

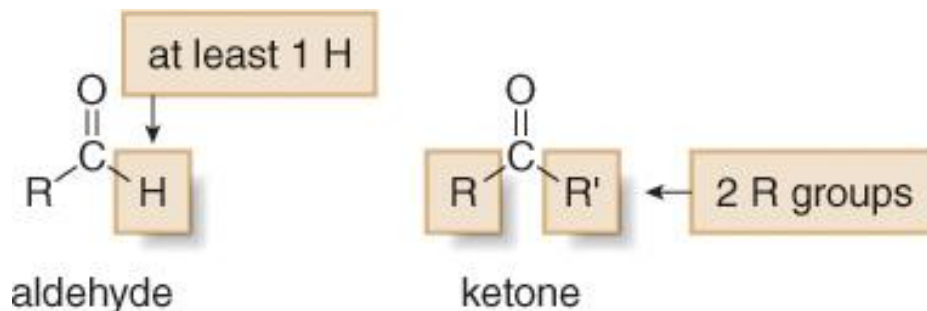
Carbonyl Compounds

Introduction

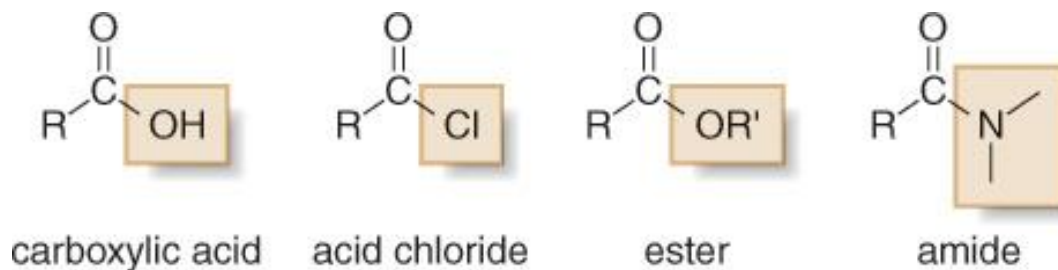
Introduction

Two broad classes of compounds contain the carbonyl group:

- [1] Compounds that have only carbon and hydrogen atoms bonded to the carbonyl

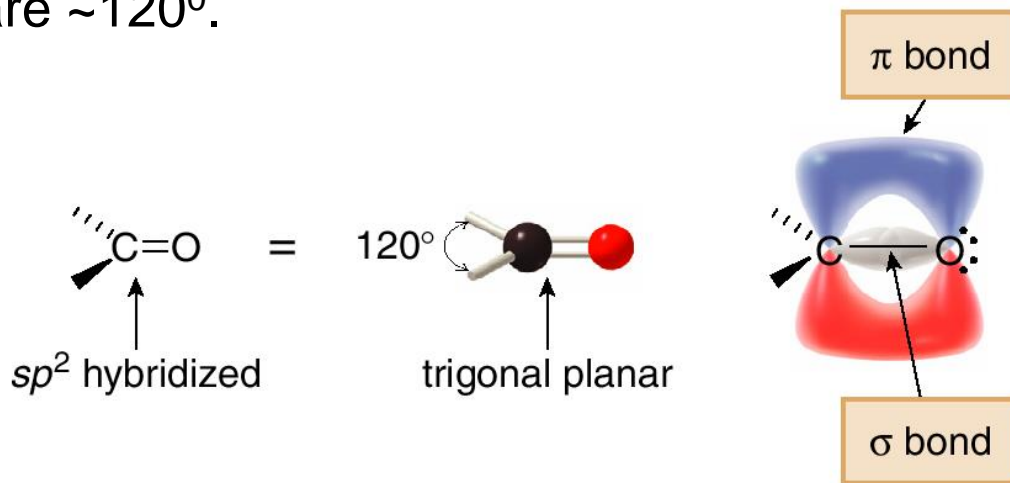


- [2] Compounds that contain an eteroatom (N, O, S, Cl) bonded to the carbonyl

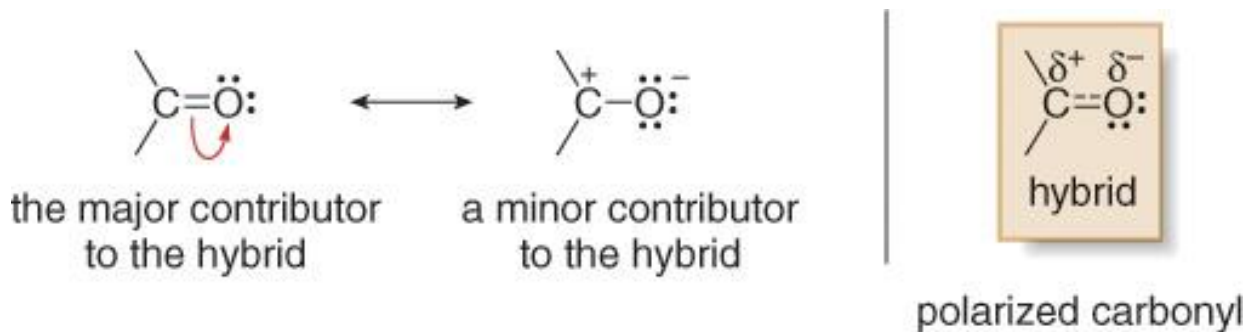


Introduction

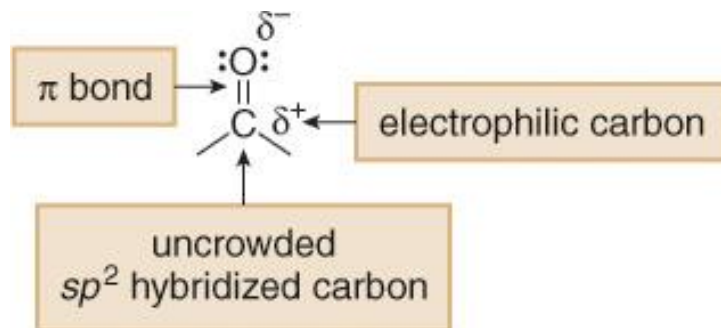
- Carbonyl carbons are sp^2 hybridized, trigonal planar, and have bond angles that are $\sim 120^\circ$.



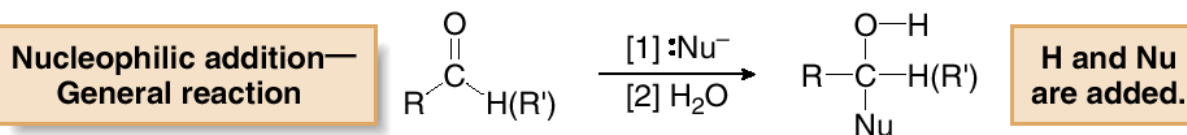
- The electronegative oxygen atom in the carbonyl group means that the bond is polarized, making the carbonyl carbon electron deficient.



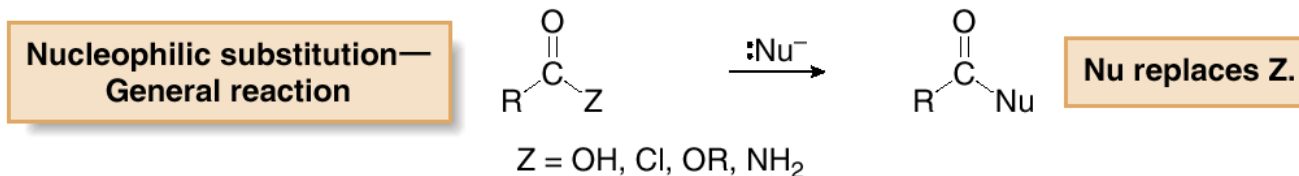
General Reactions of Carbonyl Compounds



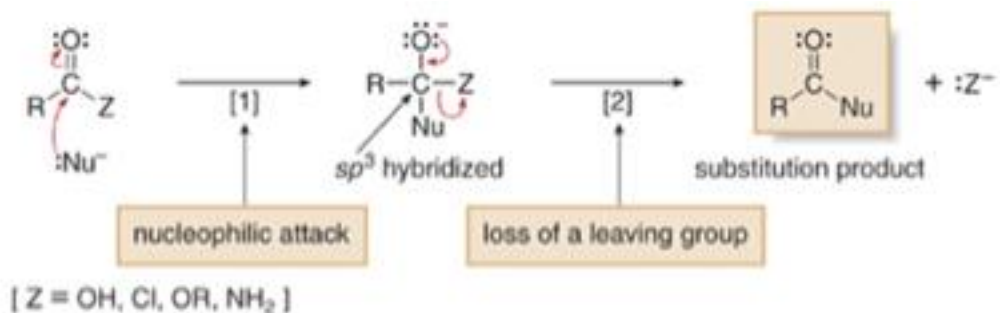
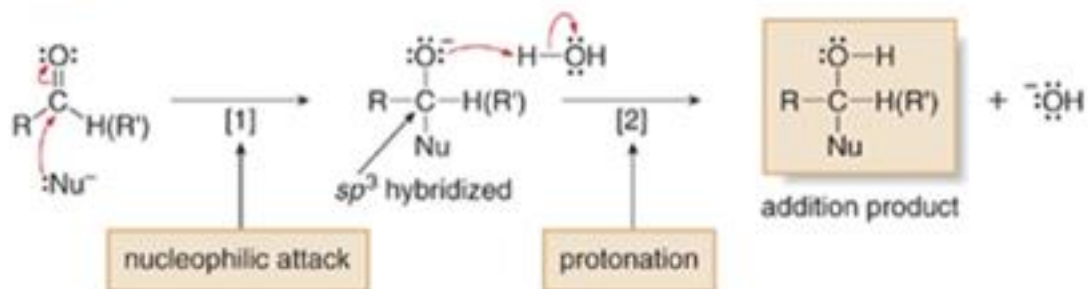
- Aldehydes and ketones undergo nucleophilic addition.



- Carbonyl compounds that contain leaving groups undergo nucleophilic substitution.



General Reactions of Carbonyl Compounds



Aldehydes and Ketones

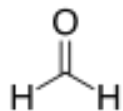
Chapter 19

Organic Chemistry, *8th Edition*

John McMurry

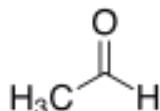
Nomenclature of Aldehydes

- Find the longest chain containing the CHO group, and change the –e ending of the parent alkane to the suffix *-al*. If the CHO group is bonded to a ring, name the ring and add the suffix *-carbaldehyde*.
- A common name for an aldehyde is formed by taking the common parent name and adding the suffix *-aldehyde*.



methanal

(formaldehyde)



ethanal

(acetaldehyde)



propanal

(propionald.)



butanal

(butyraldehyde)



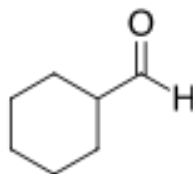
pentanal

(valeraldehyde)

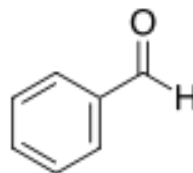


hexanal

(caproic aldehyde)

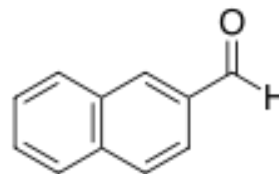


cyclohexanecarbaldehyde

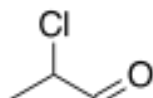


benzenecarbaldehyde

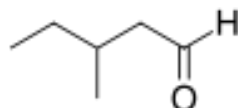
(benzaldehyde)



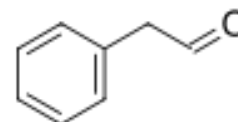
2-naphthalenecarbaldehyde



2-chloropropanal

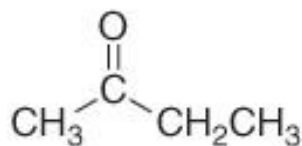


3-methylhexanal



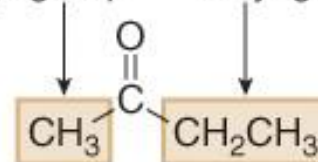
phenylethanal

Nomenclature of Ketones

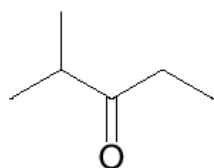


IUPAC name: **2-butanone**

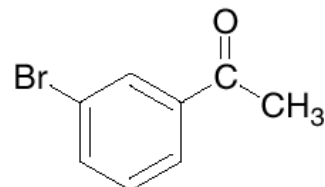
methyl group ethyl group



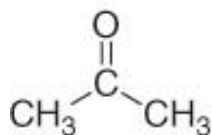
Common name: **ethyl methyl ketone**



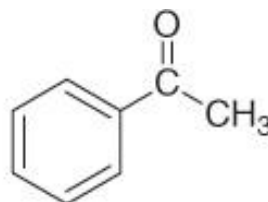
IUPAC name: 2-methyl-3-pentanone
Common name: ethyl isopropyl ketone



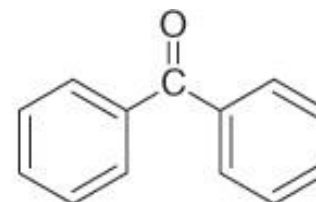
m-bromoacetophenone
or
3-bromoacetophenone



acetone

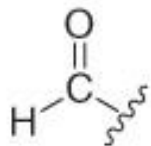


acetophenone

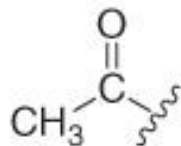


benzophenone

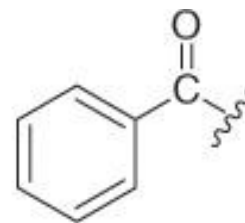
Nomenclature of Aldehydes and Ketones



formyl group

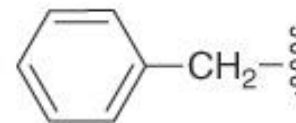


acetyl group



benzoyl group

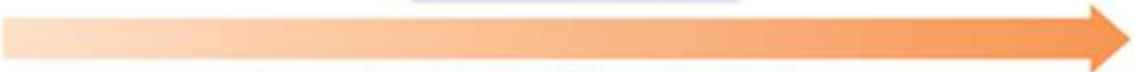
Do not confuse a **benzyl** group with a **benzoyl** group.



