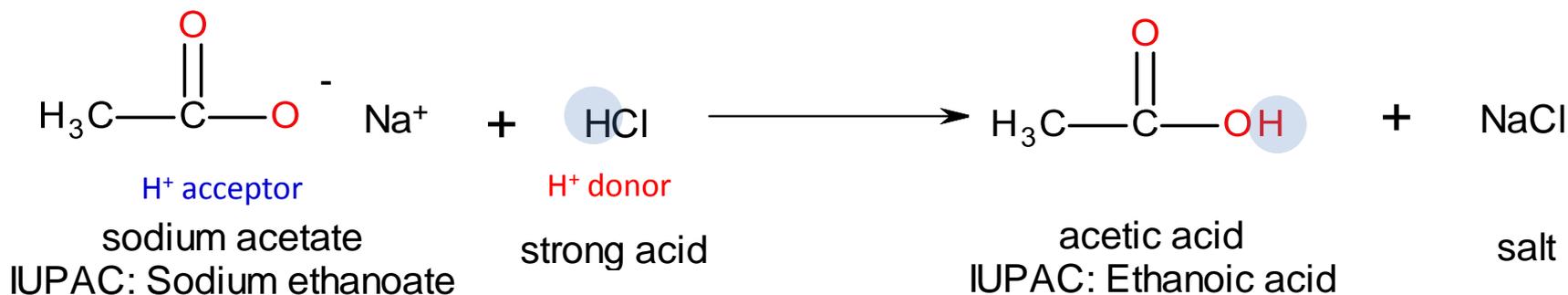


- When carboxylic acids are reacted with strong bases, they are converted to **salts** as follows:



Carboxylic acid salts

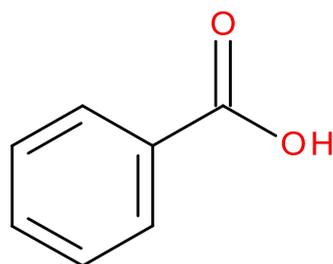
- Salts of carboxylic acids are much more water-soluble than the acids themselves.
- Also, they can be converted back to the acid form by reacting them with a strong acid:



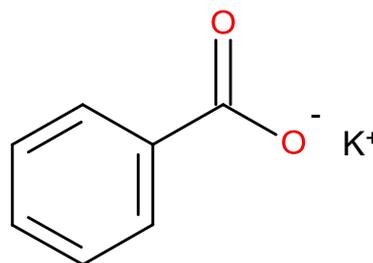
Handy rule: things that are charged tend to be more water-soluble than things that aren't (when comparing two similar structures)

Uses of carboxylic acid salts

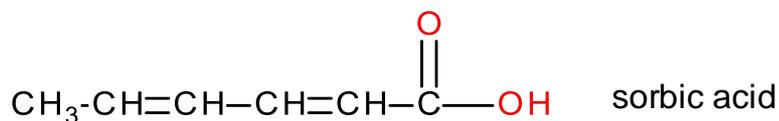
- Because of their enhanced solubility in water compared to the acid form, many drugs and medicines that possess acid groups are marketed as carboxylic acid salts (sodium or potassium salts).



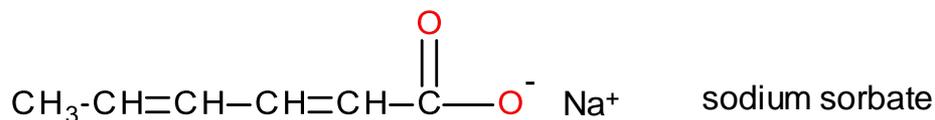
Benzoic acid



Potassium benzoate



sorbic acid

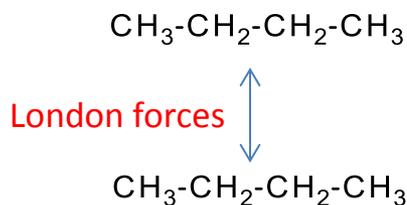


sodium sorbate

A brief review of boiling point trends

- Boiling points are determined by attractions between molecules; the stronger the attractions are, the higher the boiling point for the substance

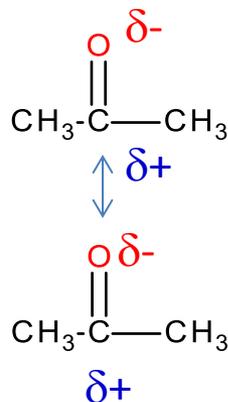
Weakest intermolecular attraction (lowest b.p.)



In simple hydrocarbons (alkanes, alkenes, etc.) there are only non-polar bonds. No dipole-dipole or H-bonding possible. Only **London**

Alkanes, alkenes, alkynes, aromatics

mid-range b.p.

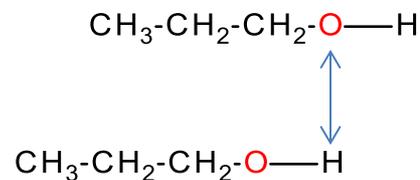


Dipole-dipole forces

Polar molecules have **dipole-dipole** attractive forces, in addition to London forces.

Aldehydes, ketones, esters

Strongest intermolecular attraction (highest b.p.)



H-bonding

In certain molecules, a H-atom may be involved in a bond to an O, N, or F-atom. This kind of H can **H-bond** to O, N, or F-atoms of other molecules.

Alcohols, carboxylic acids, amines, amides

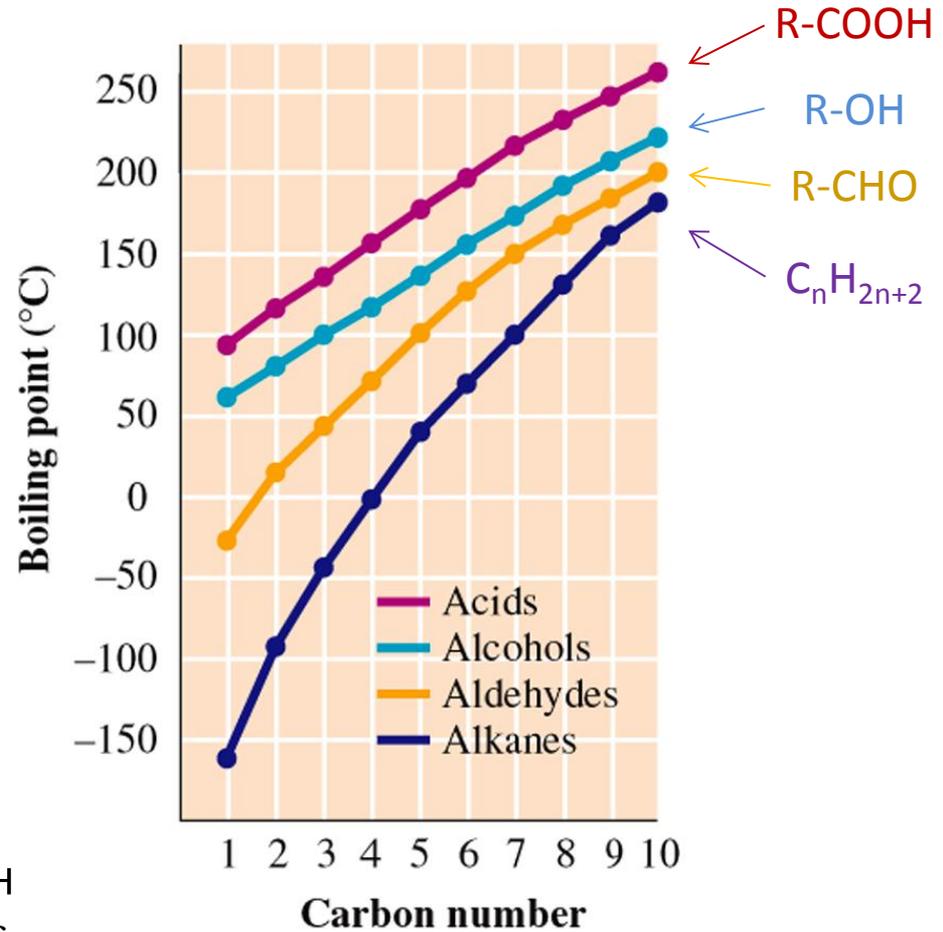
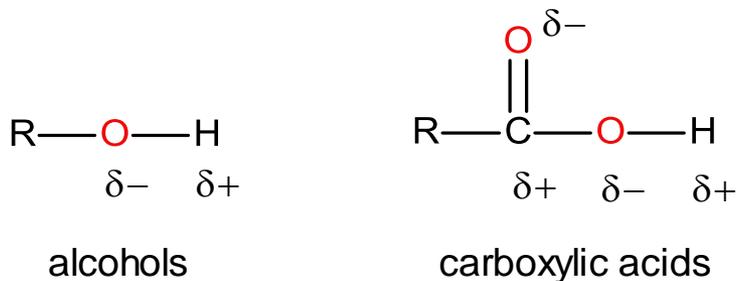
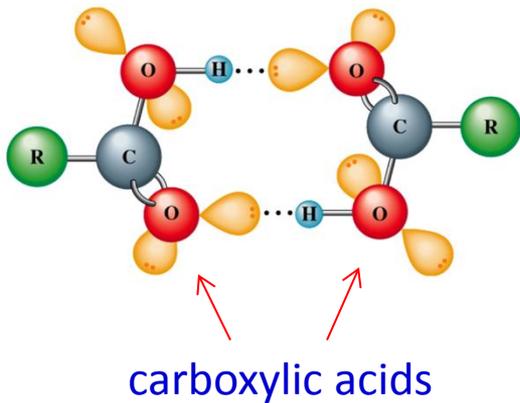
Physical properties of carboxylic acids

