

HYDROLYSIS OF ESTER

Ester is an organic compound that resulted from the reaction between an acid (carboxylic acid, phosphoric acid, phosphonic acid derivatives, or sulfuric acid) and an alcohol moiety with elimination of water molecule.

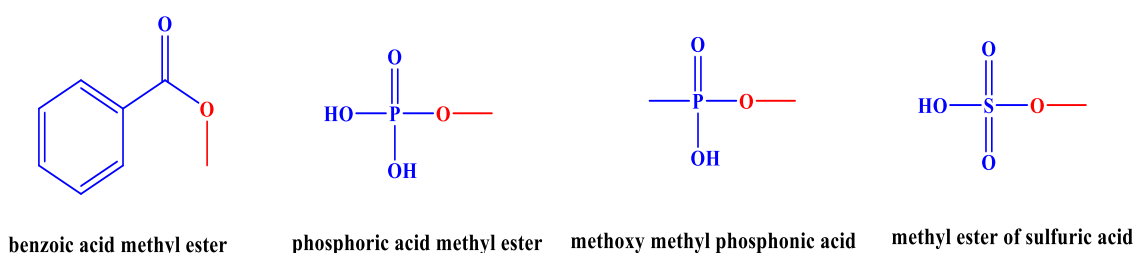


Figure 1: examples of esters from different types of acid.

In organic pharmaceutical chemistry, ester is an important approach in designing of drugs in order to overcome problems inherent in that drug; this approach is called **prodrug**. What's about soft drugs??

Ester prodrugs can either be lipophilic or hydrophilic by using appropriate moiety to circumvent problem related to solubility. Once the problem solved the prodrug will be hydrolyzed enzymatically back to the parent active drug. For example phosphate ester is designed to be water soluble as in prednisolone sodium phosphate while dipivefrin was designed to decrease polarity (increase lipophilicity) of epinephrine to be administered as eye drops.

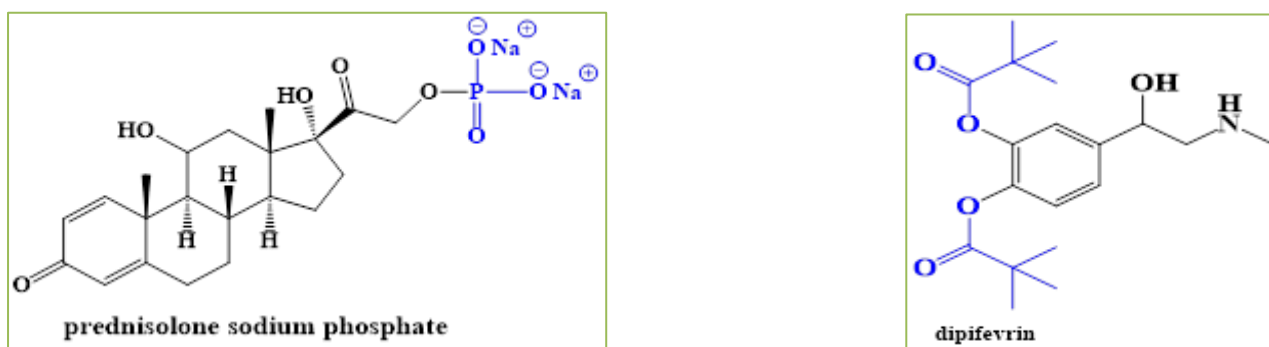
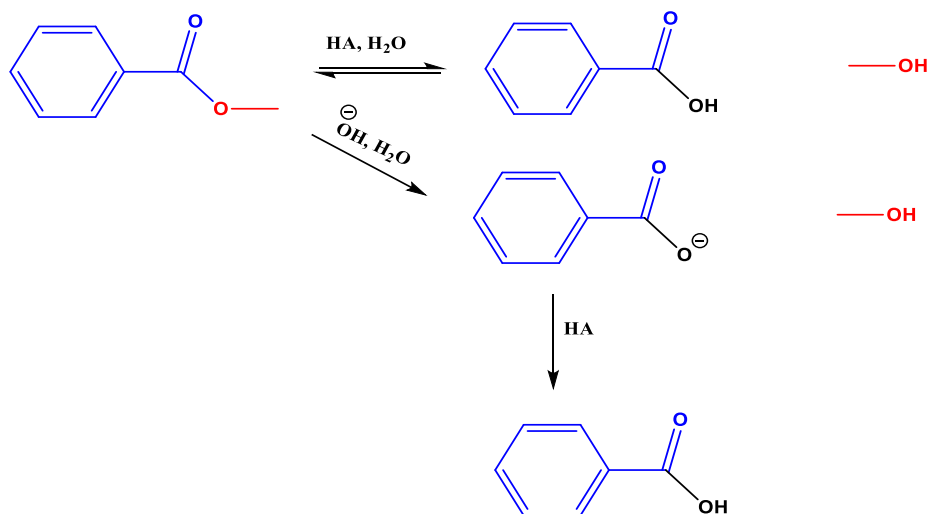
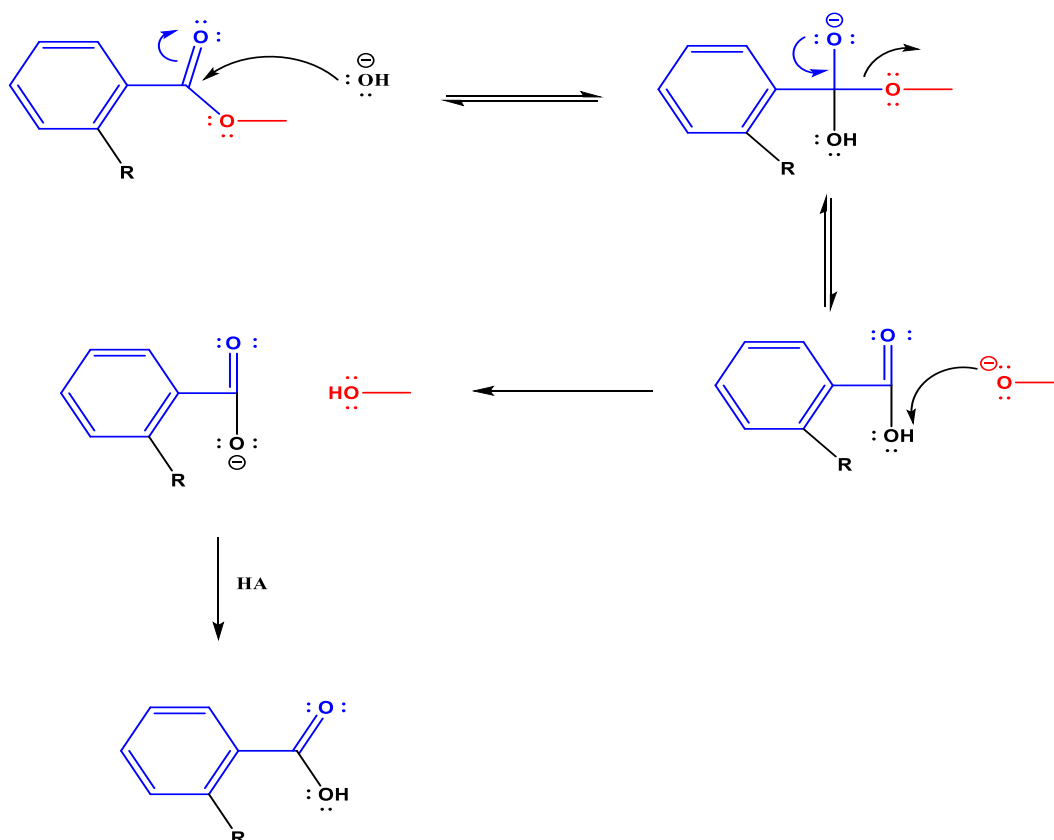


