CH 318 N LECTURE 9

Textbook Assignment: Chapter 16

Homework (for credit): POW 4 posted

Today's Topics: Aldehydes & Ketones

Notice & Announcements:

Exam 1-Grading in Progress

Organometallic Compounds

Carbenes and Carbenoids

- **Carbene**, R_2C: a neutral molecule in which a carbon atom is surrounded by only six valence electrons
- Methylene, the simplest carbene
  - prepared by photolysis or thermolysis of diazomethane

$$H_2\overset{-}{\ddot{C}}-\overset{+}{N}\equiv N: \xrightarrow{h\nu} H_2C: + :N\equiv N:$$

Methylene (the simplest carbene)

  - methylene prepared in this manner is so nonselective that it is of little synthetic use

Carbenes and Carbenoids

Dichlorocarbene

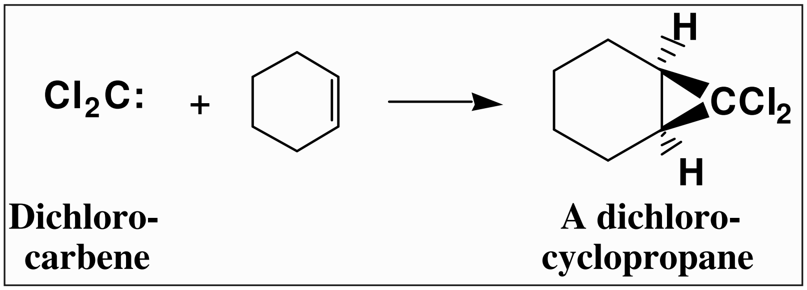
- prepared by treating chloroform with potassium *tert*-butoxide

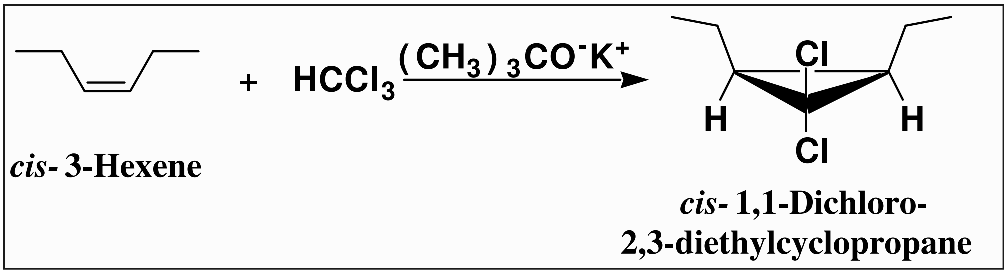
$$CHCl_3 + (CH_3)_3CO^-K^+ \longrightarrow Cl_2C: + (CH_3)_3COH + K^+Cl^-$$

Trichloromethane (Cloroform) | Potassium *tert*-butoxide | Dichloro-carbene | *tert*-Butyl alcohol

Dichlorocarbene

reacts with alkenes to give dichlorocyclopropanes





- **Simmons-Smith reaction**
  - a way to add methylene to an alkene to form a cyclopropane
  - generation of the Simmons-Smith reagent

$$CH_2I_2 + Zn(Cu) \xrightarrow[\text{diethyl ether}]{} ICH_2ZnI$$

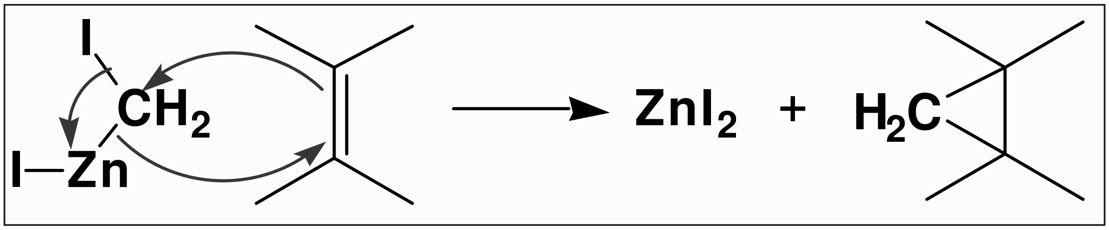
Diiodo-methane | **Zinc-copper couple** | **Iodomethylzinc iodide (Simmons-Smith reagent)**

  - this organozinc compound reacts with a wide variety of **alkenes to give cyclopropanes**

(prepared by: Zn dust; CuCl & heat)

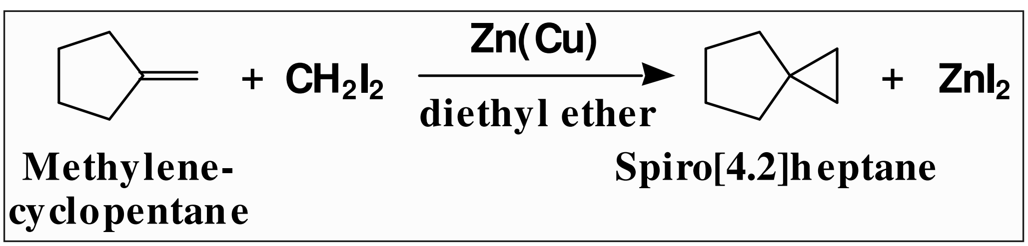
Simmons-Smith reaction:

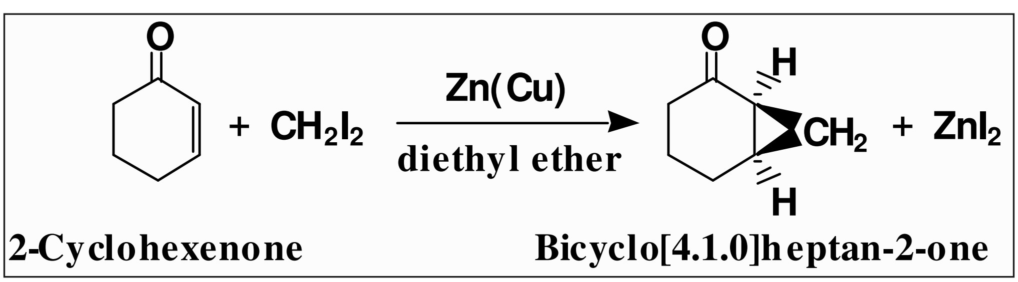
the organozinc compound reacts with an alkene by a concerted mechanism*



*__concerted mechanism__-one in which there is simultaneous bond breaking and bond formation.

