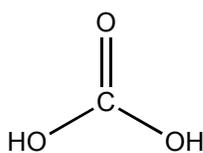
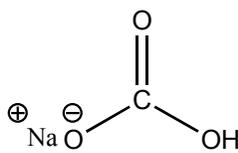
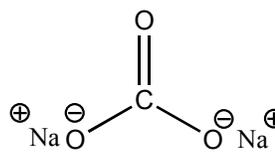


Demo-In-Class:

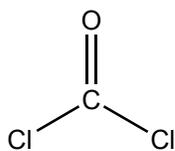
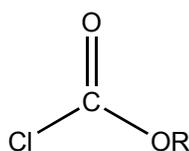
**carbon dioxide****carbonic acid**

Carbon dioxide (CO<sub>2</sub>) is a solid at -78°C. It is dry ice. When it is added to water, we made carbonated water (as in soda pop). The equilibrium for the above reaction lies far to the left (starting materials CO<sub>2</sub> and water).

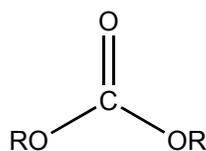
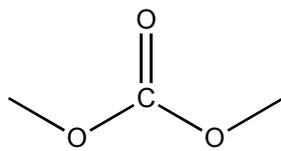
Carbonic acid has two OH groups attached to the central carbonyl. It can be deprotonated twice using base such as NaOH (shown below).

**carbonic acid****sodium bicarbonate****sodium carbonate**

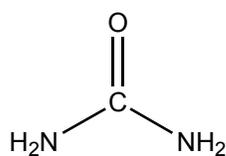
Carbonic acid can be used to make other derivatives:

**phosgene****alkyl chloroformate**

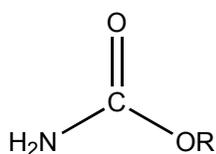
Phosgene is a toxic war gas. You are responsible for its structure on the exam. When one of the chlorine is replaced with an alkoxide group, it becomes alkyl chloroformate.

**dialkyl carbonate****dimethyl carbonate**

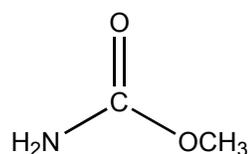
When there are two alkoxide group attached to a carbonyl, it is called dialkyl carbonate. An example of this is dimethyl carbonate which has two methoxy groups attached to the central carbonyl (dimethyl ester of carbonic acid)



**urea**



**alkyl carbamate**  
or  
**urethane**

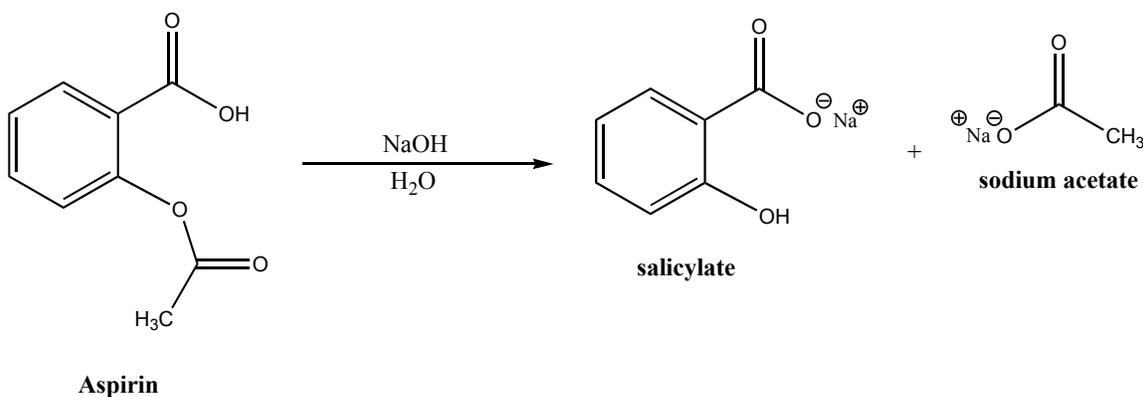


**methyl carbamate**  
or  
**methyl urethane**

Urea is the major product in metabolism of nitrogen that occurs in our body. You are responsible for its structure. When one of the amine is replaced with alkoxy group, it is called a carbamate or urethane. An example would be methyl carbamate.

