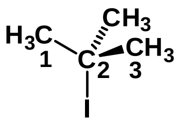
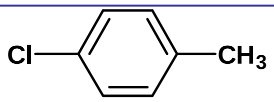
Topic 6 – Alkyl halide and carbonyl compounds

Organic compounds containing a halogen

- Compounds are named in standard way, eg:

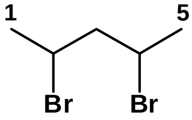


2-iodo-2-methylpropane
(tertiary alkyl halide)



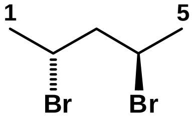
4-chlorotoluene
(aryl halide)

$CHCl_3$
trichloromethane
(chloroform)



2,4-dibromopentane
(two secondary alkyl halides)

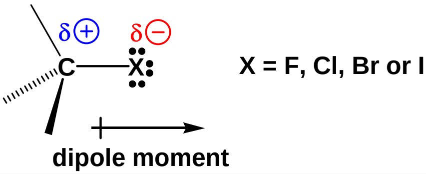
CCl_4
tetrachloromethane
(carbon tetrachloride)



(2*R*, 4*R*)-2,4-dibromopentane
(two secondary alkyl halides)

Structure and properties

- Dense liquids and solids which are insoluble in water .
- The C-X bond is polar with a slight positive charge (δ+) residing on the carbon end of the bond and a slight negative charge (δ -) on the halogen end .
- The carbon-halogen bond strength decreases in the order C-F > C-Cl > C-Br > C-I.
- Alkyl fluorides tend to be less reactive than other alkyl halides, mainly due to the higher strength of the C-F bond.

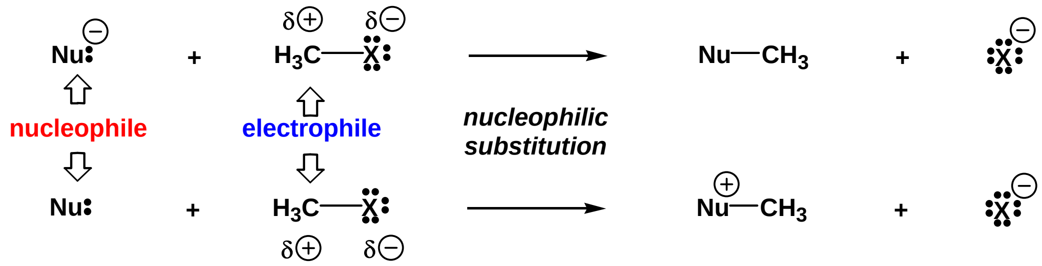


	Bond length (pm)	Bond strength (kJ mol^{-1})	Dipole moment (D)
CH_3-F	139	452	1.85
CH_3-Cl	178	351	1.87
CH_3-Br	193	293	1.81
CH_3-I	214	234	1.62

1. *Nucleophilic substitution*

***Electrophile*: A species that seeks an electron pair**

***Nucleophile*: A species that supplies an electron pair**

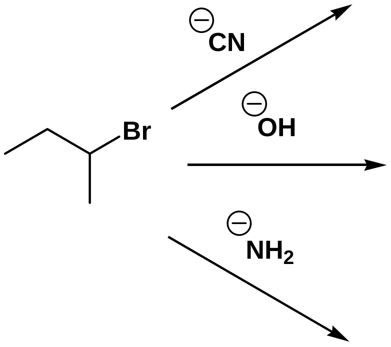


Examples:

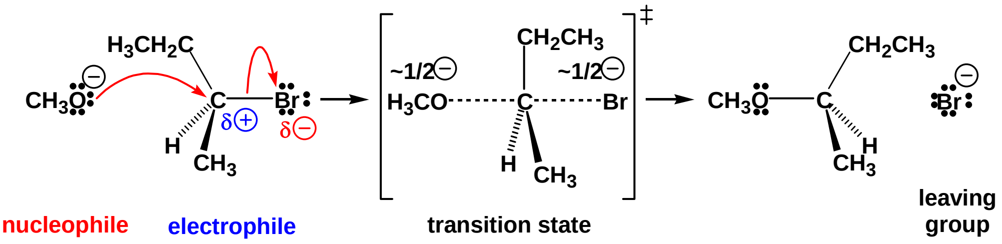
A wide range of charged and uncharged nucleophiles may be employed