Uses of the Simmons-Smith reagent:





Note: regioselectivity-alkene vs carbonyl

Aldehydes And Ketones

The Carbonyl Group

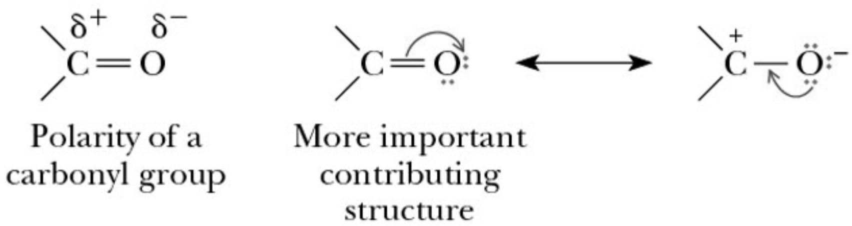
The next units cover the physical and chemical properties of classes of compounds containing the carbonyl group,

C=O

- aldehydes and ketones (Chapter 16)
- carboxylic acids (Chapter 17)
- acid halides, acid anhydrides, esters, amides (Chapter 18)
- enolate anions (Chapter 19)

Physical Properties

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



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

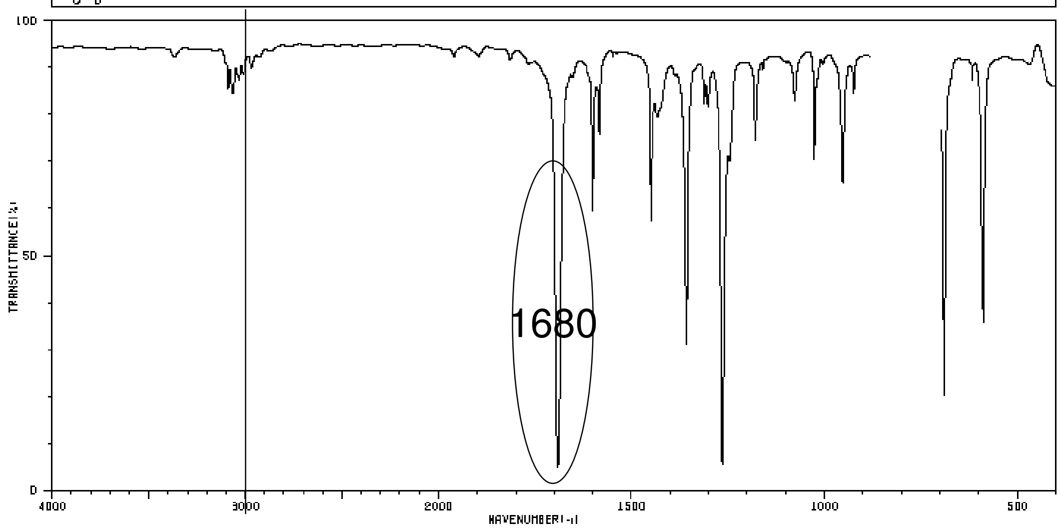
Spectral Properties

- **IR:** Carbonyl-Aldehydes 1720-1725; also show m C-H @ 2720; Ketones 1710-1715 (aryl ketones 1680)
- **NMR:** Aldehydes 9.5-10.2 (s) ketones protons α to 2.1-2.3 can be 2.2-2.6
- **^{13}CNMR:** carbonyl carbon 180-215 ppm
- **MS:** Aldehydes (M-1) loss of aldehyde H; loss of CO (M-28); both groups undergo α cleavage

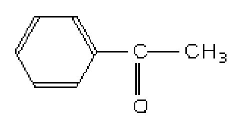
HIT-NO=1117	SCORE= ( )	SDBS-NO=722	IR-NIDA-08653 : CCL4 SOLUTION

