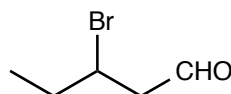
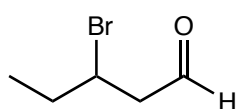
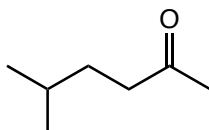
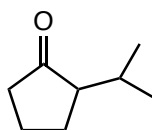
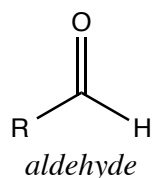
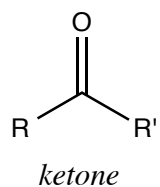


Chapter 20: Aldehydes and Ketones

[Chapter 20 Sections: 20.1-20.7, 20.9-10.10, 20.13]

Nomenclature of Aldehydes and Ketones

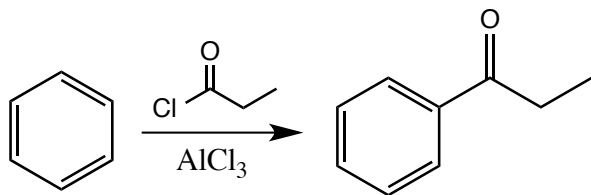


- for both aldehydes and ketones, the parent chain is the longest continuous carbon chain that contains the carbon of the carbonyl group
- numbering (locant) priority is given to the carbonyl carbon
- aldehydes always have the carbonyl group at carbon 1, so a number is not needed
- ketones have the "one" suffix, aldehydes have the "al" suffix

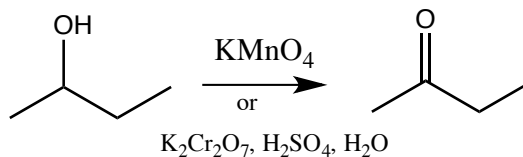
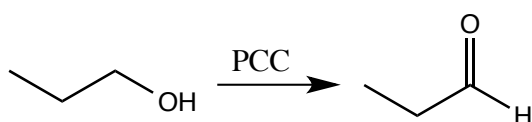
Problems: 1

Review of the Synthesis of Aldehydes and Ketones

A. Friedel-Crafts Acylation

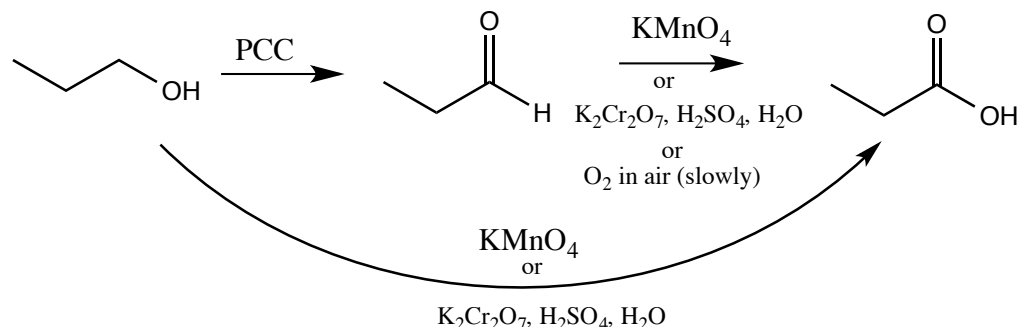


B. Oxidation of Alcohols (most common method)



Review of Reactions of Aldehydes and Ketones

A. Oxidation of Aldehydes

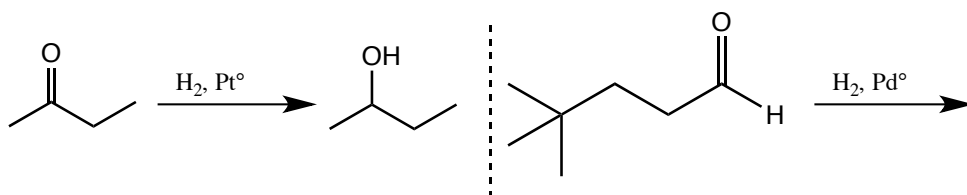


- aldehydes may be oxidized using KMnO_4 or Jones reagent to the carboxylic acid
- since aldehydes are usually synthesized via oxidation of 1° alcohols, the synthesis of carboxylic acids is usually accomplished via direct oxidation of 1° alcohols with the strong oxidizing agents
- ketones CANNOT be oxidized further

