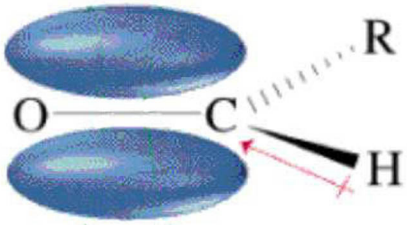

REACTIONS AND SPECTROSCOPY OF ALDEHYDES AND KETONES

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Shahid Matangini Hazra Govt. General Degree College for Women

Carbonyl Compounds

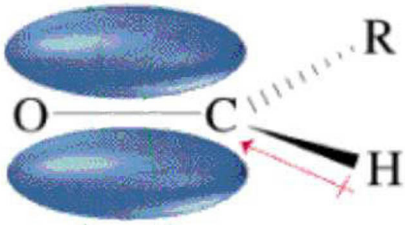
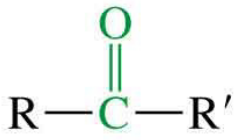
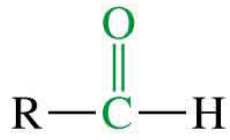
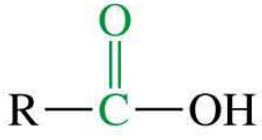
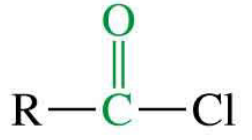
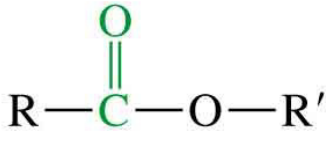
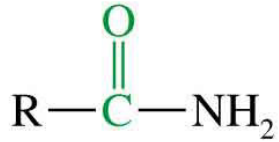


TABLE 18-1 Some Common Classes of Carbonyl Compounds

Class	General Formula	Class	General Formula
ketones		aldehydes	
carboxylic acids		acid chlorides	
esters		amides	

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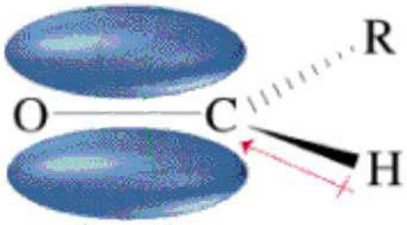
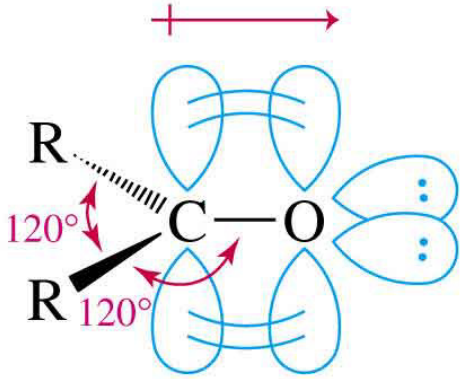
Carbonyl Structure



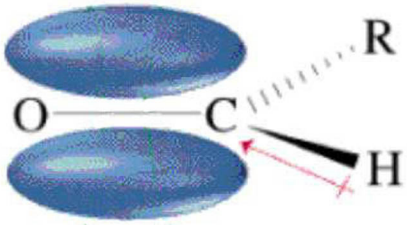
- Carbon is sp^2 hybridized.
- C=O bond is shorter, stronger, and more polar than C=C bond in alkenes.



	length	*energy*
ketone C=O bond	1.23 Å	178 kcal/mol (745 kJ/mol)
alkene C=C bond	1.34 Å	146 kcal/mol (611 kJ/mol)

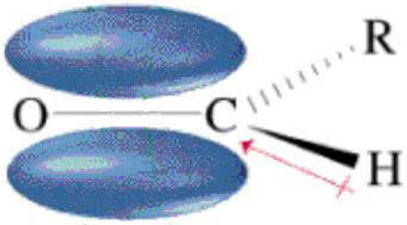
=>

IUPAC Names for Ketones

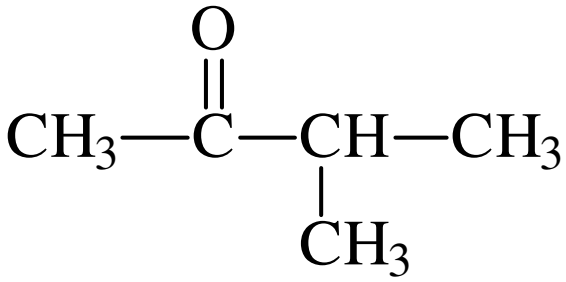


- Replace -*e* with -*one*. Indicate the position of the carbonyl with a number.
- Number the chain so that carbonyl carbon has the lowest number.
- For cyclic ketones the carbonyl carbon is assigned the number 1.

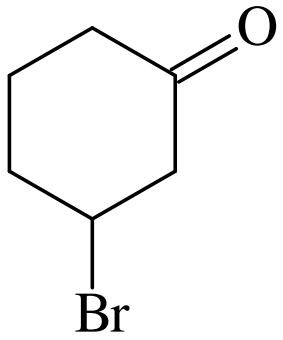
=>



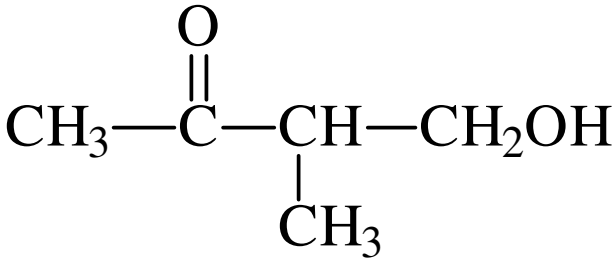
Examples



3-methyl-2-butanone

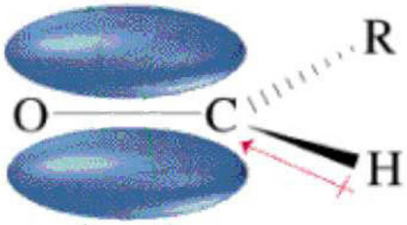


3-bromocyclohexanone



4-hydroxy-3-methyl-2-butanone

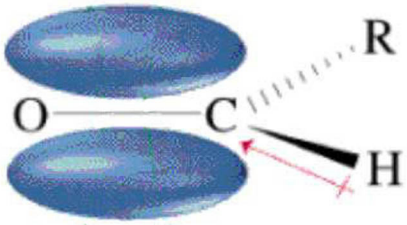
=>



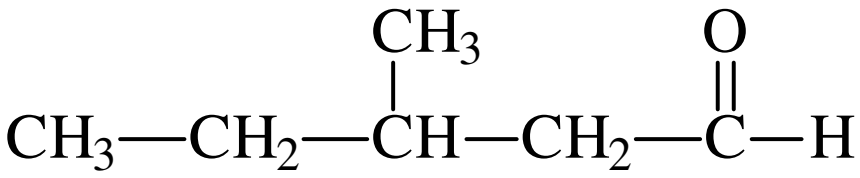
Naming Aldehydes

- IUPAC: Replace -*e* with -*al*.
- The aldehyde carbon is number 1.
- If -CHO is attached to a ring, use the suffix -*carbaldehyde*.

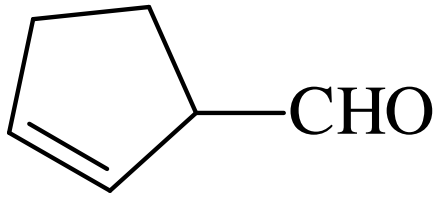
=>



Examples



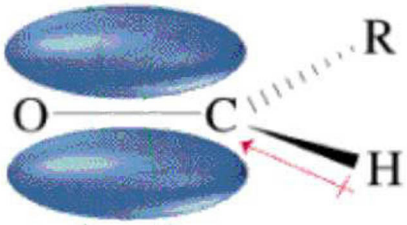
3-methylpentanal



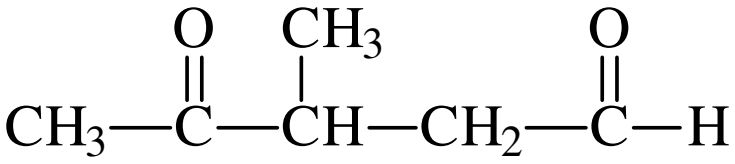
2-cyclopentenecarbaldehyde

=>

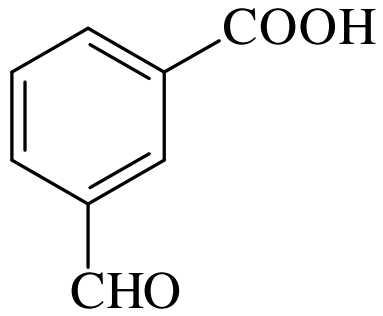
Name as Substituent



- On a molecule with a higher priority functional group, C=O is *oxo*- and -CHO is *formyl.*
- Aldehyde priority is higher than ketone.



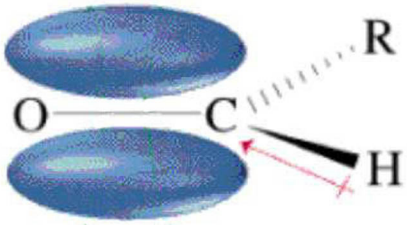
3-methyl-4-oxopentanal



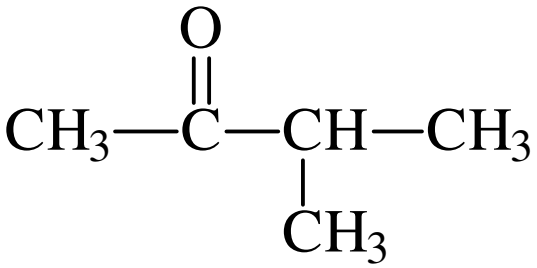
3-formylbenzoic acid

=>

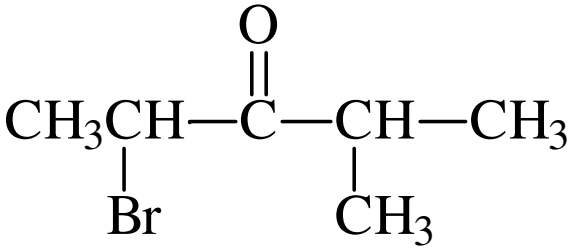
Common Names for Ketones



- Named as alkyl attachments to -C=O.
- Use Greek letters instead of numbers.



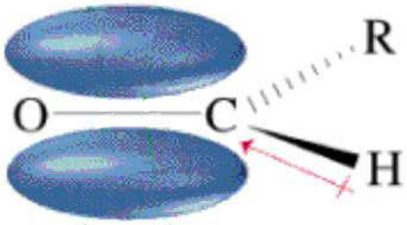
methyl isopropyl ketone

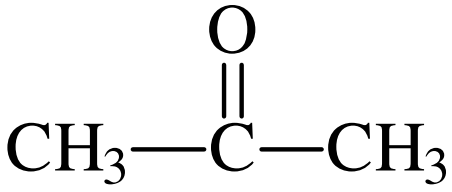


α–bromoethyl isopropyl ketone

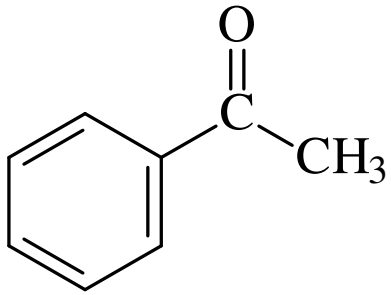
=>

Historical Common Names

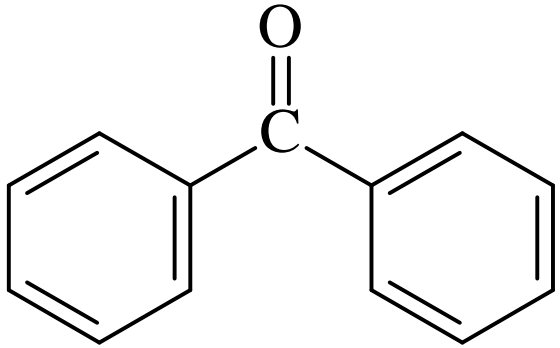




acetone



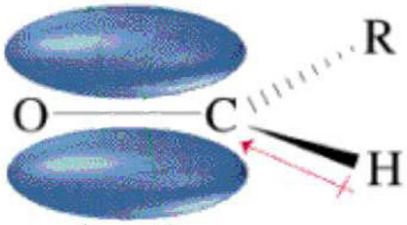
acetophenone



benzophenone

=>

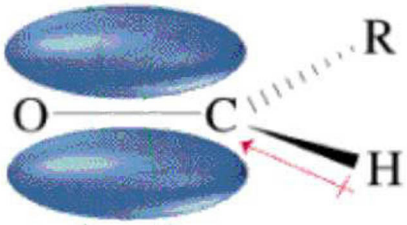
Aldehyde Common Names



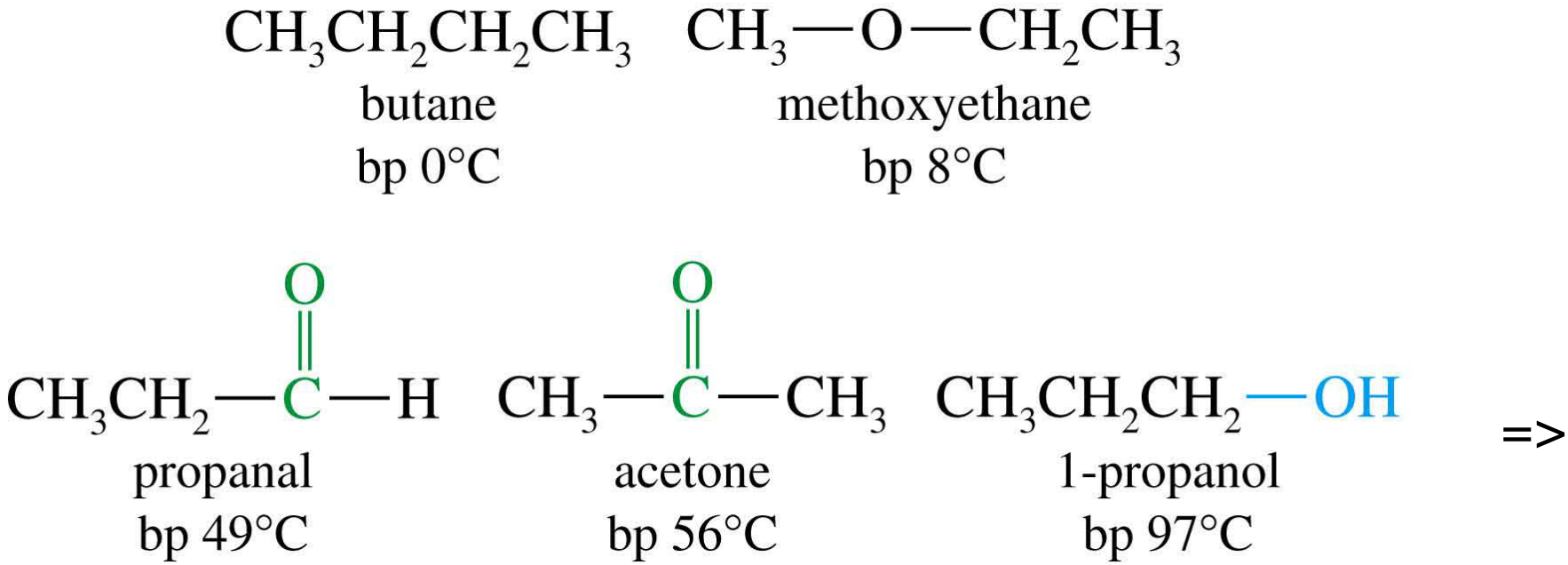
- Use the common name of the acid.
- Drop -*ic acid* and add -*aldehyde*.
  - 1 C: formic acid, formaldehyde
  - 2 C's: acetic acid, acetaldehyde
  - 3 C's: propionic acid, propionaldehyde
  - 4 C's: butyric acid, butyraldehyde.

