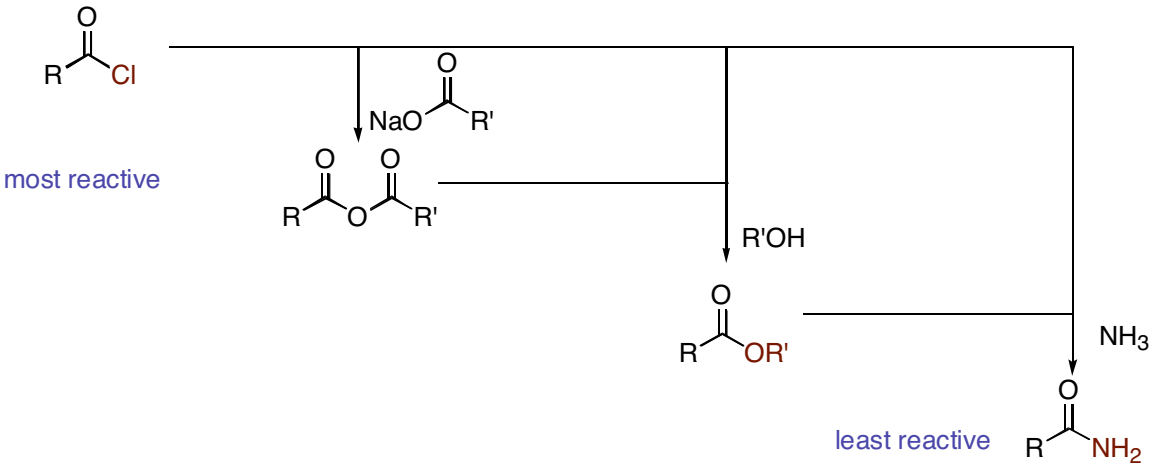
These notes can be obtained at: http://www.ndsu.nodak.edu/instruct/grcook/chem342/notes.shtml

Chapter 21: Carboxylic Acid Derivatives and Nucleophilic Acyl Subsitution Reactions

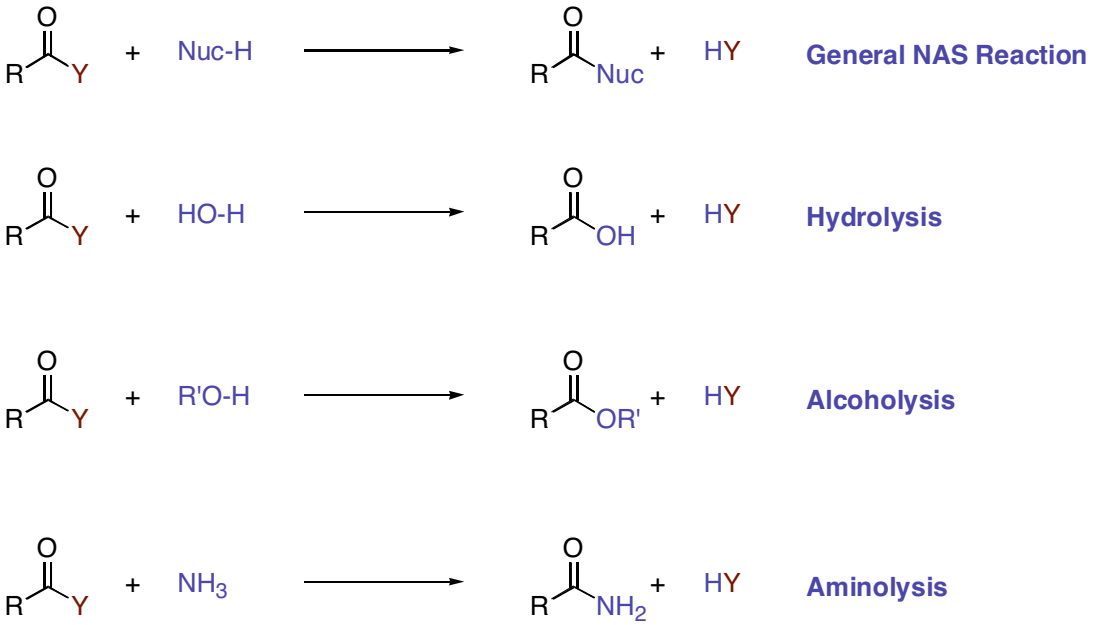
Nucleophilic Acyl Substitution

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.

