

Learning Guide for Chapter 19 - Aldehydes and Ketones

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- VII. Reactions of ketones and aldehydes with nitrogen nucleophiles
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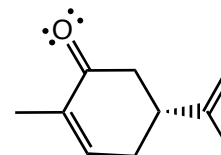
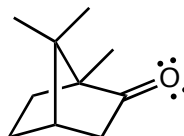
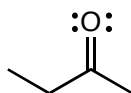
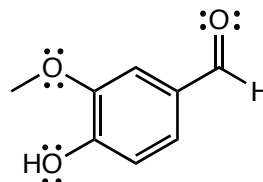
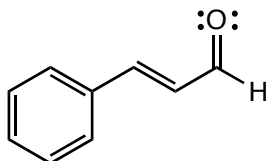
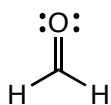
I. Introduction to aldehydes and ketones

What does an aldehyde look like? Draw an example.

What does a ketone look like? Draw an example

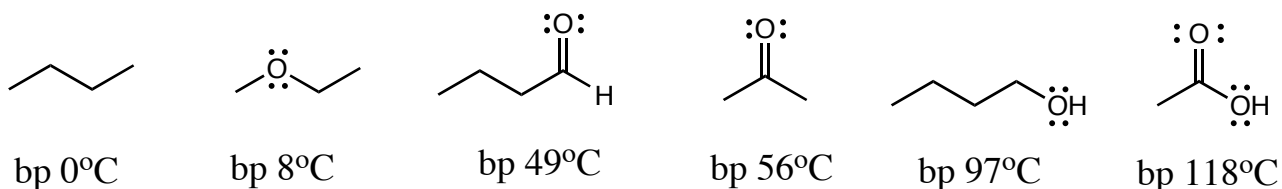
Aldehydes and ketones undergo very similar reactions, and are considered together. All other carbonyl compounds are derivatives of carboxylic acids.

Aldehydes and ketones are very common in nature, and their chemistry is critical to understanding the chemistry of biological systems. Below are some familiar aldehydes and ketones.



Properties of aldehydes and ketones

Ketones and aldehydes have melting and boiling points higher than alkanes and ethers, but lower than alcohols and carboxylic acids. Why?



Can ketones and aldehydes form hydrogen bonds with themselves?

Can they form hydrogen bonds to water?

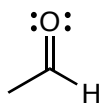
Bonding and Reactivity

What is the hybridization of the C and O in an aldehyde or ketone?

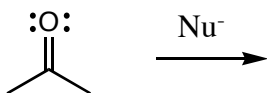
What is the geometry of the C?

Is it possible for the C=O to be a stereocenter?

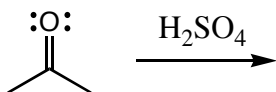
The C=O bond is quite polar. Which end is partially positive, and which is partially negative?



Where would a nucleophile attack this molecule? What would happen?



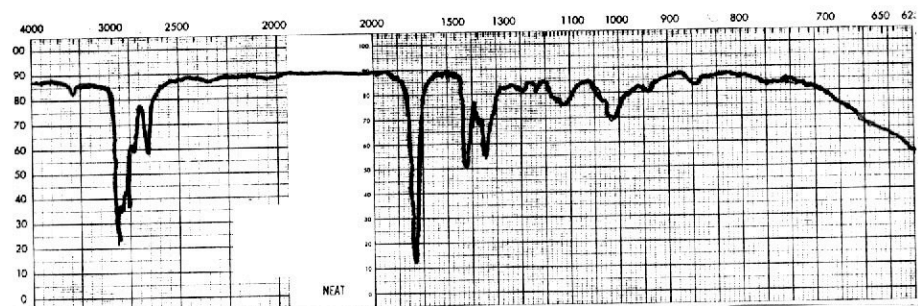
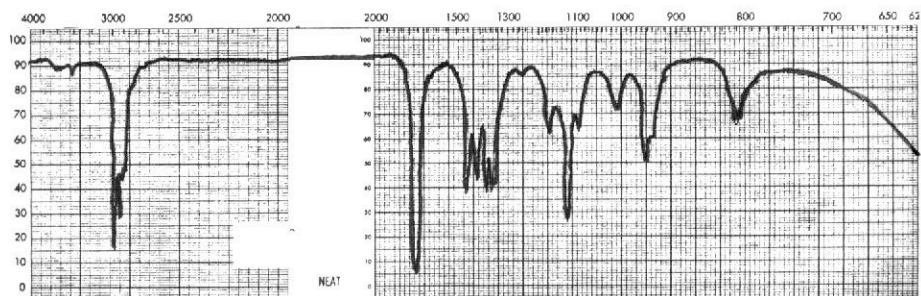
If a ketone or aldehyde reacts with a strong acid, what compound will result?
What will its reactivity be?



IR Spectroscopy

What is the characteristic band that both ketones and aldehydes have?