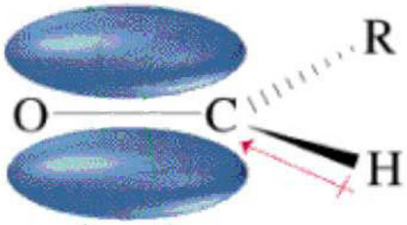
=>

Boiling Points



- More polar, so higher boiling point than comparable alkane or ether.
- Cannot H-bond to each other, so lower boiling point than comparable alcohol.

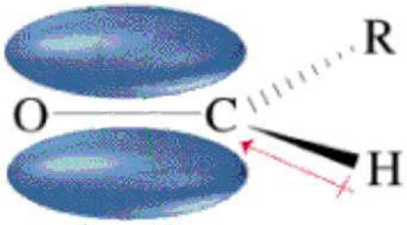




Solubility

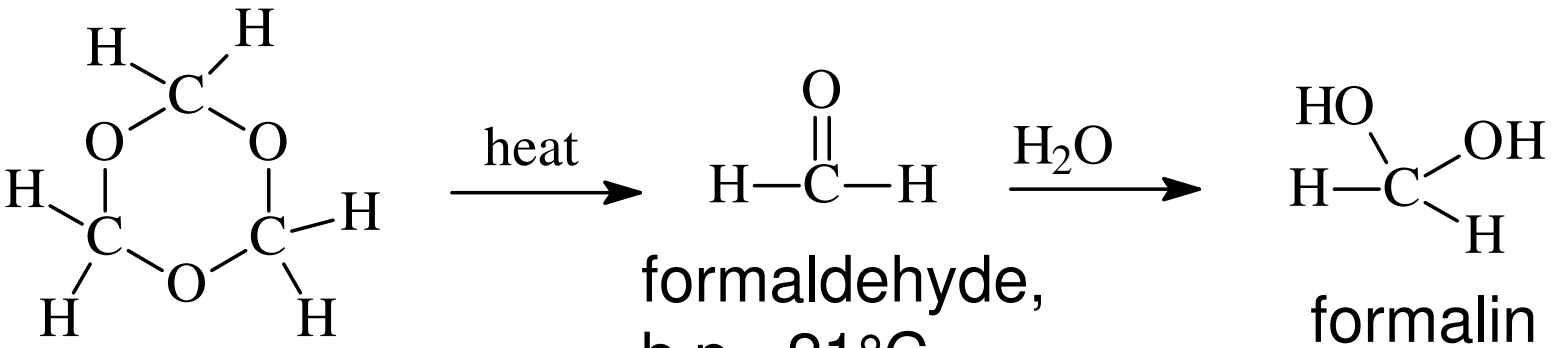
- Good solvent for alcohols.
- Lone pair of electrons on oxygen of carbonyl can accept a hydrogen bond from O-H or N-H.
- Acetone and acetaldehyde are miscible in water.

=>



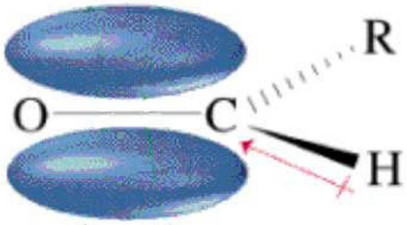
Formaldehyde

- Gas at room temperature.
- Formalin is a 40% aqueous solution.



trioxane, m.p. 62°C

=>

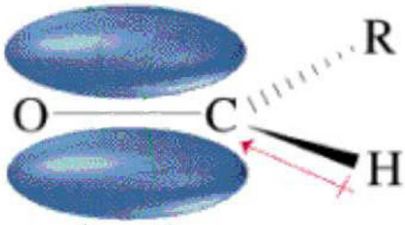


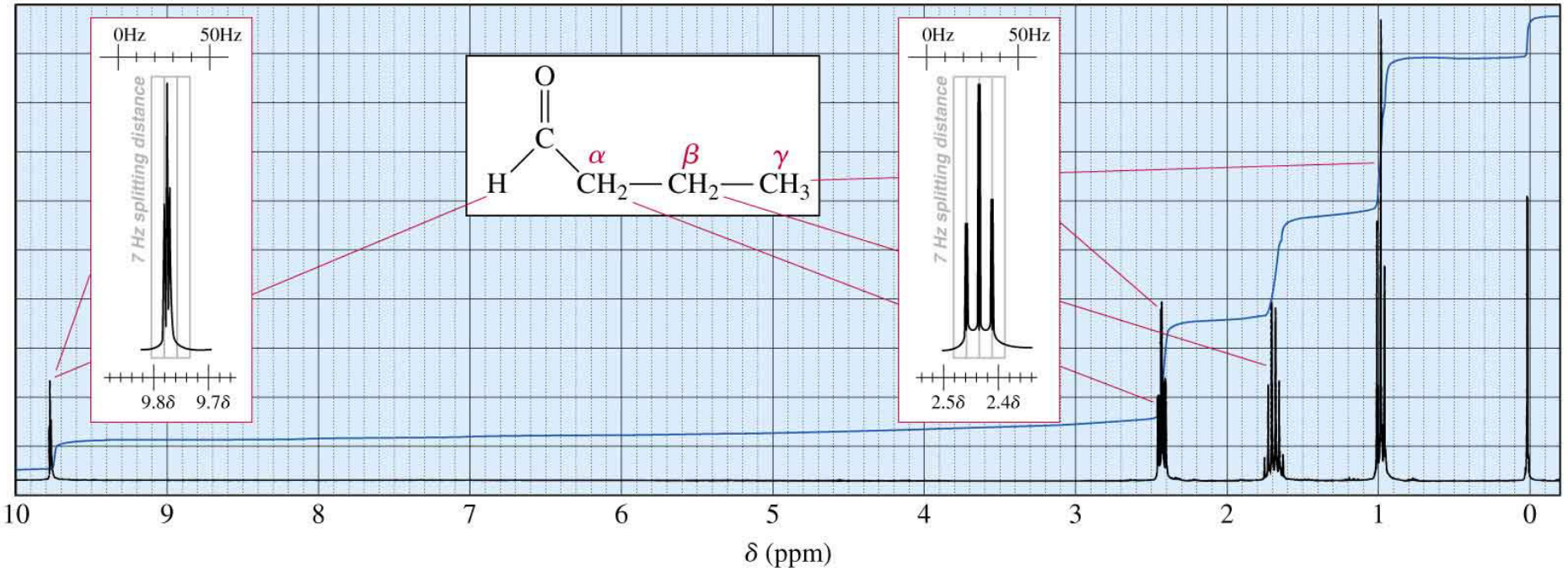
IR Spectroscopy

- Very strong C=O stretch around 1710 cm^{-1}.
- Conjugation lowers frequency.
- Ring strain raises frequency.
- Additional C-H stretch for aldehyde: two absorptions at 2710 cm^{-1} and 2810 cm^{-1}.

=>

^{1}H NMR Spectroscopy





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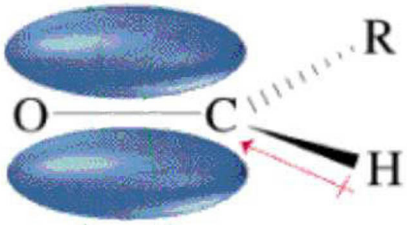
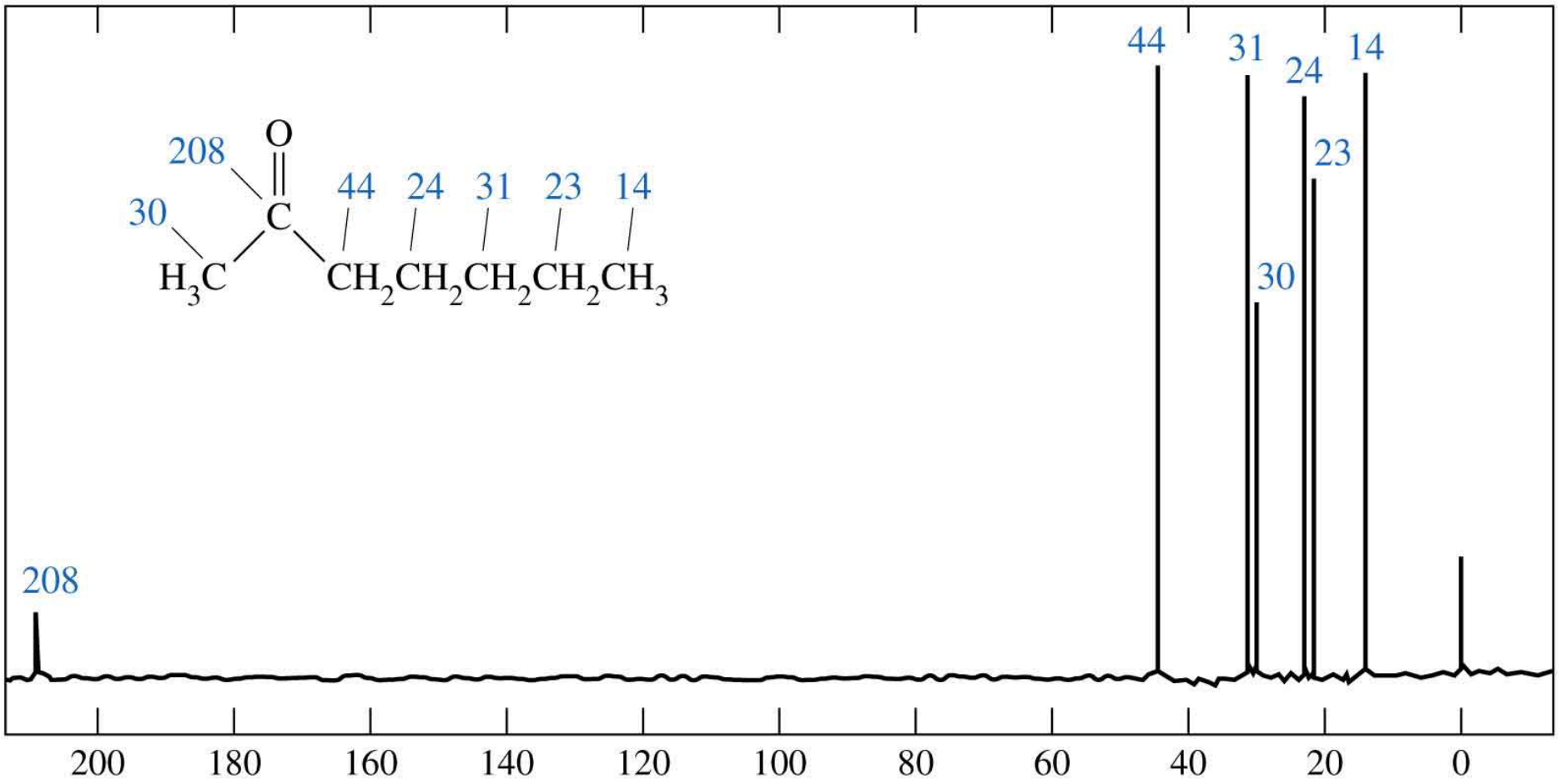
^{13}C NMR Spectroscopy





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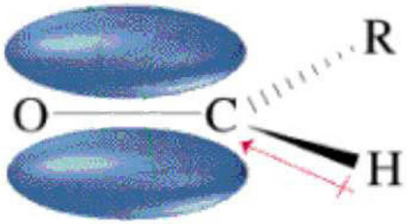
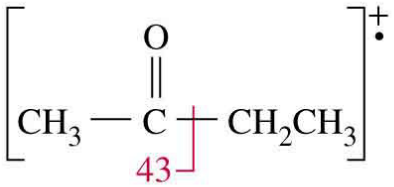
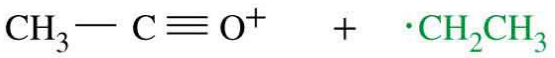
MS for 2-Butanone



