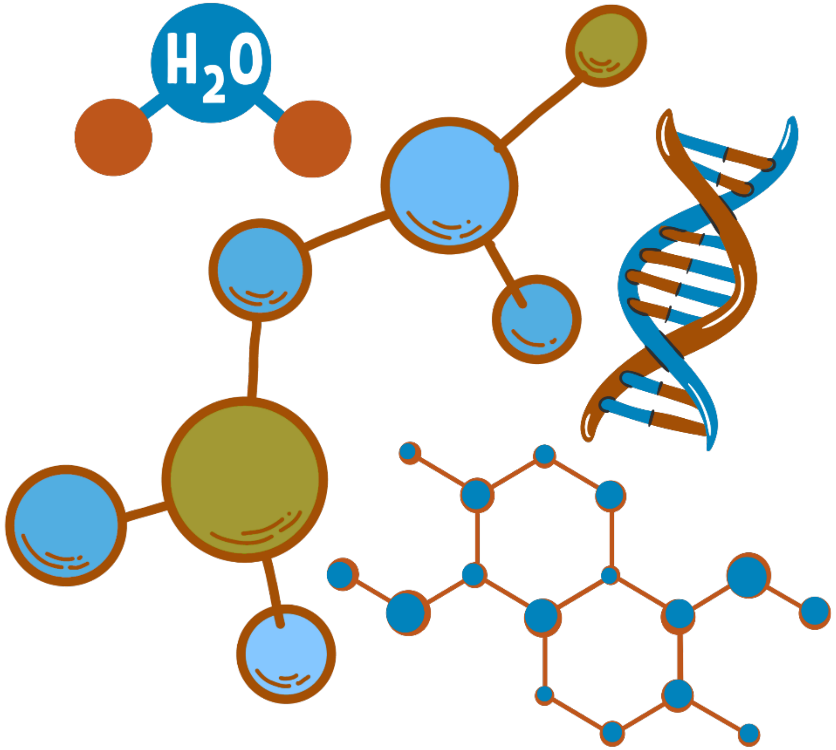
Introduction to Organic Chemistry
CHEM 109

جامعة الملك سعود
King Saud University
1957
COLLEGE OF SCIENCES
CHEMISTRY DEPARTMENT

Chapter 5: Organic Reactions



Elimination Reactions

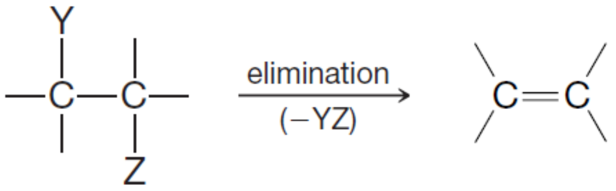
1. Elimination Reactions

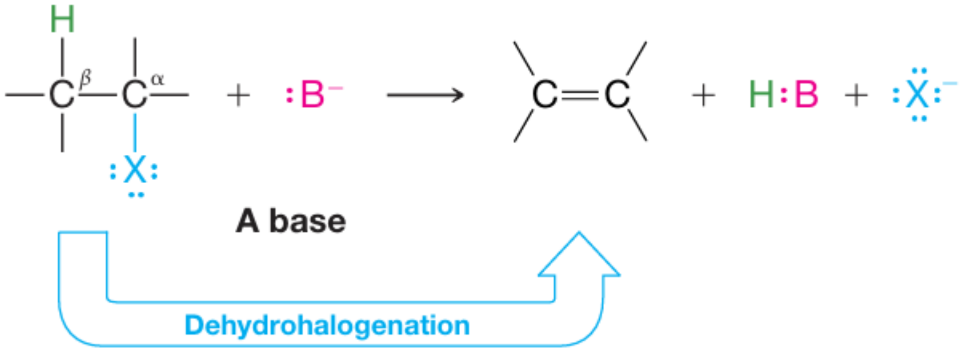
1.1 Synthesis of Alkenes

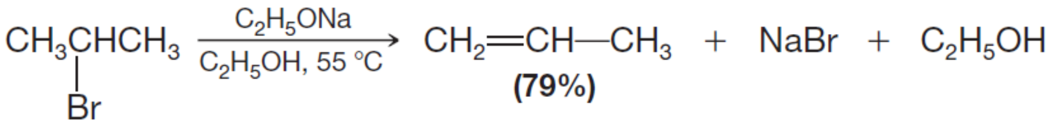
- **Elimination reactions** are the most important means for synthesizing alkenes.

A) Dehydrohalogenation; Elimination of Alkyl Halide

- **Heating** the **alkyl halide** with a **strong base** causes the reaction to take place. Examples;

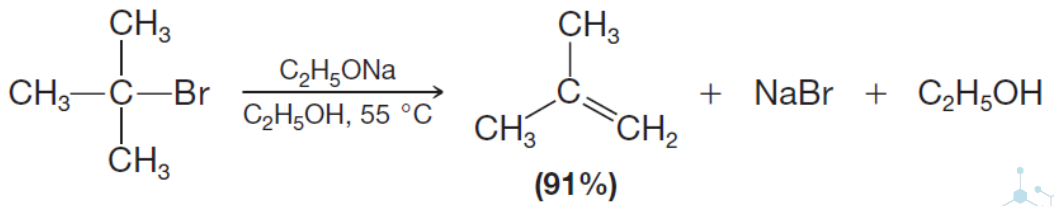






$$CH_3\underset{\substack{|\\Br}}{C}HCH_3 \xrightarrow[C_2H_5OH,\ 55\ ^\circ C]{C_2H_5ONa} CH_2{=}CH{-}CH_3 + NaBr + C_2H_5OH$$

(79%)



(91%)

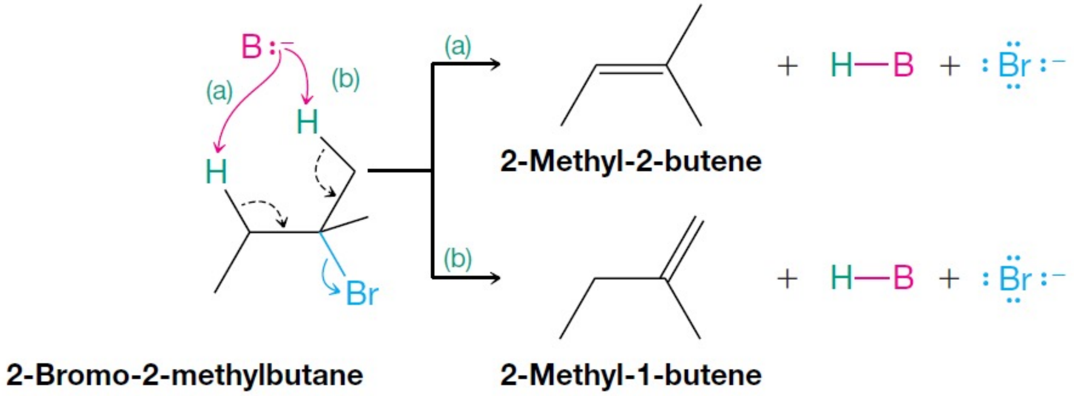
1. Elimination Reactions

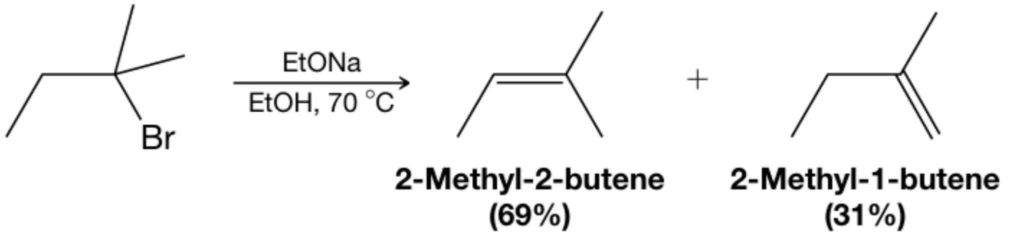
1.1 Synthesis of Alkenes

A) Dehydrohalogenation; Elimination of Alkyl Halide

- **Zaitsev's Rule:** Formation of the more substituted alkene (more stable) is favored with a small base.

- Dehydrohalogenation of alkyl halides, can often yield more than one product.
- For example; dehydrohalogenation of 2-bromo-2-methylbutane:





Trisubstituted: more stable

Disubstituted: less stable

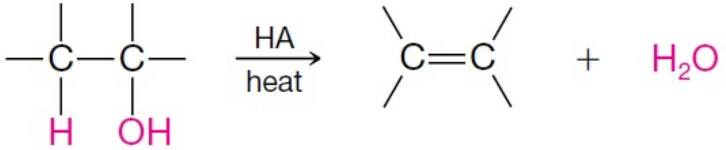
Chapter 5: Organic Reactions

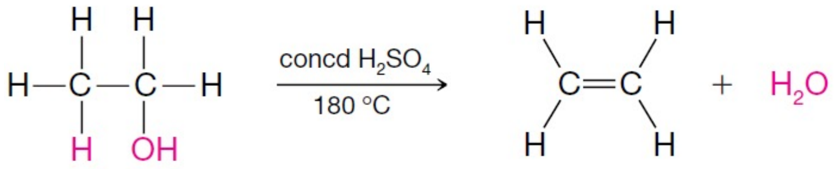
1. Elimination Reactions

1.1 Synthesis of Alkenes

B) Elimination of Alcohols: Acid-catalyzed Dehydration

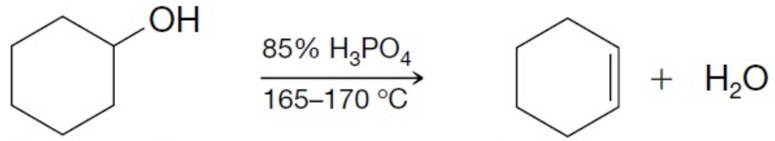
- Most alcohols undergo dehydration (*lose a molecule of water*) to form an alkene when heated with a strong acid.
- The temperature and concentration of acid required to dehydrate an alcohol depend on the structure of the alcohol substrate.
  - Dehydration of ethanol (primary alcohol) requires concentrated sulfuric acid and a temperature of 180 °C.
  - Cyclohexanol (secondary alcohol) dehydrates in 85% phosphoric acid at 165–170 °C.
  - *tert*-Butyl alcohol (tertiary alcohol) dehydrates in 20% aqueous sulfuric acid at a temperature of 85 °C.





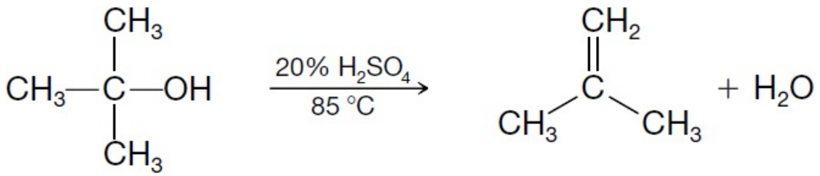
Ethanol (a 1° alcohol)

Ethene



Cyclohexanol

Cyclohexene (80%)



***tert*-Butyl alcohol**

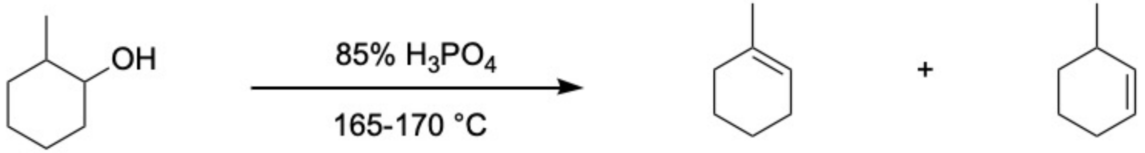
2-Methylpropene (84%)

1. Elimination Reactions

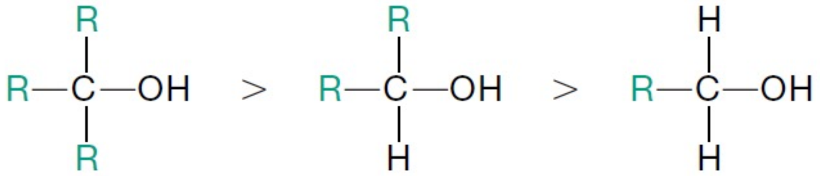
1.1 Synthesis of Alkenes

B) Elimination of Alcohols: Acid-catalyzed Dehydration

- Sometimes a single alcohol gives two or more alkenes because the proton lost during dehydration can come from any carbon atom that is directly attached to the hydroxyl-bearing carbon.
- For example, 2-methylcyclhexanol can give two alkenes.
- In these cases, the alkene with the most substituted double bond usually predominates.
- By "most substituted," we mean the alkene with the greatest number of alkyl groups on the doubly bonded carbons. Thus, in the example shown, the major product is 1-methylcyclohexene.
- The relative ease with which alcohols undergo dehydration is 3° > 2° > 1°.



2-Methylcyclohexanol **1-Methylcyclohexene** major product **3-Methylcyclohexene** minor product



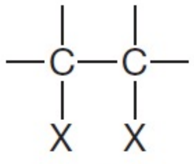
$$R-\overset{\overset{R}{|}}{\underset{\underset{R}{|}}{C}}-OH > R-\overset{\overset{R}{|}}{\underset{\underset{H}{|}}{C}}-OH > R-\overset{\overset{H}{|}}{\underset{\underset{H}{|}}{C}}-OH$$

3° Alcohol **2° Alcohol** **1° Alcohol**

1. Elimination Reactions

1.2 Synthesis of Alkynes

- Alkynes can be synthesized from alkenes via compounds called vicinal dihalides.

