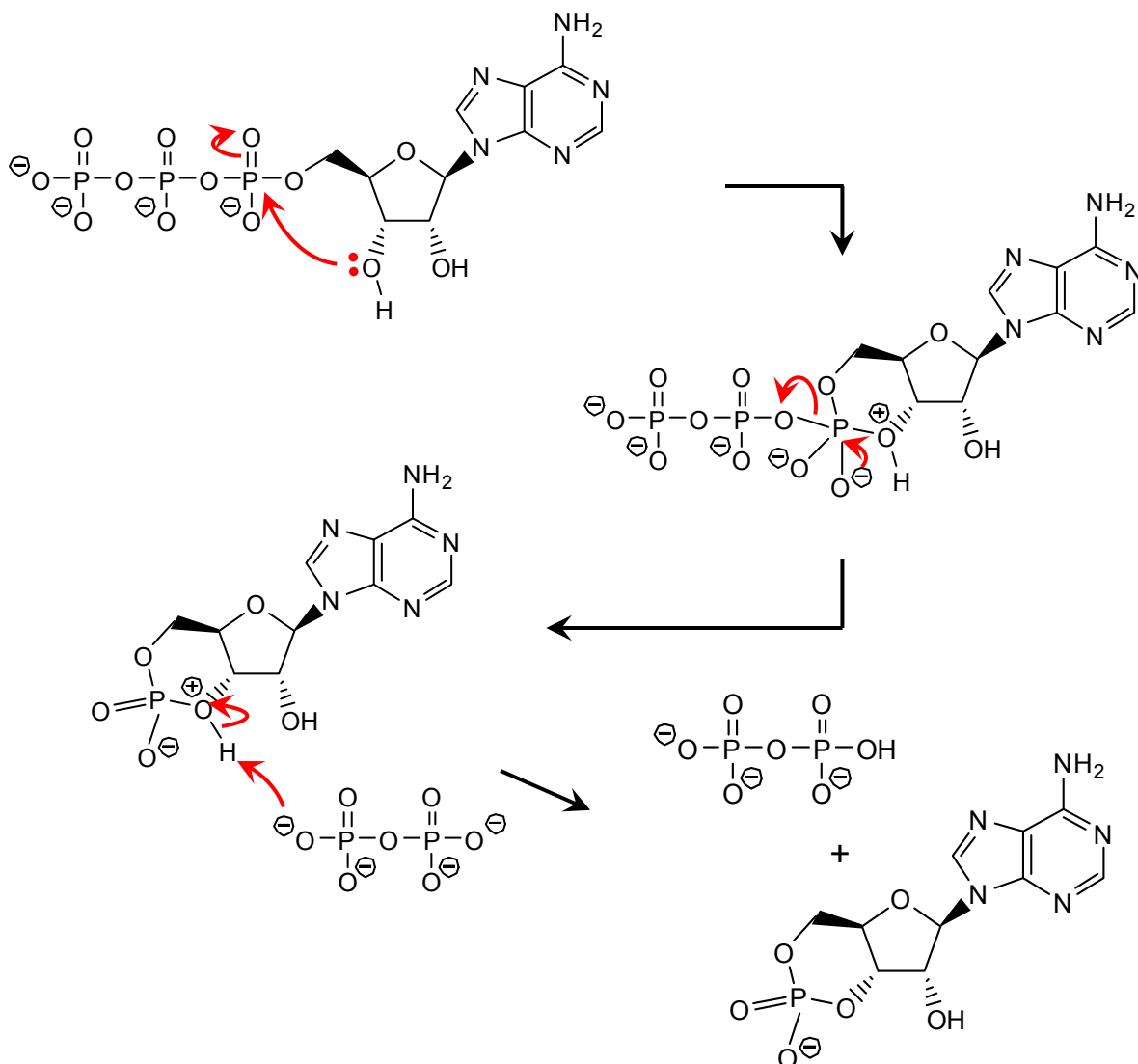
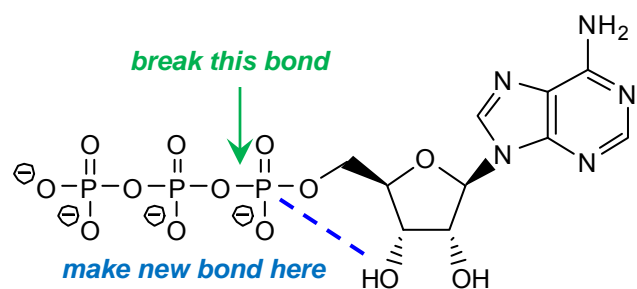


