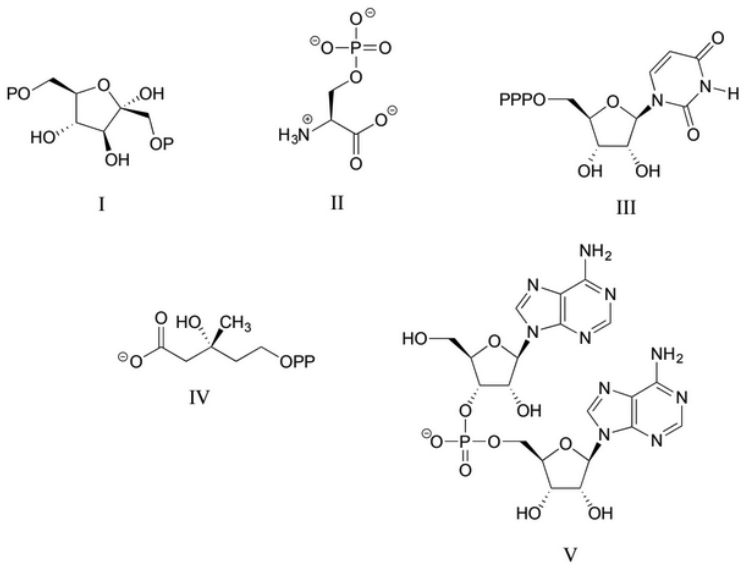
Exercise 8.1. Terms and abbreviations of phosphate

Consider the biological compounds below, some of which are shown with abbreviated structures:



a) Which contain one or more phosphate anhydride linkages? Specify the number of phosphate anhydride linkages in your answers.

b) Which contains one or more phosphate monoesters? Again, specify the number for each answer.

c) Which contains a phosphate diester?

d) Which could be described as an organic diphosphate?

e) For each compound, specify the number of bridging and non-bridging oxygens in the phosphate group.

Exercise 8.2. Role of Phosphates in Biological Systems

Phosphates have various important roles in biological systems, including the installment of post-translational modifications, activation in biochemical pathways or as bridging links for DNA.

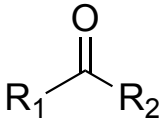
a) Show the different resonance structures that an organic monophosphate has. The organic rest can be depicted as R. Are all four P-O bonds equal?
b) Show the mechanism for the linkage of two nucleotide triphosphates, draw the according arrows and name the different bridging and non-bridging oxygens and highlight the phosphate diester. The base can be abbreviated.
c) The amino acid serine can be phosphorylated, can you name a substrate that is willing to donate a phosphate to the amino acid? Draw the phosphorylated product.

Exercise 8.3. Carbonyl Chemistry – The basics

The carbonyl functional group essential in chemistry and also highly abundant in molecules of life. Can you name five functional groups that contain a carbonyl group and sort them by their reactivity. Choose one of the five and explain where the reactivity is coming from.

Exercise 8.4. Carbonyl Addition

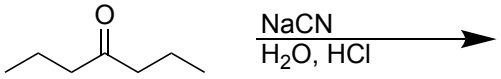
For the generic keton shown:

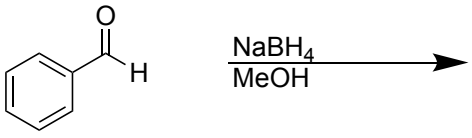


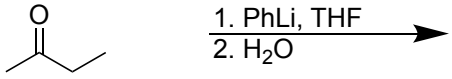
a) Can you draw a generic nucleophilic addition using ":Nu^-"
b) If $R_1 \neq R_2$, what enantiomeric products can you expect? Explain why.
c) Carbonyl additions also play a role in nature, draw an enzyme that could catalyze this reaction. Do you think enzymes can control the stereochemistry? If yes, any idea how?

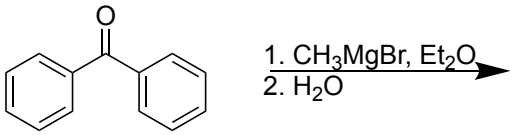
Exercise 8.5. Some Carbonyl Reactions

Show the expected products for the reaction examples below. Mark electrophile and nucleophile. (Drawing arrows and step by steps mechanisms is not required but can definitely help.)