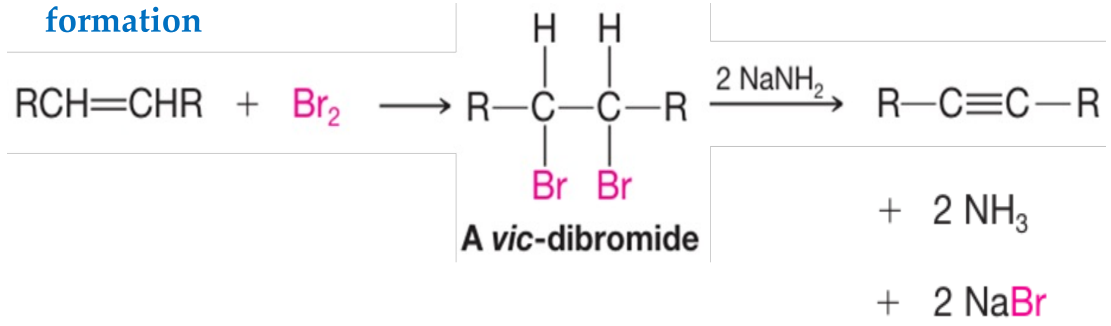


A *vic*–dihalide

- The *vic*-dibromide can be subjected to a double dehydrohalogenation reaction with a strong base to yield an alkyne.

Vicinal dihalide formation

Double dehydrohalogenation



$$RCH{=}CHR + Br_2 \longrightarrow R-\underset{Br}{\overset{H}{C}}-\underset{Br}{\overset{H}{C}}-R \xrightarrow{2\,NaNH_2} R-C\equiv C-R + 2\,NH_3 + 2\,NaBr$$

A *vic*-dibromide

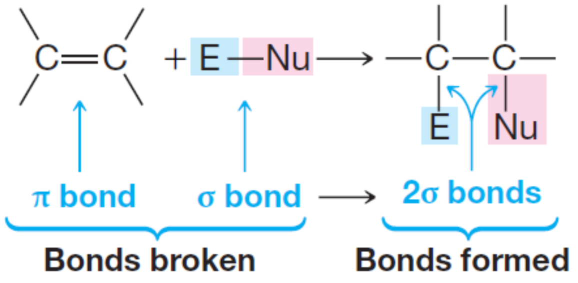
Electrophilic Addition Reactions

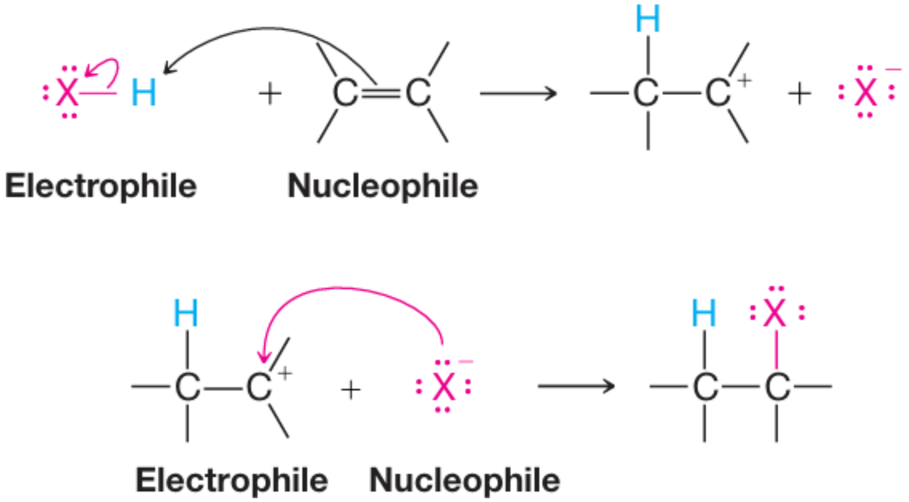
2. Electrophilic Addition Reactions

2.1 Electrophilic Addition to an Alkene

- **Generally, the reaction is exothermic because one π and one σ bond are converted to two σ bonds.**

- **In addition, reactions the alkene changes from a nucleophile in the first step to an electrophile in the second.**





2. Electrophilic Addition Reactions

2.1 Electrophilic Addition to an Alkene

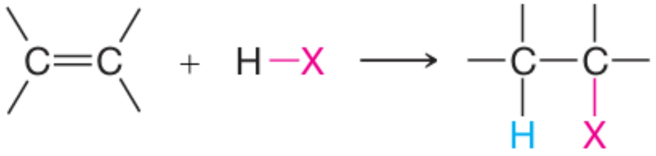
A) Addition of Hydrogen Halides (Hydrohalogenation) to Alkenes: Markovnikov's Rule

- Hydrogen halides (**HI**, **HBr**, **HCl**, and **HF**) add to the double bond of alkenes:

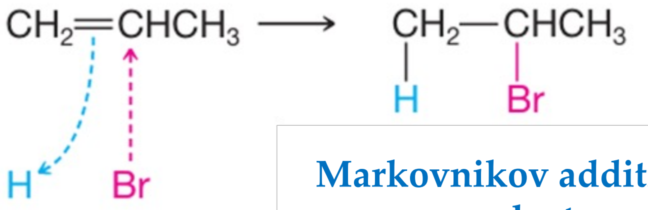
- The order of reactivity of the hydrogen halides in alkene addition is **HI** > **HBr** > **HCl** > **HF**

- The addition of HX to an unsymmetrical alkene could occur in two ways.

- One way to state **Markovnikov's rule** is to say that in the addition of **HX** to an **alkene**, the **hydrogen atom adds** to the **carbon atom** of the double bond that **already has the greater number of hydrogen atoms**.



The alkene carbon atom with the greater number of hydrogen atoms receives the hydrogen.



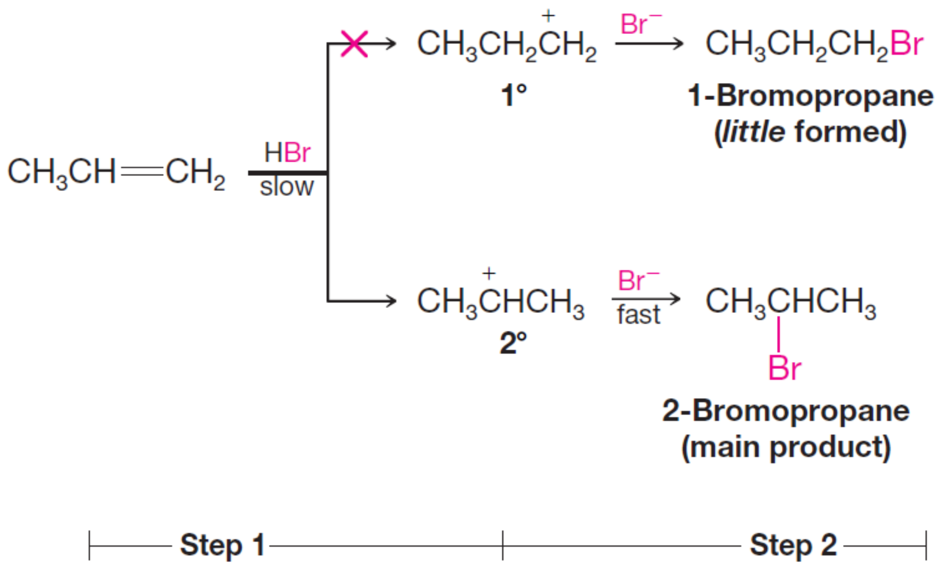
Markovnikov addition product

2. Electrophilic Addition Reactions

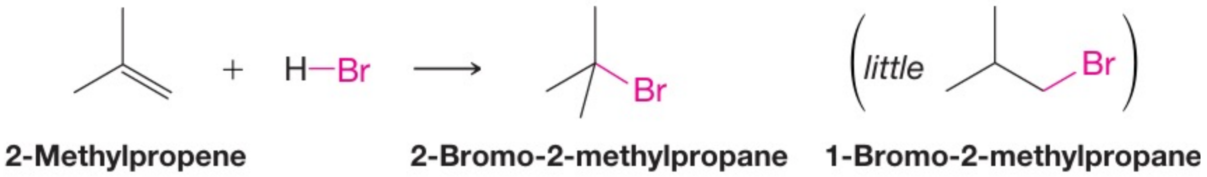
2.1 Electrophilic Addition to an Alkene

A) Addition of Hydrogen Halides (Hydrohalogenation) to Alkenes: Markovnikov's Rule

- **Theoretical Explanation of Markovnikov's Rule**
  - These two carbocations are not of equal stability.



- Example; Addition of HBr to 2-methylpropene;
  The main product is 2-bromo-2-methylpropane, not 1-bromo-2-methylpropane.



- Anti-Markovnikov Addition of HBr in the Presence of Peroxides (see Section 2.5).

2. Electrophilic Addition Reactions

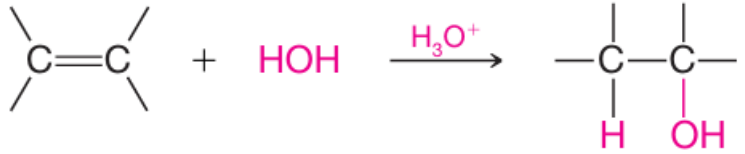
2.1 Electrophilic Addition to an Alkene

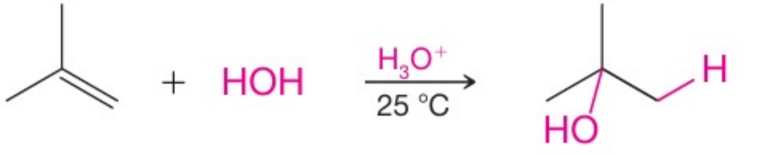
B) Acid-Catalyzed Hydration; Addition of Water to Alkenes

- The reaction of alkenes with dilute aqueous acid leads to Markovnikov addition of water.
- Example; the hydration of 2-methylpropene.
- Because the reactions follow Markovnikov's rule, acid-catalyzed hydrations of alkenes do not yield primary alcohols except in the special case of the hydration of ethane.

C) Alcohols from Alkenes through Hydroboration–Oxidation: Anti-Markovnikov Syn Hydration

- Hydroboration–oxidation takes place as anti-Markovnikov.
- Example; the hydroboration of 1-methylcyclopentene.

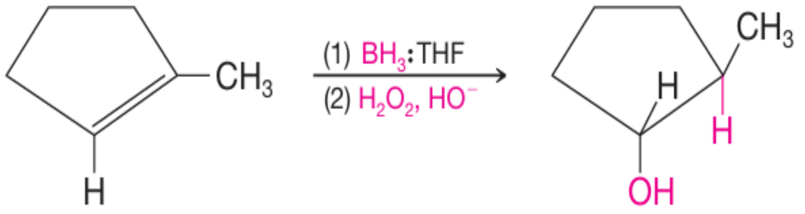




2-Methylpropene (isobutylene)

2-Methyl-2-propanol (*tert*-butyl alcohol)

$$CH_2{=}CH_2 + HOH \xrightarrow[300\ ^{\circ}C]{H_3PO_4} CH_3CH_2OH$$



1-Methylcyclopentene

2-Methylcyclopentanol

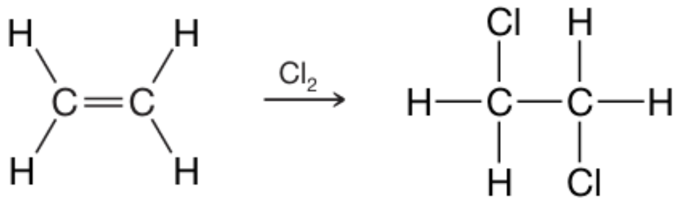
2. Electrophilic Addition Reactions

2.1 Electrophilic Addition to an Alkene

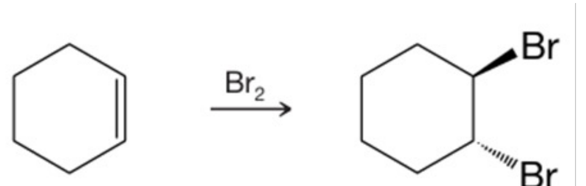
D) Addition of Bromine and Chlorine (Halogenation) to Alkenes

- Alkenes react rapidly with bromine and chlorine to form vicinal dihalides.
- The addition of halogens is an anti addition to the double bond.

- Example; addition of bromine to cyclohexene to yield *trans*-1,2-dibromocyclohexane.