From last lecture: all carboxylic derivatives can be converted to carboxylic acid (RCOOH) using acid/H<sub>2</sub>O, or they can be converted to carboxylate salt (RCOO<sup>-</sup>) using NaOH/H<sub>2</sub>O. A derivative that is more reactive can be converted directly (spontaneously) to a derivative that's less reactive (reactivity order of the derivatives is acid halide > anhydride > ester > amide). To convert a less reactive derivative to a more reactive derivative, you need to first convert the less reactive derivative to carboxylic acid or carboxylate salt, which can then be converted to acid halide with thionyl chloride (SOCl<sub>2</sub>). From the acid halide (the most reactive derivative), other derivative can be generated.

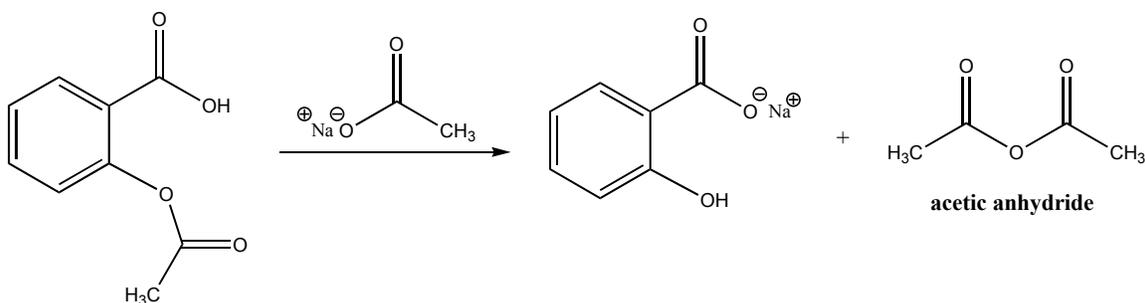
Example:



Aspirin or *acetylsalicylic acid* is a drug, often used as an analgesic (against minor pains and aches), antipyretic (against fever), and anti-inflammatory. It has also an anticoagulant ("blood-thinning") effect and is used in long-term low-doses to prevent heart attacks.

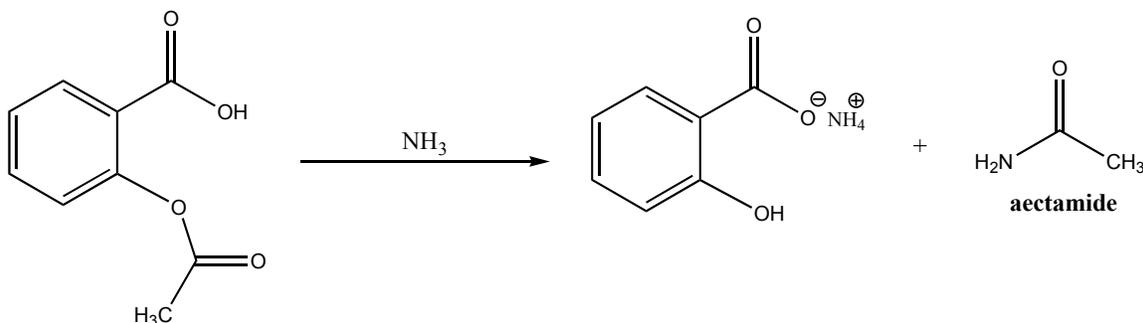
Aspirin has ester and carboxylic acid functional groups. When treated with a base such as NaOH, the first thing occurs is the deprotonation of the carboxylic acid to form a salt. The ester of aspirin also reacts and gives alcohol as product. The other product is sodium acetate. One thing to keep in mind is that the singly bonded oxygen, nitrogen or halogen is what always breaks away from the parent carbonyl.

Example below: *Is this reaction possible (can one make acetic anhydride)?*



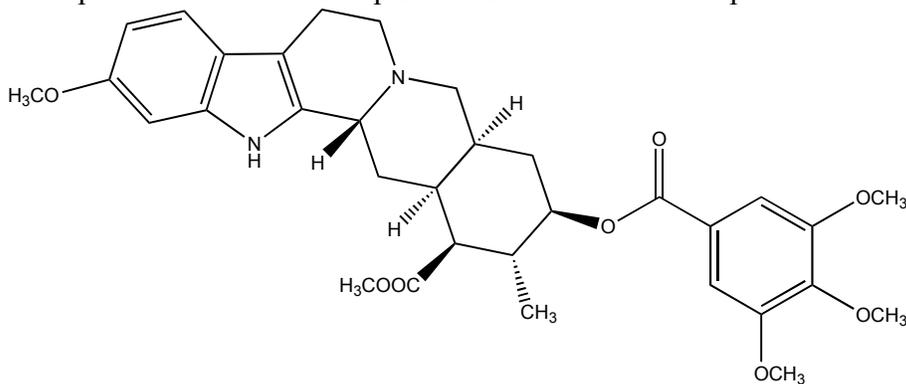
Answer: No. You cannot convert ester (less reactive) directly to anhydride (more reactive). You must convert the less reactive derivative (ester) to carboxylic acid, and then to acid halide, which can be converted to anhydride.