B. Reduction of Aldehydes and Ketones



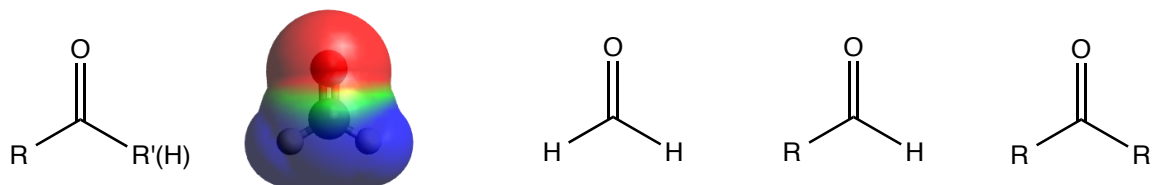
- Clemmensen or Wolff-Kishner reduction of aldehydes and ketones leads to reduction of the carbonyl group to a CH_2 group



- hydrogenation of ketones forms 2° alcohols (the opposite reaction of the oxidation process)
- hydrogenation of aldehydes forms 1° alcohols

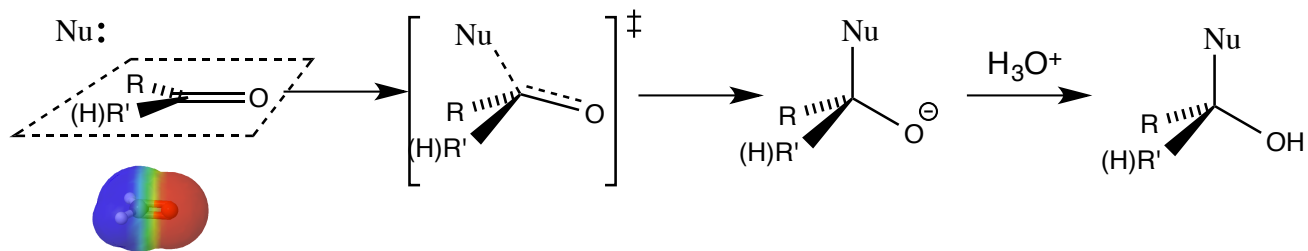
Problems: 2

General Reactivity of Aldehydes and Ketones



- both aldehydes and ketones have partial positive charge at the carbon of the carbonyl group due to the polar $\text{C}=\text{O}$ bond
- the partial charge on the aldehyde is greater since it is flanked by a single electron-donating alkyl group
- while both aldehydes and ketones are reactive towards nucleophilic addition, aldehydes are more reactive due to i) the greater partial positive charge and ii) less steric interference

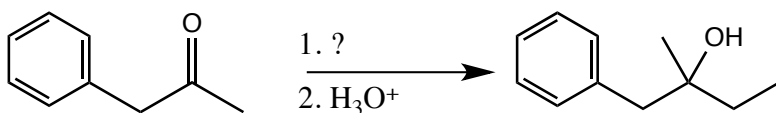
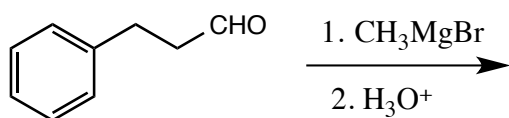
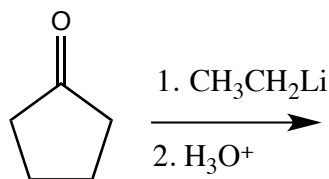
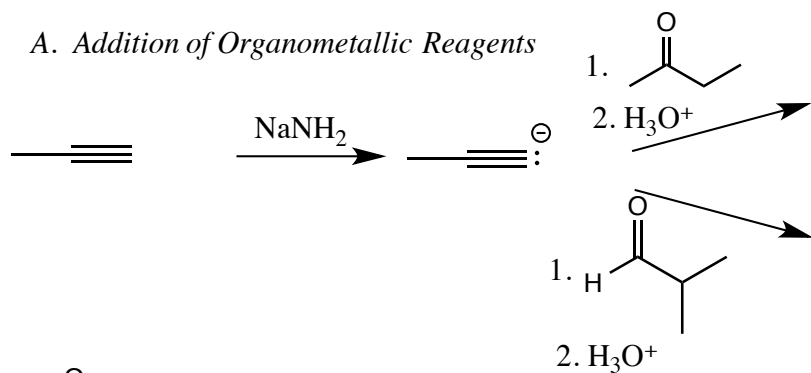
Mode of Attack of Strong Nucleophiles on the Carbonyl Group of Aldehydes and Ketones



