Ketones and Aldehydes

Carbonyl Compounds

$(C=O)$
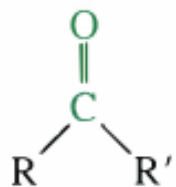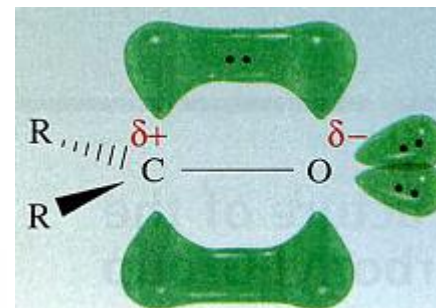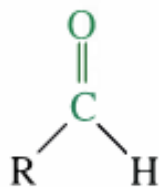
condensed structures:

	ketone	aldehyde	carbonyl group
	RCOR′	RCHO	

Ketone: Two alkyl groups bonded to a carbonyl group.

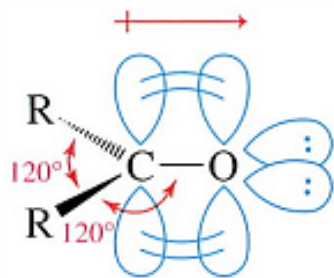*Aldehyde*:   One alkyl group and one hydrogen bonded to a carbonyl group.

TABLE 18-1   Some Common Classes of Carbonyl Compounds

Class	General Formula	Class	General Formula
ketones	R—C(=O)—R′	aldehydes	R—C(=O)—H
carboxylic acids	R—C(=O)—OH	acid chlorides	R—C(=O)—Cl
esters	R—C(=O)—O—R′	amides	R—C(=O)—NH$_2$

Structure of the Carbonyl Group

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

major   minor

Compare with:

μ = 2.7 D
acetaldehyde

μ = 2.9 D
acetone
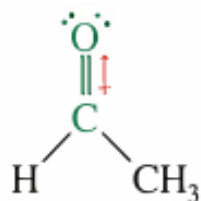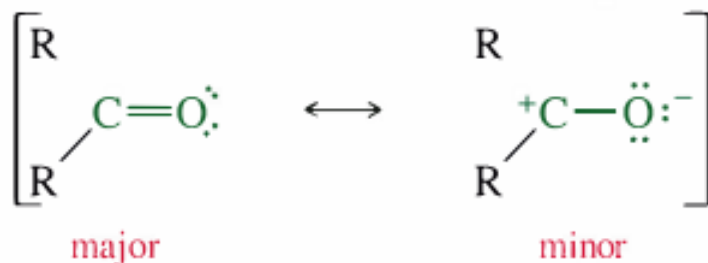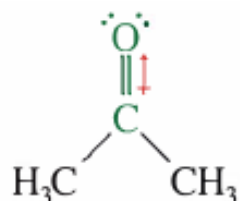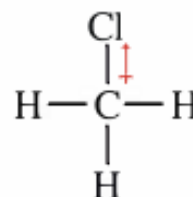
μ = 1.9 D
chloromethane
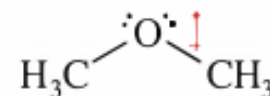
μ = 1.30 D
dimethyl ether

Nomenclature of Ketones and Aldehydes

IUPAC Names   Systematic names of ketones are derived by replacing the final -*e* in the alkane name with -*one*. The "alkane" name becomes "alkanone." In open-chain ketones, we number the longest chain that includes the carbonyl carbon from the end closest to the carbonyl group, and we indicate the position of the carbonyl group by a number. In cyclic ketones, the carbonyl carbon atom is assigned the number 1.
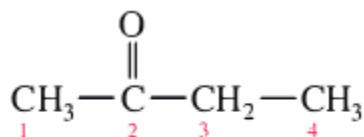
2-butanone
butan-2-one
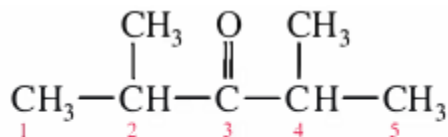
2,4-dimethyl-3-pentanone
2,4-dimethylpentan-3-one

1-phenyl-1-propanone
1-phenylpropan-1-one
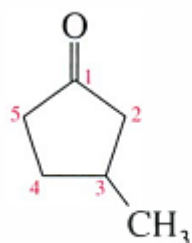
3-methylcyclopentanone
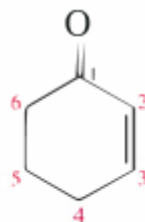
2-cyclohexenone
cyclohex-2-en-1-one
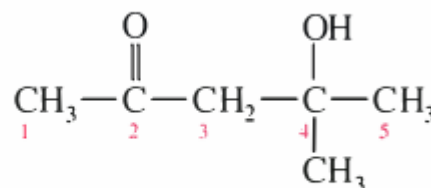
4-hydroxy-4-methyl-2-pentanone
4-hydroxy-4-methylpentan-2-one

Systematic names for aldehydes are derived by replacing the final -e of the alkane name with -al. An aldehyde carbon is at the end of a chain, so it is number 1. If the aldehyde group is attached to a large unit (usually a ring), the suffix *carbaldehyde* is used.
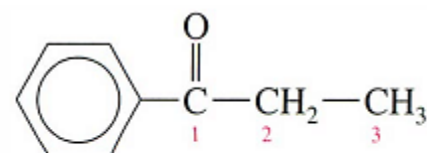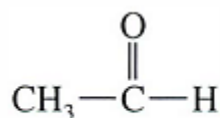
ethanal
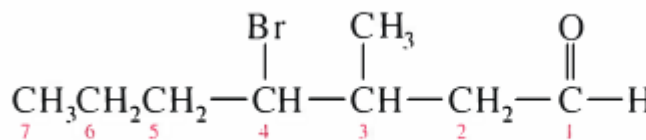
4-bromo-3-methylheptanal
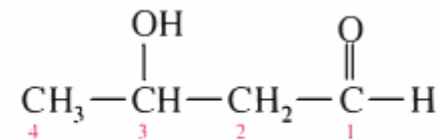
3-hydroxybutanal

2-pentenal
pent-2-enal
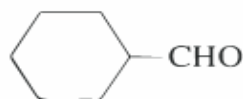
cyclohexanecarbaldehyde
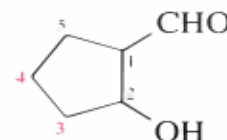
2-hydroxycyclopentane-1-carbaldehyde

A ketone or aldehyde group can also be named as a substituent on a molecule with another functional group as its root. The ketone carbonyl is designated by the prefix *oxo-*, and the —CHO group is named as a *formyl* group. Carboxylic acids frequently contain ketone or aldehyde groups named as substituents.