- Because of the **very polar** -COOH group, carboxylic acids exhibit strong intermolecular attractions.
- As expected, carboxylic acids of a given number of carbon atoms have higher **boiling points** than alcohols.

| Name | Functional-Group Class | Molecular Mass | Boiling Point ($^{\circ}\text{C}$) |
|----------------|------------------------|----------------|--------------------------------------|
| diethyl ether | ether | 74 | 34 |
| ethyl formate | ester | 74 | 54 |
| methyl acetate | ester | 74 | 57 |
| butanal | aldehyde | 72 | 76 |
| 1-butanol | alcohol | 74 | 118 |
| propionic acid | acid | 74 | 141 |

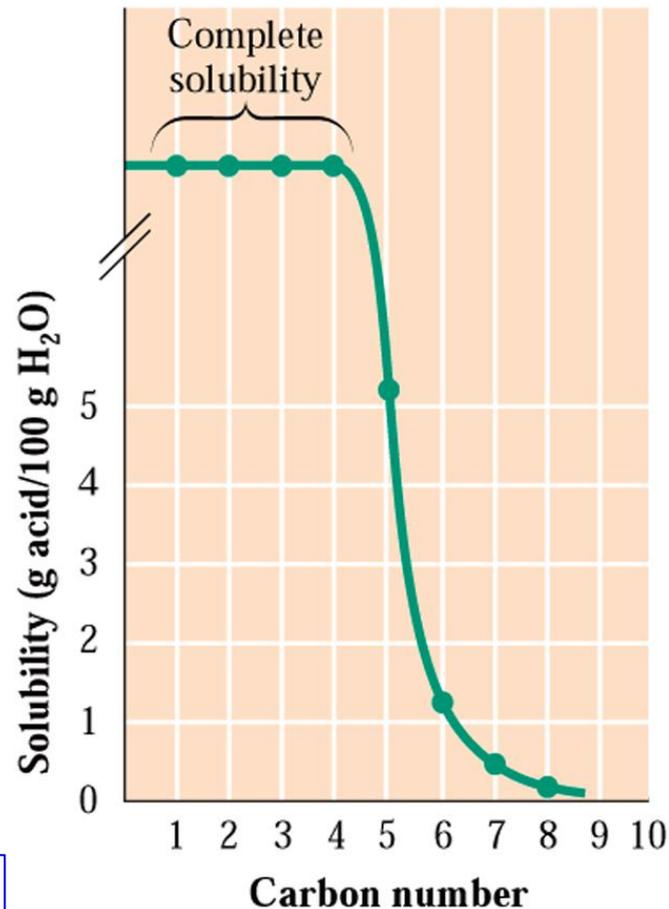
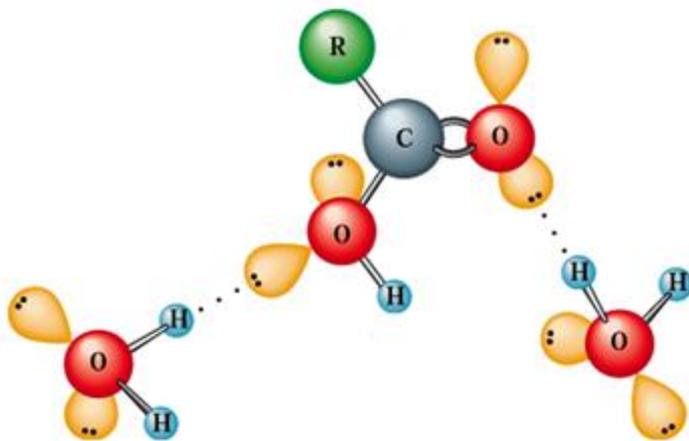
Boiling point trends

stronger H-bond
than between alcohols



Physical properties of carboxylic acids

- In terms of **water-solubility**, because of H-bonding, carboxylic acids dissolve well in water (up to 4-carbon chains).
- Beyond 4 carbons, water-solubility drops off rapidly.

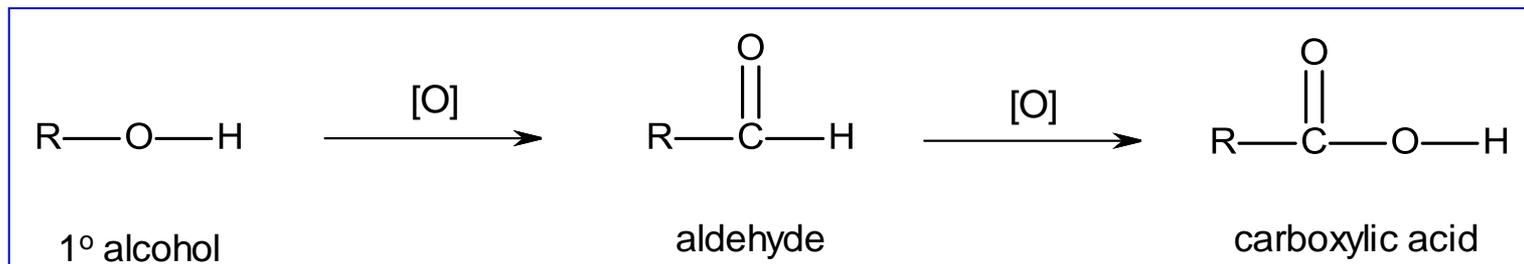


Water-solubility:

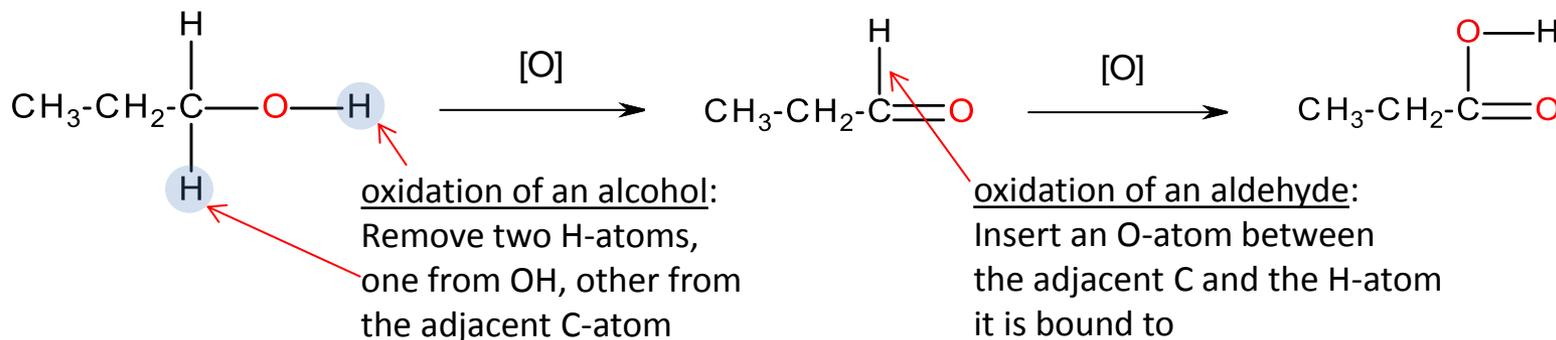
- Is the molecule polar? What about chain length?
- Can it H-bond with water? Can water H-bond to it?

Preparation of carboxylic acids

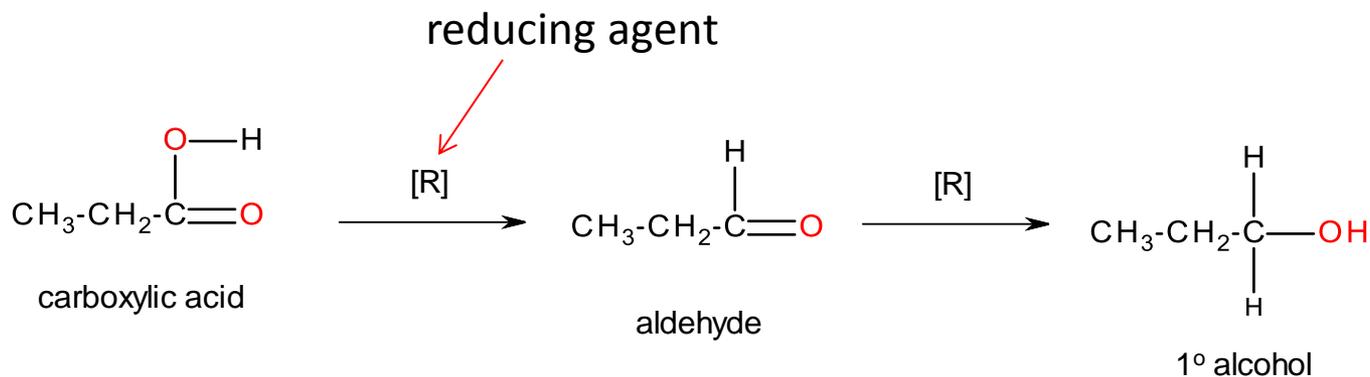
- We saw in Ch-15 that carboxylic acids can be prepared from aldehydes (which can be prepared from primary alcohols):



"adjacent" C-atom



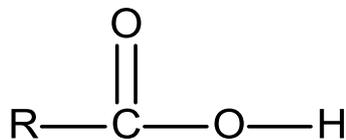
- Reduction will accomplish the reverse of these reactions



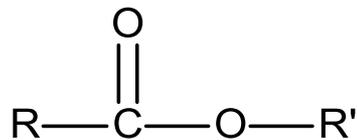
If you can remember that 1° alcohols can be oxidized to aldehydes, and then to ketones, the reduction reactions are much easier to do (just reverse of the oxidation reactions)

Structure of esters

- Esters are carboxylic acid derivatives having an alkoxy group instead of a hydroxyl group.



