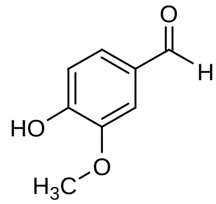
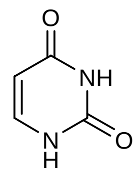
CHE326, Spring 2009	**Aldehydes and Ketones 1**	Workshop 6 Mar. 2-3, 2009

Why?

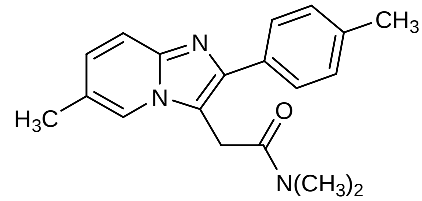
Compounds containing a carbon-oxygen double bond, carbonyl compounds, are ubiquitous in life. They are found in flavors and fragrances, proteins, carbohydrates, nucleic acids, and compounds that affect biological processes. They have a very rich chemistry whose understanding is fundamental to understanding life at a molecular level.



vanillin

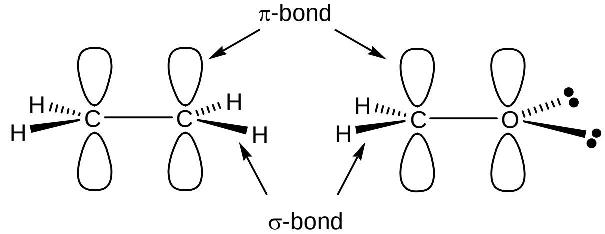


uracil



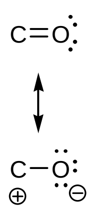
ambien

What is their structure?

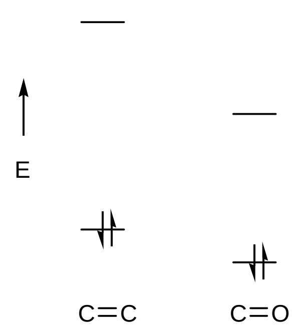


Carbon-carbon and carbon-oxygen double bonds have similar structures. As predicted by VSEPR they both have all of their atoms arranged in the same plane. Orbitals to accommodate these structures can approximately be provided by sp^2 hybridized atoms.

What is their bonding?



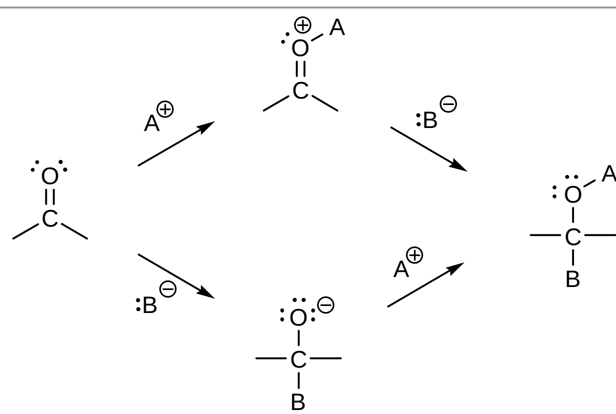
resonance model



molecular orbital model

Because of the greater electronegativity of the oxygen atom, *C=O* groups are polarized compared to *C=C* groups. This results in a greater reactivity with nucleophiles. This polarization is suggested by both a resonance and molecular orbital models. In contrast to *C=C* bonds, *C=O* bonds contain two nonbonding electron pairs on the oxygen atom that can participate in the chemistry of this group.

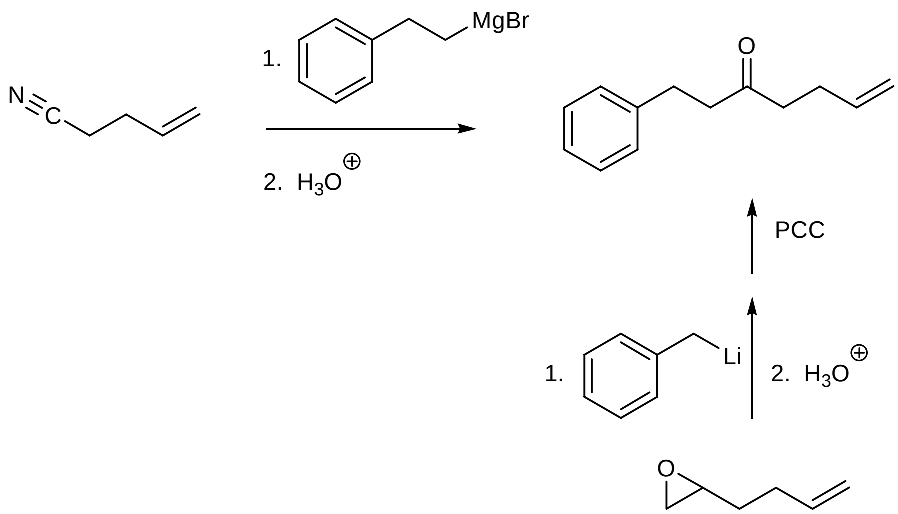
What is their chemistry?