What additional bands do aldehydes have?



NMR Spectroscopy

Where do H's on C next to C=O appear?

Where do aldehyde H's appear?

Where do C's in C=O appear on ¹³C NMR?

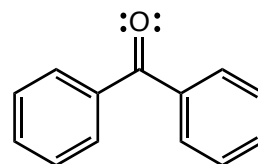
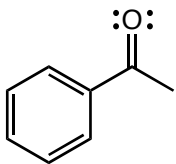
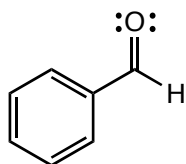
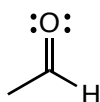
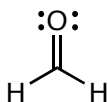
What compound could have the following spectrum?

- a - 1.0 ppm (3H t)
- b - 1.8 ppm (2H, m)
- c - 2.4 ppm (2H, t)
- d - 9.8 ppm (1H, s)

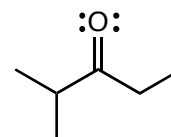
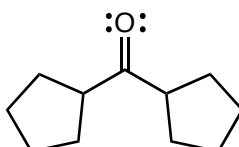
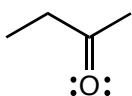
II. Nomenclature of Aldehydes and Ketones

Common names

The simplest aldehydes and ketones have common names which are used exclusively.



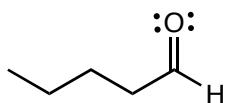
Common names for ketones may also be derived by listing the groups that are attached to the C=O, followed by the word "ketone". This is often done when the substitutive name would be inconvenient.



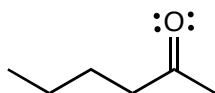
Substitutive names

Ketones and aldehydes are both principle groups. They have priority over alcohols. Aldehydes have priority over ketones.

How do you change the ending for an aldehyde?



How do you change the ending for a ketone?



Is it necessary to give the number of an aldehyde?

What about a ketone?

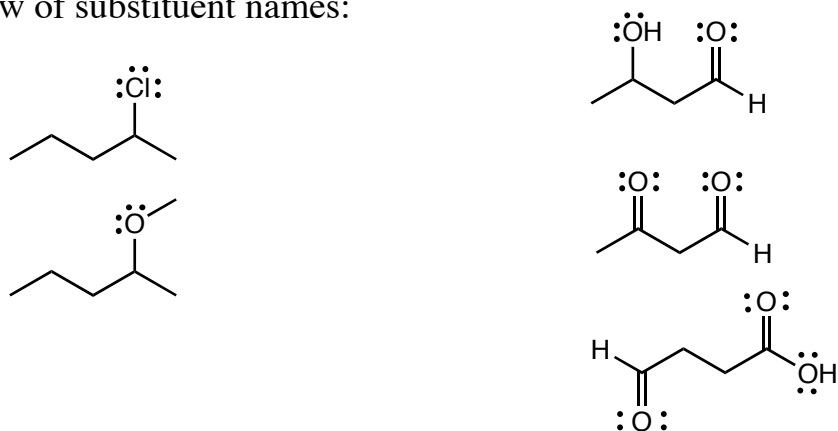
Review of suffixes:



Review of suffixes for double functional groups:

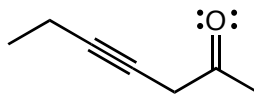
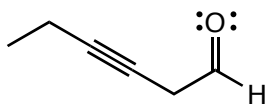
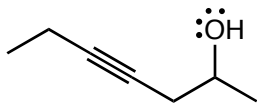


Review of substituent names:

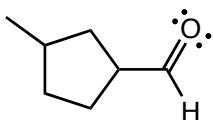


Combining multiple bonds and principle groups:

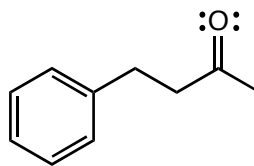
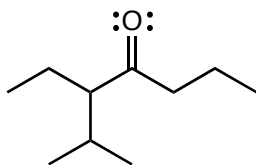
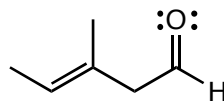
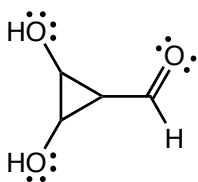
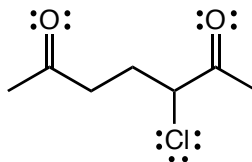
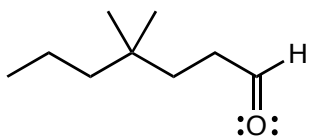




Terminal principle groups attached to cycloalkanes:



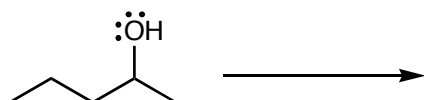
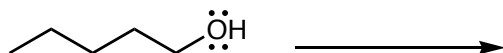
Name the following compounds.