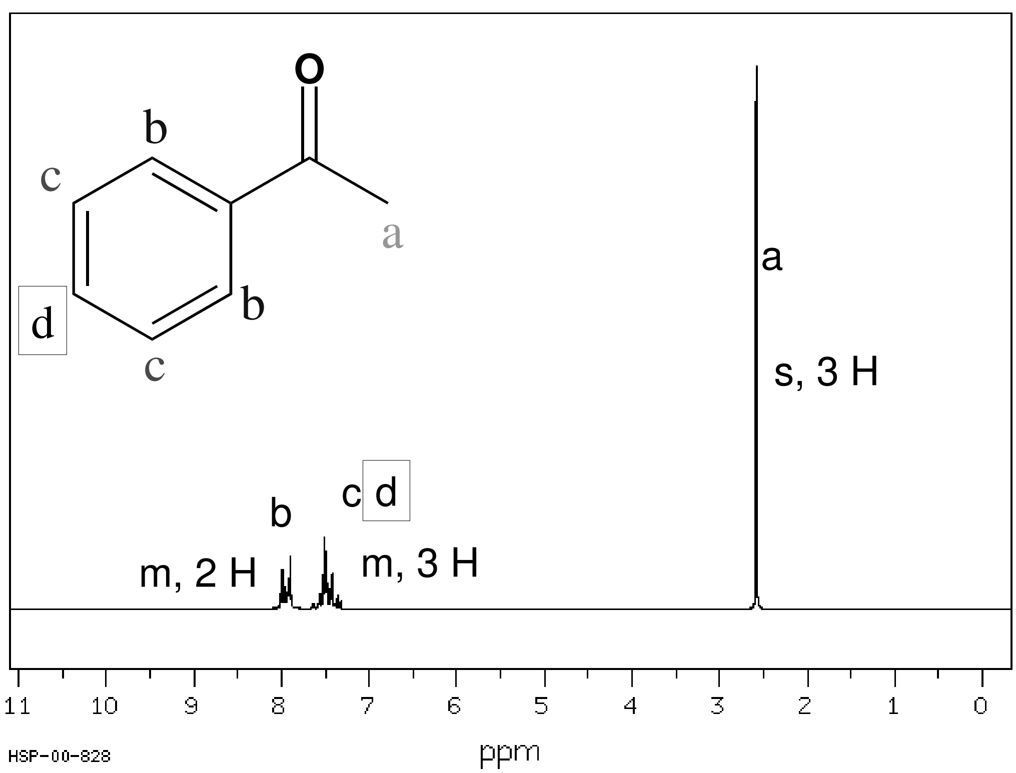
ACETOPHENONE

C_8H_8O

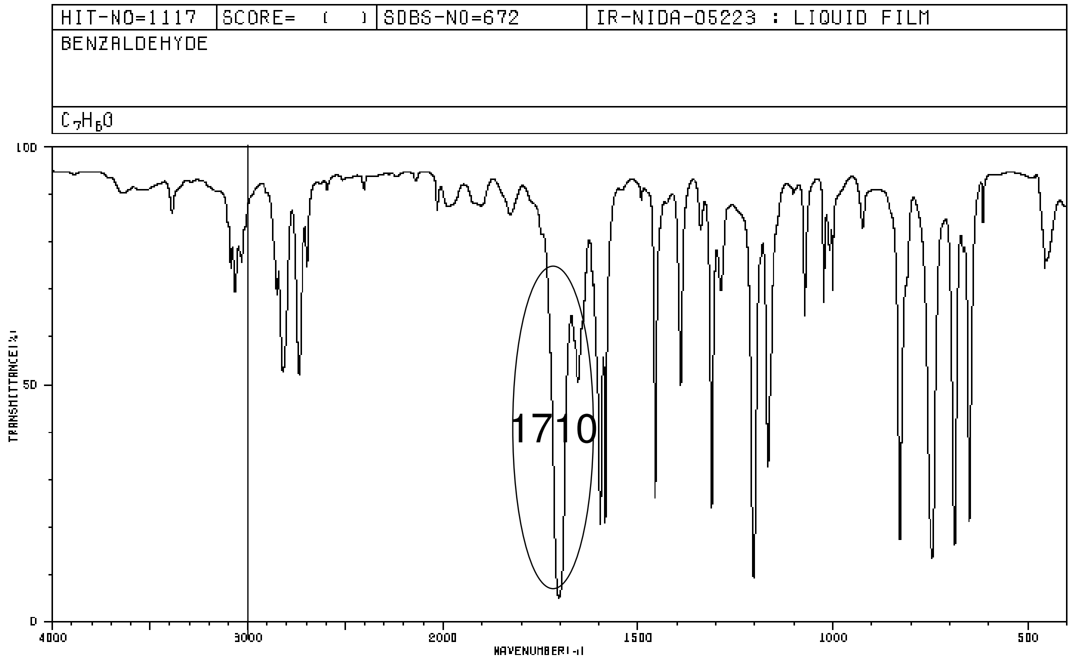


3089	81	1684	72	1246	68	690	19
3066	81	1450	55	1180	72	618	84
3031	84	1433	77	1159	86	588	34
3008	84	1368	30	1077	79		
2969	86	1312	79	1026	68		
1691	4	1302	79	953	82		
1601	67	1266	6	924	81		

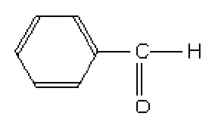


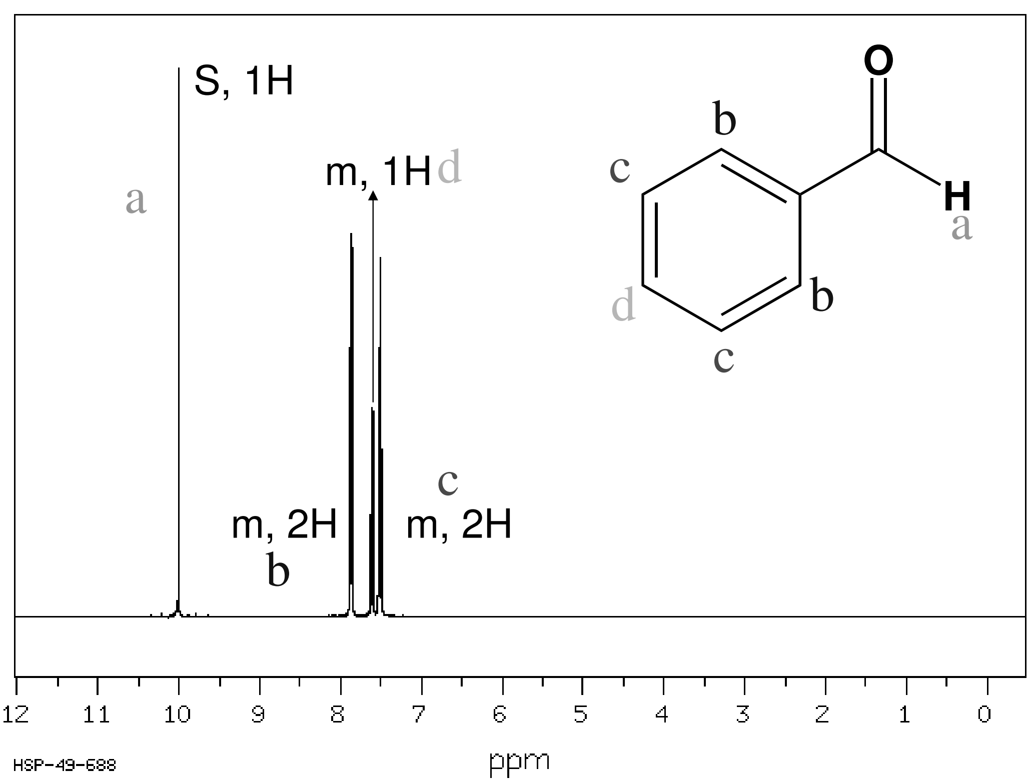


HSP-00-828



3086	72	1981	84	1697	20	1204	8	828	16
3065	66	1916	84	1584	20	1168	31	746	13
3031	72	1909	84	1456	25	1073	62	688	15
2850	66	1901	84	1391	47	1023	64	667	74
2820	50	1828	81	1339	79	1008	74	650	20
2736	50	1703	4	1311	23	1001	66	615	61
2696	72	1664	49	1288	68	924	78	457	72

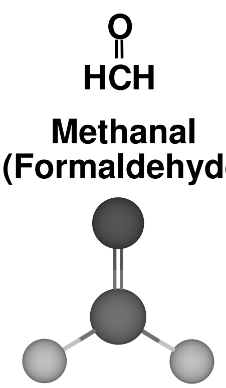




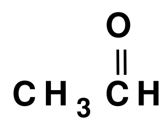
400mHz

– the functional group of an **aldehyde** is a carbonyl group bonded to a H atom and a carbon atom