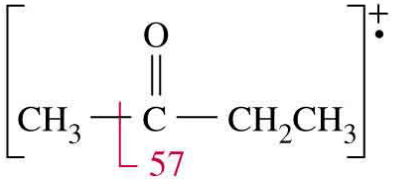


radical cation
m/z 72

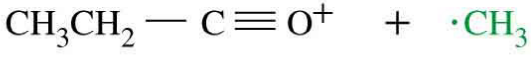


acylium ion
m/z 43 (base peak)

ethyl radical
loss of 29

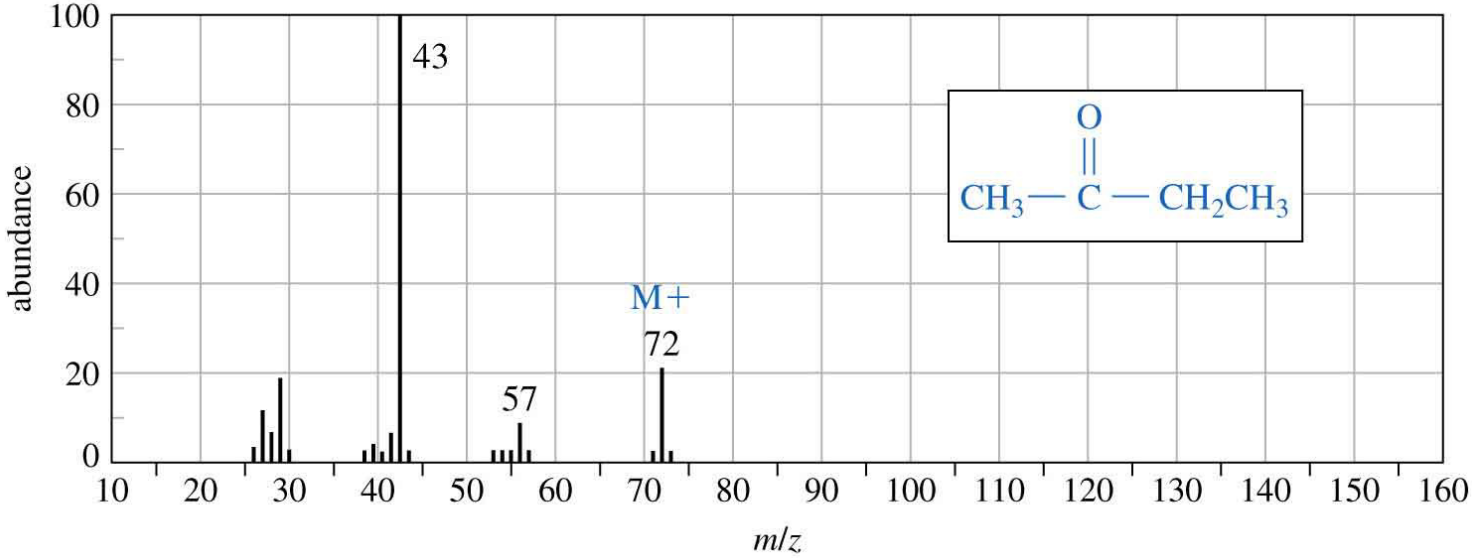


radical cation
m/z 72



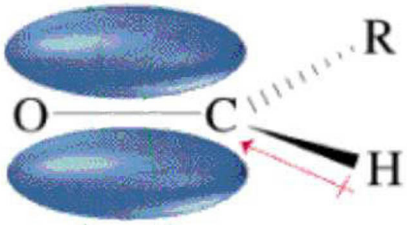
acylium ion
m/z 57

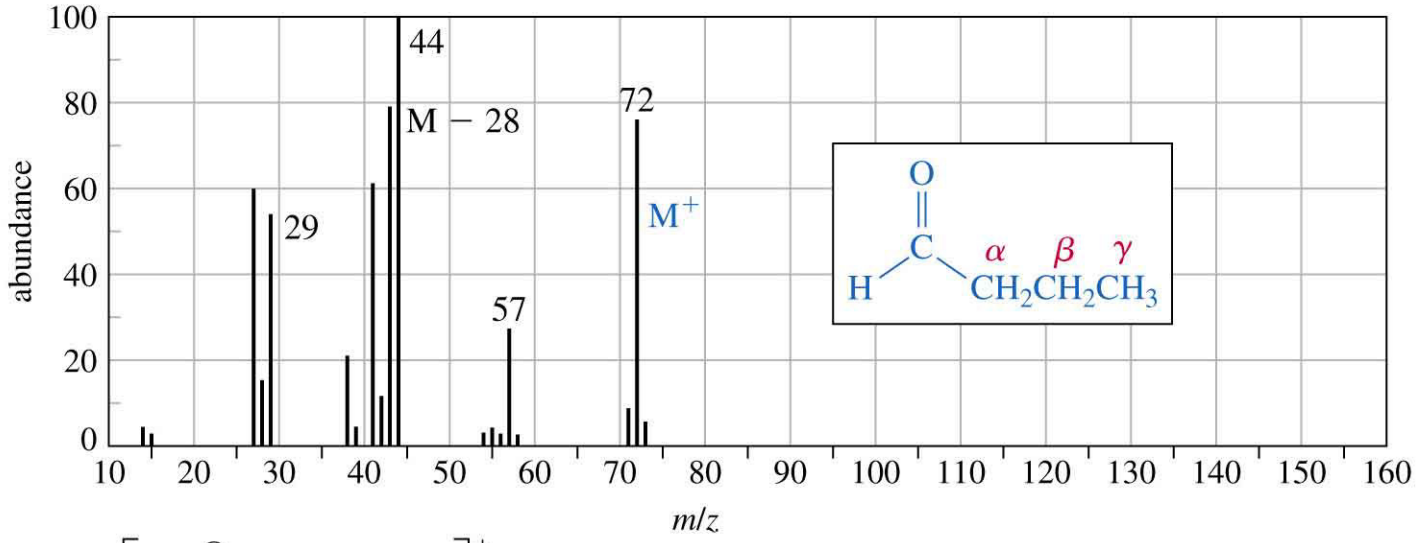
methyl radical
loss of 15

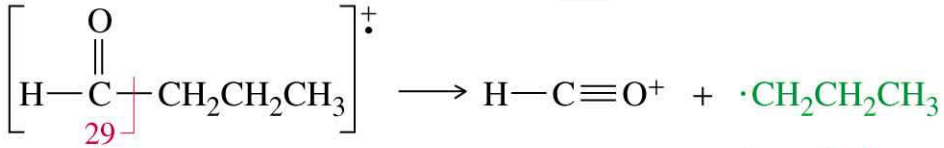


=>

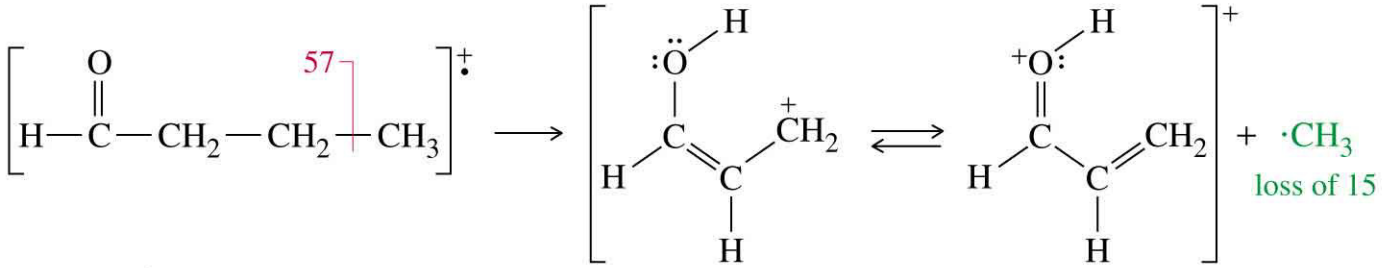
MS for Butyraldehyde







m/z 72 *m/z* 29 loss of 43



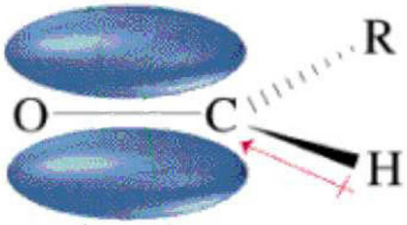
loss of 15

β, γ cleavage stabilized cation *m/z* 57

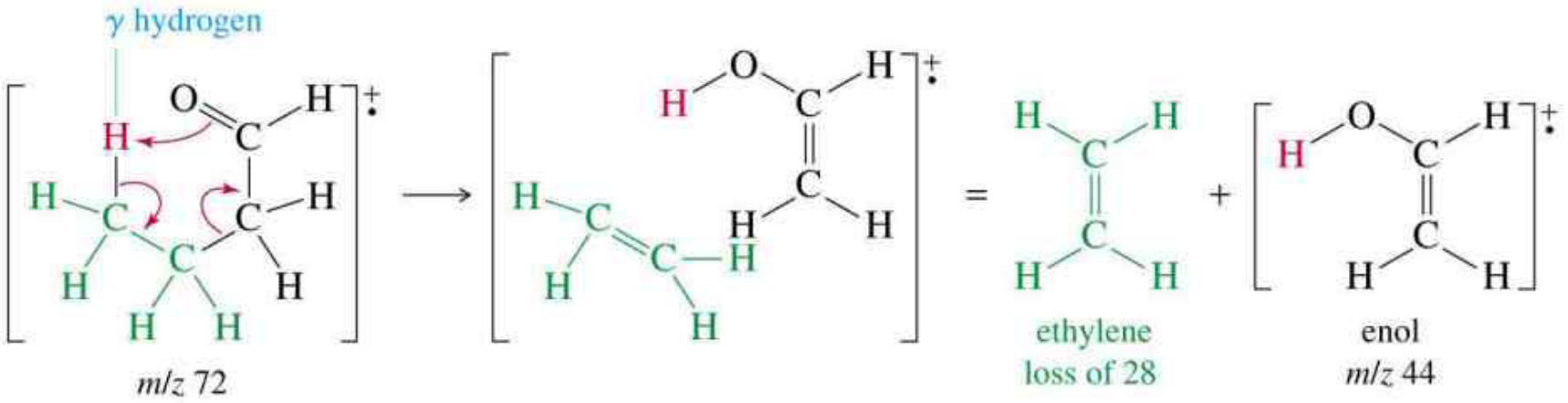
=>

McLafferty rearrangement *m/z* 72 ⟶ *m/z* 44 (base peak) + loss of 28

McLafferty Rearrangement



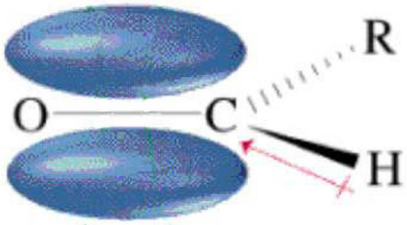
- Loss of alkene (even mass number)
- Must have γ-hydrogen



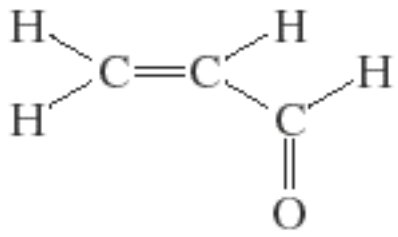
McLafferty rearrangement of butyraldehyde

=>

UV Spectra, $\pi \rightarrow \pi^*$

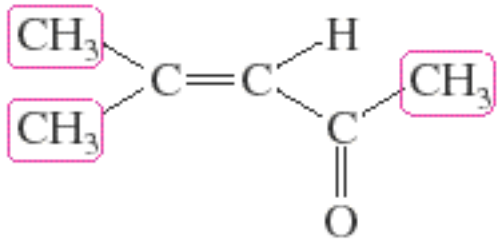


- C=O conjugated with another double bond.
- Large molar absorptivities (> 5000)