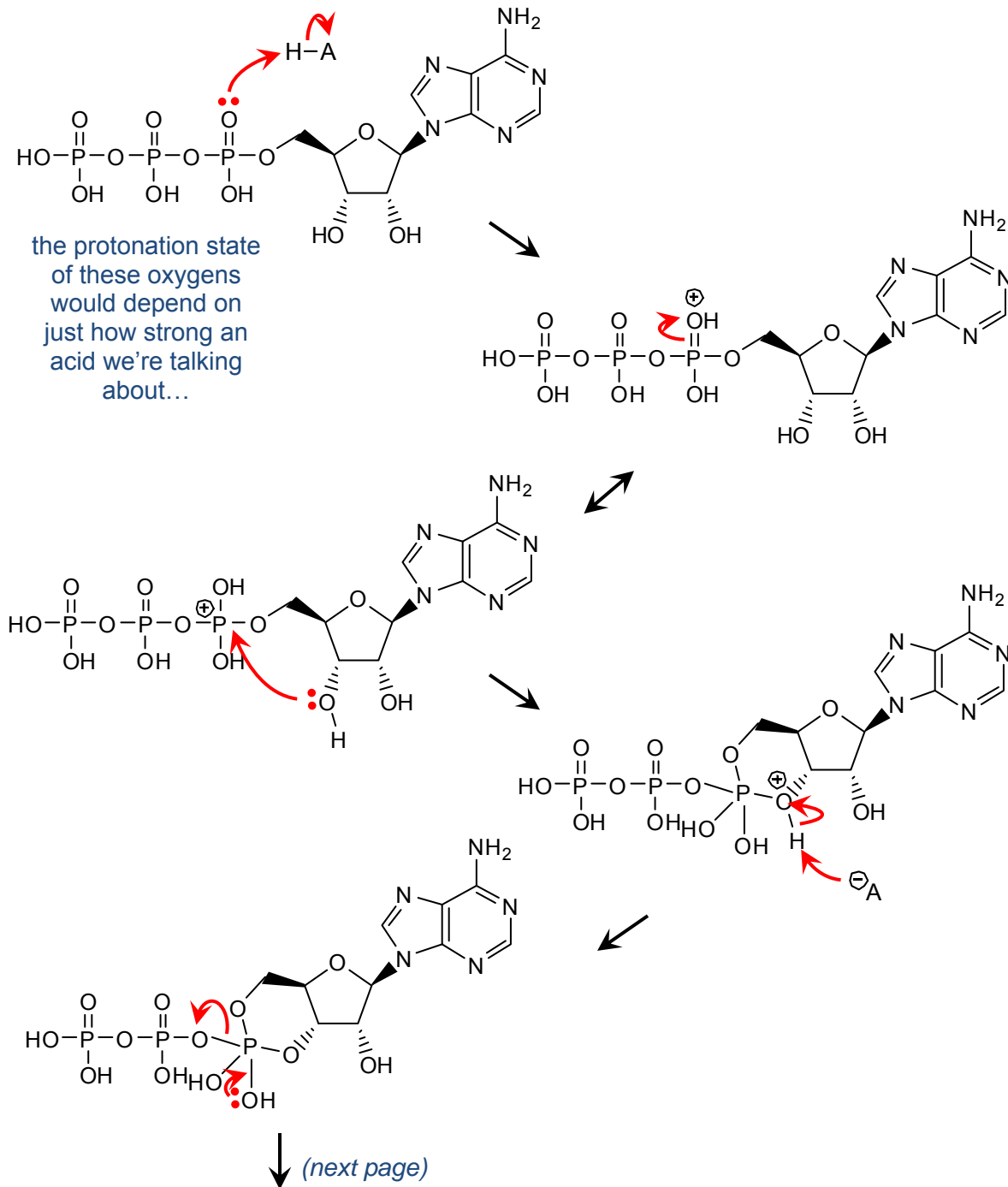
Workshop 23 Solutions Catalyzing Transphosphoesterification

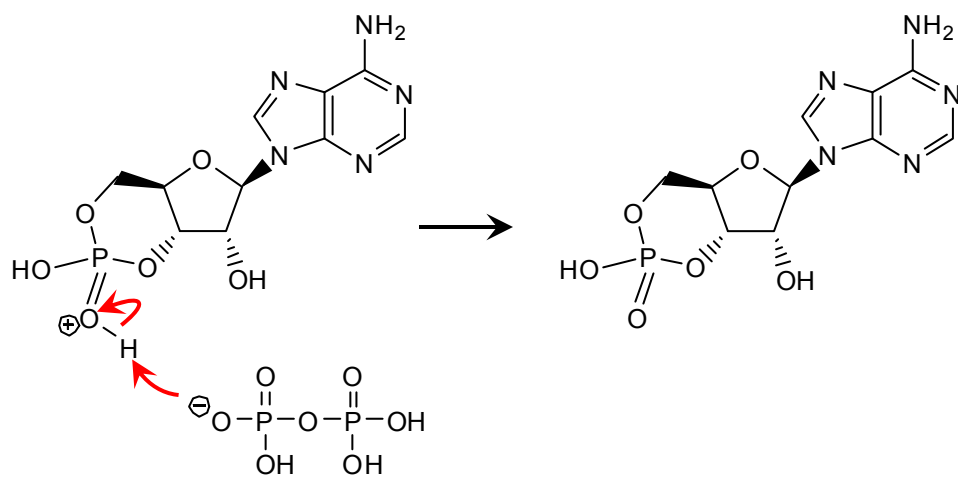
1. Looking at the starting material, we're going to need to create a new bond between the 3'-alcohol oxygen and the first phosphorus of the triphosphate, and we need to break the bond between the first phosphorus and the second phosphorus' oxygen. We can do that via transphosphoesterification, using the 3'-oxygen as a nucleophile and pyrophosphate as the leaving group.



