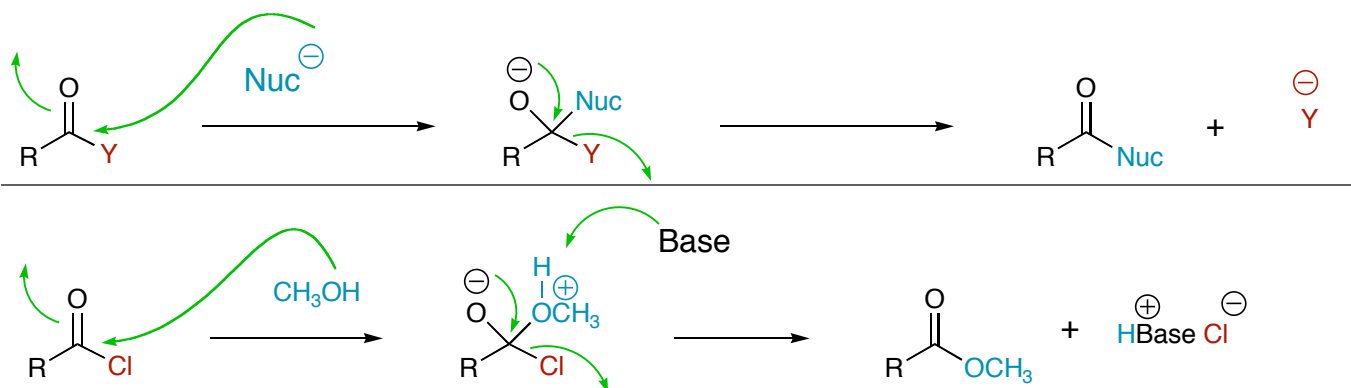


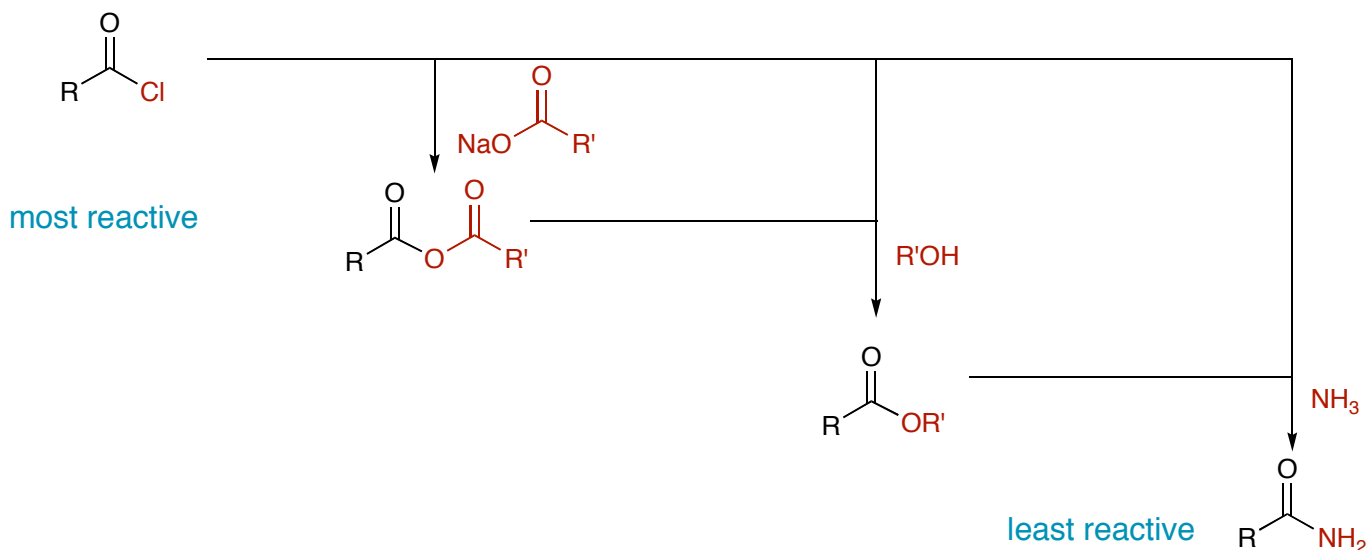
Chapter 21 - Carboxylic Acid Derivatives and Nucleophilic Acyl Substitution

Nucleophilic Acyl Substitution

Nearly all the chemistry of carboxylic acid derivatives involves the addition of a nucleophile to the carbonyl carbon followed by loss of a leaving group to affect a nucleophilic substitution on the acyl carbon. This is a two step process. Often the leaving group is very electronegative and the nucleophile is weak (neutral). An example is the formation of an ester from an acid chloride. These reactions form HCl and a base is used to neutralize the acid by deprotonating the intermediate.