Ethene **1,2-Dichloroethane**



Cyclohexene ***trans*-1,2-Dibromocyclohexane**

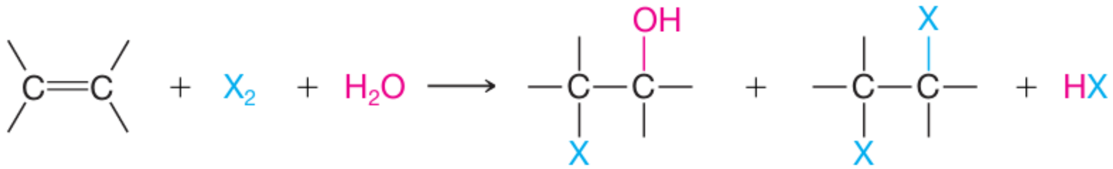
2. Electrophilic Addition Reactions

2.1 Electrophilic Addition to an Alkene

E) Halohydrin Formation

- Halogenation of an alkene in aqueous solution, the major product is a halohydrin (halo alcohol)
- If the halogen is bromine, it is called a bromohydrin.
- If the halogen is chlorine, it is called a chlorohydrin.

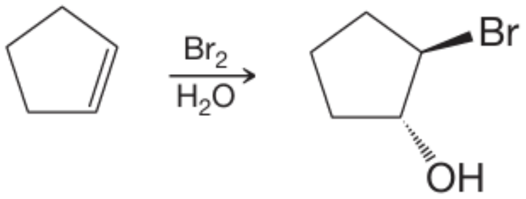
- Example; addition of bromine to cyclopentene to yield *trans*-2-bromocyclopentanol.



X = Cl or Br

Halohydrin (major)

***vic*-Dihalide (minor)**



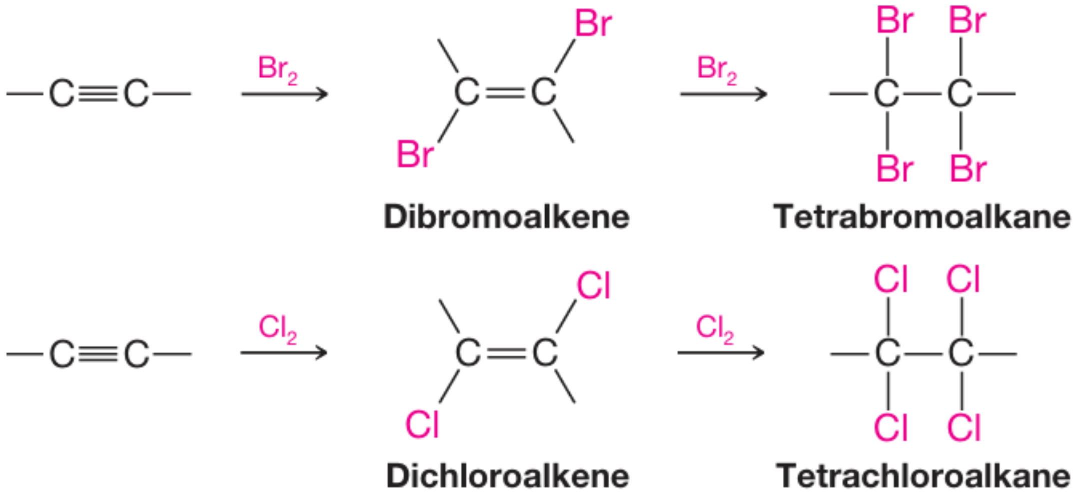
Cyclopentene **2-Bromocyclopentanol**

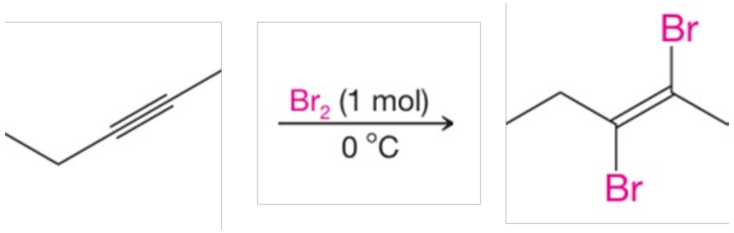
2. Electrophilic Addition Reactions

2.2 Electrophilic Addition to an Alkyne

A) Addition of Bromine and Chlorine (Halogenation) to Alkynes

- Alkynes show the same kind of addition reactions with chlorine and bromine that alkenes do.
- With alkynes the addition may occur once or twice, depending on the number of molar equivalents of halogen added.
- Addition of one molar equivalent of chlorine o bromine to an alkyne generally results in anti addition and yields a *trans*-dihaloalkene.
- Example; Addition of bromine to 2-pentyne gives the *trans* isomer.





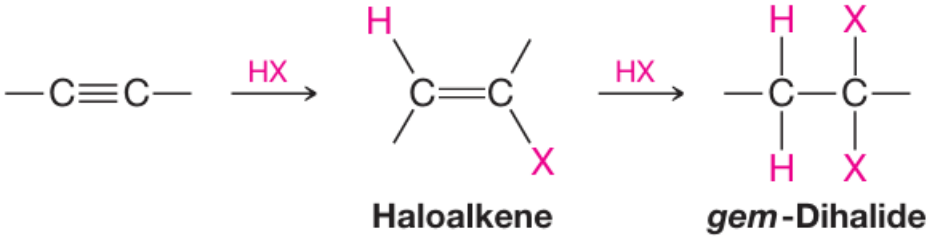
2-Pentyne **_trans_-2,3-Dibromo-2-pentene**

2. Electrophilic Addition Reactions

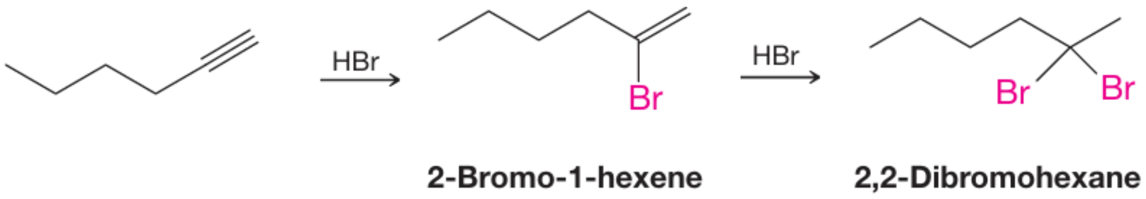
2.2 Electrophilic Addition to an Alkyne

B) Addition of Hydrogen Halides (Hydrohalogenation) to Alkynes

- **Alkynes** react with **one molar** equivalent of hydrogen chloride or hydrogen bromide to form **haloalkenes**, and with **two molar** equivalents to form **geminal dihalides** and follow **Markovnikov's rule**.



- **Example; Addition of HBr to 1-hexyne.**



- **Anti-Markovnikov addition of HBr occurs in the presence of peroxide (see Section 2.5) .**

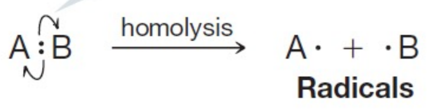
Radical Reactions

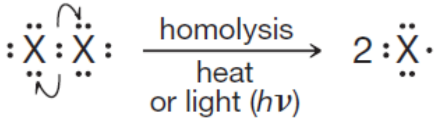
3. Radical Reactions

3.1 Production of Radicals

- Homolytic bond cleavage leads to the formation of radicals (or free radicals).
- Radicals are highly reactive, and short-lived species.

Each atom takes one electron from the covalent bond that joined them.

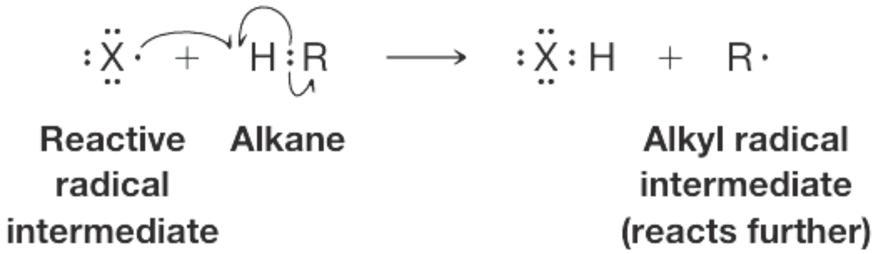




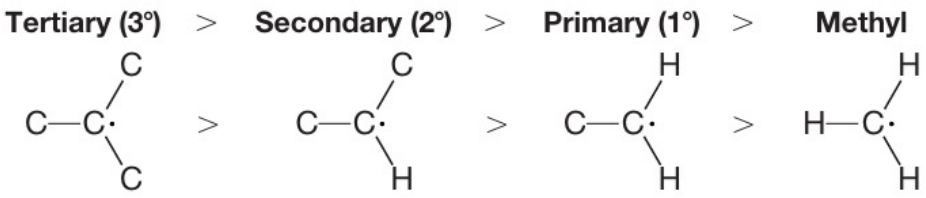
Homolysis of a halogen molecule

3.2 Reactions of Radicals

- Radicals tend to react in ways that lead to pairing of their unpaired electron. Hydrogen abstraction is one way a halogen radical can react to pair its unshared electron.



- The relative stabilities of radicals are 3° > 2° > 1° > methyl, follows the same trend as for carbocations. Radicals are electron deficient, as are carbocations, and the most substituted radical is most stable

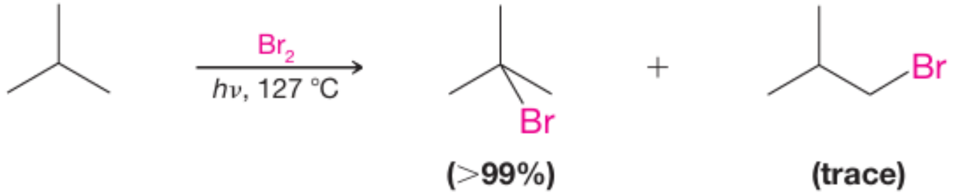


3. Radical Reactions

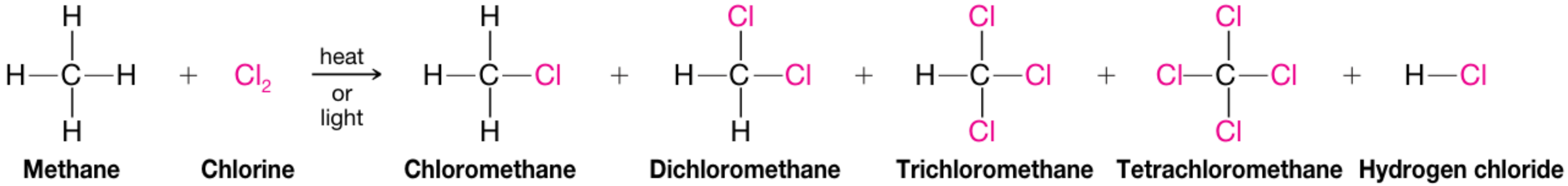
3.3 Reactions of Alkanes with Halogens

- Radical halogenation; A halogen atom replaces one or more of the hydrogen atoms of the alkane to produce alkyl halides by a substitution reaction.
- Alkanes undergo substitution reactions with halogens, fluorine, bromine and chlorine, in the presence of heat or light.
- Tertiary hydrogens are more reactive than secondary hydrogens which are more reactive than primary hydrogens.

$$R{-}H + X_2 \longrightarrow R{-}X + HX$$



- Radical halogenation can yield a mixture of halogenated compounds by substitution of all hydrogen atoms in alkane.



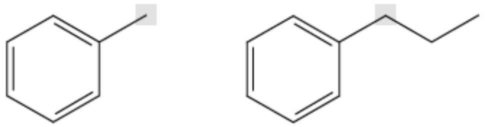
3. Radical Reactions

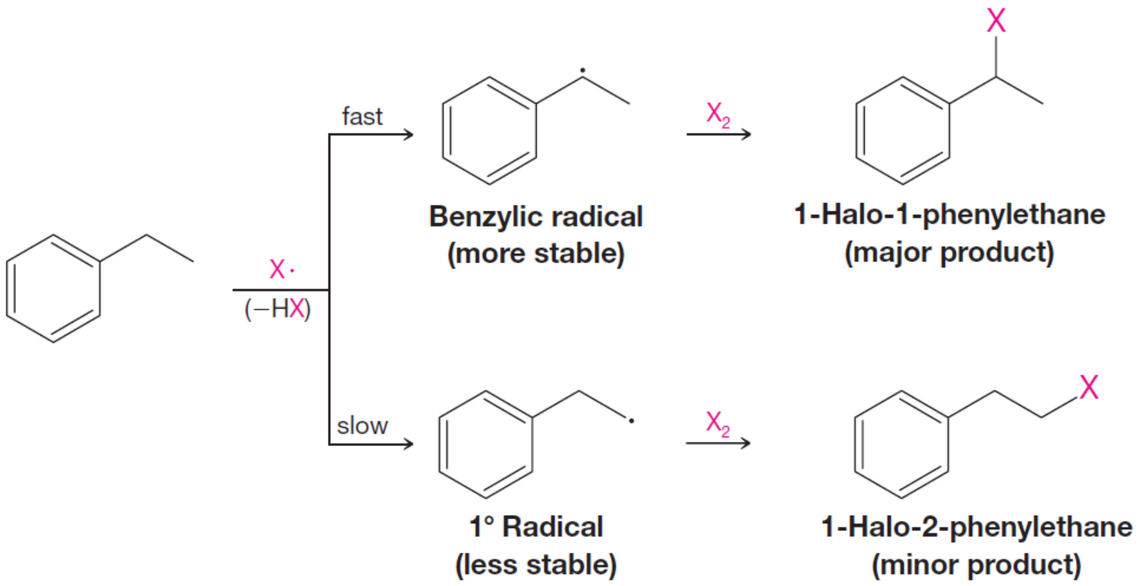
3.4 Benzylic Substitution and Benzylic Radicals

- An atom or group bonded to a *sp*3-hybridized carbon adjacent to a benzene ring is called a benzylic group.