$$CH_3CH_2-\overset{\overset{\displaystyle O}{\|}}{C}-CH_2-CHO$$
3-oxopentanal

2-formylbenzoic acid

$$CH_3-\overset{\overset{\displaystyle O}{\|}}{C}-CH_2-COOH$$
3-oxobutanoic acid
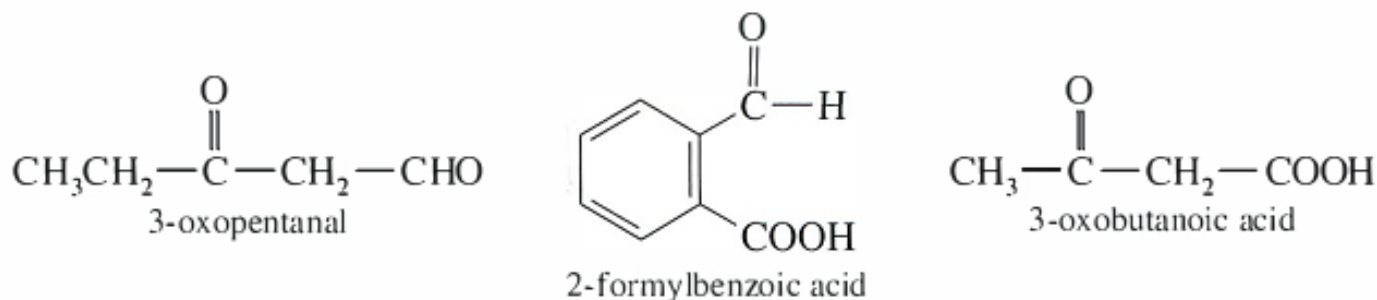
Common Names   As with other classes of compounds, ketones and aldehydes are often called by common names instead of their systematic IUPAC names. Ketone common names are formed by naming the two alkyl groups bonded to the carbonyl group. Substituent locations are given using Greek letters, beginning with the carbon *next to* the carbonyl group.

$$CH_3CH_2-\overset{\overset{\displaystyle O}{\|}}{C}-CH_3$$
methyl ethyl ketone

$$CH_3CH_2-\overset{\overset{\displaystyle CH_3}{|}}{C}H-\overset{\overset{\displaystyle O}{\|}}{C}-\overset{\overset{\displaystyle CH_3}{|}}{C}H-CH_2CH_3$$
di-*sec*-butyl ketone

$$Br-\overset{\beta}{C}H_2-\overset{\alpha}{C}H_2-\overset{\overset{\displaystyle O}{\|}}{C}-\overset{\overset{\displaystyle CH_3}{|}}{C}H-CH_3$$
β-bromoethyl isopropyl ketone

$$\overset{\gamma}{C}H_3-\overset{\beta}{C}H_2-\overset{\alpha}{\overset{\overset{\displaystyle OCH_3}{|}}{C}}H-\overset{\overset{\displaystyle O}{\|}}{C}-C(CH_3)_3$$
t-butyl α-methoxypropyl ketone

4
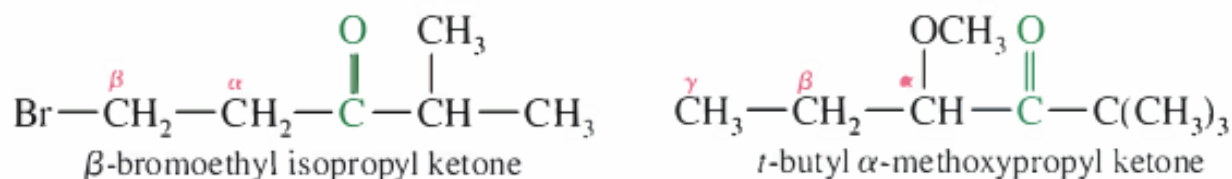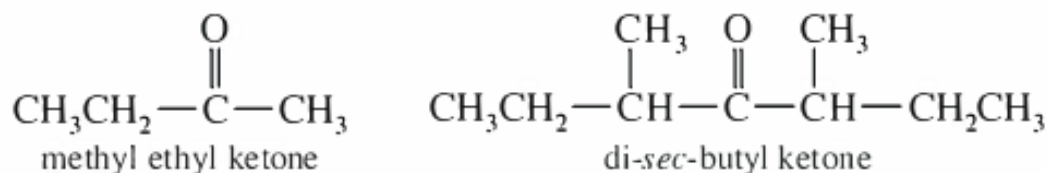
Some ketones have historical common names. Dimethyl ketone is always called *acetone*, and alkyl phenyl ketones are usually named as the acyl group followed by the suffix *-phenone*.

acetone   acetophenone   propiophenone   benzophenone
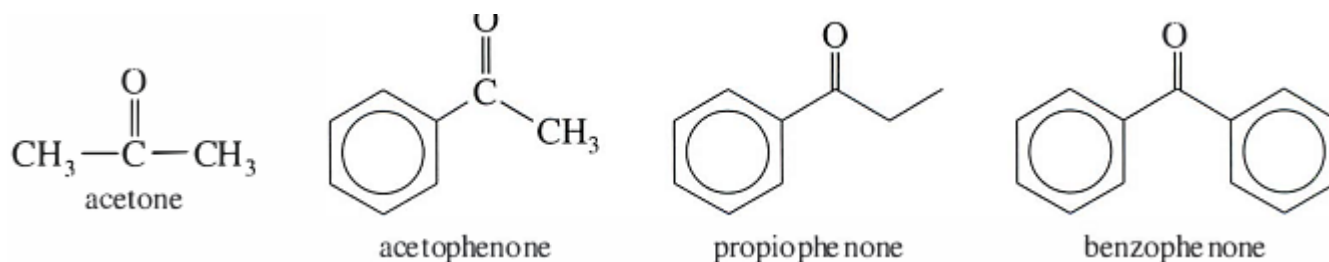
Common names of aldehydes are derived from the common names of carboxylic acids (Table 18-2). These names often reflect the Latin or Greek term for the original source of the acid or the aldehyde. Greek letters are used with common names of aldehydes to give the locations of substituents. The first letter (α) is given to the carbon atom *next to* the carbonyl group.
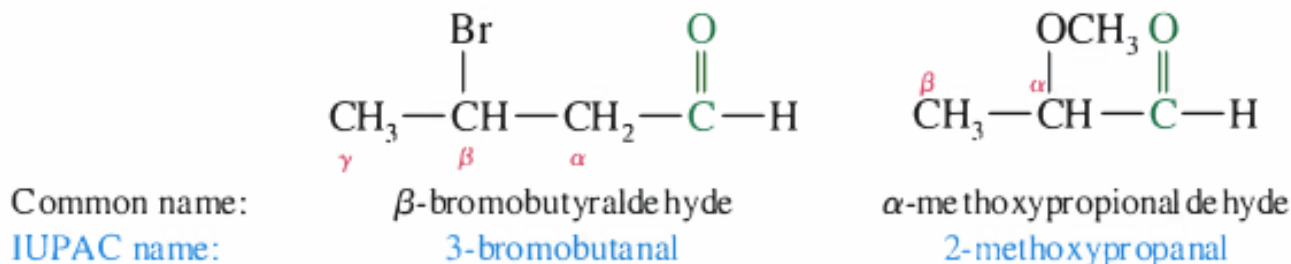

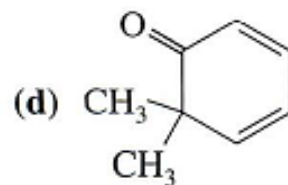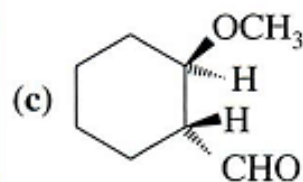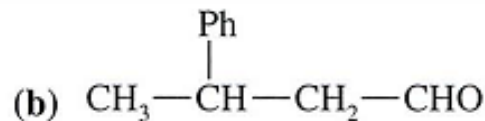|		
Common name:	β-bromobutyraldehyde	α-methoxypropionaldehyde
IUPAC name:	3-bromobutanal	2-methoxypropanal

