Ex17

Analgesics, TLC Analysis

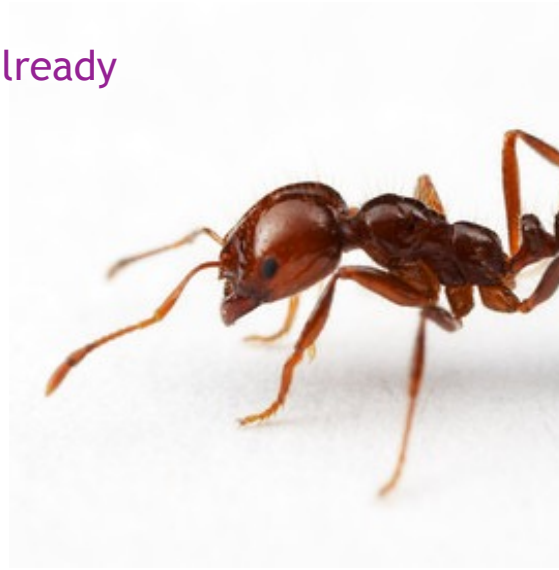
- Analgesics
  - Carboxylic Acids
    - Structure
    - Properties
  - Willow Bark
  - Esters & Esterification
  - Aspirin
- The Experiment
  - Part A
    - Use TLC to Separate Compounds
  - Part B
    - Determine Elution Solvents for Separation
- For Next Week

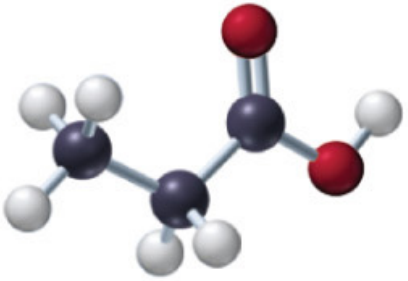
Carboxylic Acids

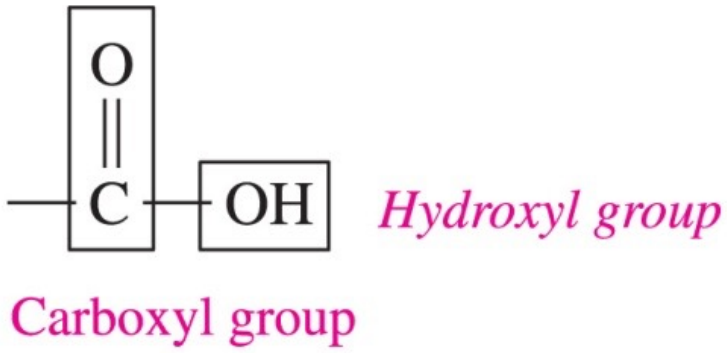
- Carboxylic Acids have many interesting properties.
  - Many of the sharp flavors we enjoy in food (vinegar, grapefruit, lemon…) are produced by simple substances of the carboxylic acid family of organic substances.
  - These organic molecules are acids. Like the simple binary acids you're already familiar with (HCl, HBr) they release free protons (H^+).
    - These substances have high acidity (low pH).
    - They neutralize bases like NaOH to form water.
  - Many toxins are simple carboxylic acids, like the formic acid in ant venom.
  - Salts formed from carboxylic acids cause food to be resistant to mold and microorganisms that cause spoilage.
  - They play important roles in how animals store and process energy.

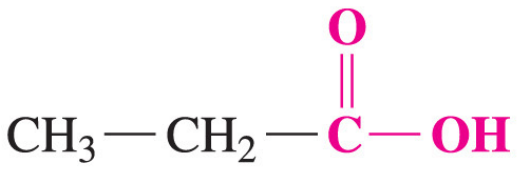
Carboxyl Functional Group

- Carboxylic Acids are defined by the carboxyl functional group.
  - The carboxyl group is a composite of two functional groups you're already familiar with.
    - The hydroxyl group.
    - The carbonyl group.









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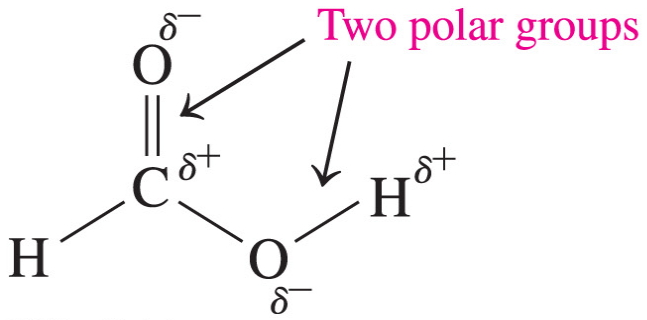