- Example; Halogenation of ethylbenzene.
  - The major product is the 1-halo-1-phenylethane.
  - The benzylic radical is formed much faster than the 1° radical due to the greater stability of benzylic radicals.

The hydrogen atoms bonded at the highlighted carbons are benzylic hydrogens

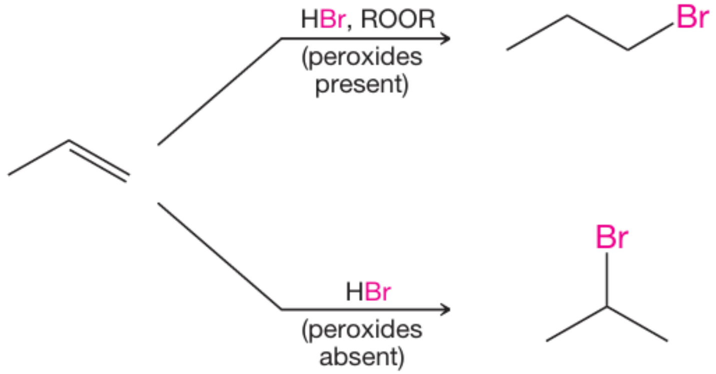




3. Radical Reactions

3.5 Radical Addition to Alkenes: Anti-Markovnikov Addition of Hydrogen Bromide

- **Ionic Addition; The result is Markovnikov addition**
- **Radical Addition; In the presence of peroxides (R-O-O-R), The result is anti-Markovnikov addition.**
- **Hydrogen bromide is the only hydrogen halide that gives anti-Markovnikov addition when peroxides are present.**
- **Hydrogen fluoride, hydrogen chloride, and hydrogen iodide do not give anti-Markovnikov addition even with peroxides.**



Anti-Markovnikov addition

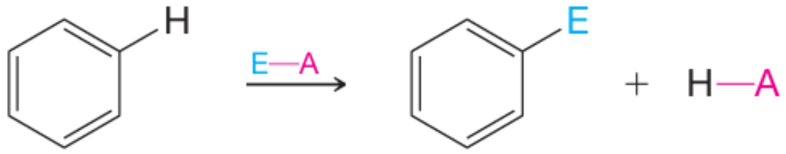
Markovnikov addition

Electrophilic Aromatic Substitution

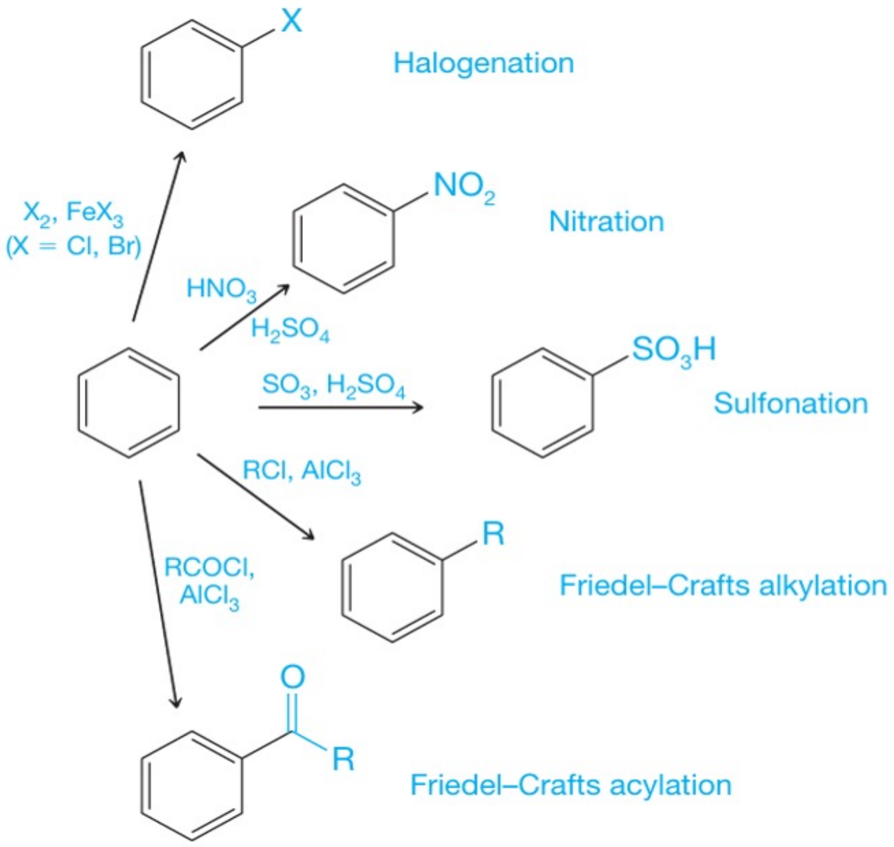
4. Electrophilic Aromatic Substitution Reactions

- Some of the most important reactions of aromatic compounds are those in which an electrophile replaces one of the hydrogen atoms of the ring.
- These reactions, called electrophilic aromatic substitutions (EAS)

- **Five different types of electrophilic aromatic substitutions** including carbon–carbon bond-forming reactions and halogenations.



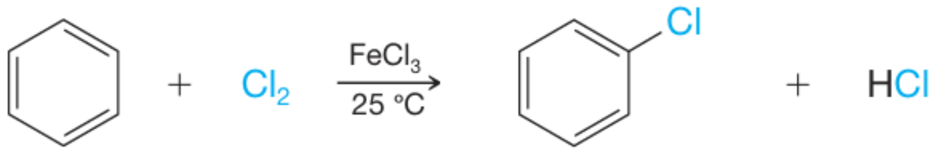
(E—A is an electrophilic reactant)



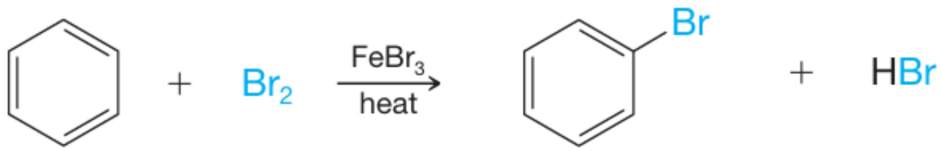
4. Electrophilic Aromatic Substitution Reactions

4.1 A Halogenation of Benzene

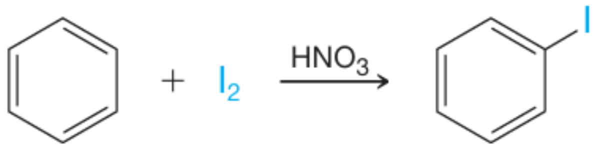
- Benzene reacts with bromine and chlorine in the presence of Lewis acids to give halogenated substitution products.
- Fluorine reacts so rapidly with benzene, and it is difficult to limit the reaction to monofluorination.
- Iodine is so unreactive; the reaction must be carried out in the presence of an oxidizing agent such as nitric acid.



Chlorobenzene (90%)



Bromobenzene (75%)



Iodobenzene (86%)

4. Electrophilic Aromatic Substitution Reactions

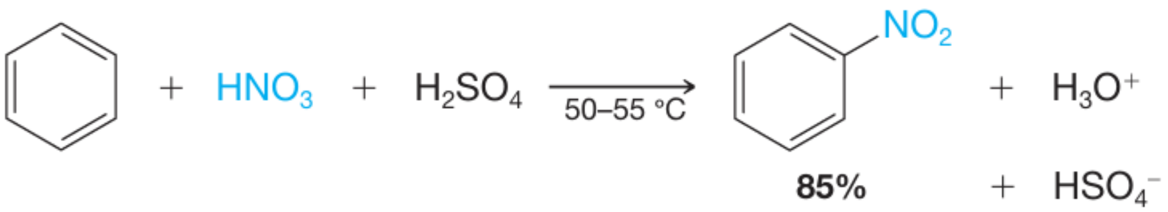
4.2 Nitration of Benzene

- **Benzene undergoes nitration on reaction with a mixture of concentrated nitric acid and concentrated sulfuric acid.**
- **The electrophile for the reaction is the nitronium ion (NO_2^+).**

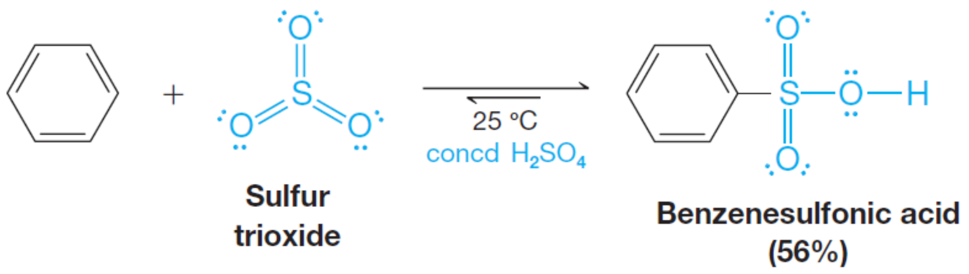
4.4 Sulfonation of Benzene

- **Benzene reacts with fuming sulfuric acid (sulfuric acid contains added sulfur trioxide (SO_3)) at room temperature to produce benzenesulfonic acid.**

$$HNO_3 + 2H_2SO_4 \longrightarrow NO_2^+ + 2HSO_4^- + H_3O^+$$



$$SO_3 + H_2SO_4 \longrightarrow SO_3H^+ + HSO_4^-$$

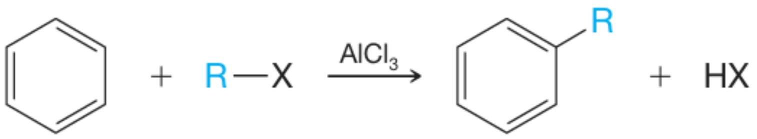


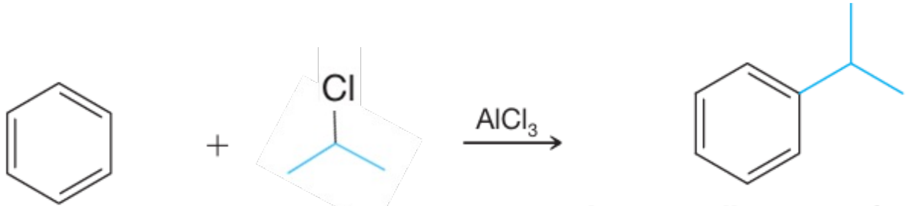
4. Electrophilic Aromatic Substitution Reactions

4.4 Friedel–Crafts Alkylation

- An aromatic ring can be alkylated by an alkyl halide in the presence of a Lewis acid.
- The Lewis acid serves to generate a carbocation electrophile.

$$RCl + AlCl_3 \longrightarrow R^+ + AlCl_4^-$$

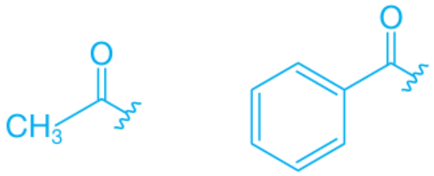




Isopropylbenzene (cumene)
(84%)

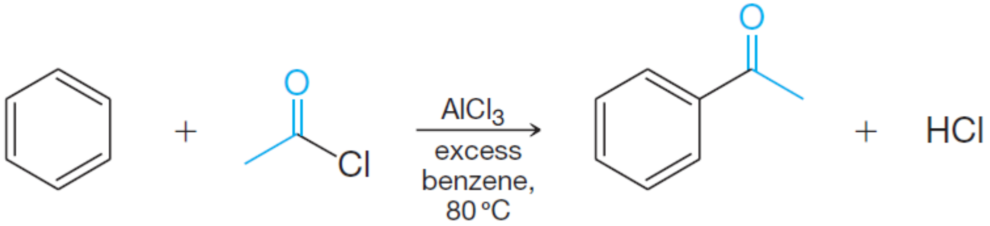
4.5 Friedel–Crafts Acylation

- An acyl group has a carbonyl attached to some R group
- Friedel-Crafts acylation requires reaction of an acid chloride with a Lewis acid such as aluminum chloride.



