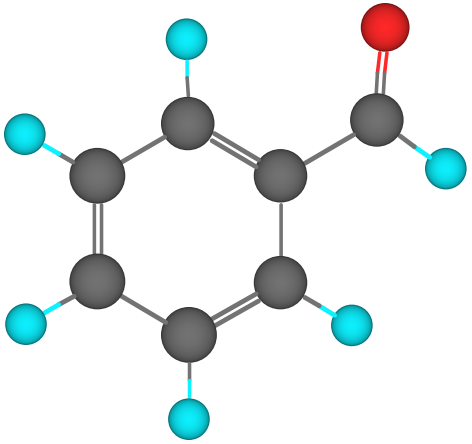
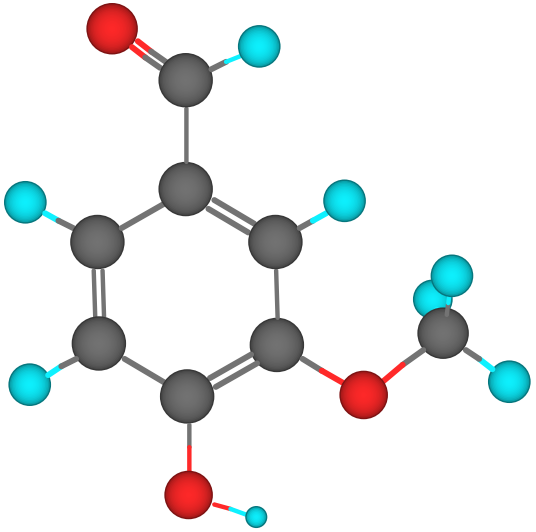


Chapter 13
Aldehydes and Ketones



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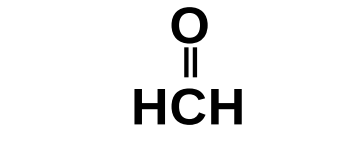
The Carbonyl Group

- **In this and several following chapters, we study the physical and chemical properties of classes of compounds containing the carbonyl group, C=O**
  - **aldehydes and ketones (Chapter 13)**
  - **carboxylic acids (Chapter 14)**
  - **acid halides, acid anhydrides, esters, amides (Chapter 15)**
  - **enolate anions (Chapter 16)**

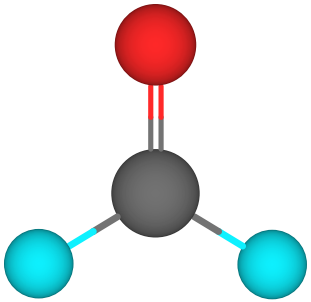
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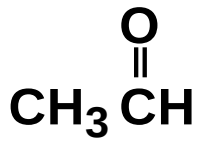
Structure

- the functional group of an aldehyde is a carbonyl group bonded to a H atom
- the functional group of a ketone is a carbonyl group bonded to two carbon atoms

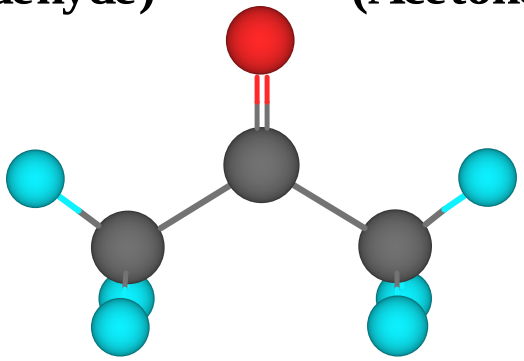


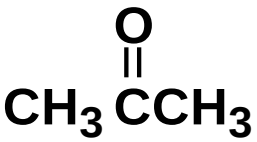
Methanal
(Formaldehyde)





Ethanal
(Acetaldehyde)





Propanone
(Acetone)

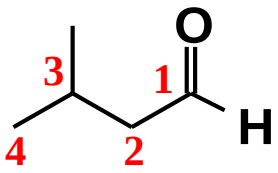
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Nomenclature

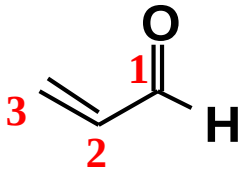
- **IUPAC names:**
  - **the parent chain is the longest chain that contains the carbonyl group**
  - **for an aldehyde, change the suffix from -e to -al**
  - **for an unsaturated aldehyde, show the carbon-carbon double bond by changing the infix from -an- to -en-; the location of the suffix determines the numbering pattern**
  - **for a cyclic molecule in which -CHO is bonded to the ring, add the suffix -carbaldehyde**

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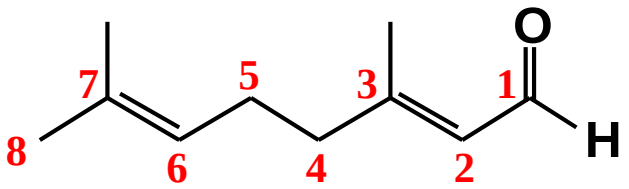
Nomenclature



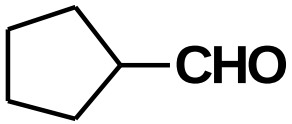
3-Methylbutanal



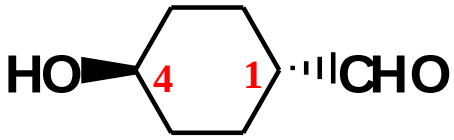
2-Propenal
(Acrolein)



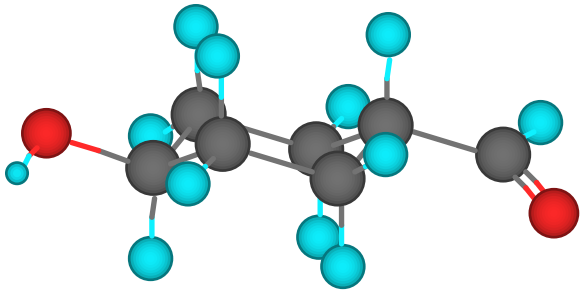
(2*E*)-3,7-Dimethyl-2,6-octadienal
(Geranial)

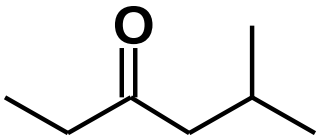


Cyclopentane-
carbaldehyde

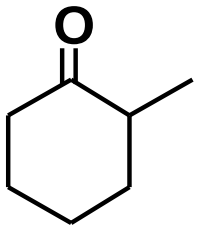


trans-4-Hydroxycyclo-
hexanecarbaldehyde

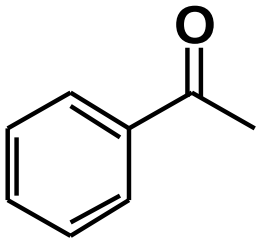




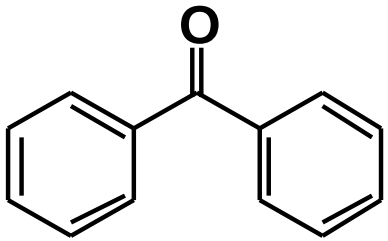
5-Methyl-3-
hexanone



2-Methyl-
cyclohexanone



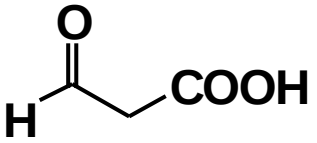
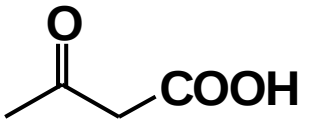
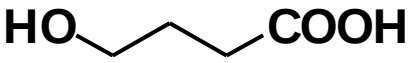
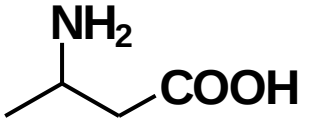
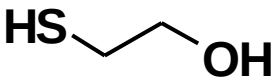
Acetophenone



Benzophenone

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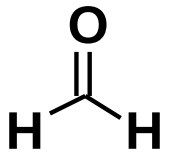
Nomenclature

Functional Group	Suffix	Prefix	Example of When the Functional Group Has a Lower Priority	
Carboxyl	-oic acid	——		
Aldehyde	-al	oxo-	3-Oxopropanoic acid	
Ketone	-one	oxo-	3-Oxobutanoic acid	
Alcohol	-ol	hydroxy-	4-Hydroxybutanoic acid	
Amino	-amine	amino-	3-Aminobutanoic acid	
Sulfhydryl	-thiol	mercapto-	2-Mercaptoethanol	

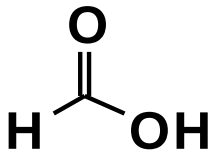
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Nomenclature

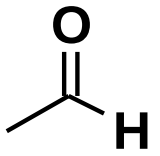
- **Common names**
  - **for an aldehyde, the common name is derived from the common name of the corresponding carboxylic acid**
  - **for a ketone, name the two alkyl or aryl groups bonded to the carbonyl carbon and add the word ketone**



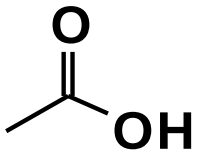
Formaldehyde



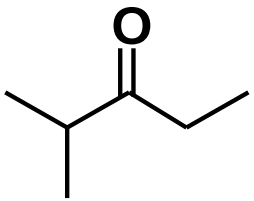
Formic acid



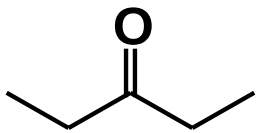
Acetaldehyde



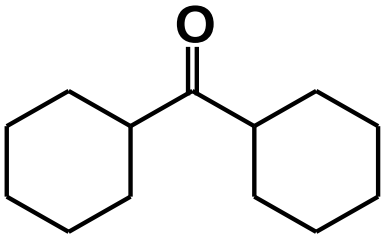
Acetic acid



Ethyl isopropyl ketone



Diethyl ketone

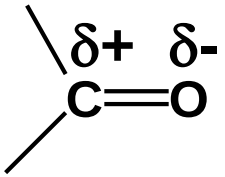


Dicyclohexyl ketone

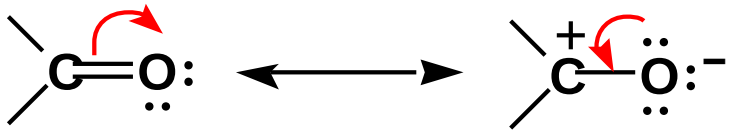
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Physical Properties

