

Chapter 21 - Carboxylic Acid Derivatives and Nucleophilic Acyl Substitution

Nucleophilic Acyl Substitution

Remember that nucleophilic acyl substitution occurs by a stepwise addition of a nucelophile followed by elimination of a leaving group. 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. We will discuss this in more detail later.



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. We have discussed this chemistry in previous chapters.



Reactions of Carboxylic Acids - Preparation of Acid Chlorides

Acid chlorides can be directly converted into more reactive acid chlorides using thionyl chloride. This is very convenient and the byproducts are all gasses. This helps drive the reaction forward.



Daily Quiz

Carboxylic acids can be prepared in one step from a Grignard reagent and an ester.
• ² Carboxylic acids are essentially fully deprotonated in aqueous NaOH solution.
³¹ Treatment of nitriles with LiAlH ₄ will produce a carboxylic acid product.
⁴ Carboxylic acid chlorides are less reactive than amides for nucleophilic acyl substitution.