benzyl group

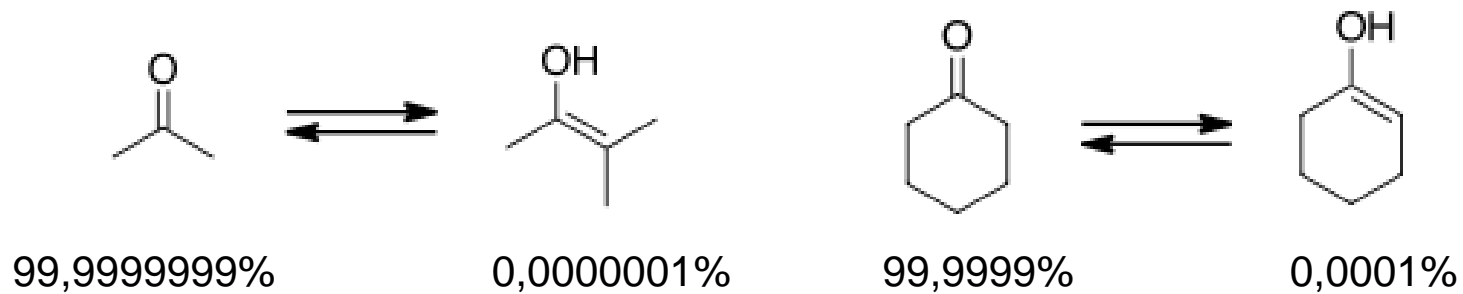
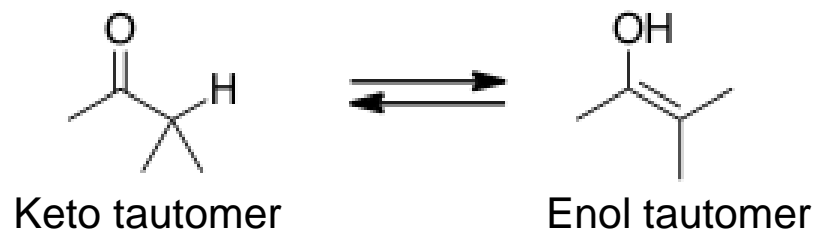
Physical Properties

Table 21.1 Physical Properties of Aldehydes and Ketones

| Property | Observation |
|---------------------------------|---|
| Boiling point and melting point | <ul style="list-style-type: none"> For compounds of comparable molecular weight, bp's and mp's follow the usual trend: The stronger the intermolecular forces, the higher the bp or mp. <div style="display: flex; justify-content: space-around; align-items: center; margin-top: 20px;"> <div style="text-align: center;"> $\text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_3$ VDW MW = 72 bp 36 °C </div> <div style="border: 1px solid black; padding: 10px; text-align: center;"> $\text{CH}_3\text{CH}_2\text{CH}_2\text{CHO}$ VDW, DD MW = 72 bp 76 °C $\text{CH}_3\text{CH}_2\text{COCH}_3$ VDW, DD MW = 72 bp 80 °C </div> <div style="text-align: center;"> $\text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_2\text{OH}$ VDW, DD, HB MW = 74 bp 118 °C </div> </div> <div style="text-align: center; margin-top: 20px;">  <p>Increasing strength of intermolecular forces Increasing boiling point</p> </div> |
| Solubility | <ul style="list-style-type: none"> RCHO and RCOR are soluble in organic solvents regardless of size. RCHO and RCOR having ≤ 5 C's are H₂O soluble because they can hydrogen bond with H₂O (Section 3.4C). RCHO and RCOR having > 5 C's are H₂O insoluble because the nonpolar alkyl portion is too large to dissolve in the polar H₂O solvent. |

Key: VDW = van der Waals, DD = dipole–dipole, HB = hydrogen bonding, MW = molecular weight

Keto-Enol Tautomerism



Interesting Aldehydes and Ketones



formaldehyde
 $\text{CH}_2=\text{O}$

Billions of pounds of formaldehyde are produced annually from the oxidation of methanol. It is sold as a 37% solution called formalin which is used as a disinfectant, antiseptic, and preservative for biological specimens. It is a product of incomplete combustion of coal, and is partly responsible for the irritation caused by smoggy air.



acetone
 $(\text{CH}_3)_2\text{C}=\text{O}$

Acetone is an industrial solvent. It is also produced in vivo during breakdown of fatty acids. Diabetics often have unusually high levels of acetone in their blood streams.

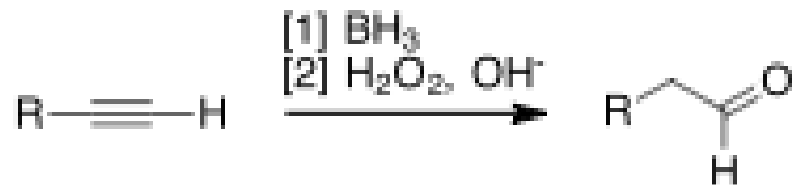
Interesting Aldehydes and Ketones

Many aldehydes and ketones with characteristic odors occur in nature.



Preparation of Aldehydes

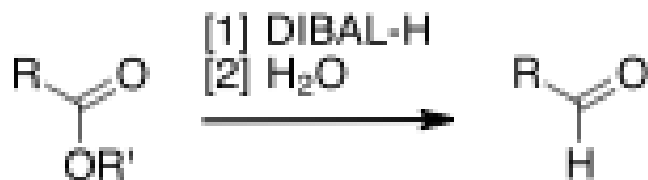
Hydration of an alkyne
(hydroboration-oxidation)



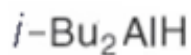
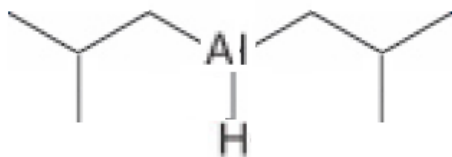
Oxidation of 1^{ry} alcohols



Reduction of esters and
acyl chlorides

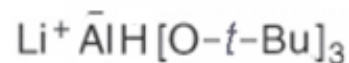
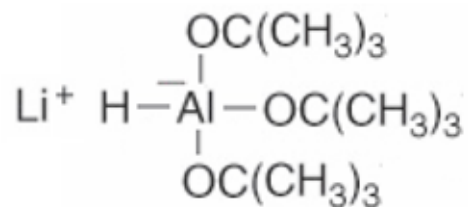


Preparation of Aldehydes and Ketones



DIBAL-H

Diisobutylaluminum hydride



Lithium tri-*tert*-butoxyaluminum hydride

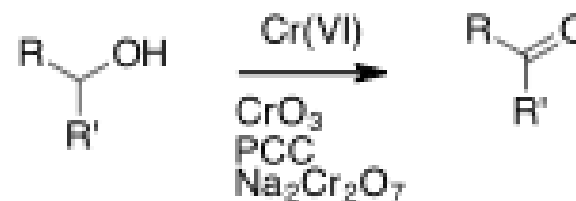
Sterically hindered - Less reactive than LiAlH_4

Preparation of Ketones

Hydration of alkynes



Oxidation of 2^{ry} alcohols



Friedel-Crafts acylation

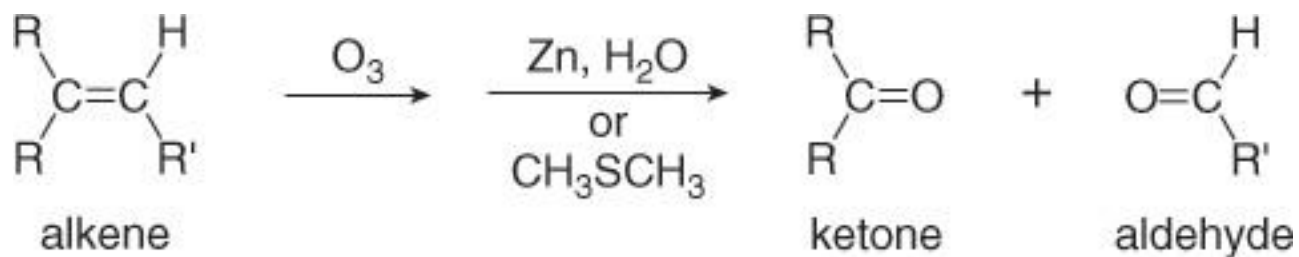


Acylation of organocuprates



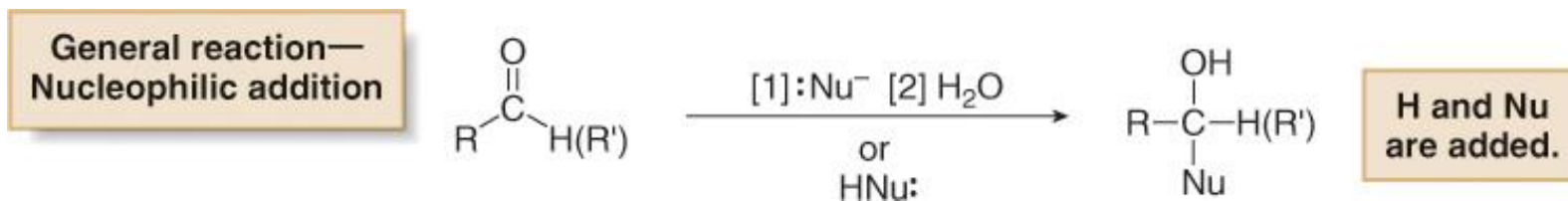
Preparation of Aldehydes and Ketones

Aldehydes and ketones are also both obtained as products of the oxidative cleavage of alkenes.



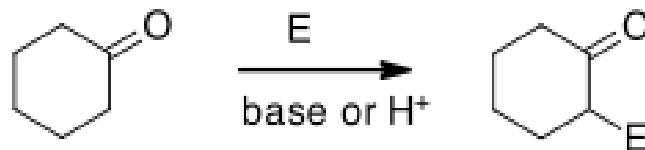
Reactions of Aldehydes and Ketones—General

[1] Nucleophilic addition

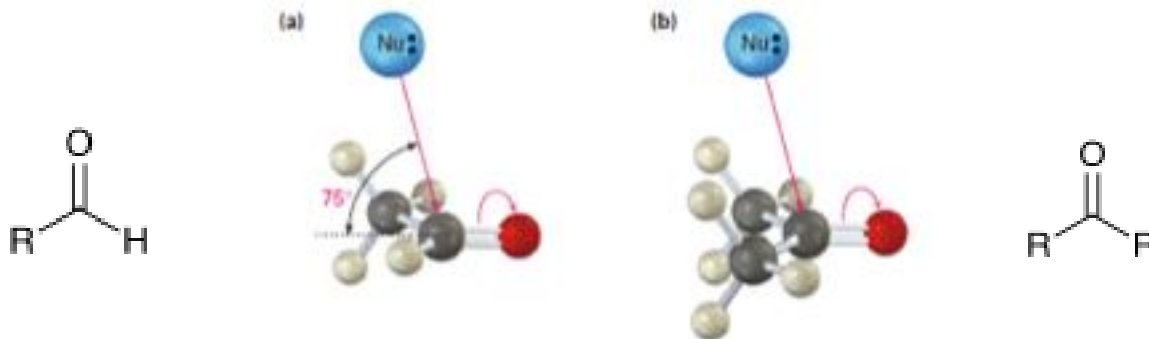
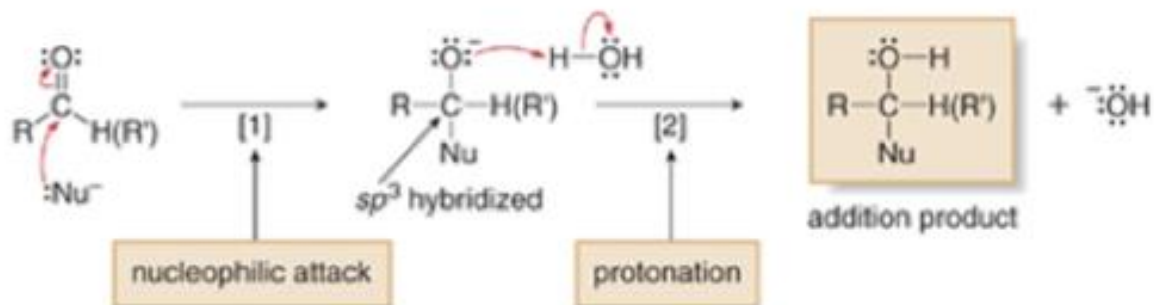