Acetyl group
(ethanoyl group)

Benzoyl
group



Acetyl
chloride

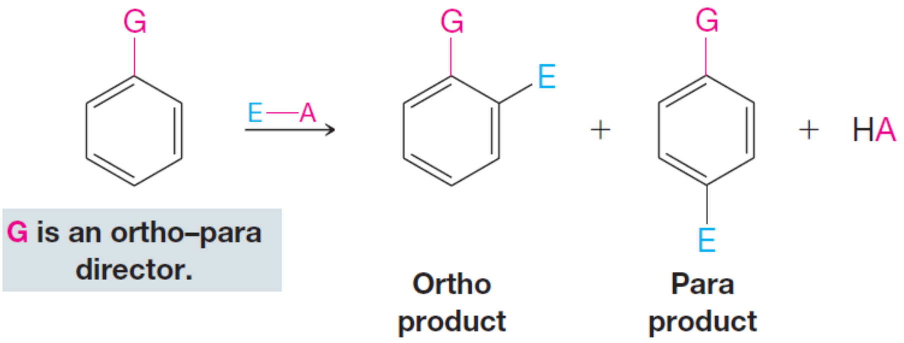
Acetophenone
(methyl phenyl ketone)
(97%)

4. Electrophilic Aromatic Substitution Reactions

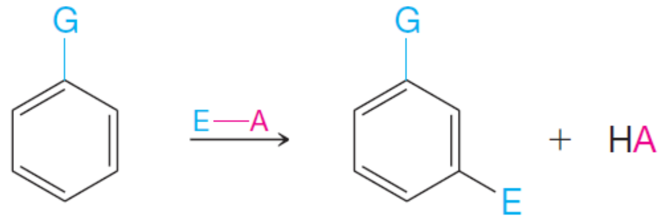
4.6 Existing Substituents Direct the Position of Electrophilic Aromatic Substitution

- **Effects of Substituents on Reactivity and Orientation**

- **The nature of groups already on an aromatic ring affect both the reactivity and orientation of future substitution.**
  - **Activating groups cause the aromatic ring to be more reactive than benzene.**
  - **Deactivating groups cause the aromatic ring to be less reactive than benzene.**
  - **Ortho-para directors direct future substitution to the *ortho* and *para* positions.**
  - **Meta directors direct future substitution to the *meta* position.**



G is an ortho–para director.

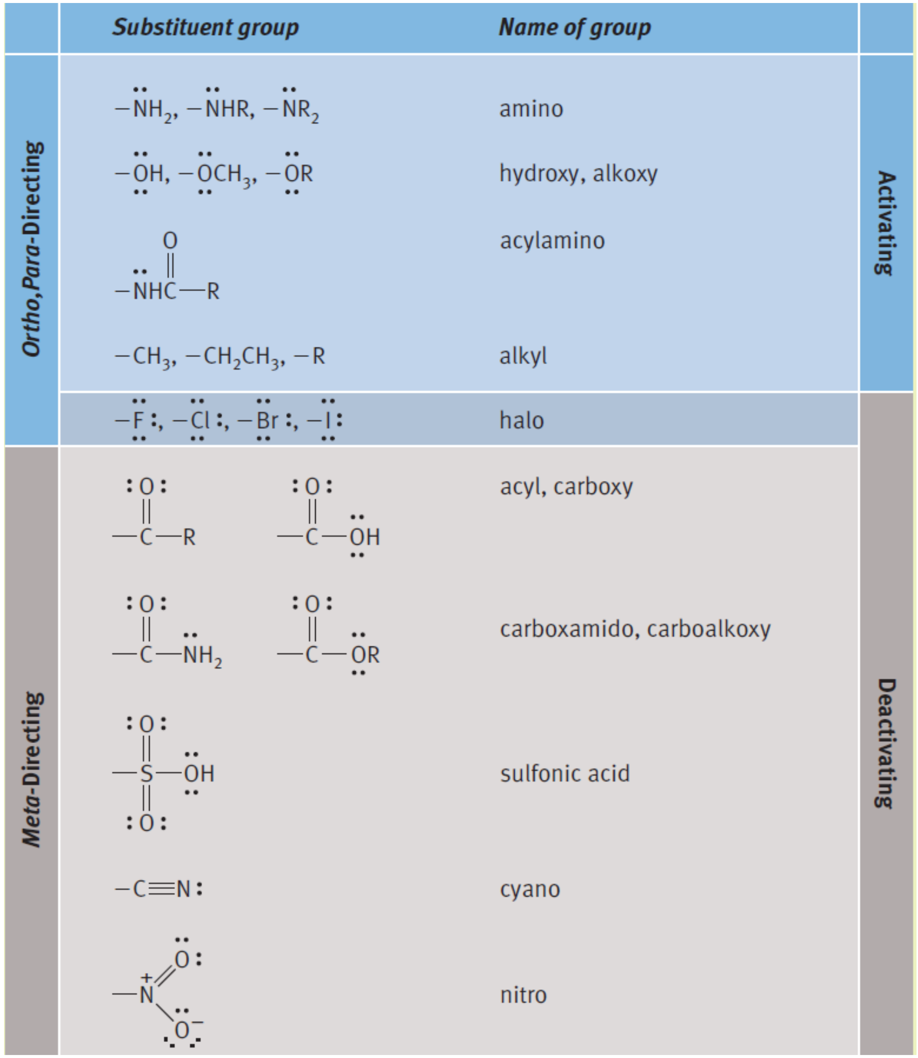


G is a meta director.

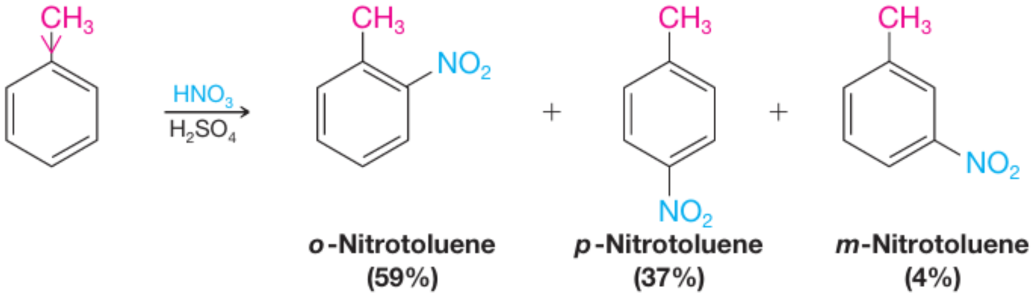
4. Electrophilic Aromatic Substitution Reactions

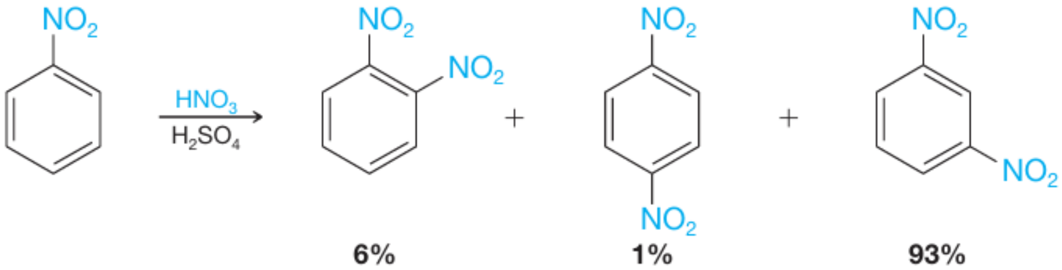
4.6 Existing Substituents Direct the Position of Electrophilic Aromatic Substitution

- **Effects of Substituents on Reactivity and Orientation**



	Substituent group	*Name of group*	
Ortho,Para-Directing	$-NH_2$, $-NHR$, $-NR_2$	amino	Activating
	$-OH$, $-OCH_3$, $-OR$	hydroxy, alkoxy	
	$-NH\overset{O}{\overset{\|}{C}}-R$	acylamino	
	$-CH_3$, $-CH_2CH_3$, $-R$	alkyl	
	$-F:$, $-Cl:$, $-Br:$, $-I:$	halo	Deactivating
Meta-Directing	$-\overset{O}{\overset{\|}{C}}-R$ $-\overset{O}{\overset{\|}{C}}-OH$	acyl, carboxy	
	$-\overset{O}{\overset{\|}{C}}-NH_2$ $-\overset{O}{\overset{\|}{C}}-OR$	carboxamido, carboalkoxy	
	$-SO_3H$	sulfonic acid	
	$-C\equiv N:$	cyano	
	$-\overset{+}{N}(=O)-O^-$	nitro	

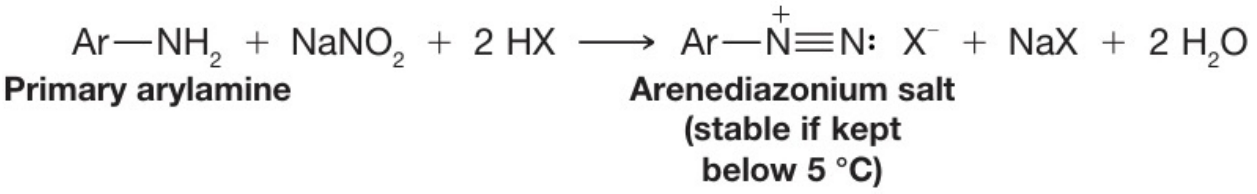




4. Electrophilic Aromatic Substitution Reactions

4.7 Reactions of Primary Arylamines with Nitrous Acid

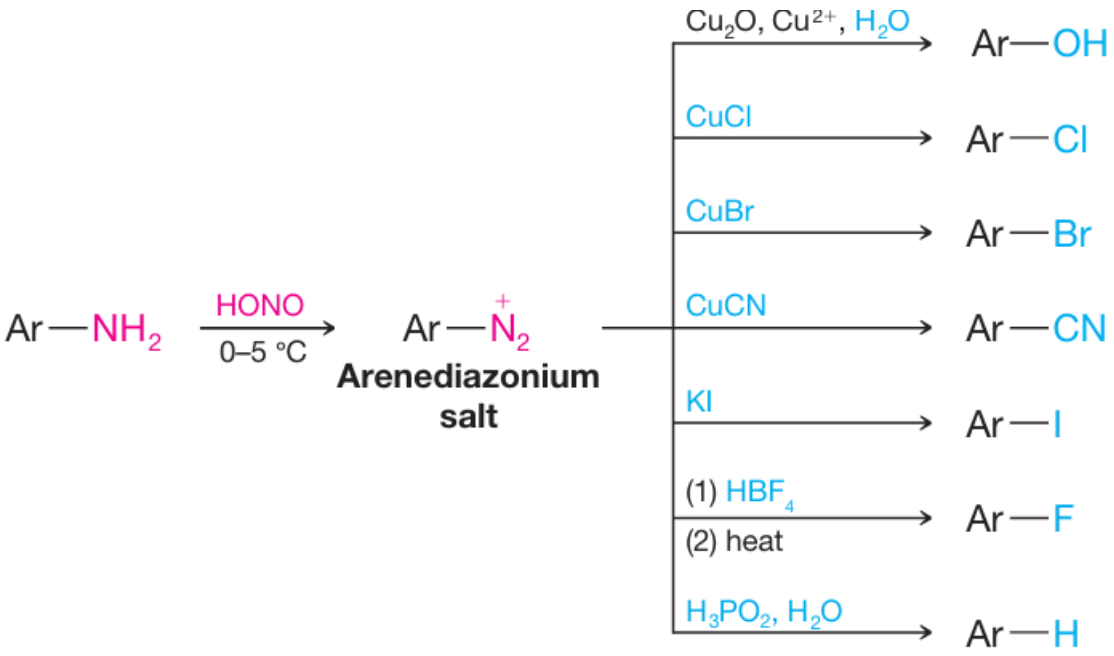
- Reaction of primary arylamines with nitrous acid results in the formation of relatively stable arenediazonium salts.



$$Ar{-}NH_2 + NaNO_2 + 2\,HX \longrightarrow Ar{-}\overset{+}{N}{\equiv}N{:}\ X^- + NaX + 2\,H_2O$$

4.8 Replacement Reactions of Arenediazonium Salts

- Arenediazonium salts are highly useful intermediates in the synthesis of aromatic compounds, because the diazonium group can be replaced by any one of a number of other atoms or groups, including –F, –Cl, –Br, –I, –CN, –OH, and –H.



