

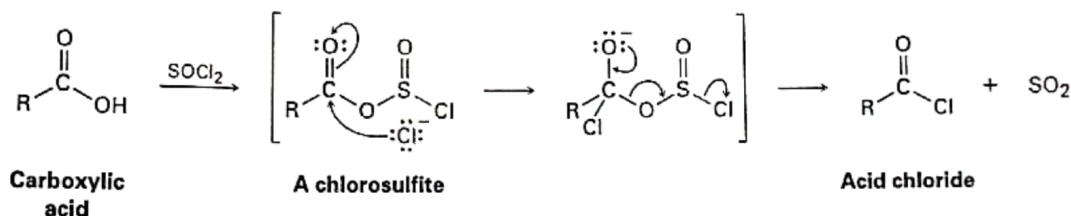
10.6

Carboxylic Acids and Their Reactions

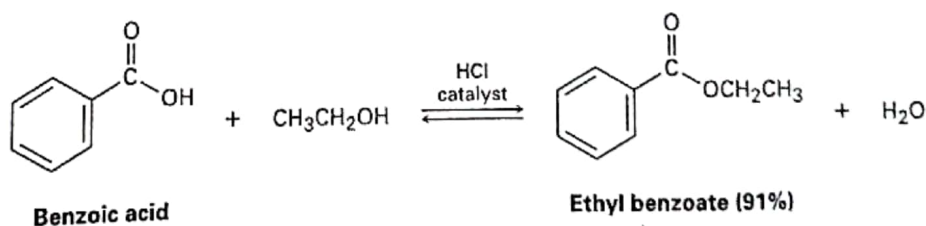
The direct nucleophilic acyl substitution of a carboxylic acid is difficult because -OH is a poor leaving group (Section 7.5). Thus, it's usually necessary to enhance the reactivity of the acid, either by using a strong acid catalyst to protonate the carboxyl and make it a better acceptor or by converting the -OH into a better leaving group. Under the right conditions, however, acid chlorides, anhydrides, esters, and amides can all be prepared from carboxylic acids.

Conversion of Acids into Acid Chlorides ($\text{RCO}_2\text{H} \rightarrow \text{RCOCl}$)

Carboxylic acids are converted into acid chlorides by treatment with thionyl chloride, SOCl_2 . The reaction occurs by a nucleophilic acyl substitution pathway in which the carboxylic acid is first converted into an acyl chlorosulfite intermediate, thereby replacing the -OH of the acid with a much better leaving group. The chlorosulfite then reacts with a nucleophilic chloride ion.

Conversion of Acids into Esters ($\text{RCO}_2\text{H} \rightarrow \text{RCO}_2\text{R}'$)

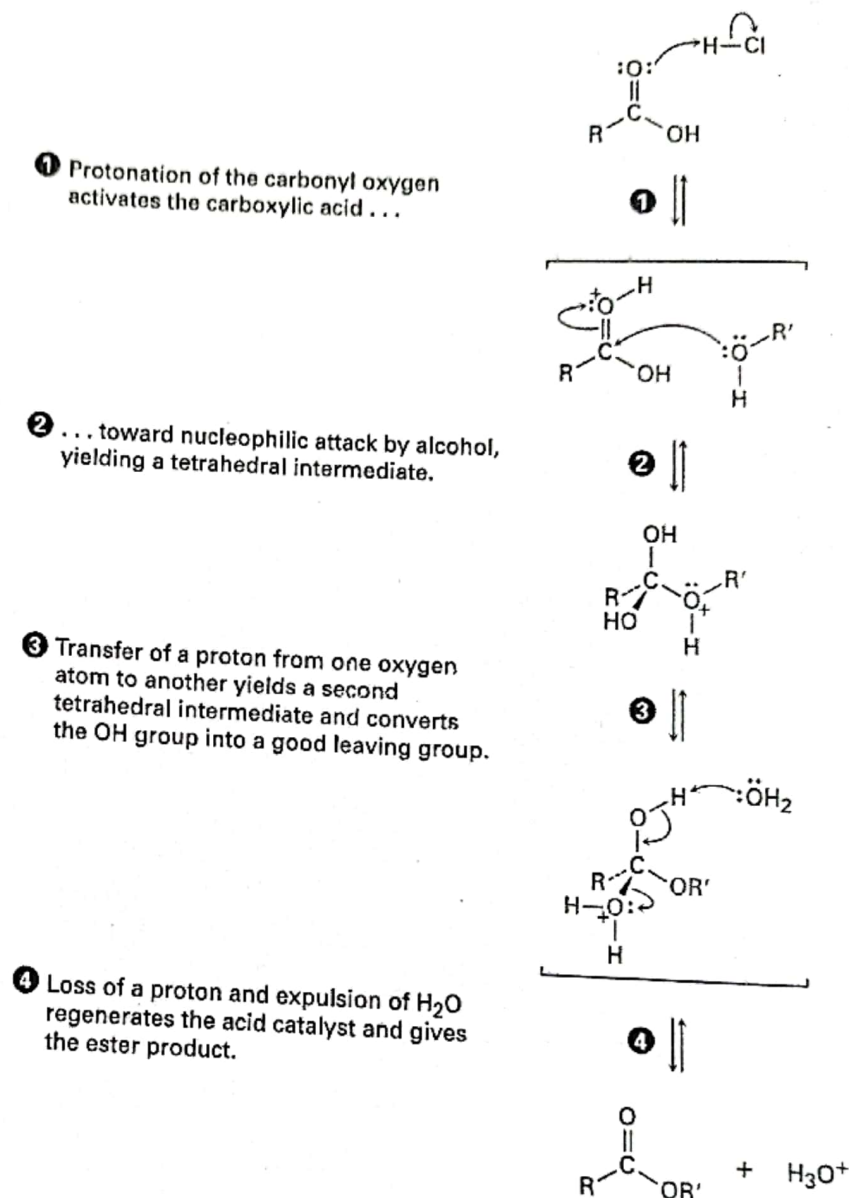
Perhaps the most useful reaction of carboxylic acids is their conversion into esters by reaction with an alcohol—the substitution of -OH by -OR . Called the **Fischer esterification reaction**, the simplest method involves heating the carboxylic acid with an acid catalyst in an alcohol solvent.