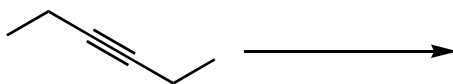
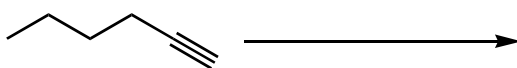
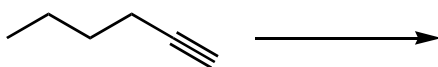
III. Synthesis of aldehydes and ketones

We have already seen the following reactions that produced aldehydes and ketones.

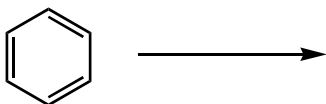
Oxidation of primary and secondary alcohols



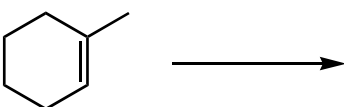
Hydration and hydroboration-oxidation of alkynes



Friedel-Crafts Acylation

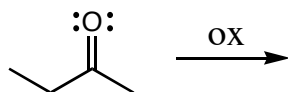
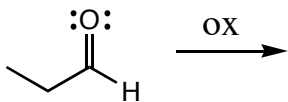


Ozonolysis

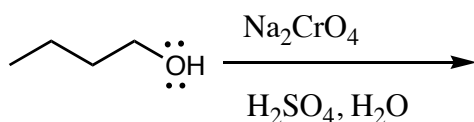
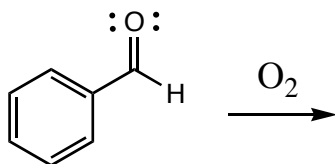


IV. Oxidations and reductions of aldehydes and ketones

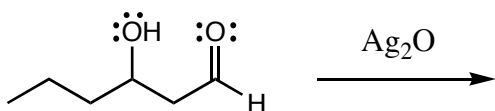
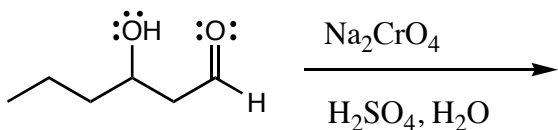
What oxidations can aldehydes and ketones undergo?



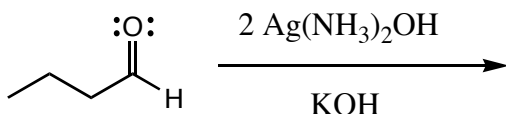
Aldehydes are very easily oxidized. Air oxidation occurs when bottles of aldehydes are left open in the lab and on TLC plates. When aldehydes are formed during the oxidation of alcohols with Jones reagent, it is impossible to stop at the aldehyde stage (this requires Collin's reagent).



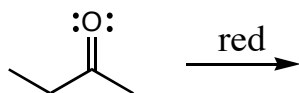
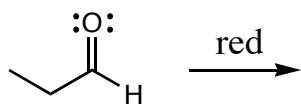
To oxidize an aldehyde on purpose, any of the reagents which make alcohols into carboxylic acids will work. However, there is also a very mild oxidizing agent - silver oxide - which only affects aldehydes and leaves other functional groups alone.



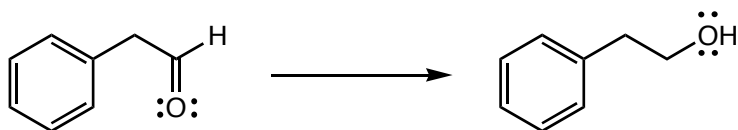
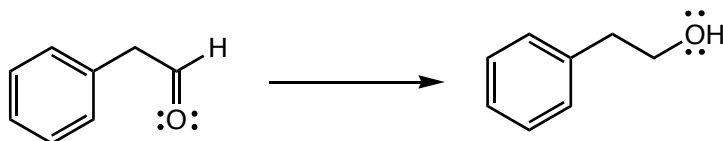
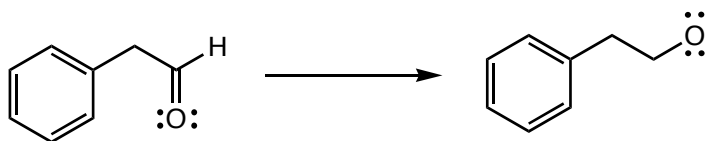
A similar reaction with Ag^+ ions is the basis of the a chemical test for aldehydes called the Tollen's test. A positive test causes silver atoms to precipitate on the inside of the test tube, forming a mirrored surface.



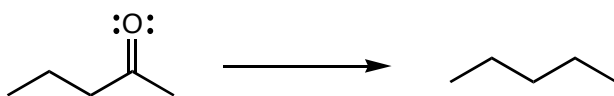
What reductions can aldehydes and ketones undergo?



What reagents are effective at reducing aldehydes and ketones to alcohols?