Nucleophile	+	H_3C-I		Product	+	$I^{\ominus}$	Product class
$HO^{\ominus}$	+	$\overset{\delta\oplus}{H_3C}-\overset{\delta\ominus}{I}$	$\longrightarrow$	H_3C-OH	+	$I^{\ominus}$	alcohol
$RO^{\ominus}$	+	H_3C-I	$\longrightarrow$	H_3C-OR	+	$I^{\ominus}$	ether
$:N\equiv C:^{\ominus}$	+	H_3C-I	$\longrightarrow$	$H_3C-C\equiv N:$	+	$I^{\ominus}$	nitrile
$R-C\equiv C:^{\ominus}$	+	H_3C-I	$\longrightarrow$	$H_3C-C\equiv C-R$	+	$I^{\ominus}$	alkyne
$H_2N:^{\ominus}$	+	H_3C-I	$\longrightarrow$	H_3C-NH_2	+	$I^{\ominus}$	amine
$R_3N:$	+	H_3C-I	$\longrightarrow$	$H_3C-\overset{\oplus}{N}R_3$	+	$I^{\ominus}$	tetraalkylammonium salt

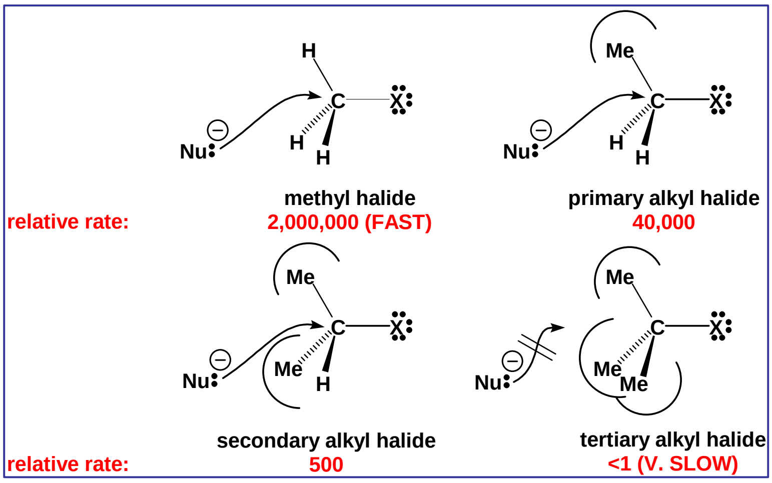
Question: Draw the organic products in the following reactions:



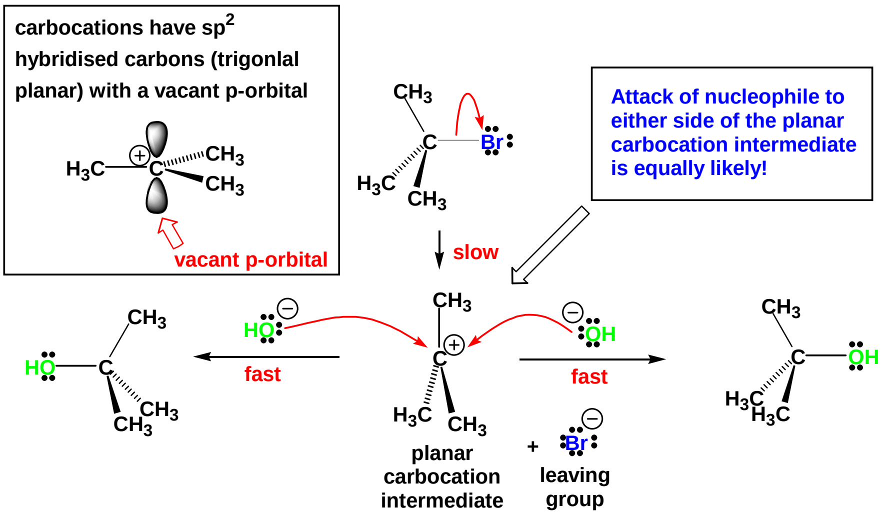
Mechanism – S_N2 (2nd order)



S_N2 reaction favoured by a primary alkyl halide as the starting material.



Mechanism – S_N1 (1st order)