- **Oxygen is more electronegative than carbon (3.5 vs 2.5) and, therefore, a C=O group is polar**



Polarity of a carbonyl group



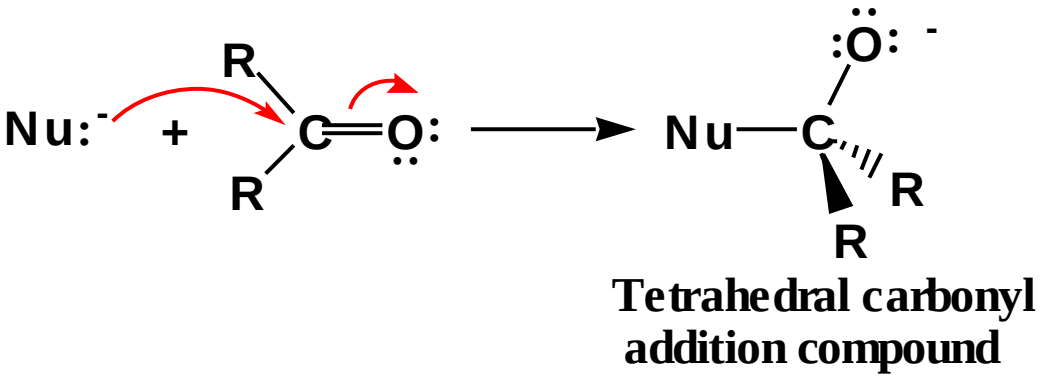
More important contributing structure

  - **aldehydes and ketones are polar compounds and interact in the pure state by dipole-dipole interactions**
  - **they have higher boiling points and are more soluble in water than nonpolar compounds of comparable molecular weight**

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Reactions

- **The most common reaction theme of a carbonyl group is addition of a nucleophile to form a tetrahedral carbonyl addition compound**



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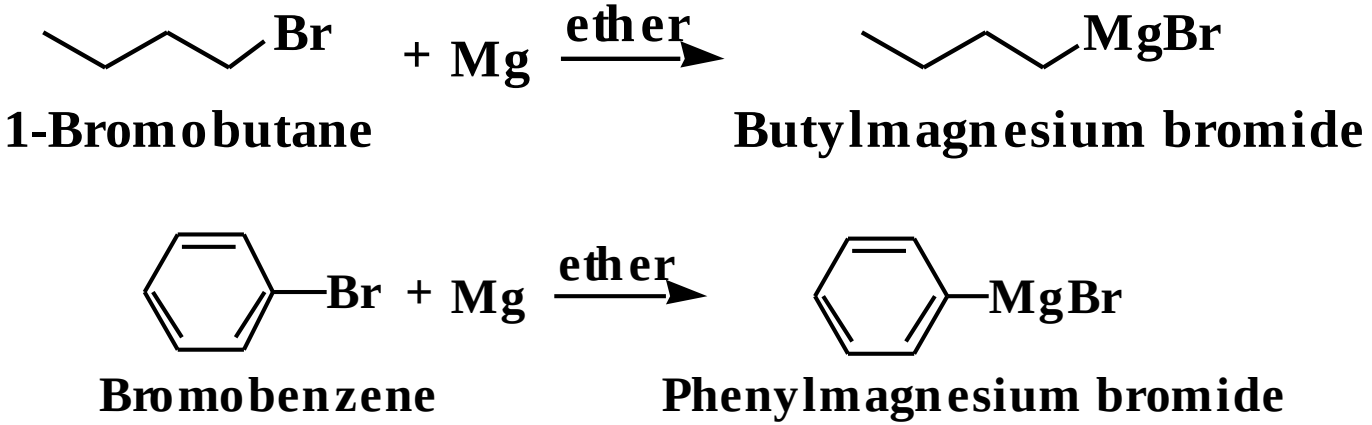
Grignard Reagents

- **Addition of carbon nucleophiles is one of the most important types of nucleophilic additions to a C=O group**
  - **a new carbon-carbon bond is formed in the process**
- **We study addition of carbon nucleophiles called Grignard reagents**
  - **Victor Grignard was awarded the Nobel Prize for chemistry in 1912 for their discovery and application to organic synthesis**
  - **Grignard reagents have the general formula RMgX, where R is an alkl or aryl group and X is a halogen**

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Grignard Reagents

- **Grignard reagents are prepared by adding an alkyl or aryl halide to a suspension of Mg metal in diethyl ether**



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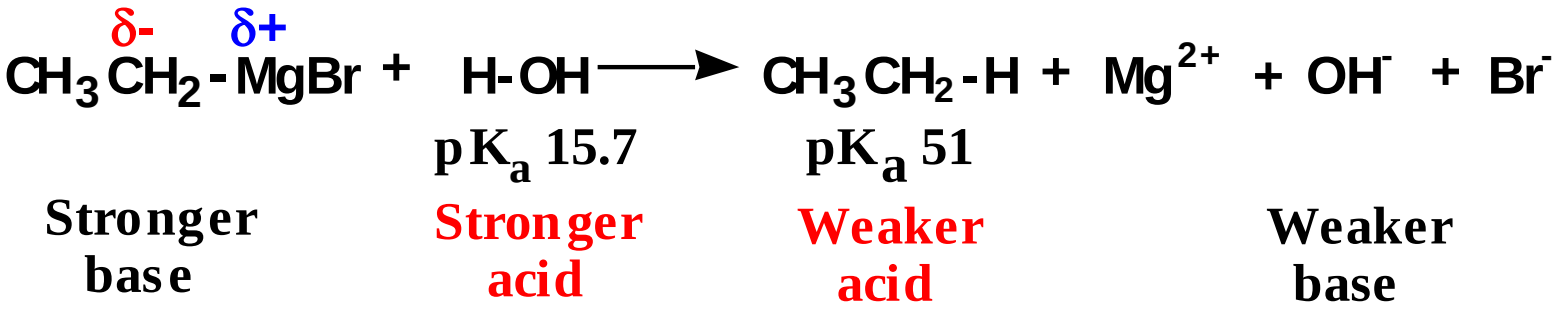
Grignard Reagents

- **Given the difference in electronegativity between carbon and magnesium (2.5 - 1.3), the C-Mg bond is polar covalent, with Cδ- and Mgδ+**
  - **in its reactions, a Grignard reagent behaves as a carbanion**
- **Carbanion: an anion in which carbon has an unshared pair of electrons and bears a negative charge**
  - **a carbanion is a good nucleophile and adds to the carbonyl group of aldehydes and ketones**

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Grignard Reagents

- **Reaction with protic acids**
  - **Grignard reagents are very strong bases and react with proton acids to form alkanes**



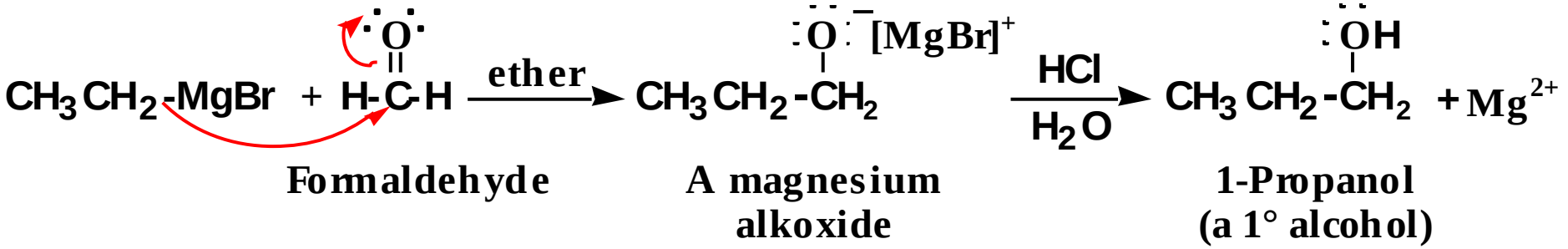
  - **any compound containing an O-H, N-H, or S-H group reacts with a Grignard reagent by proton transfer**

HOH	ROH	ArOH	RCOOH	RNH_2	RSH
Water	Alcohols	Phenols	Carboxylic acids	Amines	Thiols

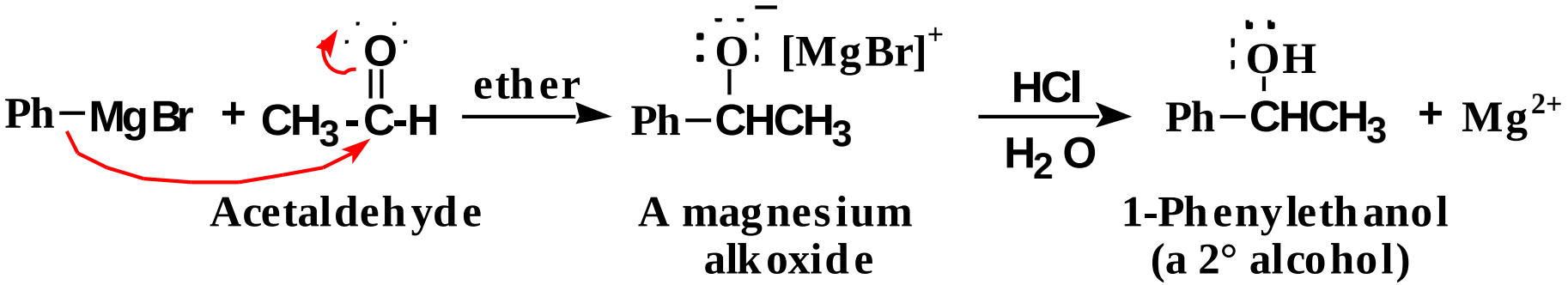
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Grignard Reagents