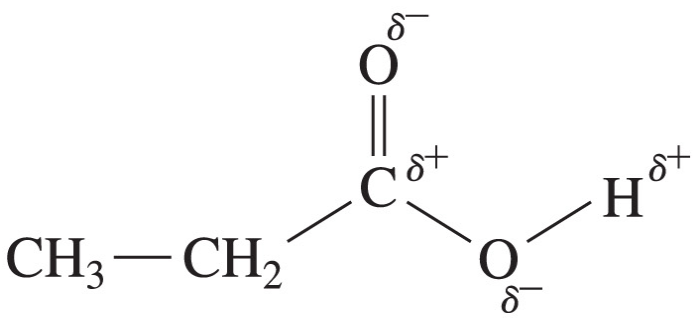

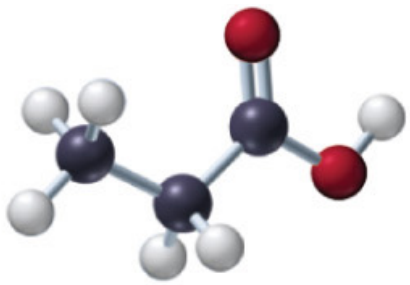

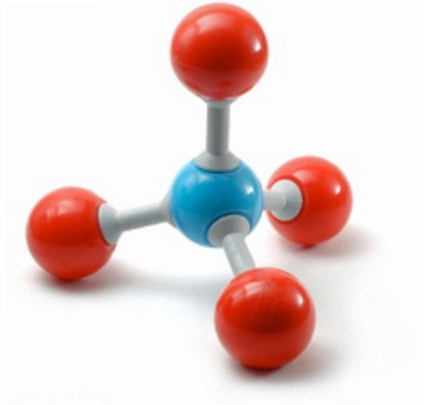

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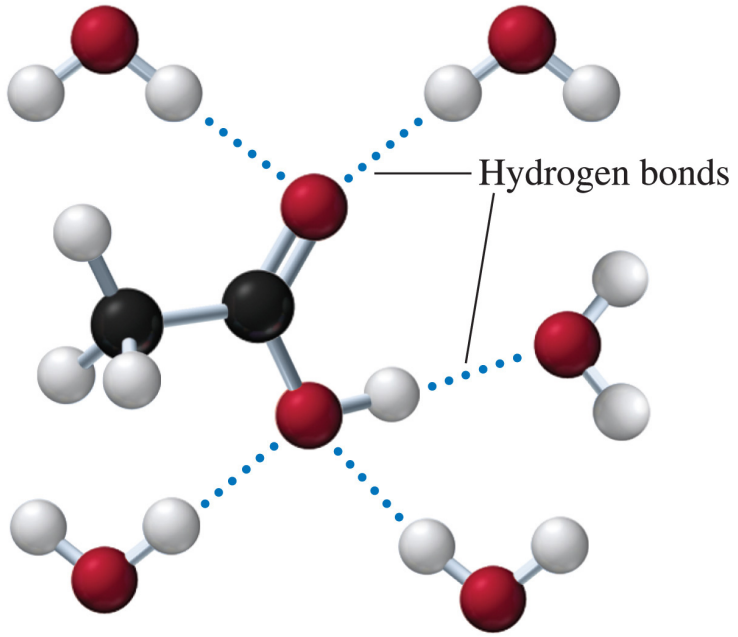
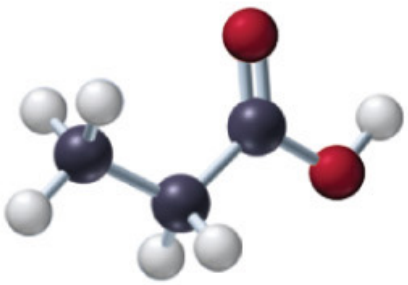
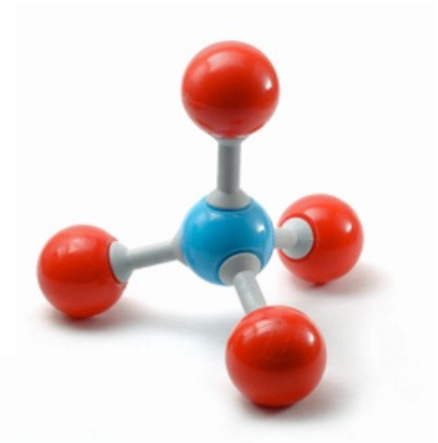
  - Carboxylic acids are strongly polar because they have two polar groups.
  - Each carboxylic acids forms hydrogen bonds with many water molecules at once.
  - Carboxylic acids with up to four carbon atoms are very soluble in water
    - As the number of carbons increases, the solubility of the carboxylic acid in water is reduced.







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Properties & Structure

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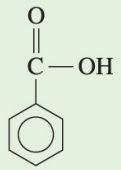
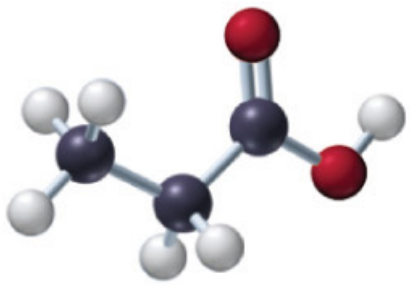
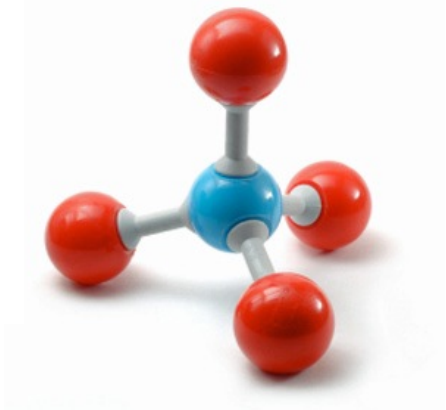
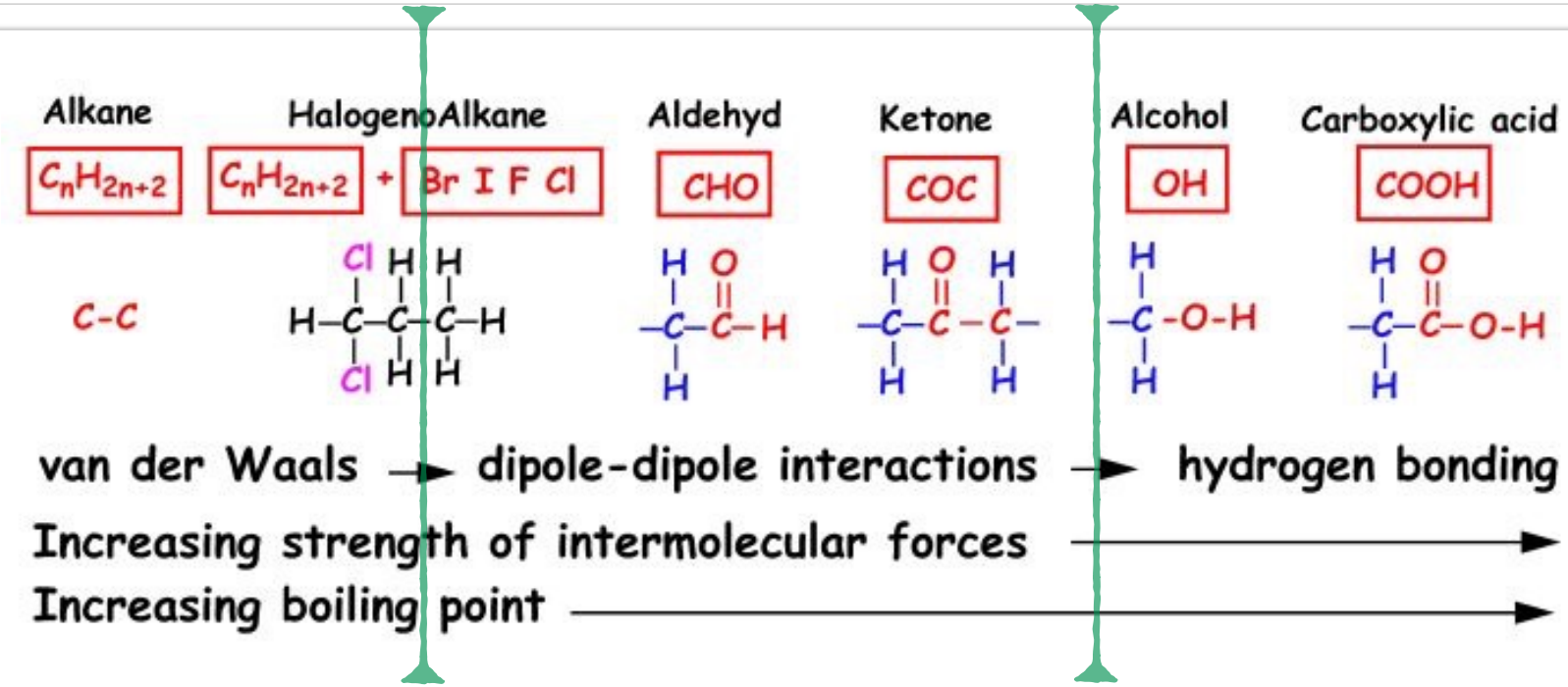
IUPAC Name	Condensed Structural Formula	Solubility in Water
Methanoic acid	$H-\overset{\overset{O}{\|\|}}{C}-OH$	Soluble
Ethanoic acid	$CH_3-\overset{\overset{O}{\|\|}}{C}-OH$	Soluble
Propanoic acid	$CH_3-CH_2-\overset{\overset{O}{\|\|}}{C}-OH$	Soluble
Butanoic acid	$CH_3-CH_2-CH_2-\overset{\overset{O}{\|\|}}{C}-OH$	Soluble
Pentanoic acid	$CH_3-CH_2-CH_2-CH_2-\overset{\overset{O}{\|\|}}{C}-OH$	Soluble
Hexanoic acid	$CH_3-CH_2-CH_2-CH_2-CH_2-\overset{\overset{O}{\|\|}}{C}-OH$	Slightly soluble
Benzoic acid		Slightly soluble