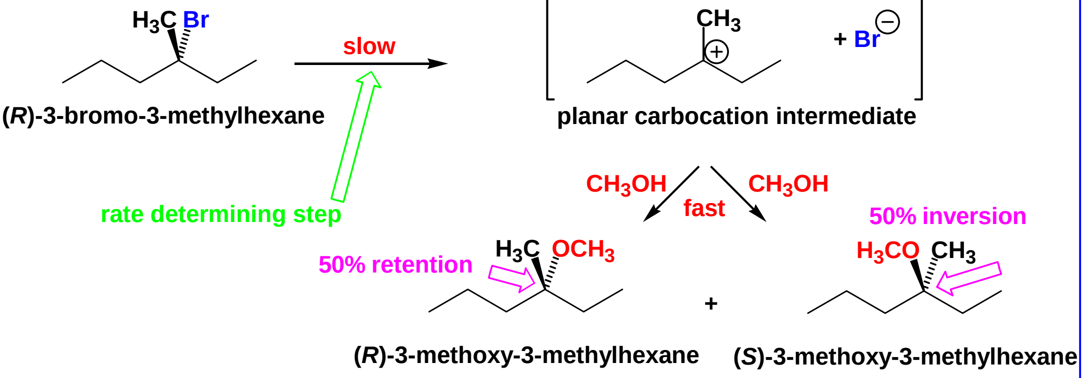

carbocations have sp^2 hybridised carbons (trigonlal planar) with a vacant p-orbital

Attack of nucleophile to either side of the planar carbocation intermediate is equally likely!

Evidence for S_N1 mechanism

Intermediacy of a planar carbocation intermediate means that any stereochemistry in the starting material is lost on conversion to the product.

The nucleophilic substitution of (*R*)-3-bromo-3-methylhexane with methanol leads to racemic methyl ether product



S_N1 stands for substitution, nucleophilic, unimolecular.

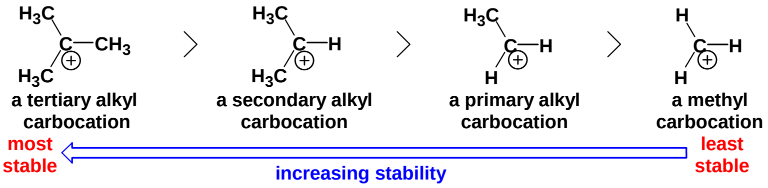
Unimolecular refers to the fact that only one molecule, the alkyl halide, is involved in the slow rate determining step. The reaction rate is therefore determined by the concentration of the alkyl halide

Reaction Rate ∝ [electrophile]

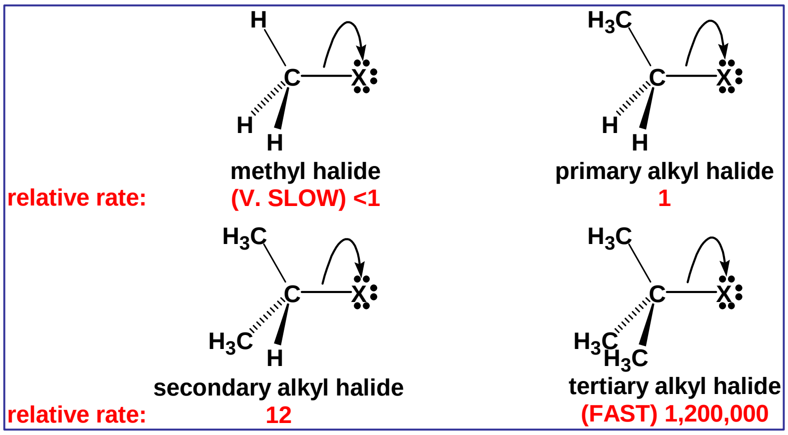
Carbocations

The intermediate in an S_N1 reaction is a carbocation.

- The C atom has six electrons and a positive charge.
- This is an unstable, highly reactive intermediate.
- Not all carbocations have the same relative (un)stability .



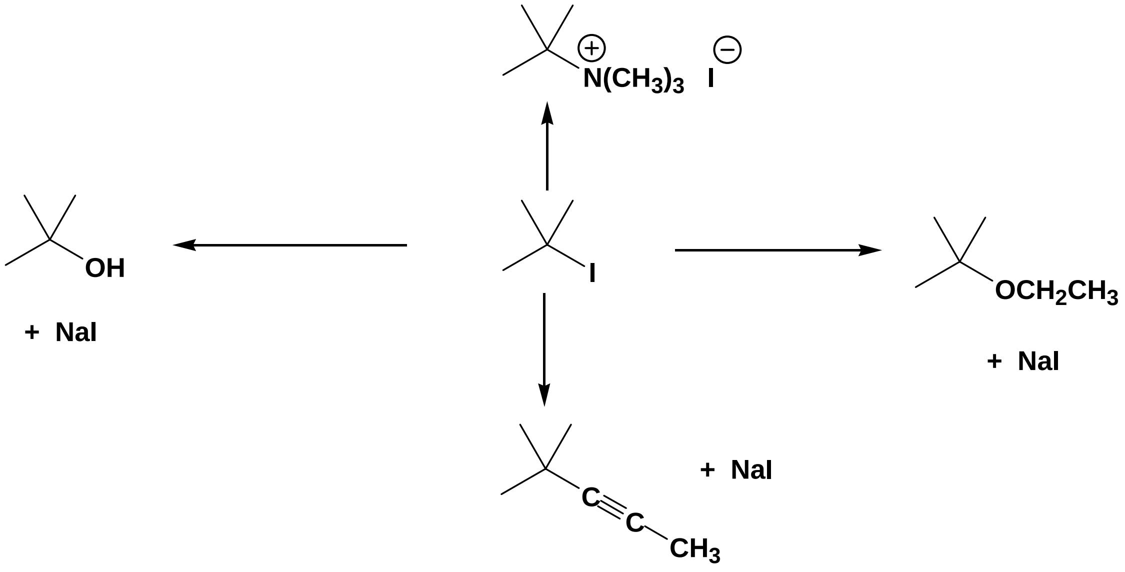
S_N1 reaction more likely when a tertiary carbocation is the intermediate