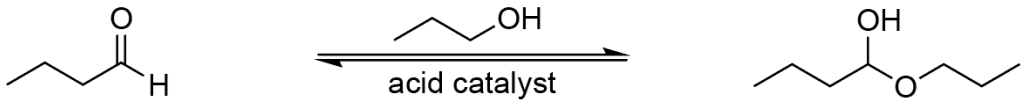




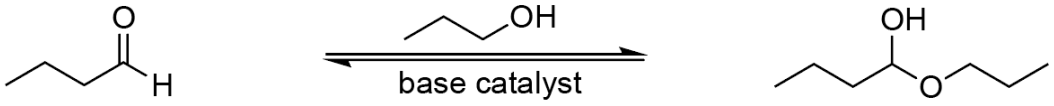


Exercise 8.6. Acid base reactions on Carbonyls

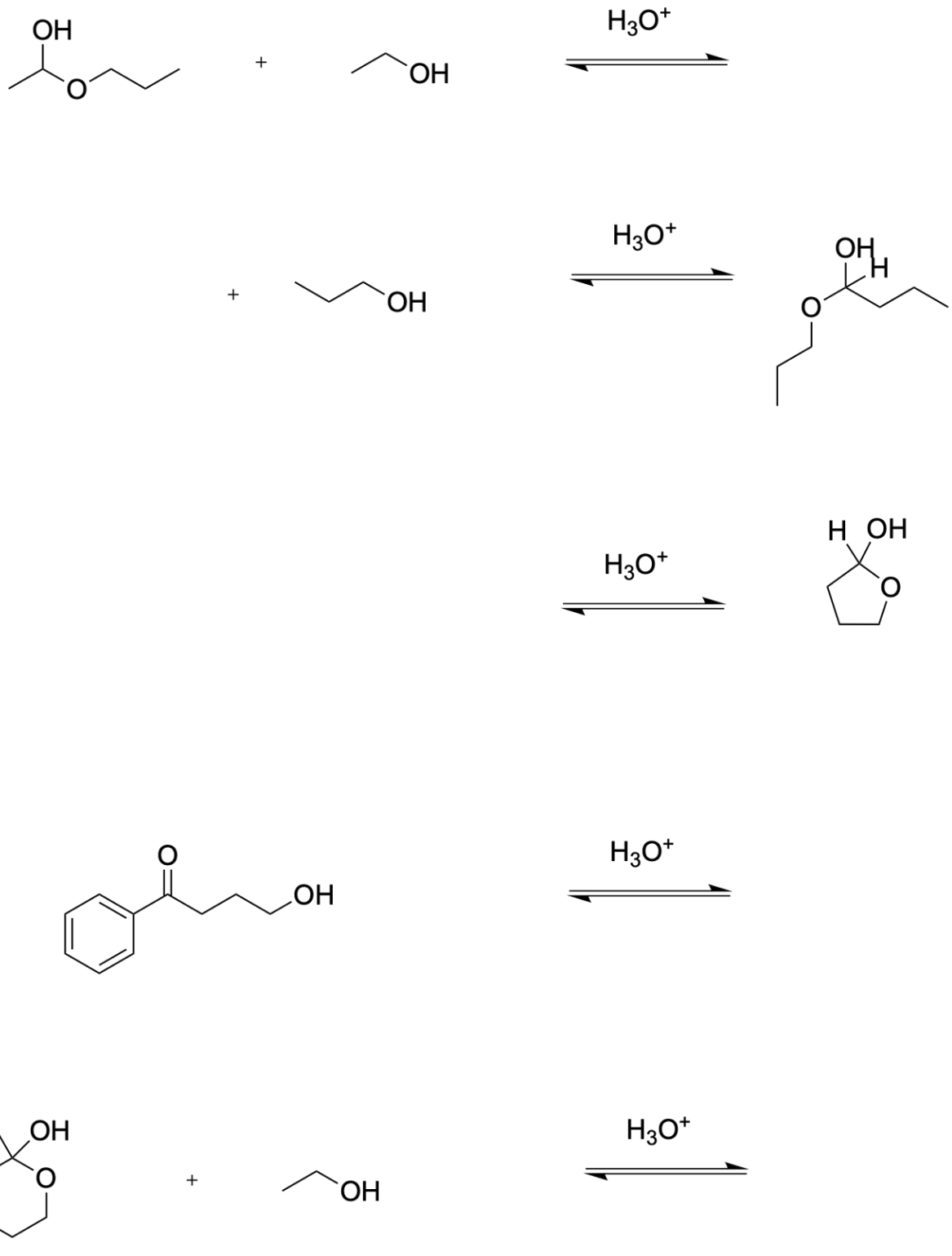
a) Addition of an alcohol to an aldehyde or ketone results in the formation of a hemiacetal and hemiketal. Draw the reaction mechanism of acid catalyzed formation of a hemiacetal below. How does the acid catalyze the reaction?



b) The formation of a hemiacetal or hemiketal can also be catalyzed by a base. Draw the reaction mechanism for the reaction below and explain how the base catalyzes the reaction.



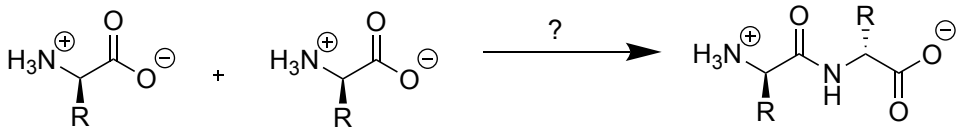
c) Provide the missing starting materials or products.



Exercise 8.7. Protein/Peptide Synthesis

All amino acids have an amino and a carboxylic acidfunctional group, these are used to build long strands of amino acids, which we know as proteins. Nature has developed enzymes which are specialized in creating amide bonds between two

amino acids. Do you think the reaction between the acid and the amine forms spontaneous in the lab? Do you have any idea how a chemist can achieve the formation of amides? (Hint: compare addition vs. substitution.)



Exercise 8.8. Protein Crosslinks through oxidation

Lysine can by oxidased to an aldehyde by the enzyme lysyl oxidase (LOX), creating a terminal aldehyde that is known as allysine. Propose potential crosslinks that can form between an allysine and a lysine and show the mechanism. Bonus: There is also the possibility of two allysine reacting together, try figuring out what could happen there.

Exercise 8.9. Acetylsalicylic acid

The compound acetylsalicylic acid, better known as Aspirin, is a widely used painkiller and blood thinner. The compound was already discovered in 1897, but its mechanism of action was not known until 1971 (*Nature New Biology* **1971***,* nobel price 1982), when it was shown to interfere with the synthesis of prostaglandins, mainly by inhibiting the enzyme cyclooxygenase (COX). This inhibition comes through a covalent modification of a serine in the substrate binding pocket, can you propose a mechanism of how aspirin is modifying COX?