TABLE 18-2 Common Names of Aldehydes

Carboxylic Acid	Derivation	Aldehyde
$H-\overset{\displaystyle O}{\overset{\|}{C}}-OH$ formic acid	*formica*, "ants"	$H-\overset{\displaystyle O}{\overset{\|}{C}}-H$ formaldehyde (methanal)
$CH_3-\overset{\displaystyle O}{\overset{\|}{C}}-OH$ acetic acid	*acetum*, "sour"	$CH_3-\overset{\displaystyle O}{\overset{\|}{C}}-H$ acetaldehyde (ethanal)
$CH_3-CH_2-\overset{\displaystyle O}{\overset{\|}{C}}-OH$ propionic acid	*protos pion*, "first fat"	$CH_3-CH_2-\overset{\displaystyle O}{\overset{\|}{C}}-H$ propionaldehyde (propanal)
$CH_3-CH_2-CH_2-\overset{\displaystyle O}{\overset{\|}{C}}-OH$ butyric acid	*butyrum*, "butter"	$CH_3-CH_2-CH_2-\overset{\displaystyle O}{\overset{\|}{C}}-H$ butyraldehyde (butanal)
⬡$-\overset{\displaystyle O}{\overset{\|}{C}}-OH$ benzoic acid	*gum benzoin*, "blending"	⬡$-\overset{\displaystyle O}{\overset{\|}{C}}-H$ benzaldehyde

PROBLEM 18-1

Give the IUPAC name and (if possible) a common name for each compound.

(a) $CH_3-\overset{\underset{\displaystyle |}{OH}}{CH}-CH_2-\overset{\underset{\displaystyle \|}{O}}{C}-CH_2CH_3$

(b) $CH_3-\overset{\underset{\displaystyle |}{Ph}}{CH}-CH_2-CHO$

(c) cyclohexane with OCH_3, H, H, CHO substituents

(d) CH_3-substituted cyclohexadienone with CH_3
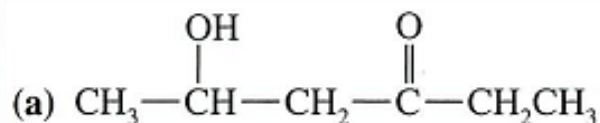
Physical Properties of Ketones and Aldehydes

$CH_3CH_2CH_2CH_3$
butane
bp 0°C

$CH_3-O-CH_2CH_3$
methoxyethane
bp 8°C

$CH_3CH_2-\overset{\underset{\displaystyle \|}{O}}{C}-H$
propanal
bp 49°C

$CH_3-\overset{\underset{\displaystyle \|}{O}}{C}-CH_3$
acetone
bp 56°C

$CH_3CH_2CH_2-OH$
1-propanol
bp 97°C

7
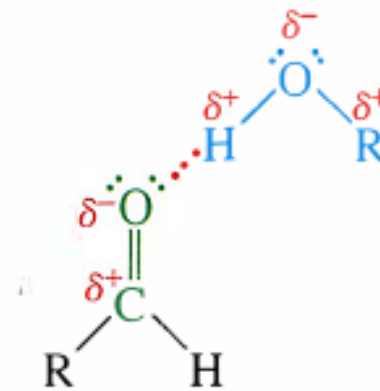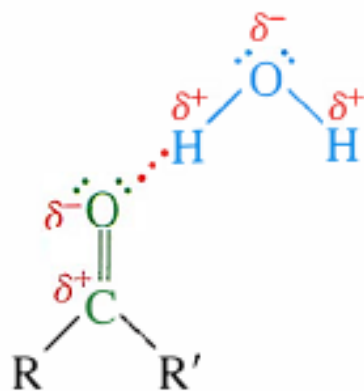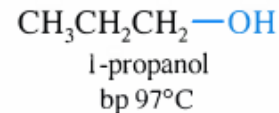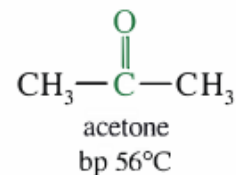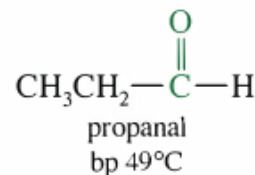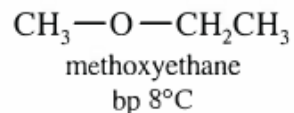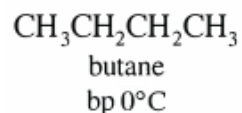
Industrial Importance of Ketones and Aldehydes

TABLE 18-4 Ketones and Aldehydes Used in Household Products
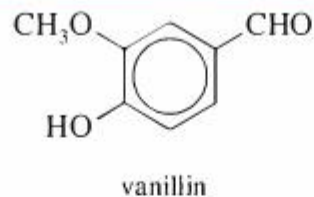
$$CH_3-CH_2-CH_2-\overset{\displaystyle O}{\overset{\|}{C}}-H$$

butyraldehyde

vanillin

acetophenone

trans-cinnamaldehyde

Odor:	buttery	vanilla	pistachio	cinnamon
Uses:	margarine, foods	foods, perfumes	ice cream	candy, foods, drugs

camphor

pyrethrin

carvone

muscone
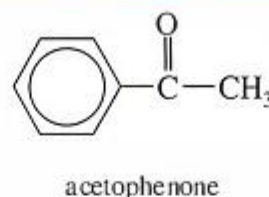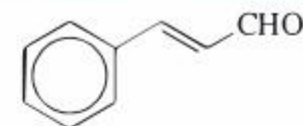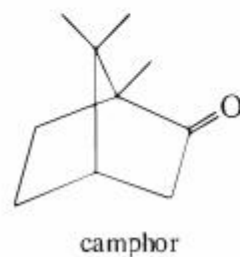
Odor:	"camphoraceous"	floral	(−) enantiomer: spearmint (+) enantiomer: caraway seed	musky aroma
Uses:	liniments, inhalants	plant insecticide	candy, toothpaste, etc.	perfumes
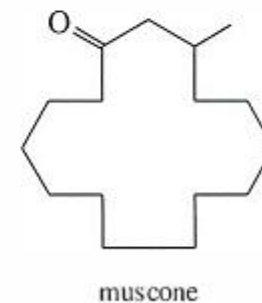
Review of Syntheses of Ketones and Aldehydes

Ketones and Aldehydes from Oxidation of Alcohols

$$R-MgX + R'-\overset{\overset{O}{\|}}{C}-H \xrightarrow[\text{ether}]{} \xrightarrow{H_3O^+} R-\overset{\overset{OH}{|}}{C}H-R' \xrightarrow[H_2SO_4]{Na_2Cr_2O_7} R-\overset{\overset{O}{\|}}{C}-R'$$

