A phosphoester bond occurs when the hydroxyl groups in phosphoric acid react with hydroxyl groups on other molecules to form an ester bonds.

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**Phosphodiesters**

A phosphodiester bond occurs when two of the hydroxyl groups in phosphoric acid react with hydroxyl groups on other molecules to form two ester bonds. Phosphodiester bonds are central to all life on Earth,[fn 1] as they make up the backbone of the strands of nucleic acid. In DNA and RNA, the phosphodiester bond is the linkage between the 3’ carbon atom of one sugar molecule and the 5’ carbon atom of another, deoxyribose in DNA and ribose in RNA. Strong covalent bonds form between the phosphate group and two 5-carbon ring carbohydrates (pentoses) over two ester bonds.

![Diagram of phosphodiester bonds](image)

*Figure 13.10.1: Diagram of phosphodiester bonds (PO₄³⁻) between nucleotides. Which presents Thymine (T) and two molecules of Adenine (A). Image used with permission of Wikipedia (G3pro)*

The phosphate groups in the phosphodiester bond are negatively charged. Because the phosphate groups have a pKa near 0, they are negatively charged at pH 7. This repulsion forces the phosphates to take opposite sides of the DNA strands and is neutralized by proteins (histones), metal ions such as magnesium, and polyamines.

For the phosphodiester bond to be formed and the nucleotides to be joined, the tri-phosphate or di-phosphate forms of the nucleotide building blocks are broken apart to give off energy required to drive the enzyme-catalyzed reaction. When a single phosphate or two phosphates known as pyrophosphates break away and catalyze the reaction, the phosphodiester bond is formed.
Hydrolysis of the Phosphoester bond in ATP

Adenosine triphosphate (ATP) is a nucleoside triphosphate used in cells as a coenzyme often called the "molecular unit of currency" of intracellular energy transfer. ATP transports chemical energy within cells for metabolism (Figure 13.10.2). The pKa's for the reactions HATP$^3-$ $\rightarrow$ ATP$^4+$ + H$^+$ and HADP$^2-$ $\rightarrow$ ADP$^3+$ + H$^+$ are about 7.0, so the overall charges of ATP and ADP at physiological pH are -3.5 and -2.5, respectively.

![01ATPhydrolysis.gif](01ATPhydrolysis.gif)

*Figure 13.10.2: ATP Hydrolysis*

Each of the phosphorous atoms are highly electrophilic and can react with nucleophiles like the OH of water or an alcohol. As we discussed earlier, anhydrides are thermodynamically more reactive than esters which are more reactive than amides. The large negative $\Delta G^0$ (-7.5 kcal/mol) for the hydrolysis (a nucleophilic substitution reaction) of one of the phosphoanhydride bonds can be attributed to a relative destabilization of the reactants (ATP and water) and relative stabilization of the products (ADP = P$_i$).

**Contributors**

- Wikipedia