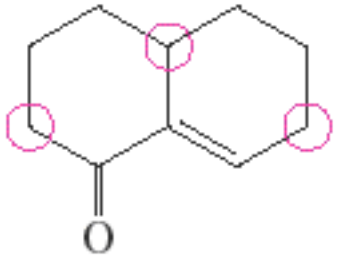
propenal

λ_{max} = 210 nm, ε = 11,000



three alkyl groups

λ_{max} = 237 nm, ε = 12,000

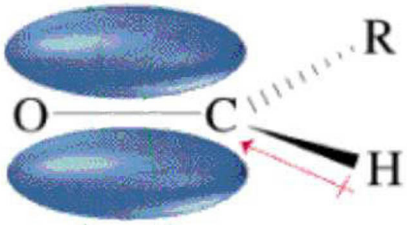


three alkyl groups

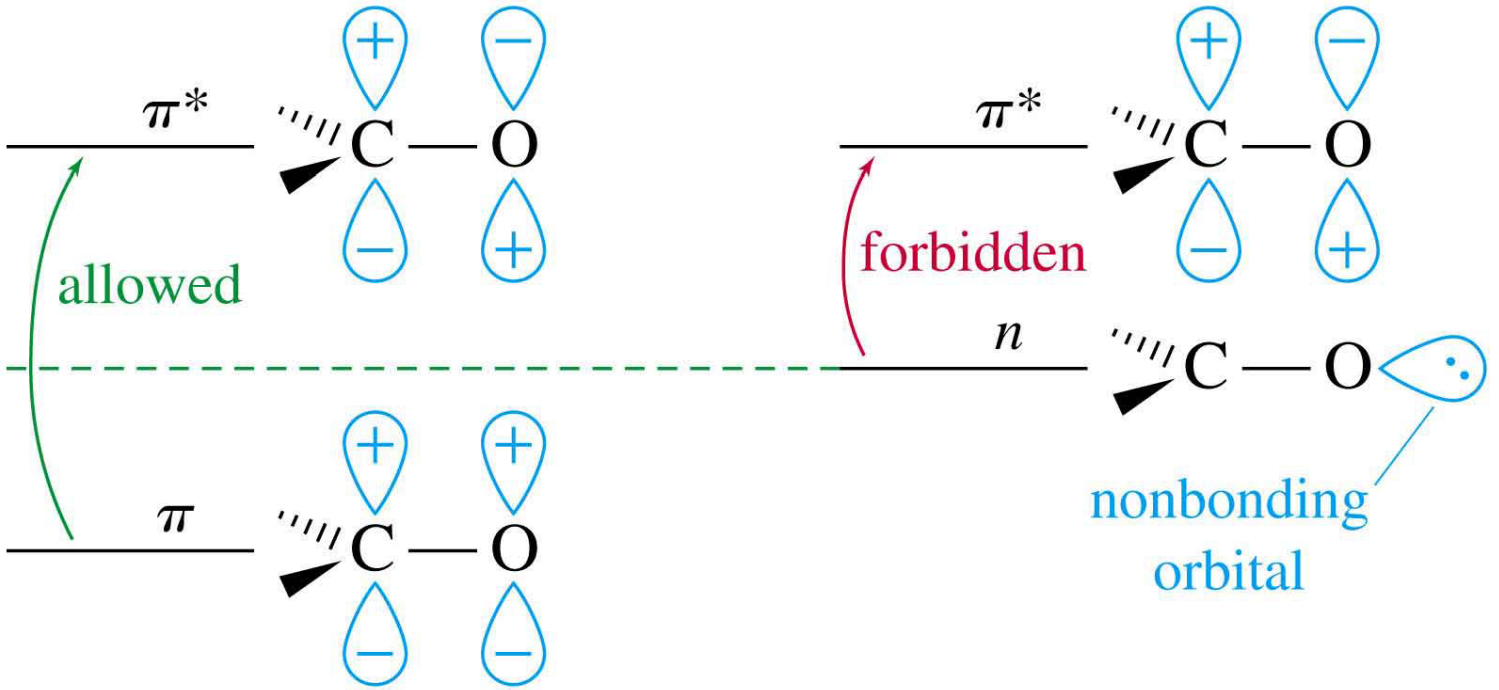
λ_{max} = 244 nm, ε = 12,500

=>

UV Spectra, $n \rightarrow \pi^*$



- Small molar absorptivity.
- "Forbidden" transition occurs less frequently.



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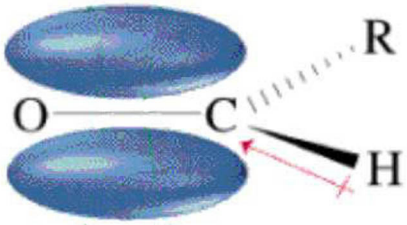
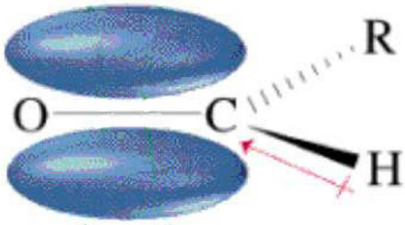
Industrial Importance



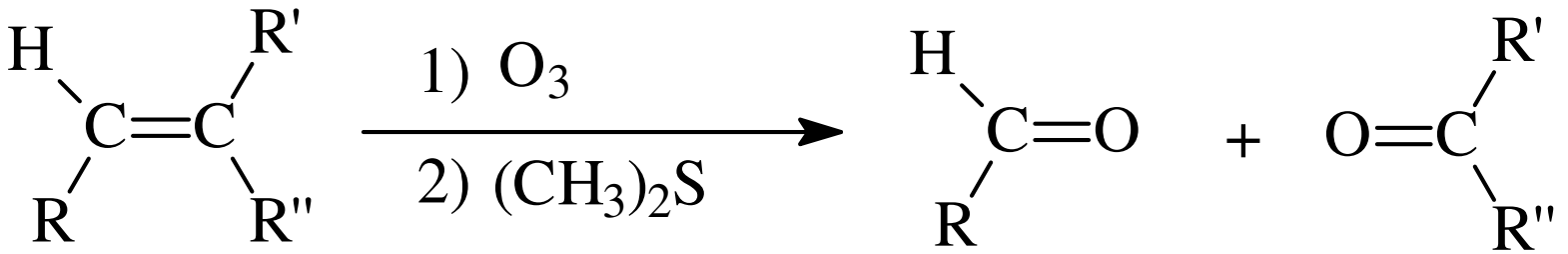
- Acetone and methyl ethyl ketone are important solvents.
- Formaldehyde used in polymers like Bakelite®.
- Flavorings and additives like vanilla, cinnamon, artificial butter.

=>

Synthesis Review



- Oxidation
  - 2° alcohol + $Na_2Cr_2O_7$ → ketone
  - 1° alcohol + PCC → aldehyde
- Ozonolysis of alkenes.



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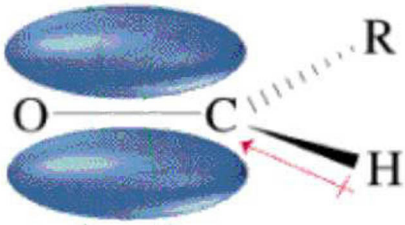
Synthesis Review (2)



- Friedel-Crafts acylation
  - Acid chloride/$AlCl_3$ + benzene $\rightarrow$ ketone
  - $CO + HCl + AlCl_3/CuCl$ + benzene $\rightarrow$ benzaldehyde (Gatterman-Koch)
- Hydration of terminal alkyne
  - Use $HgSO_4$, H_2SO_4, H_2O for methyl ketone
  - Use Sia_2BH followed by H_2O_2 in NaOH for aldehyde.

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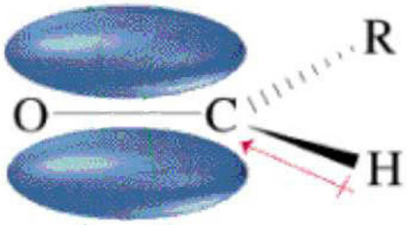
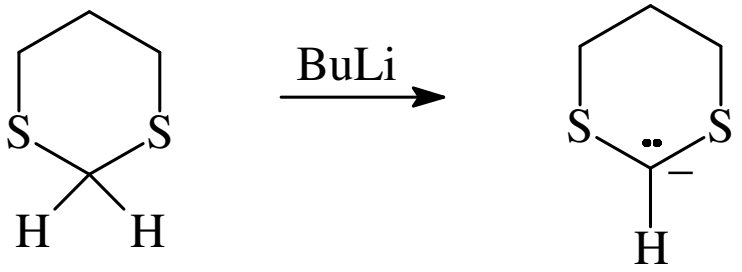
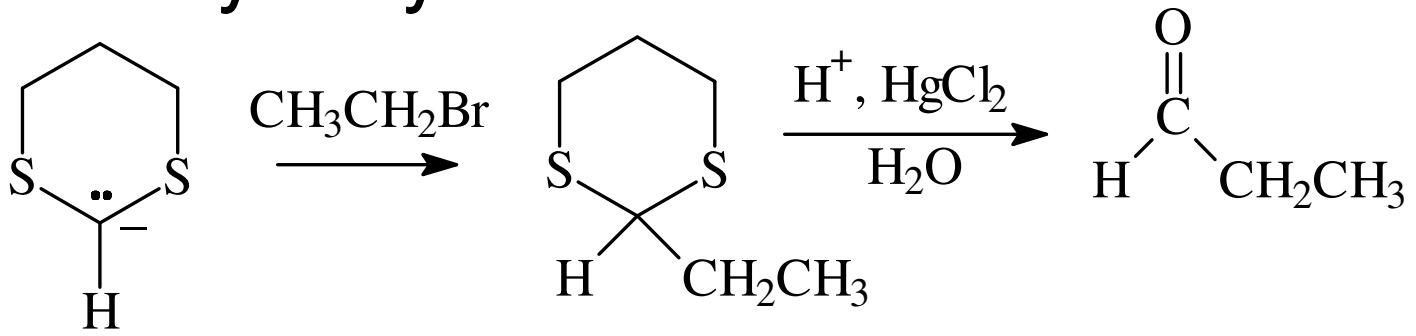
Synthesis Using 1,3-Dithiane



- Remove H^+ with *n*-butyllithium.



- Alkylate with primary alkyl halide, then hydrolyze.



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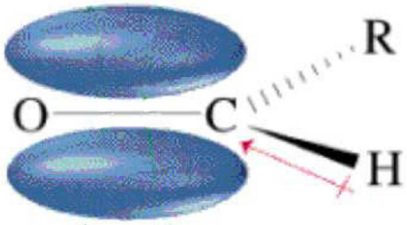
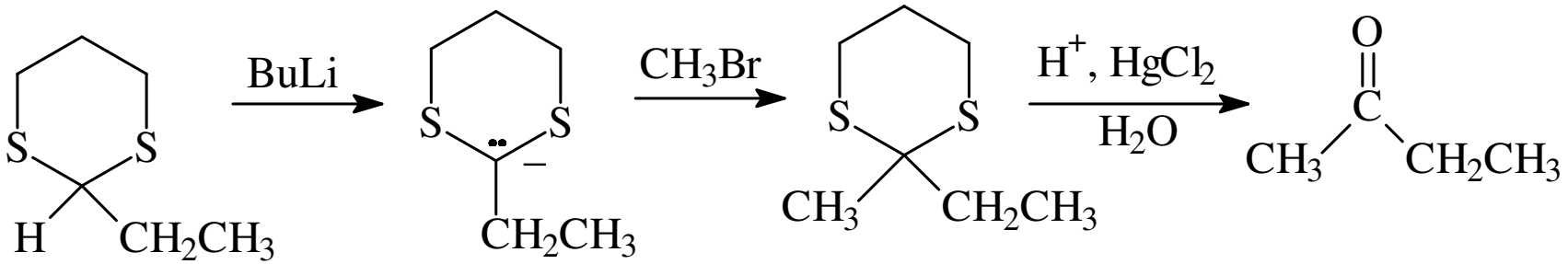
Ketones from 1,3-Dithiane



- After the first alkylation, remove the second H^+, react with another primary alkyl halide, then hydrolyze.



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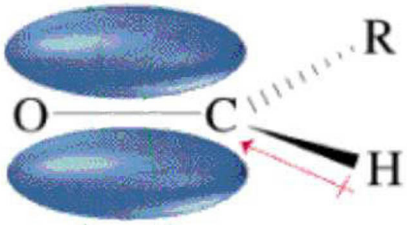
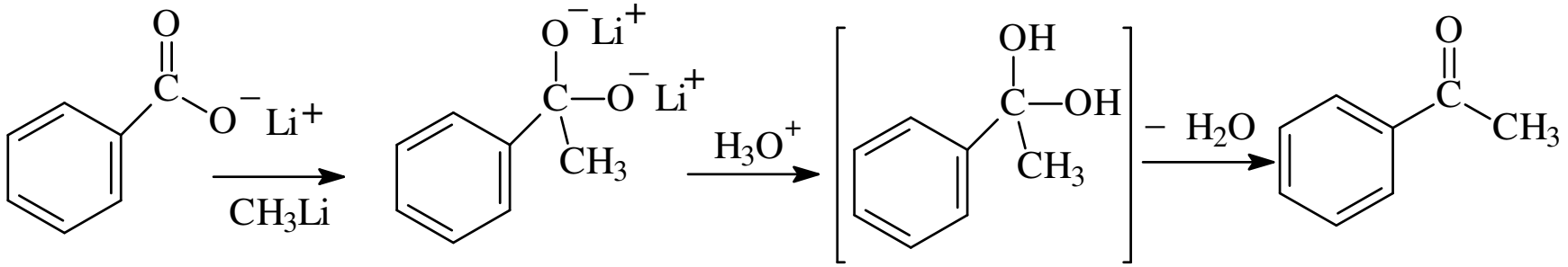
Ketones from Carboxylates



- Organolithium compounds attack the carbonyl and form a diion.
- Neutralization with aqueous acid produces an unstable hydrate that loses water to form a ketone.



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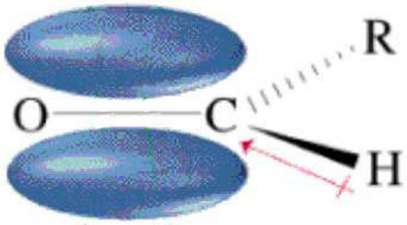
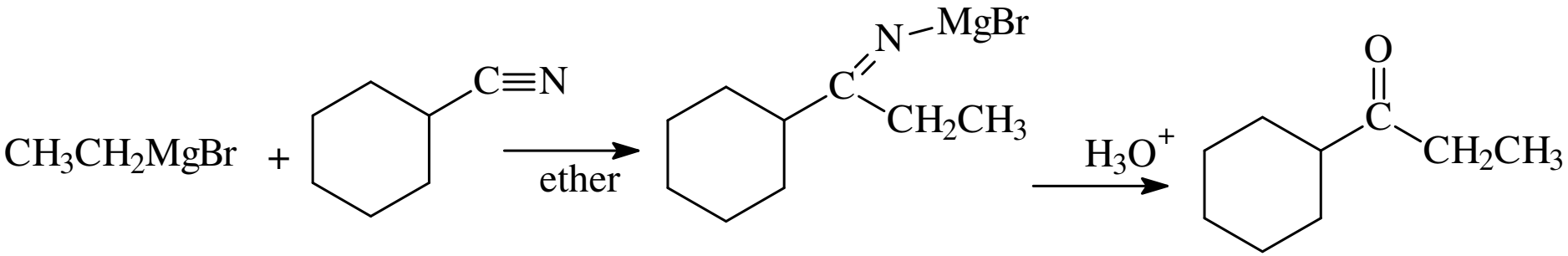
Ketones from Nitriles



- A Grignard or organolithium reagent attacks the nitrile carbon.
- The imine salt is then hydrolyzed to form a ketone.