Grignard　　　aldehyde　　　　　　　　　　　secondary alcohol　　　　　　ketone

borneol $\xrightarrow[H_2SO_4]{Na_2Cr_2O_7}$ camphor (88%)
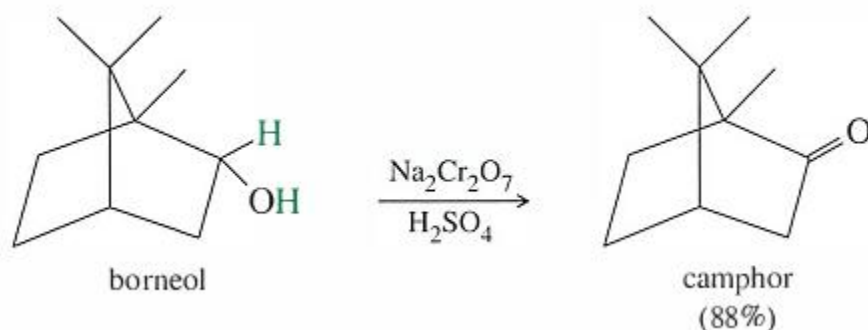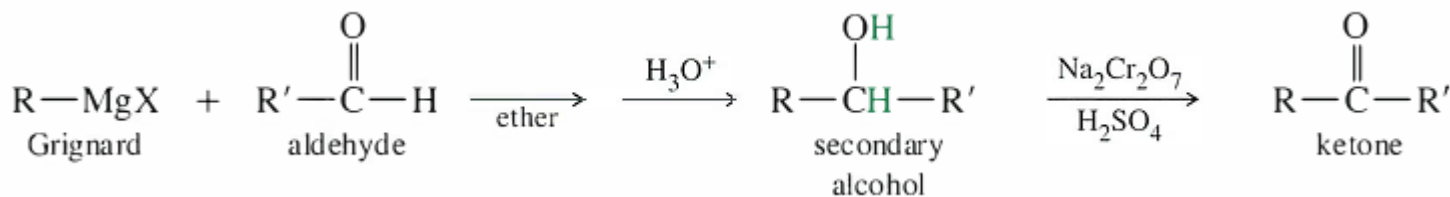
Primary alcohols → aldehydes

☞ $R-\overset{\overset{OH}{|}}{C}H_2 \xrightarrow[-2H]{[\text{oxidizing agent}]} R-\overset{\overset{O}{\|}}{C}-H \xrightarrow[\text{[O]}]{[\text{overoxidation}]} R-\overset{\overset{O}{\|}}{C}-OH$

primary alcohol　　　　　　　　　　aldehyde　　　　　　　　carboxylic acid
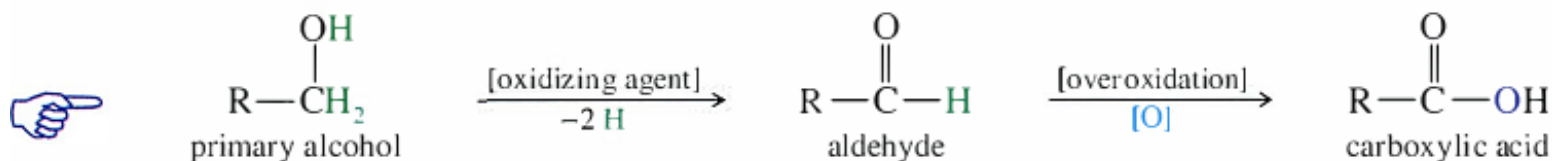
Oxidation of a primary alcohol to an aldehyde requires careful selection of an oxidizing agent to avoid over-oxidation to the carboxylic acid. *Pyridinium chlorochromate* (PCC), a complex of chromium trioxide with pyridine and HCl, provides good yields of aldehydes without over-oxidation.

cyclohexylmethanol → (PCC) → cyclohexanecarbaldehyde (90%)
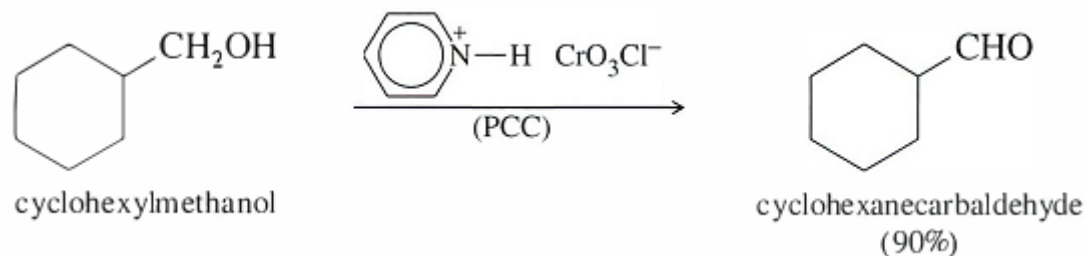
Ketones and Aldehydes from Ozonolysis of Alkenes

1-methylcyclohexene → (1) O_3 (2) $(CH_3)_2S$ → 6-oxoheptanal (65%)
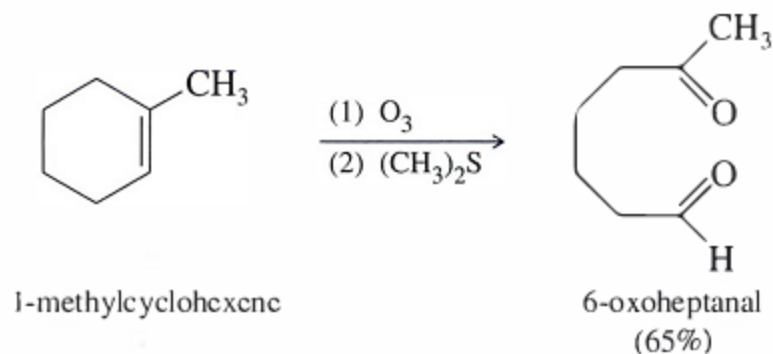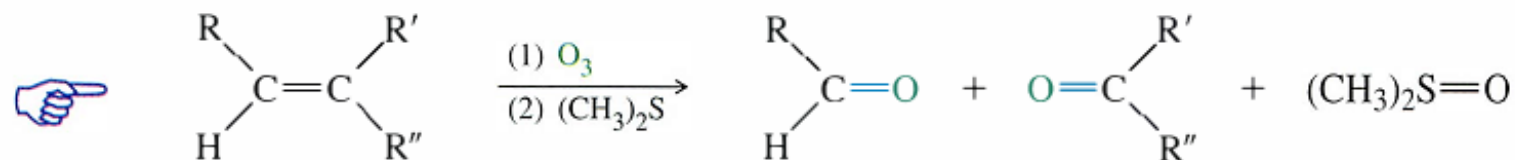
Phenyl Ketones and Aldehydes: Friedel–Crafts Acylation

$R-C(=O)-Cl$ + (benzene with G) → (1) $AlCl_3$ (2) H_2O →
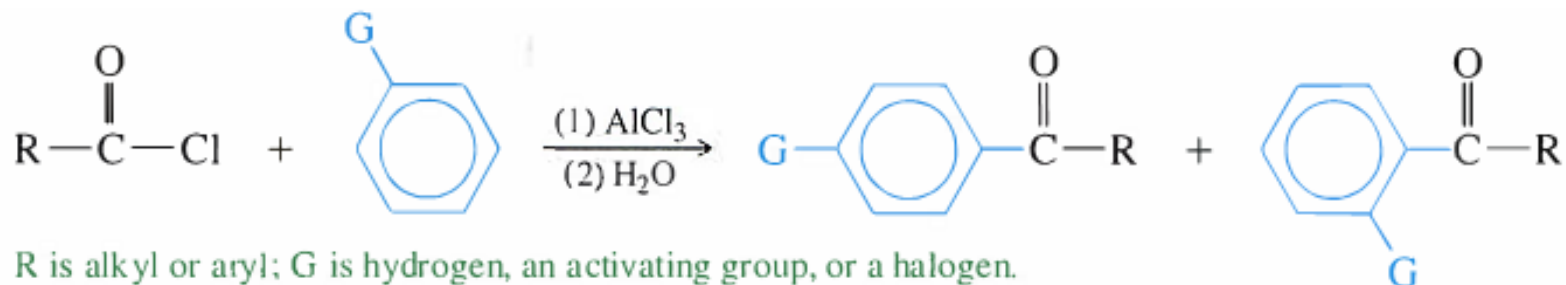
R is alkyl or aryl; G is hydrogen, an activating group, or a halogen.