[2] Oxidation

[3] Reaction at the α carbon



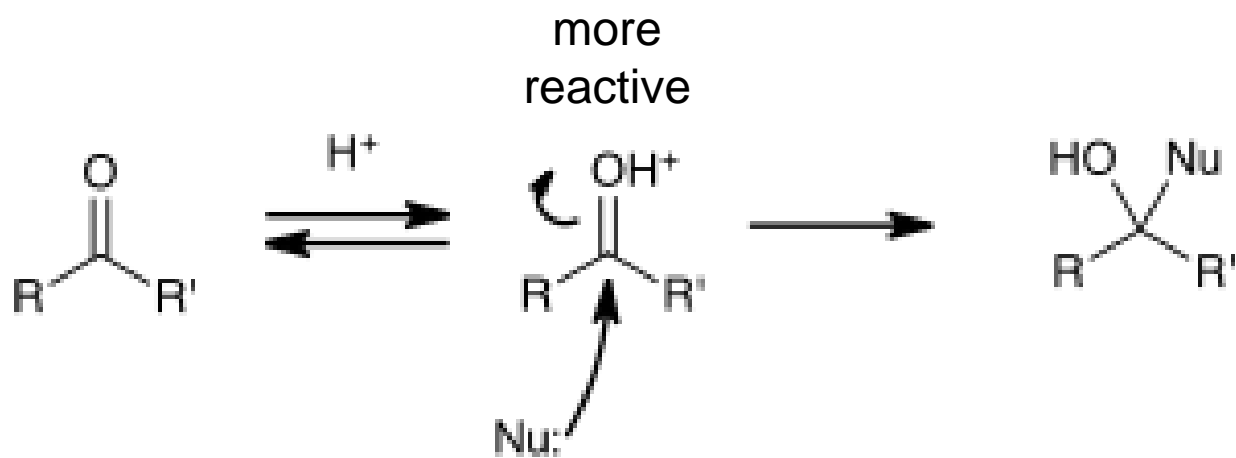
Nucleophilic Addition



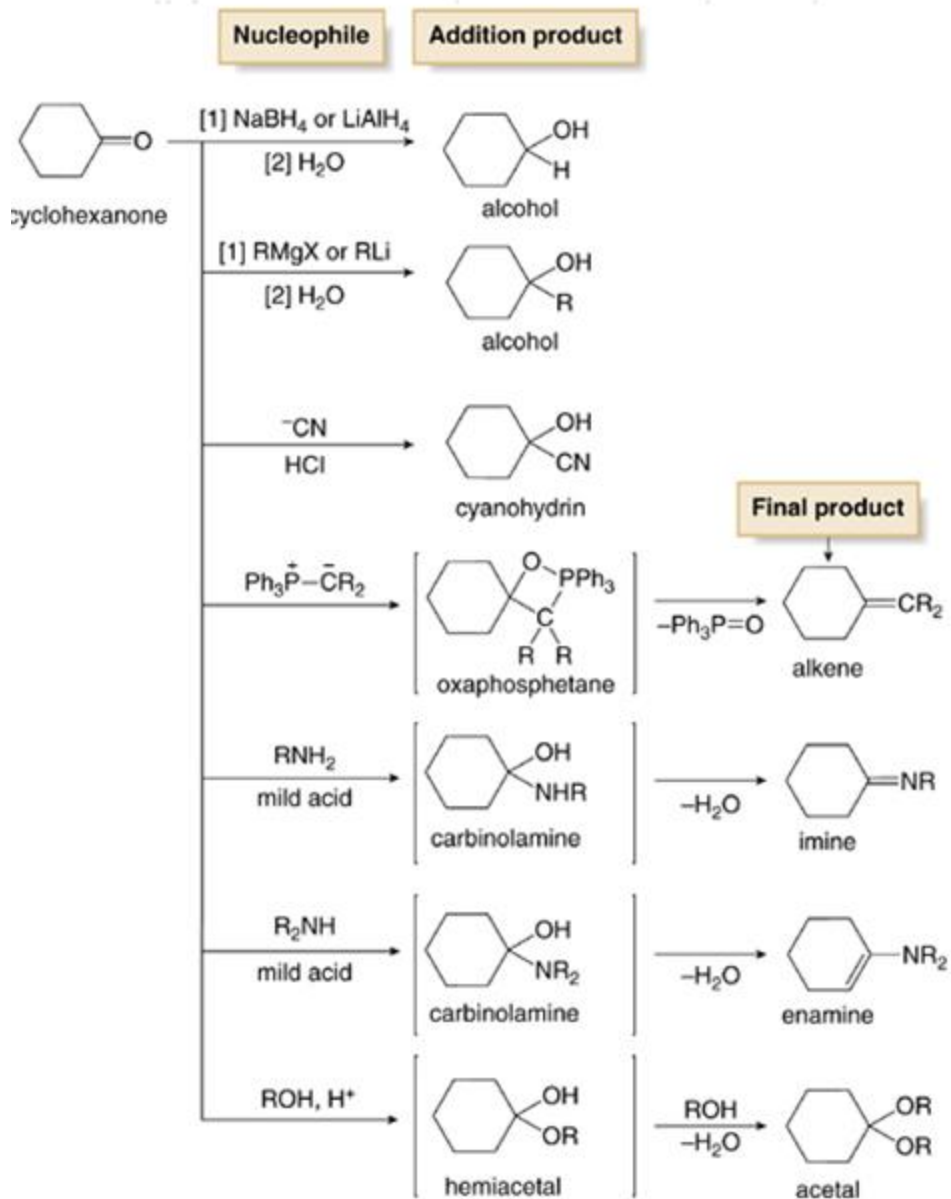
aldehyde
less crowded
more reactive

ketone
more crowded
less reactive

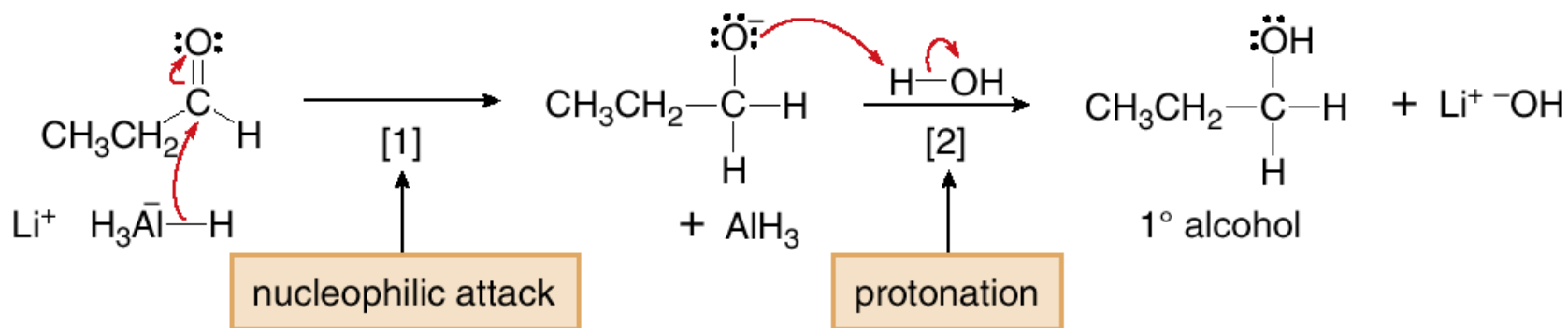
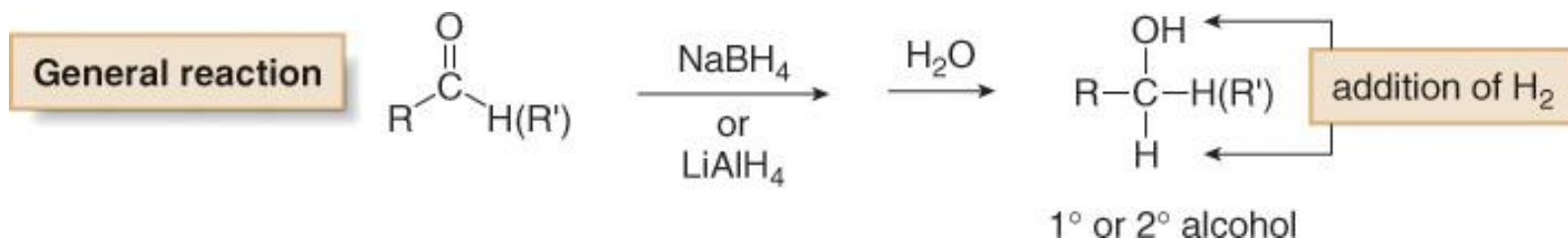
Acid Catalysis



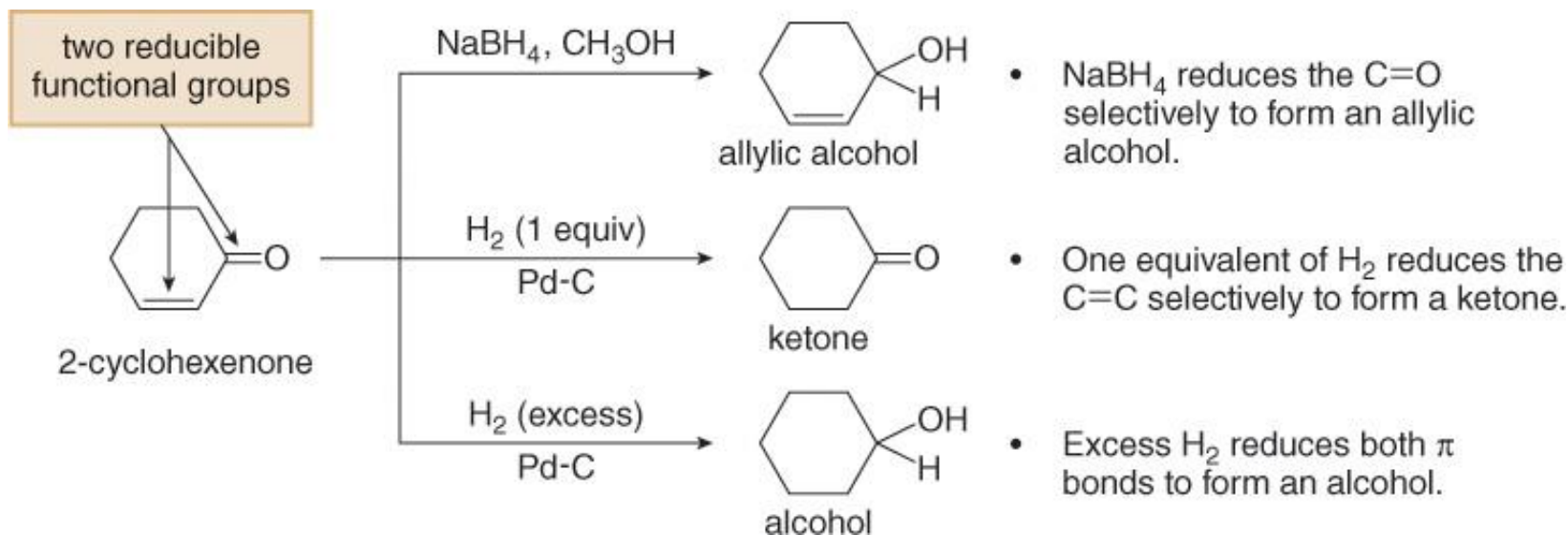
Nucleophilic Addition



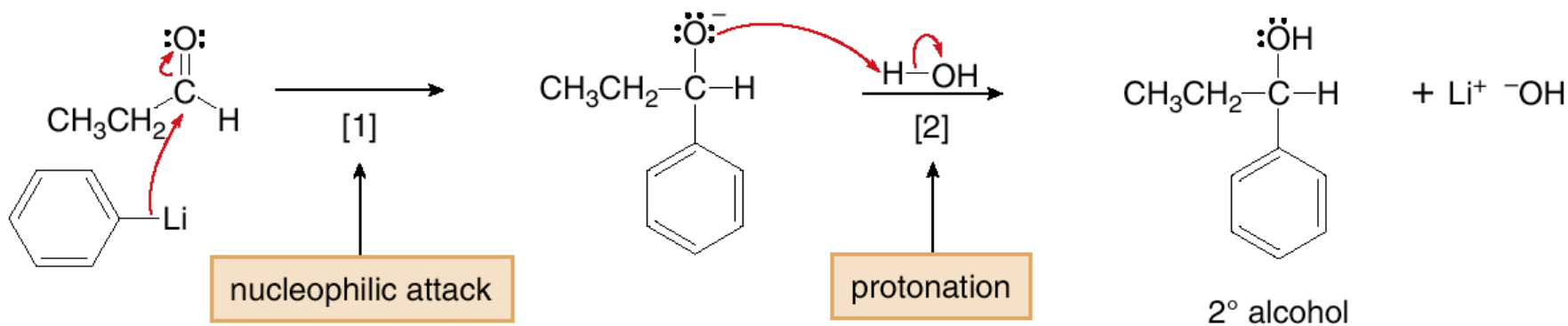
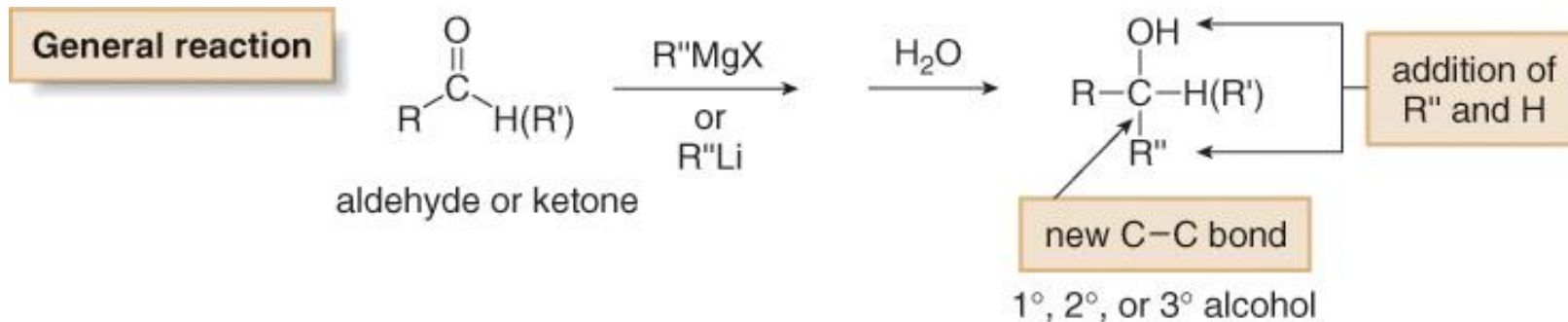
Nucleophilic Addition of H^- and R^- — A Review