Example below: Is this reaction possible ?

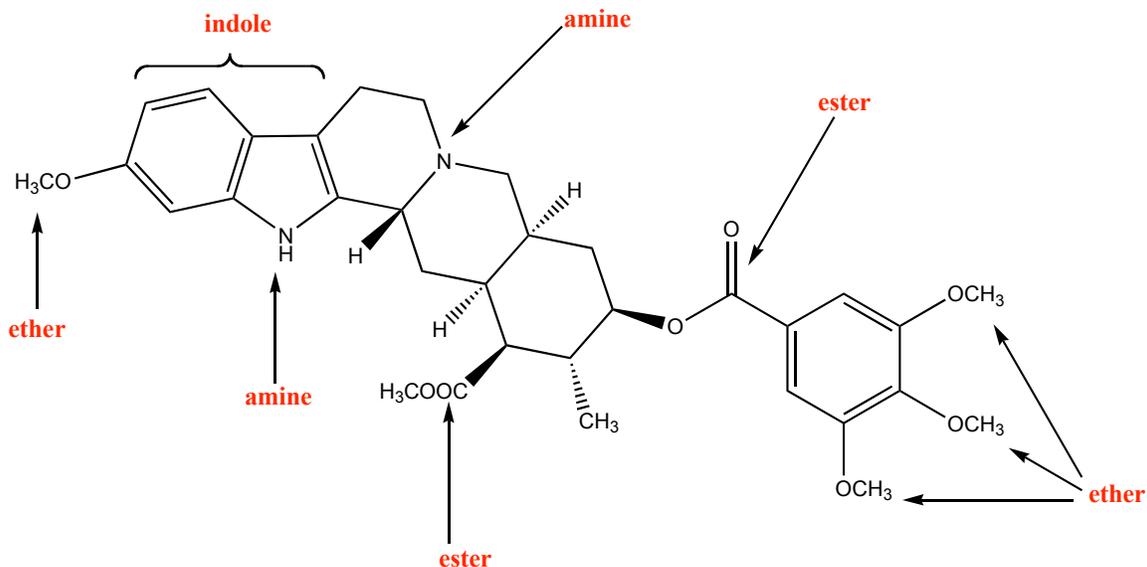


Yes. Ammonia is both a strong nucleophile and a strong base. We will learn more about its properties in later lectures. Amides are less reactive (more stable) than esters and can be made directly from esters.