10

p-nitrobenzoyl chloride

p-nitrobenzophenone
(90%)
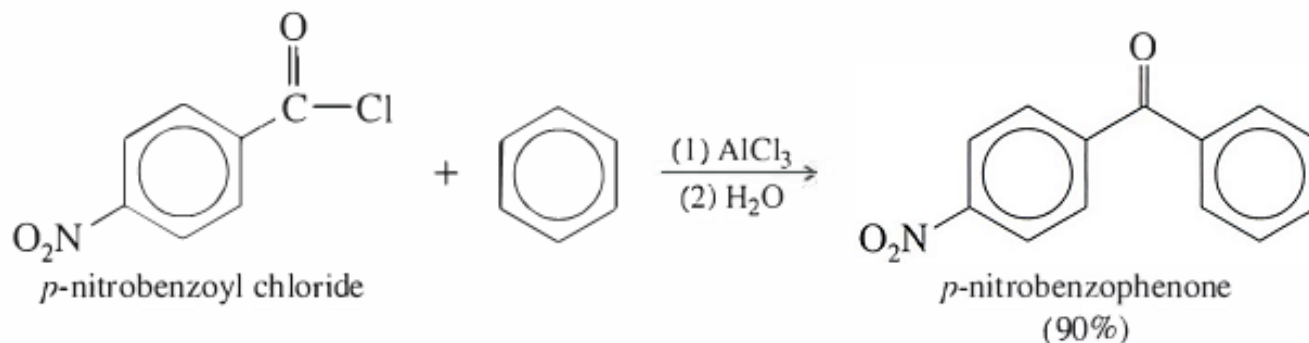
The Gatterman–Koch synthesis is a variant of the Friedel–Crafts acylation in which carbon monoxide and HCl generate an intermediate that reacts like formyl chloride. Like Friedel–Crafts reactions, the Gatterman–Koch formylation succeeds only with benzene and activated benzene derivatives.

toluene

p-methylbenzaldehyde (major)
(50%)
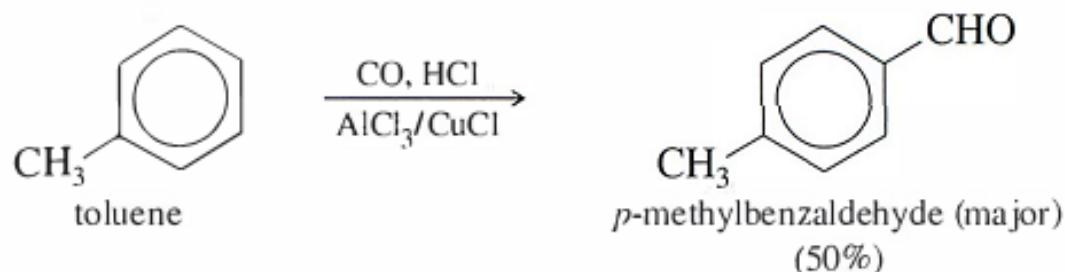
'D   Ketones and Aldehydes from Hydration of Alkynes

Catalyzed by Acid and Mercuric Salts

alkyne

enol (not isolated)

methyl ketone

ethynylcyclohexane   enol   cyclohexyl methyl ketone
                                                                                     (90%)
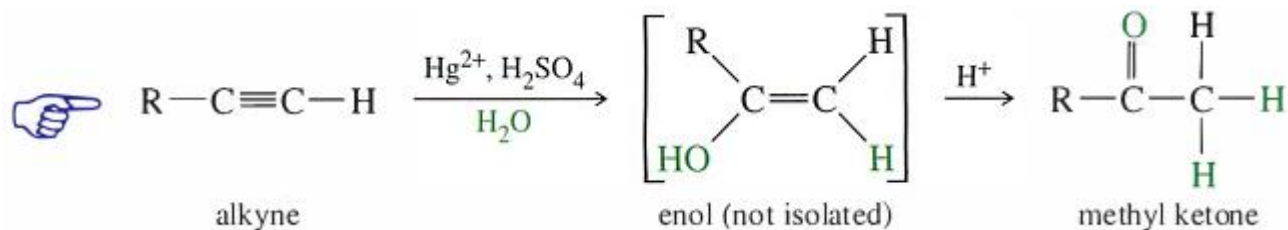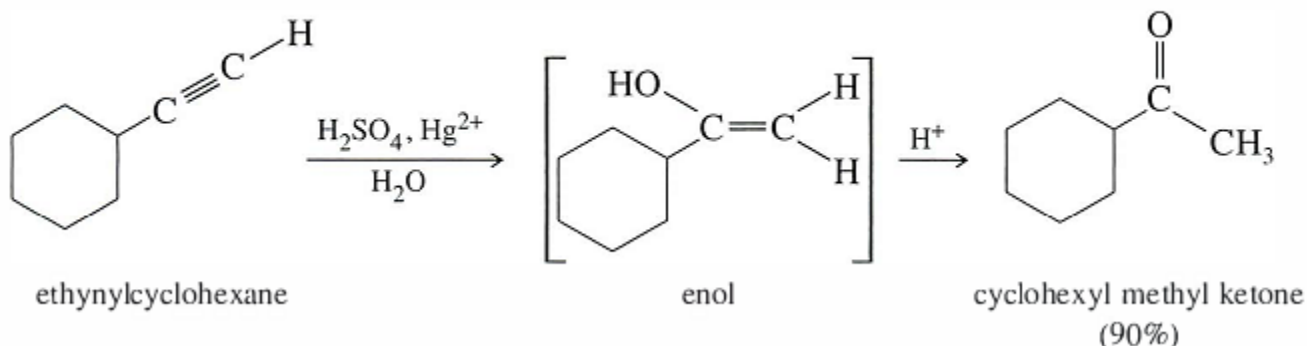
Hydroboration–Oxidation of Alkynes Hydroboration–oxidation of an alkyne gives anti-Markovnikov addition of water across the triple bond. Di(secondary isoamyl)borane, called *disiamylborane*, is used, since this bulky borane cannot add twice across the triple bond. On oxidation of the borane, the unstable enol quickly tautomerizes to an aldehyde.