Carbonyl compounds can react with acids (electrophiles), bases (nucleophiles) or both as is indicated by the adjacent scheme. The reactions of carbonyl compounds are dominated by the addition of nucleophiles to the carbon atom. Because this reaction occurs at a faster rate if the oxygen is protonated (A = $H^{\oplus}$), the reactions of weak nucleophiles with carbonyl groups are often catalyzed by acid.

Work these problems on a blank copy of your Personal Workshop Form.

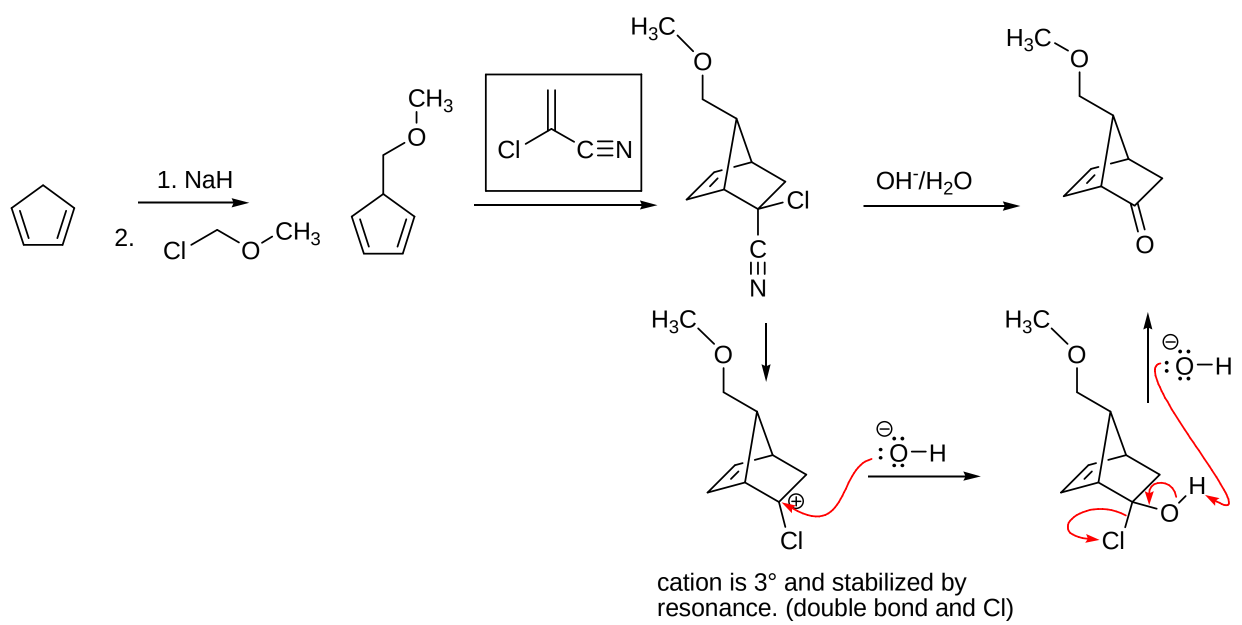
1. Propose a synthesis of the following compound from benzene and compounds containing no more than four (4) carbon atoms.



One can use either the nitrile strategy learned in chapter 16 or the alternative strategy using previously learned methods. There are many ways to prepare the intermediates in these syntheses (epoxide and nitrile) Compare your answers to those of other students in the learning center.

2. The prostaglandins are an important class of lipids. They can act as hormones and are responsible for all sorts of biological functions in the body. Among other things they regulate inflammatory responses. Aspirin acts by inhibiting prostaglandin synthesis. (See page 1095-1096 in the text.)

   The following reaction scheme is the first part of Professor E.J.Corey's (Harvard) synthesis of a Prostaglandin.



   a) The first reaction is a very unusual S_N2 substitution reaction. Explain why cyclopentadiene can be used for such a reaction, while a normal alkane cannot. Because the anion is stabilized by aromaticity, the hydrocarbon is very acidic.

   b) What is reagent X in step 2. Explain the observed stereochemistry. This product is the result of an endo transition state.

   c) Write a mechanism for the formation of the ketone.

3. A synthesis of ascorbic acid (vitamin C, 1) starting from D-(+)-galactose (2) is shown below (Haworth, W.N., et al., *J. Chem. Soc*., **1933, 1419–1423**.). Consider the following questions about the design and reactions used in this synthesis:

This is a group learning problem from the text. You should work this problem in the learning center with other students. Note the transformation of 6 to 7. Can you give a mechanism for this reaction?

(a) Why did Haworth and co-workers introduce the acetal functional groups in 3?

(b) Write a mechanism for the formation of one of the acetals.

(c) Write a mechanism for the hydrolysis of one of the acetals (4 to 5). Assume that water was present in the reaction mixture.

(d) The compound 5 was reduced to compound 6 by the sodium amalgam in the presence of an acid. From what functional group did the reduction actually proceed?

(e) Write a mechanism for the formation of a phenylhydrazone from the aldehyde carbonyl of 7. (Do not be concerned about the phenylhydrazone group at C2. We shall study the formation of bishydrazones of this type [called an osazone] in Chapter 22).

(f) What reaction was used to add the carbon atom that ultimately became the lactone carbonyl carbon in ascorbic acid (1)?