Comparison of S_N1 and S_N2

Summary S_N2 reaction:	**Summary S_N1 reaction:**
Substitution, nucleophilic, second order	**Substitution, nucleophilic, first order**
The reaction rate is determined by the concentration of both nucleophile and electrophile	**The reaction rate is determined by the concentration the electrophile only**
Involves the direct, single step substitution of an alkyl halide by a nucleophile with no intermediates	**Involves the two step substitution of an alkyl halide by a nucleophile via a carbocation intermediate**
The S_N2 reaction proceeds with inversion	**The S_N1 reaction of chiral compounds proceeds with racemisation**
The rate of the S_N2 reaction of alkyl halides decreases in the order methyl > 1° > 2° >> 3°	**The rate of the S_N1 reaction of alkyl halides decreases in the order 3° >> 2° > 1° > methyl**
Usually only methyl, 1°and 2° alkyl halides react by this pathway - less crowded	**Usually only 3° alkyl halides react by this pathway**

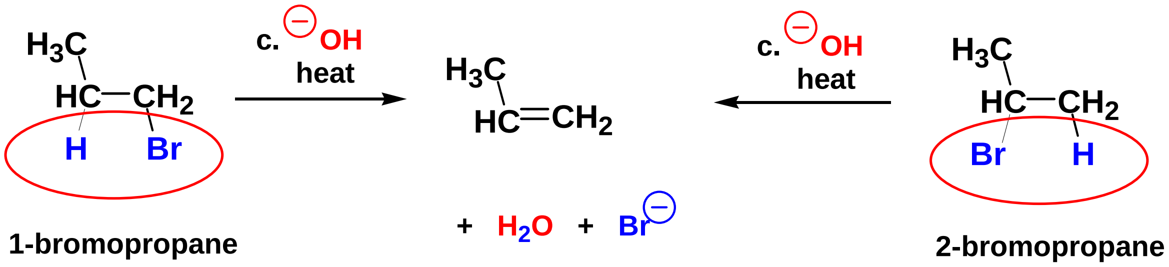
Question: Fill in the missing reagents.



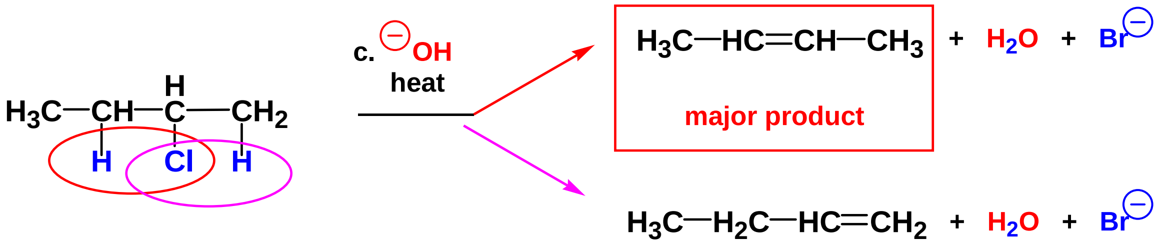
2. Elimination of HX

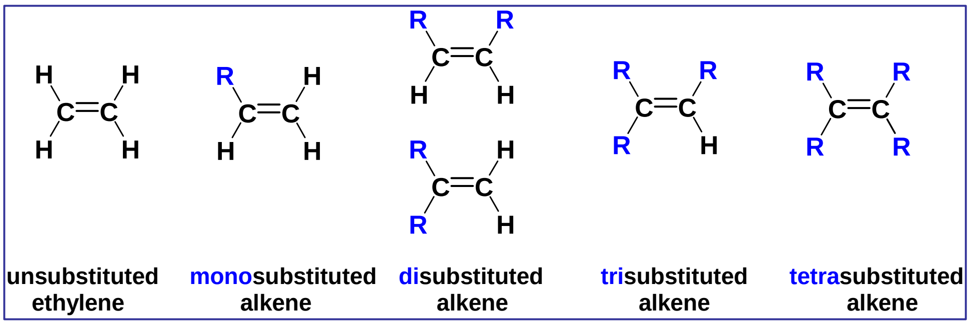
Dehydrohalogenation – require H and X on adjacent carbons.