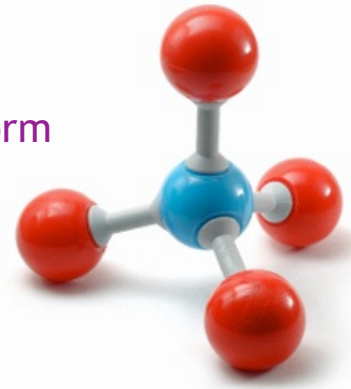




Properties & Structure

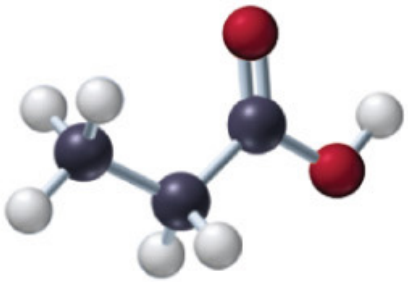


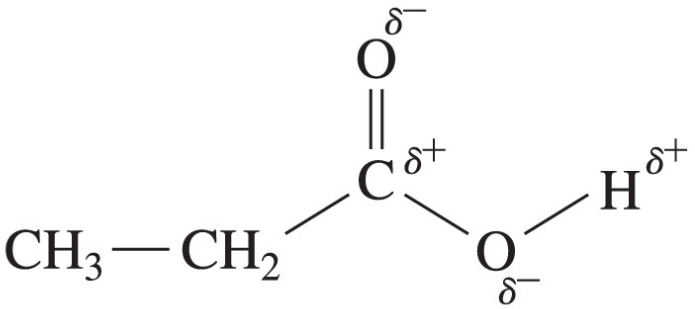
- Carboxylic Acids experience all three kinds of intermolecular forces:
  - Van der Waals Forces
  - Dipole-Dipole Forces
  - Hydrogen Bonding
- Because carboxylic acids have both a hydroxyl and carbonyl group they form more hydrogen bonds than alcohols.
- Carboxylic Acids have higher boiling points and melting points than even alcohols.

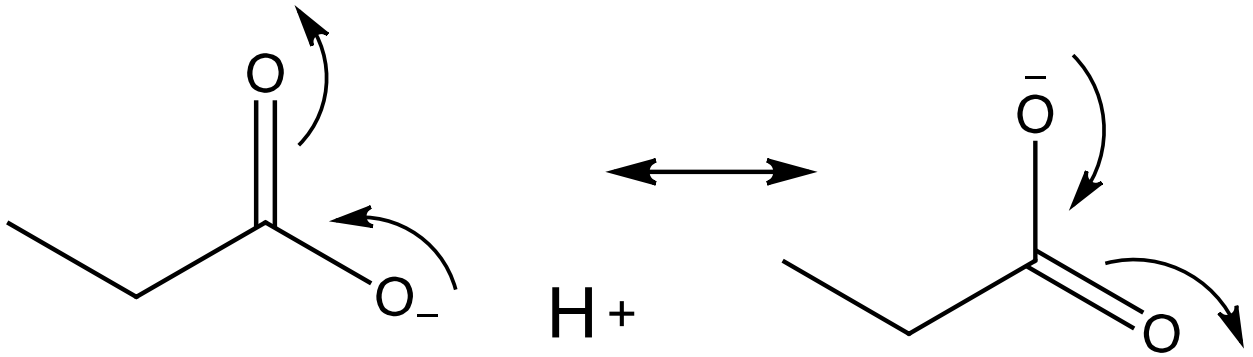


Properties & Structure

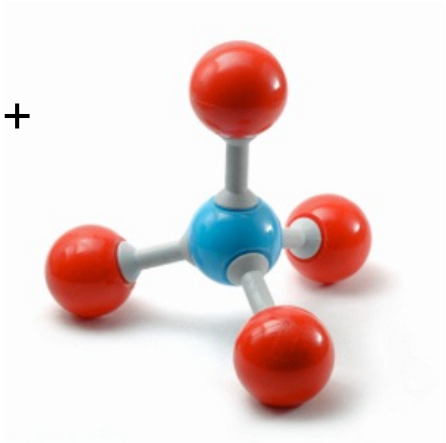
- Carboxylic Acids are defined by the carboxyl functional group.
  - Carboxylic acids are strongly polar because they have two polar groups.
  - The two polar groups cooperate to balance negative charge, stabilizing the molecule enough to allow it to release protons.
    - To act as an organic acid.