Example for review of concepts and ester reactions - Resperine

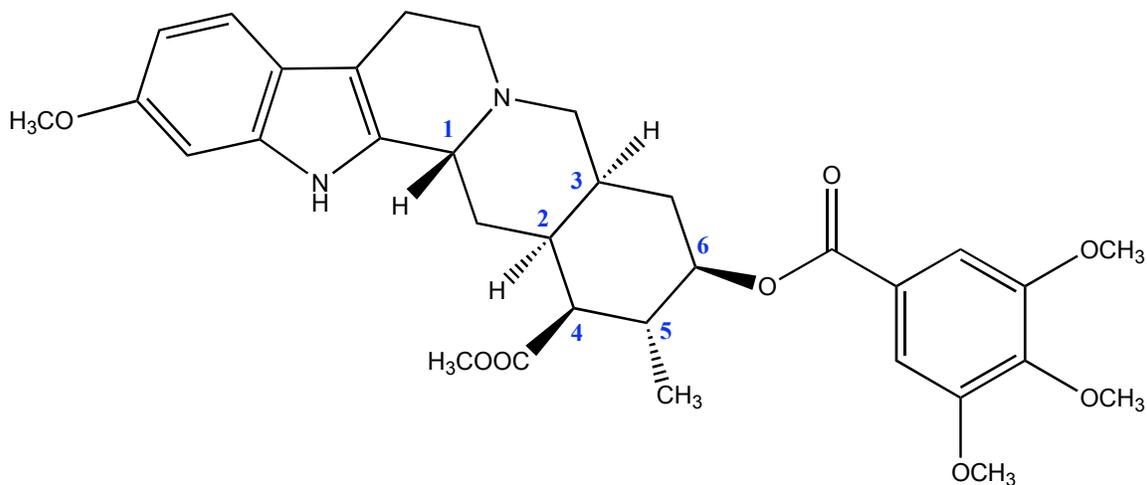


The molecule above is reserpine. It is isolated from Indian snake root (*Rauwolfia serpentina*) and was found to reduce blood pressure. However, it causes depression. Although it is a big molecule, you should be able to calculate its formula and molecular weight, as well as identify all of its functional groups (in color red).



How many stereogenic centers does it have?

Answer: 6. they are numbered below.

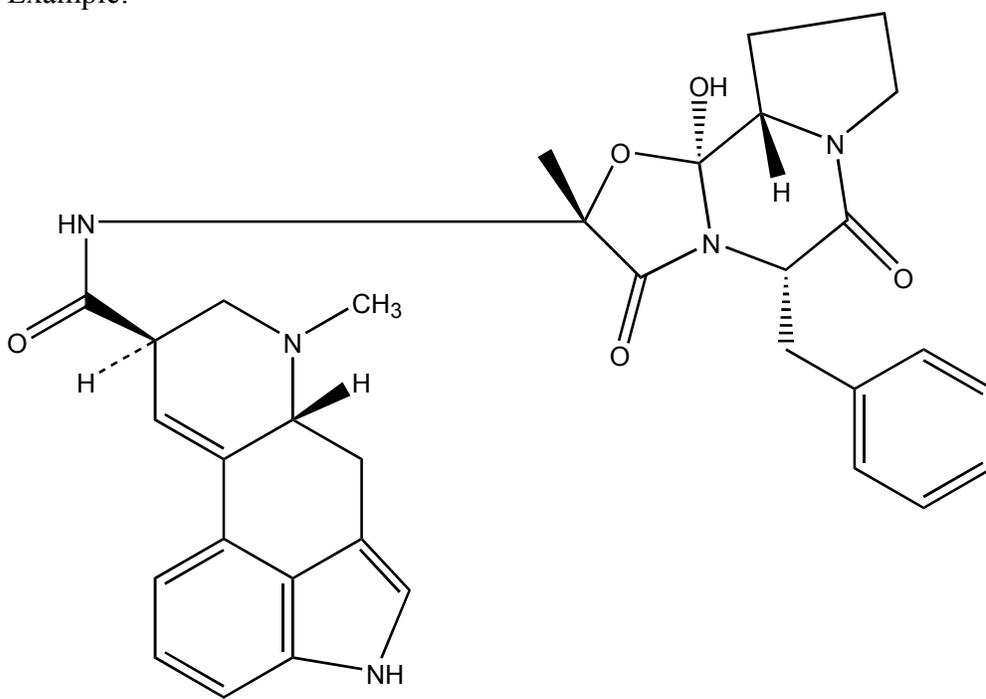


Is the stereogenic carbon #1 in R or S configuration?

Answer: It is R configuration. First we assign priority of each substituents. N gets the first priority and H is the last. The other two substituents are just carbons. However, if we look further, we see that one of the carbons is actually an alkene carbon and has a bond to nitrogen, whereas the other carbon is a methylene group with a bond to carbon and two bond to hydrogen. The carbon bearing nitrogen gets higher priority than methylene carbon (which has one carbon substituent), so the configuration is counterclockwise with

