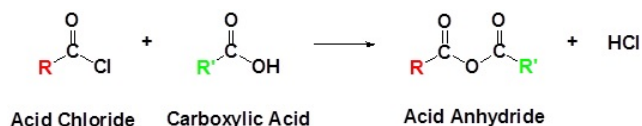


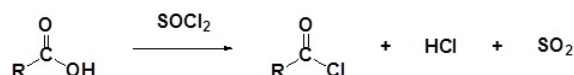
## 20.1: Reactions of Carboxylic Acids

Acid Chlorides react with carboxylic acids to form anhydrides

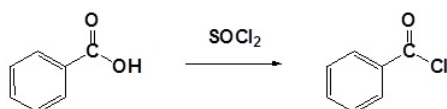


Carboxylic acids react with Thionyl Chloride ( $\text{SOCl}_2$ ) to form acid chlorides.

During the reaction the hydroxyl group of the carboxylic acid is converted to a chlorosulfite intermediate making it a better leaving group. The chloride anion produced during the reaction acts a nucleophile.

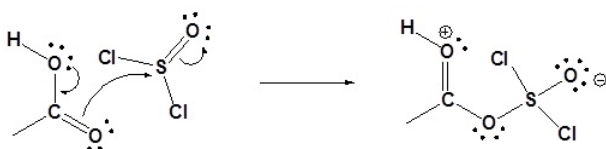


Example

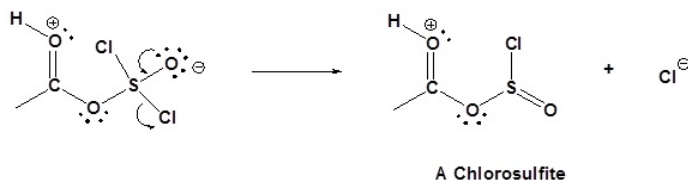


Mechanism

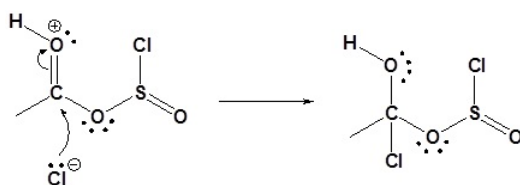
1) Nucleophilic attack on Thionyl Chloride



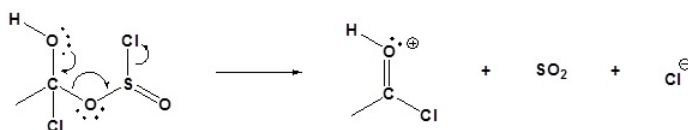
2) Removal of Cl leaving group



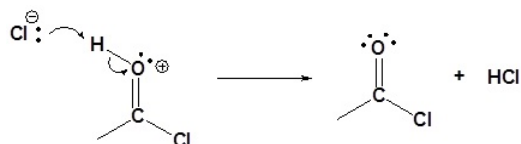
3) Nucleophilic attack on the carbonyl



4) Leaving group removal



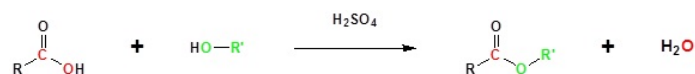
## 5) Deprotonation



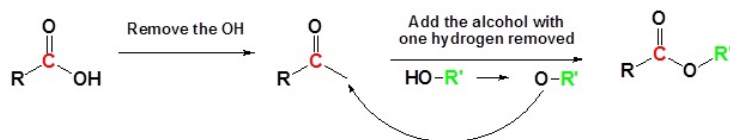
Carboxylic acids can react with alcohols to form esters in a process called Fischer esterification.

Usually the alcohol is used as the reaction solvent. An acid catalyst is required.