H+



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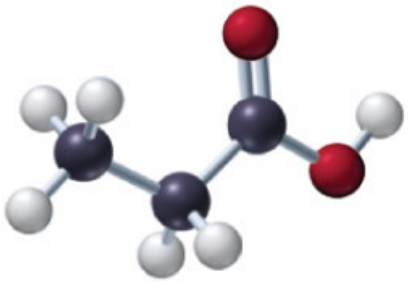
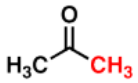
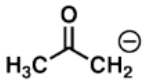
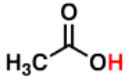
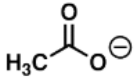
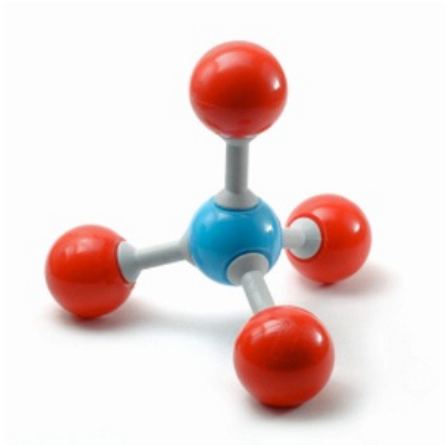


Functional group	Example	pKa	Conjugate Base
Alkane	H_3C–CH_3	~50	H_3C–$CH_2^{\ominus}$
Alkene		~43	
Ketone/ aldehyde		20-24	
Alcohol	H_3C–OH	17	H_3C–$O^{\ominus}$
Water	HO–H	16	$HO^{\ominus}$
Thiols	CH_3S–H	13	$CH_3S^{\ominus}$
Carboxylic acids		4	
Sulfuric acid	H_2SO_4	–3	$HSO_4^{\ominus}$
Hydrochloric acid	HCl	–6	$Cl^{\ominus}$



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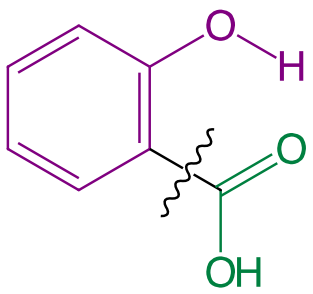
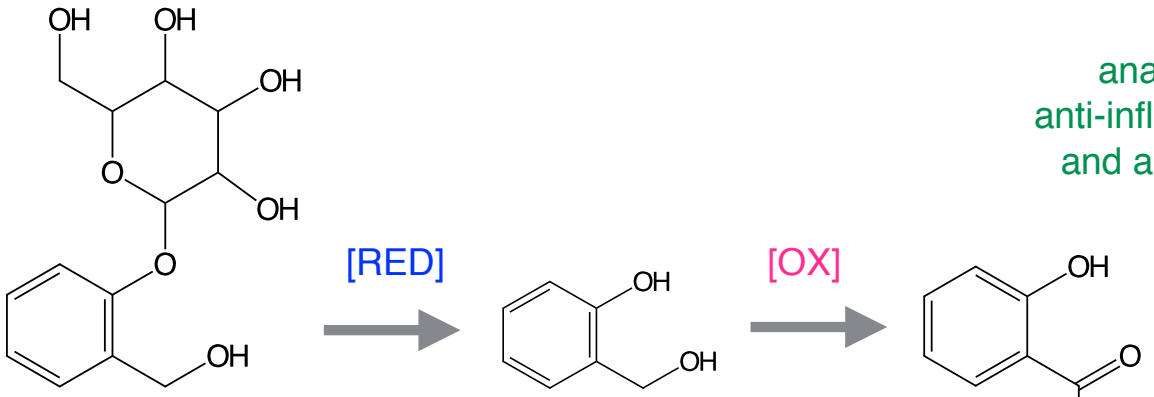
Willow Bark

salicylic acid



- By the 1800s, chemists discovered that salicin from the willow tree bark and leaves was responsible for pain relief, fever reduction and reduced inflammation.
- The body converts salicin to salicylic acid by reducing the ether and then oxidizing the primary alcohol to a carboxylic acid.
- Salicylic acid is the substance that has analgesic, anti-inflammatory, and antipyretic properties.



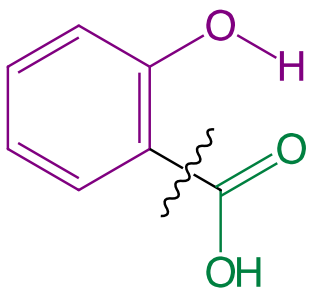
salicilin
(willow bark)

salicylic acid

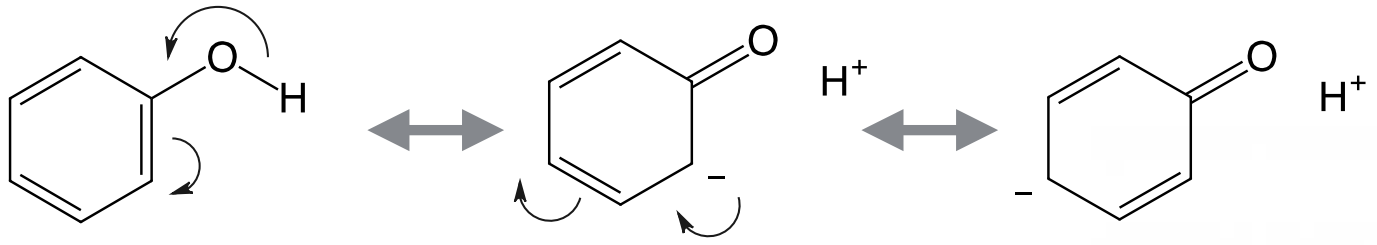
analgesic,
anti-inflammatory,
and antipyretic

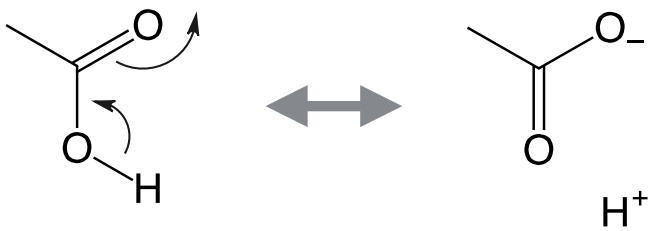
Willow Bark

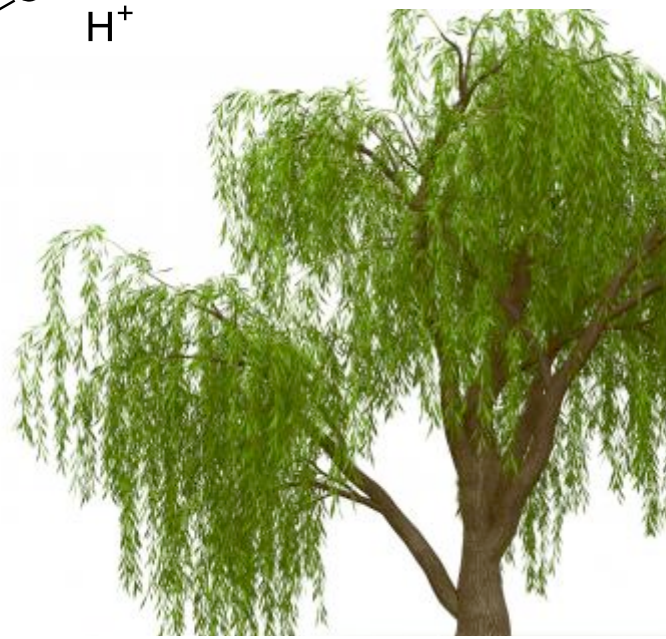
salicylic acid



- Salicylic acid is the substance that has analgesic, anti-inflammatory, and antipyretic properties.
- Salicylic acid is very acidic and can cause upset stomachs, that side effect makes it difficult to use in many cases.
- Phenols and carboxylic acids are acidic, but other substances with these functional groups don't have the same side effect.

