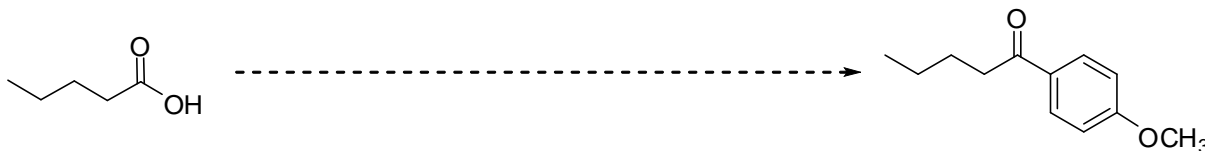


1. Complete the following syntheses by converting the starting material on the left to the product on the right. You may use any organic or inorganic reagent.

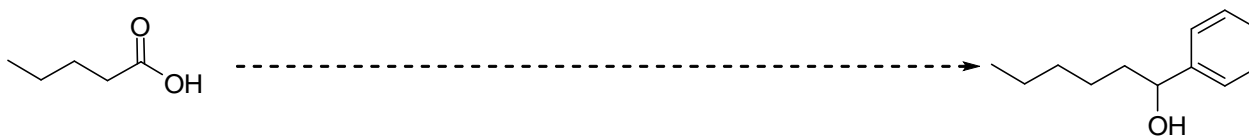
a)



b)

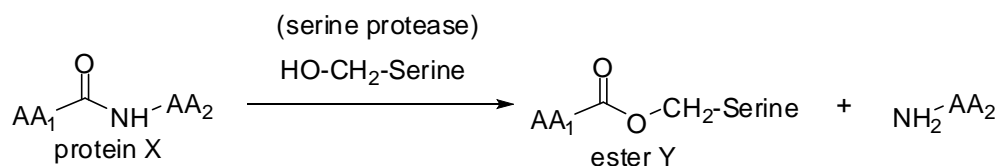


c)

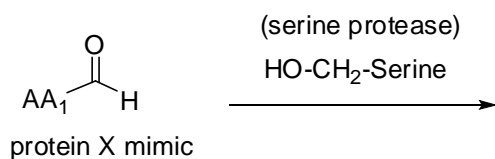


2. Serine proteases are ubiquitous in nature and are frequently the target of drug development efforts because they are key enzymes in many pathological conditions. Serine proteases catalyze the nucleophilic acyl substitution reaction shown below, eventually leading to the splitting of protein material.

a) Based on your understanding of related nucleophilic acyl substitution reactions, draw the mechanism of the transformation of protein X to ester Y. (AA<sub>1</sub> and AA<sub>2</sub> are amino acids in a protein substrate of the serine protease enzyme.)



b) The replacement of the amide bond in protein X with an aldehyde is a classic technique used by drug developers to create new drugs to interrupt the reaction of serine protease enzymes. Draw the mechanism (i.e. electron flow arrows) and product of the reaction of the serine protease enzyme with the aldehyde mimic of protein X below.



c) There are two primary chemical reasons that the aldehyde works as a good drug to inhibit serine proteases. One has to do with the nature of aldehydes that makes the reaction in part b work well. What about aldehydes makes the reaction shown in part b a successful reaction?

d) The second chemical reason for successful aldehyde inhibition of serine proteases has to do with the structure of the aldehyde product shown in part b and its ability to mimic an intermediate in part a. Which intermediate is similar and how is it similar?