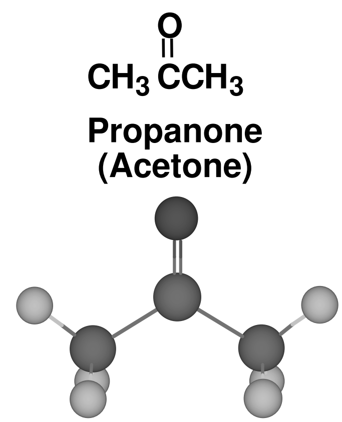
– the functional group of a **ketone** is a carbonyl group bonded to two carbon atoms



Methanal (Formaldehyde)



Ethanal (Acetaldehyde)

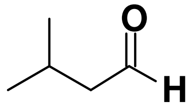


Propanone (Acetone)

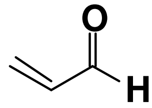
Nomenclature

IUPAC names:

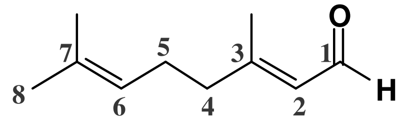
- the parent chain is the longest chain that contains the functional group
- for an aldehyde, change the suffix from -e to -al
- for an unsaturated aldehyde, change the infix from -an- to -en-; the location of the suffix determines the numbering pattern
- for a cyclic molecule in which -CHO is bonded to the ring, add the suffix -carbaldehyde



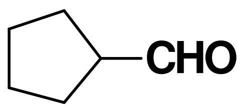
3-Methylbutanal



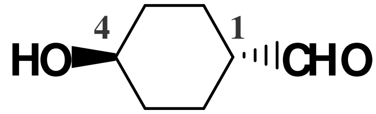
2-Propenal
(Acrolein)



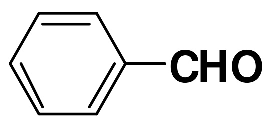
(2*E*)-3,7-Dimethyl-2,6-octadienal
(Geranial)



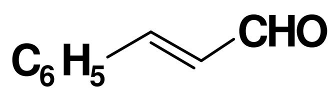
Cyclopentane-carbaldehyde



trans-4-Hydroxycyclo-hexanecarbaldehyde



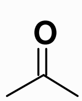
Benzaldehyde



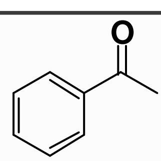
trans-3-Phenyl-2-propenal
(Cinnamaldehyde)

IUPAC names

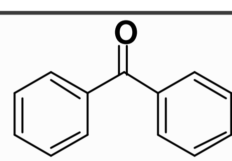
- the parent alkane is the longest chain that contains the carbonyl group
- for ketones, change the suffix -e to -one
- number the chain to give C=O the smaller number
- the IUPAC retains the common names acetone, acetophenone, and benzophenone



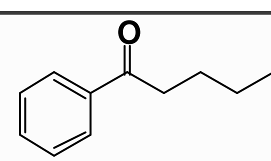
Propanone
(Acetone)



Acetophenone



Benzophenone

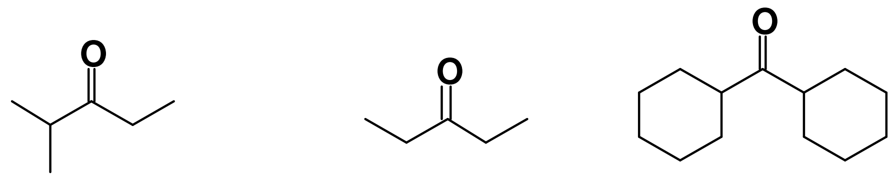


1-Phenyl-1-pentanone

Common Names

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

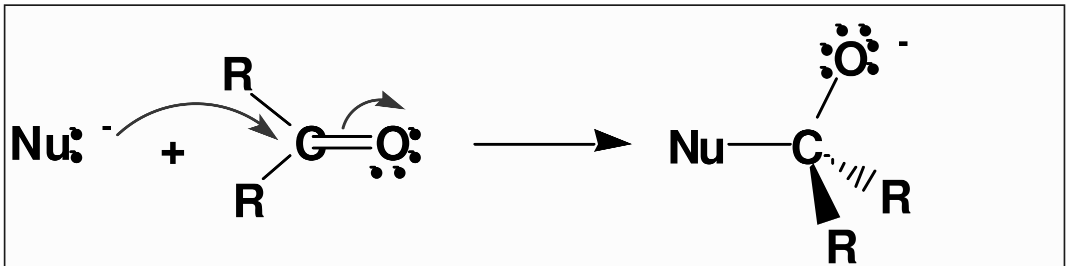
Formaldehyde   Formic acid   Acetaldehyde   Acetic acid



Ethyl isopropyl ketone   Diethyl ketone   Dicyclohexyl ketone

Reaction Themes

One of the most common reaction themes of a carbonyl group is addition of a nucleophile to form a tetrahedral carbonyl addition compound (intermediate).