- **reaction with formaldehyde gives a 1° alcohol**



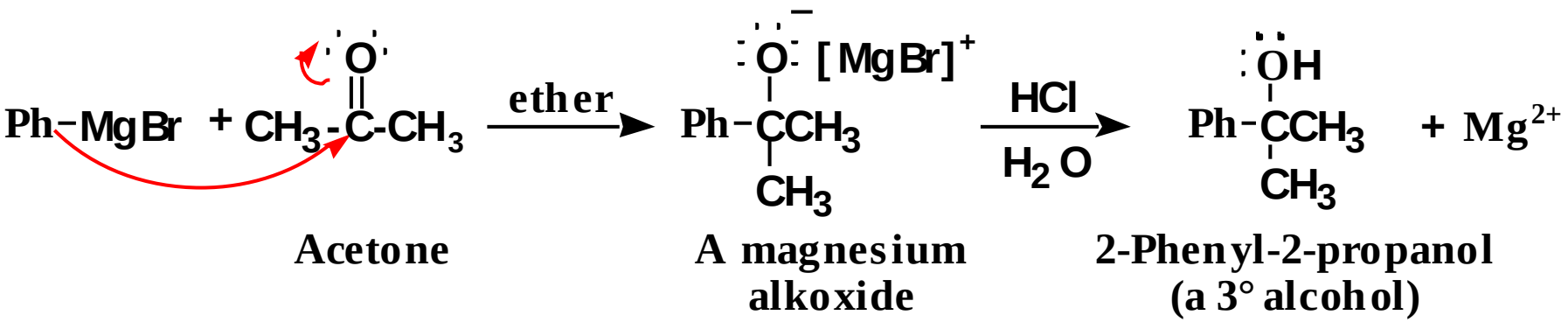
- **reaction with any aldehyde other than formaldehyde gives a 2° alcohol**



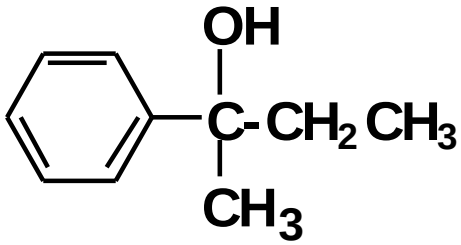
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Grignard Reagents

- reaction with a ketone gives a 3° alcohol



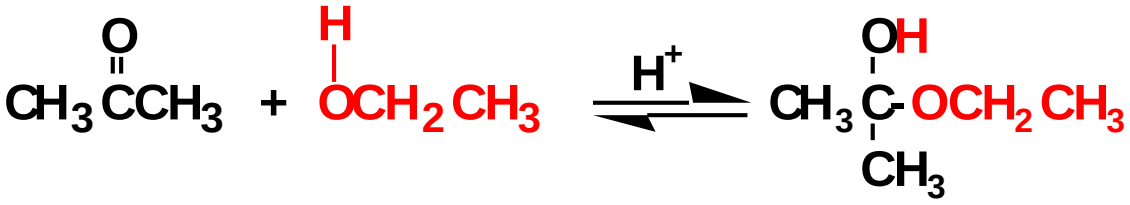
- problem: show how to synthesize this 3° alcohol by three different routes



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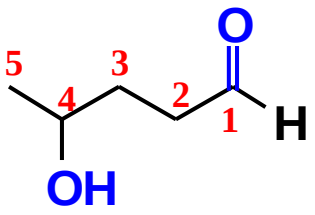
Addition of Alcohols

- **Hemiacetal: a molecule containing an -OH group and an -OR group bonded to the same carbon**



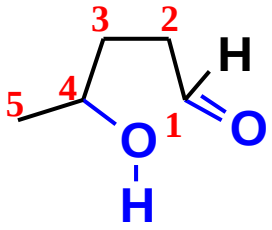
A hemiacetal

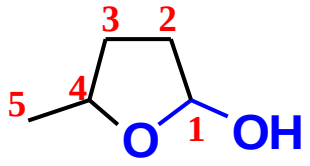
- **hemiacetals are minor components of an equilibrium mixture except where a 5- or 6-membered ring can form**



4-Hydroxypentanal

redraw to show the OH close to the CHO group



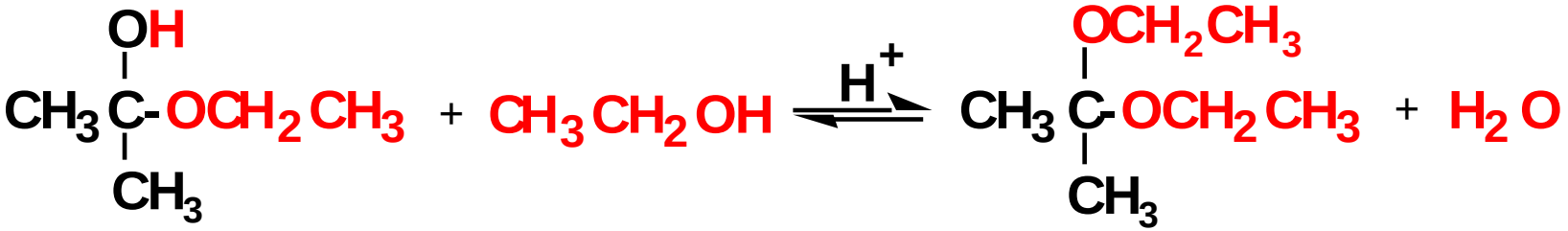


A cyclic hemiacetal (major form present at equilibrium)

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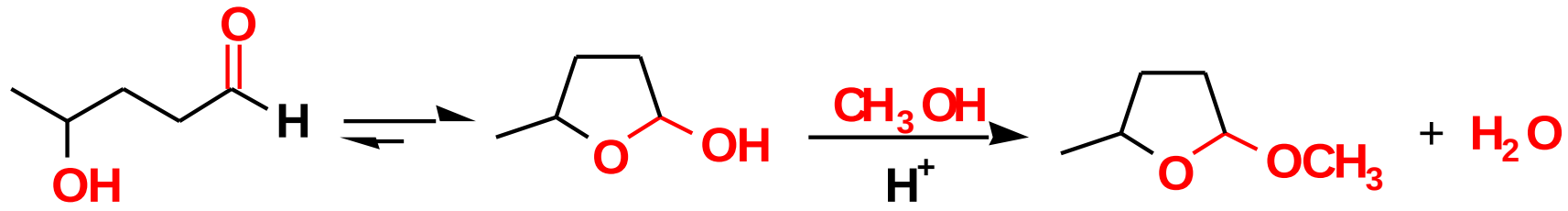
Addition of Alcohols

- **Acetal: a molecule containing two -OR groups bonded to the same carbon**



A hemiacetal

A diethyl acetal



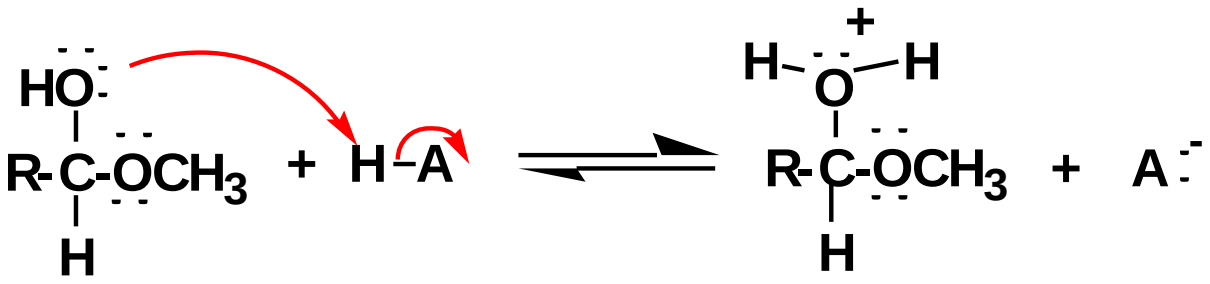
4-Hydroxypentanal

A cyclic acetal

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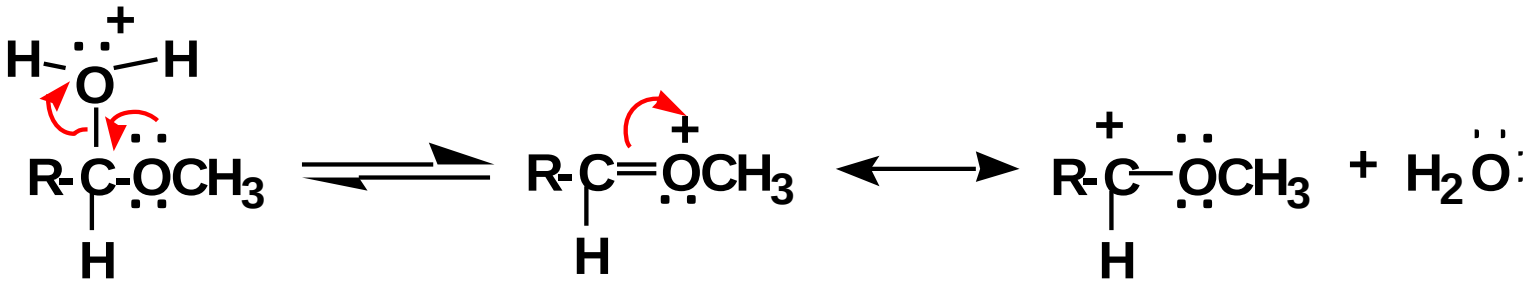
Acetal Formation