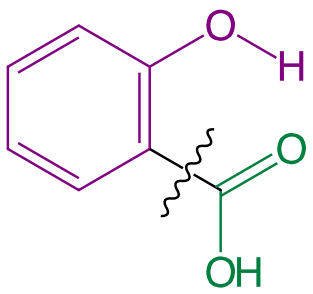






Willow Bark

salicylic acid



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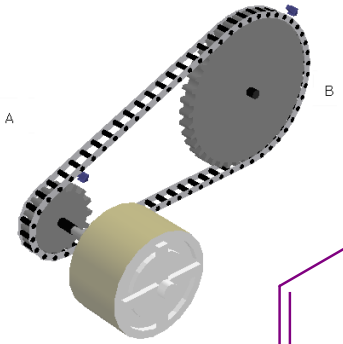
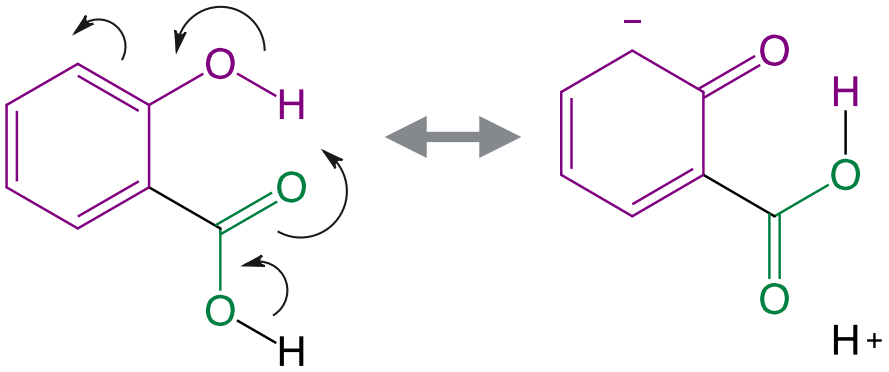
- In salicylic acid, the functional groups interact to create that greater acidity.





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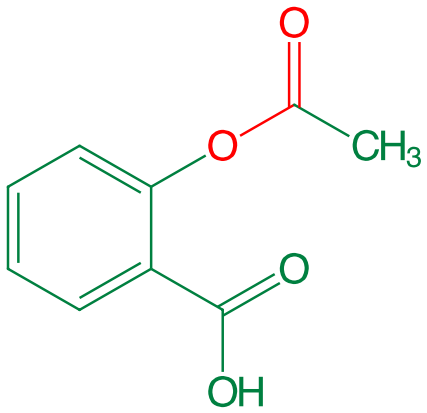
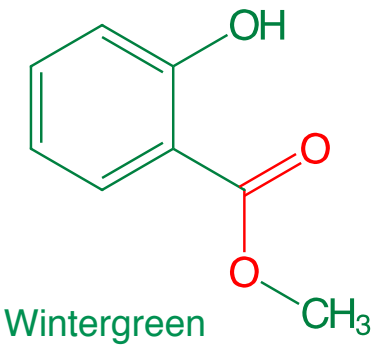
Esters

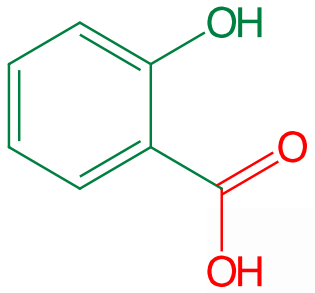
- Both oil of wintergreen and aspirin are examples of another family of organic compounds.
- Esters are substances derived from an acid (organic or inorganic) in which at least one -OH (hydroxyl) group is replaced by an -O-alkyl or -O-aryl group.
- Usually, esters are derived from a carboxylic acid and an alcohol.
- Esters comprise most naturally occurring fats and oils.



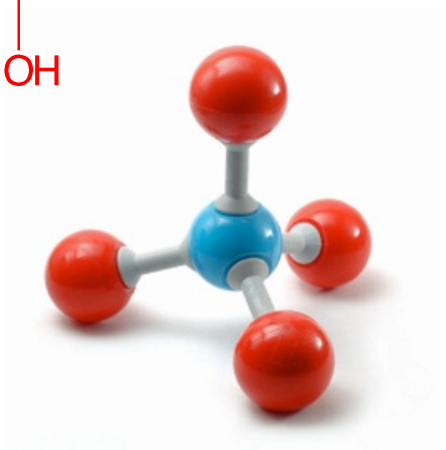
Aspirin
An Ester



Oil of Wintergreen
An Ester

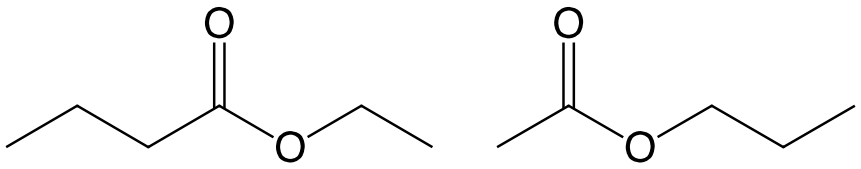


Salicylic acid
A Carboxylic Acid



Esters

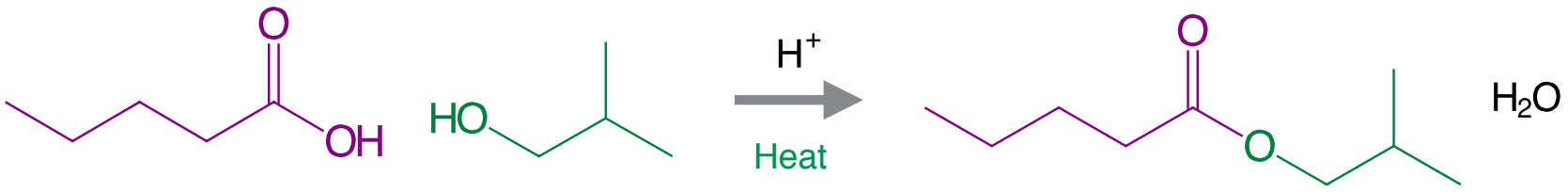
- Many of the fragrances of perfumes and flowers and the flavors of fruits are due to esters.
- Simple esters are volatile, so we can smell them, and they are soluble in water, so we can taste them.
  - Being a hydrogen bond accepter esters are reasonably water soluble.
  - Having no hydroxy group, they cannot be a hydrogen bond donator, so they have a lower boiling point (more volatile).