alkyne   enol (not isolated)   aldehyde

Example

ethynylcyclohexane   cyclohexylethanal
                                                                              (65%)
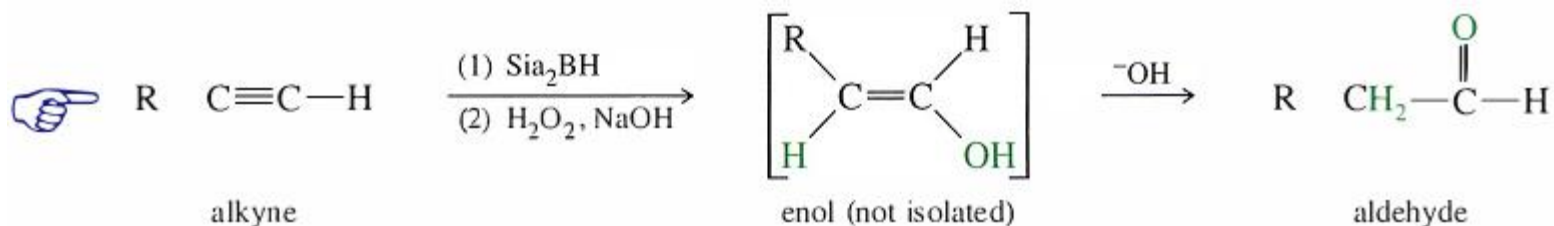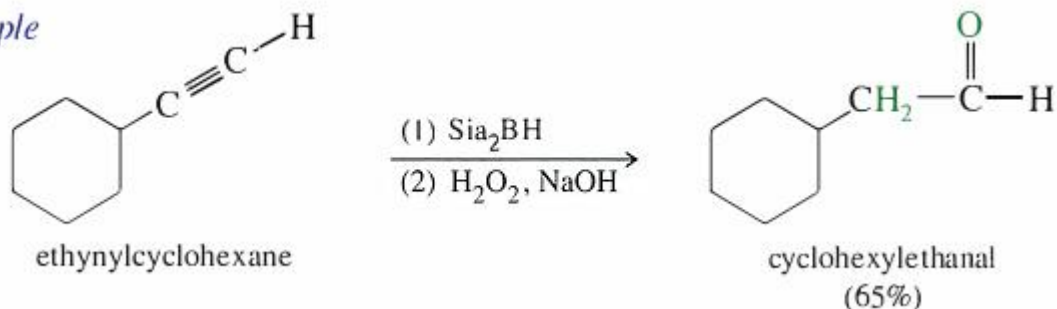
SOLVED PROBLEM 18-1

Show how you would synthesize each compound from starting materials containing no more than six carbon atoms.

(a)

(b)
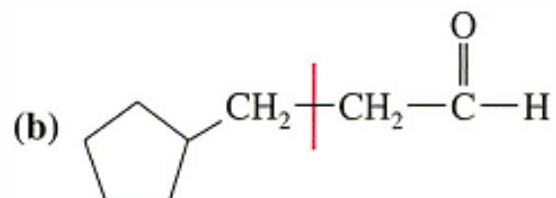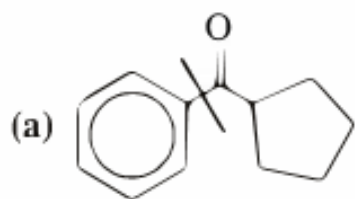
SOLUTION

(a) This compound is a ketone with 12 carbon atoms. The carbon skeleton might be assembled from two six-carbon fragments using a Grignard reaction, which gives an·alcohol that is easily oxidized to the target compound.

$$\text{MgBr} + \text{C-H} \xrightarrow[\text{(2) } H_3O^+]{\text{(1) ether solvent}} \text{OH} \xrightarrow[H_2SO_4]{Na_2Cr_2O_7} \text{target (a)}$$

An alternative route to the target compound involves Friedel–Crafts acylation.

$$\text{+ C-Cl} \xrightarrow{AlCl_3}$$

(b) This compound is an aldehyde with eight carbon atoms. An aldehyde might come from oxidation of an alcohol (possibly a Grignard product) or hydroboration of an alkyne. If we use a Grignard, the restriction to six-carbon starting materials means we need to add two carbons to a methylcyclopentyl fragment, ending in a primary alcohol. Grignard addition to an epoxide does this.
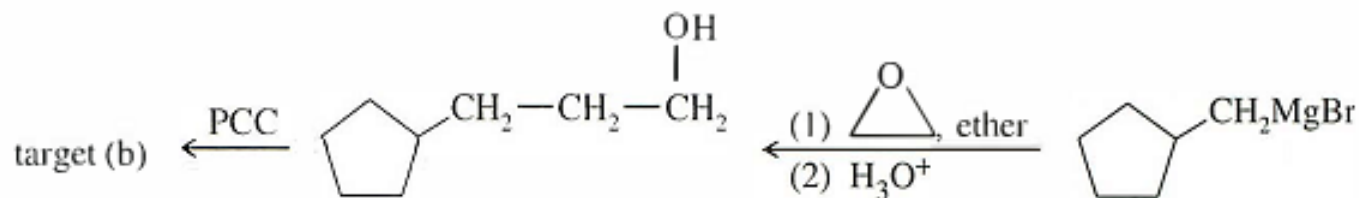
Alternatively, we could construct the carbon skeleton using acetylene as the two-carbon fragment. The resulting terminal alkyne undergoes hydroboration to the correct aldehyde.
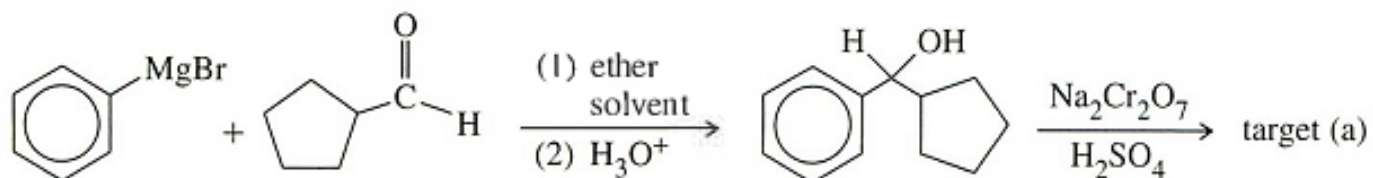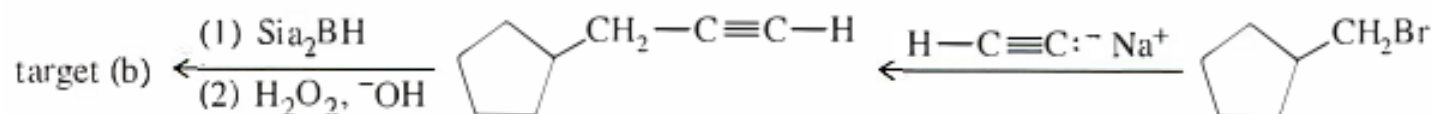

PROBLEM 18-6

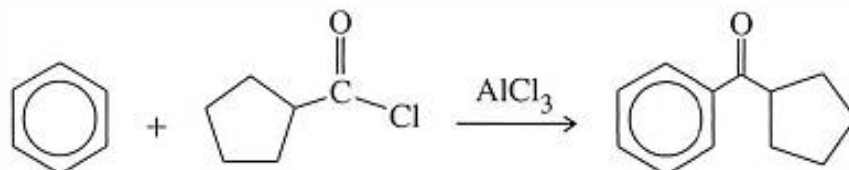Show how you would synthesize each compound from starting materials containing no more than six carbon atoms.