Nucleophilic Reactions

5. Nucleophilic Reactions

5.1 Nucleophilic Substitution Reactions

- In a nucleophilic substitution reaction, a **nucleophile** (**Nu:**) displaces a **leaving group** (**LG**) in the molecule that undergoes the substitution.

$$Nu\!:^{-} + R{-}LG \longrightarrow R{-}Nu + {}^{-}\!:\!LG$$

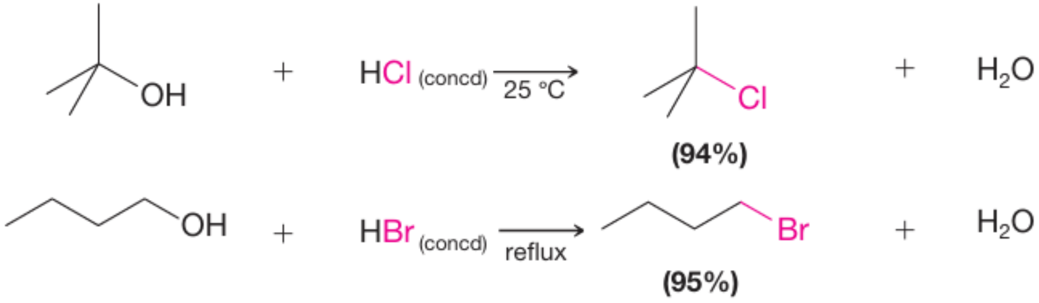
5.1.1 Nucleophilic Substitution Reactions of Alcohols: Synthesis of Alkyl halides

A) When Alcohols react with a hydrogen halide (HCl, HBr, HI), a substitution takes place producing an alkyl halide and water:

- The order of reactivity of alcohols is 3° > 2° > 1°.
- The order of reactivity of the hydrogen halides is

  HI > HBr > HCl (HF is generally unreactive).

$$R{-}OH + HX \longrightarrow R{-}X + H_2O$$



5. Nucleophilic Reactions

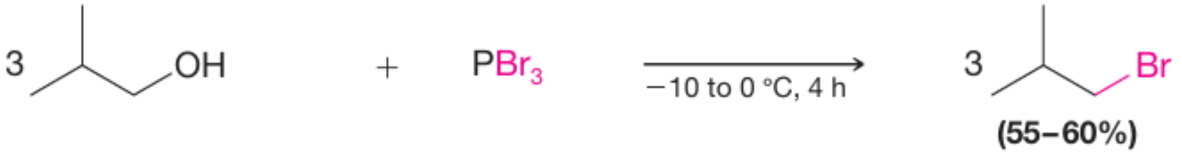
5.1 Nucleophilic Substitution Reactions

5.1.1 Nucleophilic Substitution Reactions of Alcohols: Synthesis of Alkyl halides

B) Primary and secondary alcohols react with phosphorus tribromide (PBr$_3$) to yield alkyl bromides.

$$3\ R\text{—}OH + PBr_3 \longrightarrow 3\ R\text{—}Br + H_3PO_3$$

(1° or 2°)

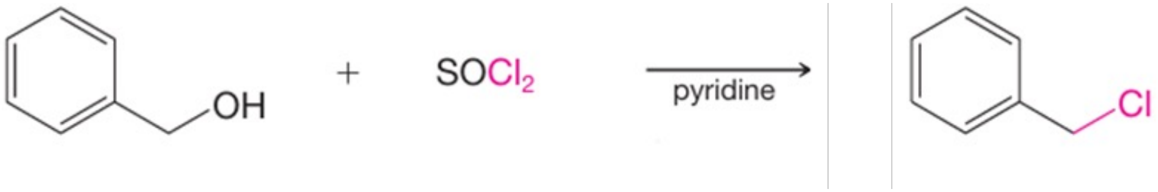


(55–60%)

C) Thionyl chloride (SOCl$_2$) converts primary and secondary alcohols to alkyl chlorides.

$$R\text{—}OH + SOCl_2 \longrightarrow R\text{—}Cl + SO_2 + HCl$$

(1° or 2°)



5. Nucleophilic Reactions

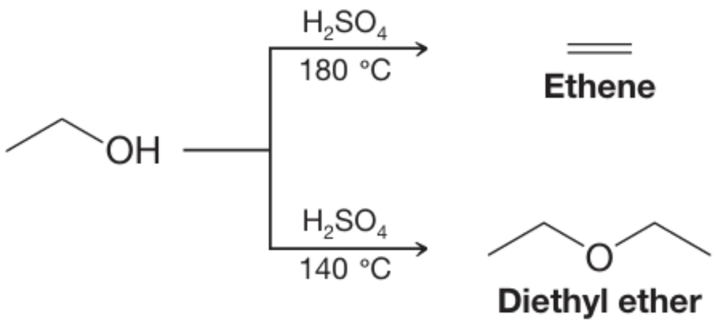
5.1 Nucleophilic Substitution Reactions

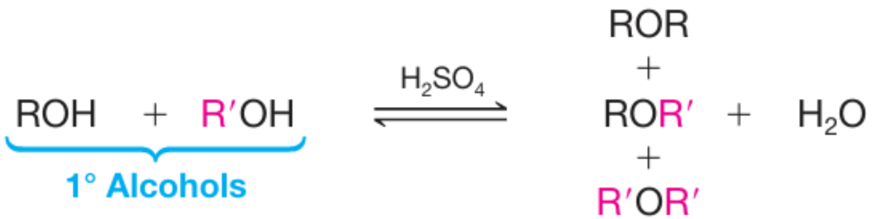
5.1.2 Nucleophilic Substitution Reactions: Synthesis of Ethers

A) Ethers by Intermolecular Dehydration of Alcohols

- Two alcohol molecules can form an ether by loss of water through an acid-catalyzed substitution reaction.
- This reaction occurs at lower temperature than the competing dehydration to an alkene at high temperature.
- Intermolecular dehydration is not useful for the preparation of unsymmetrical ethers from primary alcohols because the reaction leads to a mixture of products.

$$R{-}OH + HO{-}R \xrightarrow[-H_2O]{HA} R{-}O{-}R$$





$$\underbrace{ROH + R'OH}_{1°\ \text{Alcohols}} \xrightleftharpoons{H_2SO_4} ROR + ROR' + R'OR' + H_2O$$

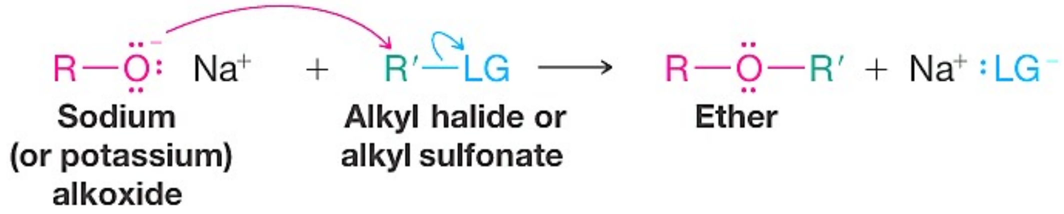
5. Nucleophilic Reactions

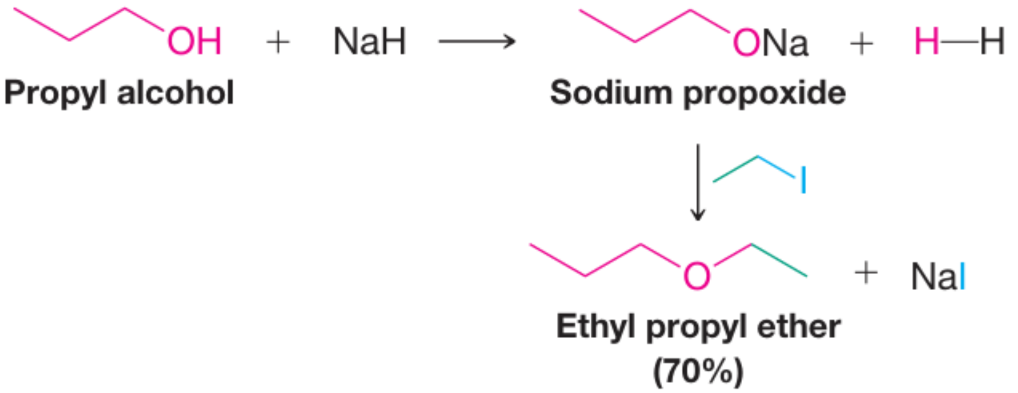
5.1 Nucleophilic Substitution Reactions

5.1.2 Nucleophilic Substitution Reactions: Synthesis of Ethers

B) The Williamson Ether Synthesis

- This is a good route for synthesis of unsymmetrical ethers.
- Best results are obtained when the alkyl halide is primary (or methyl).
- Substitution is also favored over elimination at lower temperatures.





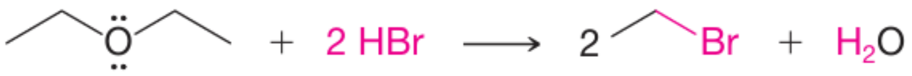
5. Nucleophilic Reactions

5.1 Nucleophilic Substitution Reactions

5.1.3 Nucleophilic Substitution Reactions: Cleavage of Ethers

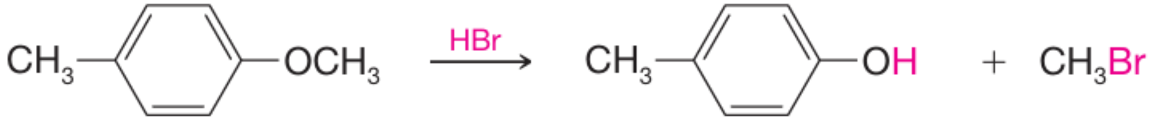
A) Cleavage of Dialkyl Ethers

- **Heating dialkyl ethers with very strong acids (HI, HBr, and H_2SO_4) causes them to undergo reactions in which the carbon–oxygen bond breaks.**



B) Cleavage of Alkyl Aryl Ethers

- **When alkyl aryl ethers react with strong acids such as HI and HBr, the reaction produces an alkyl halide and a phenol.**



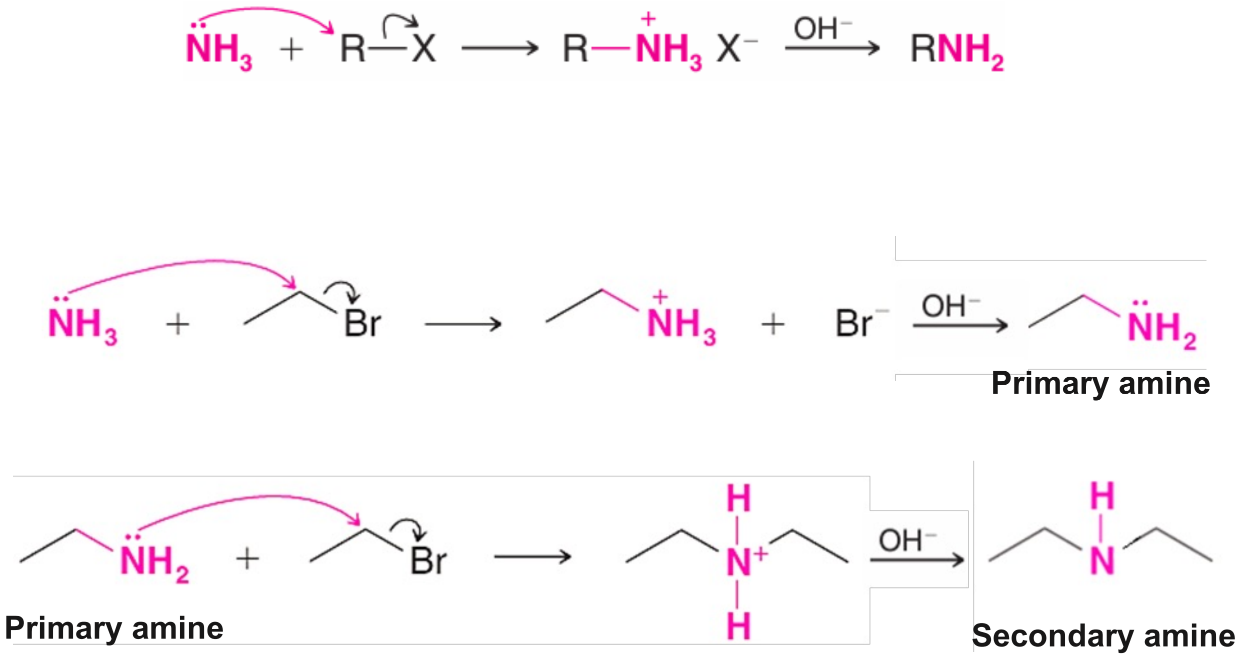
***p*-Methylanisole** **4-Methylphenol** **Bromomethane**

5. Nucleophilic Reactions

5.1 Nucleophilic Substitution Reactions

5.1.4 Nucleophilic Substitution Reactions: Preparation of Amines

- **Alkylation of Ammonia:** Reaction of ammonia with an alkyl halide leads to an ammonium salt. Subsequent treatment of the resulting ammonium salts with a base gives primary amines.
- Primary, secondary, and tertiary amines can be similarly alkylated.



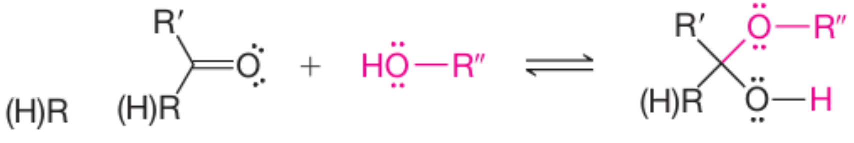
5. Nucleophilic Reactions

5.2 Nucleophilic Addition Reactions

5.2.1 Nucleophilic Addition to Aldehyde or Ketone

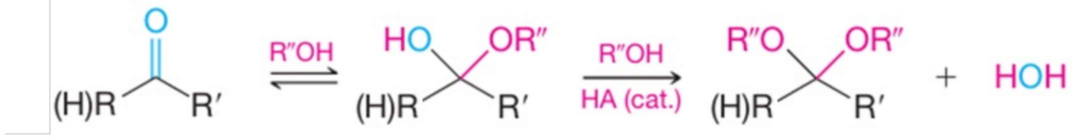
A) The Addition of Alcohols: Hemiacetals and Acetals

- Hemiacetals; an –OH and an –OR group attached to the same carbon atom.
- A hemiacetal results by nucleophilic addition of an alcohol oxygen to the carbonyl carbon of an aldehyde or ketone.
- Acetals; has two –OR groups attached to the same carbon atom.
- An acetal forms when an aldehyde or ketone is treated with an excess of alcohol in the presence of an acid catalyst. Although a hemiacetal is an intermediate, it usually cannot be isolated because it continues to become an acetal.