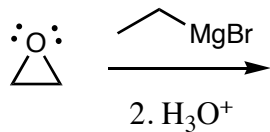
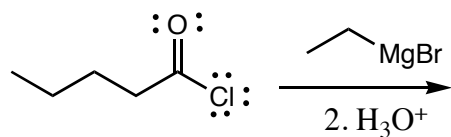
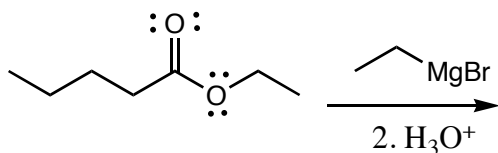
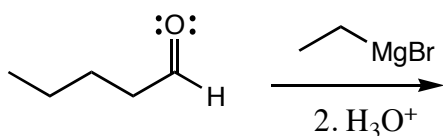
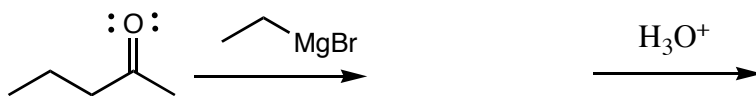
What reagents are effective at reducing aldehydes and ketones to alkanes?



V. Reactions of aldehydes and ketones with carbon nucleophiles

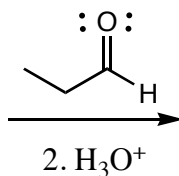
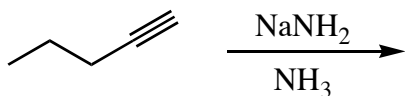
Grignards and Organolithium reagents

The primary purpose of organometallic reagents is to add a carbon group to a molecule. So far, we have seen this done with ketones, aldehydes, esters, acid chlorides, and epoxides. What kinds of products result from each?

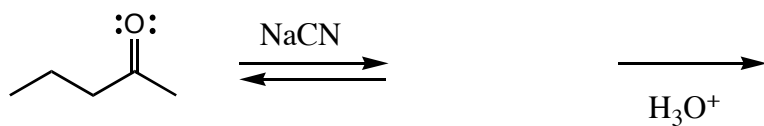


Reaction with alkyne anions and cyanide

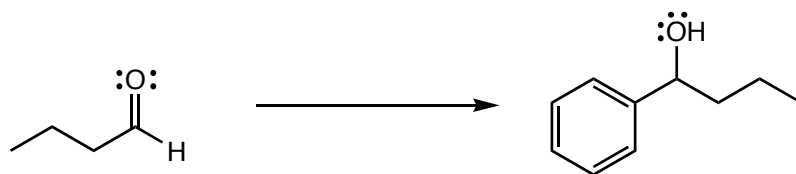
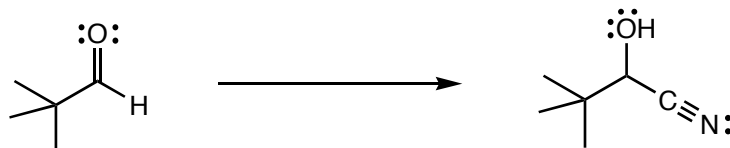
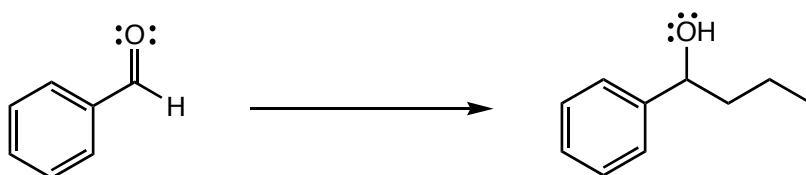
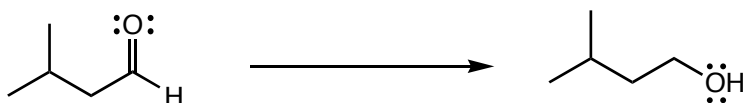
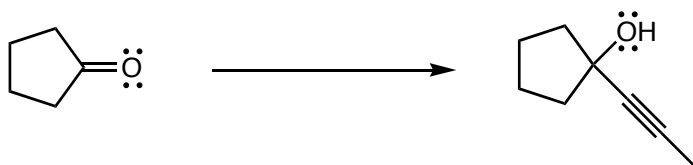
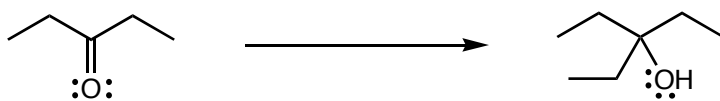
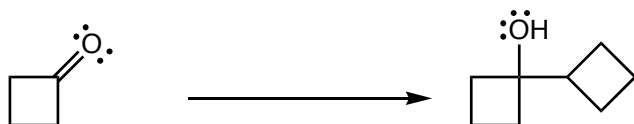
Based on the reactivity of organometallic reagents, predict the product of an acetylide anion with a ketone or aldehyde.



How would you predict that cyanide will behave?

