9.S: Phosphate Transfer Reactions (Summary)

All of the reactions detailed in this chapter involved the transfer of a phosphate group - usually a phosphate, diphosphate, or AMP group - from one molecule (the donor) to another (the acceptor). Your learning goal for this chapter is to recognize and understand what is happening in these phosphate group transfer reactions, and to gain a basic understanding of the chemistry of phosphate and other phosphate groups.

Be sure that you can identify and provide examples of the following terms:

inorganic phosphate	organic triphosphate
inorganic phosphate	phosphate (mono)ester
inorganic pyrophosphate	phosphate diester
organic (mono)phosphate	phosphate anhydride
organic diphosphate	bridging/non-bridging oxygen

- Also, make sure that you can recognize and use appropriately the various abbreviations introduced in this chapter:

P_i PP_i $R-OP$

$R-OPP$ $R-OAMP$ ATP

ADP AMP

. . . in addition to the various structural abbreviations for adenosine mono-, di-, and triphosphate.

- You should know the approximate pK_a values for phosphoric acid and an organic monophosphate, and be able to state the approximate net charge (to the nearest 0.5 charge unit) of these species in buffers of different pH levels.
- You should be able to describe, in words and pictures, the tetrahedral sp3d bonding picture for the phosphorus atom of a phosphate group. Even though the geometry is not always shown in every drawing, always keep in mind that the phosphate group is tetrahedral.
- You should be able to draw resonance contributors for different phosphate groups, identify major versus minor contributors, and explain why some are major and some are minor. Remember - charges are shared between non-bridging oxygens, even if they are not drawn that way!
- ***Absolutely critical to your success with this chapter is being able to picture and illustrate the mechanistic pattern which we refer to as a phosphate group transfer.***
- Though not usually included in reaction illustrations, always remember that charge-charge interactions with magnesium ions and hydrogen bonds to active site amino acids both serve to increase the electrophilicity of a phosphorus atom in donor compounds such as ATP.
- You should understand the distinctions between the three mechanistic models for phosphate transfer reactions - concerted, addition-elimination, and elimination-addition - and know that the concerted model probably most closely describes biochemical reactions.
- You should be able to identify the apical and equatorial positions in the pentavalent transition state of a phosphate transfer reaction, and recognize that the reaction results in inversion at the phosphorus center.
- You should be able to identify the a, b, and g phosphate groups of ATP, as well as the ribose and adenosine parts of the molecule.
- You should be able to explain how ATP acts as a phosphate group donor, and why such reactions are thermodynamically favorable.
- You should be able to draw a curved-arrow mechanism for reactions in which ATP acts as a phosphate group donor in the phosphorylation and/or diphosphorylation of an alcohol. You should be able to predict the result of nucleophilic attack at the α, β, or γ phosphates of ATP.
- In general, you should be able to propose a likely mechanism for any phosphate transfer reaction, given the starting compounds and products.
- Given information about the existence of a covalently linked enzyme-substrate complex in an enzyme mechanism, you should be able to propose a likely mechanism that accounts for such an intermediate. For example, after being told that the

phosphotyrosine phosphatase reaction involves a phosphocysteine intermediate, you should be able to propose a mechanism.