1. Proton transfer from HA to the hemiacetal oxygen



An oxonium ion

2. Loss of H_2O gives a cation

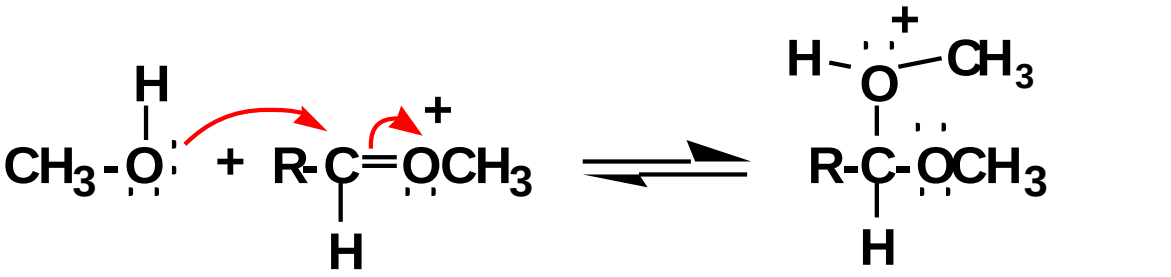


A resonance-stabilized cation

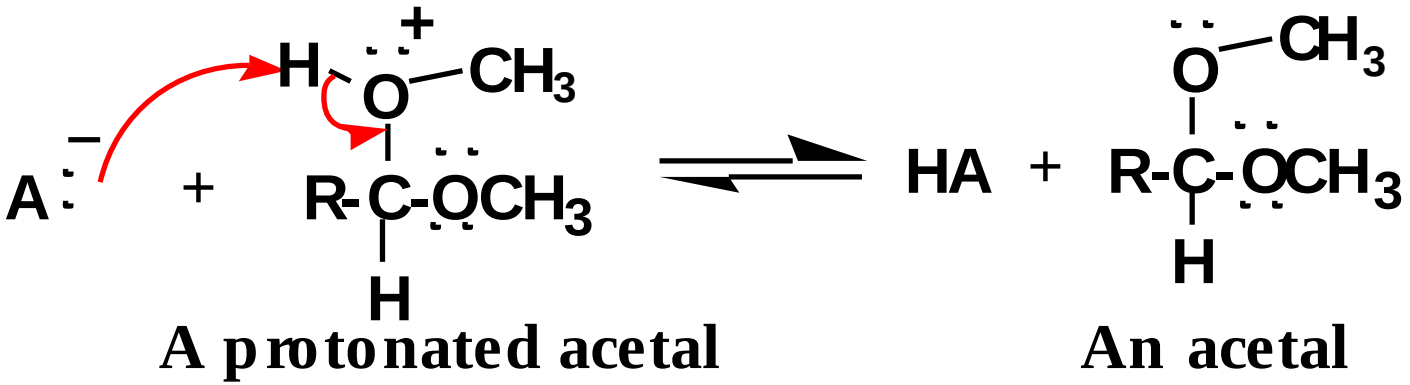
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Acetal Formation

3. reaction of the cation (an electrophile) with an alcohol (a nucleophile)



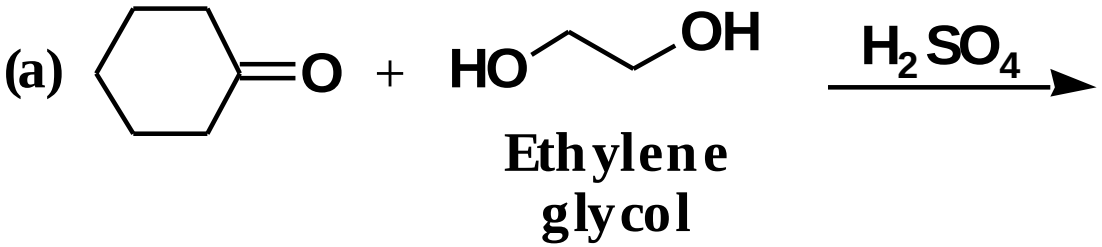
4. proton transfer to A^- gives the acetal and regenerates the acid catalyst

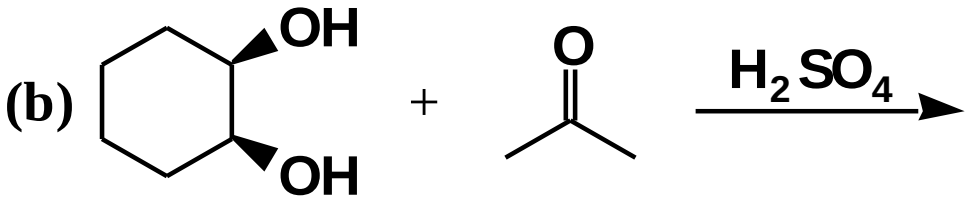


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Acetals

- **Draw a structural formula for the acetal formed in each reaction**

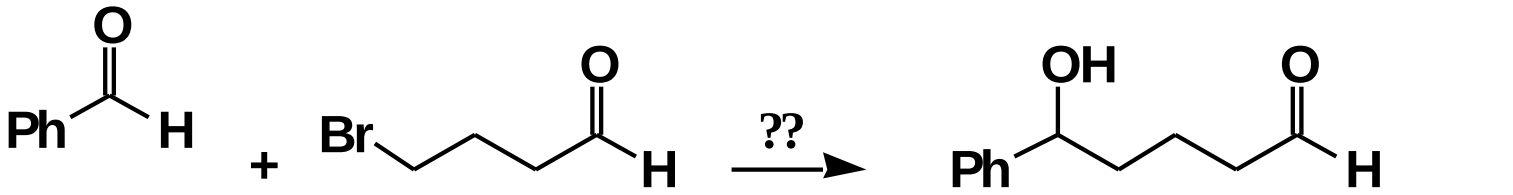




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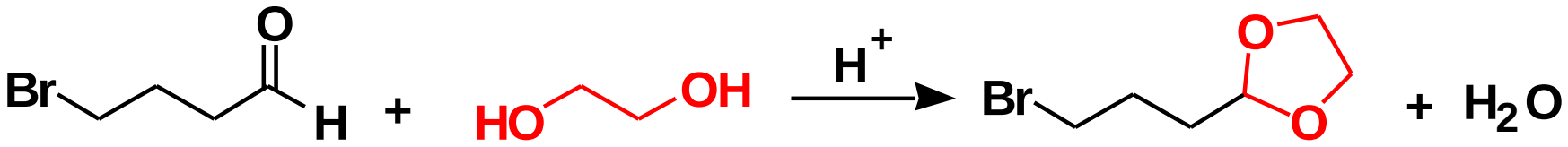
Acetals as Protecting Groups

- one way to synthesize the ketoalcohol on the right is by a Grignard reaction



Benzaldehyde 4-Bromobutanal 5-Hydroxy-5-phenylpentanal

- but first the aldehyde of the bromoaldehyde must be protected; one possibility is as a cyclic acetal

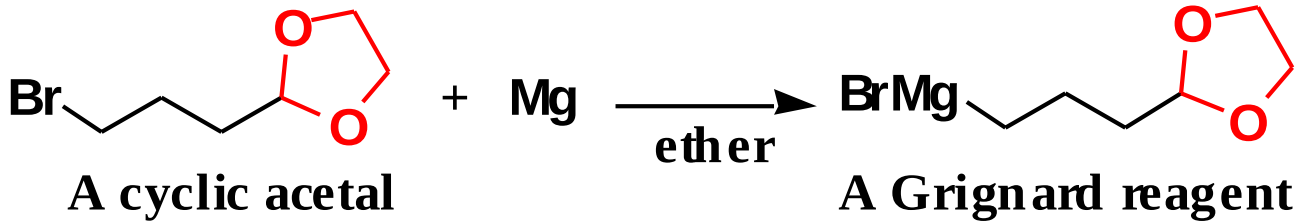


Ethylene glycol A cyclic acetal

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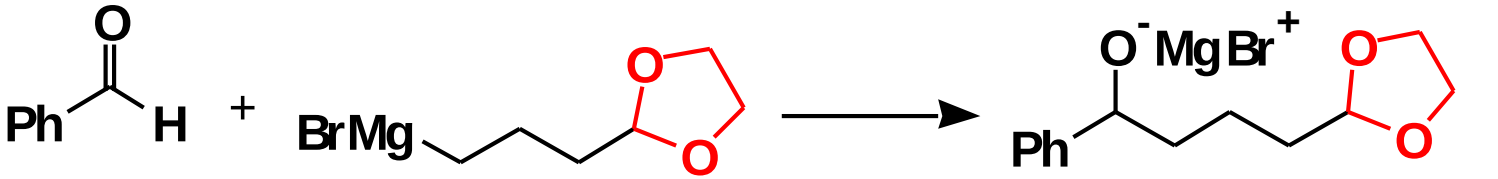
An Acetal as a Protecting Group

- now the Grignard reagent can be prepared and the new carbon-carbon bond formed



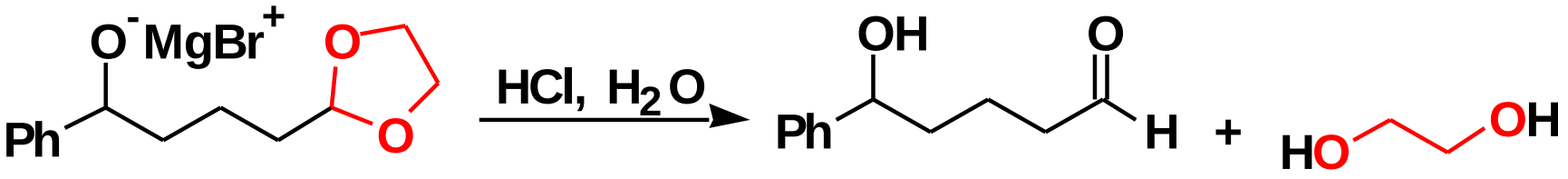
A cyclic acetal

A Grignard reagent



A magnesium alkoxide

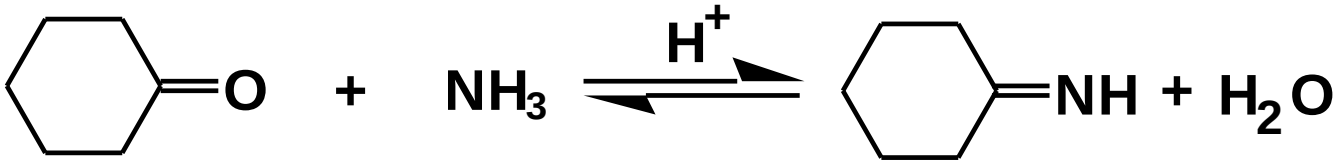
- hydrolysis gives the hydroxyaldehyde



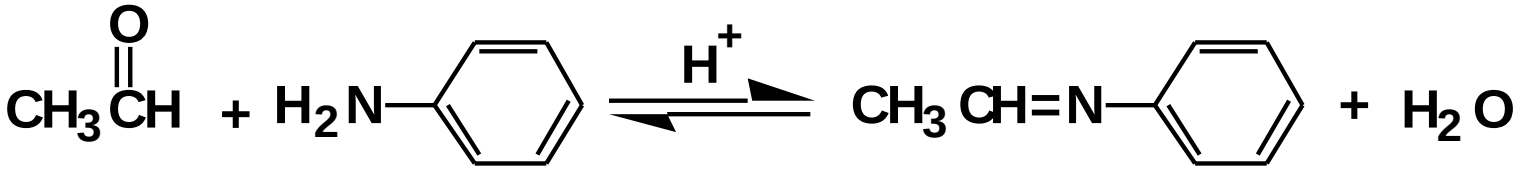
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Imines

