

## 21.4: SYNTHESIS OF CARBOXYLIC ACIDS

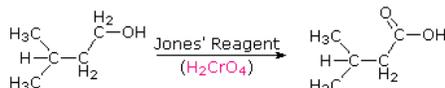
### CARBOXYLIC ACID SYNTHESIS - REVIEW

The carbon atom of a carboxyl group has a high [oxidation state](#). It is not surprising, therefore, that many of the chemical reactions used for their preparation are oxidations. Such reactions have been discussed in previous sections of this text, and the following diagram summarizes most of these. To review the previous discussion of any of these reaction classes simply click on the number (1 to 4) or descriptive heading for the group.

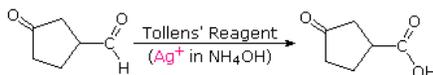
#### 1. Oxidation of Arene Side-Chains



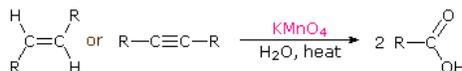
#### 2. Oxidation of 1°-Alcohols



#### 3. Oxidation of Aldehydes



#### 4. Oxidative Cleavage of Alkenes and Alkynes

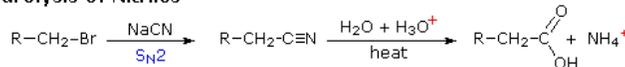


### CARBOXYLIC ACID SYNTHESIS - NEW

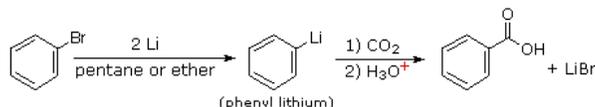
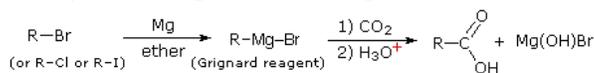
Two other useful procedures for preparing carboxylic acids involve hydrolysis of nitriles and carboxylation of organometallic intermediates. As shown in the following diagram, both methods begin with an organic halogen compound and the carboxyl group eventually replaces the halogen. Both methods require two steps, but are complementary in that the nitrile intermediate in the first procedure is generated by a  $S_N2$  reaction, in which cyanide anion is a nucleophilic precursor of the carboxyl group. The hydrolysis may be either acid or base-catalyzed, but the latter give a carboxylate salt as the initial product.

In the second procedure the electrophilic halide is first transformed into a strongly nucleophilic metal derivative, and this adds to carbon dioxide (an electrophile). The initial product is a salt of the carboxylic acid, which must then be released by treatment with strong aqueous acid.

#### Hydrolysis of Nitriles



#### Carboxylation of Organometallic Reagents

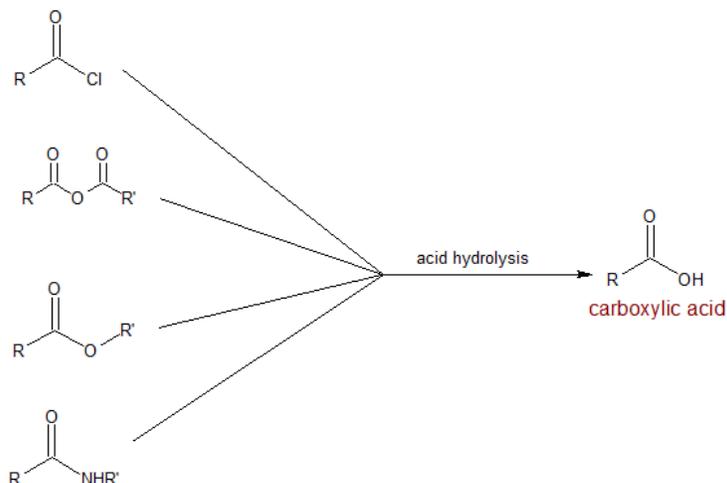


An existing carboxylic acid may be elongated by one methylene group, using a homologation procedure called the **Arndt-Eistert reaction**. To learn about this useful method [Click Here](#).

