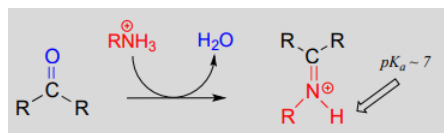


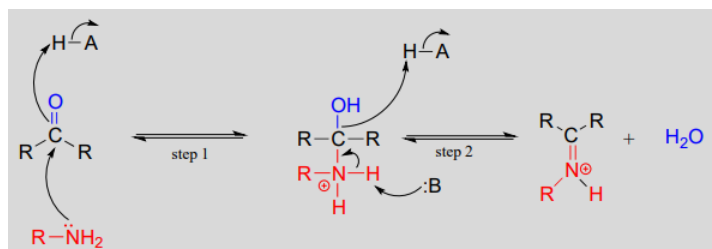
10.6: Imines

The electrophilic carbon atom of aldehydes and ketones can be the target of nucleophilic attack by amines as well as alcohols. The end result of attack by an amine nucleophile is a functional group in which the C=O double bond is replaced by a C=N double bond, and is known as an imine. (An equivalent term is 'Schiff base', but we will use 'imine' throughout this book). Recall from section 7.5B that imines have a pKa of approximately 7, so at physiological pH they can be accurately drawn as either protonated (iminium ion form) or neutral (imine).

Iminium ion formation:



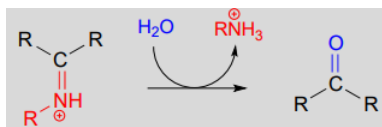
Mechanism (enzymatic):



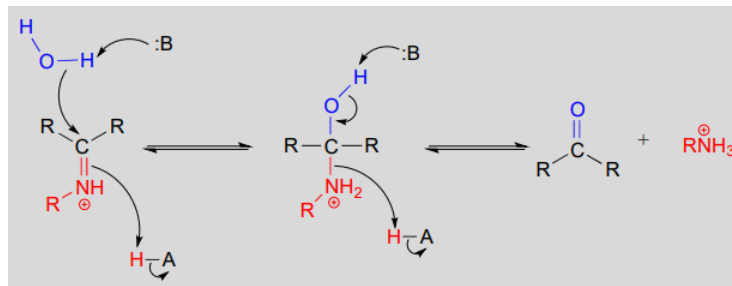
Mechanistically, the formation of an imine involves two steps. First, the amine nitrogen attacks the carbonyl carbon in a nucleophilic addition step (step 1) which is closely analogous to hemiacetal and hemiketal formation. Based on your knowledge of the mechanism of acetal and ketal formation, you might expect that the next step would be attack by a second amine to form a compound with a carbon bound to two amine groups – the nitrogen version of a ketal or acetal. Instead, what happens next (step 2 above) is that the nitrogen lone pair electrons ‘push’ the oxygen off of the carbon, forming a C = N double bond (an iminium) and a displaced water molecule.

The conversion of an iminium back to an aldehyde or ketone is a hydrolytic process (bonds are broken by a water molecule), and mechanistically is simply the reverse of iminium formation:

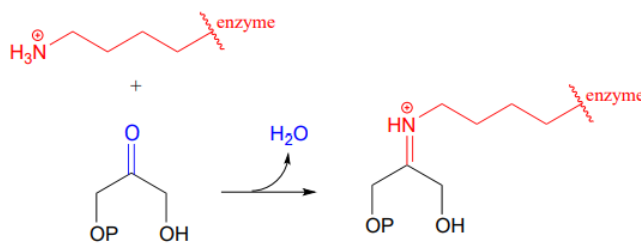
Hydrolysis of an iminium ion:



Mechanism (enzymatic):

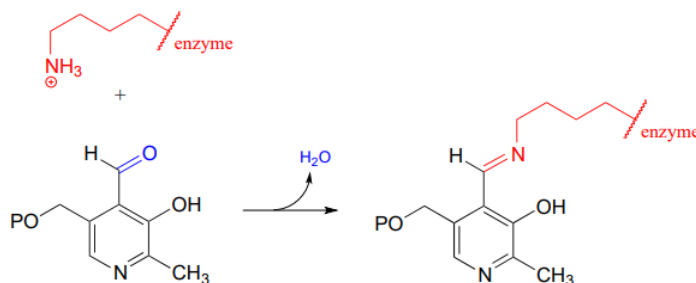


Carbon-carbon bond forming enzymes called aldolases (which we'll cover in detail in chapter 12) often form iminium links between a carbonyl carbon on a substrate and a lysine residue from the active site of the enzyme, as in this aldolase reaction from the Calvin Cycle:

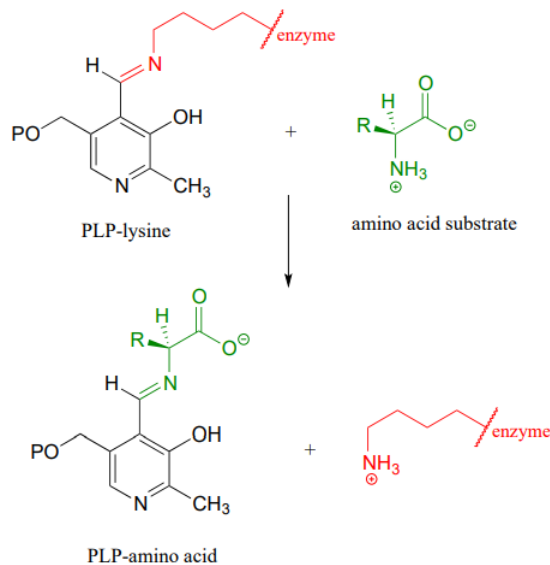


After the carbon-carbon bond forming part of an aldolase reaction is completed, the iminium linkage is hydrolyzed, freeing the product so that it can diffuse out of the active site and allow another catalytic cycle to begin.

In chapter 17, we will learn about reactions that are dependent upon a coenzyme called pyridoxal phosphate (*PLP*), also known as vitamin *B6*. In these reactions, the aldehyde carbon of *PLP* links to an enzymatic lysine in the active site:



Then, the *PLP*-lysine imine linkage is traded for an imine linkage between *PLP* and the amino group on the substrate, in what can be referred to as a transamination.

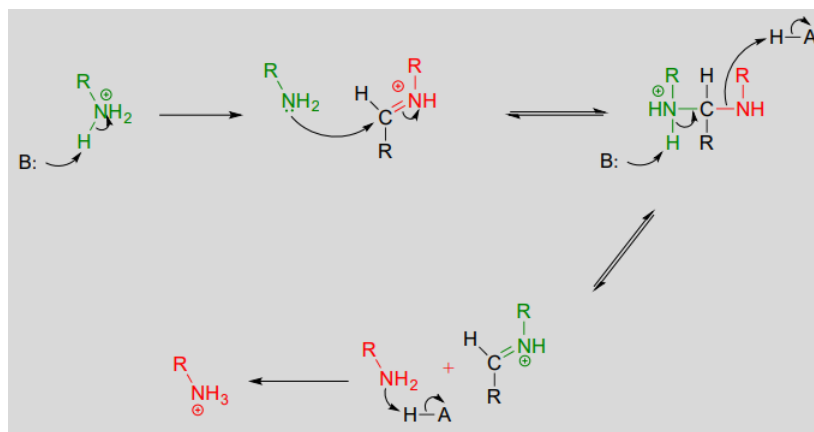


The mechanism for a transamination is very similar to that of imine formation:

Transamination reaction:



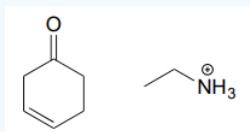
Mechanism:



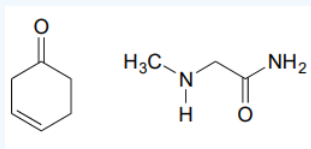
? Exercise 10.6.1

Draw an imine that could be formed between each pair of compounds.

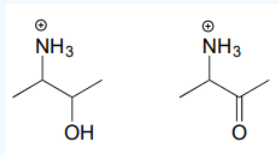
a.



b.

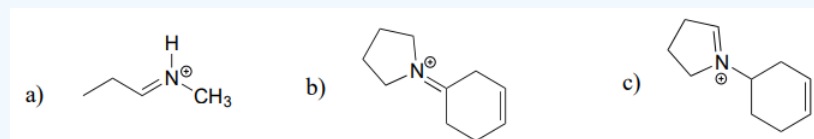


c.



? Exercise 10.6.2

Draw the iminium hydrolysis product for each of the following compounds.

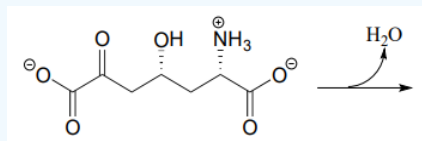


Answer

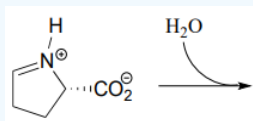
Add answer text here and it will automatically be hidden if you have a "AutoNum" template active on the page.

? Exercise 10.6.3

- a. The metabolic intermediate shown below undergoes an intramolecular imine formation as a step in the biosynthesis of lysine (EC 4.3.3.7). Draw the product of this intramolecular imine formation step.



- b. Predict the product of this iminium hydrolysis step (EC 2.3.1.117) from the proline degradation pathway.



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