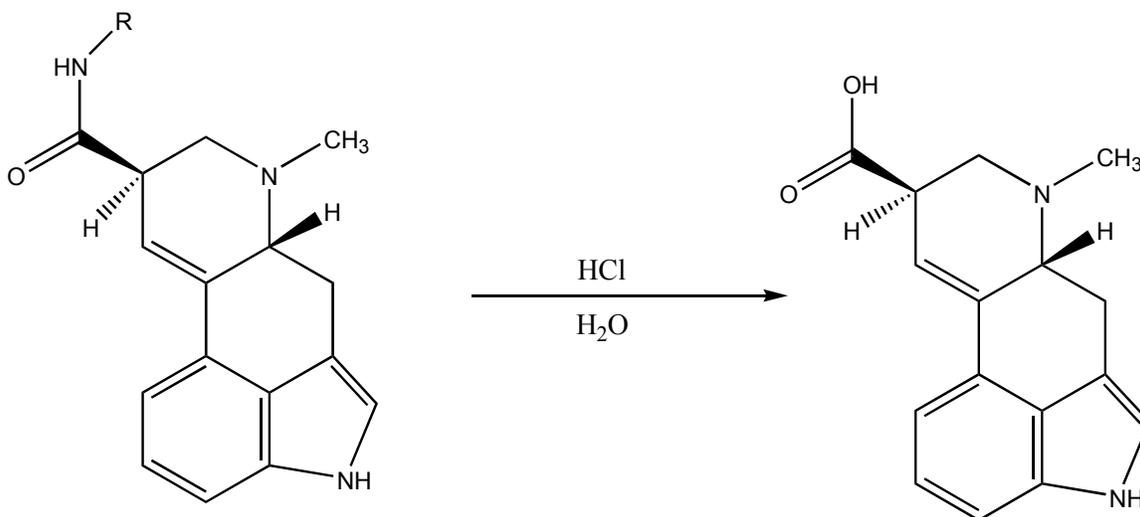


Example:



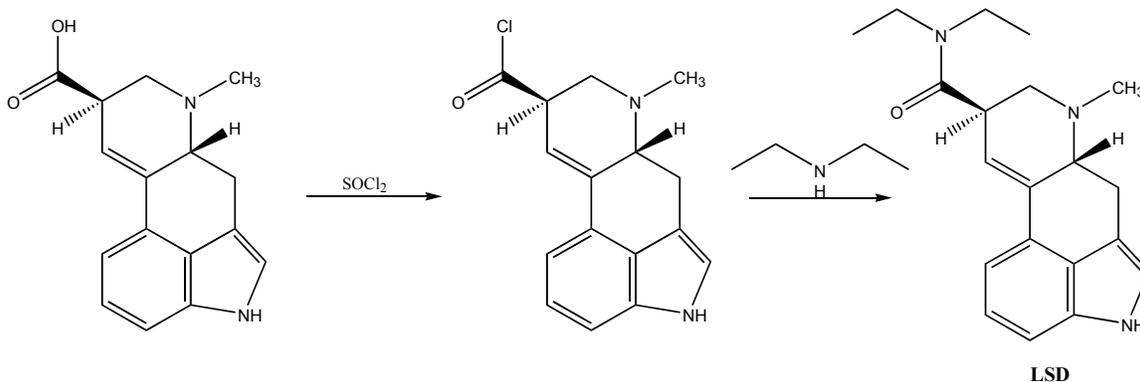
This structurally complicated molecule is called ergotamine. It is a mycotoxin produced by fungi *Claviceps paspali* and it causes constriction of blood vessels. It is the cause for the disease St. Anthony's Fire in the middle ages through contamination on rye.

When ergotamine is treated with acid/water, what is the bond that will react with the left side of the structure?



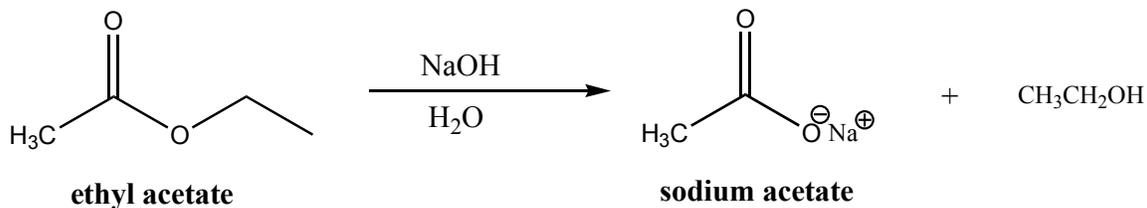
At the left hand of the structure, there is amide functionality. When treated with acid in water, the amide is hydrolyzed to carboxylic acid.

In 1960, Albert Hoffman, as part of a large research program searching for medically useful ergot alkaloid derivatives, discovered/synthesized LSD.