- nucleophiles attack the partially positively charged carbon of the carbonyl group by pushing electrons into the polarized pi bond
- the pi electrons are forced onto the electronegative oxygen atom
- these reactions are often followed up by addition of acidic water (HCl , H_2O or H_3O^+) to protonate the negatively charged oxygen and form a neutral product

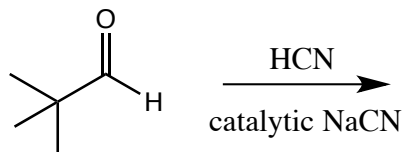
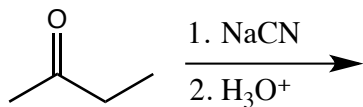
Addition of Strong Nucleophiles to Aldehydes and Ketones

A. Addition of Organometallic Reagents



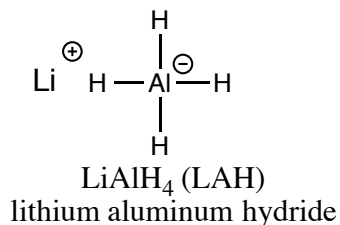
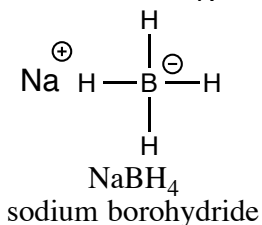
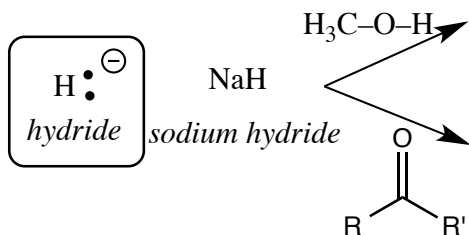
- these types of nucleophilic additions to aldehydes and ketones are critical reactions since they result in the formation of NEW C-C bonds!
- these reactions, therefore, provide a way in which to create larger molecules from readily available smaller molecules

B. Addition of HCN



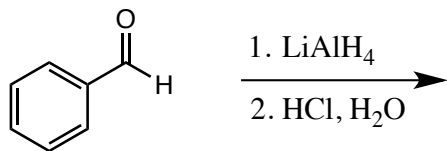
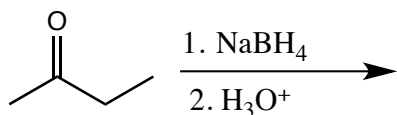
- there are two methods for addition of HCN to a carbonyl group. The net result is the same
- the product of addition is referred to as a "cyanohydrin" to reflect the presence of both the cyanide AND hydroxyl groups
- as with the organometallics, this reaction forms a new C-C bond

C. Addition of Hydride (hydride reduction)



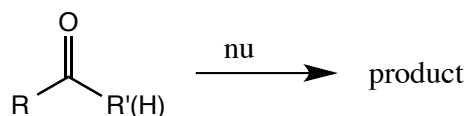
- a "hydride" is a hydrogen with an extra electron, giving it a negative charge
- sodium hydride is the simplest form of hydride, but in this form it acts only as a strong base and **never** as a nucleophile
- NaBH_4 and LiAlH_4 are both sources of nucleophilic hydride

Examples



- reduction of aldehydes with either NaBH_4 OR LiAlH_4 results in the formation of 1° alcohols
- reduction of ketones with either NaBH_4 OR LiAlH_4 results in the formation of 2° alcohols

