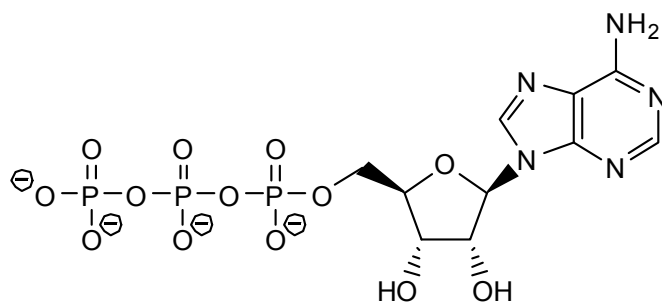


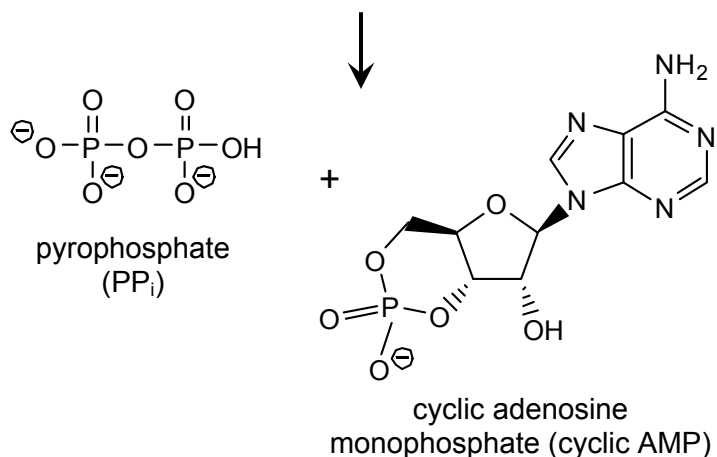
Workshop 23
Catalyzing Transphosphoesterification

The intracellular signaling molecule cyclic AMP is formed by intramolecular reaction of ATP. Though the uncatalyzed reaction is very slow, the process is catalyzed by the enzyme adenylate cyclase in cells.



adenosine triphosphate (ATP)

1. Draw a mechanism for this reaction in the absence of the enzyme catalyst. The reaction takes place in buffered biological fluids (pH \approx 7.4), and in this environment there are no strong acids or bases available.



pyrophosphate (PP_i)

cyclic adenosine monophosphate (cyclic AMP)

2. How might this reaction be accelerated by a strong acid (H-A)? A strong base (B⁻)? Draw a new mechanism for each of these cases.

3. Although protein enzymes don't contain acids or bases that are any stronger than what is found in their environment, they can catalyze reactions by donating or accepting protons via hydrogen bonding. For example, adenylate cyclase could catalyze transphosphoesterifications by forming H bonds with substrate(s).

How would this affect the uncatalyzed mechanism you drew in problem 1? How might the enzyme contact the starting material to catalyze the reaction, and what steps in the uncatalyzed mechanism could be helped by the enzyme?