Nucleophilic Addition of H^- and R^- — A Review

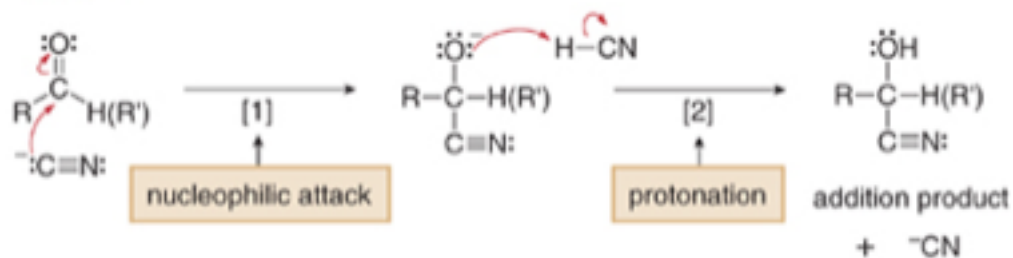
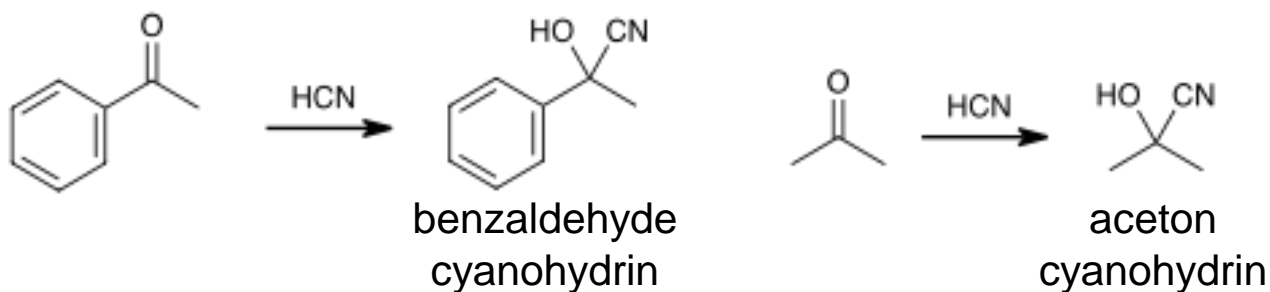


Nucleophilic Addition of H^- and R^- — A Review



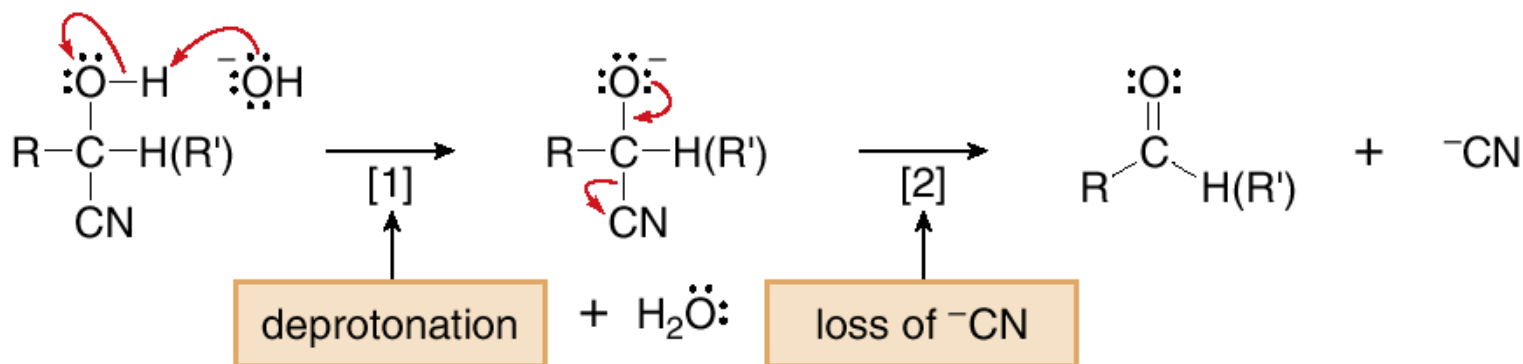
Nucleophilic Addition of CN^-

- Treatment of an aldehyde or ketone with HCN gives a cyanohydrin.

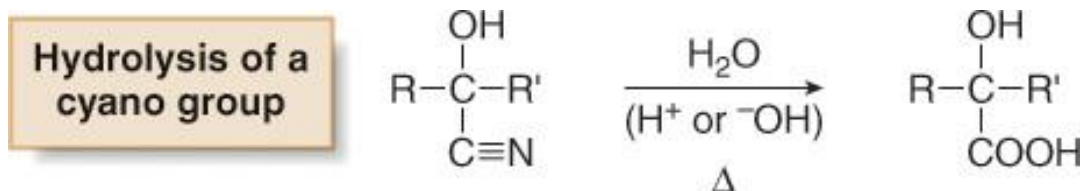


Nucleophilic Addition of CN⁻

- Cyanohydrins** can be reconverted to carbonyl compounds by treatment with base. This process is just the reverse of the addition of HCN: deprotonation followed by elimination of ⁻CN.

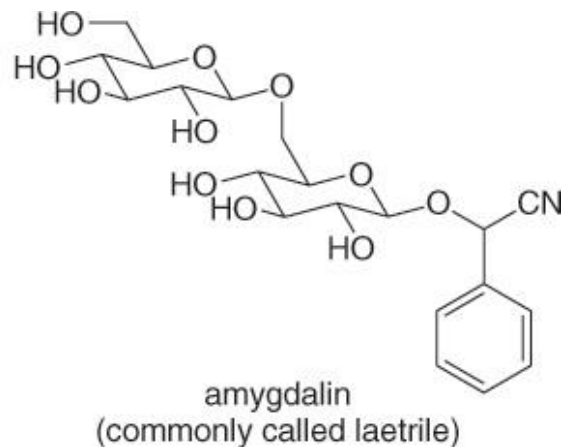
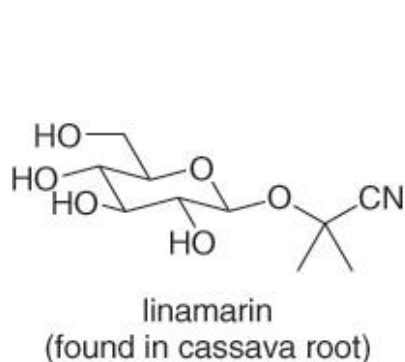


- The cyano group of a cyanohydrin is readily hydrolyzed to a carboxy group by heating with aqueous acid or base.



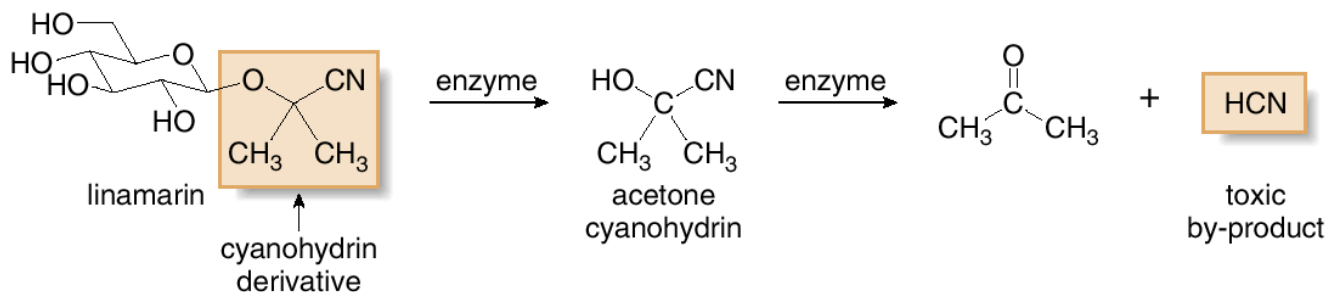
Nucleophilic Addition of CN⁻

- Linamarin and Amygdalin are two naturally occurring cyanohydrin derivatives.



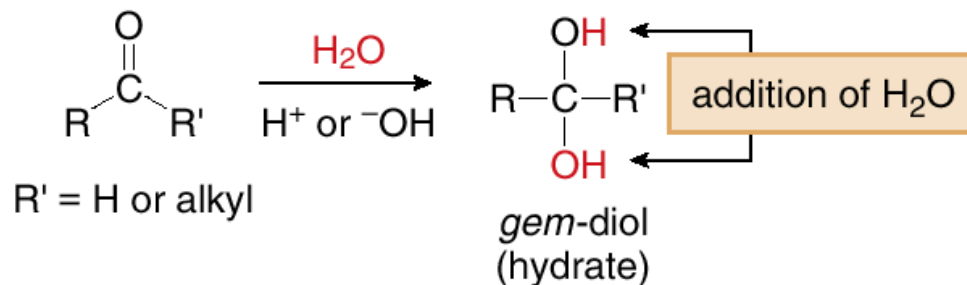
- Both compounds are toxic because they are metabolized to cyanohydrins, which are hydrolyzed to carbonyl compounds and HCN gas.

The breakdown of linamarin to HCN

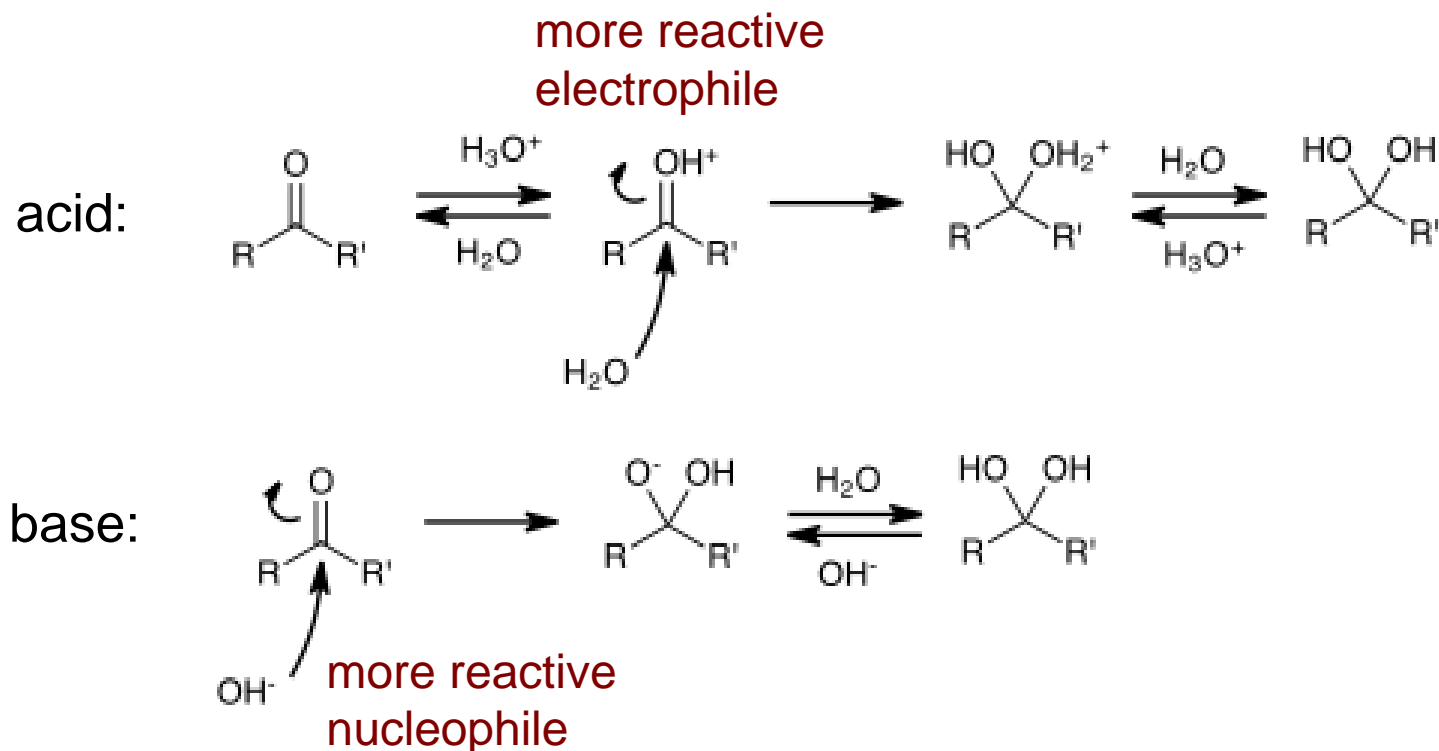


Addition of H₂O—Hydration

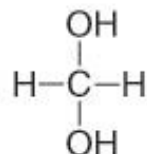
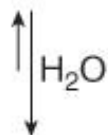
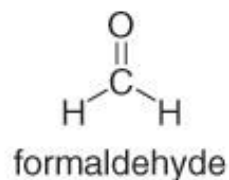
Nucleophilic addition of H₂O



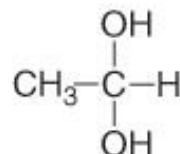
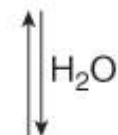
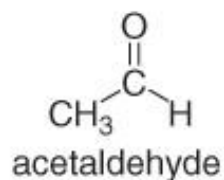
Both acid and base catalyze the addition of H₂O to the carbonyl group.



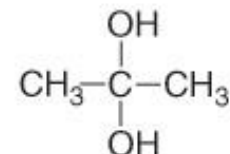
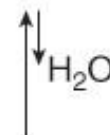
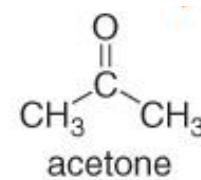
Addition of H₂O—Hydration



99.9% product



58% product

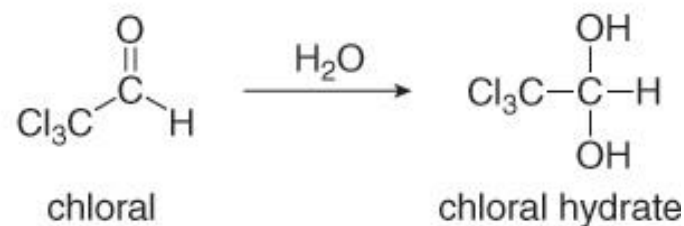
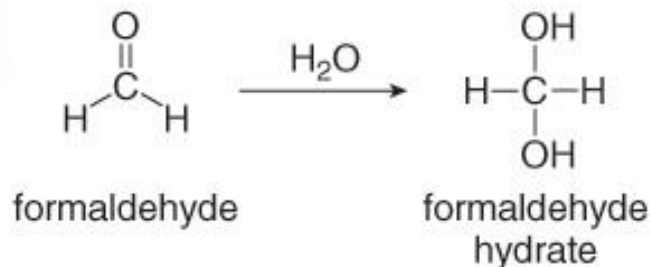


0.2% product

← Increasing amount of hydrate present at equilibrium

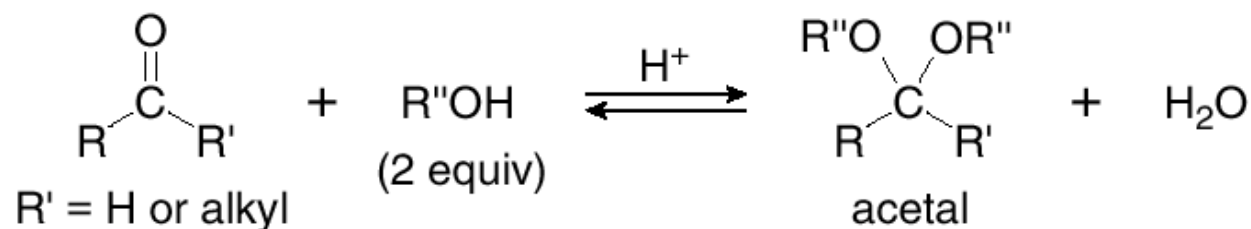
- *Gem*-diol product yields are good only when unhindered aldehydes or aldehydes with nearby electron withdrawing groups are used.

