

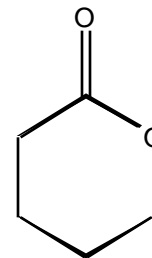
GTQ on Lactones. (30 points, reaction chem., mechanistic and recognition elements)

A lactone is a cyclic ester. Cyclic ester can be made in several ways and the simplest synthesis consists in the intramolecular esterification. Let's look at that and then we will also examine one other synthetic route to lactones.

(a) The compound shown contains two functional groups. There is a carboxy group and the other functional group corresponds to a hemiacetal (hydrate, hemiacetal, acetal). Under acid catalysis, the molecule shown will form an ester. Show the structure of the product ester. Provide a detailed mechanism for the formation of the ester showing intermediates and reagents for every step.

	<p>Product Ester (3 points):</p>
<p>Mechanism (7 points):</p> <p>Reaction 1: Acid-catalyzed hemiacetal cleavage. See SV and lecture notes for details of mechanism. Reaction 2: Acid-catalyzed ester formation. See SV and lecture notes for details of mechanism. Both reactions are equilibria. The reaction is driven to the ester as it is the “thermodynamic sink”.</p>	

(b) The lactone shown can be made in two ways: Via intramolecular cyclization of a hydroxycarboxylic acid or by Baeyer-Villiger reaction. For each of these syntheses, provide the starting materials and the reagents for the key step. Furthermore, suggest a synthesis of the precursors (the appropriate hydroxy carboxylic acid and ketone, respectively) employed in these two reactions.



Intramolecular Cyclization (10 points):

Precursor: HO-CH₂-CH₂-CH₂-CH₂-COOH

Nontrivial synthesis.

One strategy involves the introduction of the alcohol function via hydroboration.

Thus, the target is now: H₂C=CH-CH₂-CH₂-COOH

Via oxidation of H₂C=CH-CH₂-CH₂-CH₂-OH or H₂C=CH-CH₂-CH₂-CHO.

The point here is to realize that the synthesis is quite involved.

Thus, you can see the value of the BVR to make the ester in a simple fashion and to then cleave it to make this hydroxy acid (as opposed to going the other way).

Baeyer-Villiger reaction (10 points):

Via Baeyer-Villiger reaction from cyclopentanone. Using F₃C-CO₃H as the reagent.

The cyclopentanone can be made by oxidation of cyclopentanol.

Cyclopentanol is accessible from bromocyclopentane via S_N2.

There are other ways to make the precursor.