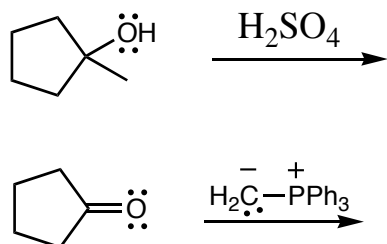


What reagents would be needed to form the following products?

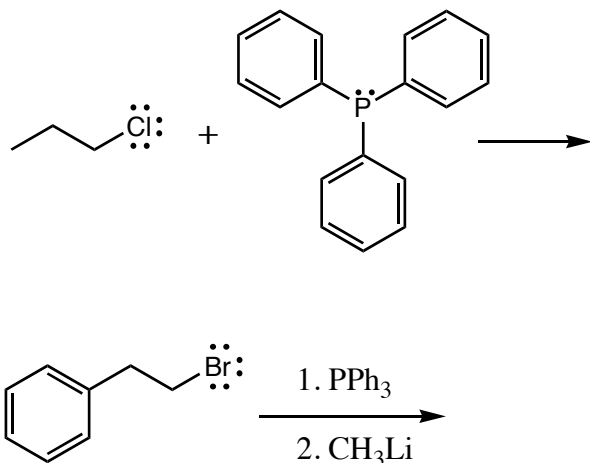


The Wittig Reaction

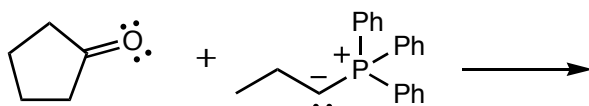
The Wittig reaction is a way to make C=C from C=O. Unlike all of the other reactions we've studied which form C=C, this one doesn't produce any regioisomers, though it may still give a mixture of stereoisomers. This is so useful that Georg Wittig received the 1979 Nobel Prize for this discovery.



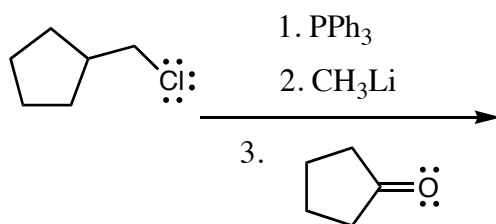
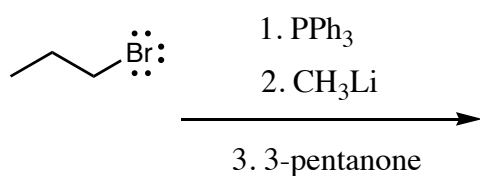
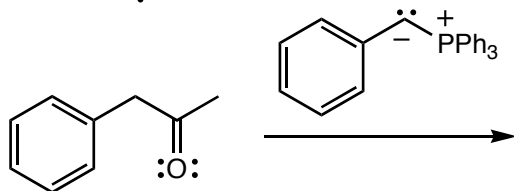
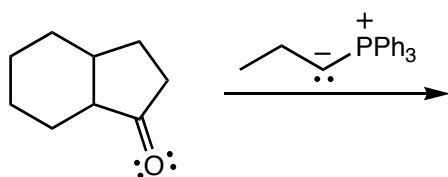
The nucleophile in this reaction is an ylide - a covalent compound which contains a positive charge next to a negative charge. It is generated by treating a primary alkyl halide with triphenylphosphine, followed by a very strong base (usually methyl lithium or butyl lithium).



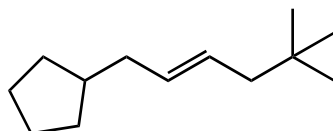
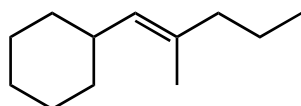
The reaction proceeds by attack of the ylide on the C=O. The negatively charged oxygen then attacks the phosphorus, forming a four-membered ring. Finally, the ring collapses to form a C=C and a P=O. The strength of the P=O bond is the driving force for the reaction.



What products will the following reactions give?



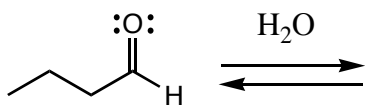
From what aldehyde or ketone and alkyl halide could the following alkenes be synthesized?



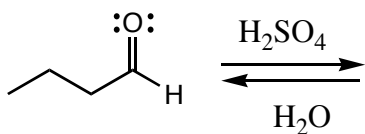
Reactions of aldehydes and ketones with oxygen nucleophiles

Formation of hydrates

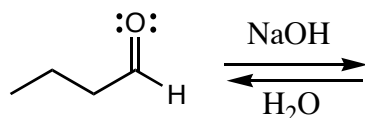
Aldehydes and ketones react with hydroxide or with water and acid to form a geminal diol, called a hydrate.