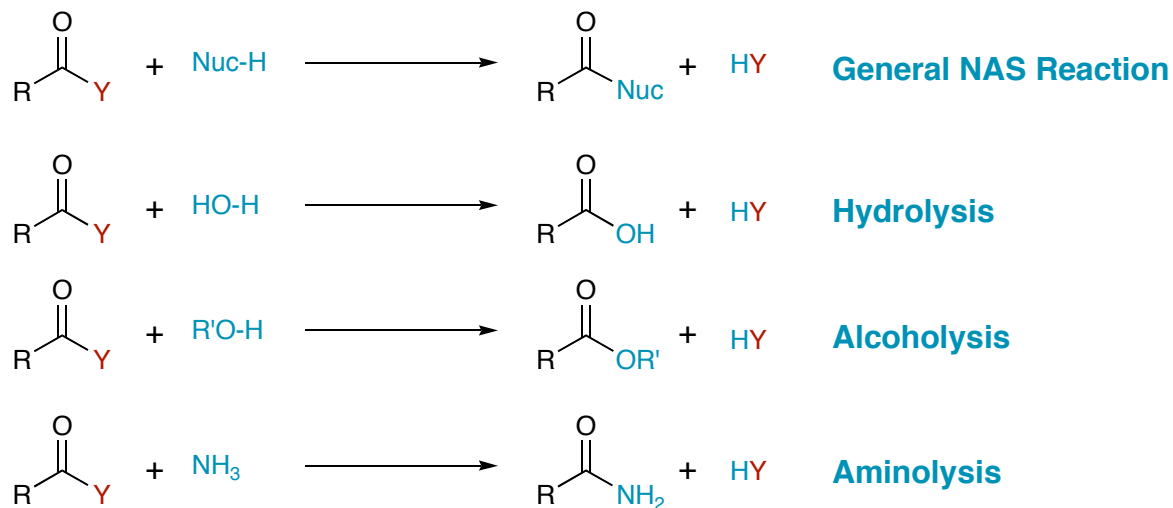


It is generally easy to go from a more reactive carboxylic acid derivative to a less reactive one. It is very difficult to go the other direction.

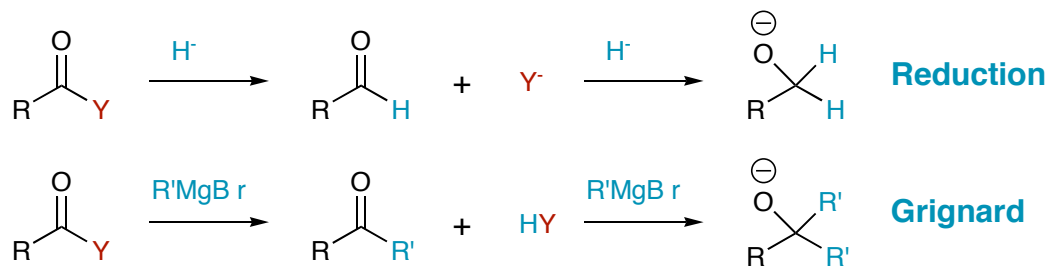


Reaction Types

The nucleophilic acyl substitution with weak nucleophiles can be classified into various reaction types depending on what kind of nucleophile is adding.

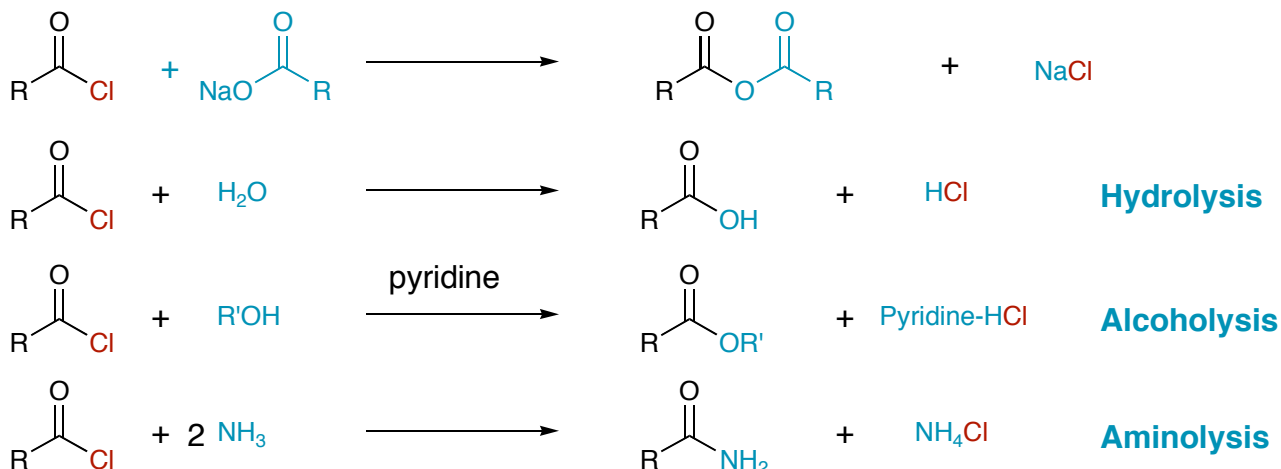


Stronger nucleophiles include reducing agents (hydrides) and Grignard reagents. They will generally add twice.



Reaction of Acid Chlorides

The most reactive and versatile derivative, acid chlorides can be used to make any derivative.



Reaction of Anhydrides

Anhydrides will react very similar to Acid Chlorides. They are limited only by the lack of different anhydrides that are readily prepared. If you want anhydrides other than acetic or cyclic anhydrides, you must make them from acid chlorides. Thus, it is easier to just use the acid chloride itself to make esters and amides.