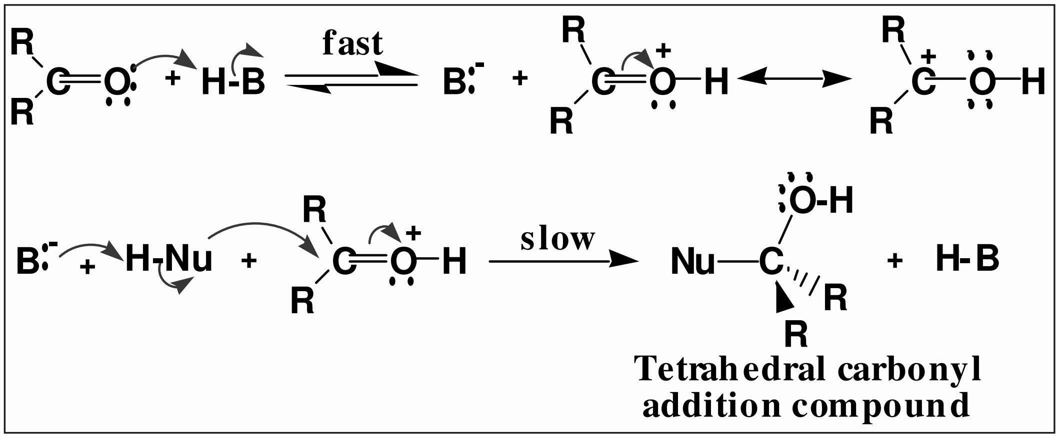


Tetrahedral carbonyl addition compound

Reaction Themes

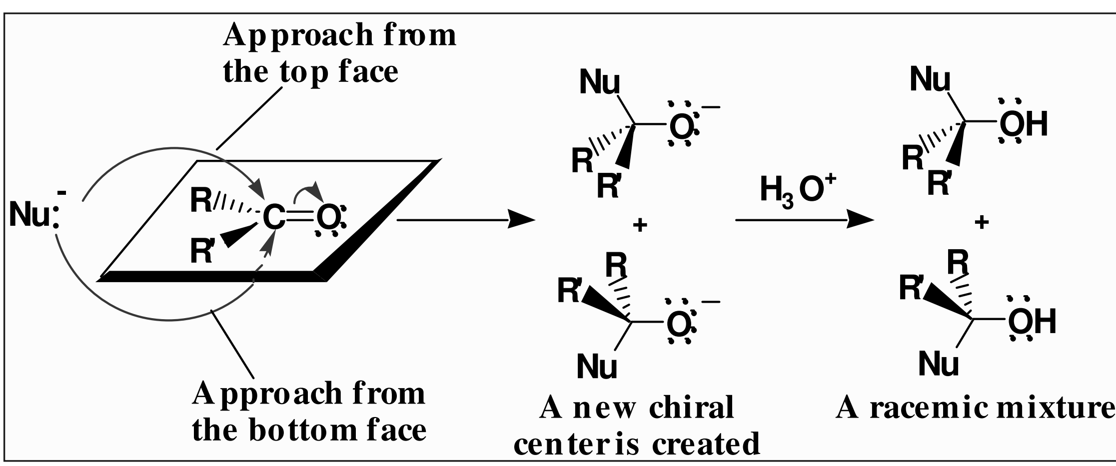
A second common theme is reaction with a proton or other Lewis acid to form a resonance-stabilized cation--

– protonation increases the electron deficiency of the carbonyl carbon and makes it more reactive toward nucleophiles



– often the tetrahedral product of addition to a carbonyl is a new chiral center

– if none of the starting materials is chiral and the reaction takes place in an achiral environment, then enantiomers will be formed as a racemic mixture



Addition of C Nucleophiles

Addition of carbon nucleophiles is one of the most important types of nucleophilic additions to a **C=O** group

- a new **carbon-carbon bond** is formed in the process
- Focus on addition of these carbon nucleophiles:

RMgX	RLi	$RC\equiv C:^-$	$^-:C\equiv N:$
A Grignard reagent	An organolithium reagent	An alkyne anion	Cyanide ion

Grignard Reagents

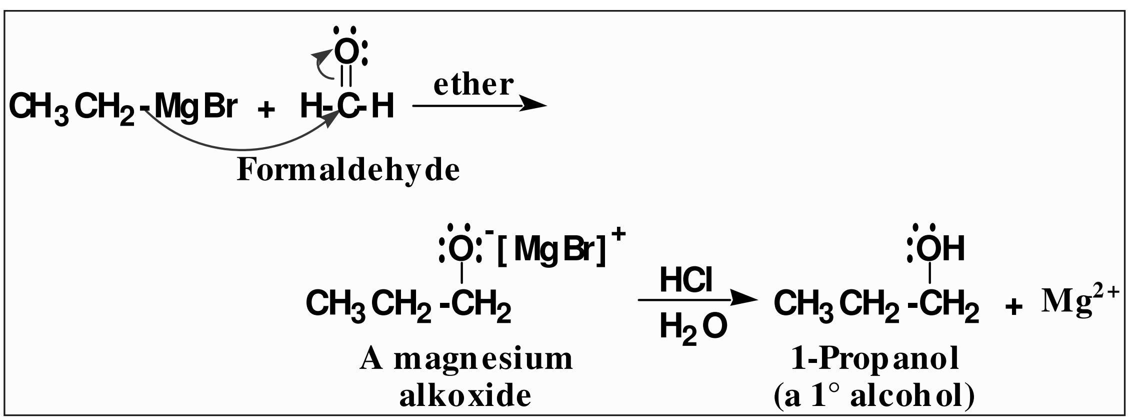
- Given the difference in electronegativity between carbon and magnesium (2.5 - 1.3), the C-Mg bond is polar covalent, with Cδ- and Mgδ+
  - in its reactions, a Grignard reagent behaves as a carbanion
- **Carbanion:** an anion in which carbon has an unshared pair of electrons and bears a negative charge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

Drawing Mechanisms

- Use double-barbed arrows to indicate the flow of pairs of e^-
- Draw the arrow from higher e^- density to lower e^- density i.e. from the nucleophile to the electrophile
- Removing e^- density from an atom will create a formal + charge
- Adding e^- density to an atom will create a formal - charge
- Proton transfer is fast (kinetics) and usually reversible

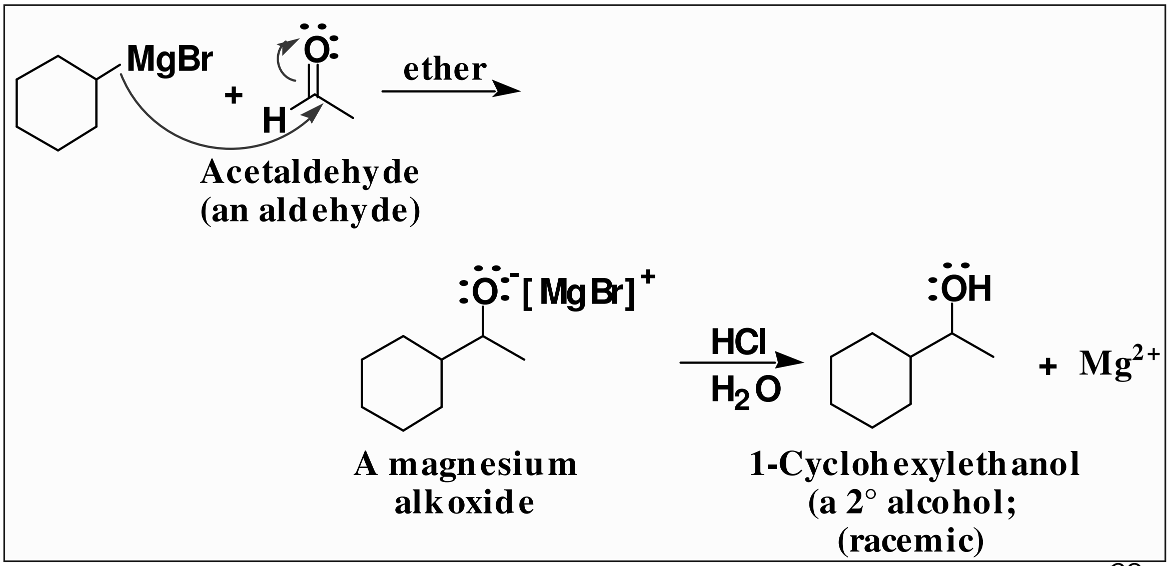
Grignard Reagents

– addition of a Grignard reagent to formaldehyde followed by H_3O^+ gives a 1° alcohol