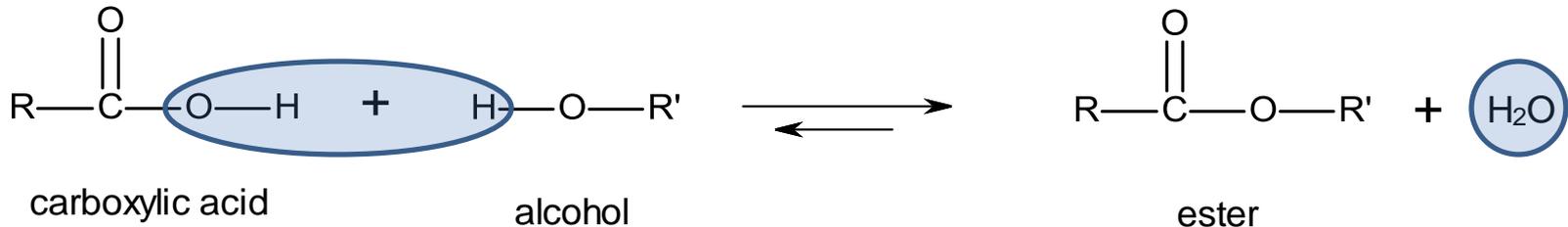
carboxylic acid



ester

Preparation of esters

- Esters are prepared by condensation reactions (called an **esterification reaction** in this case):

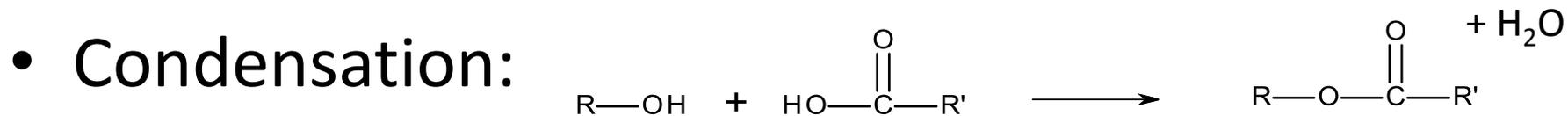
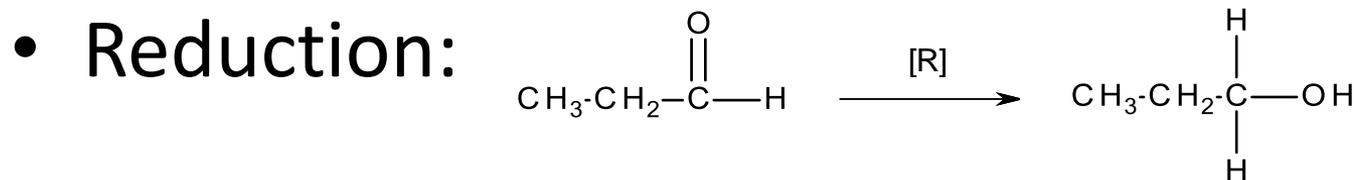
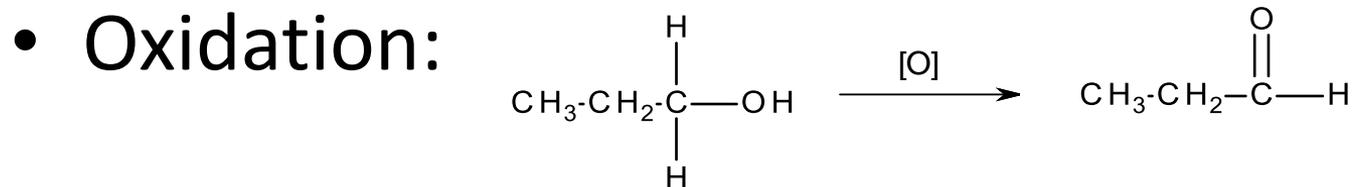
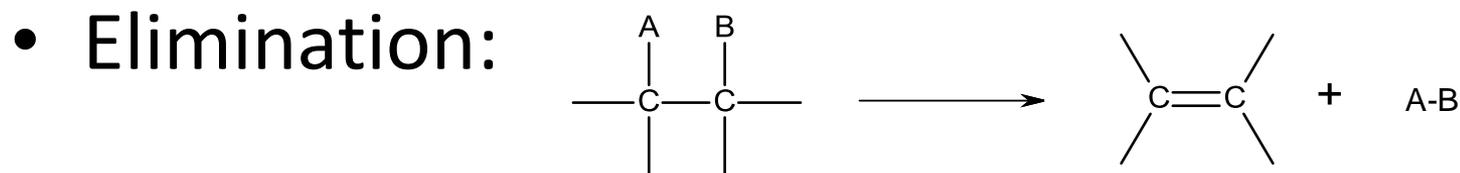
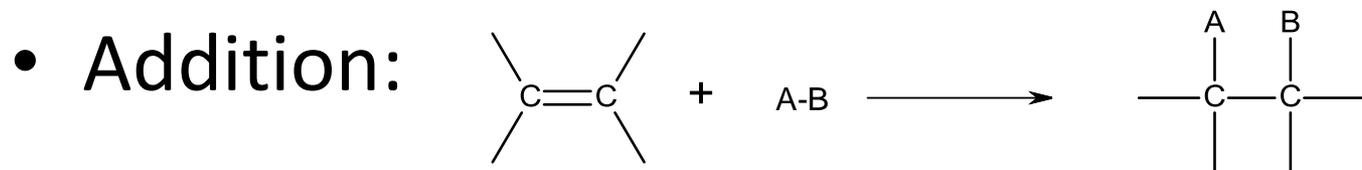


An alcohol and a carboxylic acid both have an -OH group.

In this reaction, a larger molecule (the ester) is made when the carboxylic acid and the alcohol react together to release a water molecule.

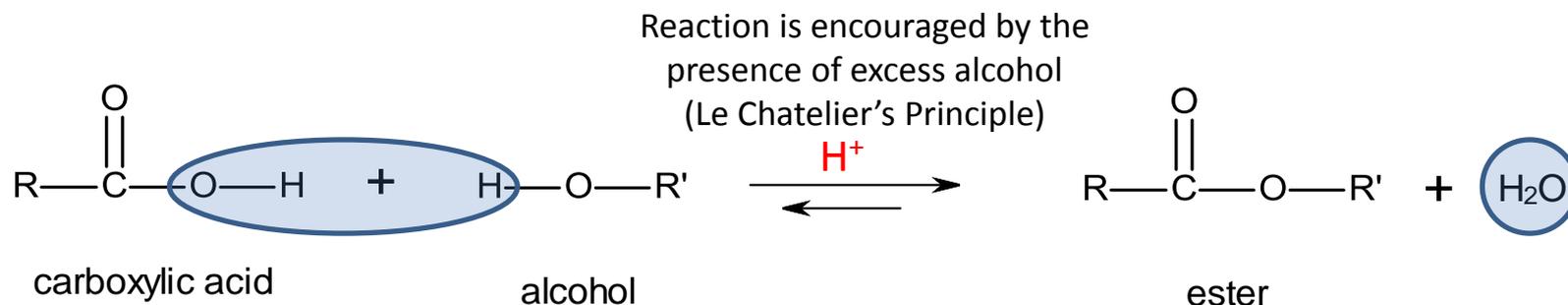
The C and the O that were bound to the OH and H become bonded together in the process

Summary of most important reactions seen so far

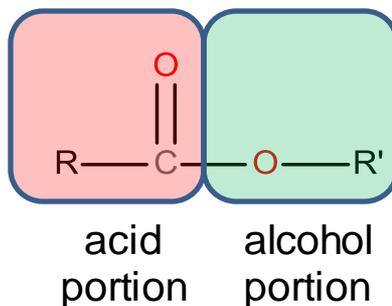


Preparation of esters

- Esters are prepared by condensation reactions involving carboxylic acids and alcohols. Such reactions are called **esterification reactions**:

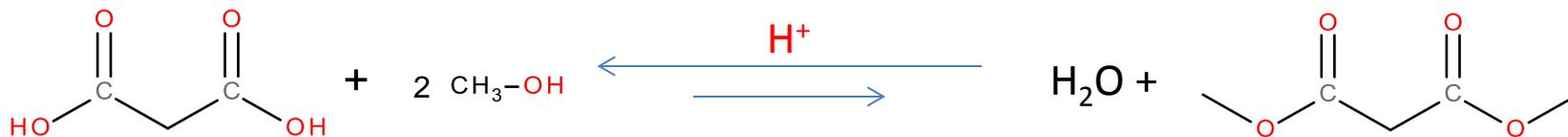
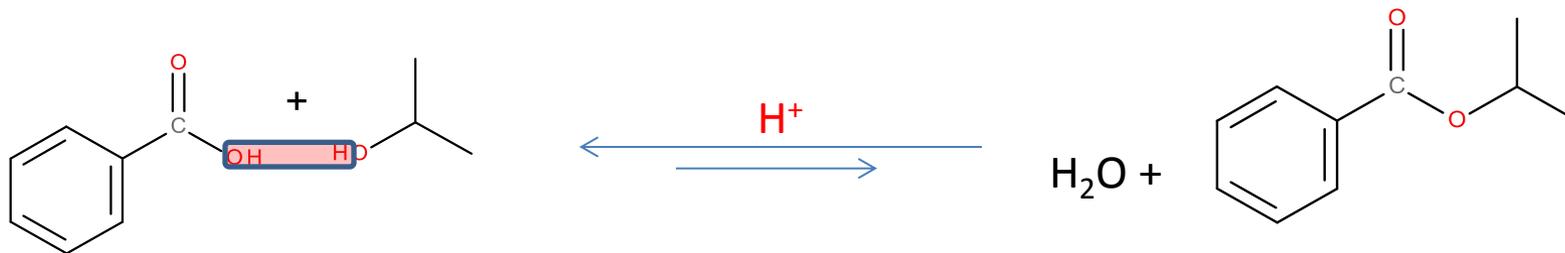
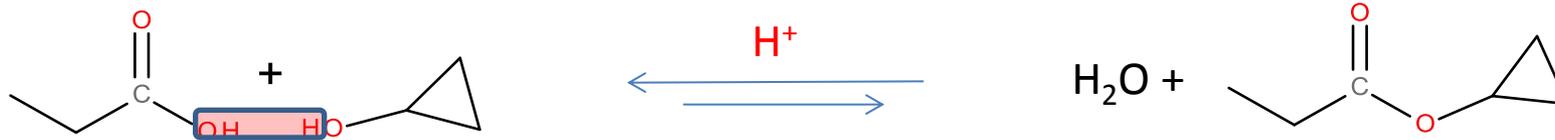
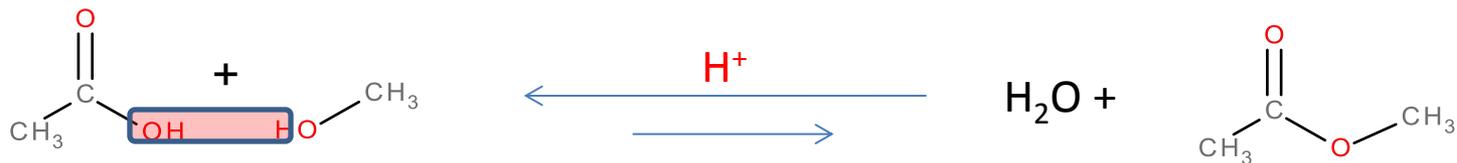
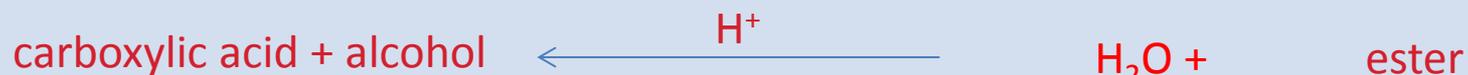


- Thus, an ester consists of an acid portion and an alcohol portion:



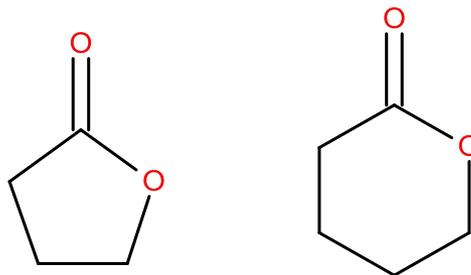
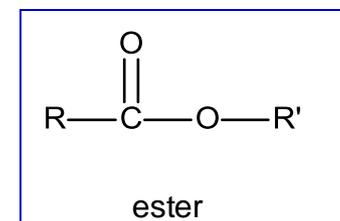
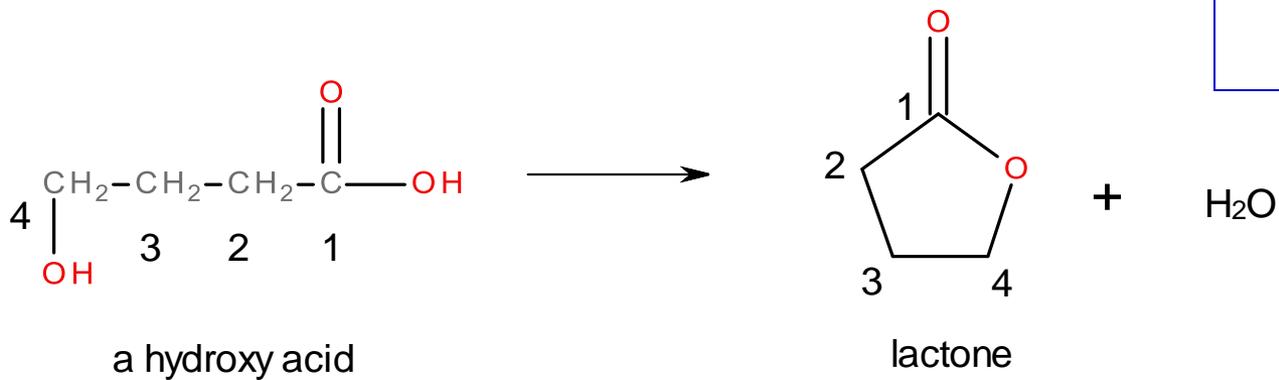
Preparation of esters

- Complete the following reactions:



Preparation of esters

- Cyclic esters (**lactones**) are created from hydroxy acids (bear both a hydroxyl group and a carboxyl group) in an *intra*molecular esterification reaction:

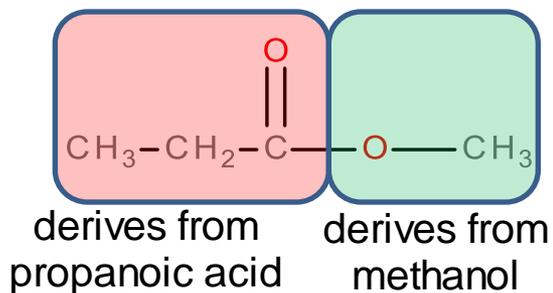


lactones

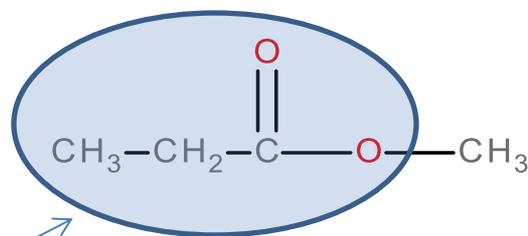
lactones (like cyclic ethers) are examples of *heterocyclic compounds* (meaning it's a cyclic compounds in which at least one member of the ring is not a carbon atom)

Nomenclature for esters

- Thinking of an ester in terms of an “alcohol portion” and a “carboxylic acid portion” is important for naming esters using the IUPAC system:
 - The name for the alcohol portion comes first: name the alkyl part of the alcohol (e.g., for the ester shown below, the first part of the ester’s name is methyl (alcohol part comes from methanol). Present the alkyl name separate from the remainder of the ester name.
 - The carboxylic acid portion is named as if it were deprotonated (i.e. the conjugate base of the carboxylic acid), changing the “-ic acid” part of that name to “-ate”



Methyl propanoate

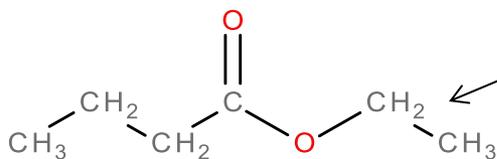


This part would be called “propanoate”

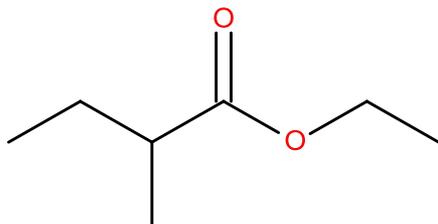
Nomenclature for esters

- Some other examples:

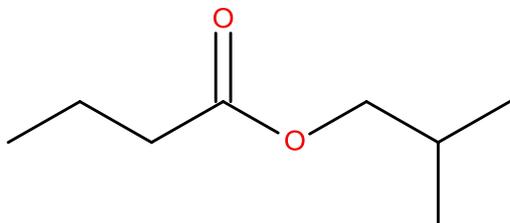
The "alcohol part" of the ester is bonded to the -O- part of the ester



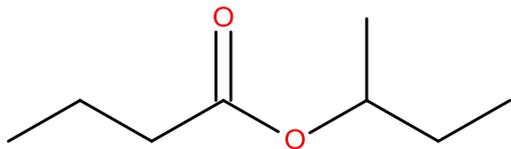
Ethyl butanoate



Ethyl 2-methylbutanoate



2-Methylpropyl butanoate
Isobutyl butanoate



2-Butyl butanoate
Sec-Butyl butanoate

Selected common esters

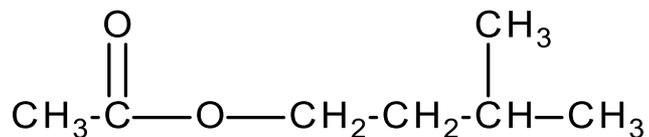
- Flavor/fragrance agents

| IUPAC Name | Structural Formula | Characteristic Flavor and Odor |
|--|--|--------------------------------|
| (methylpropyl) isobutyl methanoate | $\begin{array}{c} \text{O} & & \text{CH}_3 \\ \parallel & & \\ \text{H}-\text{C}-\text{O}-\text{CH}_2-\text{CH}-\text{CH}_3 \end{array}$ | raspberry |
| propyl ethanoate | $\begin{array}{c} \text{O} \\ \parallel \\ \text{CH}_3-\text{C}-\text{O}-(\text{CH}_2)_2-\text{CH}_3 \end{array}$ | pear |
| pentyl ethanoate | $\begin{array}{c} \text{O} \\ \parallel \\ \text{CH}_3-\text{C}-\text{O}-(\text{CH}_2)_4-\text{CH}_3 \end{array}$ | banana |
| octyl ethanoate | $\begin{array}{c} \text{O} \\ \parallel \\ \text{CH}_3-\text{C}-\text{O}-(\text{CH}_2)_7-\text{CH}_3 \end{array}$ | orange |
| pentyl propanoate | $\begin{array}{c} \text{O} \\ \parallel \\ \text{CH}_3-\text{CH}_2-\text{C}-\text{O}-(\text{CH}_2)_4-\text{CH}_3 \end{array}$ | apricot |
| methyl butanoate | $\begin{array}{c} \text{O} \\ \parallel \\ \text{CH}_3-(\text{CH}_2)_2-\text{C}-\text{O}-\text{CH}_3 \end{array}$ | apple |
| ethyl butanoate | $\begin{array}{c} \text{O} \\ \parallel \\ \text{CH}_3-(\text{CH}_2)_2-\text{C}-\text{O}-\text{CH}_2-\text{CH}_3 \end{array}$ | pineapple |

