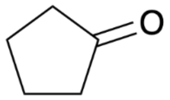
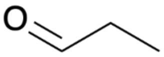
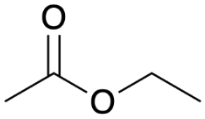
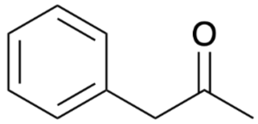
11.1 Cα-Acidity

Compared to simple hydrocarbons, the α-hydrogens of carbonyl groups are much more acidic. This opens up different reaction pathways. Below you find four compounds with a carbonyl group.


Cyclopentanone

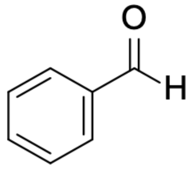

Propanal

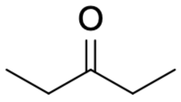

Ethyl Acetate

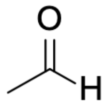

Phenylacetone

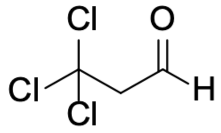
a) Mark all α-hydrogens in each compound and draw the enol-tautomer for each compound.

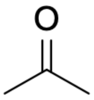
b) Here you can find more carbonyl compounds. Create a ranking starting with the highest Cα-acidity.


1


2

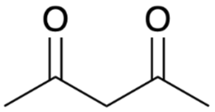

3


4


5

c) Most monocarbonyl compounds in equilibrium exist almost entirely in the keto-form. Even for good chemists it's hard to isolate the pure enol. For example, at room temperature, cyclohexanone contains only about 0.0001% of its enol-tautomer. What can we do to push the equilibrium towards the enol?

d) Have a look at 2,4 pentanedione. Why is the enol dominating here?

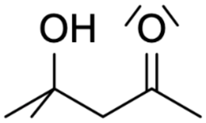


2,4 pentanedione

11.2 Aldol Reactions

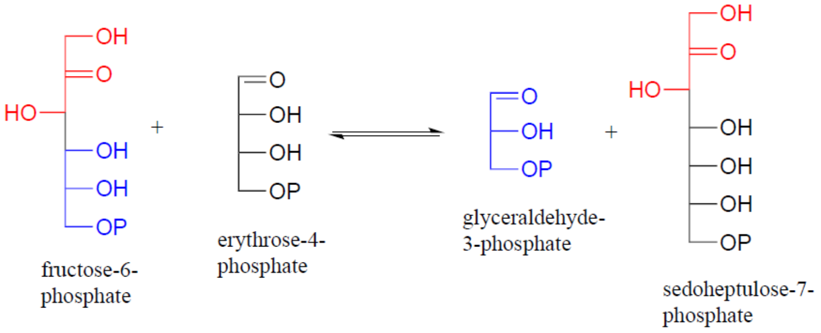
a) Formulate the reaction mechanism for the base-catalyzed aldol reaction of cyclopentanone (see alpha acidity exercise). Use arrows to illustrate the movement of electron pairs.

b) Which starting compounds will yield the compound below via an aldol reaction? Develop a reaction mechanism in which the movement of electron pairs is represented by arrows.



11.3 Transaldol Reactions

In a transaldol reaction an aldose is transferred from one molecule to another. We will be looking at a sugar-interconverting transaldol reaction. We will be walking our way through the following transaldol reaction:



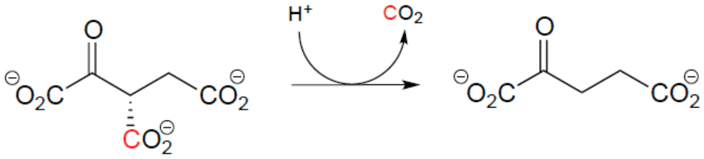
a. Step 1 – Retro-Aldol reaction: Draw the reaction mechanism for how a glyceraldehyde-3-phosphate molecule breaks from the fructose-6-phosphate:

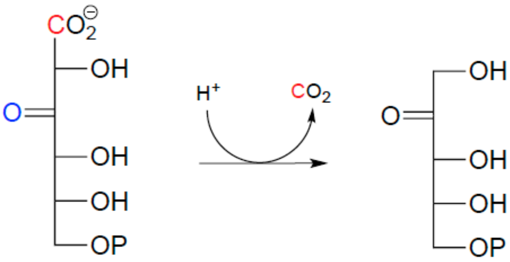
b. Step 2 – Forward-Aldol rection: Draw the reaction mechanism for the formation of the Sedoheptulose-7-phosphate:

c. Bonus: This reaction is facilitated by a transaldose enzyme, more specifically by a Lysine residue which is covalently bound to the substrate throughout the reaction cycle. Show where the enzyme binds to the substrate and explain how this facilitates the reaction:

11.4 Decarboxylation

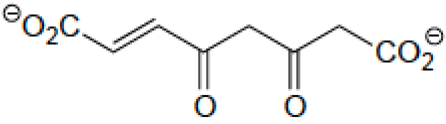
a. Below are two decarboxylation steps which are part of the central catabolic metabolism (specifically the citric acid cycle and pentose phosphate pathway catabolism). Each step represents a point at which a carbon atom is derived and released from the body in the form of CO_2.
   Draw the mechanistic arrows showing the carbon-carbon bond breaking step in each of the reactions shown below:



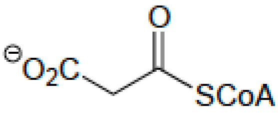


b. Which of the following compounds could be expected to undergo decarboxylation? Draw the mechanistic arrows as well as the product for the decarboxylation step of each one you choose:

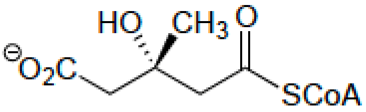
a)



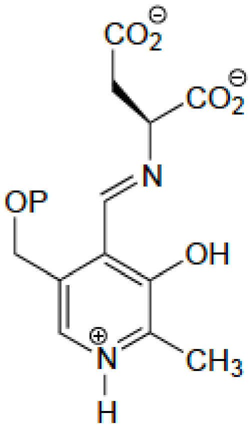
b)



c)



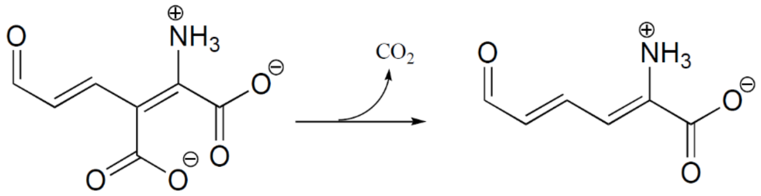
d)



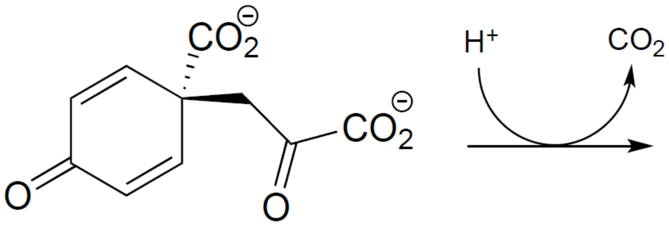
11.5 Decarboxylation in Amino Acid Synthesis

Draw the mechanisms for the two decarboxylations in the synthesis of the amino acids Tryptophan and Tyrosine:

a. Synthesis of Tryptophan – Draw a mechanism for the following decarboxylation. *Hint:* a tautomerization (shifting of a double bond through the moving of a proton, for more information check chapter 7 of the book) precedes the decarboxylation:



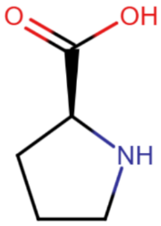
b. Synthesis of Tyrosine – Draw the product and mechanism for the following decarboxylation. *Hint:* Think about comparative stability when thinking about where the protonation will take place:



11.6 Amide Formation of Proteins

a. Draw the mechanism for the general formation of a dipeptide structure (replace the amino acid residues with an R):

b. Now, draw the mechanism for Proline and an amino acid of your choice. What sets Proline apart from the other amino acids?



Proline

c. *Bonus [exceeds scope of the course]:* how do you think this will impact the tertiary (‘3D’) structures of proteins think where they are often found (Turns and Loops, β-Sheets, or α-Helix). Feel free to scour the internet.

11.7 Build your Protein

a. Create your own amino acid. Describe the properties it has, while making sure it still has all the necessary properties and functional groups of an amino acid. Don't forget to invent a name, a three, and one letter code!

b. Now, your amino acid is the second amino acid in the protein favoritase. Your task is to draw the mechanism of how your amino acid is added to the peptide chain. Make sure to show where the reacting amino acids are connected to their respective tRNAs, as well as noting in which part of the ribosome the tRNA currently is.

c. *Optional*: For extra practice take the amino acid of one of your friends and add it to the chain.