Aldehyde or Ketone

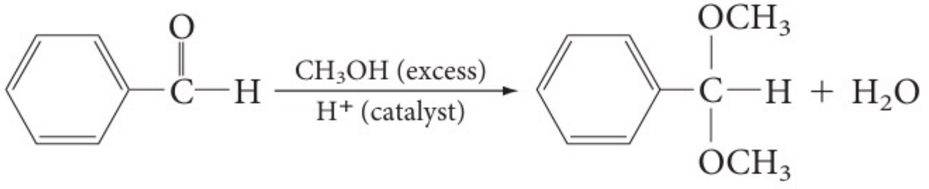
Hemiacetal



Aldehyde or Ketone

A hemiacetal

An acetal



5. Nucleophilic Reactions

5.2 Nucleophilic Addition Reactions

5.2.1 Nucleophilic Addition to Aldehyde or Ketone

B) The Addition of Primary Amines : Imine formation

- Imine formation is acid catalyzed, and the product can form from a primary amine and an aldehyde or ketone.

C) Reaction with hydroxylamine : Oxime formation

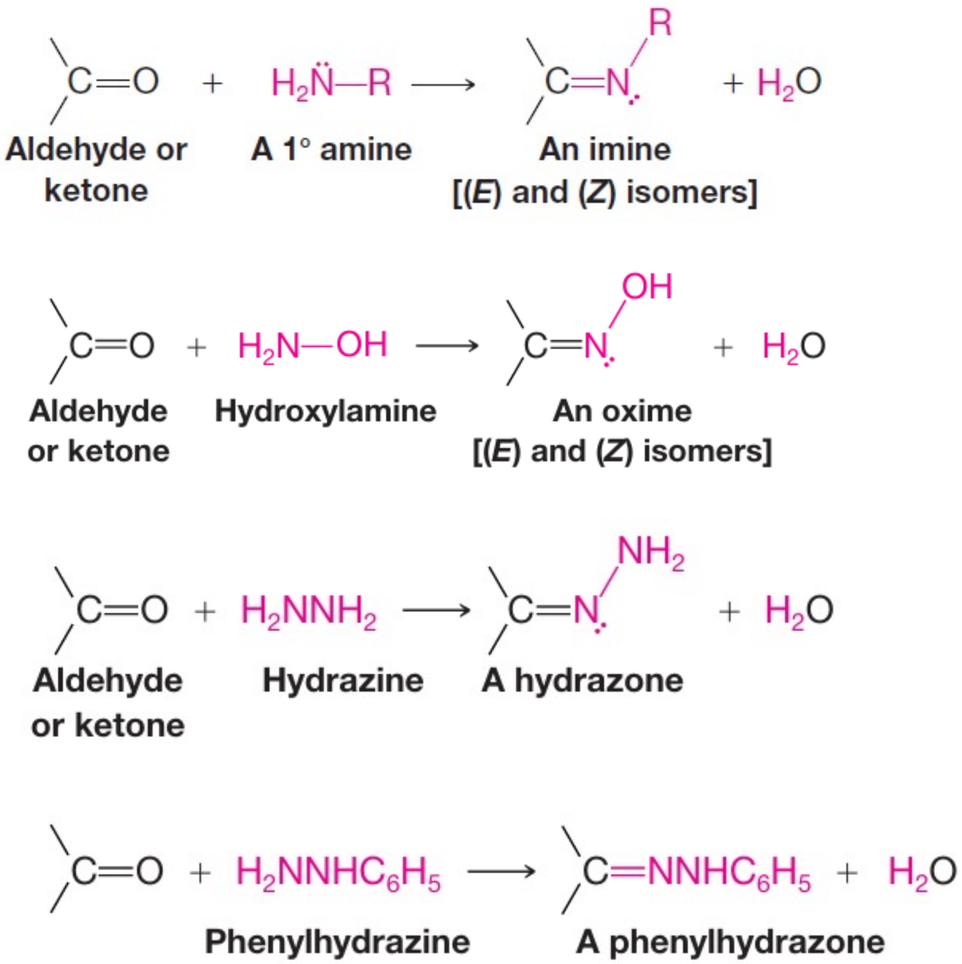
- Oximes are formed when aldehydes or ketones react with hydroxylamine (H_2N-OH).

D) Reactions with hydrazine: Hydrazone formation

- Hydrazone can be formed when aldehydes or ketones react with hydrazine (H_2N-NH_2).

E) Reactions with phenylhydrazine: Phenylhydrazone formation

- Hydrazone can be formed when aldehydes or ketones react with hydrazine (H_2N-NHC_6H_5).



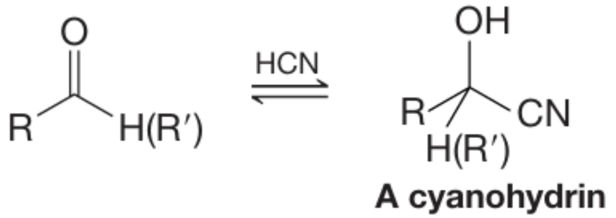
5. Nucleophilic Reactions

5.2 Nucleophilic Addition Reactions

5.2.1 Nucleophilic Addition to Aldehyde or Ketone

F) The Addition of Hydrogen Cyanide: Cyanohydrins

- **Hydrogen cyanide adds to the carbonyl groups of aldehydes and most ketones to form compounds called cyanohydrins.**



5. Nucleophilic Reactions

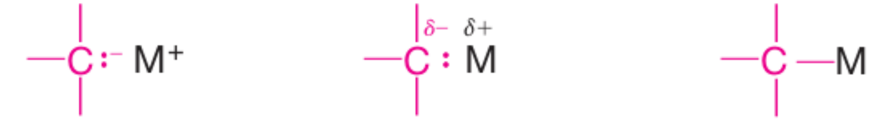
5.2 Nucleophilic Addition Reactions

5.2.2 Nucleophilic Addition Grignard Reagents

- **Compounds that contain carbon–metal bonds are called organometallic compounds.**

- **Grignard reagents are prepared by the reaction of an organic halide with magnesium metal in an anhydrous ether solvent.**

- **The order of reactivity of halides with magnesium is also**
  RI > RBr > RCl.



Primarily ionic (M = Na^+ or K^+)

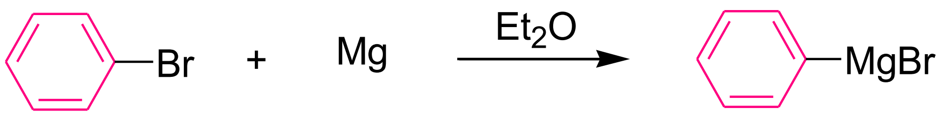
(M = Mg or Li)

Primarily covalent (M = Pb, Sn, Hg, or Tl)

$$\left.\begin{array}{l} RX + Mg \xrightarrow{Et_2O} RMgX \\ ArX + Mg \xrightarrow{Et_2O} ArMgX \end{array}\right\} \text{Grignard reagents}$$

$$CH_3I + Mg \xrightarrow{Et_2O} CH_3MgI$$

Methylmagnesium iodide



Phenylmagnesium bromide

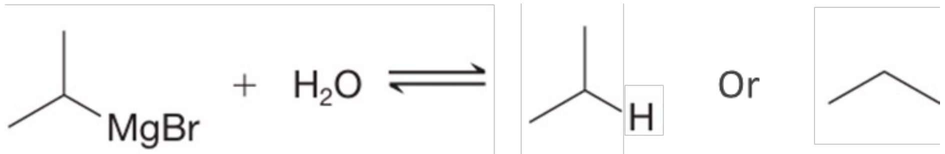
5. Nucleophilic Reactions

5.2 Nucleophilic Addition Reactions

5.2.2 Nucleophilic Addition Grignard Reagents

A) Reactions of Grignard Reagents with Compounds Containing Acidic Hydrogen Atoms

- Grignard reagents are very strong bases.
- They react with any compound that has a hydrogen atom attached to an electronegative atom such as oxygen, nitrogen, or sulfur.



Propane

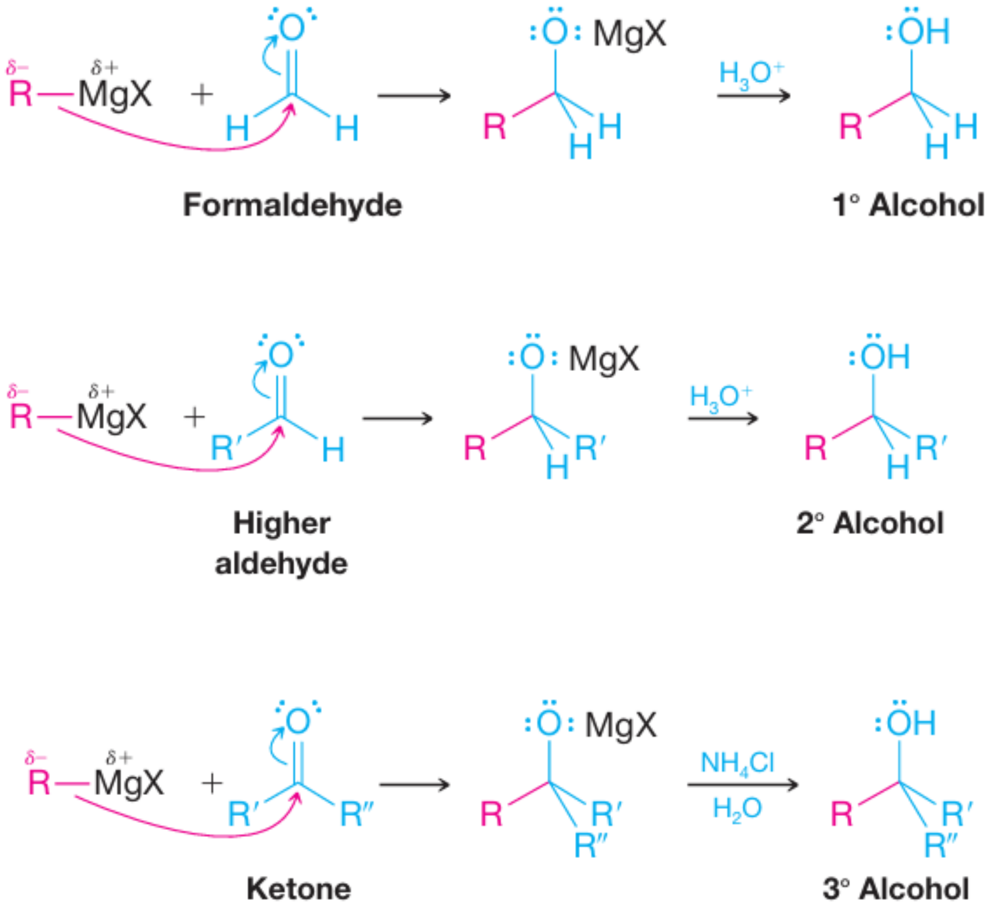
5. Nucleophilic Reactions

5.2 Nucleophilic Addition Reactions

5.2.2 Nucleophilic Addition Grignard Reagents

B) Reactions of Grignard Reagents with Aldehydes and Ketones

- Grignard reagents react as nucleophiles and attack an unsaturated carbon—the carbon of a carbonyl group (aldehyde and ketone) to prepare primary, secondary, or tertiary alcohols.
- Grignard Reagents React with Formaldehyde to Give a Primary Alcohol.
- Grignard Reagents React with All Other Aldehydes to Give Secondary Alcohols.
- Grignard Reagents React with Ketones to Give Tertiary Alcohols.



5. Nucleophilic Reactions

5.2 Nucleophilic Addition Reactions

5.2.2 Nucleophilic Addition Grignard Reagents

B) Reactions of Grignard Reagents with Aldehydes and Ketones

Examples,

Phenylmagnesium bromide **Formaldehyde** **Benzyl alcohol (90%)**

Ethylmagnesium bromide **Acetaldehyde** **2-Butanol (80%)**

Butylmagnesium bromide **Acetone** **2-Methyl-2-hexanol (92%)**

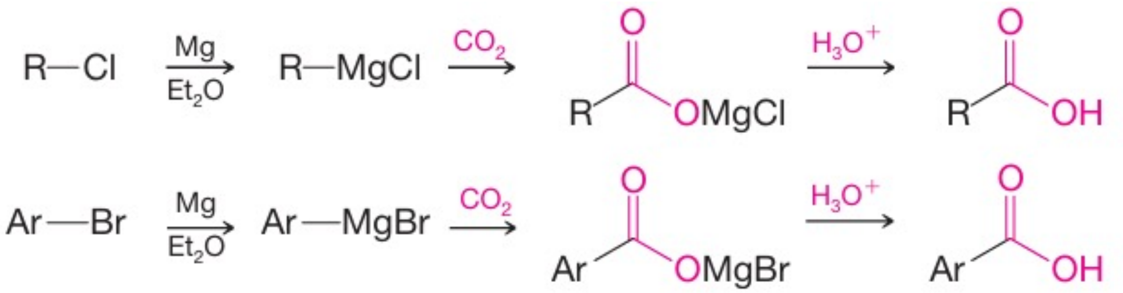
5. Nucleophilic Reactions

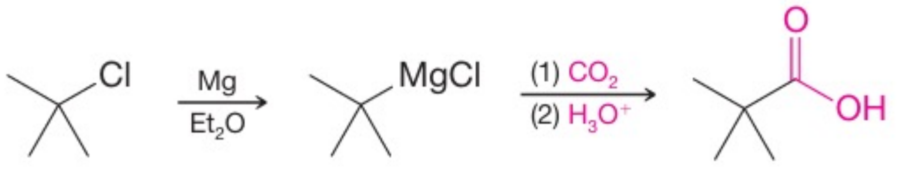
5.2 Nucleophilic Addition Reactions

5.2.2 Nucleophilic Addition Grignard Reagents

C) Carbonation of Grignard Reagents: preparation of carboxylic acids

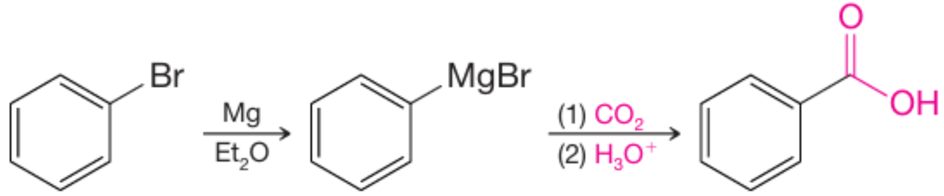
- Grignard reagents react with carbon dioxide to yield magnesium carboxylates. Acidification produces carboxylic acids.
- This synthesis of carboxylic acids is applicable to primary, secondary, tertiary, allyl, benzyl, and aryl halides.