- **Imine: a compound containing a C=N bond; also called a Schiff base**
  - **formed by the reaction of an aldehyde or ketone with ammonia or a 1° amine**



Cyclohexanone Ammonia An imine

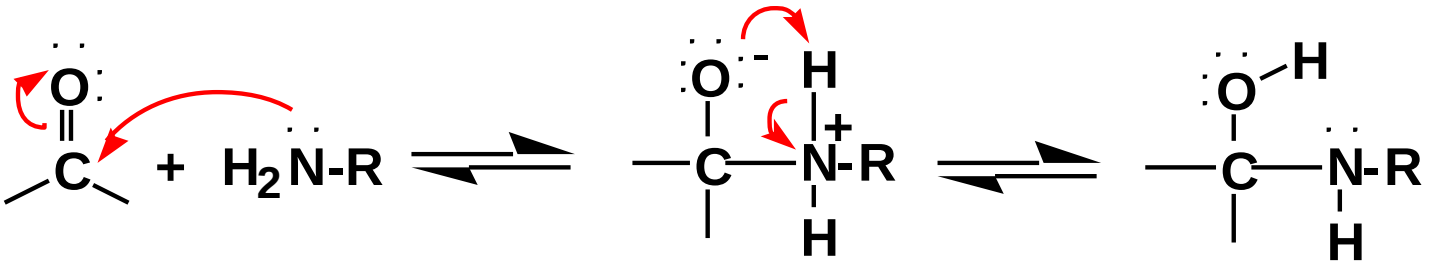


Ethanal Aniline An imine

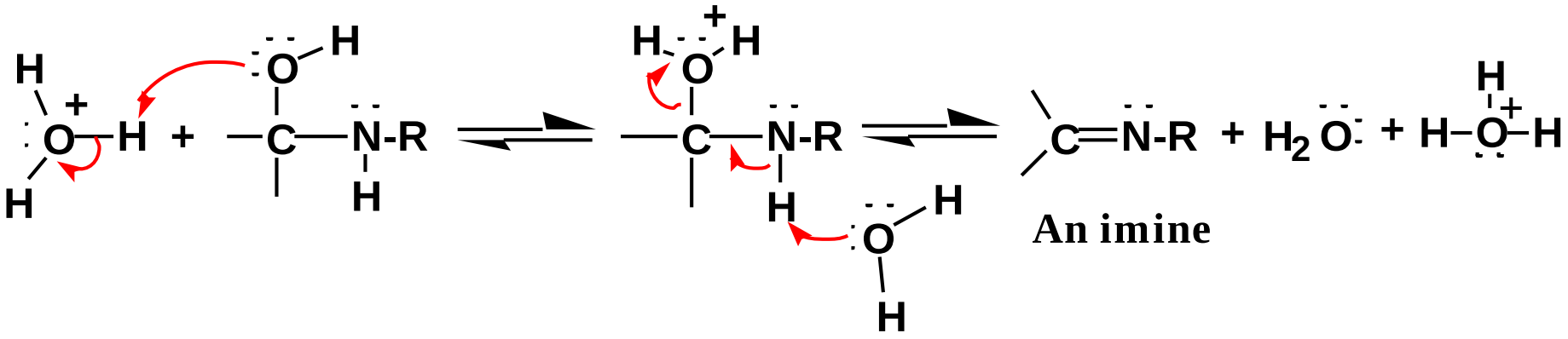
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Imines

1. addition of the amine to the carbonyl carbon followed by proton transfer



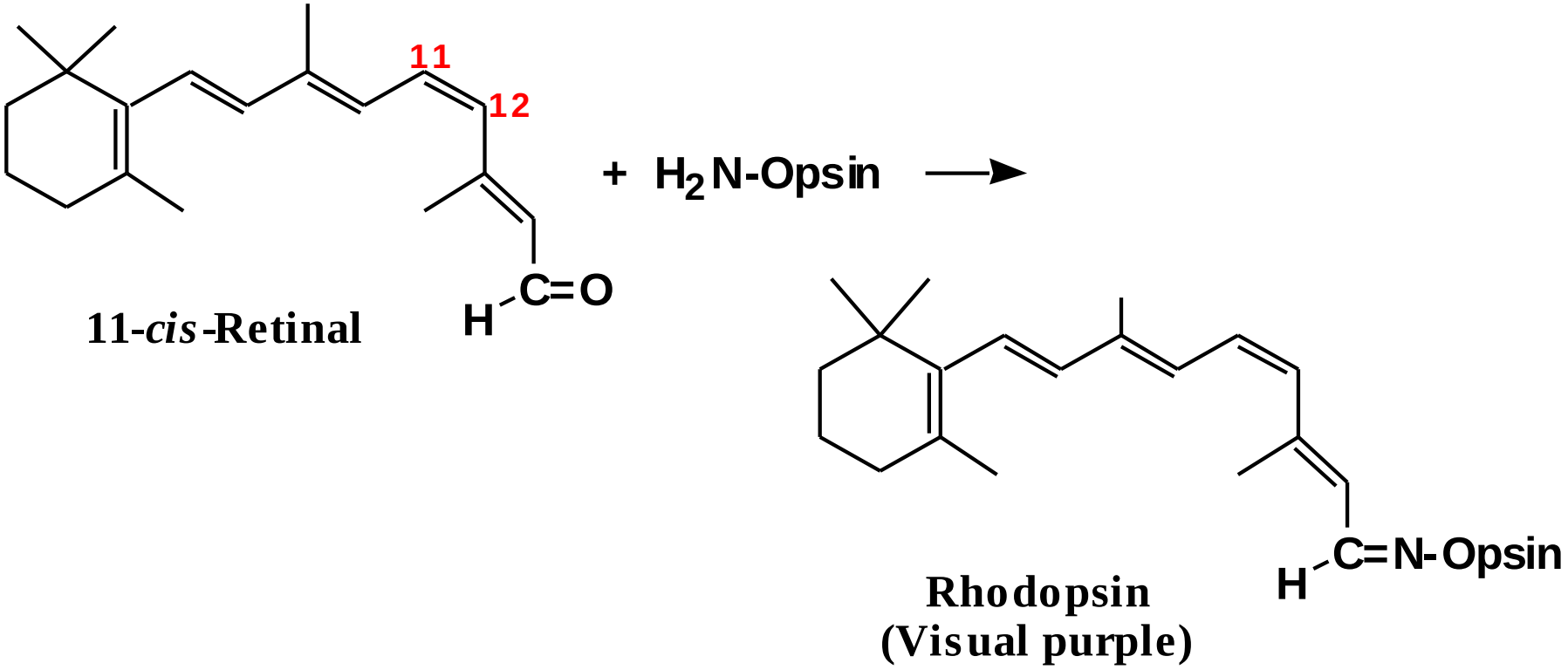
2. two proton-transfer reactions and loss of H_2O



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Rhodopsin

- **reaction of vitamin A aldehyde (retinal) with an amino group on the protein opsin gives rhodopsin**



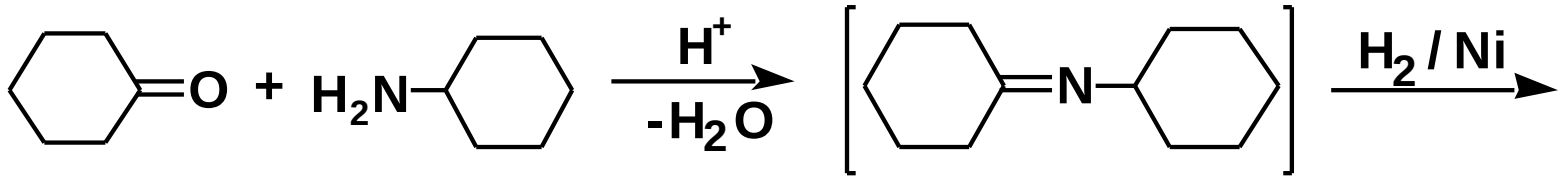
11-*cis*-Retinal

Rhodopsin
(Visual purple)

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Reductive Amination

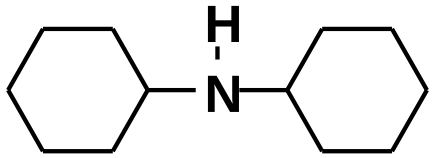
- **Reductive amination: the formation of an imine followed by its reduction to an amine**



Cyclohex-anone

Cyclohexyl-amine (a 1° amine)

An imine (not isolated)



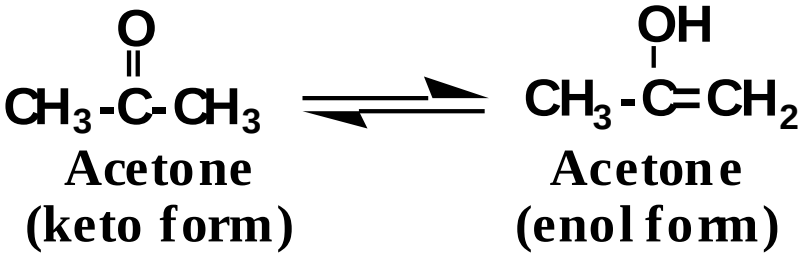
Dicyclohexylamine (a 2° amine)

- **reductive amination is a valuable method for the conversion of ammonia to a 1° amine, and a 1° amine to a 2° amine**

