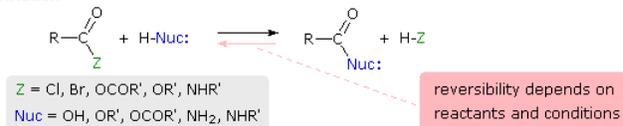


20.6: Summary of Nucleophilic Acyl Substitution Reactions

This is probably the single most important reaction of carboxylic acid derivatives. The overall transformation is defined by the following equation, and may be classified either as **nucleophilic substitution at an acyl group** or as **acylation of a nucleophile**. For certain nucleophilic reagents the reaction may assume other names as well. If Nuc-H is water the reaction is often called **hydrolysis**, if Nuc-H is an alcohol the reaction is called **alcoholysis**, and for ammonia and amines it is called **aminolysis**.

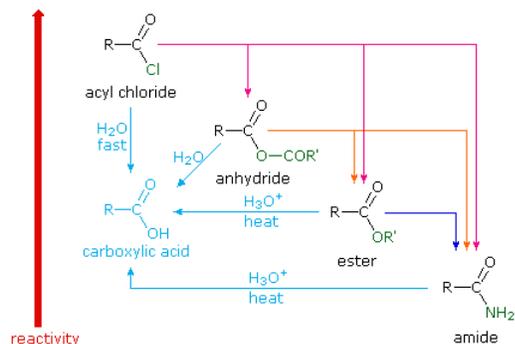
Acyl Substitution:



Different carboxylic acid derivatives have very different reactivities, acyl chlorides and bromides being the most reactive and amides the least reactive, as noted in the following qualitatively ordered list. The change in reactivity is dramatic. In homogeneous solvent systems, reaction of acyl chlorides with water occurs rapidly, and does not require heating or catalysts. Amides, on the other hand, react with water only in the presence of strong acid or base catalysts and external heating.

Reactivity: acyl halides > anhydrides >> esters \approx acids >> amides

Because of these differences, the conversion of one type of acid derivative into another is generally restricted to those outlined in the following diagram. Methods for converting carboxylic acids into these derivatives were shown in a [previous section](#), but the amide and anhydride preparations were not general and required strong heating. A better and more general anhydride synthesis can be achieved from acyl chlorides, and amides are easily made from any of the more reactive derivatives. Specific examples of these conversions will be displayed by clicking on the product formula. The carboxylic acids themselves are not an essential part of this diagram, although all the derivatives shown can be hydrolyzed to the carboxylic acid state (light blue formulas and reaction arrows). Base catalyzed hydrolysis produces carboxylate salts.



Contributors

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