Condensed Structural Formula and Name	Flavor/Odor
$CH_3-\overset{\overset{O}{\|}}{C}-O-CH_2-CH_2-CH_3$ Propyl ethanoate (propyl acetate)	Pears
$CH_3-\overset{\overset{O}{\|}}{C}-O-CH_2-CH_2-CH_2-CH_2-CH_3$ Pentyl ethanoate (pentyl acetate)	Bananas
$CH_3-\overset{\overset{O}{\|}}{C}-O-CH_2-CH_2-CH_2-CH_2-CH_2-CH_2-CH_2-CH_3$ Octyl ethanoate (octyl acetate)	Oranges
$CH_3-CH_2-CH_2-\overset{\overset{O}{\|}}{C}-O-CH_2-CH_3$ Ethyl butanoate (ethyl butyrate)	Pineapples
$CH_3-CH_2-CH_2-\overset{\overset{O}{\|}}{C}-O-CH_2-CH_2-CH_2-CH_2-CH_3$ Pentyl butanoate (pentyl butyrate)	Apricots

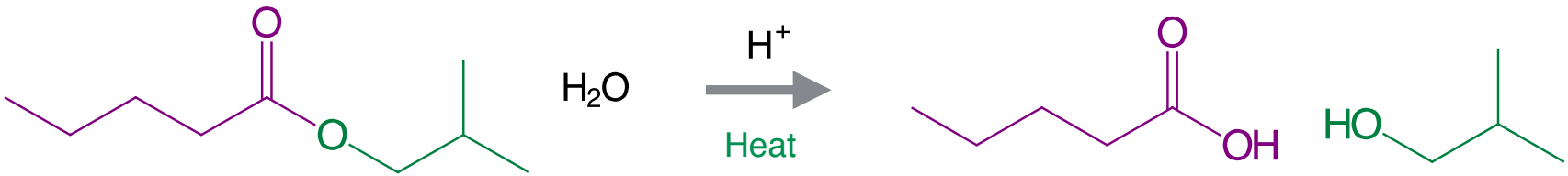
Reactions of Esters

- Esters are formed by condensing an alcohol and a carboyxlic acid.
- The reaction is also called an esterification of a carboxylic acid.
- It's an equilibrium reaction, but driven forward by using a large excess of the alcohol.



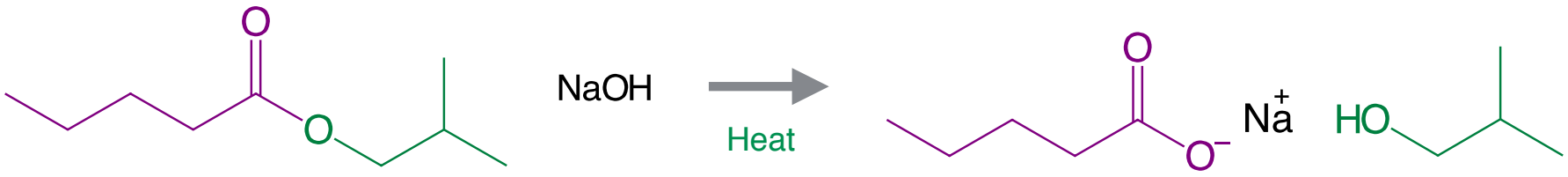
Reactions of Esters

- Hydrolysis of esters is breaking them into alcohols and carboxylic acids.
- It can be accomplished with acid and heat.
  - It's an equilibrium reaction, but driven forward by using a large excess water.
  - It's the reserve of esterification.



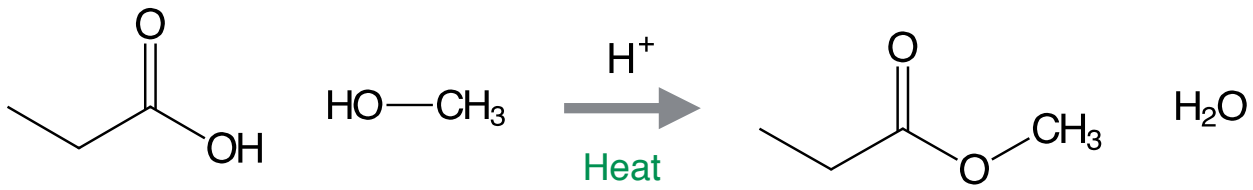
Reactions of Esters

- Hydrolysis of esters is breaking them into alcohols and carboxylic acids.
- Hydrolysis can also be accomplished with strong base.
- This type of hydrolysis is called saponification (soap making).
- It produces carboxylic acid salts instead of acids.

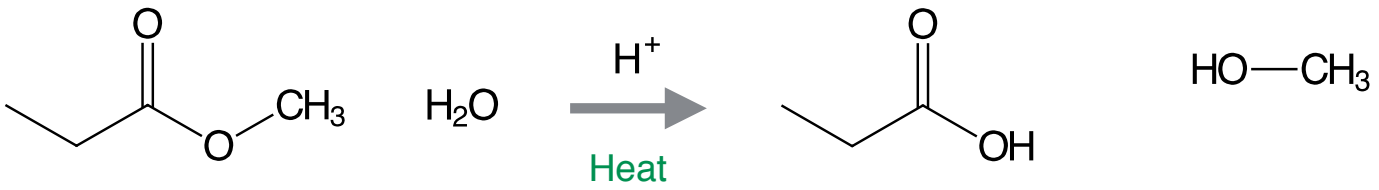


Reaction Summary

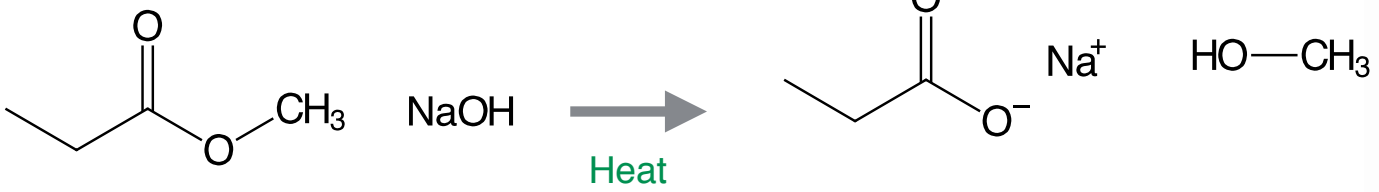
- Esterification:

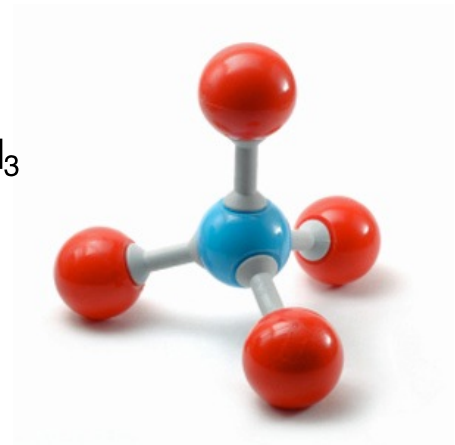


- Hydrolysis:



- Saponification:





Ex17

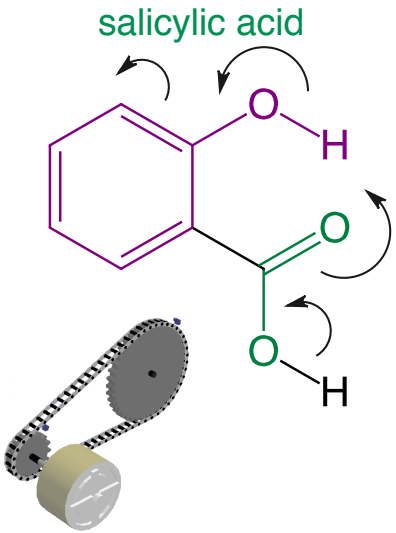
Analgesics, TLC Analysis

- Analgesics
  - Carboxylic Acids
    - Structure
    - Properties
  - Willow Bark
  - Esters & Esterification
  - Aspirin

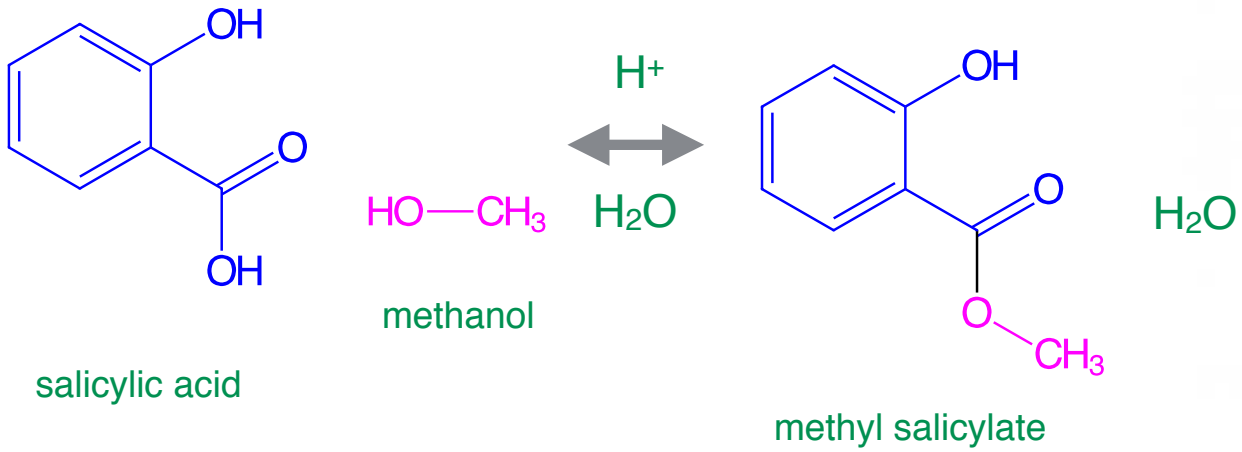
- The Experiment
  - Part A
    - Use TLC to Separate Compounds
  - Part B
    - Determine Elution Solvents for Separation

- For Next Week

Willow Bark

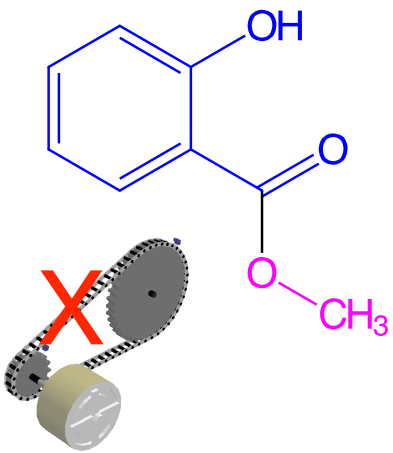


- Chemists tried to improve on salicylic acid to reduce that side effect while retaining it's other useful properties.
- The first thing they tried was replacing the hydrogen in the carboxylic acid with a methyl group.
- Carboxylic Acids and alcohols can react in acid and water to combine. This is a reversible reaction.
- This is a condensation or esterification reaction.