Examples

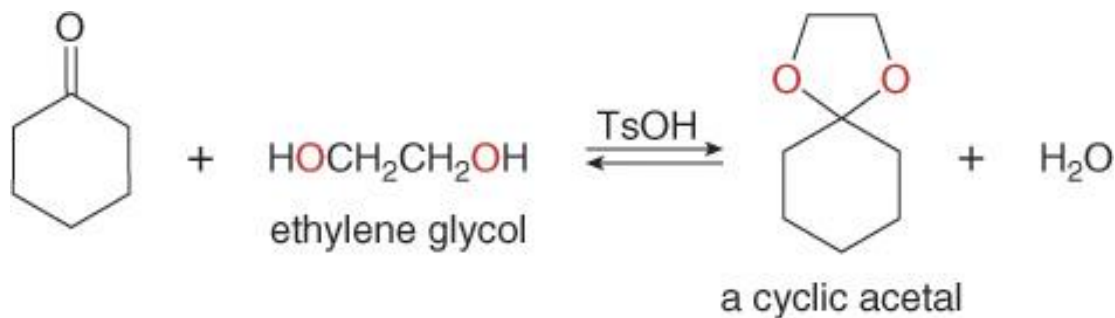
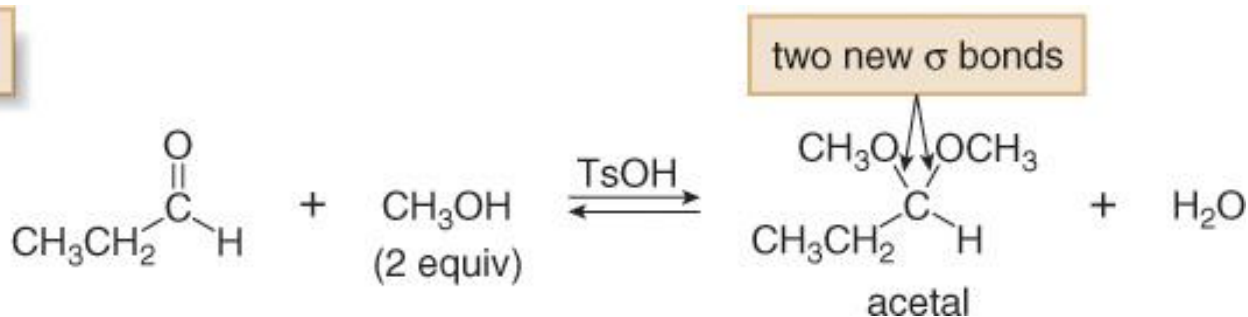


Addition of Alcohols—Acetal Formation

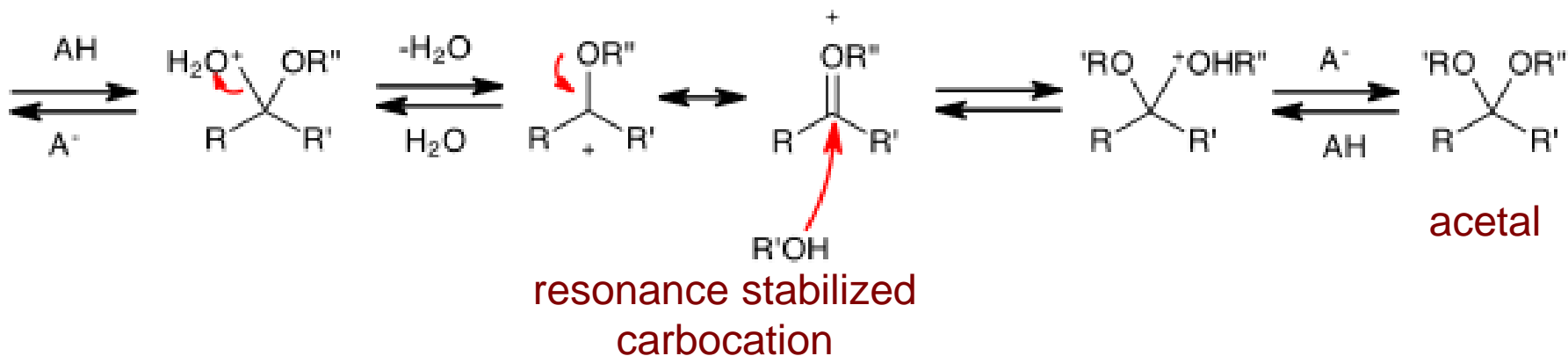
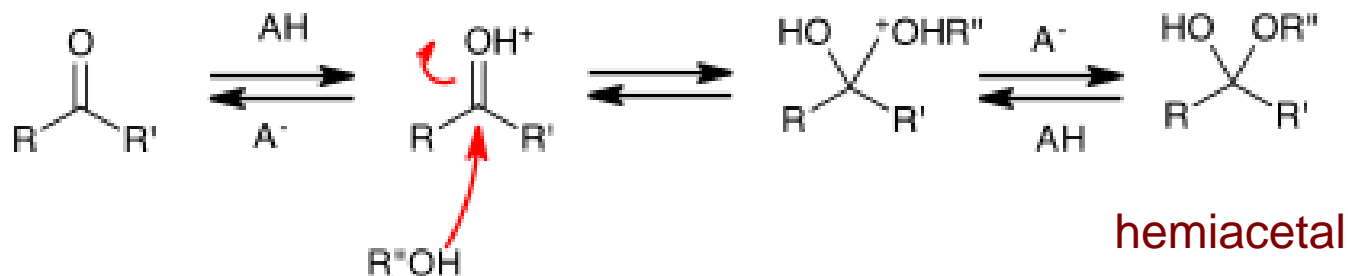
Acetal formation



Example

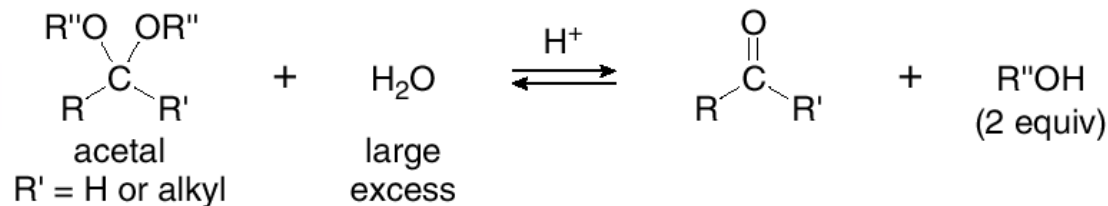


Addition of Alcohols—Acetal Formation

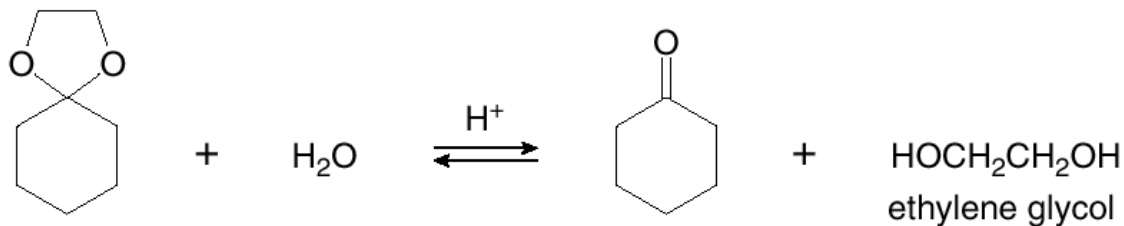


Acetal Hydrolysis

Acetal hydrolysis

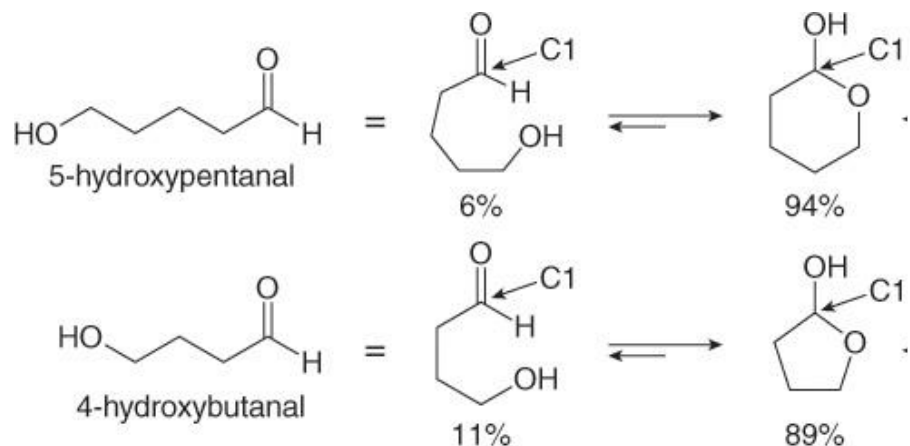


Example



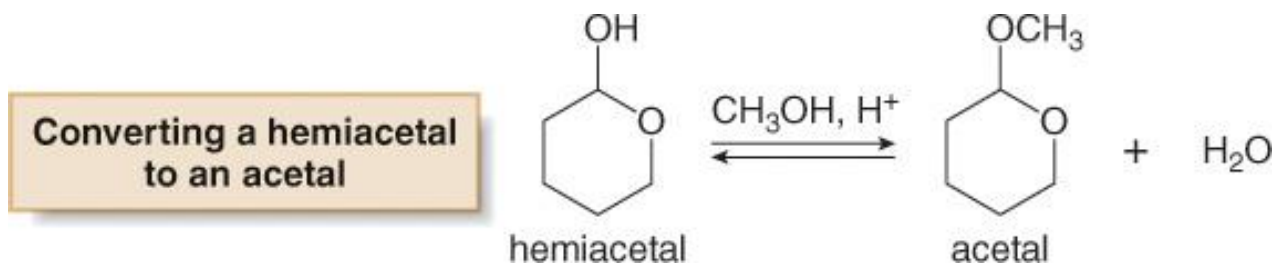
Cyclic Hemiacetals and Acetals

Cyclic hemiacetals are formed by intramolecular cyclization of hydroxy aldehydes.



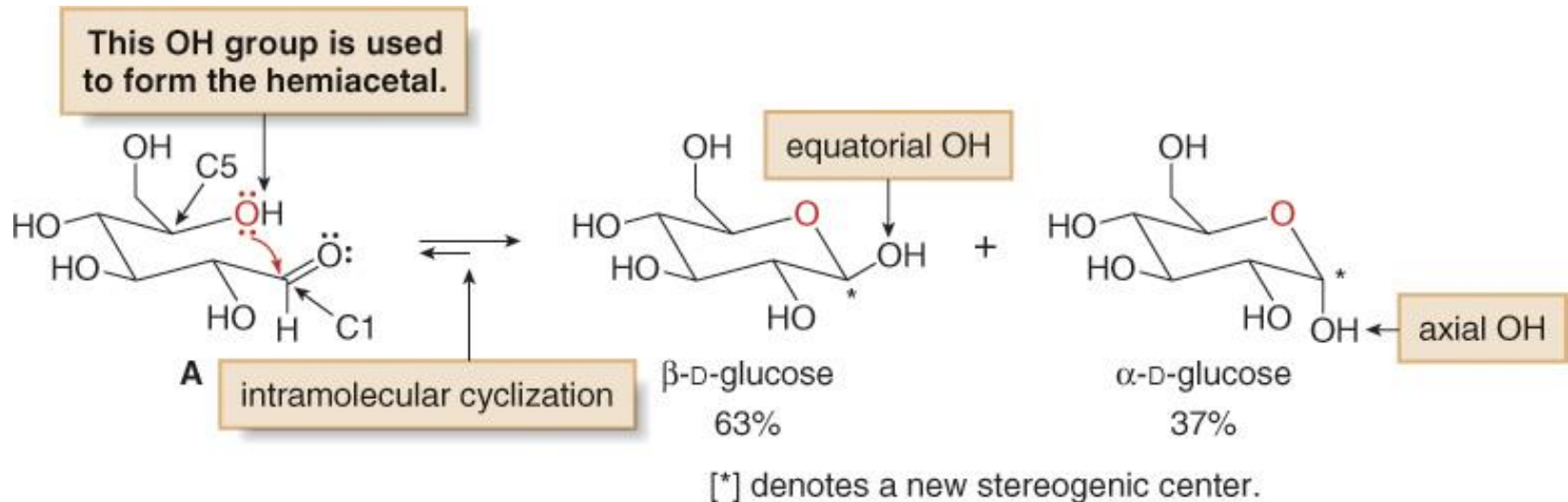
[Equilibrium proportions of each compound are given.]

Cyclic hemiacetals can be converted to acetals by treatment with an alcohol and acid.