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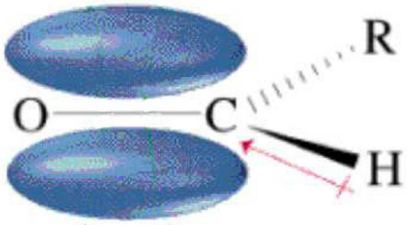
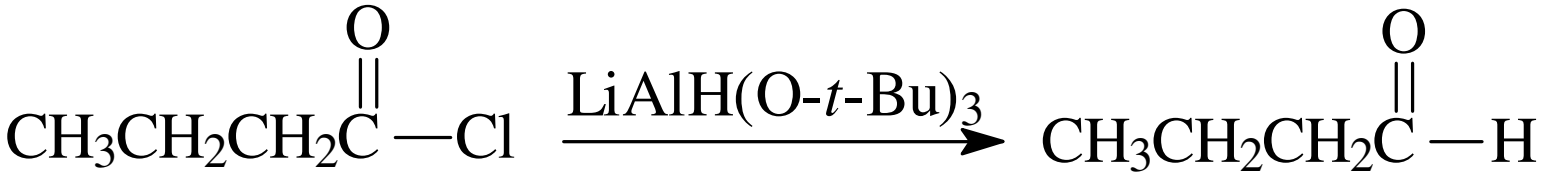
Aldehydes from Acid Chlorides



Use a mild reducing agent to prevent reduction to primary alcohol.



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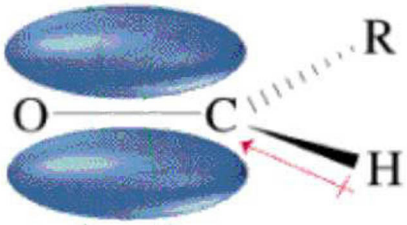
Ketones from Acid Chlorides



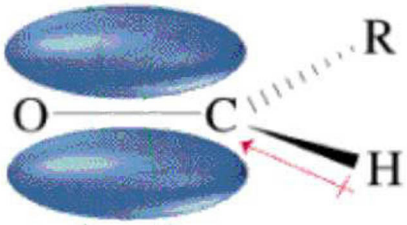
Use lithium dialkylcuprate (R_2CuLi), formed by the reaction of 2 moles of R-Li with cuprous iodide.

$$2\ CH_3CH_2CH_2Li \xrightarrow{CuI} (CH_3CH_2CH_2)_2CuLi$$

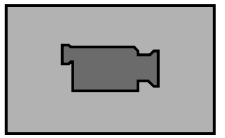
$$(CH_3CH_2CH_2)_2CuLi + CH_3CH_2\overset{\overset{O}{\|}}{C}—Cl \longrightarrow CH_3CH_2\overset{\overset{O}{\|}}{C}—CH_2CH_2CH_3$$

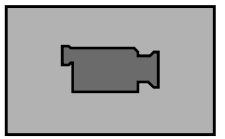
=>

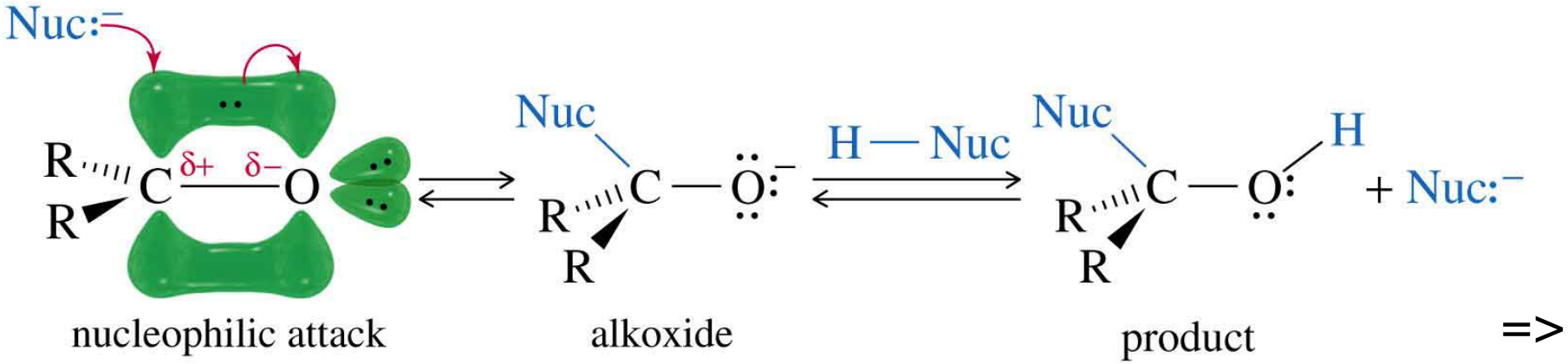
Nucleophilic Addition



- A strong nucleophile attacks the carbonyl carbon, forming an alkoxide ion that is then protonated.
- A weak nucleophile will attack a carbonyl if it has been protonated, thus increasing its reactivity.
- Aldehydes are more reactive than ketones.







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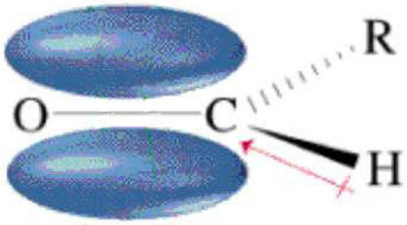
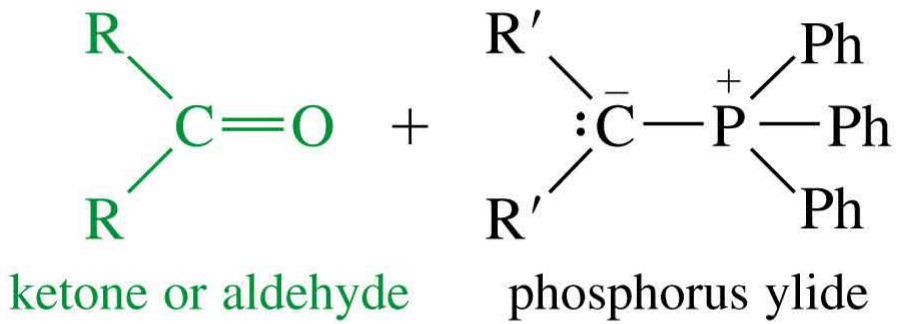
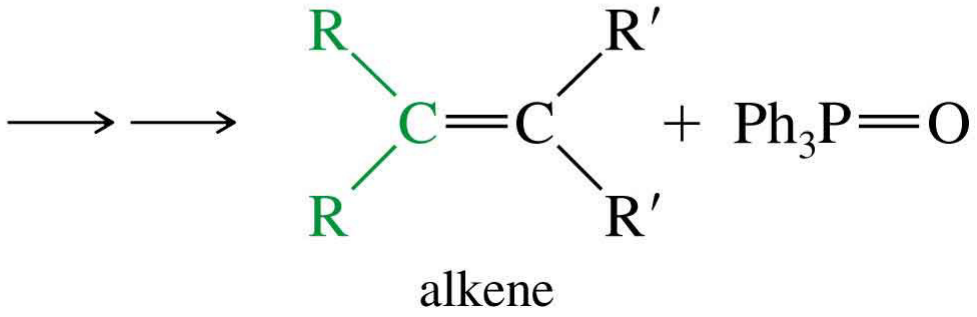
Wittig Reaction



- Nucleophilic addition of phosphorus ylides.
- Product is alkene. C=O becomes C=C.

The Wittig reaction





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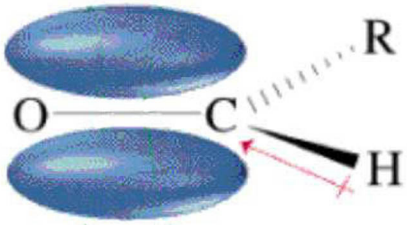
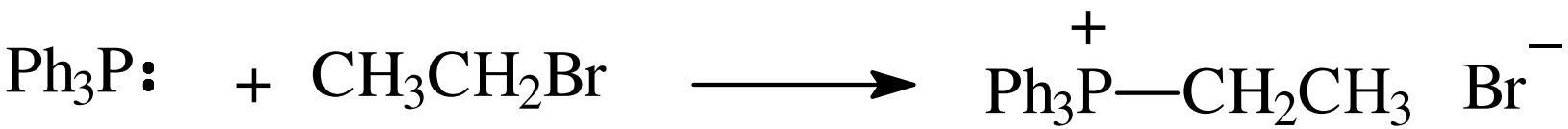
Phosphorus Ylides



- Prepared from triphenylphosphine and an unhindered alkyl halide.
- Butyllithium then abstracts a hydrogen from the carbon attached to phosphorus.



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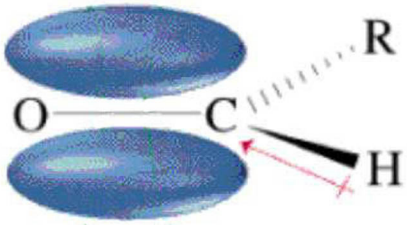
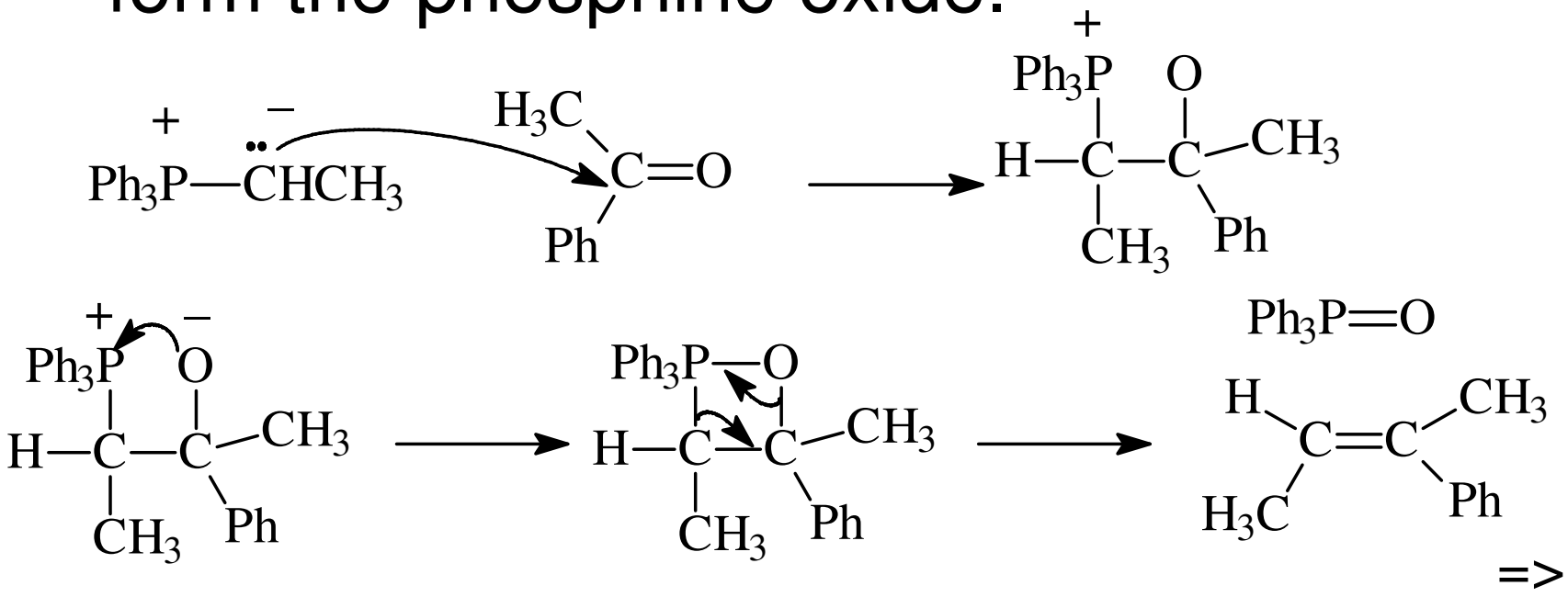
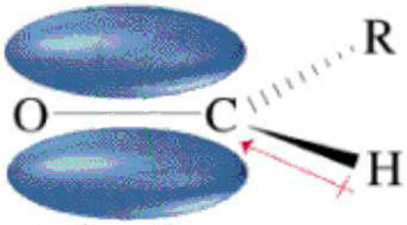
Mechanism for Wittig



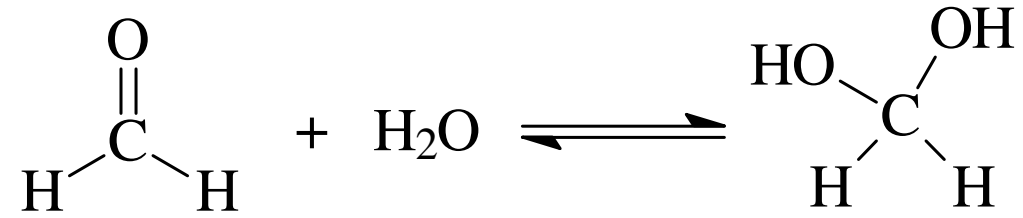
- The negative C on ylide attacks the positive C of carbonyl to form a betaine.
- Oxygen combines with phosphine to form the phosphine oxide.



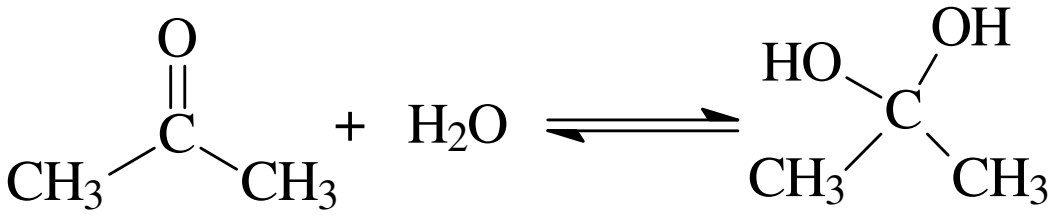
Addition of Water



- In acid, water is the nucleophile.
- In base, hydroxide is the nucleophile.
- Aldehydes are more electrophilic since they have fewer e^--donating alkyl groups.