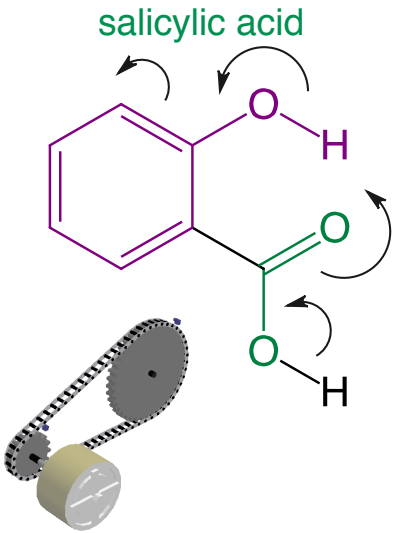
Oil of Wintergreen

methyl salicylate

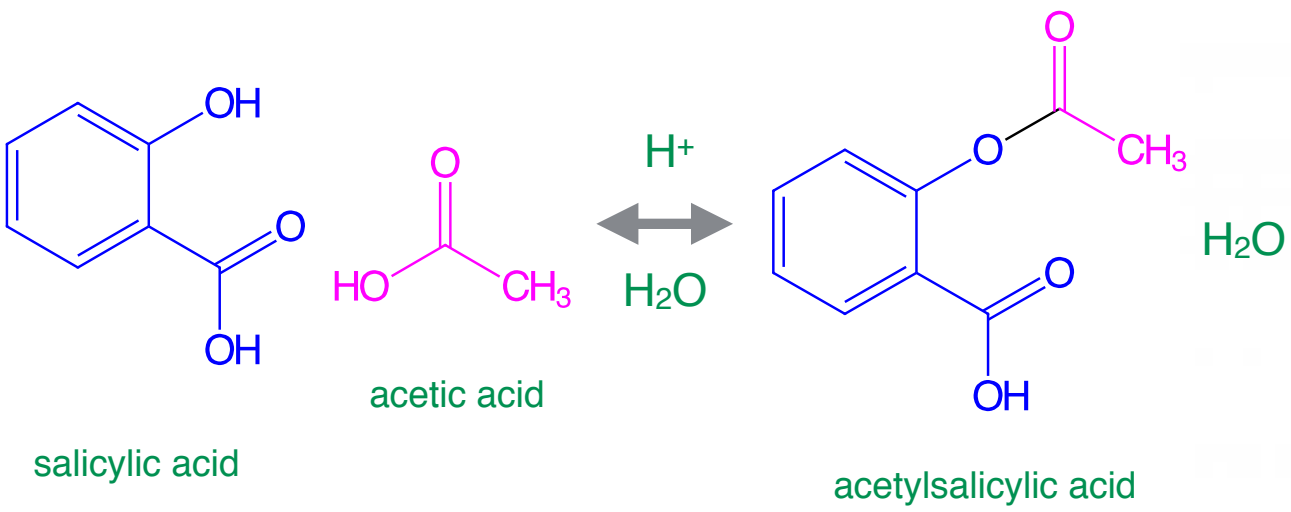


- Methyl salicylate (oil of wintergreen) retained many of the properties of salicylic acid.
  - It's still an analgesic (pain reliever).
- It lost other properties.
  - Without the carboxylic acid group it is less acidic.
    - It's also less water soluble, more greasy.
  - It's not easily consumed.
- It has other properties all it's own.
  - In small quantities it's used as food flavoring, it's responsible for the mint taste in spearmint gum.
  - It can be absorbed through the skin. It's the active ingredient in Tiger Balm, Icy Hot, and Bengay ointments.
  - It has a high toxicity. One spoonful is three times a lethal dose.
    - In 2007 a professional runner died from excessive application of Bengay.

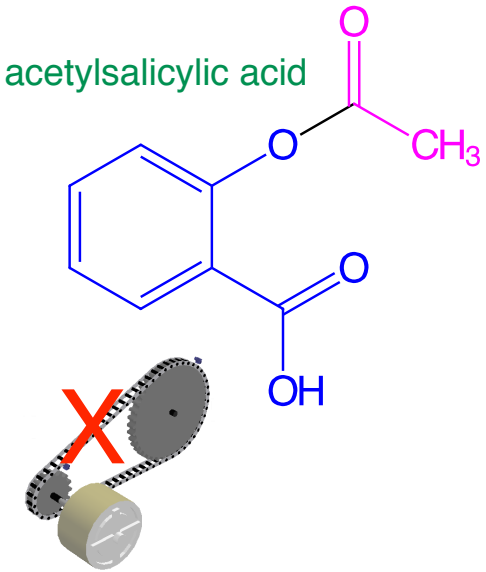
Willow Bark



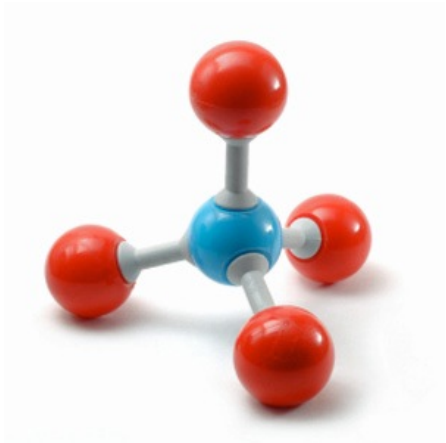
- Chemists tried to improve on salicylic acid to reduce that side effect while retaining it's other useful properties.
- The next thing they tried was replacing the hydrogen in the phenol with an acetal group.
- Carboxylic Acids and alcohols can react in acid and water to combine. This is a reversible reaction.
- They used the same esterification reaction to disrupt the phenols contribution to salicylic acids high acidity.



Aspirin



- Acetylsalicylic acid (aspirin) retained many of the properties of salicylic acid.
  - It's still an analgesic (pain reliever)
  - It's also an antipyretic (fever reducer)
  - It's an anti-inflammatory agent
- It lost other properties.
  - It doesn't have the same disruptive effect on the stomach.
- Bayer chemicals introduced aspirin as a product in 1897 and has been primary supplier aspirin for over 100 years.



Ex17

Analgesics, TLC Analysis

- Analgesics
  - Carboxylic Acids
    - Structure
    - Properties
  - Willow Bark
  - Aspirin

- The Experiment
  - A - Preparations
  - B - Reference Plate
  - C - Development Chamber
  - D

- For Next Week

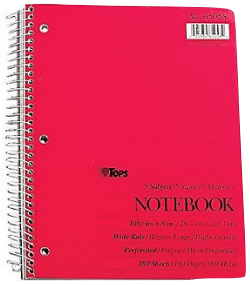
Next Meeting

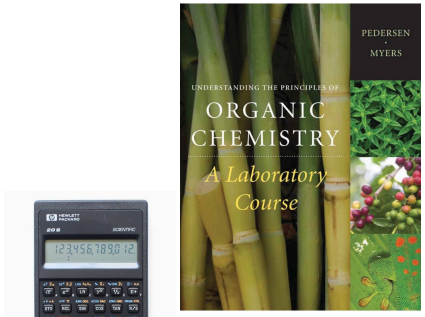
- For next Meeting:

Review: Technique 7 - Reaction Methods
Technique 12 - Extractions & Separations
section 12.5
section 12.9

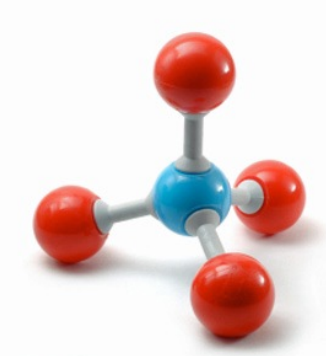
Read: Experiment 17 (page 144)
Technique 19 - Column Chromatography

Do: Identify Objectives
List Materials w/ Properties
Organize Procedures





We will start with a quiz about the experiment and reading.



Questions?