Mechanism under acidic conditions:



Mechanism under basic conditions:

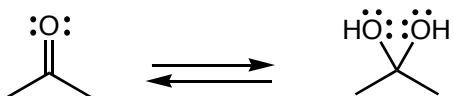
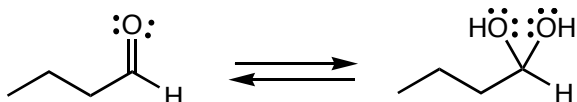
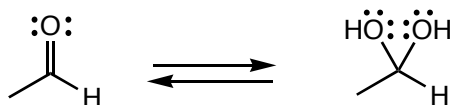
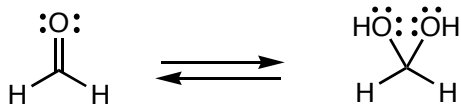


The equilibrium constant for the formation of different hydrates varies widely.

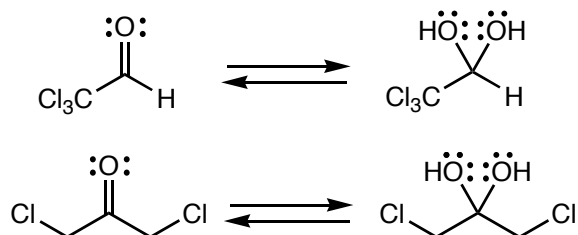
$$K = \frac{[\text{product}]}{[\text{starting material}]}$$

large K =
small K =

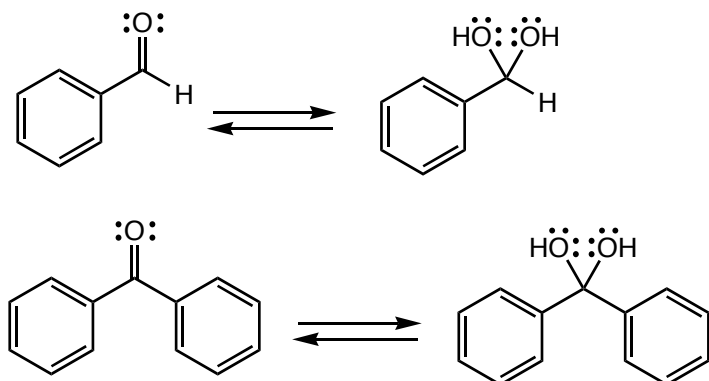
Aldehydes as a rule have more hydrate at equilibrium than ketones.



Electron-withdrawing groups close to the carbonyl increase the proportion of hydrate formed.



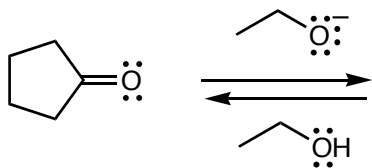
Benzene rings or C=C next to the C=O increase the proportion of the C=O form present.



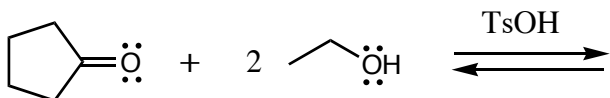
It is not unusual for aldehydes to have an IR band at 3200-3400 cm^{-1} showing that some hydrate is present.

Formation of Hemiacetals and Acetals

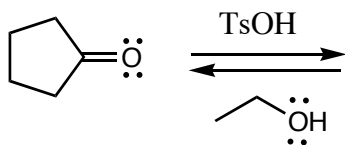
Alkoxides react reversibly with aldehydes and ketones to form hemiacetals, which are very similar to hydrates. Hemiacetals don't usually have favorable equilibrium constants, unless they are cyclic.



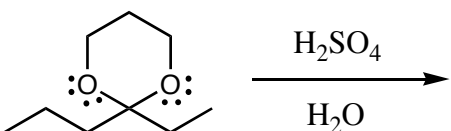
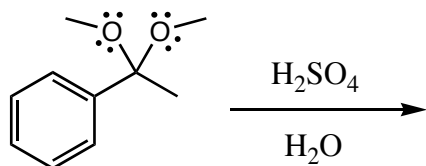
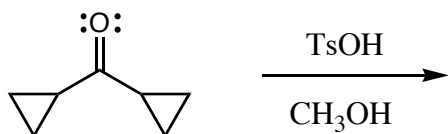
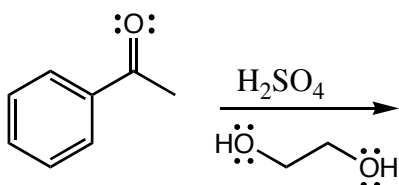
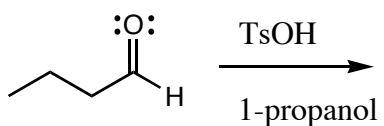
In the presence of acid, the reaction of aldehydes and ketones with alcohols goes a step further to form acetals. Tosic acid (TsOH) is often used as the acid because it is soluble in organic solvents. Equilibrium constants are around 1, so the reaction can be forced in either direction.