$K = 2000$



$K = 0.002$

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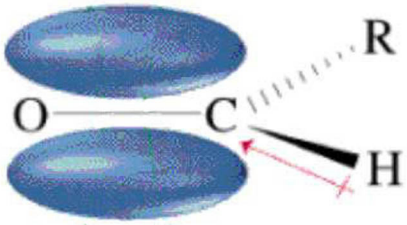
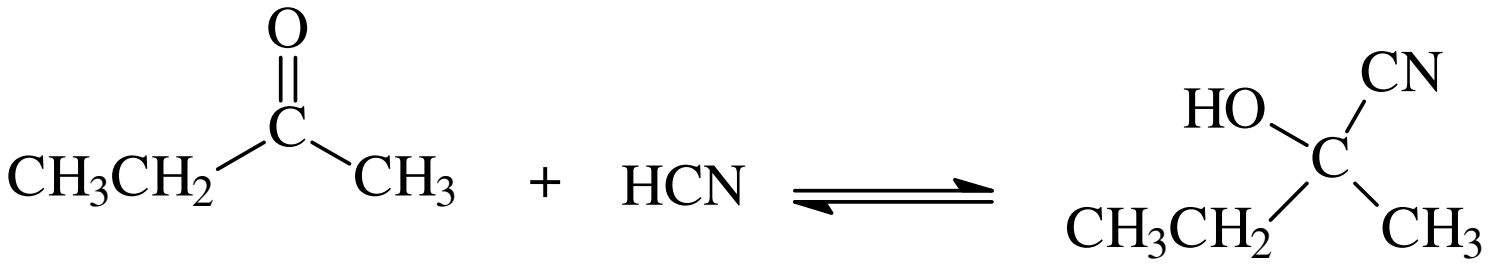
Addition of HCN



- HCN is highly toxic.
- Use NaCN or KCN in base to add cyanide, then protonate to add H.
- Reactivity formaldehyde > aldehydes > ketones >> bulky ketones.



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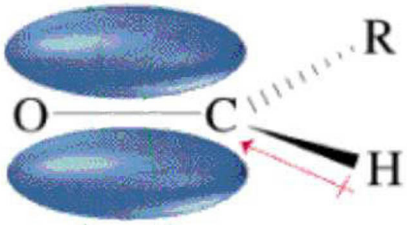
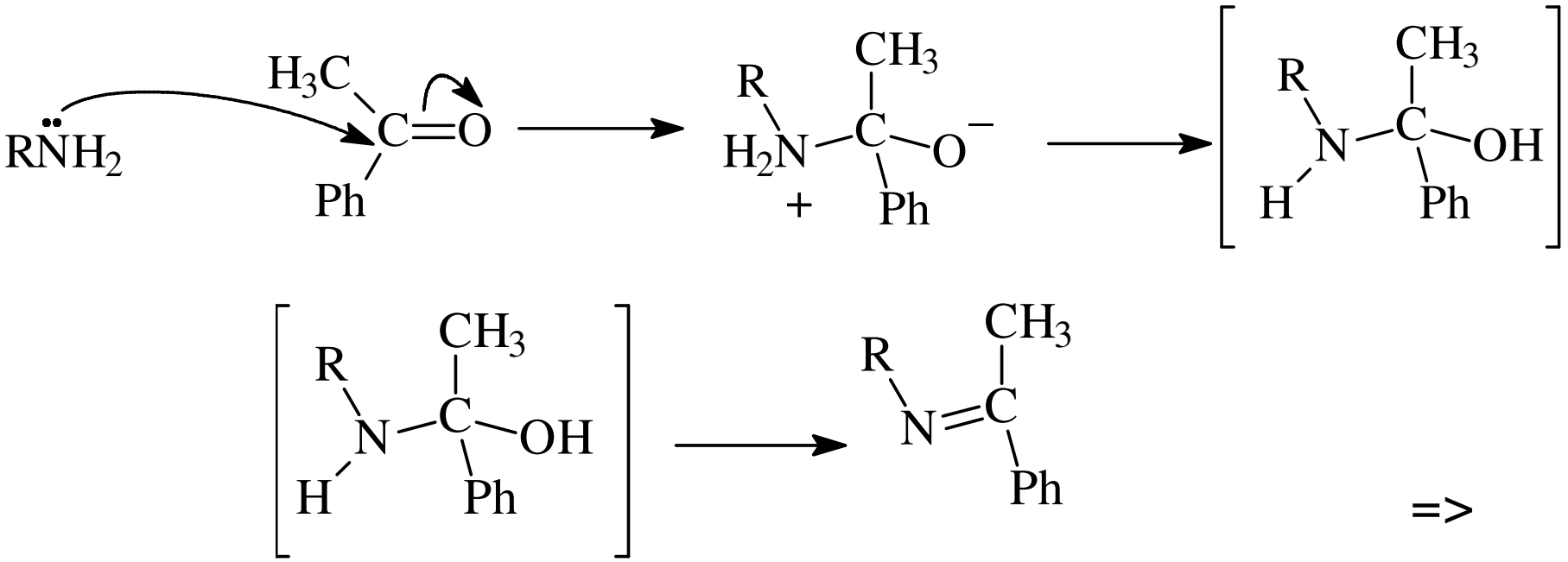
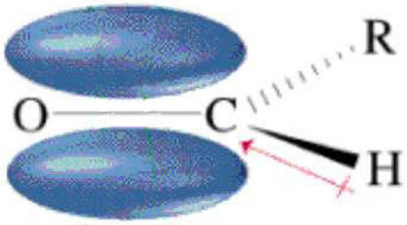
Formation of Imines



- Nucleophilic addition of ammonia or primary amine, followed by elimination of water molecule.
- C=O becomes C=N-R



pH Dependence



- Loss of water is acid catalyzed, but acid destroys nucleophiles.
- $NH_3 + H^+ \rightarrow NH_4^+$ (not nucleophilic)
- Optimum pH is around 4.5

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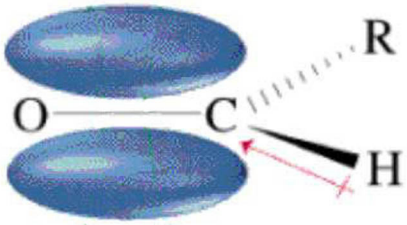
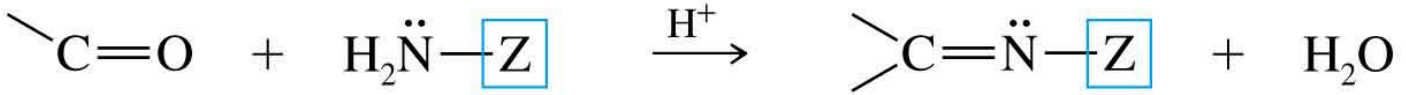
Other Condensations





Z in Z—NH$_2$	*Reagent*	*Product*
—H	$H_2\ddot{N}$—H ammonia	>C=$\ddot{N}$—H an imine
—R	$H_2\ddot{N}$—R primary amine	>C=$\ddot{N}$—R an imine (Schiff base)
—OH	$H_2\ddot{N}$—OH hydroxylamine	>C=$\ddot{N}$—OH an oxime
—NH$_2$	$H_2\ddot{N}$—NH$_2$ hydrazine	>C=$\ddot{N}$—NH$_2$ a hydrazone
—NHPh	$H_2\ddot{N}$—NHPh phenylhydrazine	>C=$\ddot{N}$—NHPh a phenylhydrazone
—NHCNH$_2$ (O)	$H_2\ddot{N}$—NHCNH$_2$ (O) semicarbazide	>C=$\ddot{N}$—NHCNH$_2$ (O) a semicarbazone

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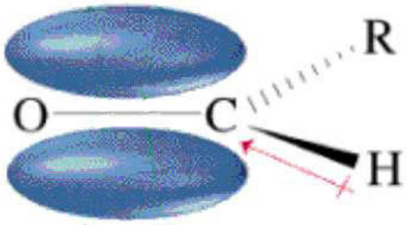
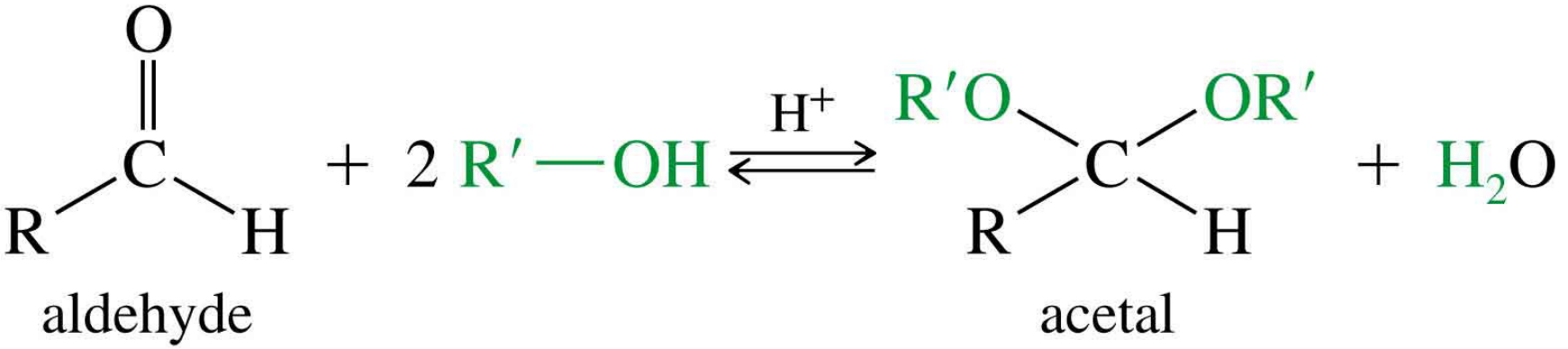
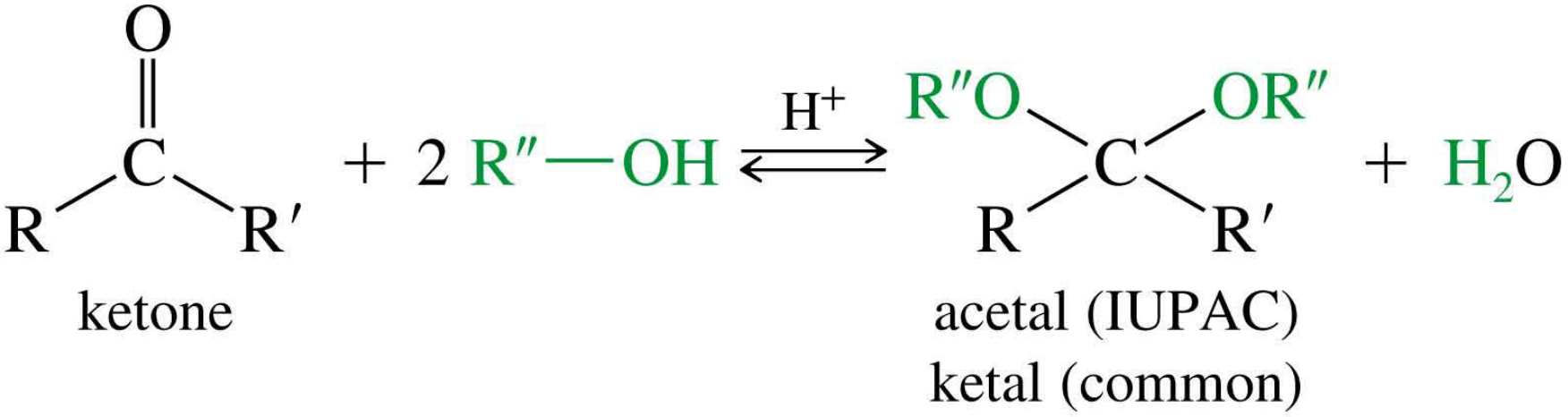
Addition of Alcohol







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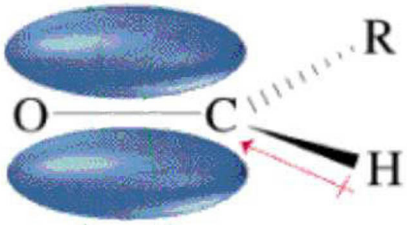

Mechanism

- Must be acid-catalyzed.
- Adding H^+ to carbonyl makes it more reactive with weak nucleophile, ROH.
- Hemiacetal forms first, then acid-catalyzed loss of water, then addition of second molecule of ROH forms acetal.
- All steps are reversible.