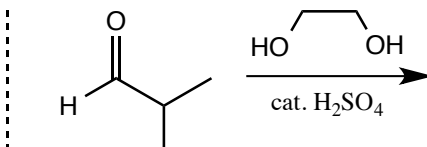
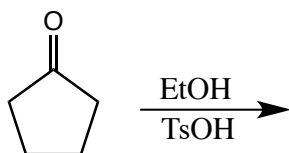
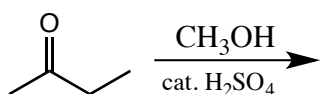
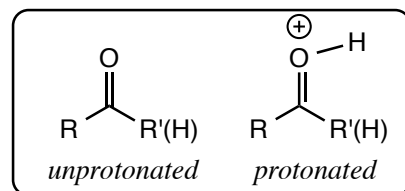
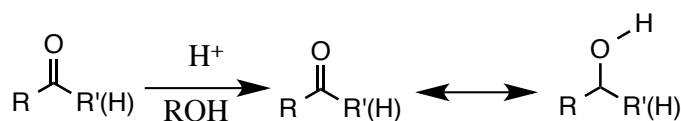
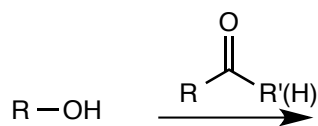
Summary of Nucleophilic Addition Reactions of Aldehydes and Ketones



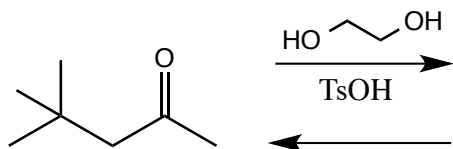
nucleophile	catalyst	type of product	
H^- (hydride, NaBH_4 or LiAlH_4)	none	alcohol (1° from aldehyde, 2° from ketone)	$\text{R}-\overset{\text{H}}{\underset{\text{OH}}{\text{C}}}-\text{R}'(\text{H})$
R^- (Grignard, alkyllithium)	none	alcohol (2° from aldehyde, 3° from ketone)	$\text{R}-\overset{\text{R}}{\underset{\text{OH}}{\text{C}}}-\text{R}'(\text{H})$
$\ominus\text{C}\equiv\text{N}$ (cyanide)	none	cyanohydrin	$\text{R}-\overset{\text{NC}}{\underset{\text{OH}}{\text{C}}}-\text{R}'(\text{H})$

D. Addition of Alcohols

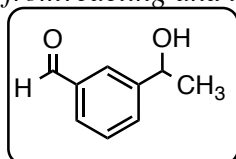
- alkoxides are strong nucleophiles but alcohols are poor nucleophiles
- alcohols will not react with aldehydes or ketones in the absence of an acid catalyst
- an acid catalyst protonates a lone pair of the oxygen atom of the carbonyl group
- protonation increases the partial positive charge on the carbon and enhances the reactivity of the carbonyl towards nucleophilic addition
- under acidic conditions, aldehydes and ketones will react with the weaker alcohol nucleophile
- the most common acid catalysts are H_3PO_4 , H_2SO_4 , HCl or para-toluenesulfonic acid (TsOH)



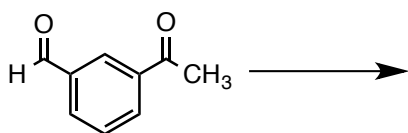
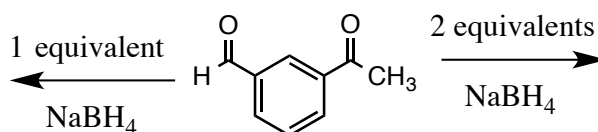
- reaction of aldehydes or ketones with alcohols under acid catalysis results in the addition of TWO equivalents of the alcohol to the carbonyl group. The product is called a "ketal" from a ketone and an "acetal" from an aldehyde
- if a diol such as ethylene glycol is used, both ends of the diol add across the carbonyl group to form a cyclic ketal
- cyclic ketals are the most often utilized type of ketal