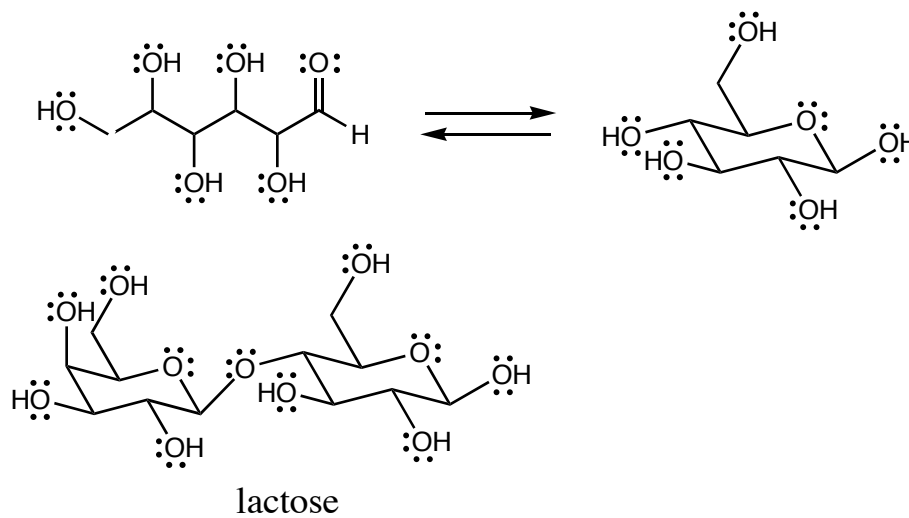
The mechanism of acetal formation involves first the formation of a hemiacetal, followed by an S_N1 substitution of the second alcohol molecule.



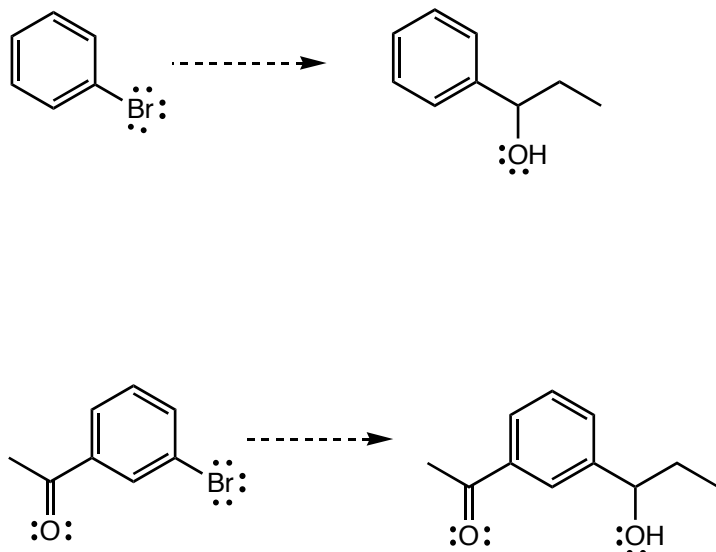
Predict the products of the following reactions:



Acetal formation is very important in sugar chemistry. Simple sugars are usually found in their cyclic form, as hemiacetals. When linkages between sugars are formed, an acetal is generated.

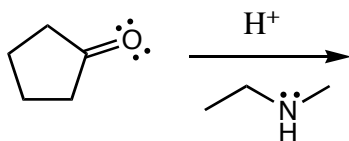
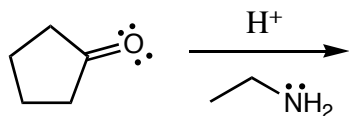


Acetals are very useful in synthesis because they turn a C=O into a group that does not react with bases or nucleophiles, but can be changed back into the C=O with mild acid and water. This reaction can also be used to protect 1,2 or 1,3 diols.

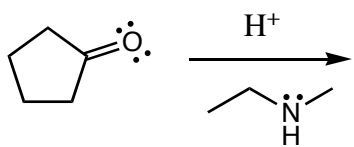
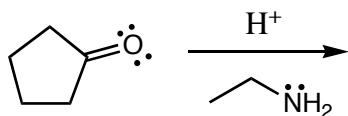


Reactions of aldehydes and ketones with nitrogen nucleophiles

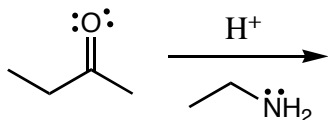
Aldehydes and ketones react with ammonia and primary amines to form imines. When they react with secondary amines, an enamine is formed. No reaction occurs with tertiary amines.

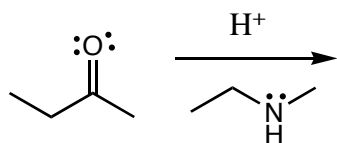


The mechanisms of these reactions closely resembles both hydration and acetal formation. The pH of the reaction is critical - acid must be present to make water into a leaving group, but the solution must not be acidic enough to protonate the amine. A pH of 4.5 is optimal.