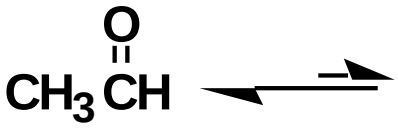
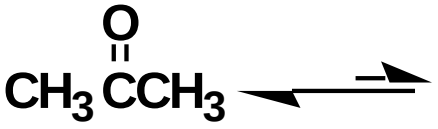
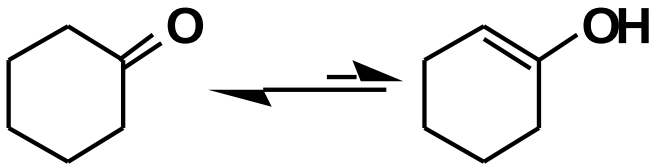
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Keto-Enol Tautomerism

- **Enol: a molecule containing an -OH group on a carbon-carbon double bond of an alkene**



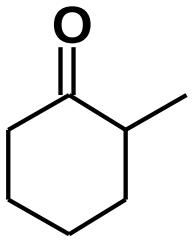
the keto form predominates for most simple aldehydes and ketones

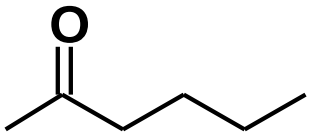
Keto form	Enol form	% Enol at Equilibrium
		6×10^{-5}
		6×10^{-7}
		4×10^{-5}

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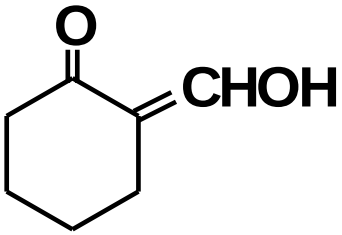
Keto-Enol Tautomerism

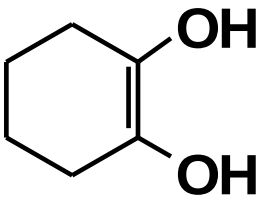
- **Problem:** draw two enol forms for each ketone

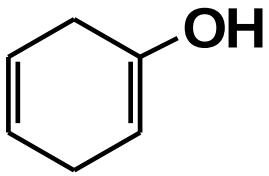
(a) 

(b) 

- **Problem:** draw the keto form of each enol

(a) 

(b) 

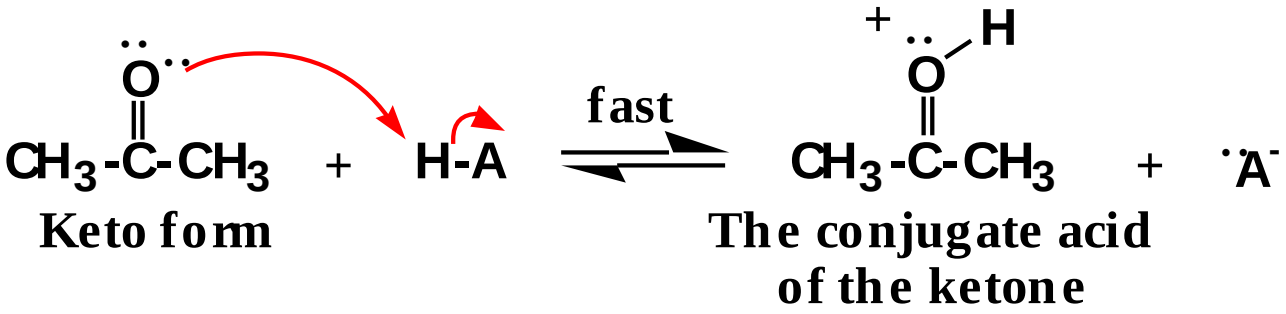
(c) 

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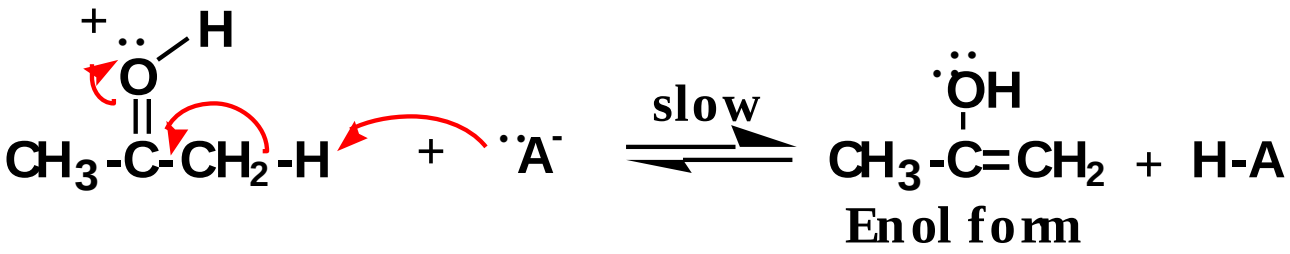
Keto-Enol Tautomerism

- **Interconversion of keto and enol forms is catalyzed by both acid and base**
  - **following is a mechanism for acid catalysis**

1. proton transfer to the carbonyl oxygen



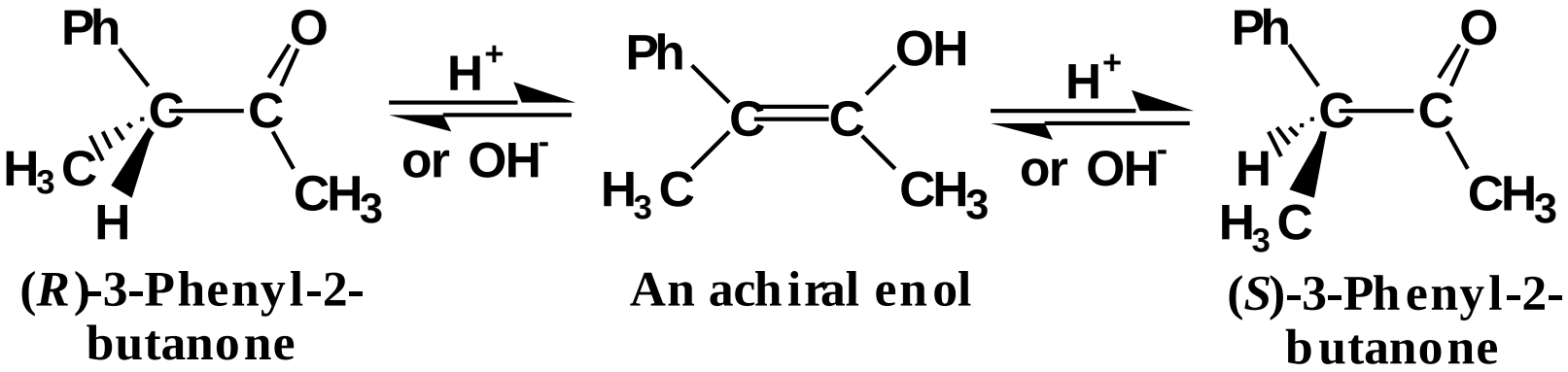
2. proton transfer from the α-carbon to A:⁻



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Racemization an at α-Carbon

- **when an enantiomerically pure aldehyde or ketone with at least one α-hydrogen is treated with a trace of acid or base, it gradually becomes a racemic mixture; it loses all optical activity**



(*R*)-3-Phenyl-2-butanone

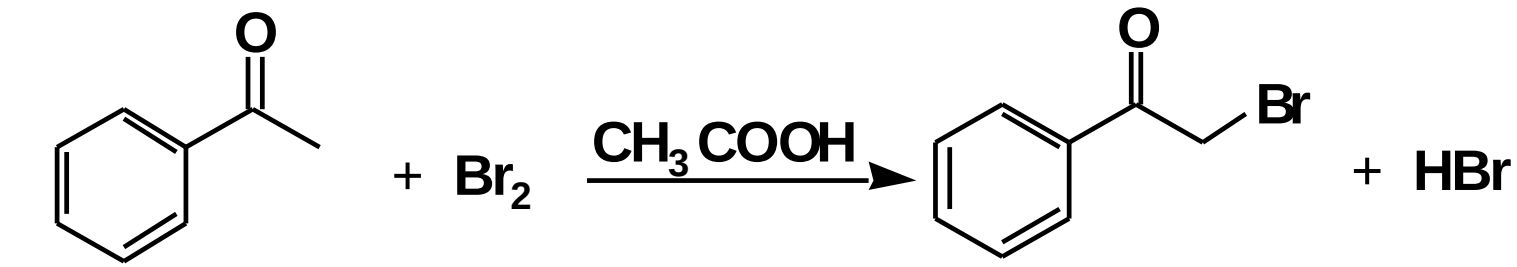
An achiral enol

(*S*)-3-Phenyl-2-butanone

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α-Halogenation

- **Aldehydes and ketones with an α-hydrogen react with Br_2 and Cl_2 to give an α-haloaldehyde or an α-haloketone**



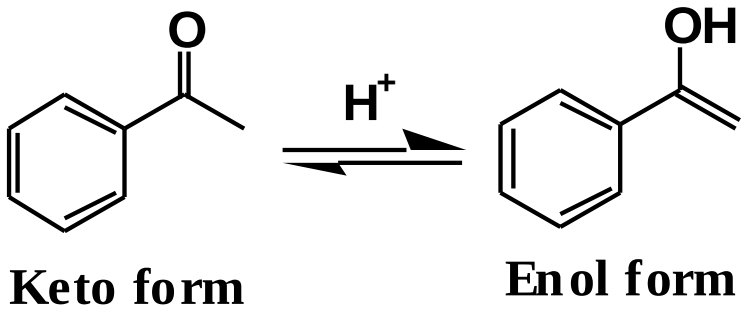
Acetophenone α-Bromoacetophenone

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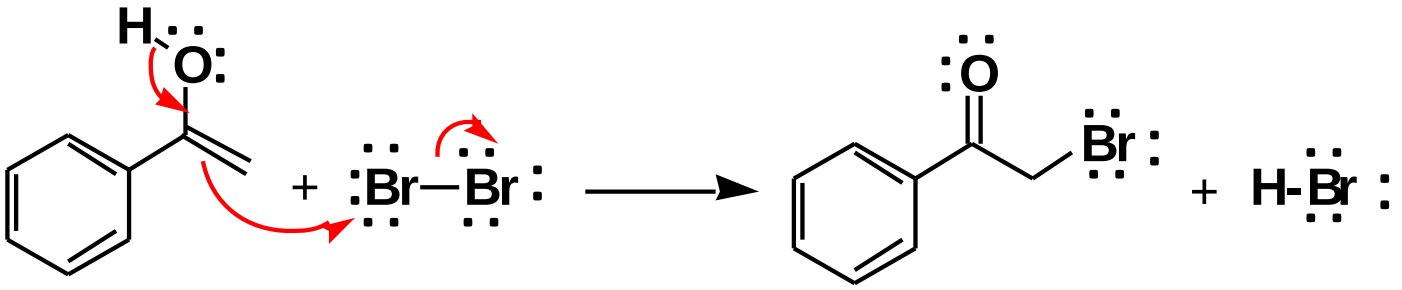
α-Halogenation

