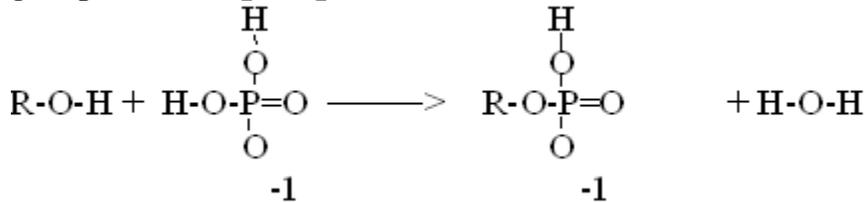
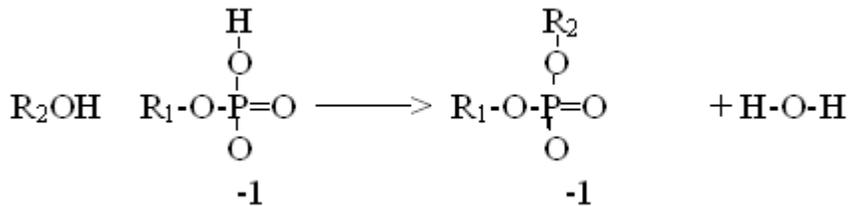


4.17 Phosphate esters

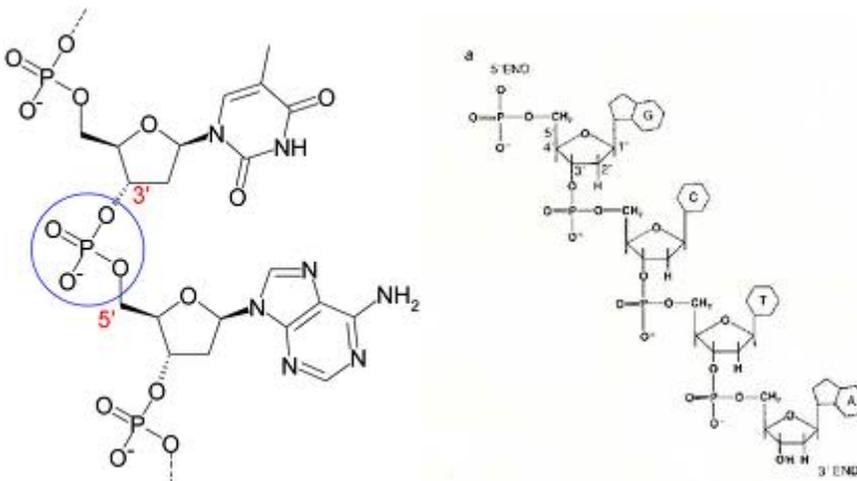
Similarly we can react phosphoric acid (really phosphate ions) with alcohol groups to form **phosphate esters**:



Again the P=O in the phosphate is analogous to the C=O in a regular ester. A phosphate ester can react with a second alcohol and form a **phosphodiester**.



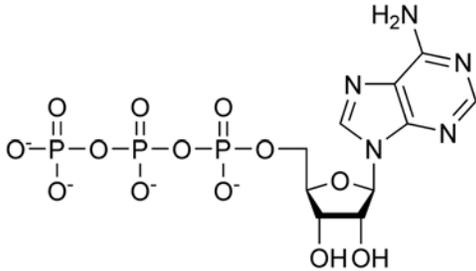
Alcohol phosphate ester phosphodiester



Phosphodiester bonds link the ribose sugars of DNA together.

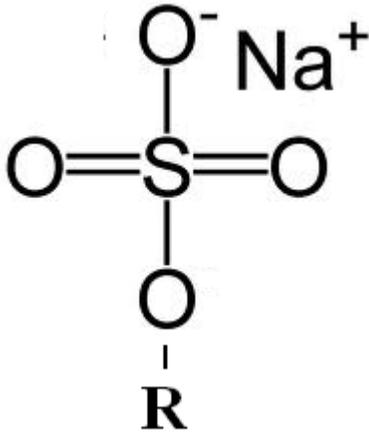
Phosphate groups are used to activate (raise the energy level of) alcohol and other functional groups. Reacting two or three phosphate together forces the negatively charged phosphates closely together and requires energy (it is **endergonic**)! When the phosphate ions hydrolyze, energy is released

(**exergonic**)! The most well known molecule that utilizes this principle is the major high energy molecule of the cell, **adenosine triphosphate**.



Adenosine triphosphate

Sulfate esters

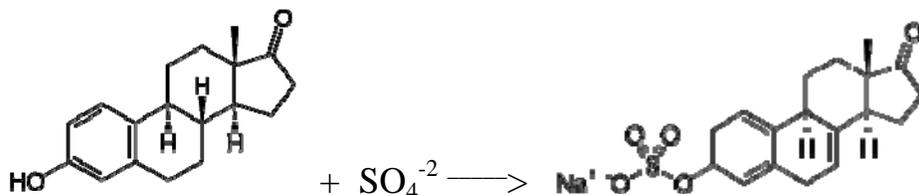


The liver metabolizes many hormones as well as drugs by adding a sulfate group onto an OH group of a molecule. The ionic sulfate group increases the water solubility and expedites excretion of the sulfated molecule in the urine or feces.

A medically important example is the metabolism of estrogens. The body does not want these hormones to stay active forever and one way of terminating their activity is to add either a **sulfate group** or a **glucuronic acid** onto an OH group of the estrogen, a process called **conjugation**. This not only increases the water solubility, but decreases the biological activity of the estrogen.

Example. The estrogen molecule estrone is metabolized in the liver into estrone sulfate which is readily excreted in the urine.

This excretion has been used pharmacologically. Pregnant mares excrete large amounts of sulfated estrone which can be purified from their urine and taken orally by menopausal women as Premarin. The Premarin can have its sulfate removed in the human liver and be regenerated into active estrone.



The estrogens with sulfate covalently attached are collectively referred to as **conjugated estrogens**. This is analogous to the term conjugated bilirubin which is used to describe a bilirubin molecule in which glucuronic acid has been covalently attached. Indeed the active ingredients of Premarin are listed as **conjugated estrogens**.



When taken orally, the sulfate group is removed from the conjugated estrogens to make them active again.

Sulfation of drugs does not always lead to inactivation. Minoxidil (Rogaine) is used in the treatment of male baldness. It turns out that minoxidil is actually a pro-drug and is sulfated on the O atom to produce minoxidil sulfate, the actual active drug.