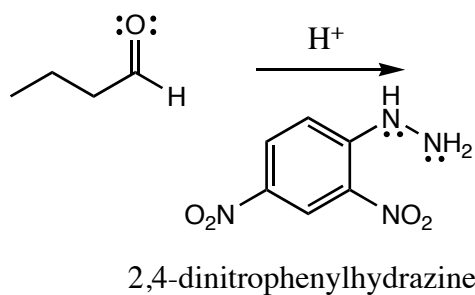
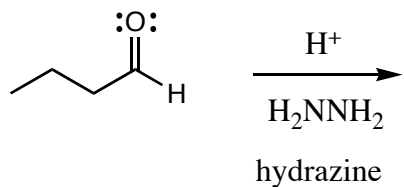
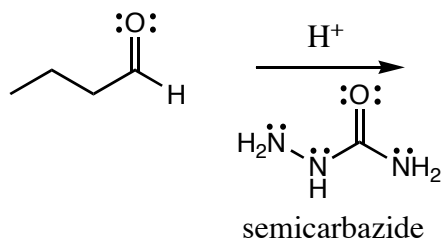
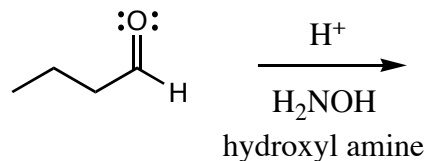


Imines may have E/Z stereoisomers. Enamines may also have constitutional isomers if there are 2 sets of beta hydrogens.



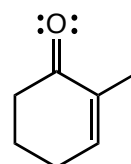
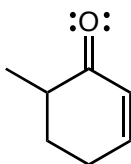


Other derivatives of ammonia are also used in this reaction.



This is an old trick from before spectroscopy to distinguish closely related compounds by the difference in the melting point of their derivative.

ketone

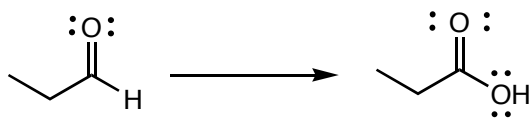


semicarbazide derivative

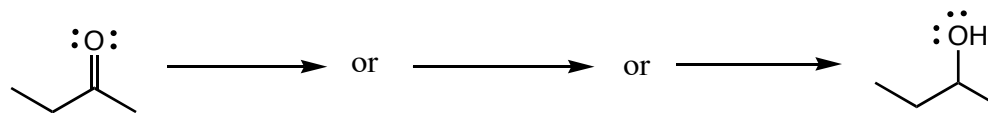
2,4-dinitrophenylhydrazone derivative

Summary of Aldehyde and Ketone Reactions

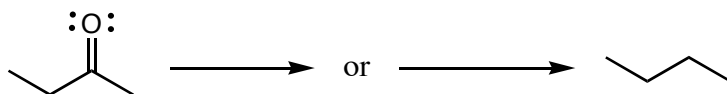
Oxidation of aldehydes:



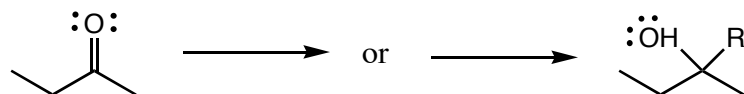
Reduction to alcohols:



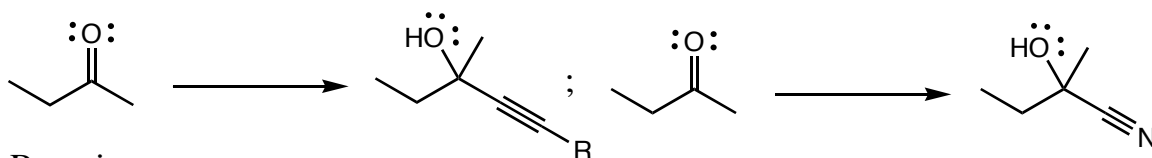
Reduction to alkanes:



Reaction with Grignards and organolithium reagents:



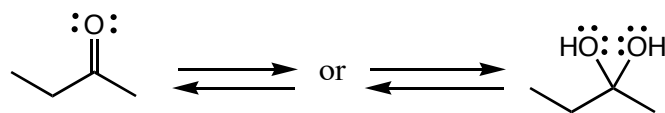
Reaction with acetylide anions or cyanide:



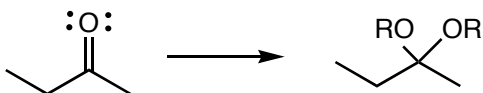
Wittig Reaction:



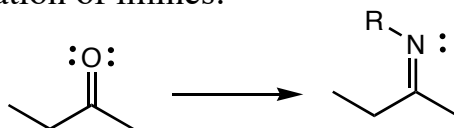
Hydration:



Formation of acetals:



Formation of imines:



Formation of enamines:

