

Carboxylic Acids

Section Agenda

- 1) Problem Set #4 (due today) will be graded by Wednesday morning
- 2) Handout: Carboxylic Acids
- 3) Handout: Practice Problem Set
- 4) Handout: Practice Solution Set
- 5) Office Hours: Thursday in Bauer, 3-4PM and 8-9PM

Carboxylic Acids

Structure

- The protonated oxygen is sp^2 hybridized despite having four structural pairs. This allows for favorable orbital overlap with the π system of the carbonyl group.
- The most stable conformation, the (Z) form, allows the protonated oxygen's sp^2 lone pair to overlap with and donate into the C-O σ^* bond.

Reactivity

- The acid carbonyl group is still electrophilic, but less so than aldehydes and ketones, because the conjugation with the alkoxy substituent stabilizes the system. Deprotonated carboxylate anions are even less electrophilic.
- The hydroxyl substituent can act as a leaving group, especially if protonated so it leaves as neutral water.

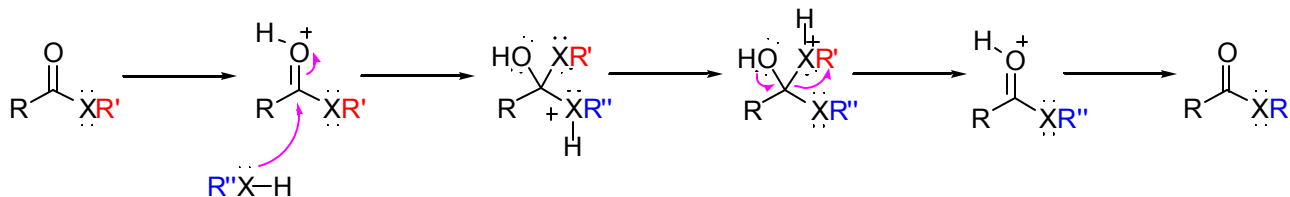
Carboxylic Acid Derivatives

General Mechanisms for Reactions of Carboxylic Acid Derivatives

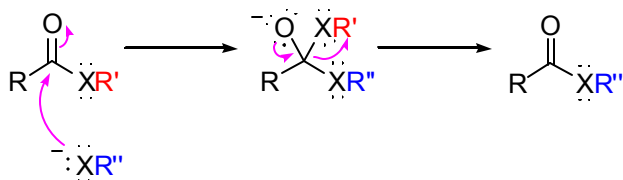
Acidic: Nucleophiles are neutral, carbonyl electrophiles are activated as cations, leaving groups are neutral

Basic: Nucleophiles are charged anions, electrophiles are neutral, leaving groups are charged anions

Mechanism under Acidic Conditions



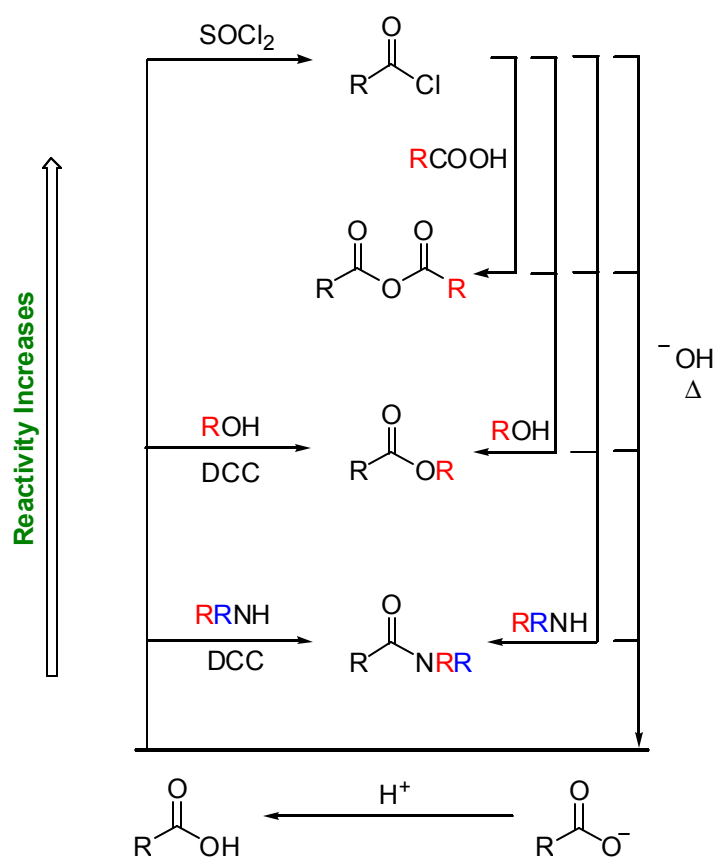
Mechanism under Basic Conditions



Note that both mechanisms proceed through tetrahedral intermediates!

Carboxylic Acid Derivative Interconnectivity

Relative Reactivity of Carboxylic Acid Derivatives



- Know these transformations for synthesis
- You can go “down in energy” on the chart by reacting with a lower energy ligand. For instance, you can react an anhydride with an alcohol or alkoxide to form an ester.
- It is harder to go “up in energy” on the chart. Often, you must hydrolyze to an acid, treat the acid with thionyl chloride to go “all the way up” to an acid chloride, then perform another reaction to “come back down” to an anhydride, ester, or amide.
- Know the mechanism by which DCC activates carboxylic acids. Essentially, it makes the hydroxyl substituent a good leaving group