- Generally concentrated reagents and elevated temperatures are used.
- Concentrated OH^- is used (often KOH in ethanol solvent).

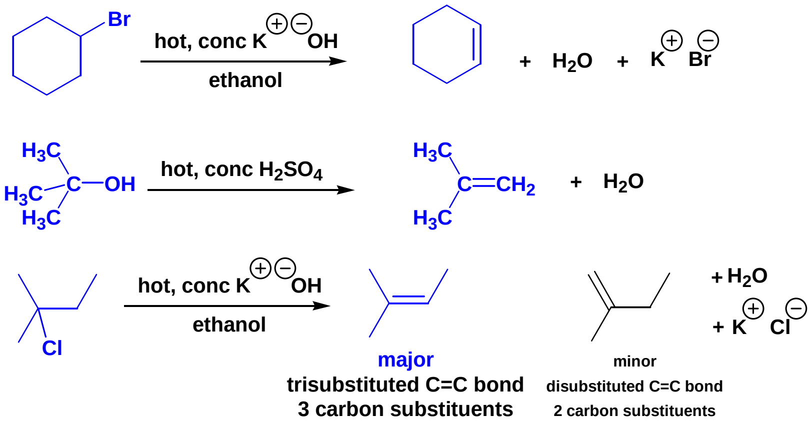


Zaitsev's Rule applies – where there is a choice, the most substituted alkene forms.

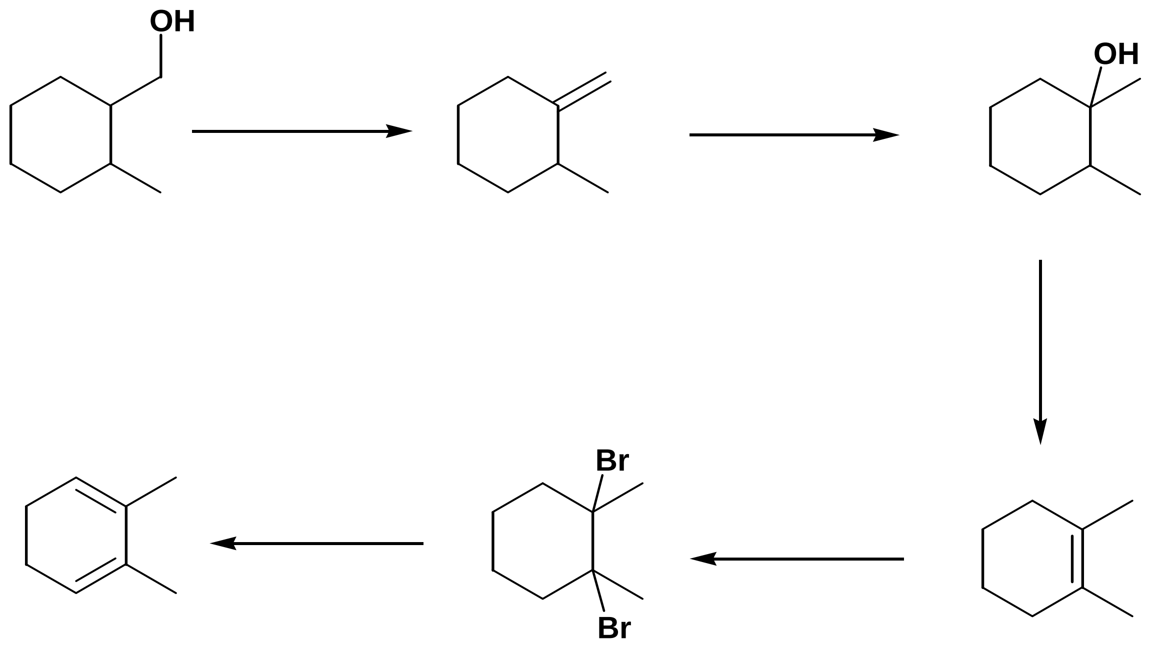




Examples of eliminations



Question: Fill in the reagents in the following sequence of reactions.