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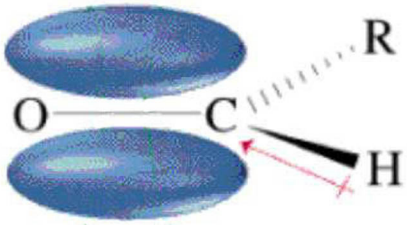
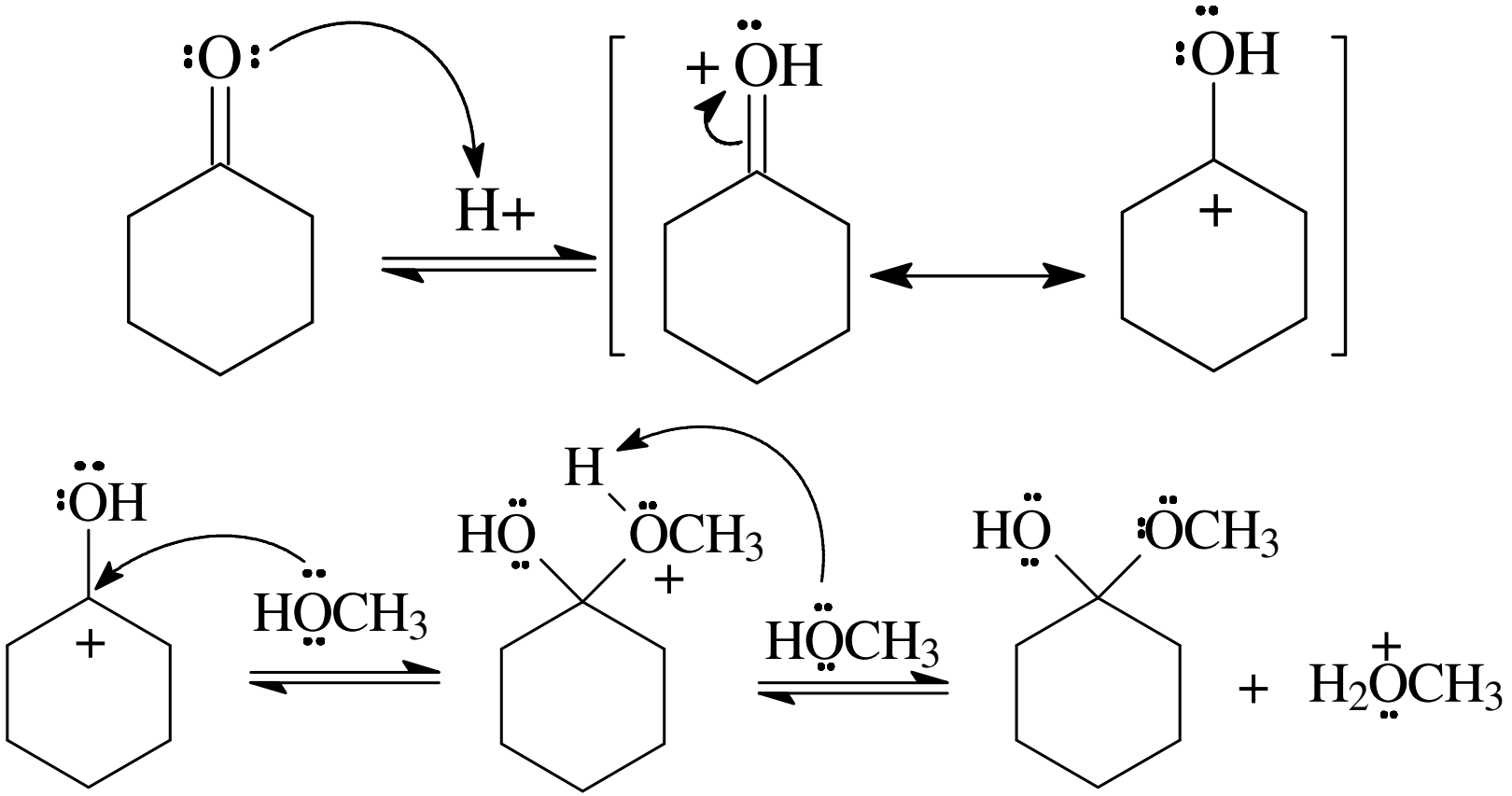
Mechanism for Hemiacetal





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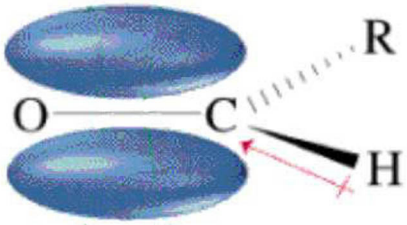
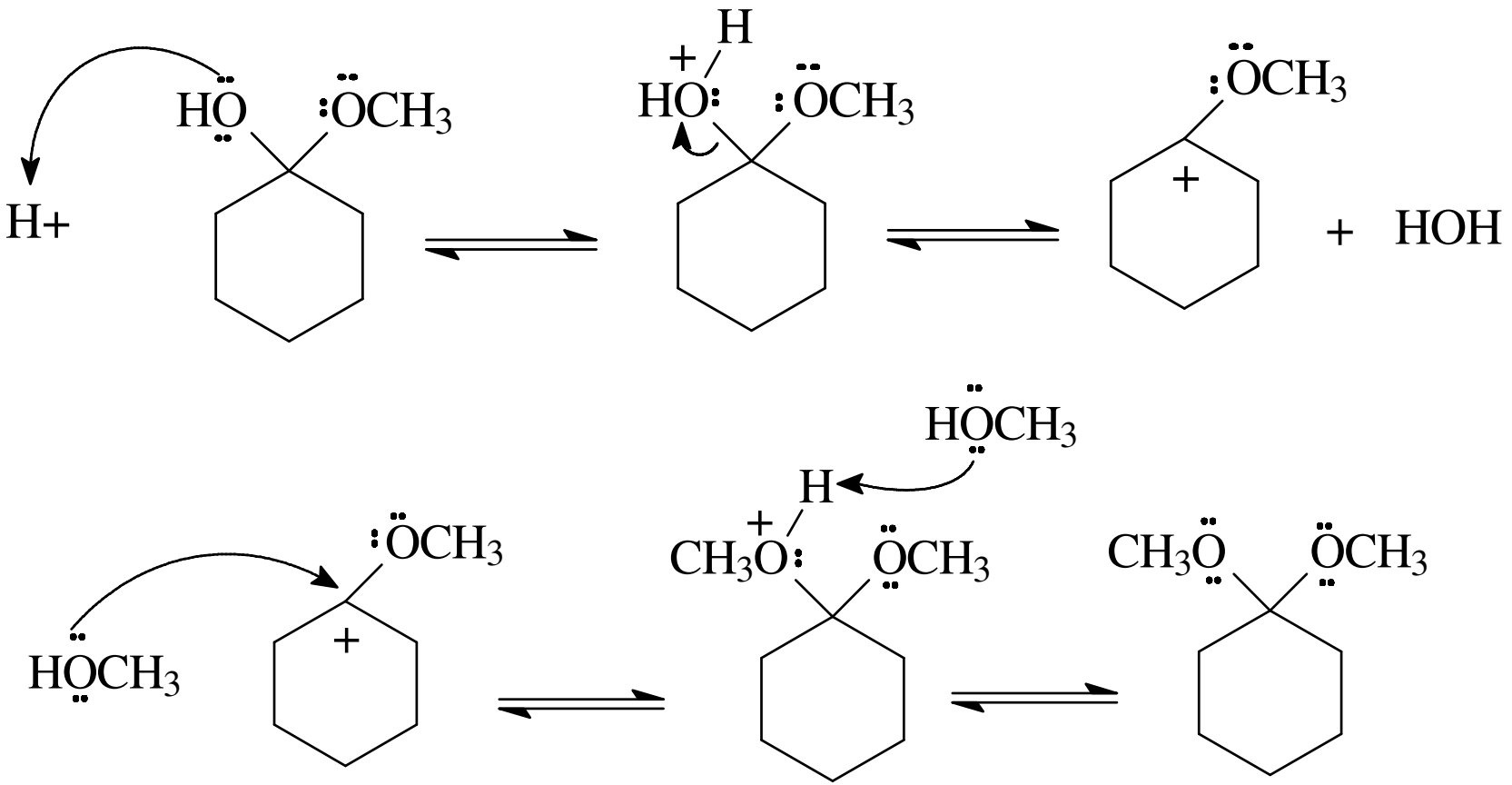
Hemiacetal to Acetal





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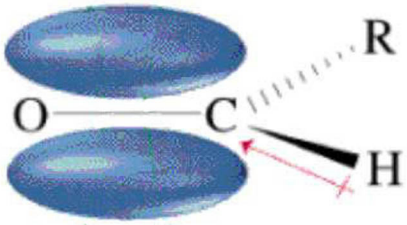
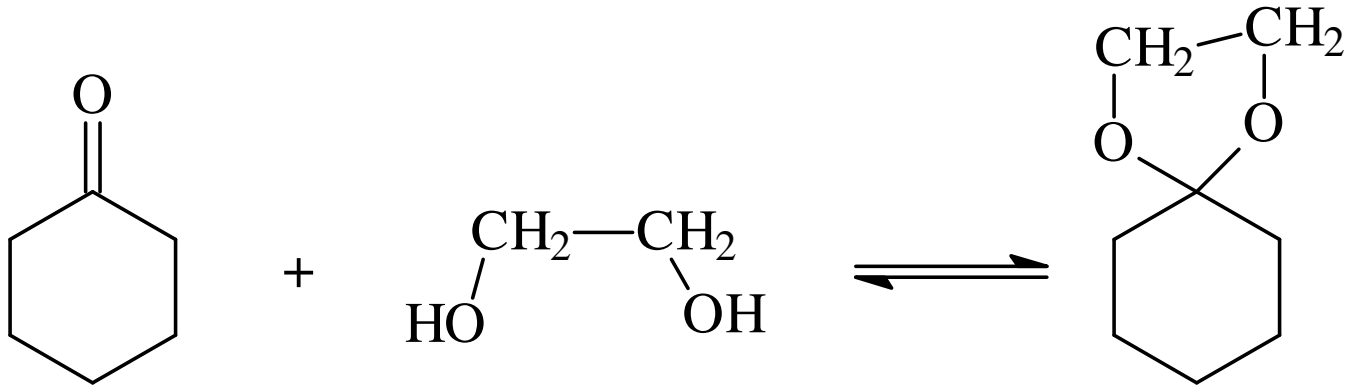


Cyclic Acetals

- Addition of a diol produces a cyclic acetal.
- Sugars commonly exist as acetals or hemiacetals.



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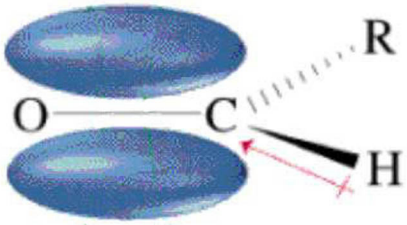
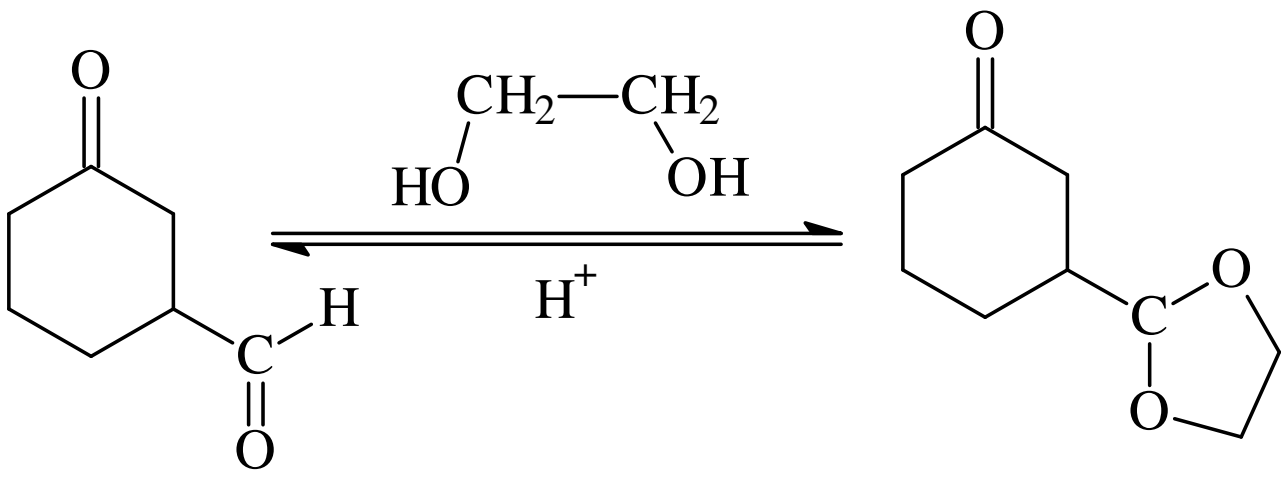
Acetals as Protecting Groups



- Hydrolyze easily in acid, stable in base.
- Aldehydes more reactive than ketones.



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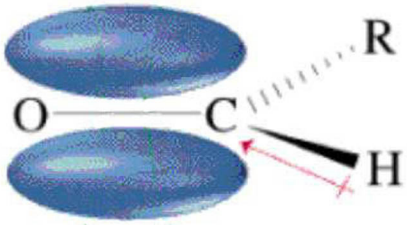
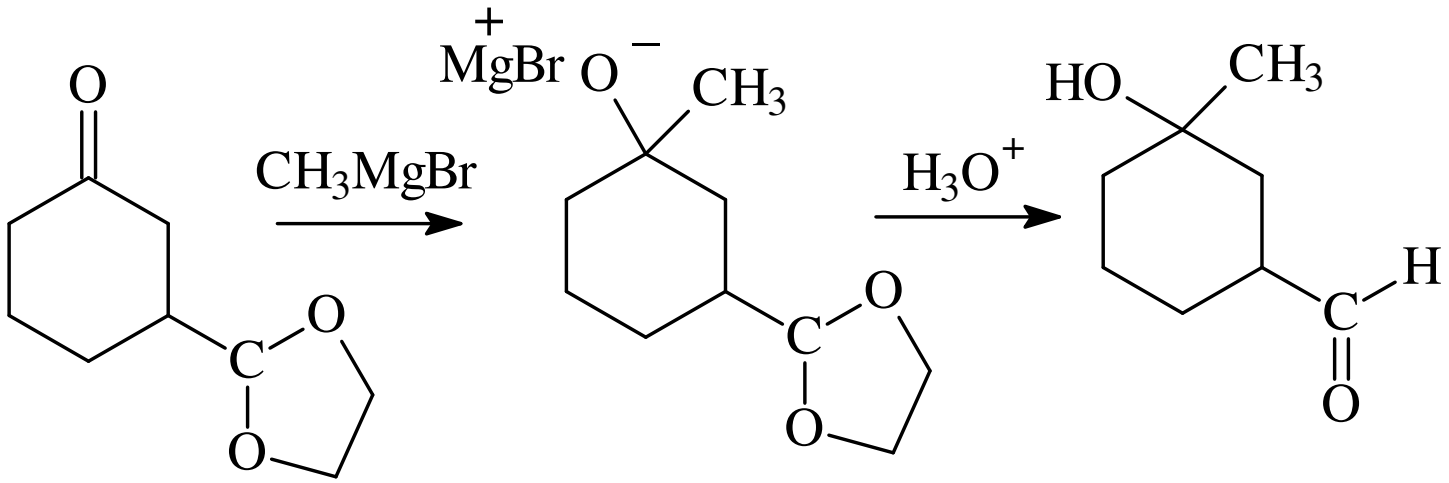
Selective Reaction of Ketone



- React with strong nucleophile (base)
- Remove protective group.