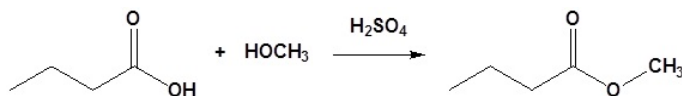
## Basic Reaction



## Going from reactants to products simplified

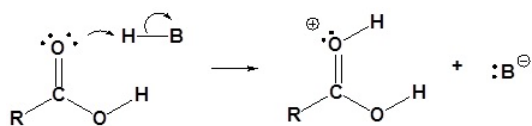


## Example

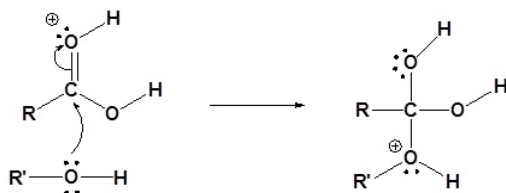


## Mechanism

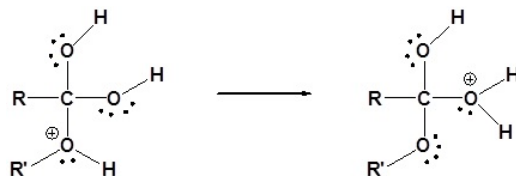
1) Protonation of the carbonyl by the acid. The carbonyl is now activated toward nucleophilic attack.



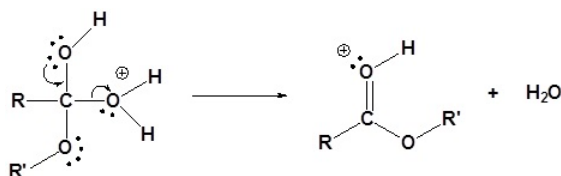
2) Nucleophilic attack on the carbonyl



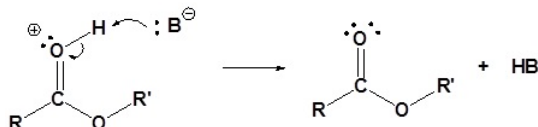
3) Proton transfer



4) Water leaves



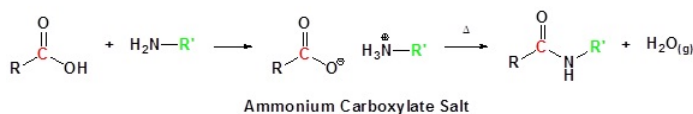
#### 5) Deprotonation



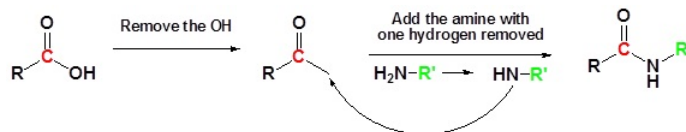
### Conversion of Carboxylic Acids to Amides

The direct reaction of a carboxylic acid with an amine would be expected to be difficult because the basic amine would deprotonate the carboxylic acid to form a highly unreactive carboxylate. However when the ammonium carboxylate salt is heated to a temperature above 100 °C water is driven off and an amide is formed.

#### General Reaction

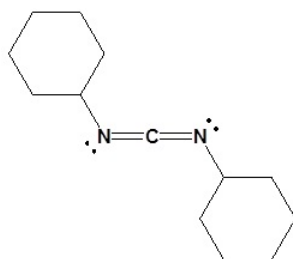


#### Going from reactants to products simply



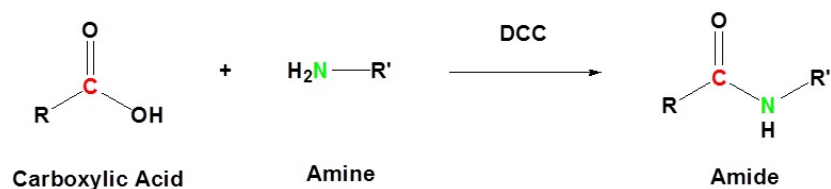
### Conversion of Carboxylic acids to amide using DCC as an activating agent

The direct conversion of a carboxylic acid to an amide is difficult because amines are basic and tend to convert carboxylic acids to their highly unreactive carboxylates. In this reaction the carboxylic acid adds to the DCC molecule to form a good leaving group which can then be displaced by an amine during nucleophilic substitution. DCC induced coupling to form an amide linkage is an important reaction in the synthesis of peptides.