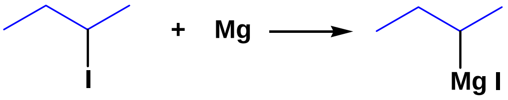
3. Formation of Grignard reagent

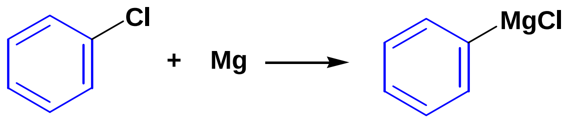
This is the reaction of an alkyl- or aryl-halide and magnesium.

$$\overset{\delta\oplus}{R}-\overset{\delta\ominus}{X} + Mg \longrightarrow \overset{\delta\ominus}{R}-\overset{\delta\oplus}{Mg}-X$$

X = Cl, Br, I
R = alkyl, aromatic

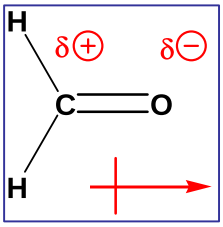
eg $CH_3Br + Mg \longrightarrow CH_3MgBr$

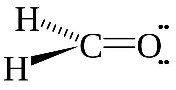


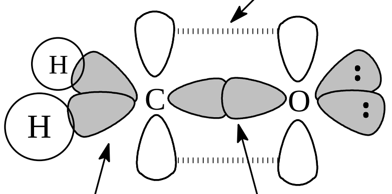


Carbonyl Compounds – aldehydes and ketones

- The double bond is composed of one σ and one π bond.
- The electron density of a π bond is above and below the plane of the double bond.
- The C=O double bond is polarised.
- Aldehydes have at least one H attached to the carbonyl group, ketones have two carbon groups attached to the carbonyl group.
- Carbon of the carbonyl group is *sp*^{2} hybridised.







overlap of electrons in p-orbitals give rise to a π-bond

oxygen has two lone pairs of electrons

overlap of electrons in *sp*^{2}-hybridised orbitals gives a σ-bond

in formaldehyde, overlap of electrons in an *sp*^{2}-hybridised orbital from C and a 1s orbital from H gives a σ-bond

Nomenclature

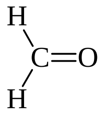
Aldehydes

- The longest chain containing the CHO group gives the stem; ending *–al.*
- If substituents are present, start the numbering from the aldehyde group - C1.

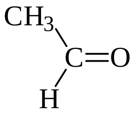
Ketones

- The longest chain containing the carbonyl group gives the stem; ending *–one.*
- If substituents are present number from the end of the chain so the carbonyl group has the lowest possible number.

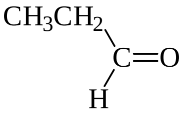
- There are non-systematic names for the common aldehydes and ketone, for example:



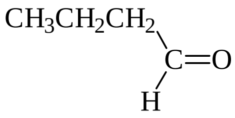
formaldehyde
(methanal)



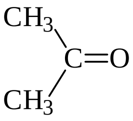
acetaldehyde
(ethanal)



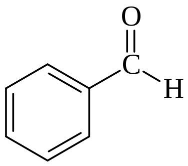
propionaldehyde
(propanal)



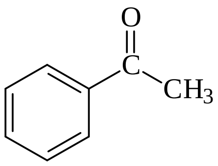
butyraldehyde
(butanal)



acetone
(propanone)

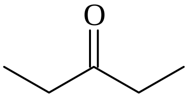


benzaldehyde

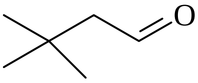


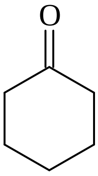
acetophenone

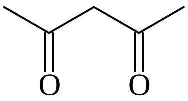
Question: Name the following compounds.



CH_2O



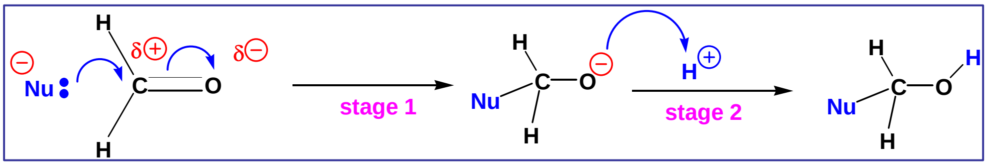




Reactions of carbonyl group – nucleophilic addition

Dominated by weak and accessible π-bond

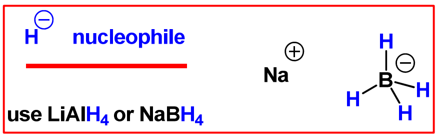
- Polarity of C=O directs addition reaction
- Reaction conducted in two stages
    - Nucleophile (eg hydride or carbanion) adds to C
    - Then O^- adds to H^+