## HYDROLYSIS OF CARBOXYLIC ACID DERIVATIVES AND NITRILES

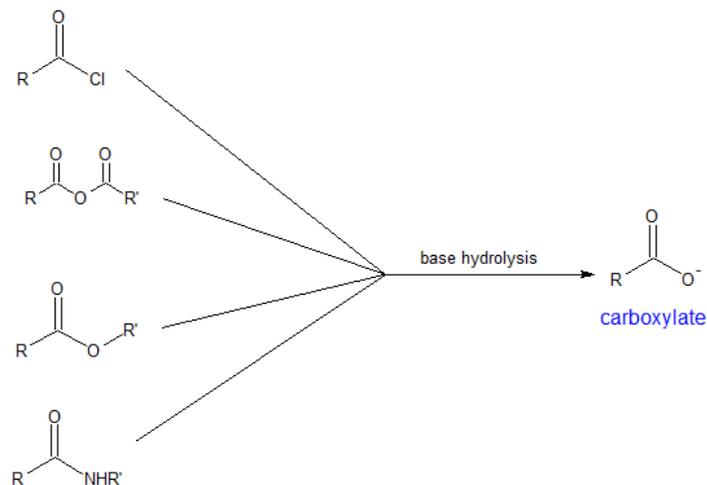
In this chapter we learn that all of the carboxylic acid derivatives can be synthesized from carboxylic acids. These reactions tend to be more useful for multiple-step syntheses to build large and complex molecules. The carboxylic acid derivatives along can be hydrolyzed to produce carboxylic acids. These hydrolysis reactions have limited use in multiple-step synthesis because the acidic proton can be problematic for many organic reactions. Biochemically, hydrolysis reactions are very important in the metabolism of food, drugs, and other nutrients. Hydrolysis can occur under acidic or basic conditions that determine the ionization of the carboxylic acid. Reactions under basic conditions will require a final neutralization step with dilute  $H^+$  to recover the carboxylic acid. To reinforce our awareness of the pH sensitivity of carboxylic acids, both reaction maps are shown below.

- Acid Hydrolysis of the Carboxylic Acid Derivatives



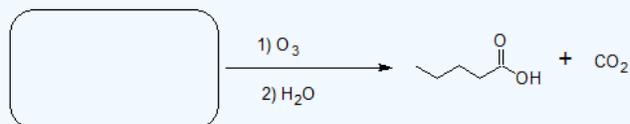
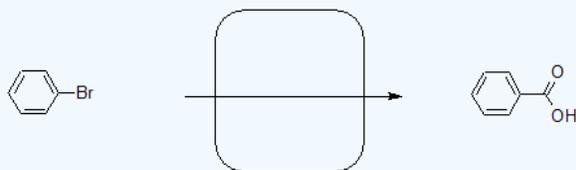
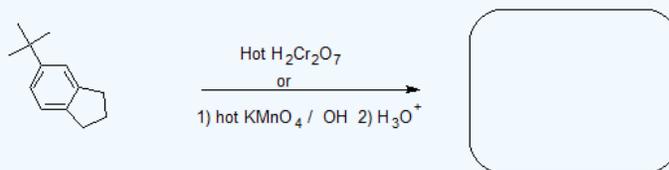
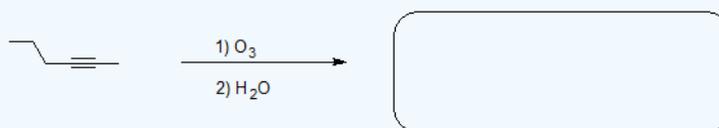
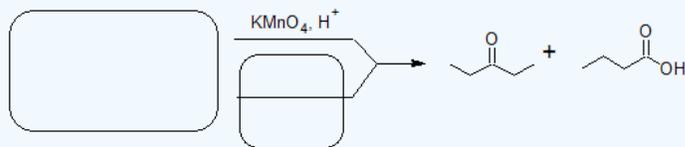
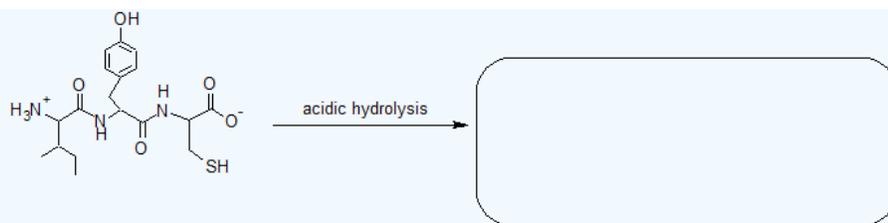
Helpful Hint: Different professors tend to use different proton sources. It is helpful to recognize reagents for their role in a reaction. For example,  $H_2SO_4$ ,  $HCl$ ,  $H_3PO_4$ ,  $CH_3CO_2H$ , and p-TSA are all sources of  $H^+$ . It does not matter which one is used for catalysis or neutralization. Nitric acid is oxidizing, so it is typically only used in oxidation reactions. As we continue learning more reactions/reagents, it can help to group them by their reactivity: acids, bases, neutral, oxidizing, reducing, protic, aprotic, etc. For example, peroxides are oxidizing - whether it is  $H_2O_2$  or MCPBA (m-chloroperoxybenzoic acid).