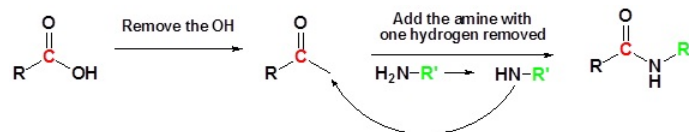


Dicyclohexylcarbodiimide (DCC)

#### Basic reaction

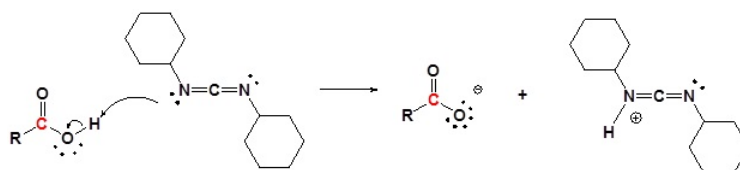


Going from reactants to products simplified

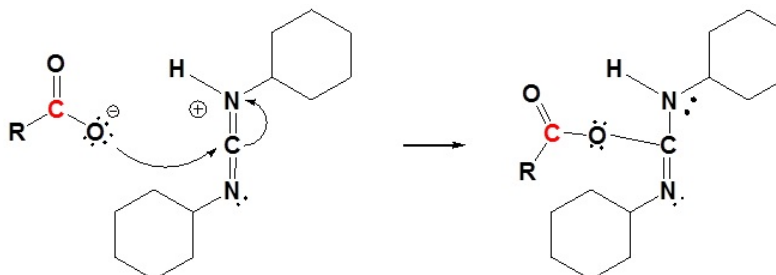


## Mechanism

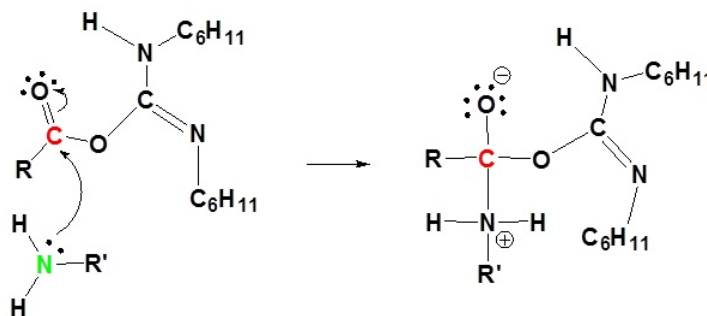
### 1) Deprotonation



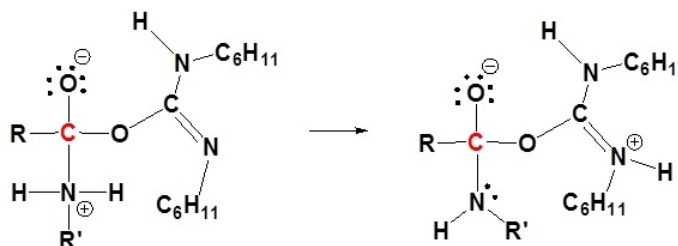
### 2) Nucleophilic attack by the carboxylate



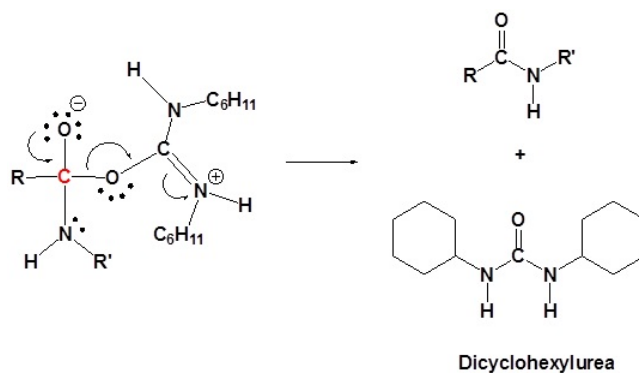
### 3) Nucleophilic attack by the amine



### 4) Proton transfer



## 5) Leaving group removal



## Contributors

- Prof. Steven Farmer ([Sonoma State University](#))

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