(a)

(b)

(c)
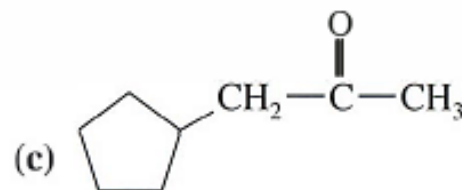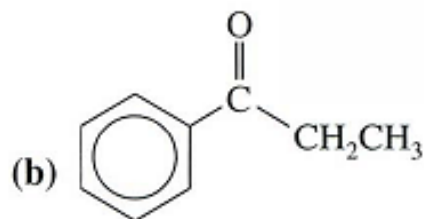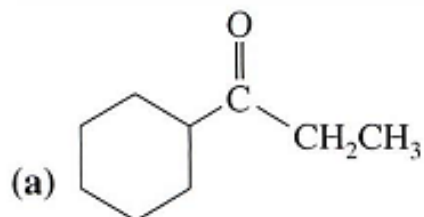
Synthesis of Ketones from Carboxylic Acids

carboxylic acid →(LiOH)→ lithium carboxylate →(R'—Li)→ dianion →(H_3O^+)→ hydrate →($-H_2O$)→ ketone

cyclohexane carboxylic acid →(2 phenyllithium)→ dianion →(H_3O^+)→ hydrate →($-H_2O$)→ cyclohexyl phenyl ketone
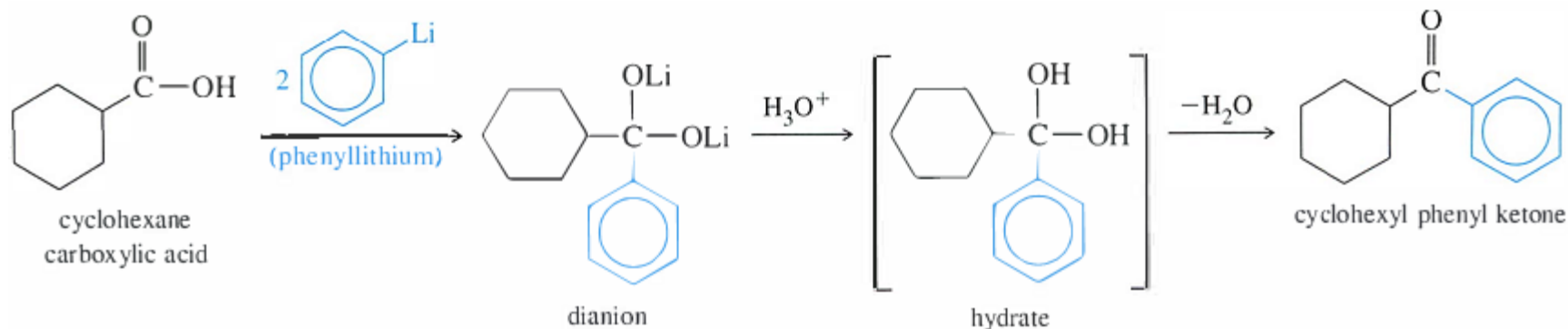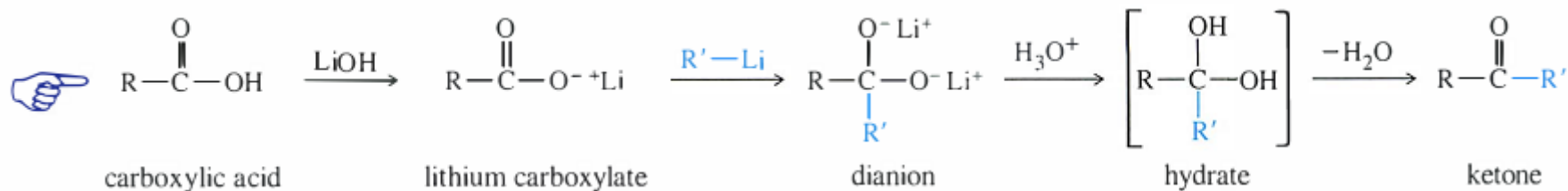
PROBLEM 18-8

Predict the products of the following reactions.

(a) [benzoic acid structure] $\xrightarrow[(2) H_3O^+]{(1) \text{ excess } CH_3Li}$

(b) CH_3COOH $\xrightarrow[(2) H_3O^+]{(1) \ 2 \text{ [cyclohexyllithium]}}$

(c) $CH_3(CH_2)_3COOH$ $\xrightarrow[(2) H_3O^+]{(1) \text{ excess } CH_3CH_2Li}$
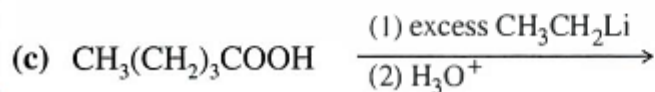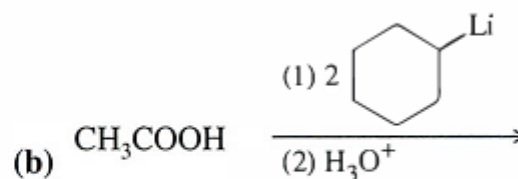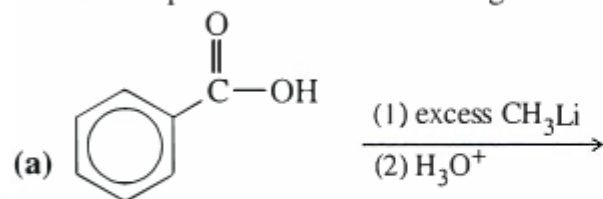
Synthesis of Ketones from Nitriles

$R'-Mg-X$

$R-C\equiv N:$ → Mg salt of imine → imine → ketone

nucleophilic attack · · · Mg salt of imine · · · imine · · · ketone

$$R'-C\equiv N: \longrightarrow \underset{R}{\overset{R'}{C}}=N \cdot MgX \xrightarrow{H^+} \underset{R}{\overset{R'}{C}}=N \cdot H \xrightarrow{H_3O^+} \underset{R}{\overset{R'}{C}}=O: + NH_4^+$$

Example

benzonitrile + phenylmagnesium bromide $\xrightarrow{\text{ether}}$ benzophenone imine (magnesium salt) $\xrightarrow{H_3O^+}$ benzophenone (80%)
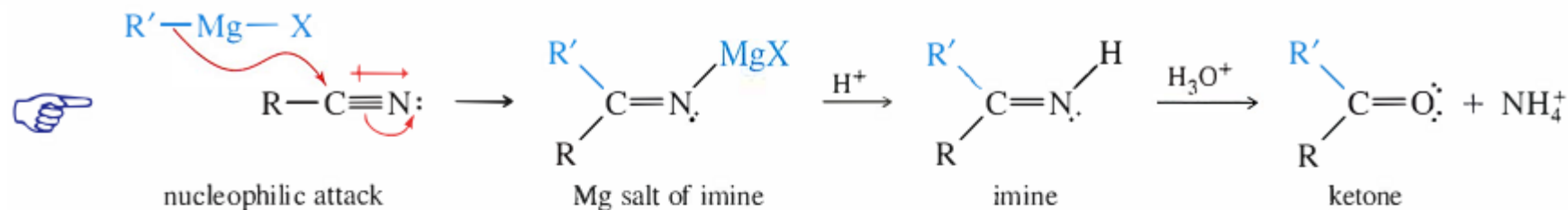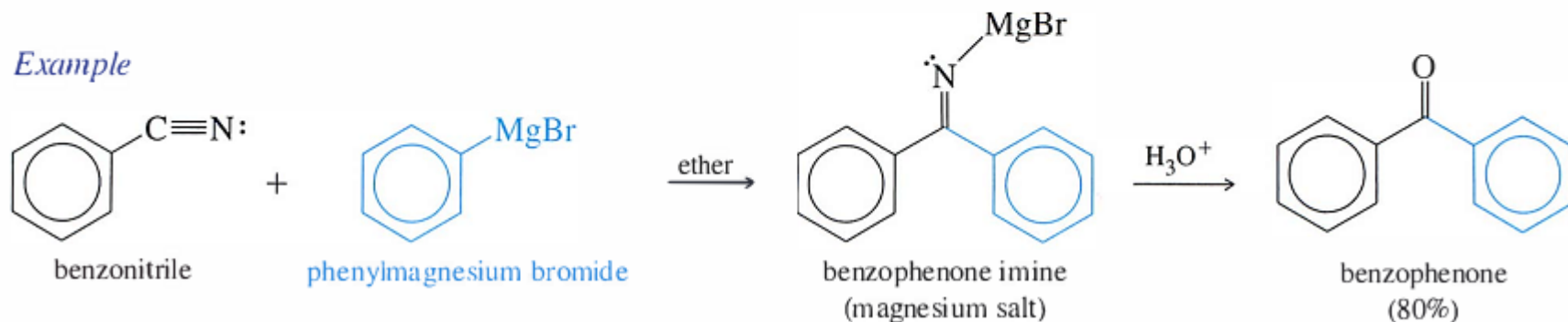
PROBLEM 18-9