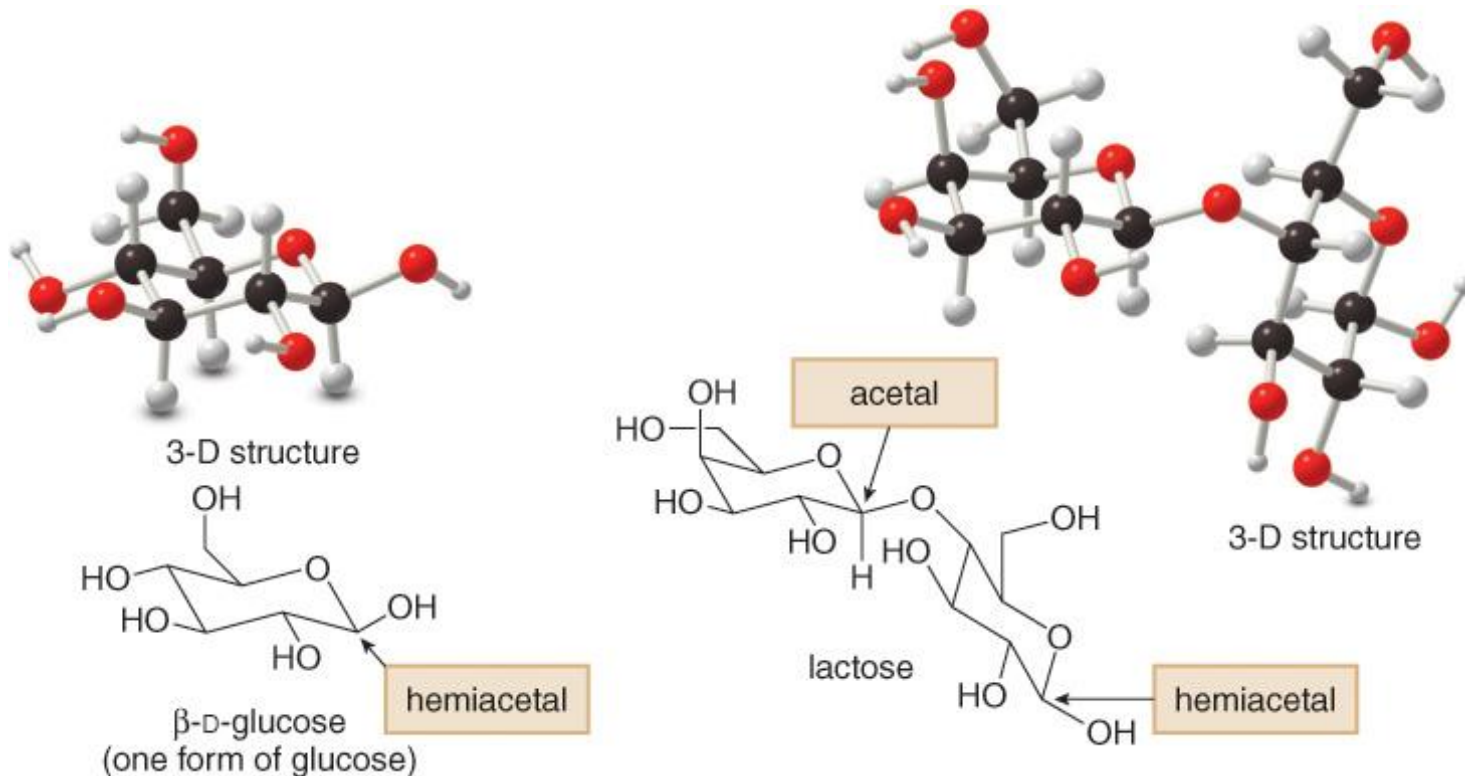
Introduction to Carbohydrates

- **Carbohydrates**, commonly referred to as sugars and starches, are **polyhydroxy aldehydes** and ketones, or compounds that can be hydrolyzed to them.
- Many carbohydrates contain cyclic acetals or hemiacetals. Examples include glucose and lactose.

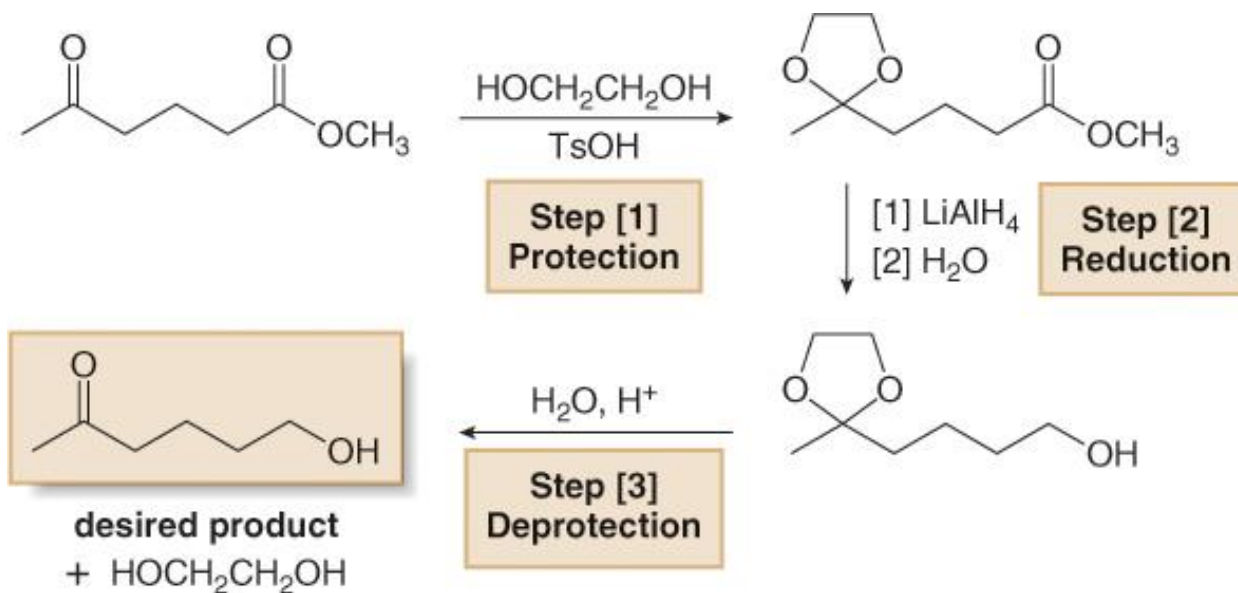
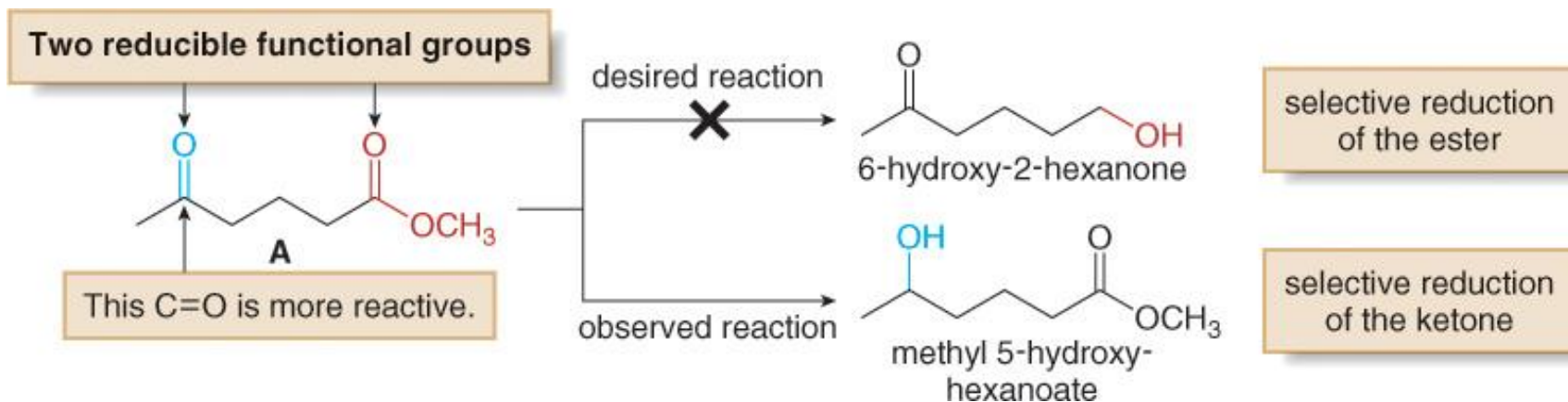


Introduction to Carbohydrates

- **Carbohydrates**, commonly referred to as sugars and starches, are **polyhydroxy aldehydes** and ketones, or compounds that can be hydrolyzed to them.
- Many carbohydrates contain cyclic acetals or hemiacetals. Examples include glucose and lactose.



Acetals as Protecting Groups



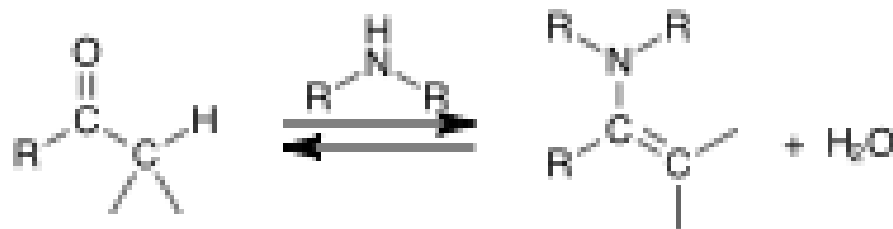
Addition of Amines

- Treatment of an aldehyde or a ketone with a 1ry amine affords an **imine** (also called a **Schiff base**).



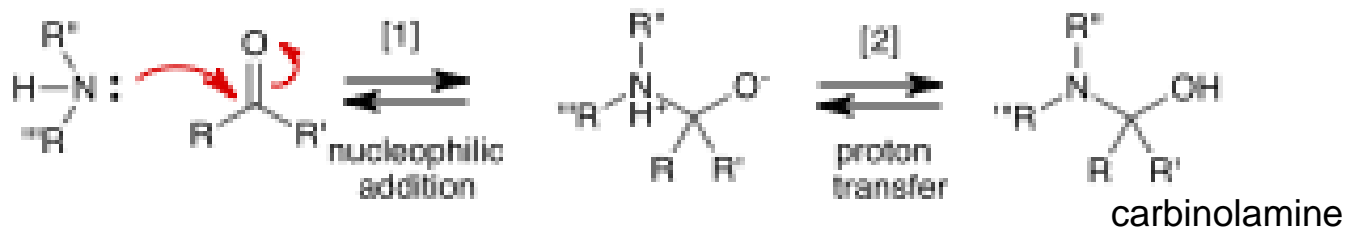
The N atom of an imine is sp^2 hybridized, making the C—N—R bond angle 120° , (not 180°).

- Treatment of an aldehyde or a ketone with a 2ry amine affords an **enamine**.

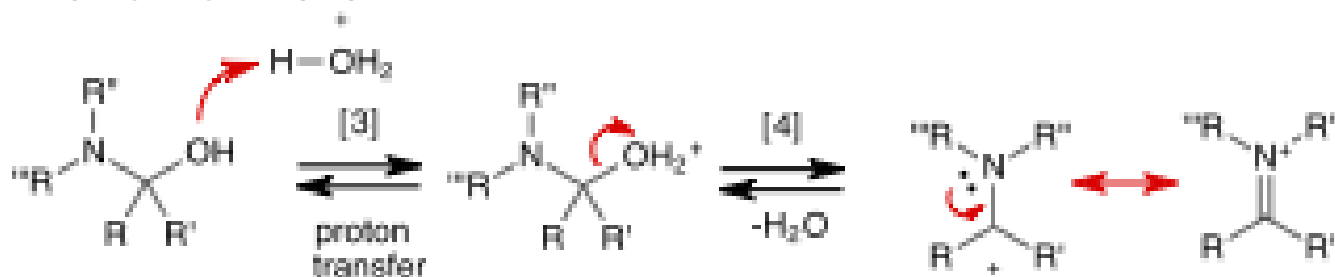


Imines and Enamines: Mechanism

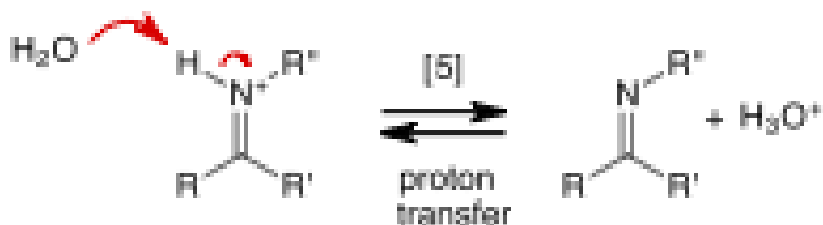
1. Amine addition



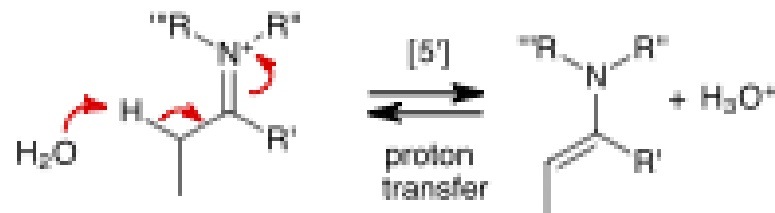
2. Elimination of water



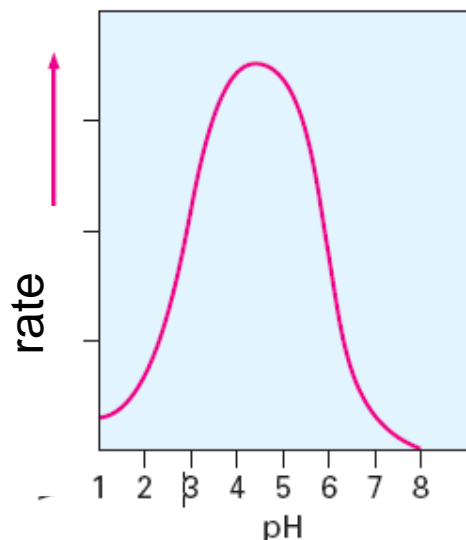
a: NH_3 , $\text{R}''\text{NH}_2$



b: $\text{R}''\text{R}'''\text{NH}$



Addition of Amines – Effect of pH



General pH-rate profile for addition of amines to carbonyl compounds

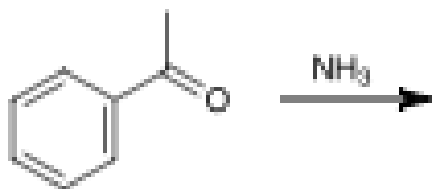
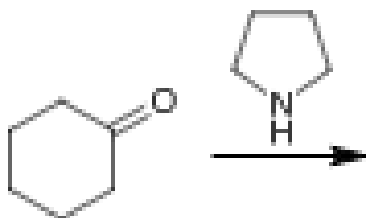


protonation activates the electrophile



protonation deactivates the nucleophile

Addition of Amines

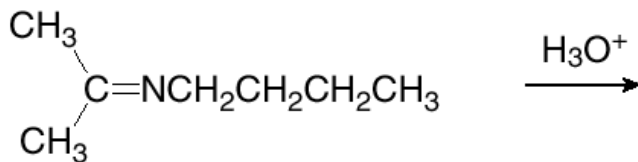


Imine and Enamine Hydrolysis

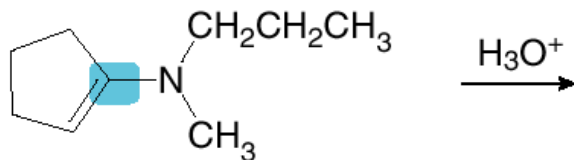
- Because imines and enamines are formed by a reversible set of reactions, both can be converted back to carbonyl compounds by **hydrolysis** with mild acid.
- The mechanism of hydrolysis is the exact reverse of the mechanism written for formation of imines and enamines.