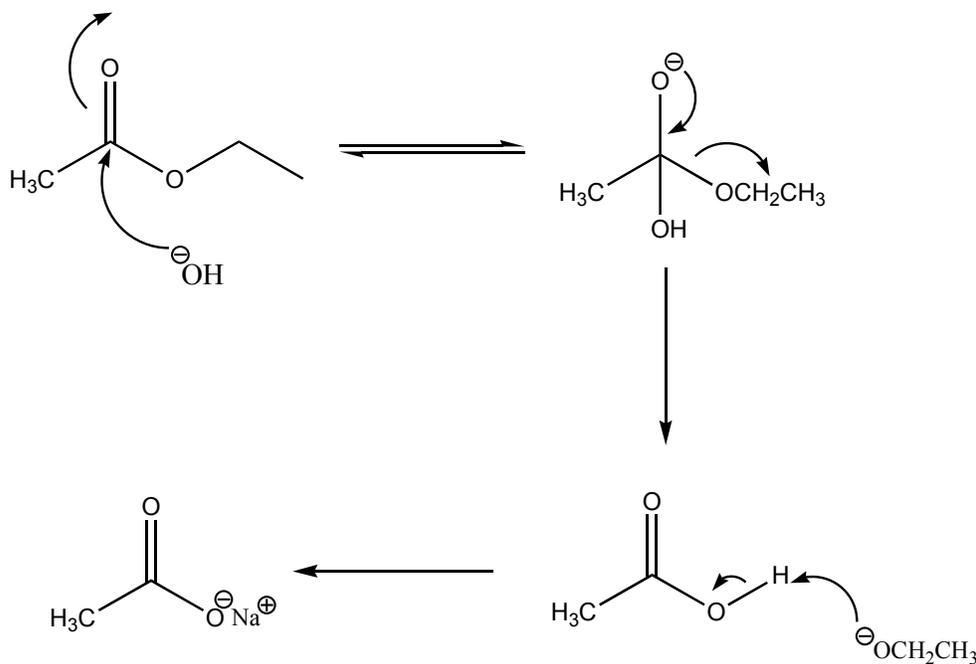


Note that acid cannot go directly to amide. It must go through the acid halide intermediate before being finally converted to amide.

## Hydrolysis of Esters



Mechanism:

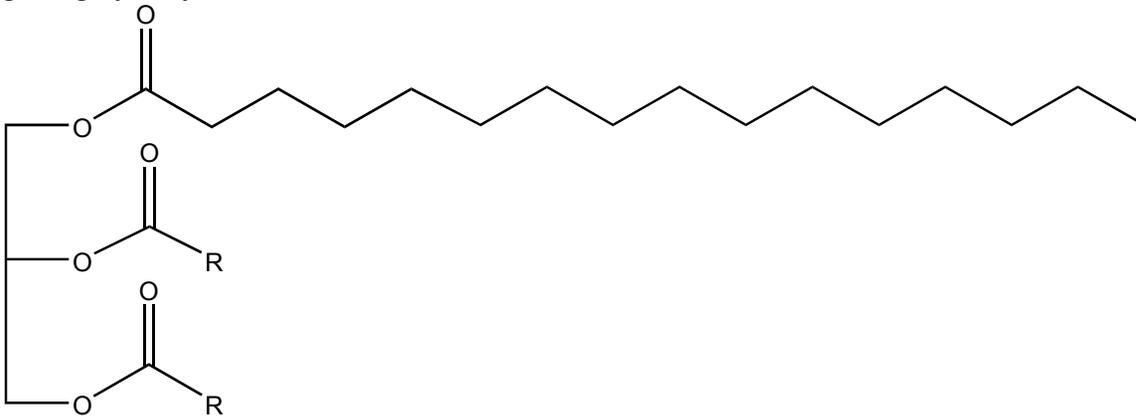


The hydroxide anion attacks the carbonyl carbon in the first step, and a tetrahedral intermediate is formed. This process is reversible (so if the negative charge on oxygen comes down and kicks out the OH group instead of ethoxide anion in the second step, we get the starting material again).

In the second step, The ethoxide anion is ejected and carboxylic acid is formed. However, under the basic conditions, the proton on carboxylic acid is abstracted by the ethoxide anion to form carboxylate anion and ethanol.

The pKa for acetic acid is 4.5, whereas the pKa of ethanol is 17. Ethoxide is a stronger base, therefore it will deprotonate the acetic acid to give acetate.

The process of hydrolyzing esters with base is called **saponification**. Saponification means process of making soap. When you accidentally pour NaOH in your hand, you feel your hand has a soapy feeling. What occurs is that the fat (triglyceride) in your hand is getting hydrolyzed. We will discuss more about it in the next lecture.



glycerol triester = triglyceride