Predict the products of the following reactions.
(a) $CH_3CH_2CH_2CH_2-C\equiv N + CH_3CH_2-MgBr$, then H_3O^+
(b) benzyl bromide + sodium cyanide
(c) product of (b) + cyclopentylmagnesium bromide, then acidic hydrolysis

PROBLEM 18-10

Show how the following transformations may be accomplished in good yield. You may use any additional reagents that are needed.
(a) bromobenzene → propiophenone   (b) CH_3CH_2CN → 3-heptanone
(c) pentanoic acid → 3-heptanone   (d) toluene → benzyl cyclopentyl ketone

Synthesis of Aldehydes and Ketones from Acid Chlorides

$$R-\overset{\overset{\displaystyle O}{\|}}{C}-OH \xrightarrow[\text{(slow)}]{LiAlH_4} \left[R-\overset{\overset{\displaystyle O}{\|}}{C}-H\right] \xrightarrow[\text{(fast)}]{LiAlH_4} R-CH_2-O^-$$

acid   aldehyde (not isolable)   alkoxide

👉 $$R-\overset{\overset{\displaystyle O}{\|}}{C}-OH \;+\; Cl-\overset{\overset{\displaystyle O}{\|}}{S}-Cl \longrightarrow R-\overset{\overset{\displaystyle O}{\|}}{C}-Cl \;+\; HCl \;+\; SO_2\uparrow$$

acid   thionyl chloride   acid chloride

👉 $$R-\overset{\overset{\displaystyle O}{\|}}{C}-Cl \xrightarrow[\text{lithium aluminum tri}(t\text{-butoxy})\text{hydride}]{Li^+ \; ^-AlH(O\text{-}t\text{-Bu})_3} R-\overset{\overset{\displaystyle O}{\|}}{C}-H$$

acid chloride   aldehyde

Example

$$\underset{\text{isovaleric acid}}{CH_3CHCH_2-\overset{\overset{\displaystyle O}{\|}}{C}-OH} \xrightarrow{SOCl_2} \underset{\text{isovaleroyl chloride}}{CH_3CHCH_2-\overset{\overset{\displaystyle O}{\|}}{C}-Cl} \xrightarrow{Li^+ \; ^-AlH(O\text{-}t\text{-Bu})_3} \underset{\text{isovaleraldehyde (65\%)}}{CH_3CHCH_2-\overset{\overset{\displaystyle O}{\|}}{C}-H}$$

(with CH_3 substituents shown on the CH positions)

Synthesis of Ketones

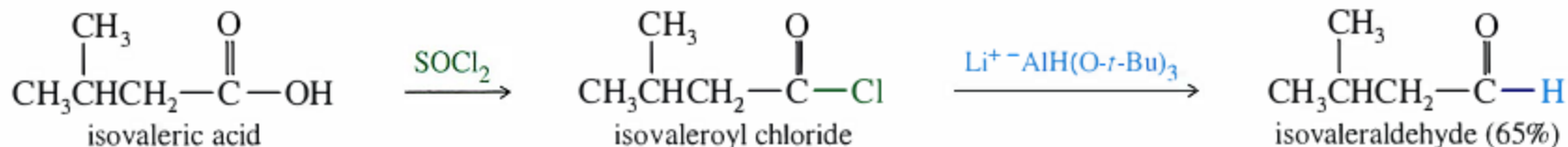$$\underset{\text{acid chloride}}{R'-\overset{\overset{\displaystyle O}{\|}}{C}-Cl} \xrightarrow[\text{(fast)}]{RMgX} \underset{\text{ketone}}{\left[R'-\overset{\overset{\displaystyle O}{\|}}{C}-R\right]} \xrightarrow[\text{(fast)}]{RMgX} \underset{\text{alkoxide}}{R'-\overset{\overset{\displaystyle O^-\,^+MgX}{|}}{\underset{\underset{\displaystyle R}{|}}{C}}-R}$$

To stop at the ketone stage, a weaker organometallic reagent is needed: one that reacts faster with acid chlorides than with ketones. A **lithium dialkylcuprate (Gilman reagent)** is such a reagent.

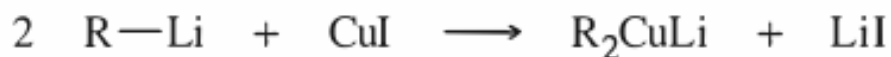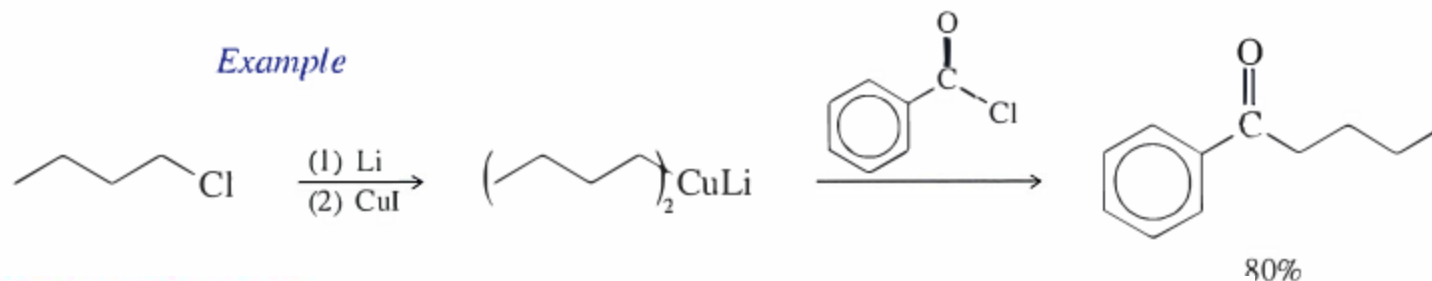$$R_2CuLi \quad + \quad R'-\overset{\overset{\displaystyle O}{\|}}{C}-Cl \quad \longrightarrow \quad R'-\overset{\overset{\displaystyle O}{\|}}{C}-R \quad + \quad R-Cu \quad + \quad LiCl$$

a lithium dialkylcuprate

$$2 \quad R-Li \quad + \quad CuI \quad \longrightarrow \quad R_2CuLi \quad + \quad LiI$$

Example

80%

PROBLEM 18-11

Predict the products of the following reactions:

(a) $\xrightarrow[\text{(2) H}_3\text{O}^+]{\text{(1) LiAlH}_4}$

(b) $\xrightarrow{\text{LiAlH(O-}t\text{-Bu)}_3}$

(c) $\xrightarrow[\text{(2) H}_3\text{O}^+]{\text{(1) excess} \quad \diagup\!\!\diagdown \text{MgCl}}$

(d) $\xrightarrow{(\diagup\!\!\diagdown)_2\text{CuLi}}$