- Hydrolysis of imines and enamines forms aldehydes and ketones.

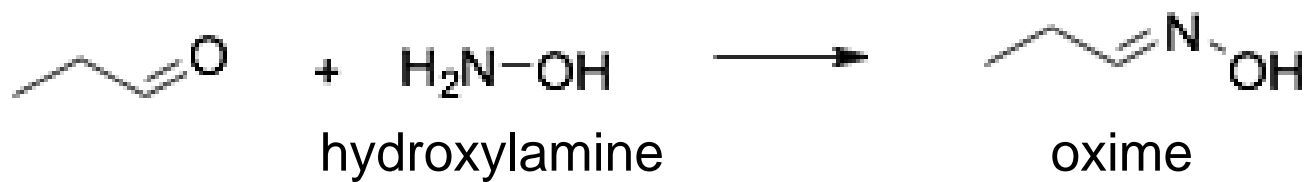
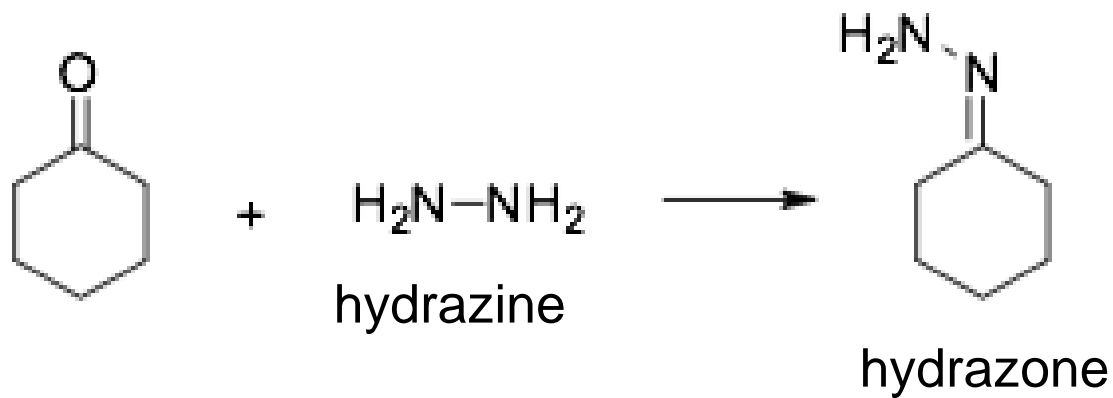
Imine hydrolysis



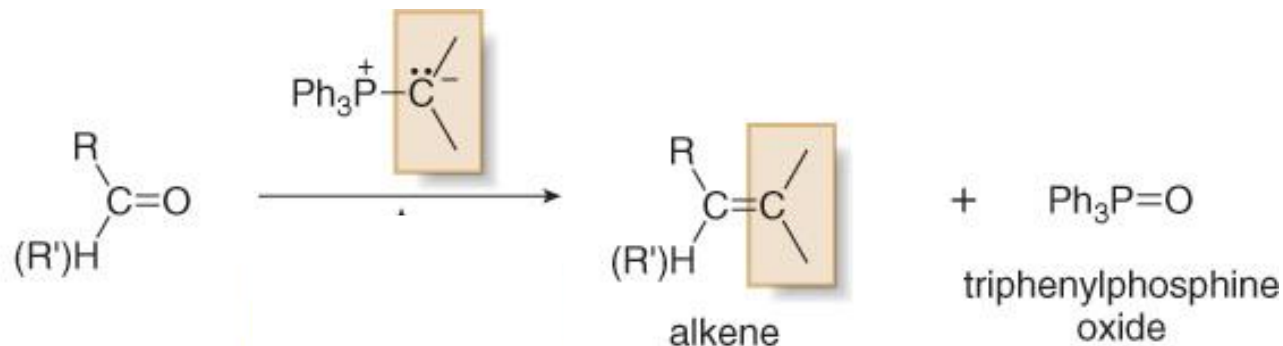
Enamine hydrolysis



Other Amines

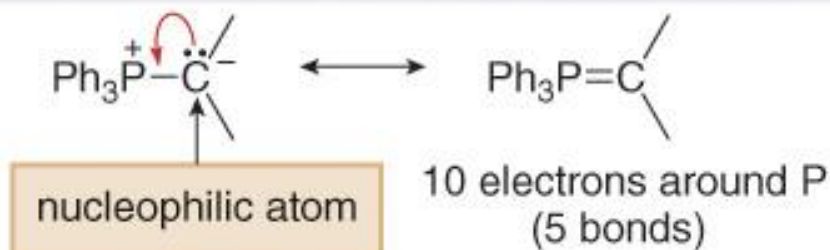


The Wittig Reaction

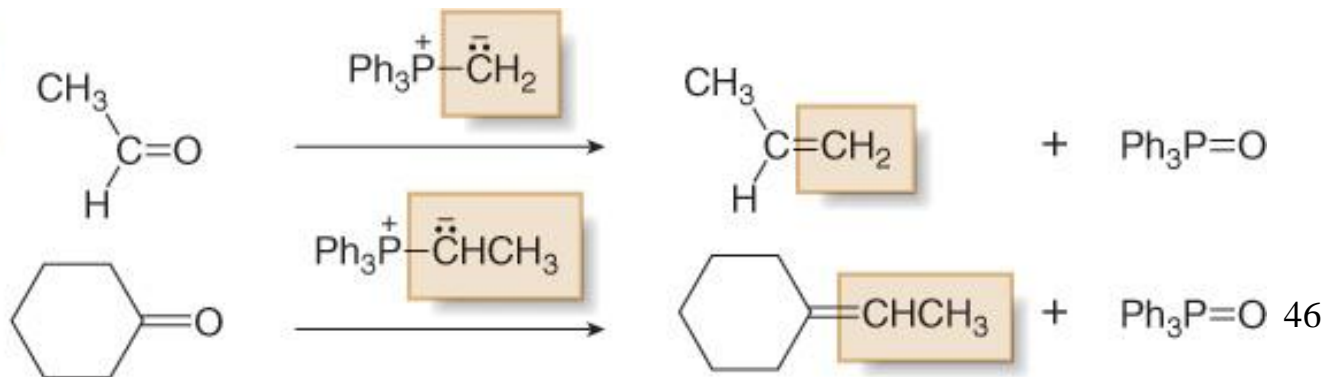


Two resonance structures for the Wittig reagent

phosphonium ylids
(Wittig reagents)



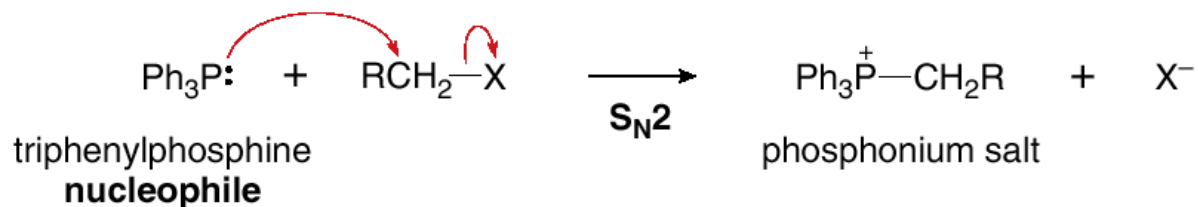
Examples



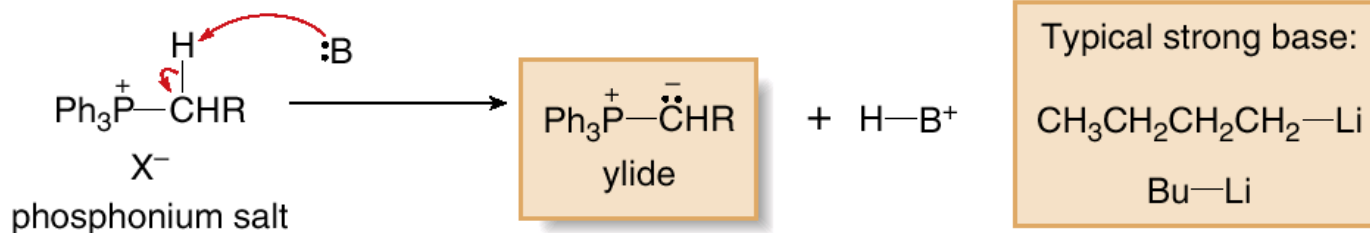
The Wittig Reaction

Preparation of phosphorus ylides (phosphoranes)

Step [1] S_N2 reaction of triphenylphosphine with an alkyl halide forms a phosphonium salt.

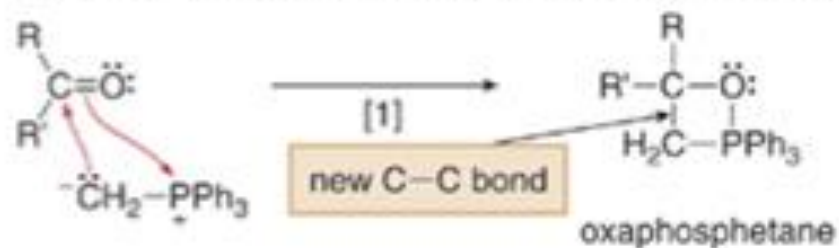


Step [2] Deprotonation of the phosphonium salt with a strong base (:B) forms the ylide.

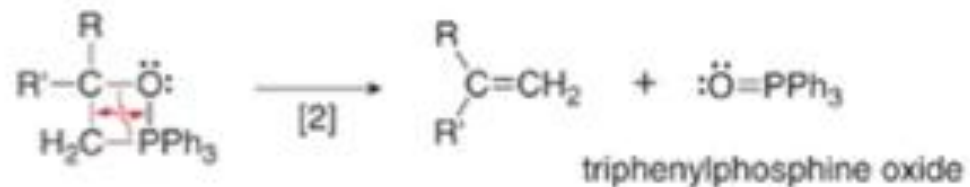


The Wittig Reaction

Step [1] Nucleophilic addition forms a four-membered ring.

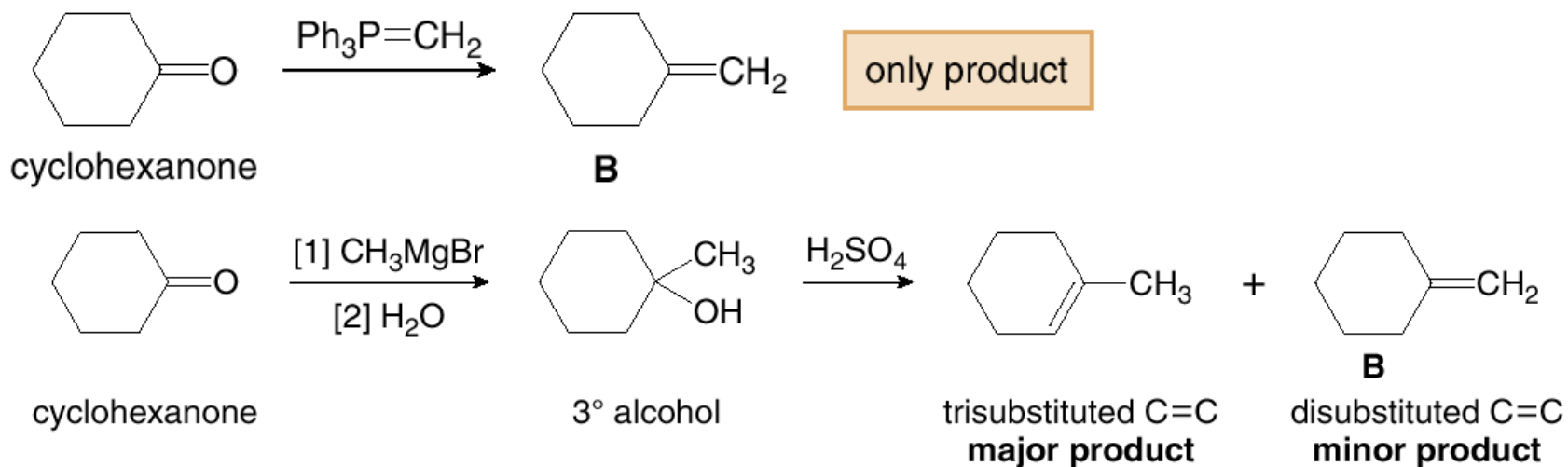


Step [2] Elimination of $\text{Ph}_3\text{P}=\text{O}$ forms the alkene.