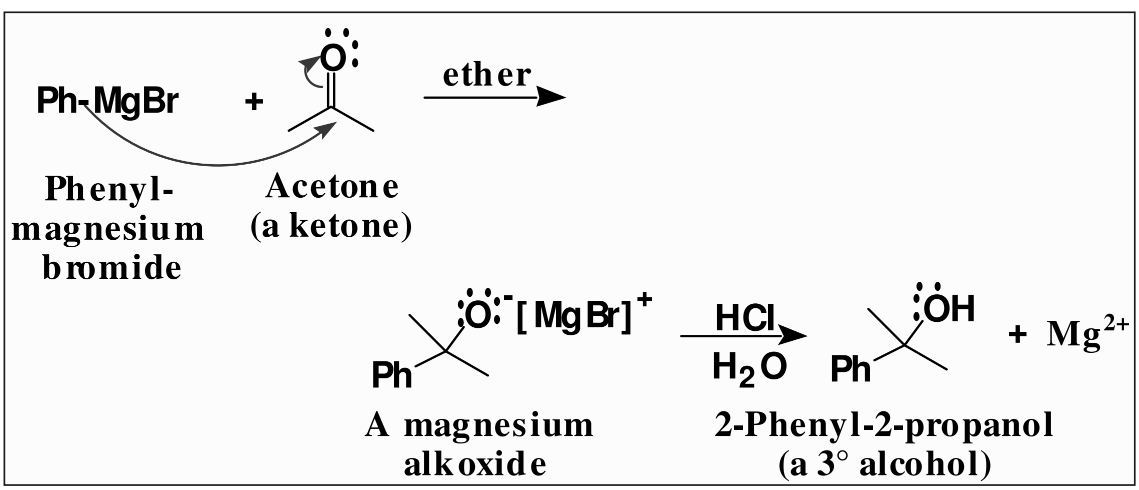
Grignard Reagents

– addition to any other RCHO gives a 2° alcohol

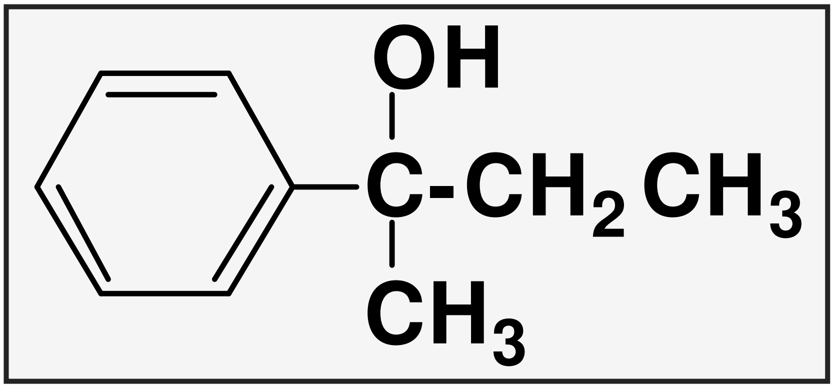


Grignard Reagents

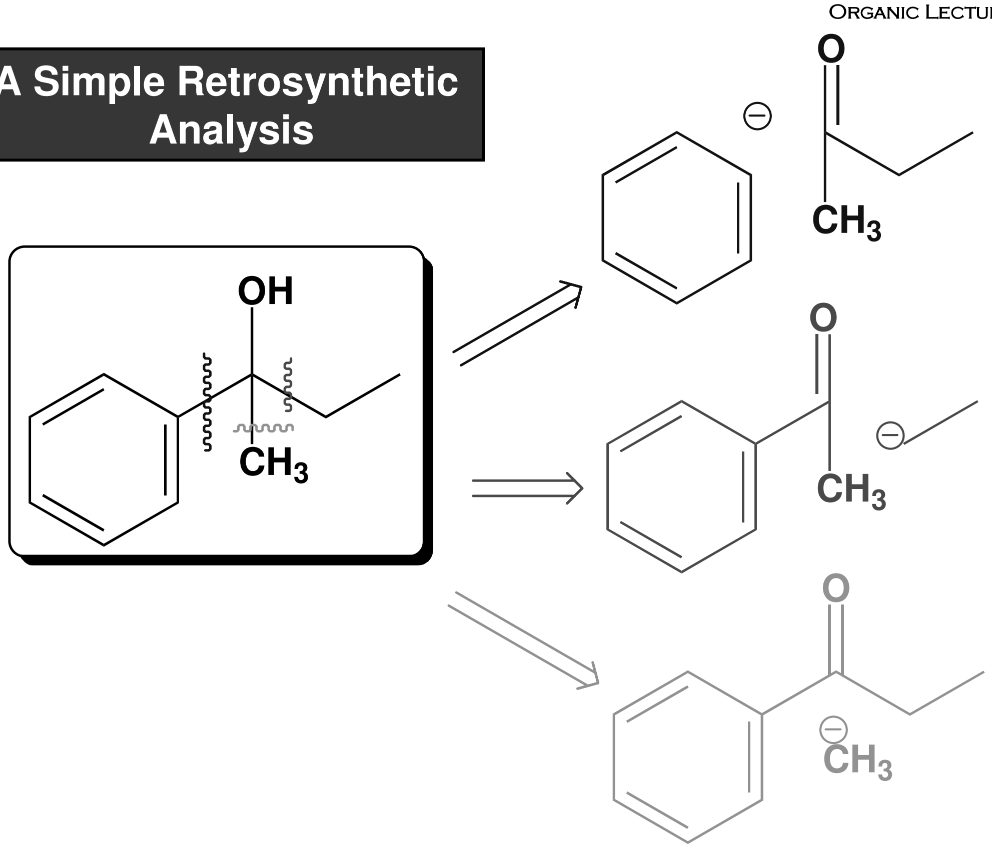
– addition to a ketone gives a 3° alcohol