- **the key intermediate in α-halogenation is an enol**

1. formation of the enol



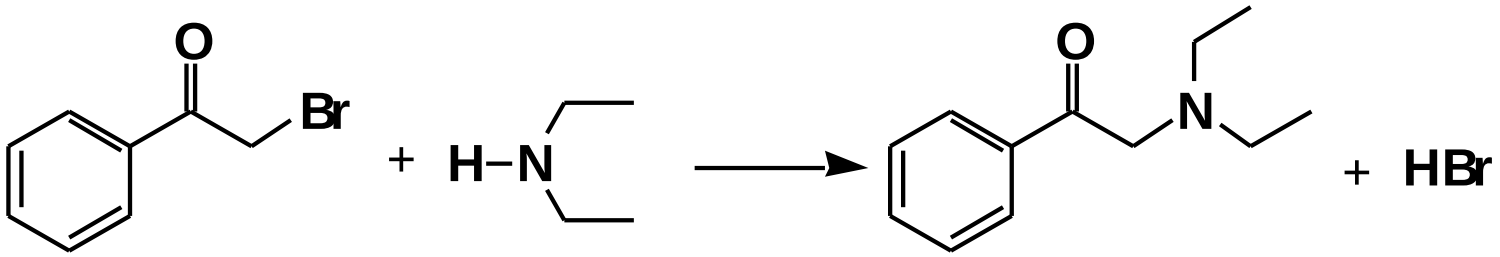
2. nucleophilic attack of the enol on the halogen



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α-Halogenation

- **A value of α-halogenation is that the carbon adjacent to the aldehyde or ketone now bears a good leaving group and is susceptible to nucleophilic attack**

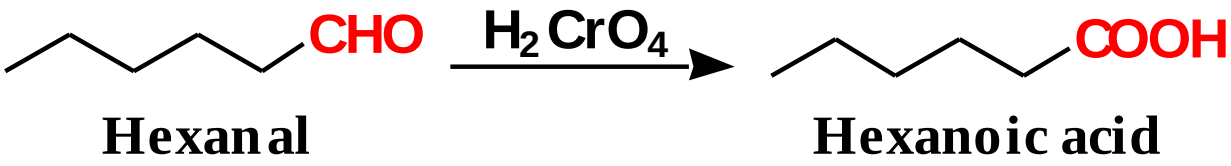


An α-bromo-ketone | Diethyl-amine | An α-diethylaminoketone

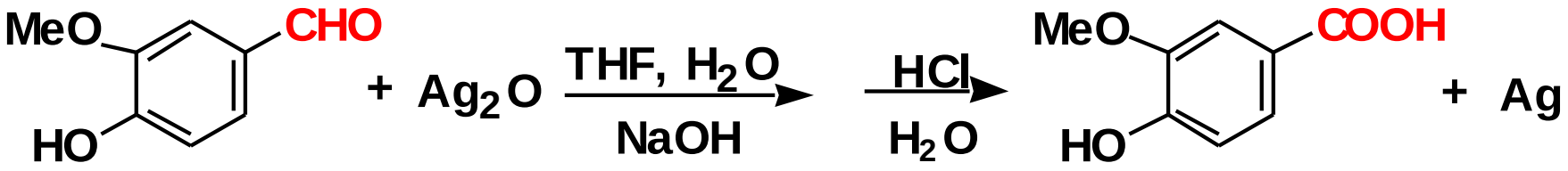
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Oxidation

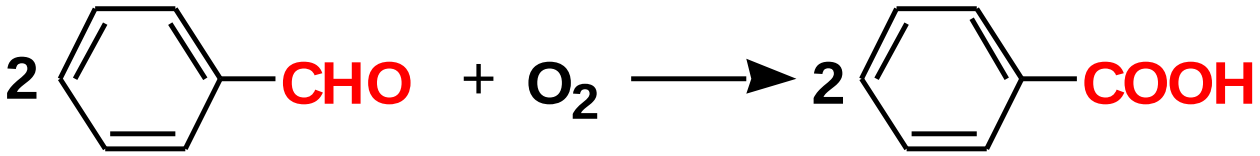
- **Aldehydes are one of the most easily oxidized of all functional groups**



Hexanal — Hexanoic acid



Vanillin — Vanillic acid

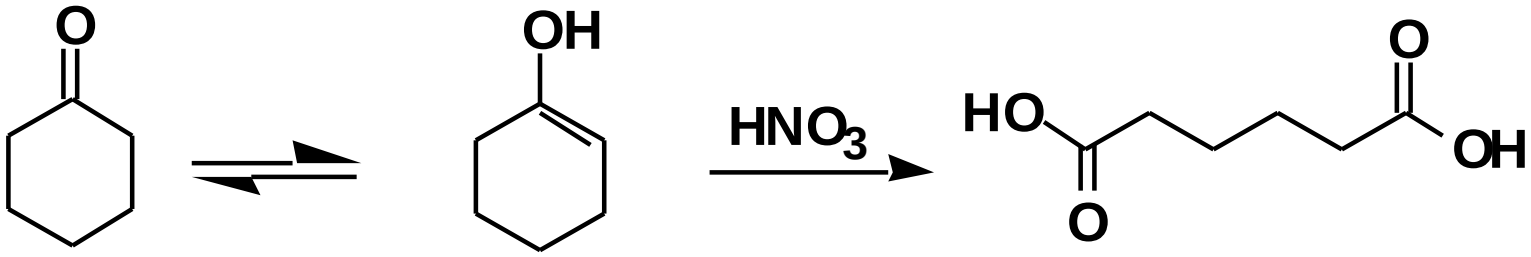


Benzaldehyde — Benzoic acid

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Oxidation

- **Ketones are not normally oxidized by H_2CrO_4; in fact this reagent is used to oxidize 2° alcohols to ketones**
  - **they are oxidized by HNO_3 at higher temperatures**
  - **oxidation is via the enol**



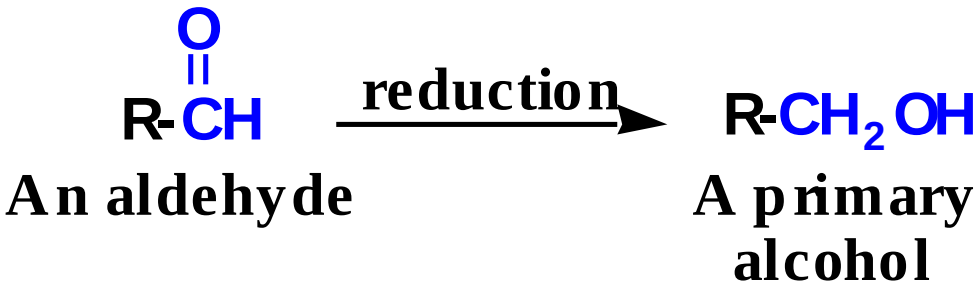
Cyclohexanone (keto form) | Cyclohexanone (enol form) | Hexanedioic acid (Adipic acid)

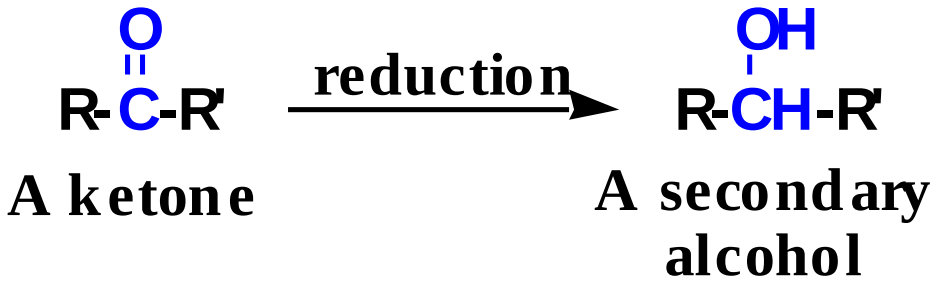
- **adipic acid is one of the starting materials for the synthesis of nylon 66**

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Reduction

- aldehydes can be reduced to 1° alcohols
- ketones can be reduced to 2° alcohols

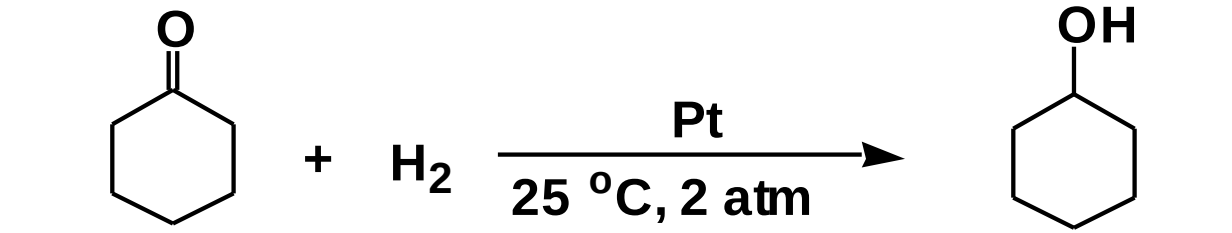




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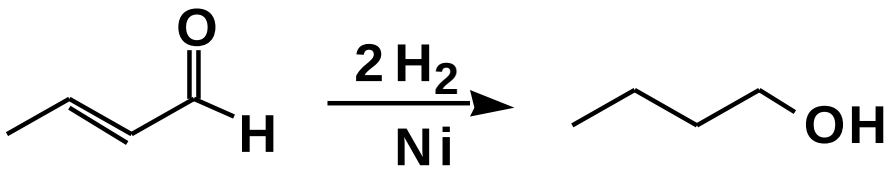
Catalytic Reduction