Figure 2: examples of ester prodrugs.

In **organic synthesis**; esterification is method for protection of carboxyl group as in peptide synthesis. After that the ester hydrolyzed either in strong acidic media or strong basic media to make carboxyl group available for the next step if needed.



The mechanism of hydrolysis will operate as in the following:

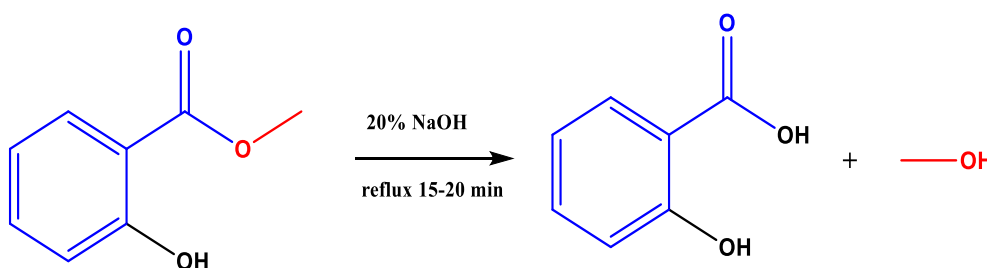


Scheme (1): Mechanism of hydroxyl ion-promoted hydrolysis of ester.

In our lab.; we will use methyl salicylate as ester to obtain salicylic acid by hydroxyl ion promoted hydrolysis. "Methyl salicylate will undergo base promoted hydrolysis to obtain salicylic acid".

PROCEDURE

- 1.** Place 1.25ml of methyl salicylate in 250ml distilling flask.
- 2.** Add 12.5ml of 20% (w/v) aqueous solution of NaOH, mix well, the sodium salt of methyl salicylate phenolic group may separate out at this point, but will re-dissolve on heating.
- 3.** Then reflux at the boiling point for 15-20 min.
- 4.** Transfer the mixture to 125ml beaker, cool and acidify with diluted H₂SO₄ (check acidification by litmus paper if available).
- 5.** Filter the precipitated salicylic acid, dry, and crystallize.
- 6.** Store the product for the next procedure.



H.W:

- ❖ Medicinal uses of methyl salicylate....
- ❖ Medicinal uses of salicylic acid....