- Basic Hydrolysis of the Carboxylic Acid Derivatives

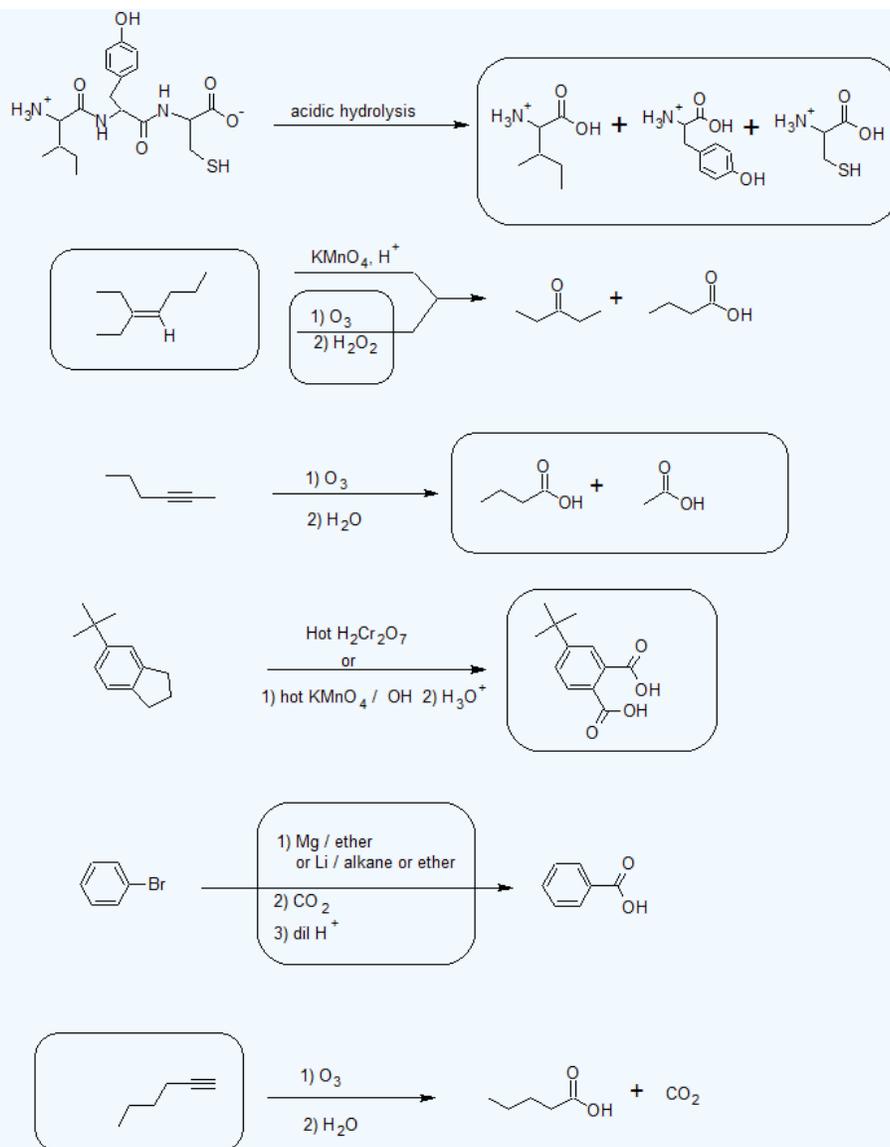


### Exercise

4. Complete the reactions below.



Answer  
4.



## CONTRIBUTORS AND ATTRIBUTIONS

- Dr. Dietmar Kennepohl FCIC (Professor of Chemistry, Athabasca University)
- Prof. Steven Farmer (Sonoma State University)
- William Reusch, Professor Emeritus (Michigan State U.), Virtual Textbook of Organic Chemistry

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