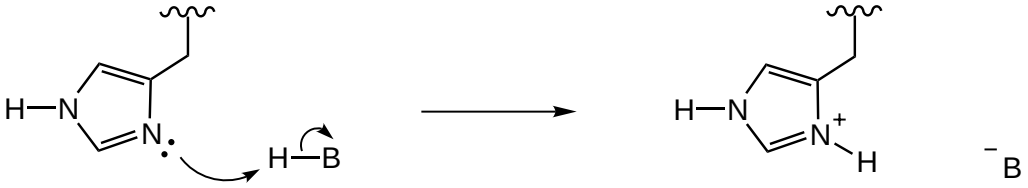
Organic Chemistry c3444y

Problem Set 9 - Amino Acids and Proteins II

Relevant Reading: 26.5, 26.6, 26.7, 26.8, 26.10, 26.11, 26.13, 26.14, 26.15.

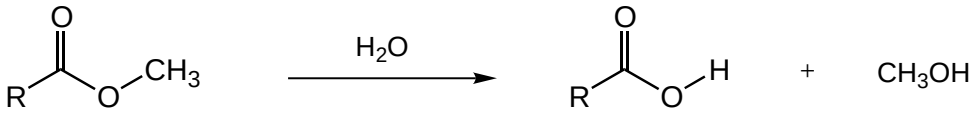
Relevant Book Problems: 26.54, 26.56, 26.62

1. The imidazole of histidine is often used by proteins as a base at the active site.

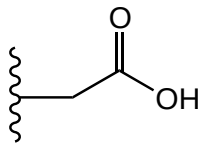


Although imidazole is a reasonably competent base (pK_a of protonated imidazole = 7), proteins often use a "trick" to increase its basicity. Show with structures how the basicity of imidazole may be increased. You may use any other reasonable chemical entity likely to be found in a protein that you desire.

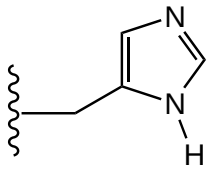
2. You are evolution and you are attempting to "design" a protein for the hydrolysis of esters (a lipase) as shown in the following reaction, using water as the nucleophile:



You only have two active site residues at your disposal, an aspartic acid (not aspartate) and a histidine:



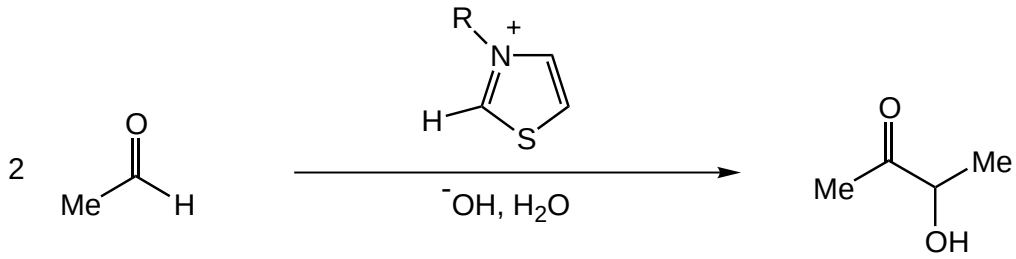
Aspartic acid



Histidine

Propose a two step mechanism for the hydrolysis of an ester with water, using these two amino acid residues in the manner which you feel would be most efficient. You may place the amino acid residues anywhere that you feel is appropriate. Your tasks are 1) to make the water as good a nucleophile as possible, and 2) to stabilize any charge that might be produced on any part of the substrate ester. (Creating some charge on your amino acid residues is OK.)

3. In class we have seen how the cofactor thiamine (vitamin B_1) can catalyze the decarboxylation of pyruvate. Another reaction that thiamine can catalyze is shown below (abbreviated thiamine used):



Write a mechanism for this reaction. (Hint: the first couple of steps will be similar to what we did before. But at some point you need to decide how to generate an anion that is capable of doing the carbon-carbon bond forming step.)