- **Catalytic reductions are generally carried out from 25° to 100°C and 1 to 5 atm H_2**



Cyclohexanone → Cyclohexanol

- **a carbon-carbon double bond may also be reduced under these conditions**

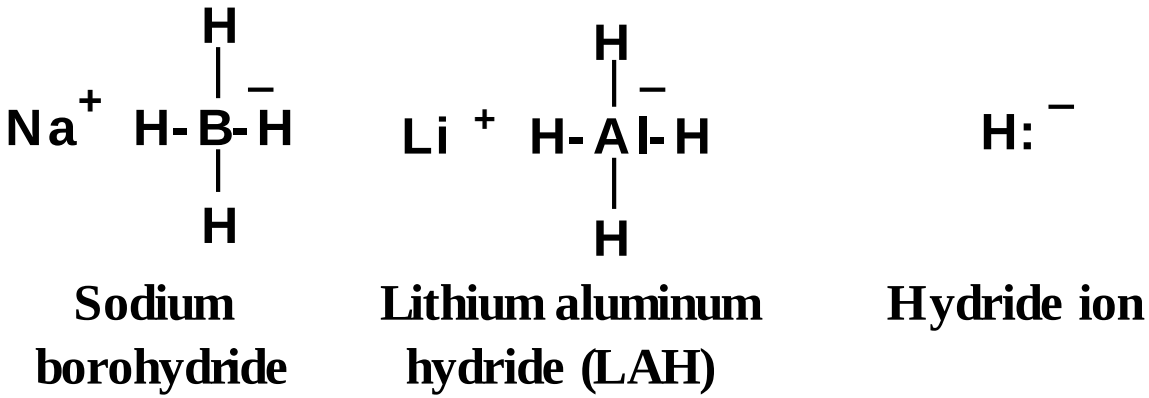


trans- 2-Butenal (Crotonaldehyde) → 1-Butanol

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Metal Hydride Reductions

- **The most common laboratory reagents for the reduction of aldehydes and ketones are $NaBH_4$ and $LiAlH_4$**
  - **both reagents are sources of hydride ion, $H:^-$, a very strong nucleophile**

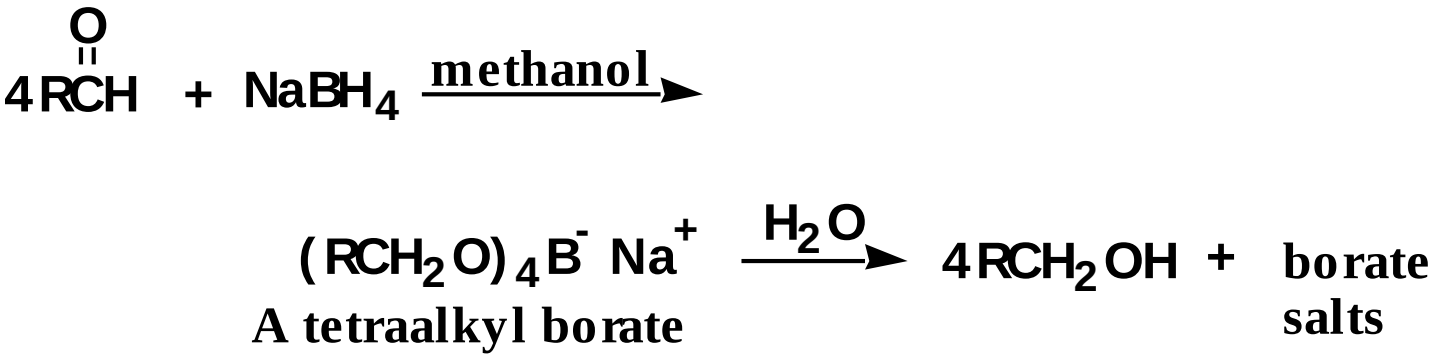


Sodium borohydride **Lithium aluminum hydride (LAH)** **Hydride ion**

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$NaBH_4$ Reductions

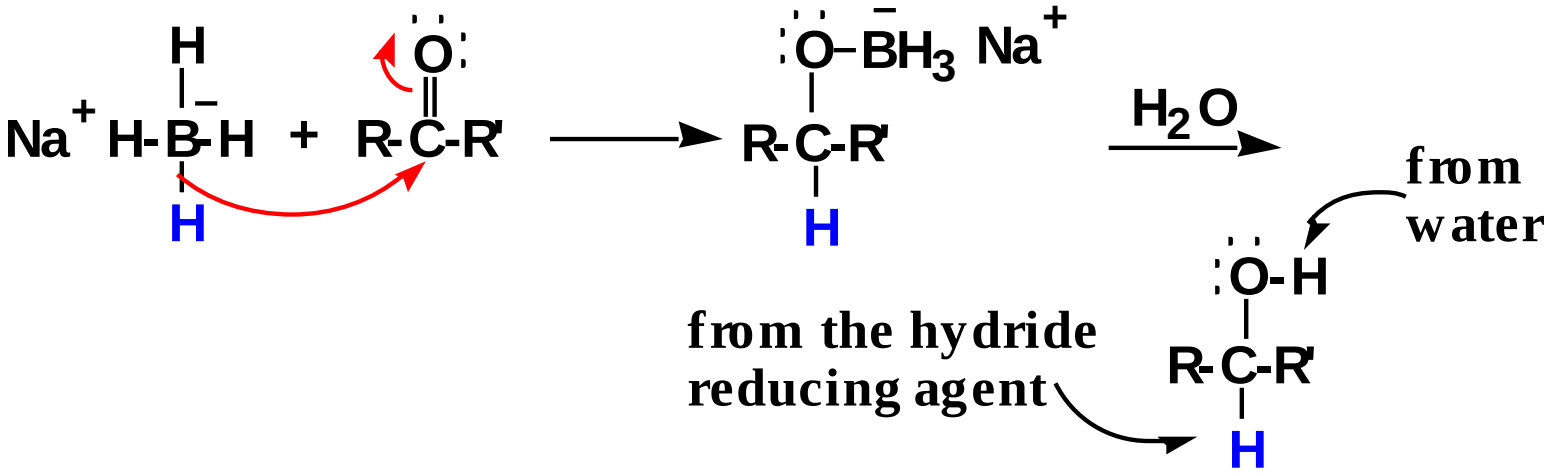
- reductions with $NaBH_4$ are most commonly carried out in aqueous methanol, in pure methanol, or in ethanol
- one mole of $NaBH_4$ reduces four moles of aldehyde or ketone



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$NaBH_4$ Reductions

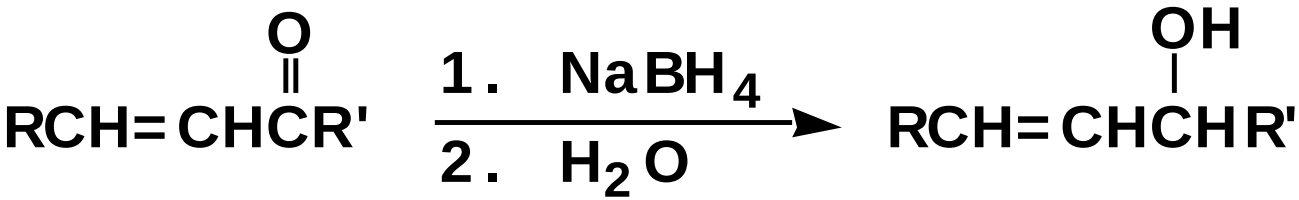
- **the key step in metal hydride reductions is transfer of a hydride ion to the C=O group to form a tetrahedral carbonyl addition compound**

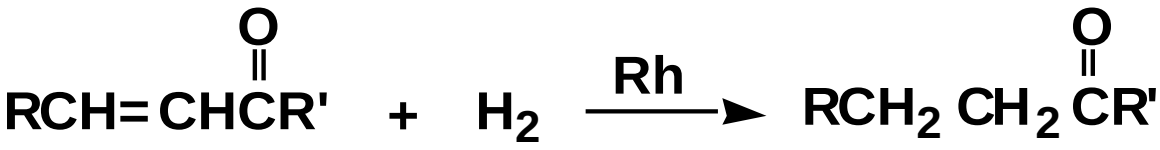


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Metal Hydride Reductions

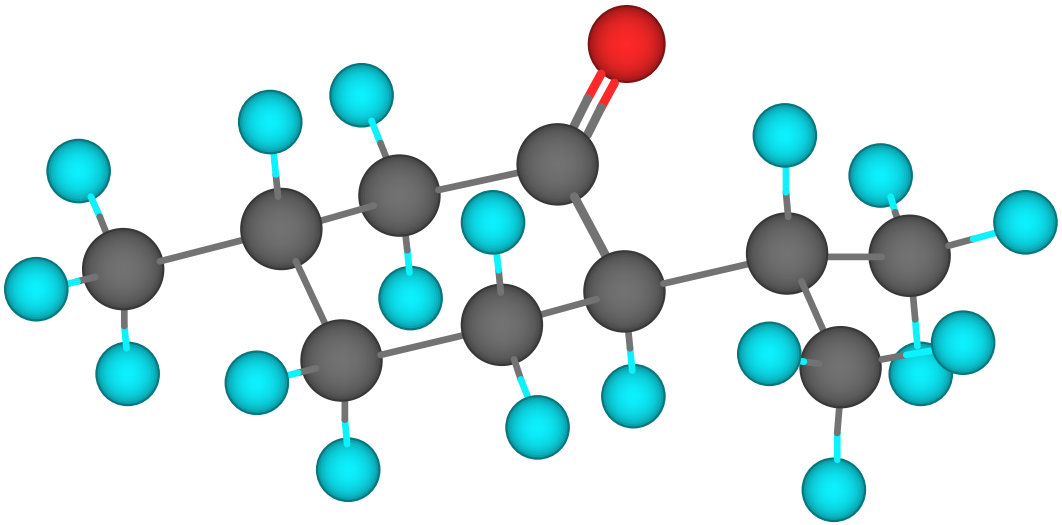
- **metal hydride reducing agents do not normally reduce carbon-carbon double bonds, and selective reduction of C=O or C=C is often possible**





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Aldehydes and Ketones



End Chapter 13

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