5.9: Getting Towed Uphill

The uphill carboxyloids are useful materials in terms of being able to make other compounds. For example, a thioester such as acetyl coenzyme A may be able to make a variety of acyl esters. In the laboratory, acid chlorides are very common starting materials to make other carboxyloids. However, if they are so far uphill, how are they formed in the first place?

The two most common methods of making acid chlorides are treatment with thionyl chloride or with oxalyl chloride.

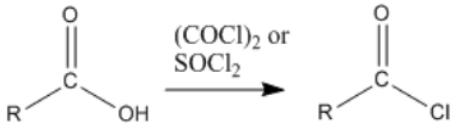


Figure 5.9.1: Possible syntheses of an acid chloride.

The key part of making the uphill acid chloride out of the downhill carboxylic acid is the reagent used. Structurally, the reagents can be compared to acid chlorides themselves. They can be though of as being a little bit like uphill carboxyloids themselves. Thus, as one compound gives its chloride and gets oxygenated on its way downhill, it provides the energy needed to drive the carboxylic acid uphill.

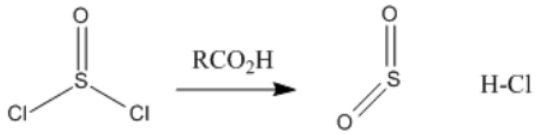


Figure 5.9.2: Conversion of thionyl chloride to sulfur dioxide and hydrochloric acid.

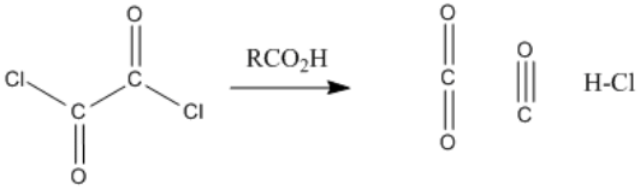
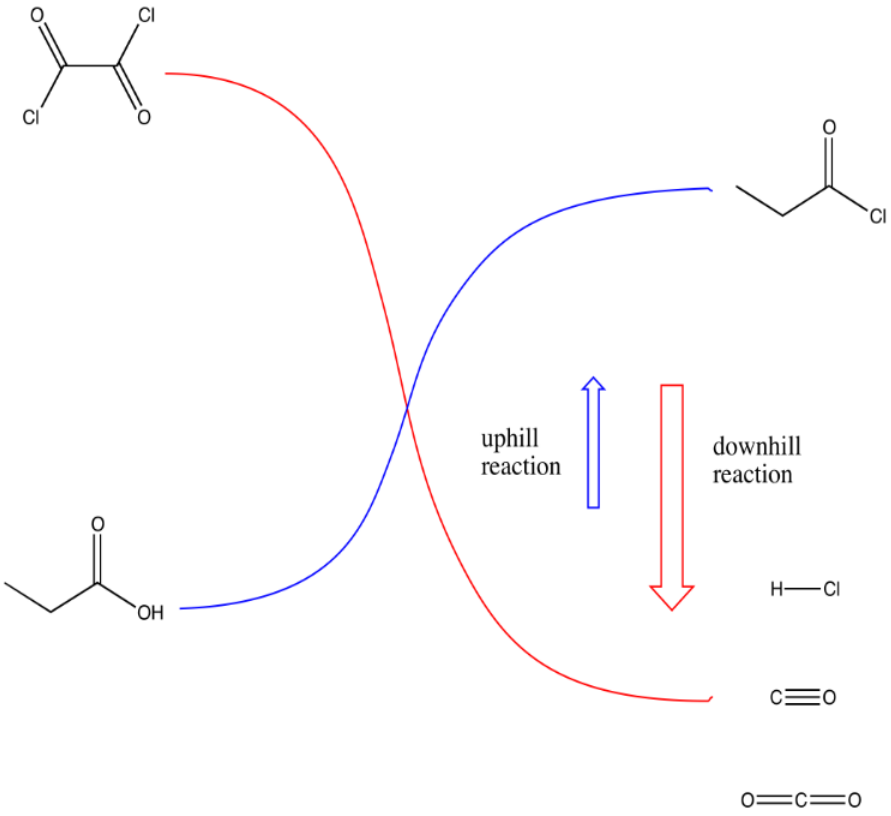


Figure 5.9.3: Conversion of oxalyl chloride to carbon dioxide, carbon monoxide and hydrochloric acid.



Exercise 5.9.1

Reaction of a carboxylic acid with oxalyl chloride starts with a carboxyloid substitution using the oxalyl chloride as electrophile and carboxylic acid as nucleophile. The chloride ion that is liberated then acts as a nucleophile in a cascade reaction that releases CO_2 and CO as an acid chloride forms. Draw the mechanism.

Exercise 5.9.2

Reaction of a carboxylic acid with thionyl chloride is very similar to reaction with oxalyl chloride, described above. Draw the mechanism of the reaction.

Exercise 5.9.3

Provide additional factors (such as energetics, equilibrium concepts) that explain why oxalyl chloride and thionyl chloride can drive the conversion of a carboxylic acid to an acid chloride.