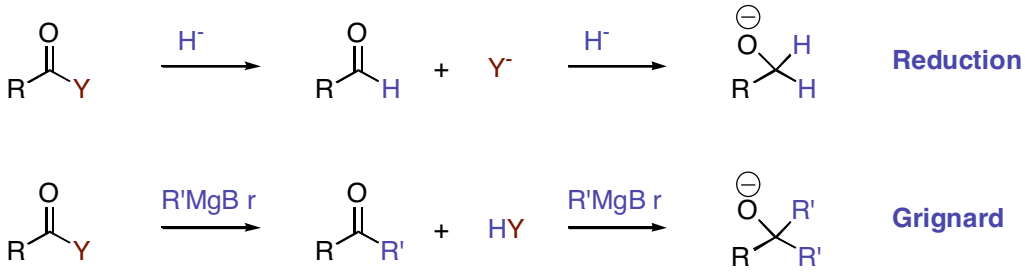


Reaction Types

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



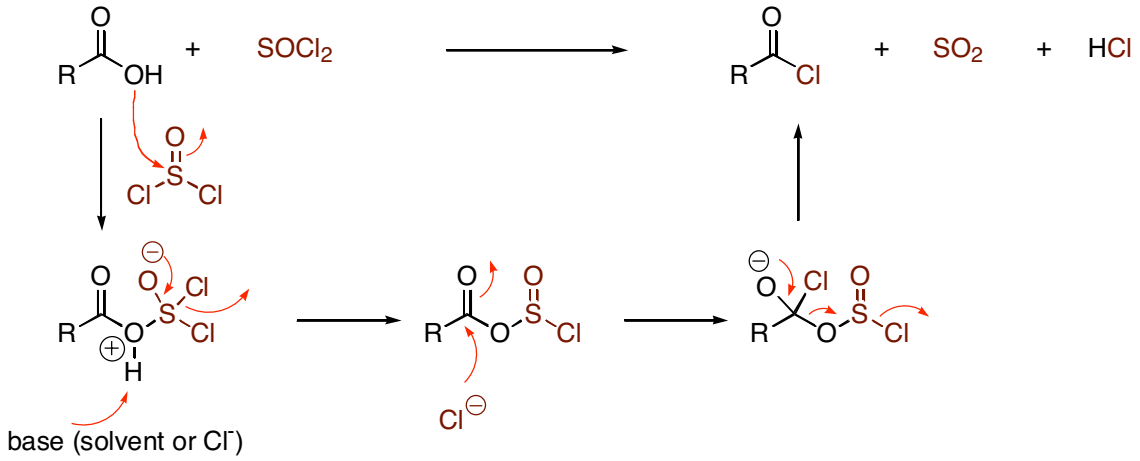
Stronger nucleophiles include reducing agents (hydrides) and Grignard reagents. They will generally add twice.



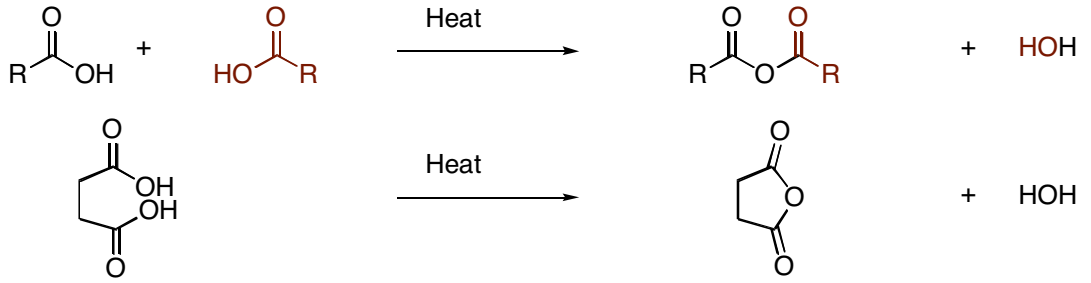
Preparation of Carboxylic Acid Derivatives from Carboxylic Acids

How does one obtain the reactive acid chlorides or anhydrides for use in making other derivatives? They can be prepared from the carboxylic acid directly. For anhydrides, the direct preparation is only practical for symmetrical anhydrides like acetic anhydride or cyclic anhydrides from dicarboxylic acids.

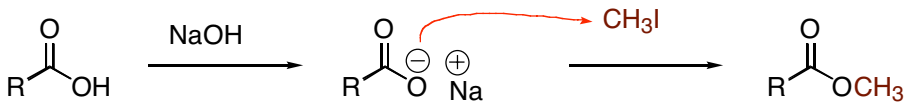
Acid Chlorides



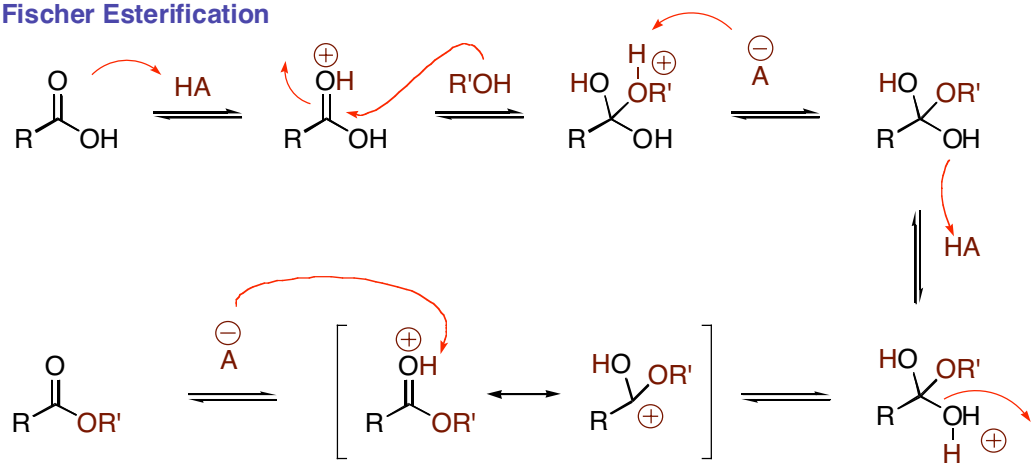
Acid Anhydrides



The preparation of esters from acids is limited. The deprotonated acid will react with methyl or primary alkyl halides via a S_N2 reaction. With a large excess of alcohol and an acid catalyst, a Fischer Ester Synthesis can be undertaken.



Fischer Esterification



It is very very difficult to make amides directly from acids as the amine utilized will simply deprotonate the acid and make a salt.

Reactions of Acid Chlorides

Acid chlorides are the most versatile carboxylic acid derivative and can be used to make any of the others.