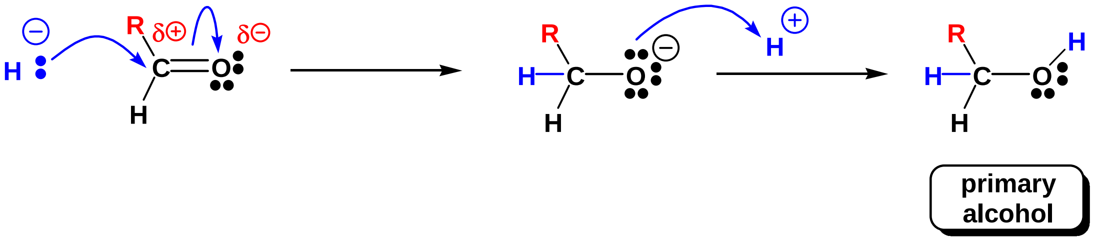
1. Hydride addition (reduction)

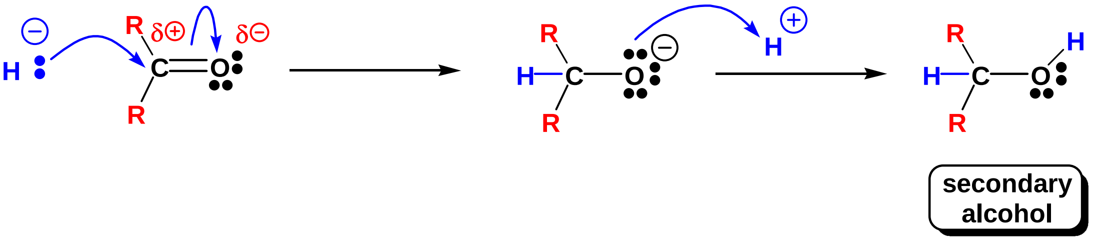
Use H^- ($LiAlH_4$ or $NaBH_4$) followed by H^+

- Aldehydes give primary alcohols, ketones give secondary alcohols



Examples:

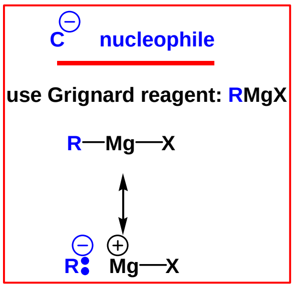




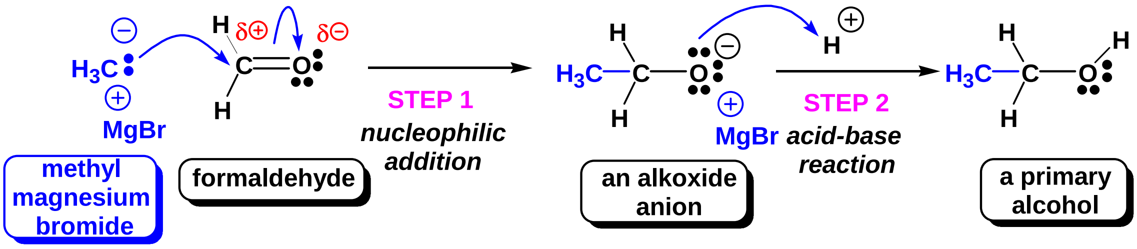
2. Grignard reaction

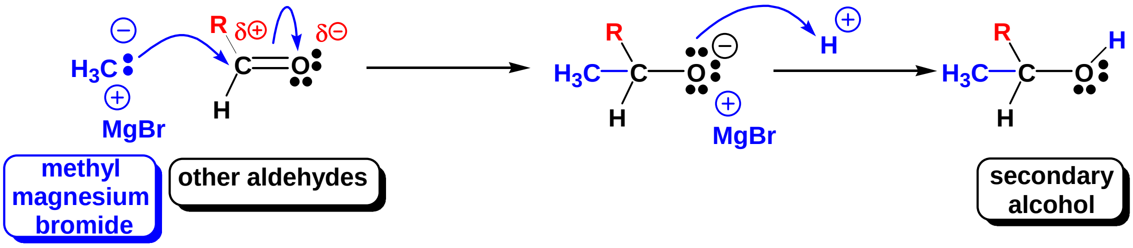
This is a very versatile reaction.