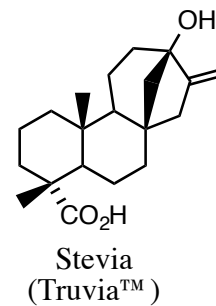
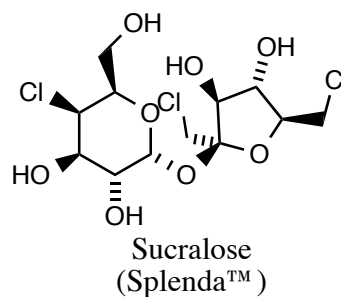
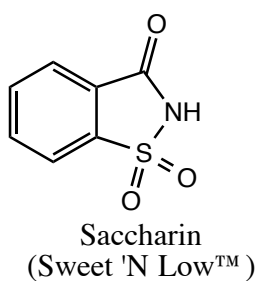
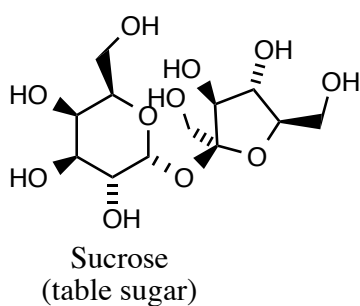
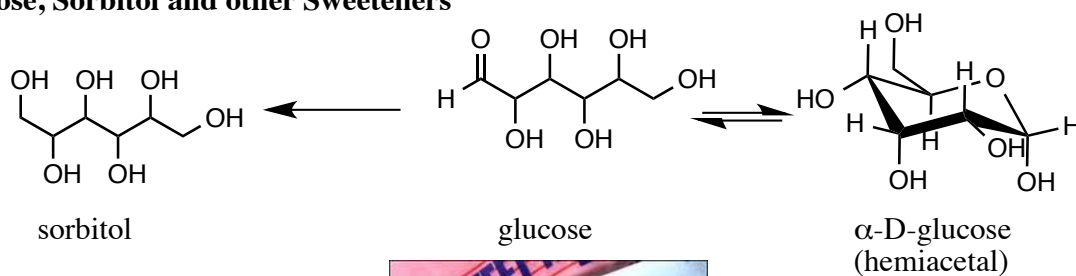
- ketals are "ether-like" compounds that behave like ethers, i.e., they are fairly unreactive
- the ketal formation process can be reversed by addition of water under acidic conditions
- ketals act as carbonyl "protecting groups" in that they can be placed on a carbonyl group to keep it from reacting and then removed when desired



target molecule



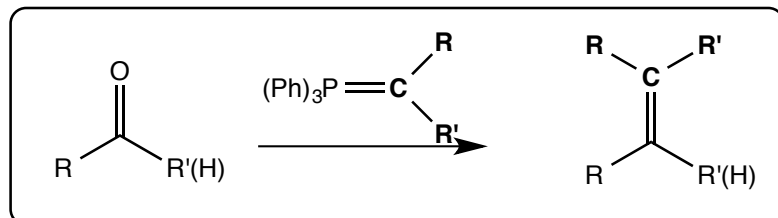
Glucose, Sorbitol and other Sweeteners



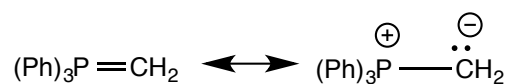
Addition/Elimination Reactions of Aldehydes and Ketones

A. The Wittig Reaction

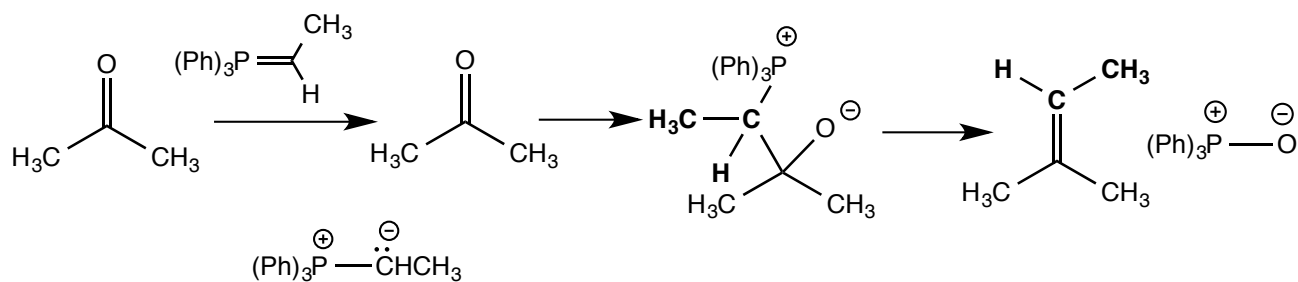
Overall Reaction:



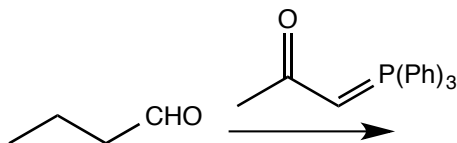
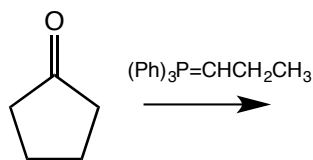
- the Wittig reaction takes place between an aldehyde or a ketone and a Wittig reagent
- the final product is replacement of the C=O double bond by a C=C double bond



Reaction Steps

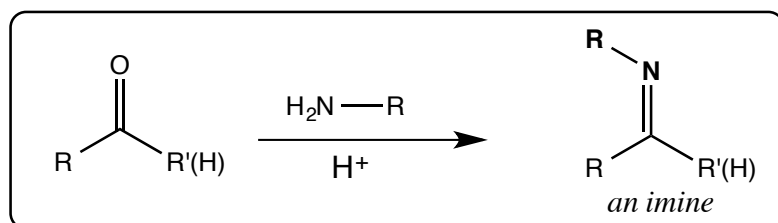


Examples



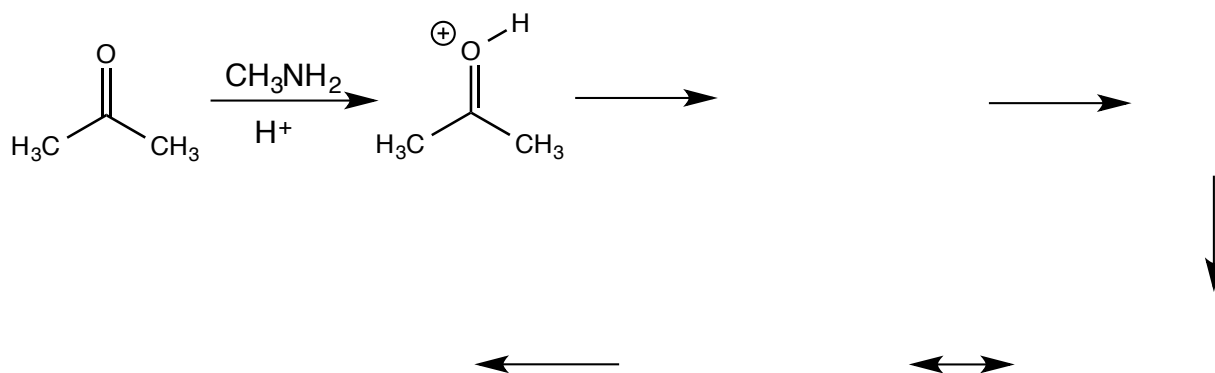
B. Imine Formation

Overall Reaction:

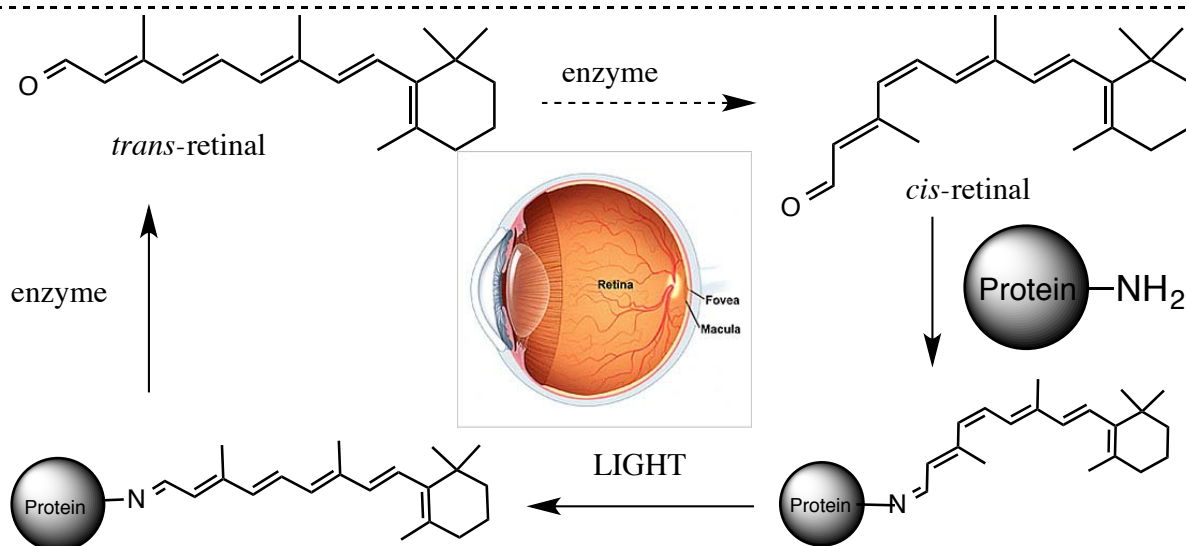
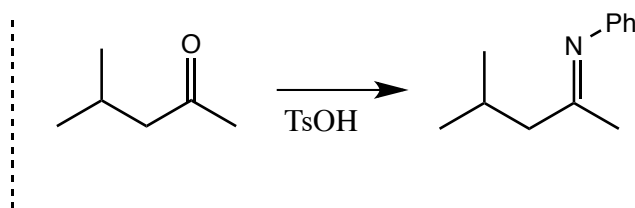
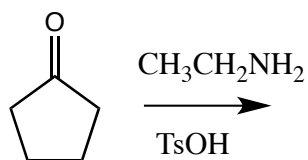


- when a 1° amine reacts with a ketone or aldehyde, an imine product results
- an acid catalyst [usually TsOH or HCl] is often needed
- the final product is replacement of the C=O double bond by a C=N double bond

Reaction Steps

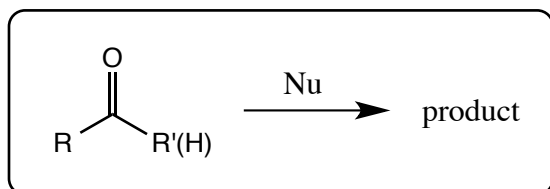


Examples



Problems: 4-6

Summary of Nucleophilic Addition Reactions of Aldehydes and Ketones



nucleophile	catalyst	type of product	
<i>single addition reactions</i>			
H^- (hydride, NaBH_4 or LiAlH_4)	none	alcohol (1° from aldehyde, 2° from ketone)	$\begin{array}{c} \text{H} \quad \text{OH} \\ \diagdown \quad / \\ \text{R}-\text{C}-\text{R}'(\text{H}) \end{array}$
R^- (Grignard, alkyllithium)	none	alcohol (2° from aldehyde, 3° from ketone)	$\begin{array}{c} \text{R} \quad \text{OH} \\ \diagdown \quad / \\ \text{R}-\text{C}-\text{R}'(\text{H}) \end{array}$
$\ominus \text{C} \equiv \text{N}$ (cyanide)	none	cyanohydrin	$\begin{array}{c} \text{NC} \quad \text{OH} \\ \diagdown \quad / \\ \text{R}-\text{C}-\text{R}'(\text{H}) \end{array}$

<i>double addition reactions</i>			
ROH (alcohols)	H^+	acetal	$\begin{array}{c} \text{RO} \quad \text{OR} \\ \diagdown \quad / \\ \text{R}-\text{C}-\text{R}'(\text{H}) \end{array}$

<i>addition-elimination reactions</i>			
$(\text{Ph})_3\text{P}=\text{CR}_2$ (Wittig reagents)	none	alkene	$\begin{array}{c} \text{R} \quad \text{R} \\ \diagdown \quad / \\ \text{C} \\ \parallel \\ \text{R}-\text{C}-\text{R}'(\text{H}) \end{array}$
$\text{R}-\text{NH}_2$ (1° amine)	H^+ sometimes	imine	$\begin{array}{c} \text{N}-\text{R} \\ \parallel \\ \text{R}-\text{C}-\text{R}'(\text{H}) \end{array}$

Chapter 20 *Essential Concepts*

1. Know how to name cyclic and acyclic ketones and aldehydes.
2. Know the common ways (and reagents required) for the synthesis of aldehydes and ketones.
3. Understand, and be able to apply, the theory regarding relative reactivities of aldehydes and ketones with regards to electronic and steric considerations.
4. Know the common reactions of aldehydes and ketones discussed in the notes, the reagents necessary to carry out these reactions, and the nature of the products formed.
5. Understand how acetal and ketal protecting groups can be applied to affect reactivity.
6. Know how “serendipity” played a large role in the development of artificial sweeteners and the dietetic difference between sucrose and the artificial sweeteners.