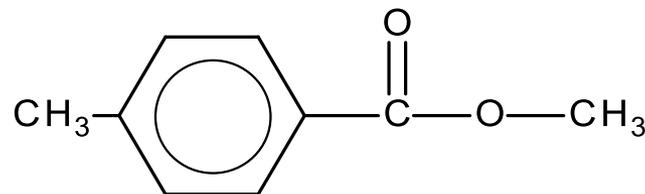


Selected common esters

- Pheromones:

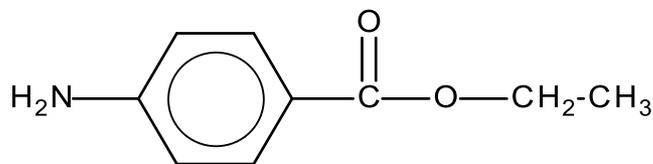


alarm pheromone for honeybee

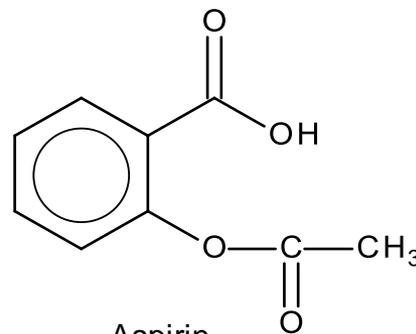


sexual attractant for canines

- Medications:



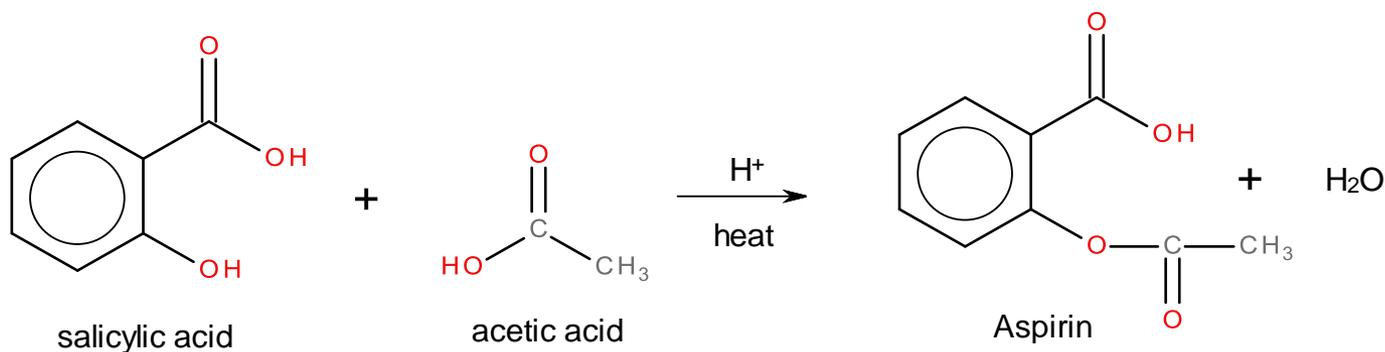
benzocaine



Aspirin

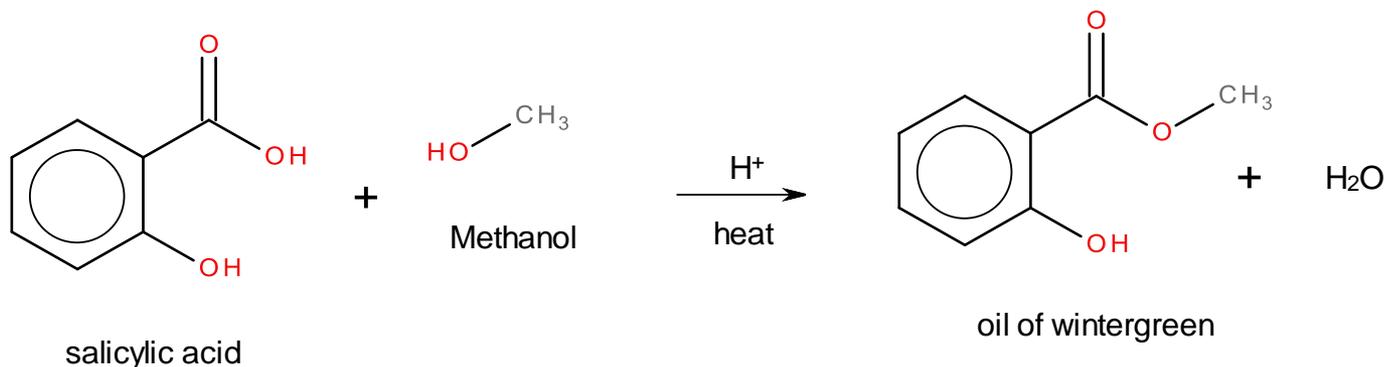
Selected common esters

- Synthesis of Aspirin



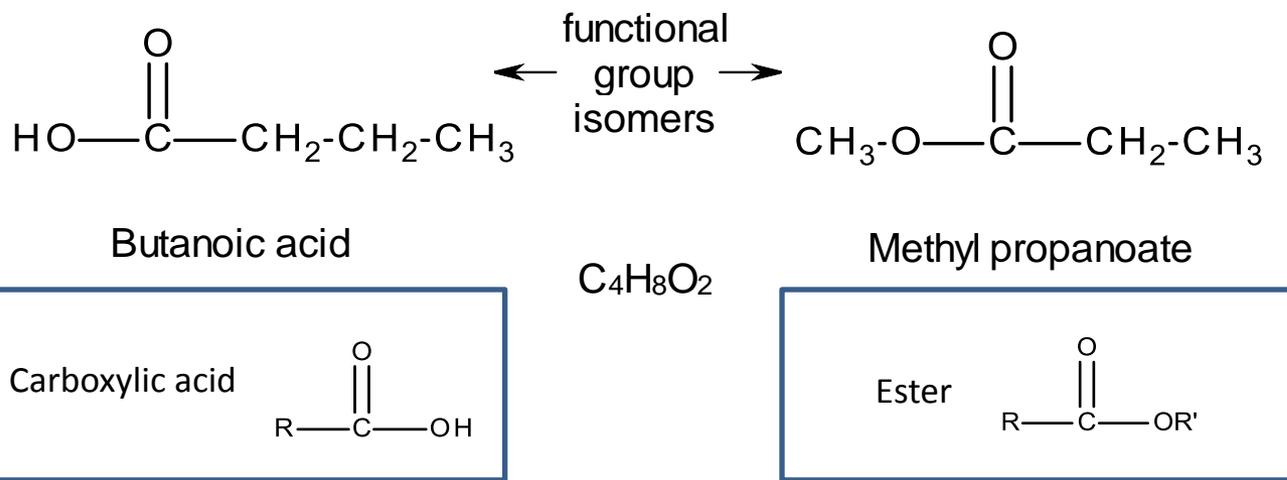
(better yield if acetic anhydride is used instead of acetic acid)

- Synthesis of oil of wintergreen:



Isomerism in carboxylic acids and esters

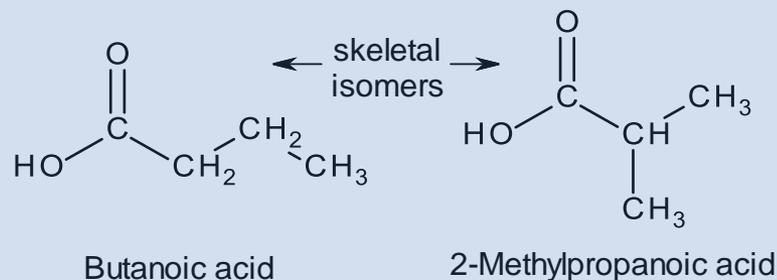
- Recall that **constitutional isomers** are molecules that share the same formula but differ in their atom-to-atom connectivities.
- Three kinds of constitutional isomers (in the order we encountered them):
 - **positional isomers** (position of the functional group differs, C-chain is same)
 - **skeletal isomers** (have different C-chains)
 - **functional group isomers** (have different functional groups)
- **Carboxylic acids and esters** that have a given number of carbon atoms form another example of functional group isomers:



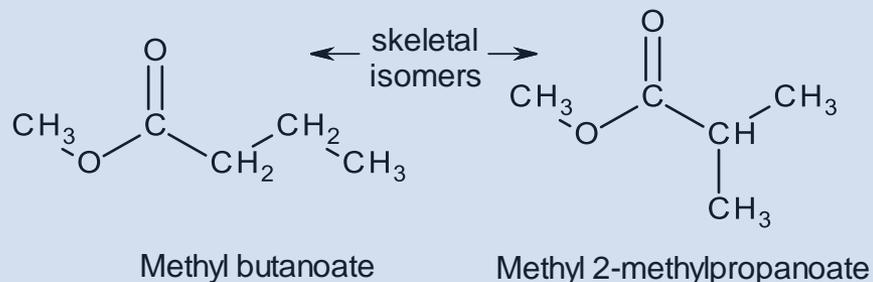
Isomerism in carboxylic acids and esters

- For both carboxylic acids and esters, skeletal isomers are possible:

(carboxylic acids)

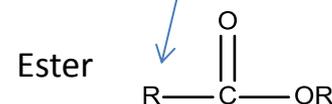
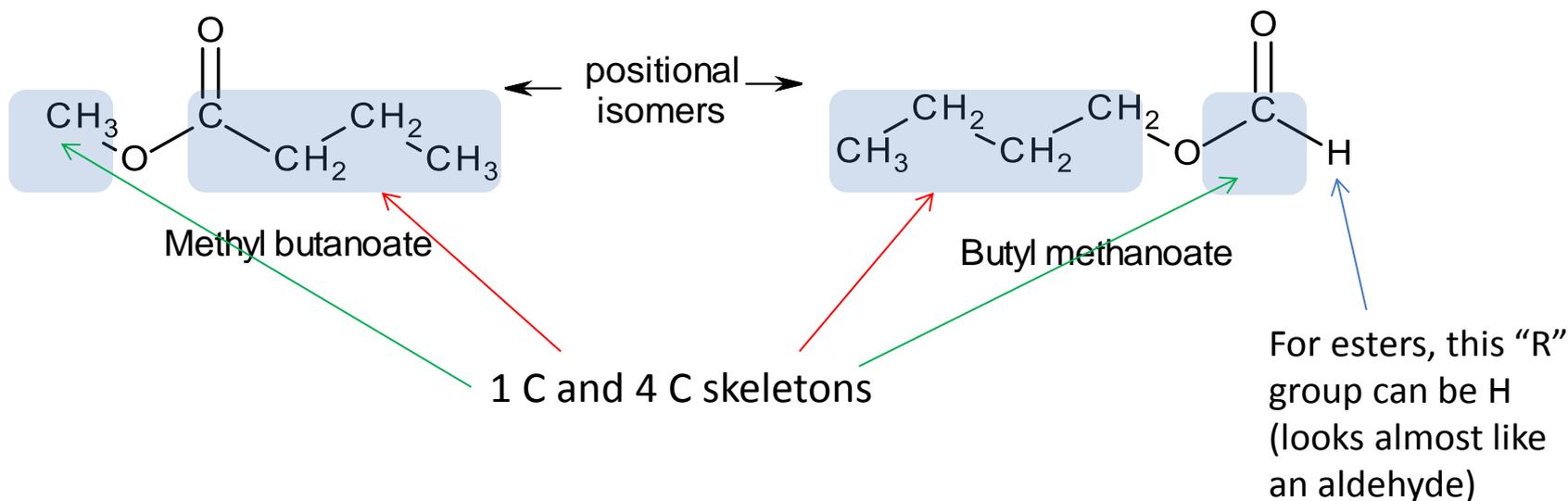


(esters)



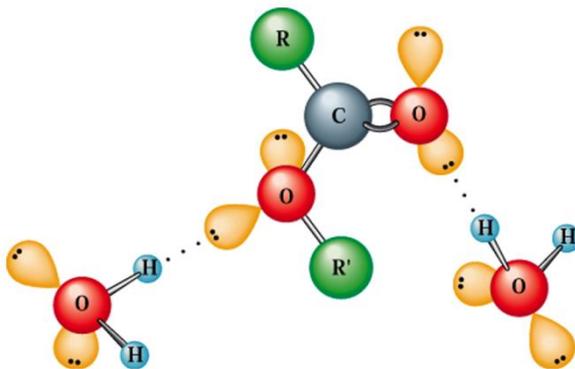
Isomerism in carboxylic acids and esters

- Positional isomers are possible for esters, but not carboxylic acids.



Physical properties of esters

- Because they don't possess OH groups, esters cannot form H-bonds with other ester molecules. As a result, *esters have lower boiling points than carboxylic acids and alcohols that have approximately the same molar mass.*
- They do have a C=O bond (polar) so their boiling points are between alcohols and alkanes.
- Water molecules can H-bond to esters, at the oxygen atoms. This makes *low molecular weight* esters water-soluble.



Chemical reactions of esters

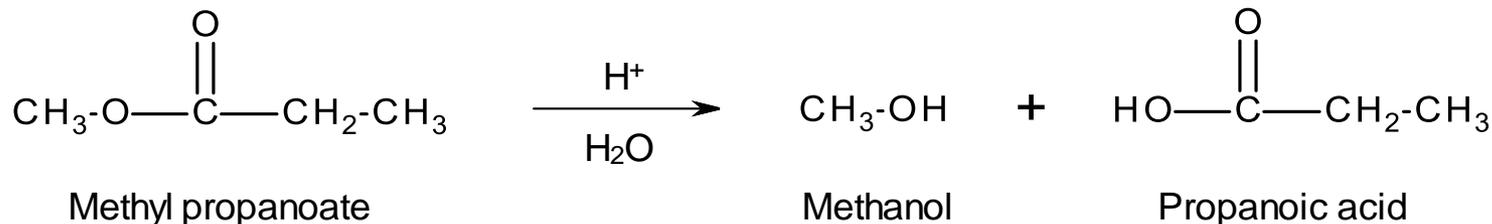
hydrolysis = reverse of condensation reaction

- Ester hydrolysis: the hydrolysis of an ester is accomplished by reacting water with the ester in the presence of an acid catalyst (ester hydrolysis is the reverse reaction of esterification).



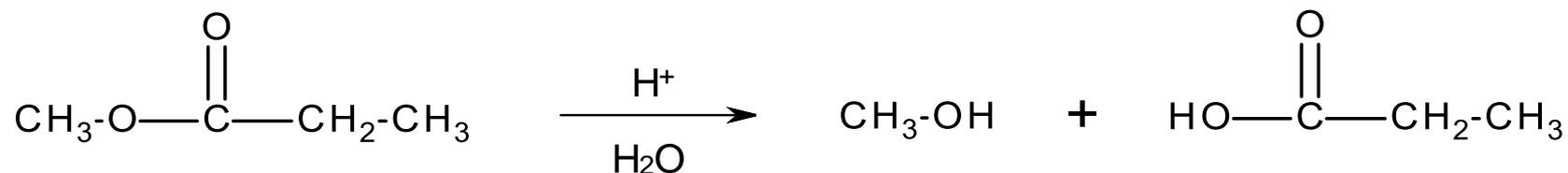
acidic conditions
used for hydrolysis

- An example:



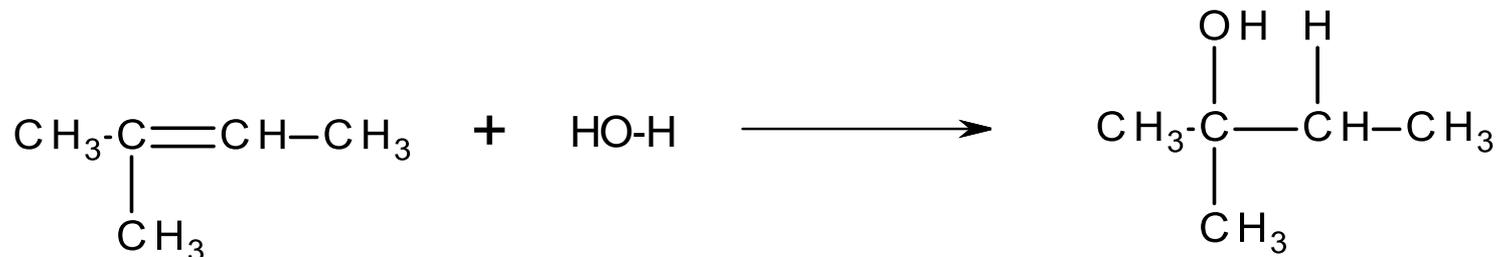
Some things that sound the same but mean different things

- Hydrolysis: reverse of condensation → water is reacted with a large molecule to break it into two smaller molecules



one organic molecule becomes two

- Hydration: water is added across a multiple bond, breaking a π -bond and producing new C-H and C-OH bonds. Example:



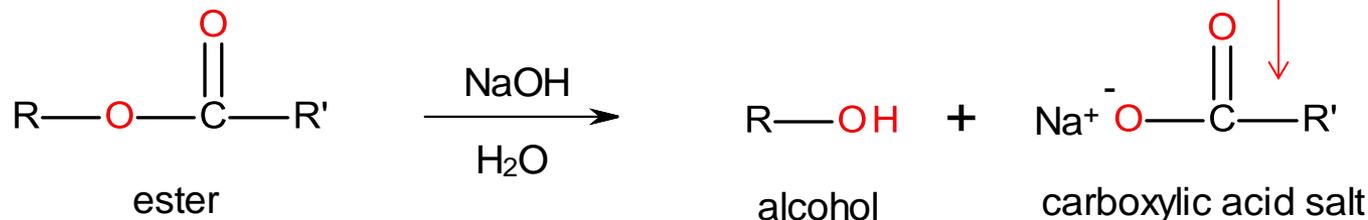
one organic molecule on reactant and product sides

Chemical reactions of esters

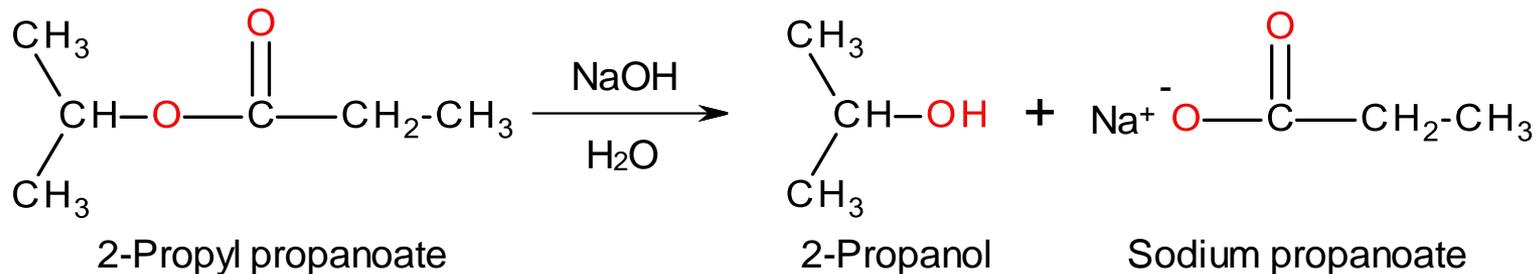
Hydrolysis in basic conditions = saponification

- Ester saponification: another hydrolysis reaction, but this time, under basic conditions. Rather than a carboxylic acid, the acid salt is produced here.

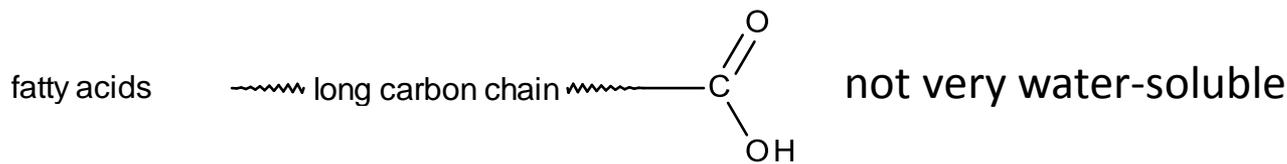
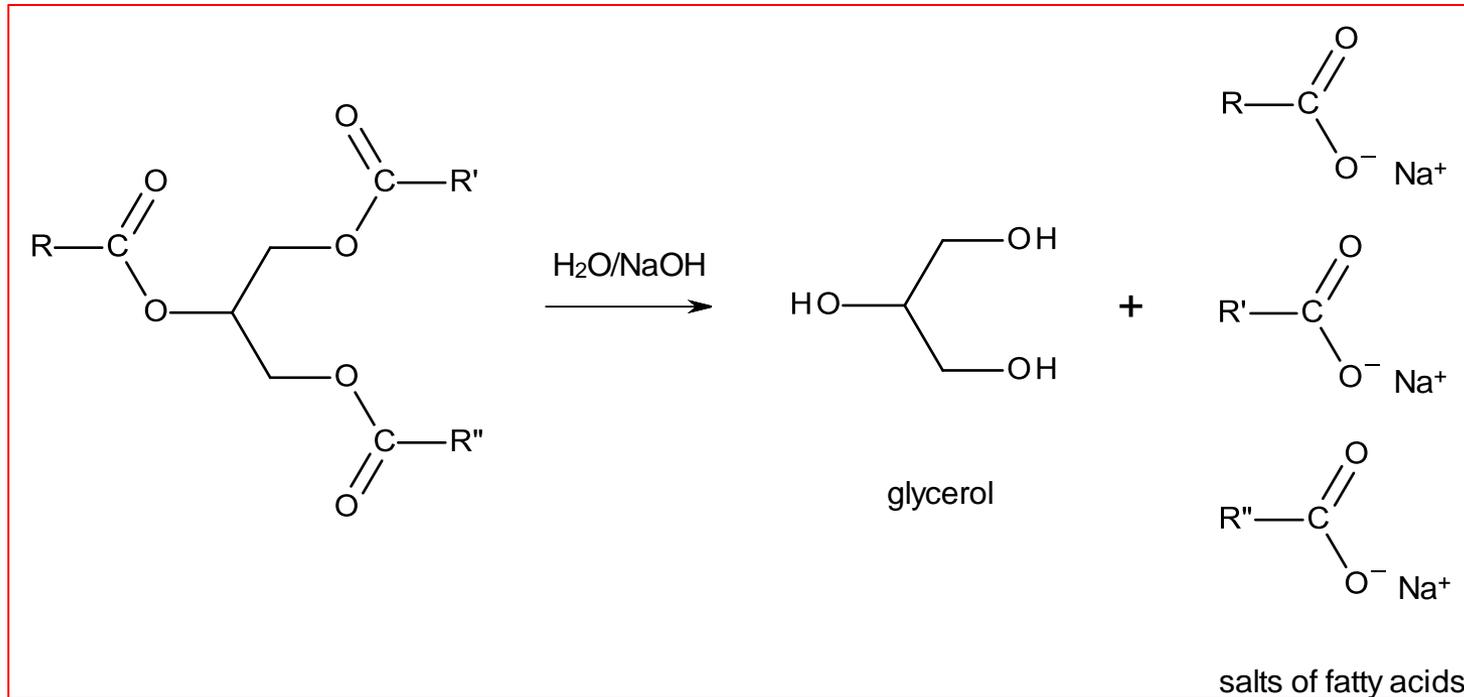
because the carboxylic acid that *would* form during hydrolysis can't exist in basic conditions



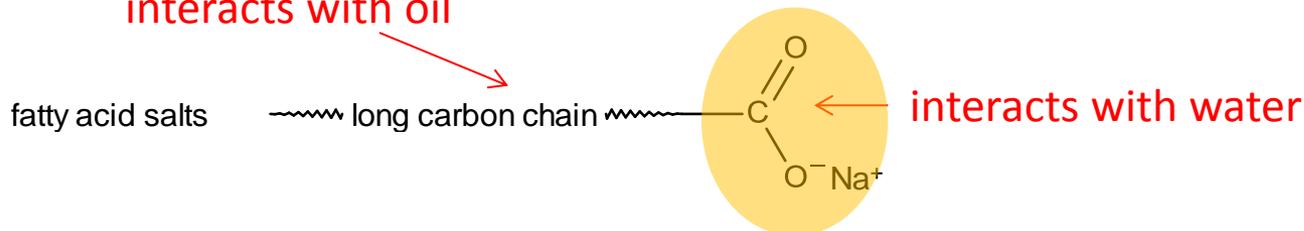
- Example:



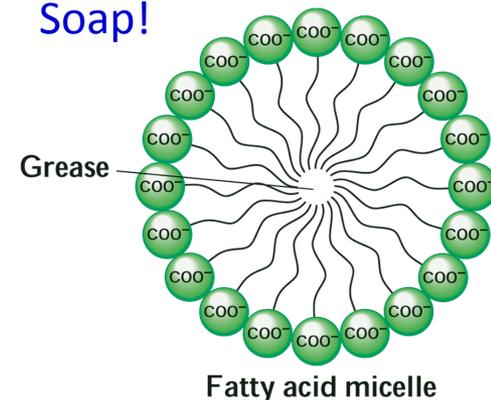
Saponification of a triglyceride



interacts with oil



Soap!

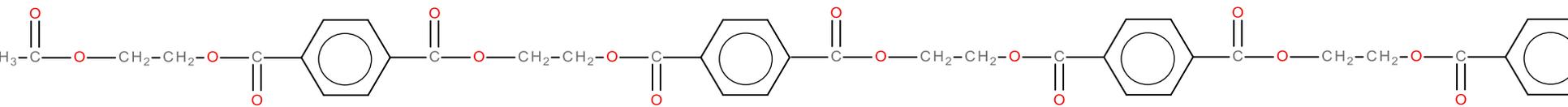
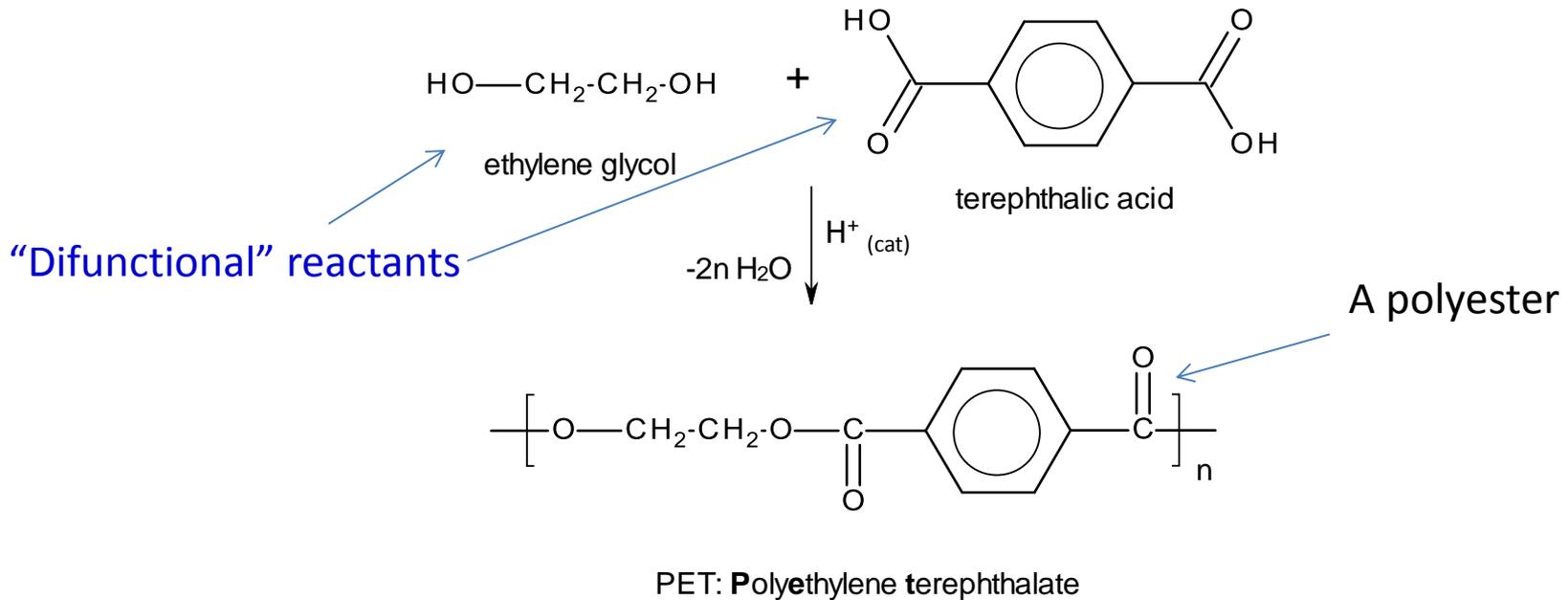


Polyesters

“poly” means *many*

“polyester” means many esters linked together in one big molecule

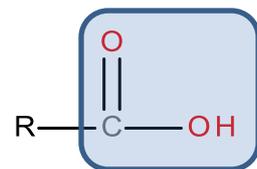
- **Condensation polymerization** creates polymers through the loss of water molecules:



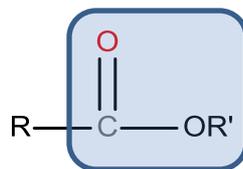
Acid chlorides and acid anhydrides

carboxylic acid derivatives

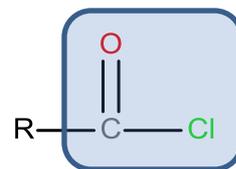
- Acid chlorides and anhydrides have structures that are quite similar to carboxylic acids and esters.
- Both are able to be hydrolyzed* to produce carboxylic acids.



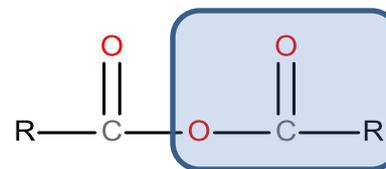
carboxylic acid



ester



acid chloride

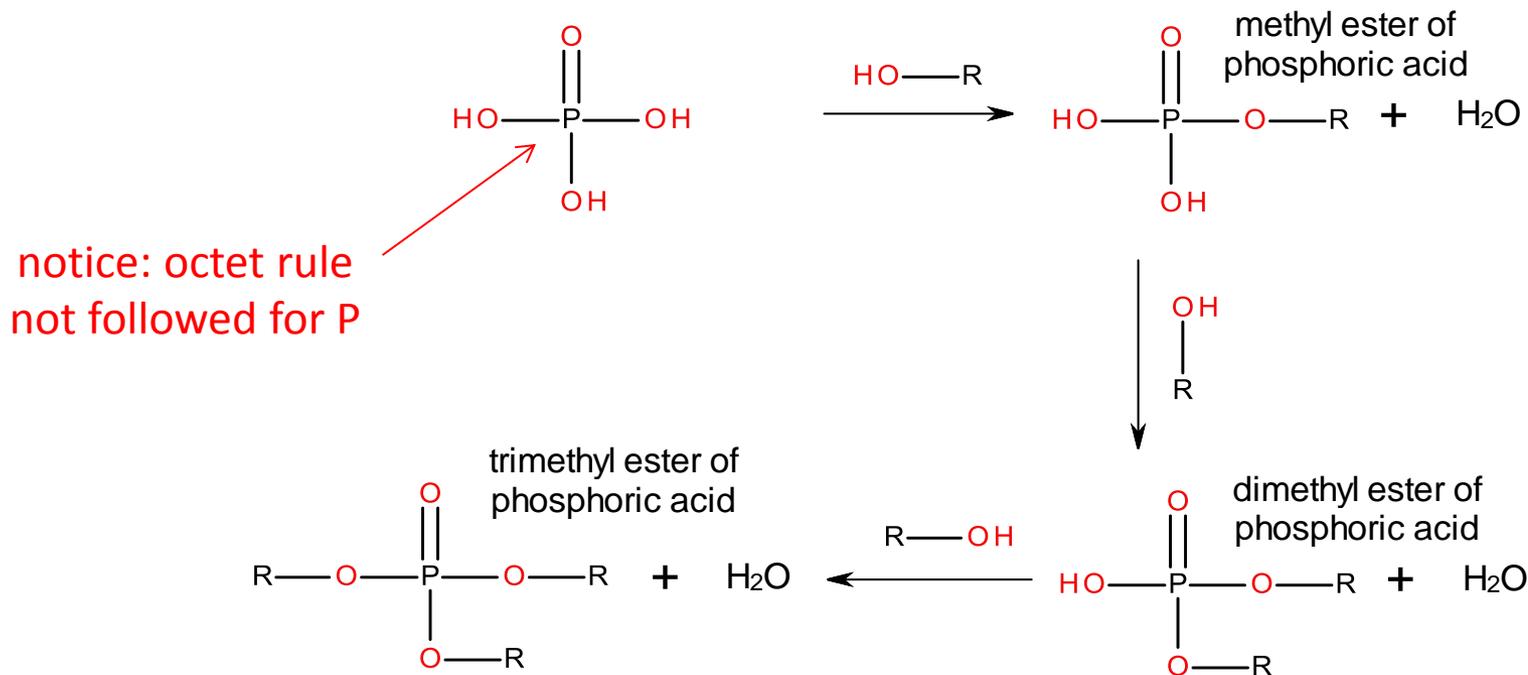


acid anhydride

* Hydrolysis reaction

Esters and anhydrides of inorganic acids

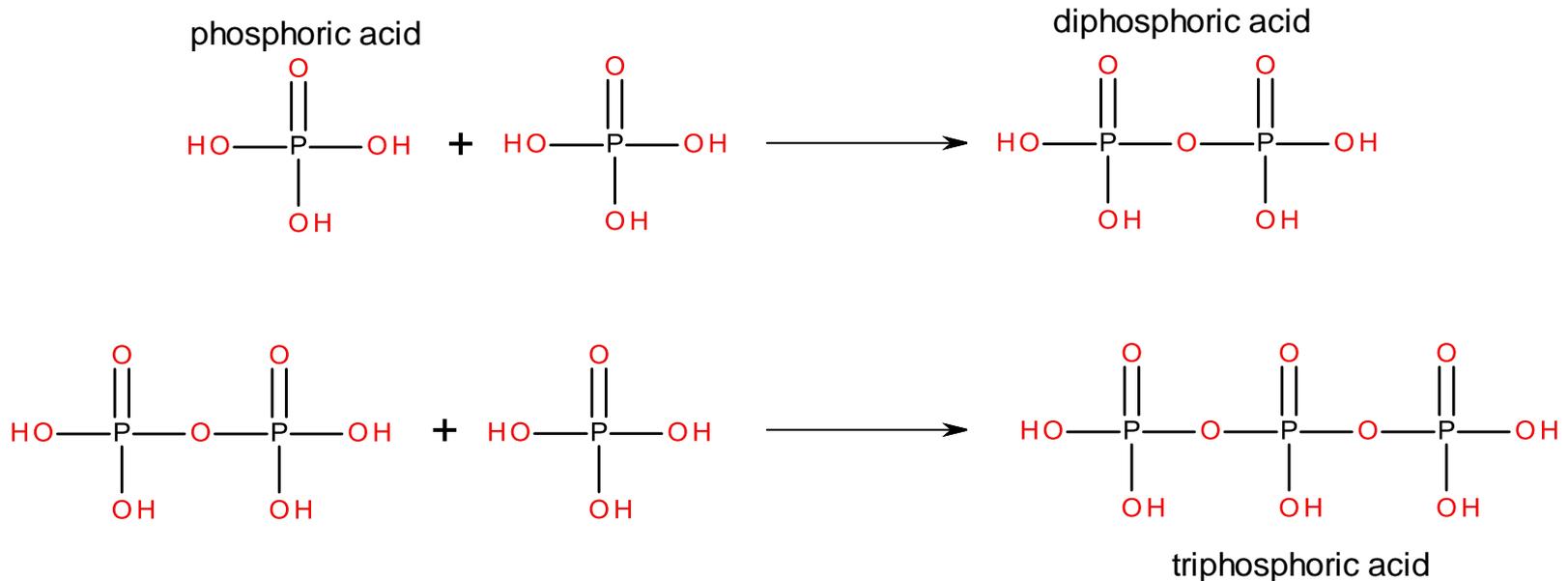
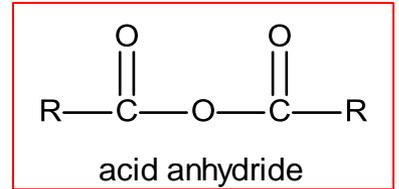
- **Phosphate esters** are the most important class of inorganic esters.
- Because phosphoric acid has three OH groups, it can form mono-, di- and tri-esters:



R-OH = CH₃OH here

Esters and anhydrides of inorganic acids

- Phosphoric acid anhydrides are also made via condensation reactions:



- These systems are important components of cellular processes for biochemical energy production.

ATP

phosphoanhydride component