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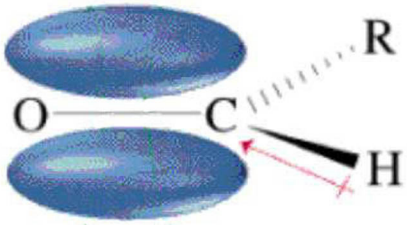
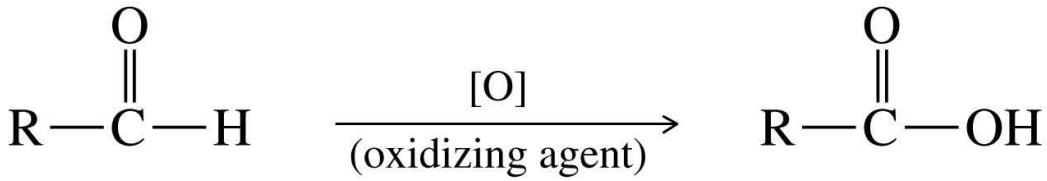
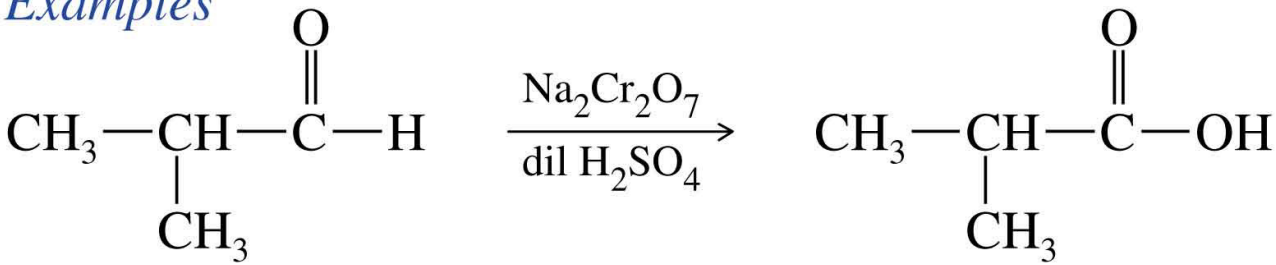
Oxidation of Aldehydes



Easily oxidized to carboxylic acids.

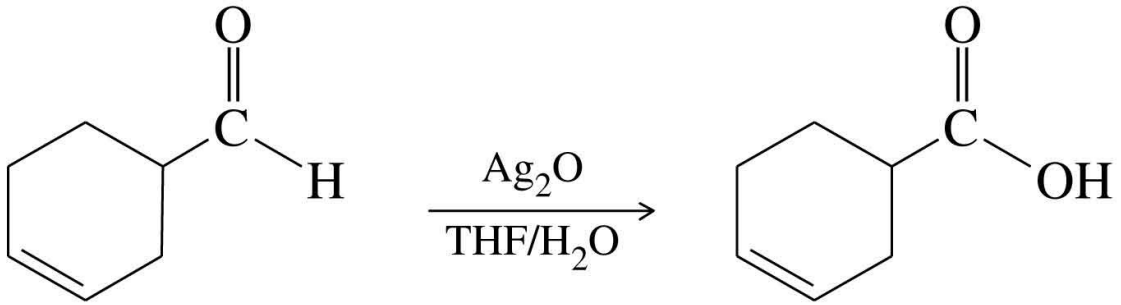


Examples



isobutyraldehyde

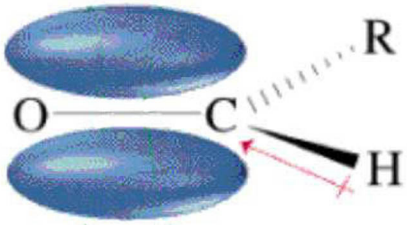
isobutyric acid (90%)



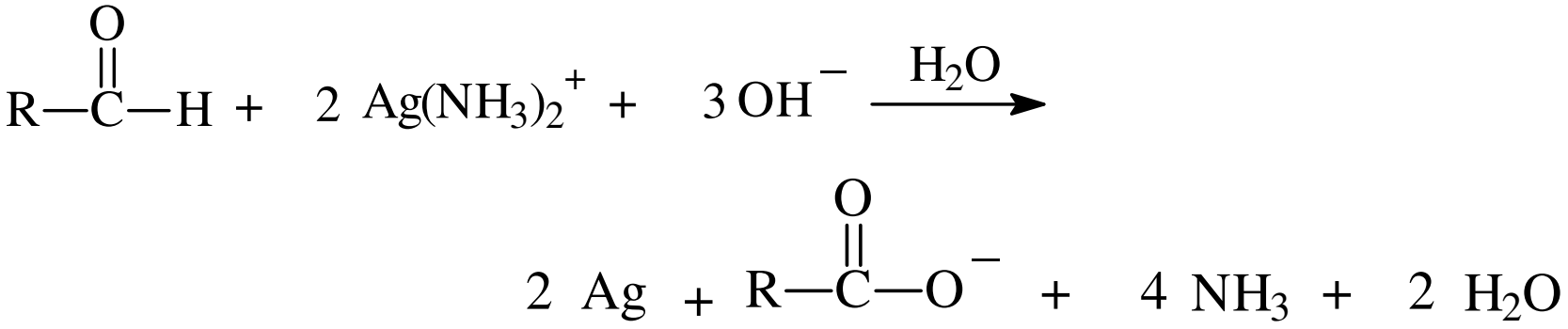
(97%)

=>

Tollens Test



- Add ammonia solution to $AgNO_3$ solution until precipitate dissolves.
- Aldehyde reaction forms a silver mirror.



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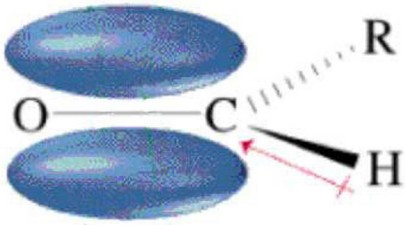
Reduction Reagents



- Sodium borohydride, $NaBH_4$, reduces C=O, but not C=C.
- Lithium aluminum hydride, $LiAlH_4$, much stronger, difficult to handle.
- Hydrogen gas with catalyst also reduces the C=C bond.

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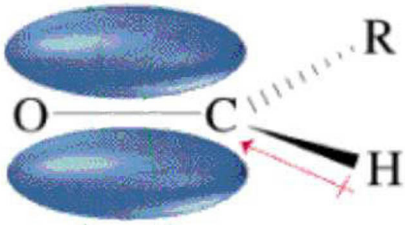
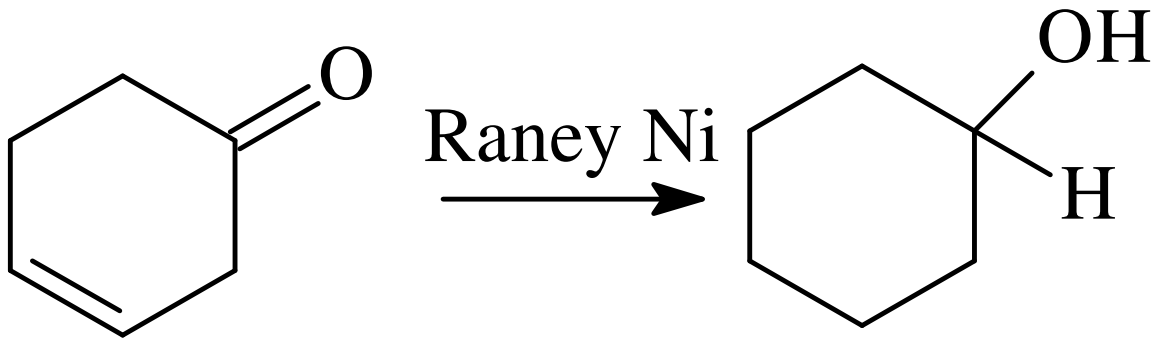
Catalytic Hydrogenation



- Widely used in industry.
- Raney nickel, finely divided Ni powder saturated with hydrogen gas.
- Pt and Rh also used as catalysts.



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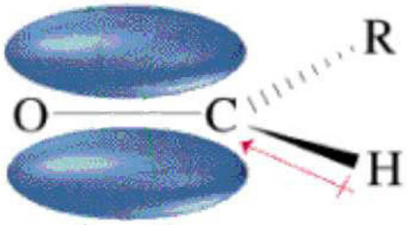
Deoxygenation



- Reduction of C=O to CH_2
- Two methods:
  - Clemmensen reduction if molecule is stable in hot acid.
  - Wolff-Kishner reduction if molecule is stable in very strong base.

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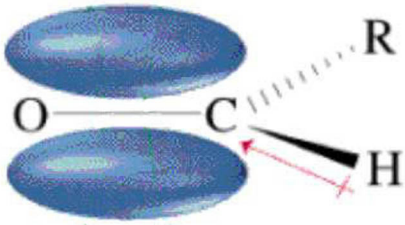
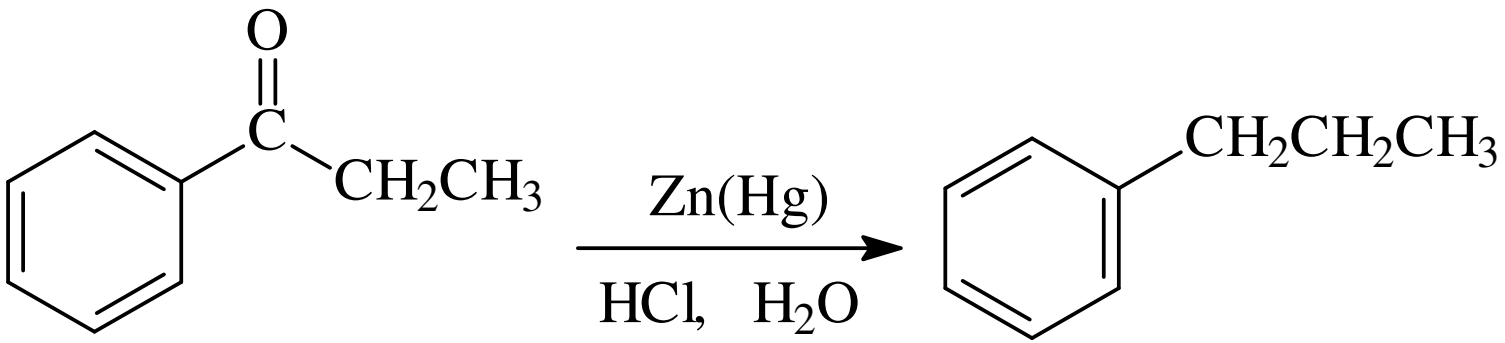
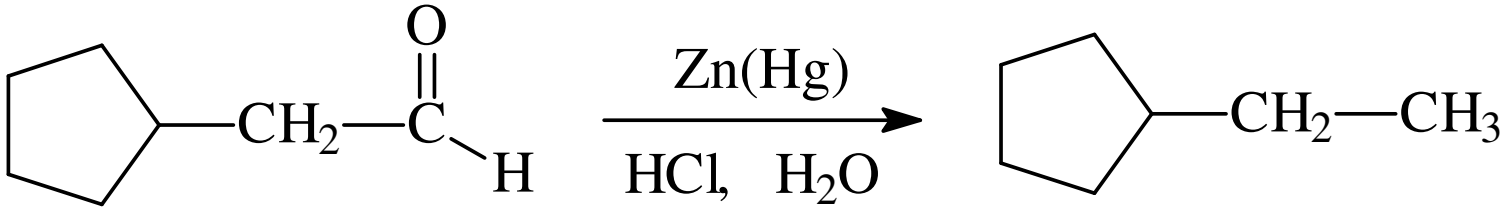
Clemmensen Reduction







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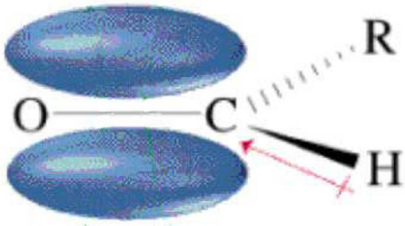
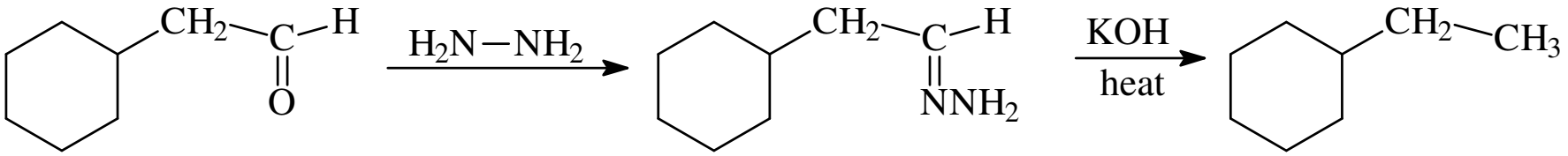
Wolff-Kisher Reduction



- Form hydrazone, then heat with strong base like KOH or potassium *t*-butoxide.
- Use a high-boiling solvent: ethylene glycol, diethylene glycol, or DMSO.



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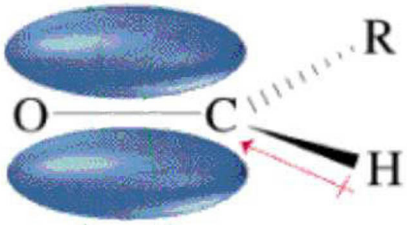

THANK YOU