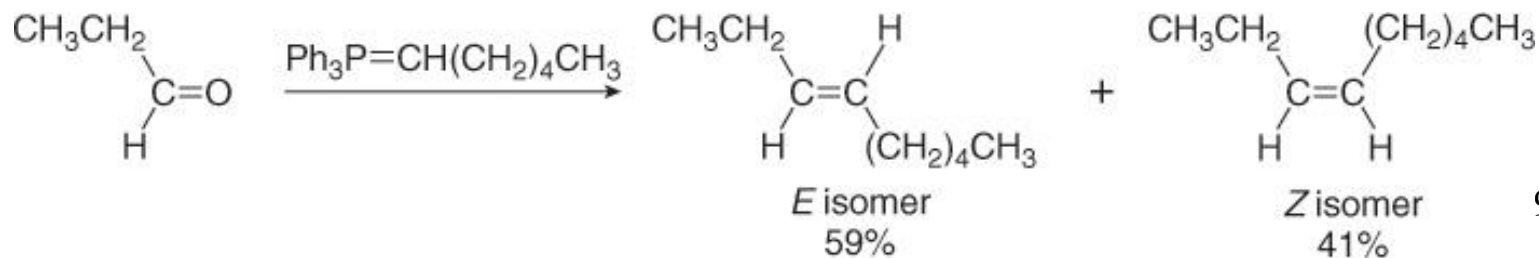


The Wittig Reaction

- Advantage:** the Wittig reaction always gives a single constitutional isomer.



- Limitation:** a mixture of stereoisomers is sometimes formed.

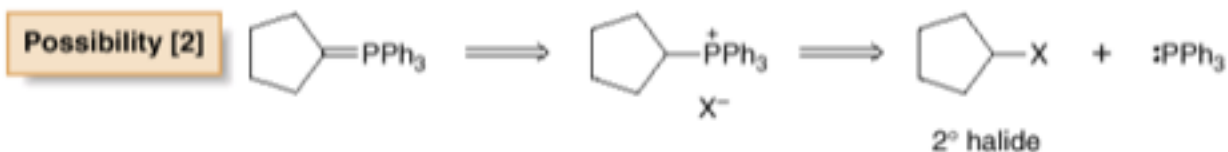
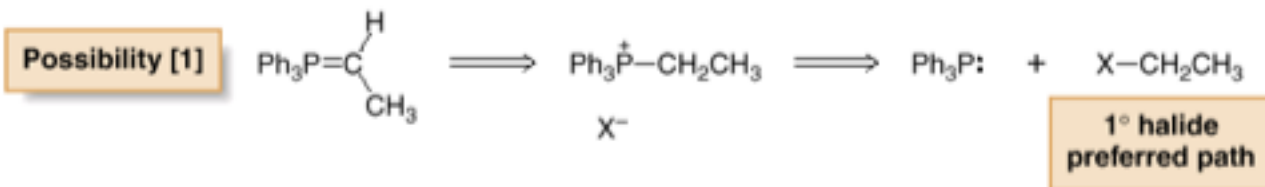
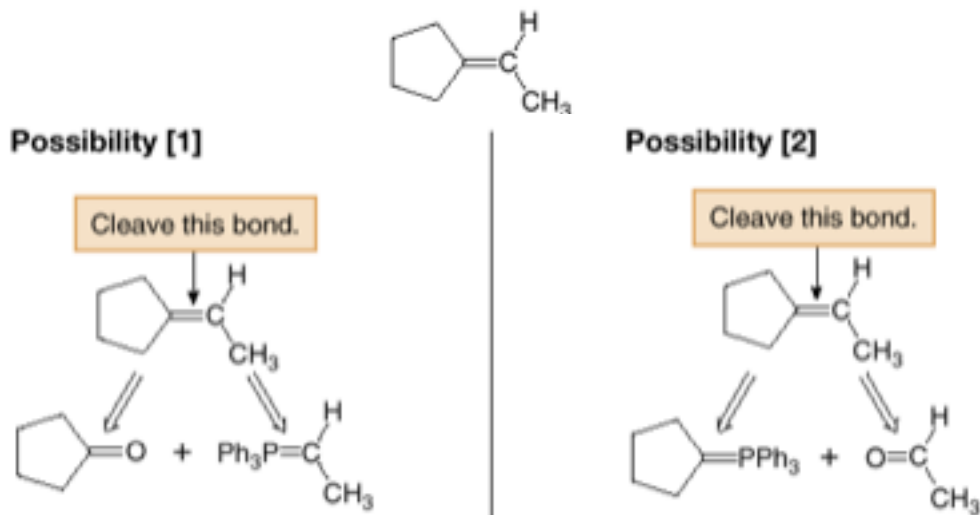


The Wittig Reaction

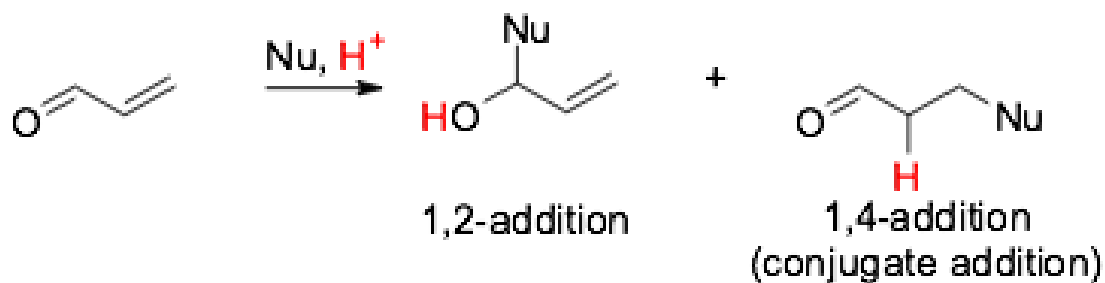
How To

Determine the Starting Materials for a Wittig Reaction Using Retrosynthetic Analysis

Example What starting materials are needed to synthesize alkene A by a Wittig reaction?

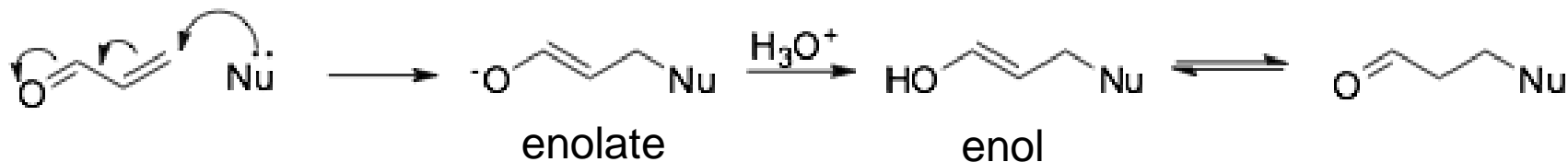


α,β -Unsaturated Carbonyl Compounds

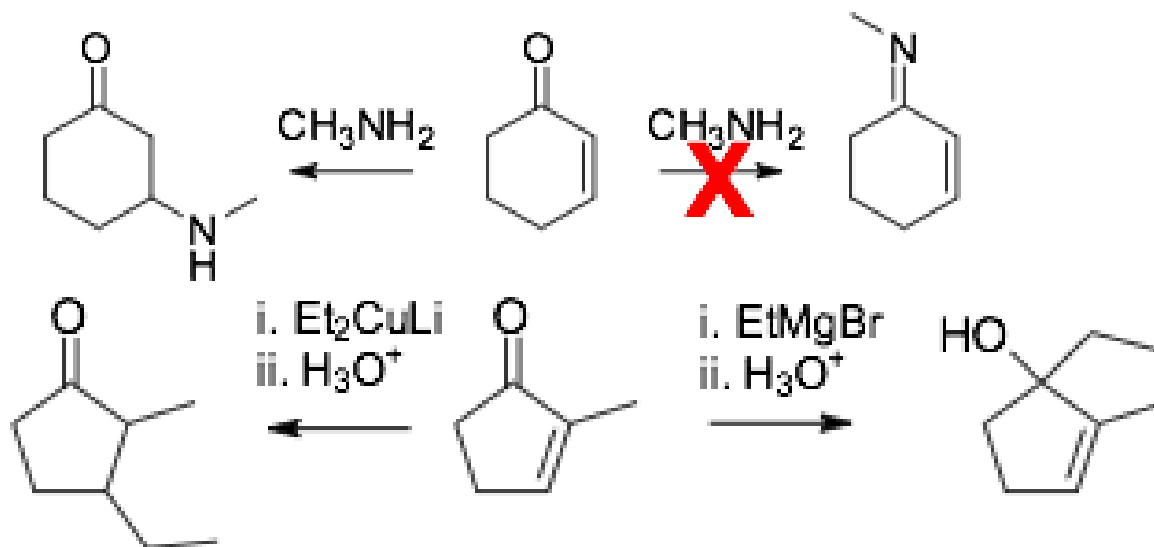


Conjugate Addition

general mechanism:

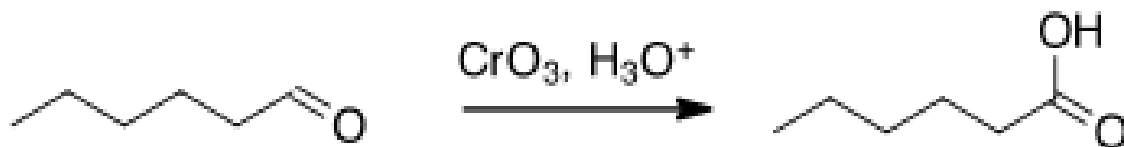


examples:

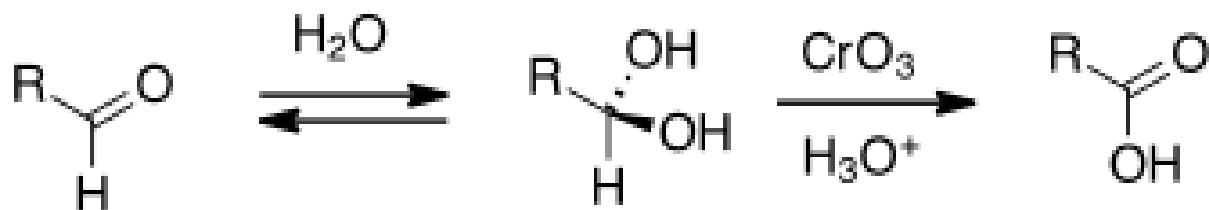


In generale nucleofili deboli come organocuprati danno addizione 1,4 mentre nucleofili forti come organolitio e reattivi di Grignard danno addizione 1,2.

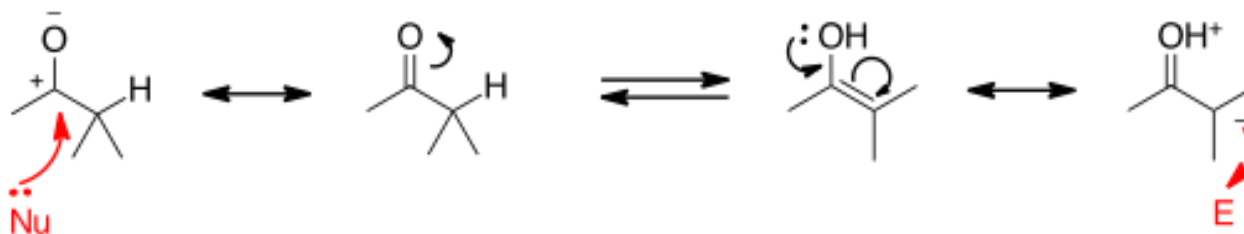
Oxidation



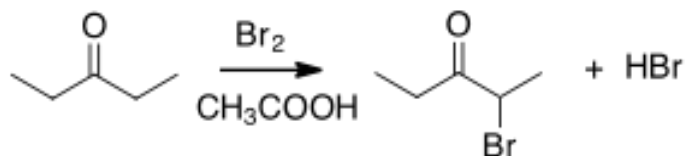
mechanism



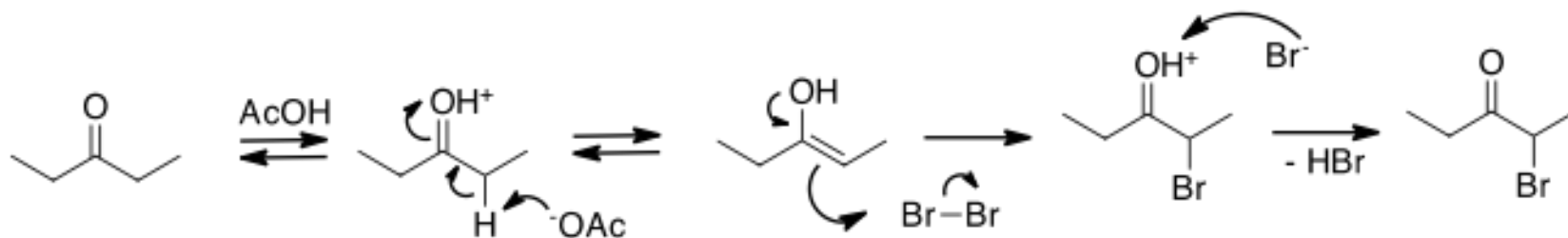
Keto-Enol Tautomerism. Reaction at the α -Carbon



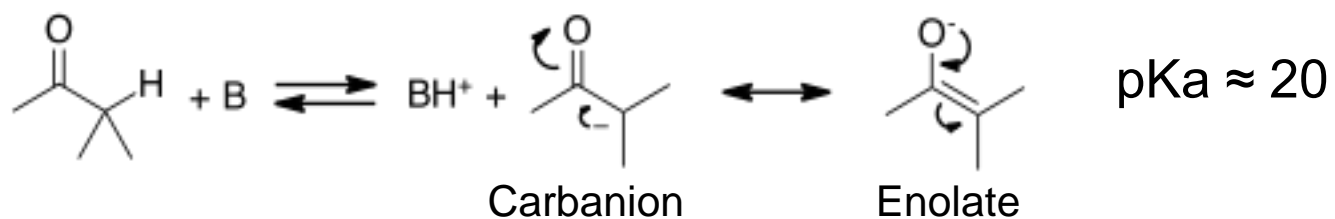
α -halogenation:



mechanism:



Enolates. Reaction at the α -Carbon



Example: 2-methylcyclohexanone