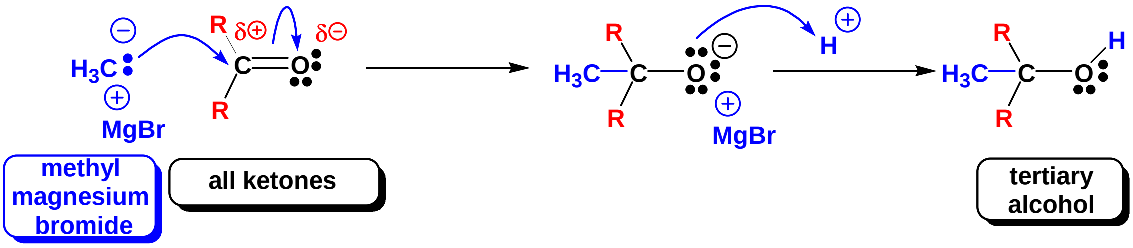
- Can use most organohalide compounds to generate Grignard reagent.
- Grignard reagent reacts with aldehydes, ketones and CO_2.
- Must employ anhydrous conditions.

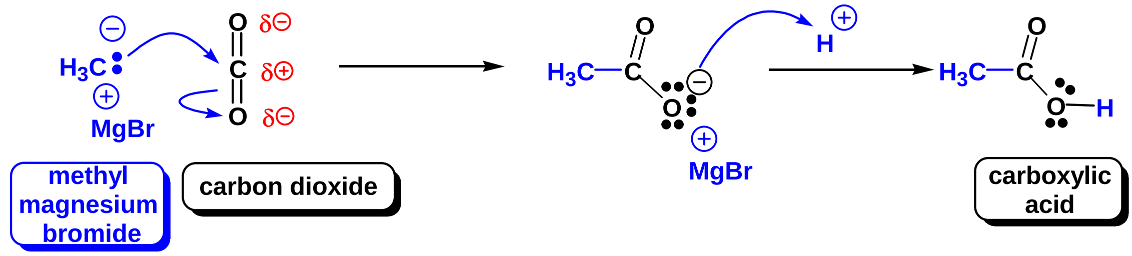


Examples:

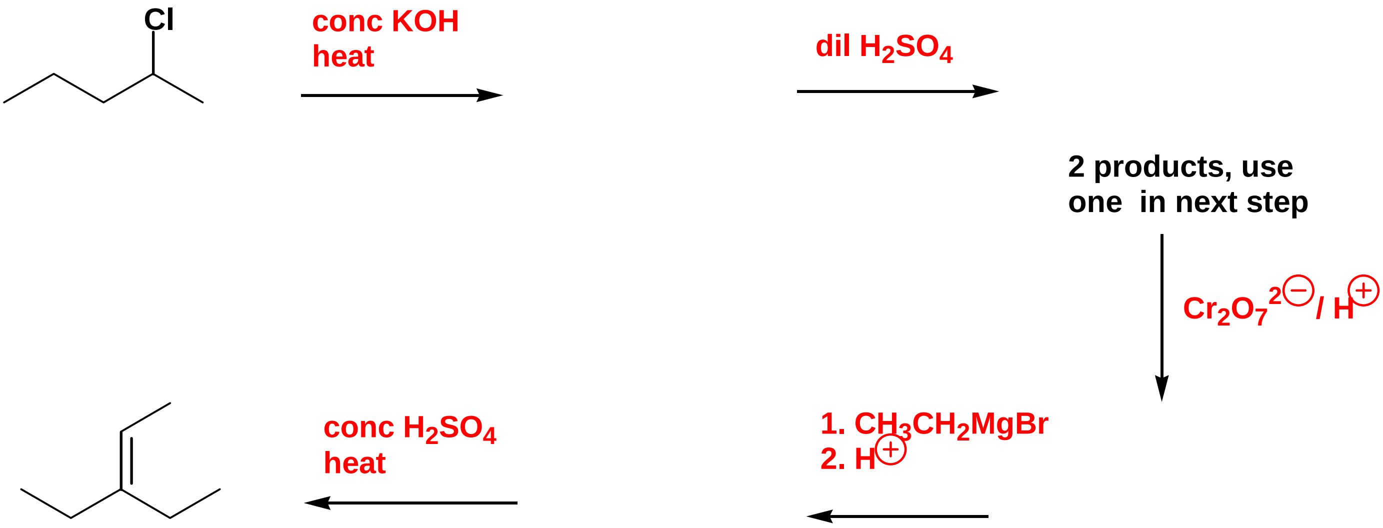








Question: Draw the products of the following sequence of reactions.



Question: In the Grignard reaction to form 3-methylhexan-3-ol there are three possible ketones that could be used as a starting material. Identify the three ketones and the Grignard reagent they need to react with to give the desired product.