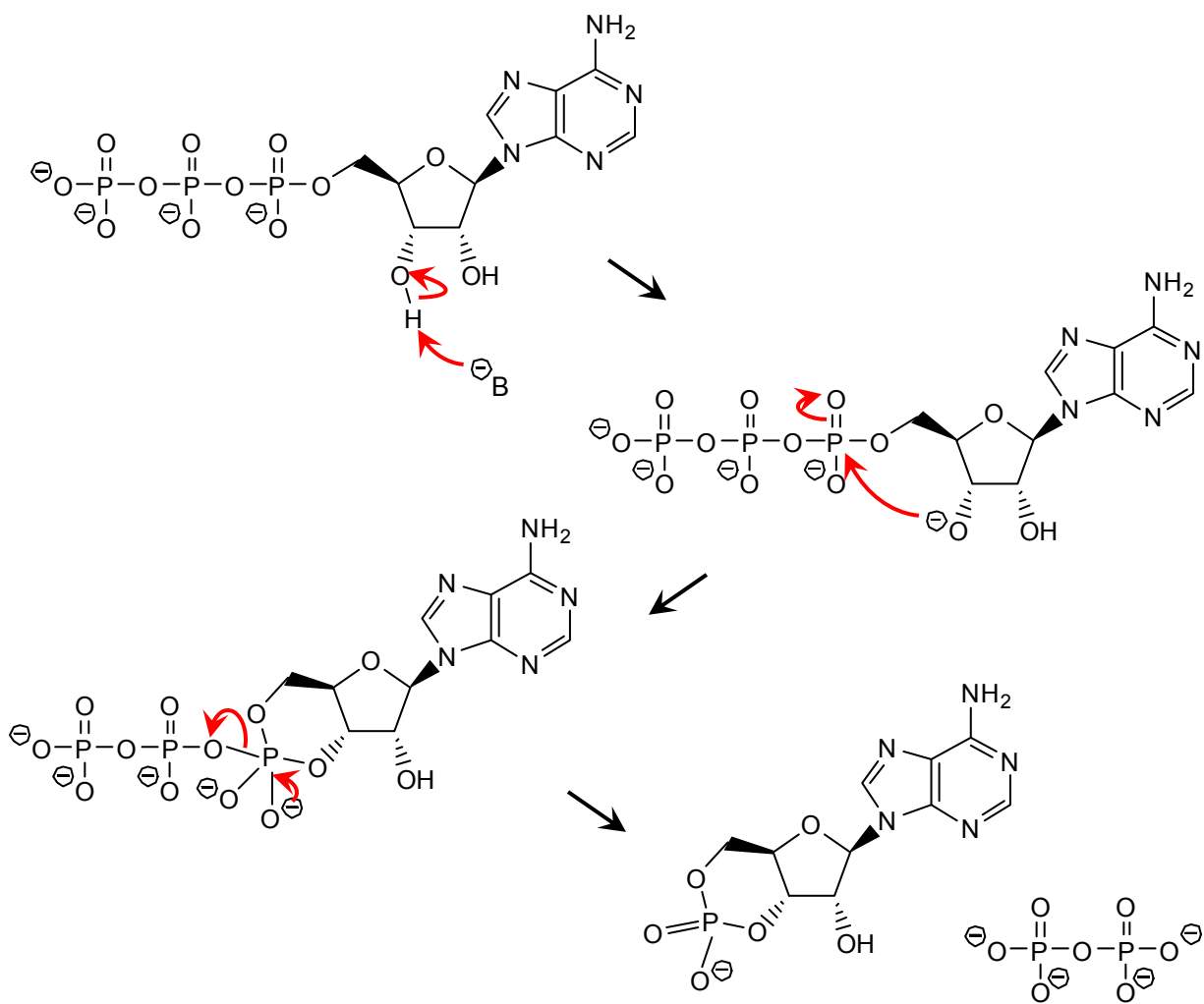
2. The first step in the uncatalyzed reaction—where a zwitterion is produced by intramolecular reaction of a nucleophilic oxygen and an electrophilic phosphorus—is the slow step. A catalyst could help it out by either making the oxygen more nucleophilic, or making the phosphorus more electrophilic.

A strong acid would make the phosphorus more electrophilic by protonating the P=O oxygen. Well, actually, a strong acid would protonate many of the phosphate oxygens:





A strong base would make the attacking oxygen more nucleophilic by deprotonating it:



3. An enzyme could catalyze the uncatalyzed reaction by first making the first step go faster, and both making the P=O bond more electrophilic and making the attacking oxygen more nucleophilic would accomplish that goal.