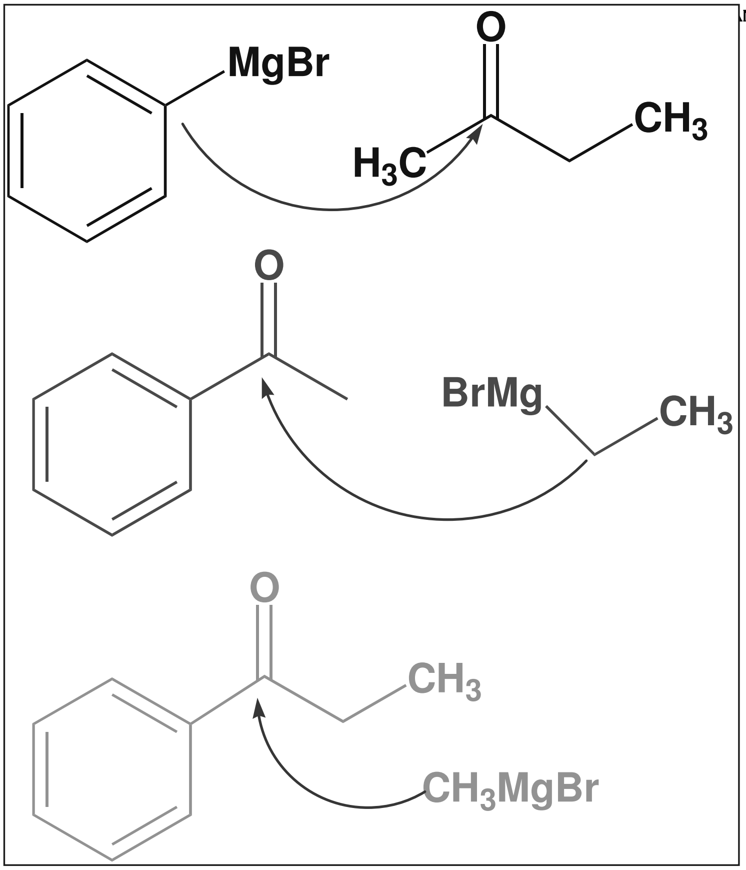


Problem: 2-phenyl-2-butanol can be synthesized by three different combinations of a Grignard reagent and a ketone. Show each combination.



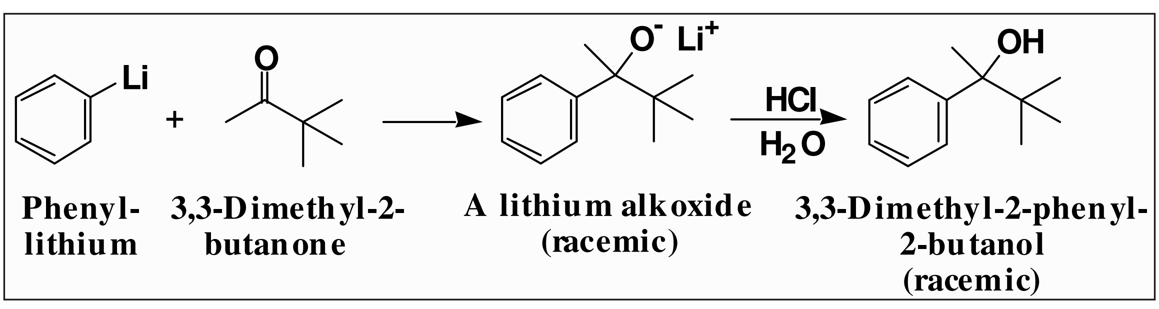
A Simple Retrosynthetic Analysis





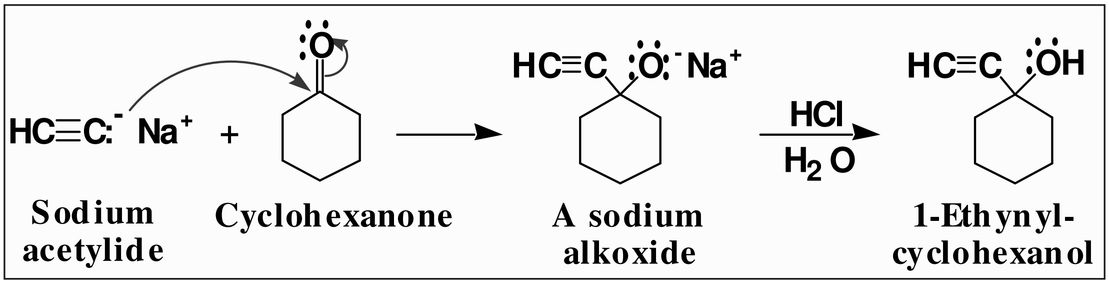
Organolithium Reagents

Organolithium compounds are generally more reactive in C=O addition reactions than RMgX, and typically give higher yields