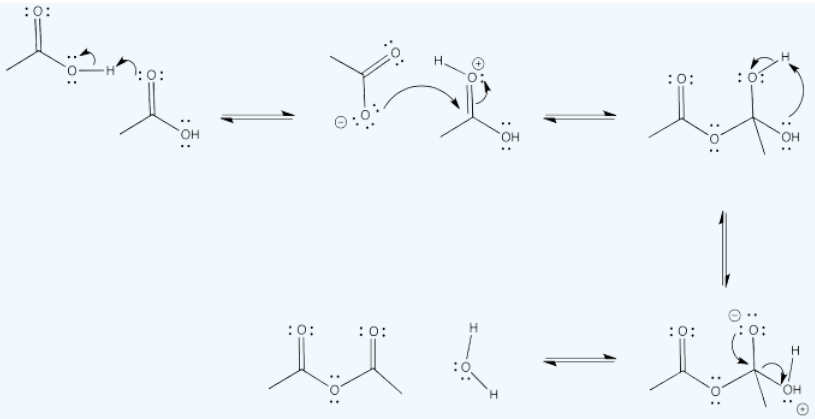
Acid anhydrides are usually made from the corresponding carboxylic acids. One molecule of carboxylic acid acts as a nucleophile and a second acts as an electrophile. Because the same kind of molecule acts as nucleophile and electrophile, acid anhydrides are typically symmetric: they havae a (C=O)O(C=O) unit in the middle, with the same alkyl groups on either side of it.

To aid formation of acid anhydrides, carboxylic acids are often heated strongly (well above 100 ^oC). Otherwise, they are sometimes heated in the presence of a strong drying agent, such as phosphorus pentoxide (empirically, P_2O_5). In the presence of water, phosphorus pentoxide is converted to phosphoric acid, H_3PO_4.

Exercise 5.9.4

Draw a mechanism for the conversion of ethanoic acid to ethanoic anhydride.

Answer



Exercise 5.9.5

Show the *reverse reaction* to the conversion of ethanoic acid to ethanoic anhydride (the same reaction, in the other direction). Which of the two directions do you think is favorable, based on the ski hill?

Exercise 5.9.6

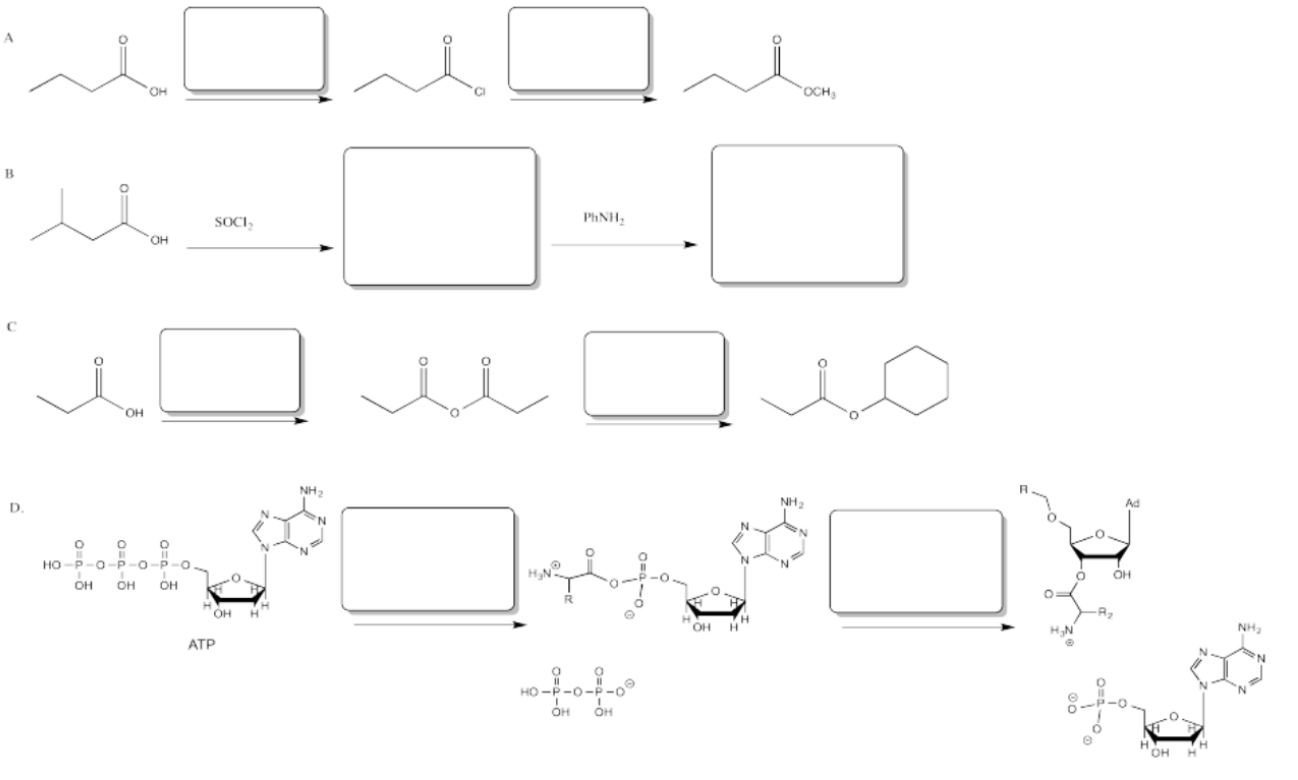
Draw a mechanism for the conversion of phosphorus pentoxide to phosphoric acid.

Exercise 5.9.7

Explain why the conditions outlined above lead to acid anhydride formation.

Exercise 5.9.8

Fill in the blanks in the following problem.



Answer