As shown in Figure 10.5, the acid catalyst first protonates an oxygen atom of the $\text{-CO}_2\text{H}$ group, which gives the carboxylic acid a positive charge and makes it more reactive toward nucleophiles. An alcohol molecule then adds to the protonated carboxylic acid, and subsequent loss of water yields the ester product.

MECHANISM

Figure 10.5 Mechanism of the Fischer esterification reaction of a carboxylic acid to yield an ester. The reaction is an acid-catalyzed nucleophilic acyl substitution.



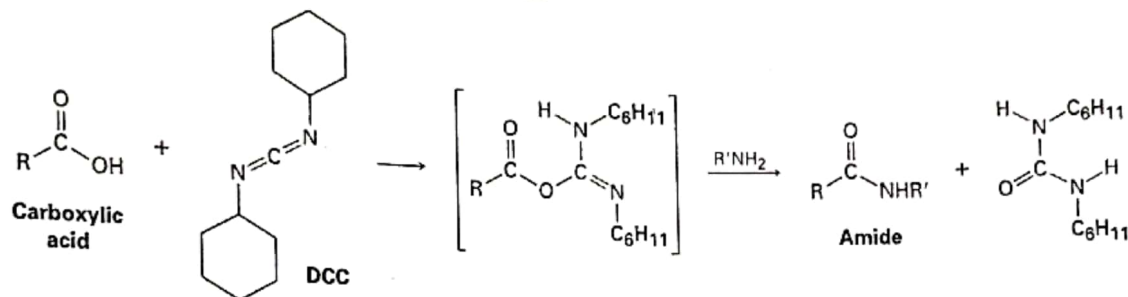
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All steps in the Fischer esterification reaction are reversible, and the position of the equilibrium can be driven either forward or backward depending on the reaction conditions. Ester formation is favored when alcohol is used as the solvent, but carboxylic acid is favored when the solvent is water.

Conversion of Acids into Amides ($\text{RCO}_2\text{H} \rightarrow \text{RCONH}_2$)

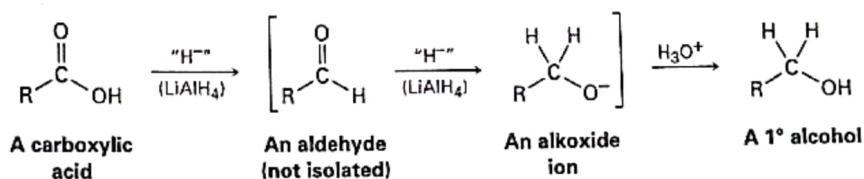
Amides are carboxylic acid derivatives in which the acid $-\text{OH}$ group has been replaced by a nitrogen substituent, $-\text{NH}_2$, $-\text{NHR}$, or $-\text{NR}_2$. Amides are difficult to prepare directly from acids by substitution with an amine because amines are bases, which convert acidic carboxyl groups into their unreactive carboxylate anions. Thus, the $-\text{OH}$ must be activated by making it a better,

nonacidic leaving group. In practice, amides are usually prepared by treating the carboxylic acid with dicyclohexylcarbodiimide (DCC) to activate it, followed by addition of the amine. We'll see in Section 15.7 that this DCC method for preparing amides is particularly useful for the laboratory synthesis of proteins from amino acids.



Conversion of Acids into Alcohols ($RCO_2H \rightarrow RCH_2OH$)

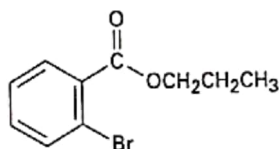
As we saw in Section 8.3, carboxylic acids are reduced by lithium aluminum hydride ($LiAlH_4$) to yield primary alcohols. The reaction occurs by initial substitution of the acid $-OH$ group by $-H$ to give an aldehyde intermediate that is further reduced to the alcohol.



Worked Example 10.3

Synthesizing an Ester from an Acid

How might you prepare the following ester using a Fischer esterification reaction?



Strategy

Begin by identifying the two parts of the ester. The acyl part comes from the carboxylic acid, and the $-OR$ part comes from the alcohol. In this case, the target molecule is propyl *o*-bromobenzoate, so it can be prepared by treating *o*-bromobenzoic acid with propan-1-ol.

Solution