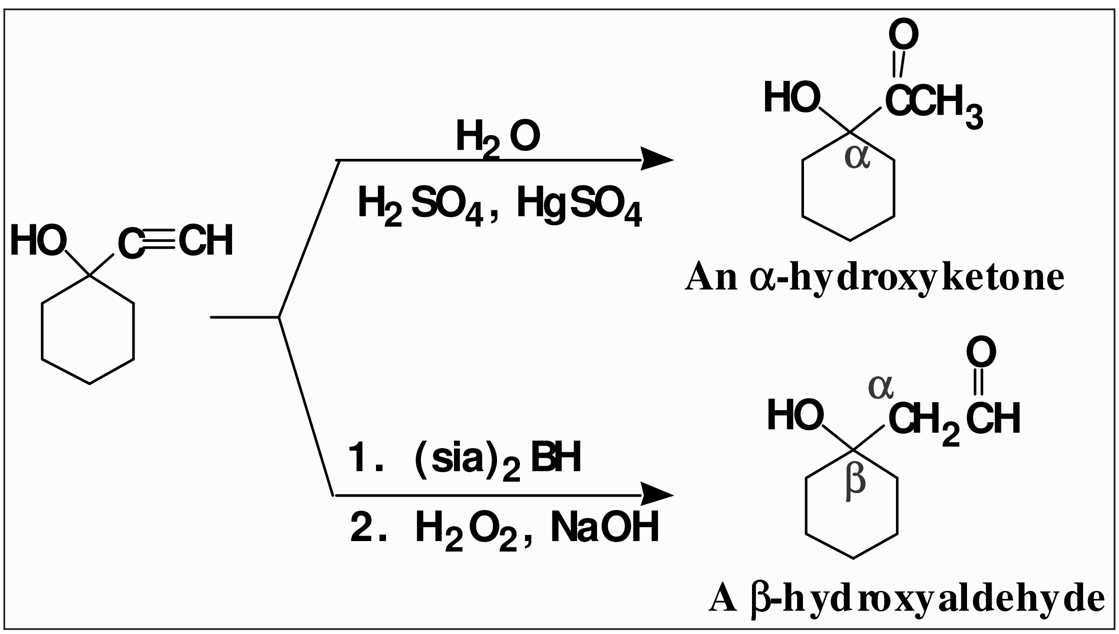
Salts of Terminal Alkynes

- Addition of an alkyne anion followed by H_3O^+ gives an α-acetylenic alcohol
- Note: this is a 2-C homologation



Homologation is a term used for extending a carbon chain

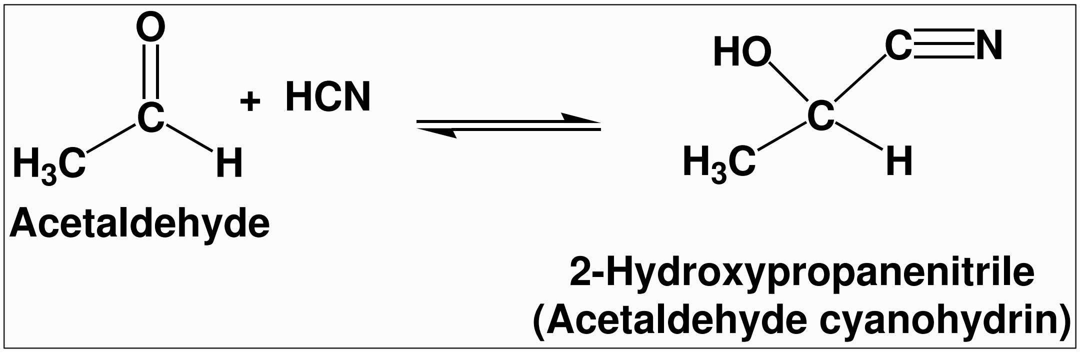
Oxidation of Terminal Alkynes



Pg 275: use of $(sia)_2BH$

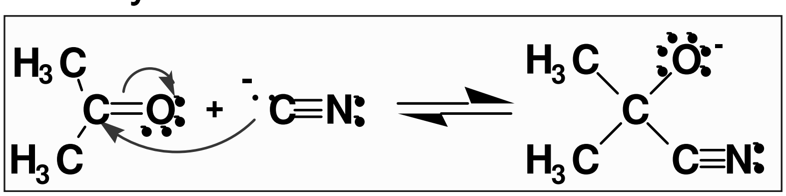
Addition of HCN

- HCN adds to the C=O group of an aldehyde or ketone to give a cyanohydrin
- Cyanohydrin: a molecule containing an -OH group and a -CN group bonded to the same carbon

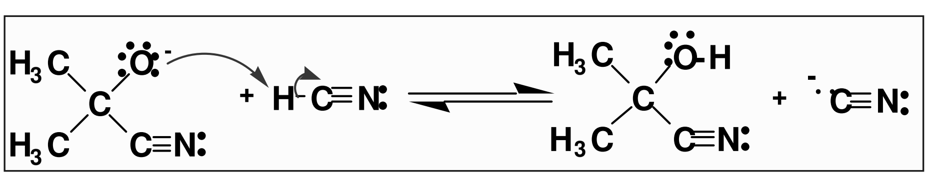


Addition of HCN

- Mechanism of cyanohydrin formation
  - Step 1: nucleophilic addition of cyanide to the carbonyl carbon



  - Step 2: proton transfer from HCN gives the cyanohydrin and regenerates cyanide ion



Cyanohydrins

- The value of cyanohydrins
  - acid-catalyzed dehydration of alcohol gives an alkene

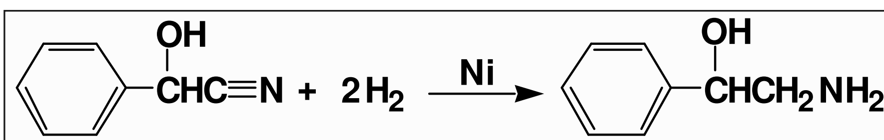
Monomer for polymers

$$CH_3CH(OH)C\equiv N \xrightarrow{\text{acid catalyst}} CH_2=CHC\equiv N + H_2O$$

2-Hydroxypropanenitrile (Acetaldehyde cyanohydrin) → Propenenitrile (Acrylonitrile)

Cyanohydrins

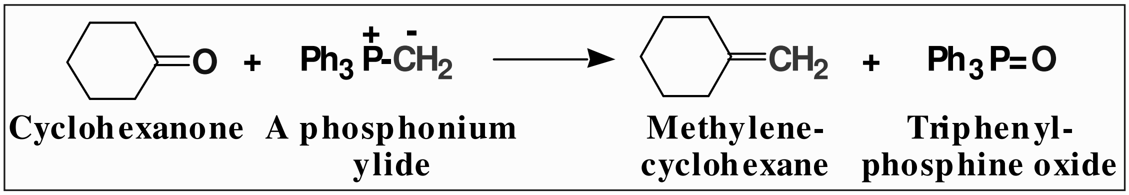
– catalytic reduction of the cyano group gives a 1° amine



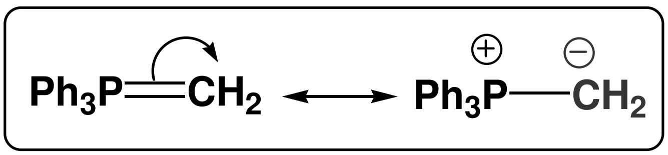
Benzaldehyde cyanohydrin (racemic) → 2-Amino-1-phenylethanol (racemic)

Wittig Reaction

The Wittig reaction is a very versatile synthetic method for the synthesis of alkenes (olefins) from aldehydes and ketones



Ylides are reagents (or reactive intermediates) which have adjacent charges:



Overall Synthetic Transformation of Wittig Reagents & Its Variations