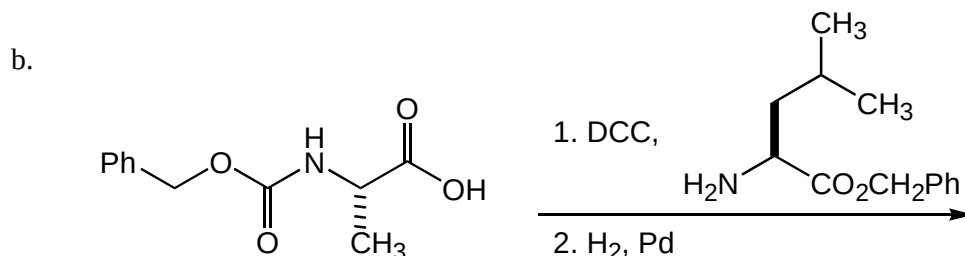
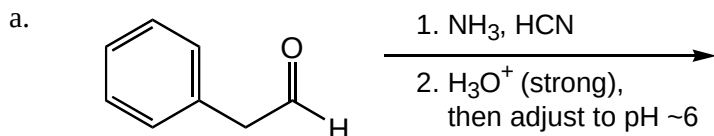


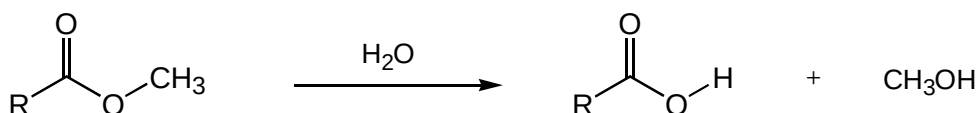
Organic Chemistry c3444y

Problem Set 10 - Amino Acids and Proteins

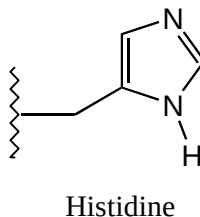
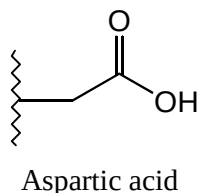
1. Draw the expected product of the following reactions:



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:

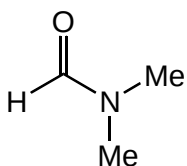


You only have two active site residues at your disposal, an aspartic acid (not aspartate) and a histidine:

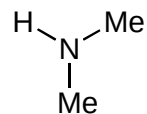


Propose a two step mechanism for the hydrolysis of an ester with water, using these two amino acid residues in the manner which you feel would be most efficient. You may place the amino acid residues anywhere that you feel is appropriate. Your tasks are 1) to make the water as good a nucleophile as possible, 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. The ^1H NMR spectrum of DMF shows two separate 3H singlets for the two methyl groups, whereas the spectrum of dimethylamine shows a 6H singlet for both methyl groups. Explain this difference. If the spectrum of DMF is taken at elevated temperatures ($> 120^\circ\text{C}$) only one 6H singlet is observed for the methyl groups. Explain.

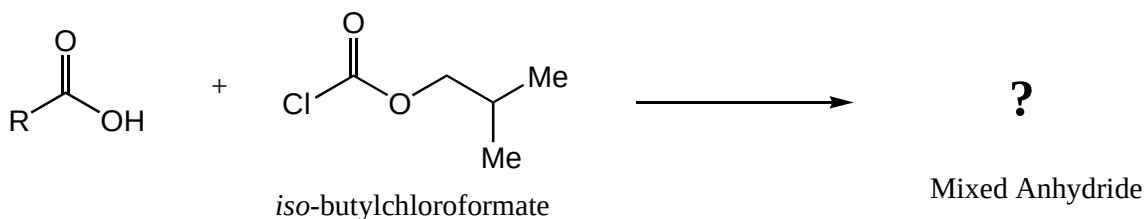


DMF (*N,N*-Dimethylformamide)

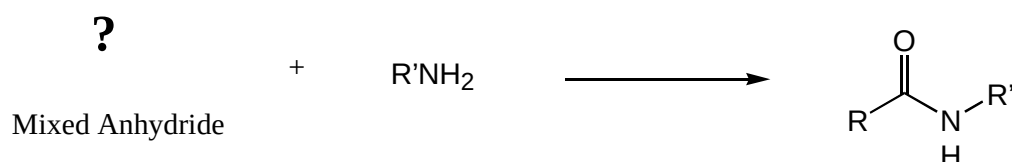


Dimethylamine

4. We have seen that DCC is an efficient reagent for the synthesis of amides from carboxylic acids and amines. Many other reagents have been developed, such as *iso*-butylchloroformate. This first reacts with the carboxylic acid to produce a "mixed anhydride." Provide the structure of the mixed anhydride and a mechanism for its formation:



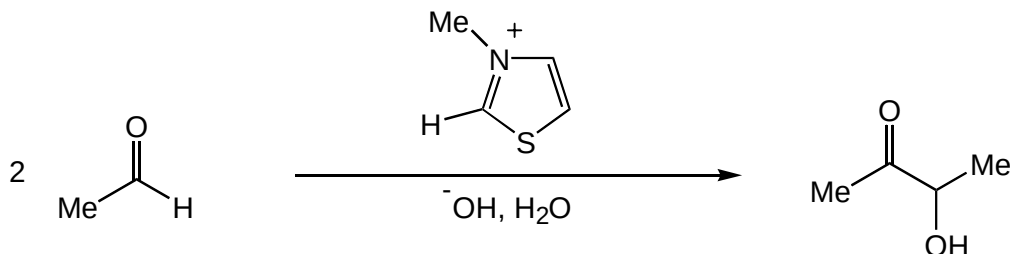
Now show the mechanism of the reaction of an amine with the mixed anhydride to produce an amide:



The mixed anhydride has two carbonyls. In principle, the amine could attack either one, but it doesn't. Why does the amine only attack the one carbonyl and not the other?

5. In class the β -sheet we drew was antiparallel, meaning that the two peptide chains were going in opposite directions. There is another kind of β -sheet that is parallel. Try to draw a parallel β -sheet. You will not be able to have perfectly linear hydrogen bonds as in the antiparallel case.

6. 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 the 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.)