***tert*-Butyl chloride**

2,2-Dimethylpropanoic acid (79–80% overall)



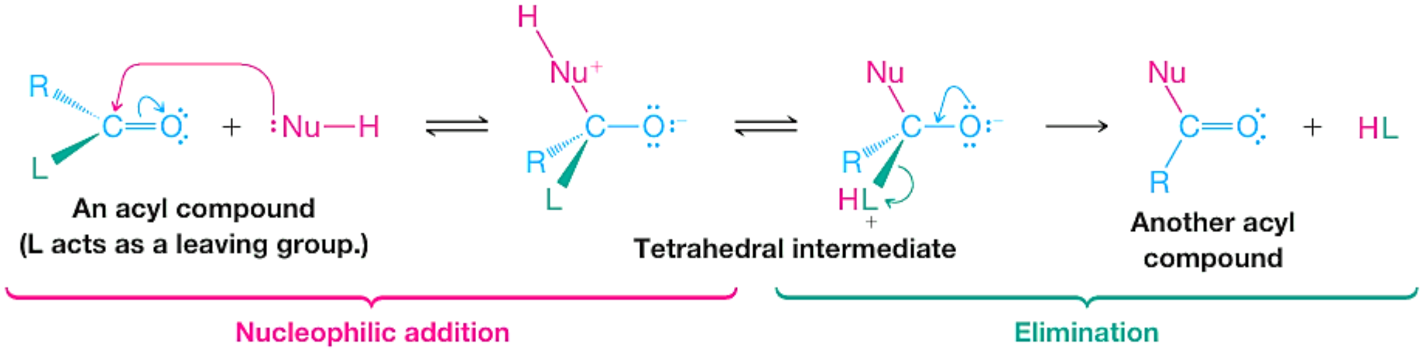
Bromobenzene

Benzoic acid (85%)

5. Nucleophilic Reactions

5.3 Substitution by Nucleophilic Addition-Elimination Reaction

- **The reactions of carboxylic acids and their derivatives are characterized by nucleophilic addition–elimination at their acyl (carbonyl) carbon atoms. The result is a substitution at the acyl carbon.**

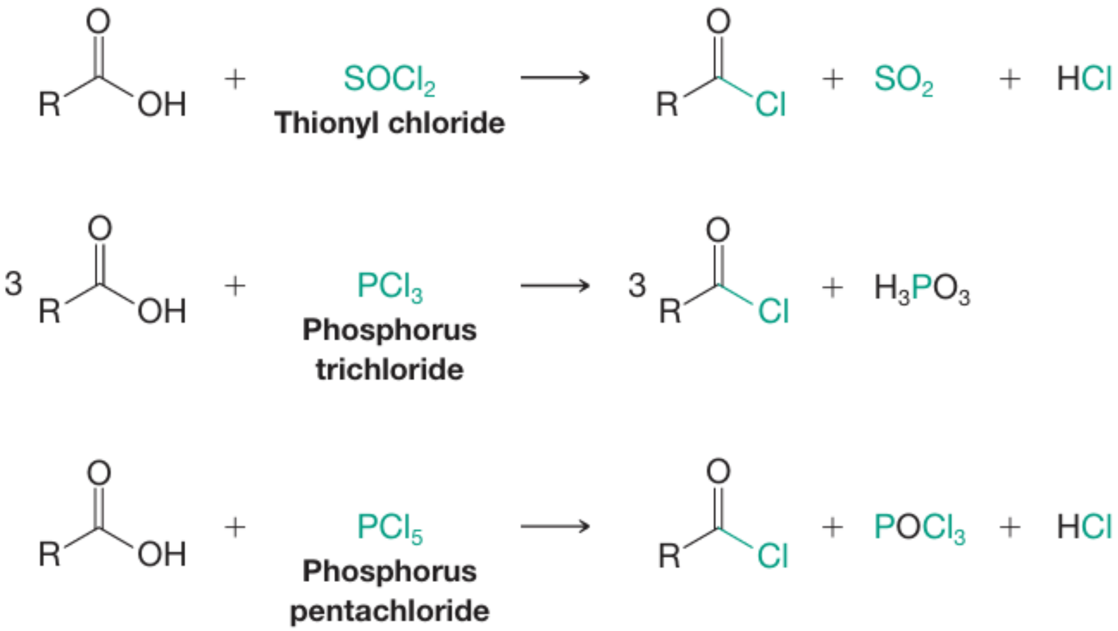


5. Nucleophilic Reactions

5.3 Substitution by Nucleophilic Addition-Elimination Reaction

5.3.1 Synthesis of Acyl Chlorides

- Acid chlorides are made from the reaction of carboxylic acids with thionyl chloride, phosphorus trichloride or phosphorus pentachloride.

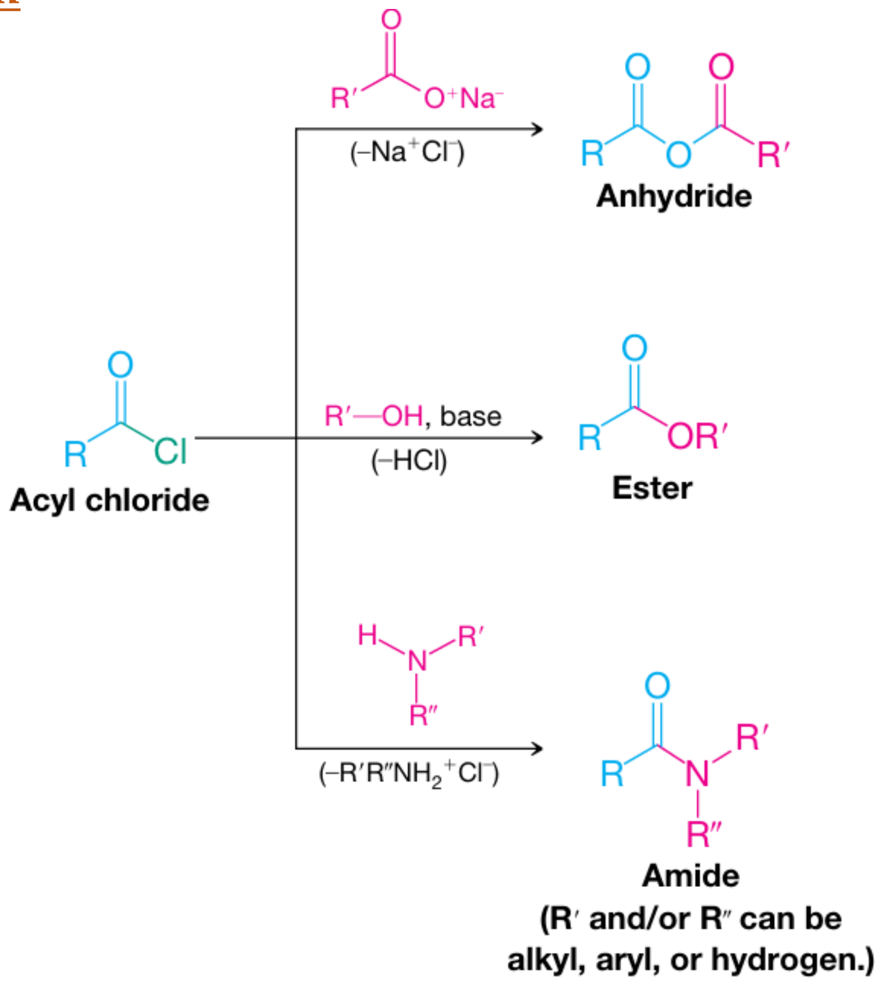


5. Nucleophilic Reactions

5.3 Substitution by Nucleophilic Addition-Elimination Reaction

5.3.2 Reactions of Acyl Chlorides

- Acyl chlorides are very reactive and can be used to synthesize anhydrides, esters and amides.



5. Nucleophilic Reactions

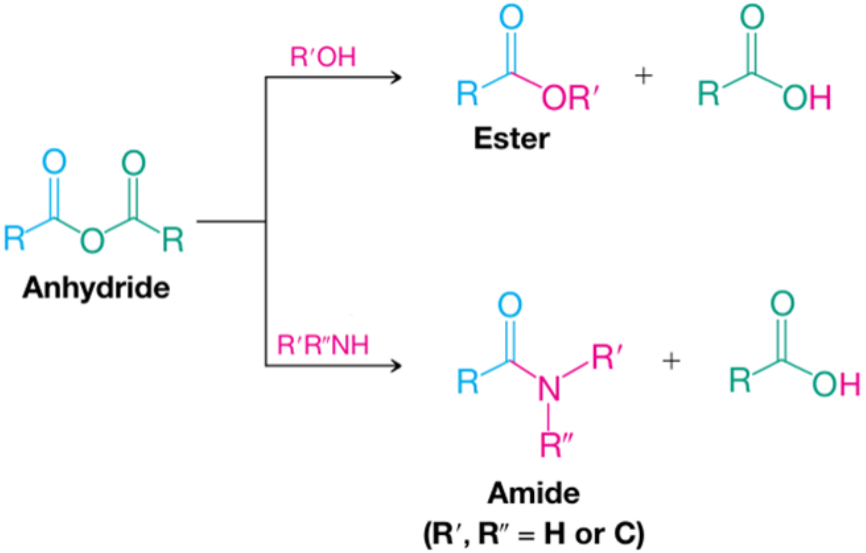
5.3 Substitution by Nucleophilic Addition-Elimination Reaction

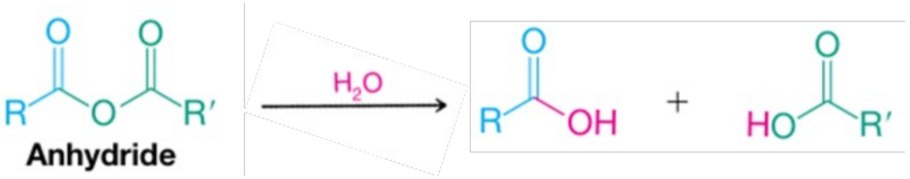
5.3.3 Synthesis of Carboxylic Acid Anhydrides

- **Sodium salts** of carboxylic acids react with **acyl chlorides** to give **anhydrides**.

5.3.4 Reactions of Carboxylic Acid Anhydrides

- Carboxylic acid anhydrides are very reactive and can be used to synthesize **esters** and **amides**.
- **Hydrolysis** of an anhydride yields the corresponding carboxylic acids.





5. Nucleophilic Reactions

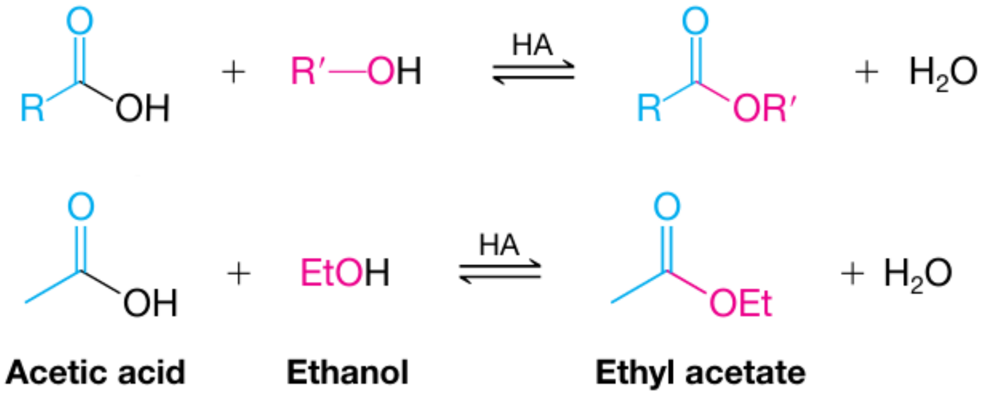
5.3 Substitution by Nucleophilic Addition-Elimination Reaction

5.3.5 Synthesis of Esters: Esterification

A) Acid-Catalyzed Esterification:

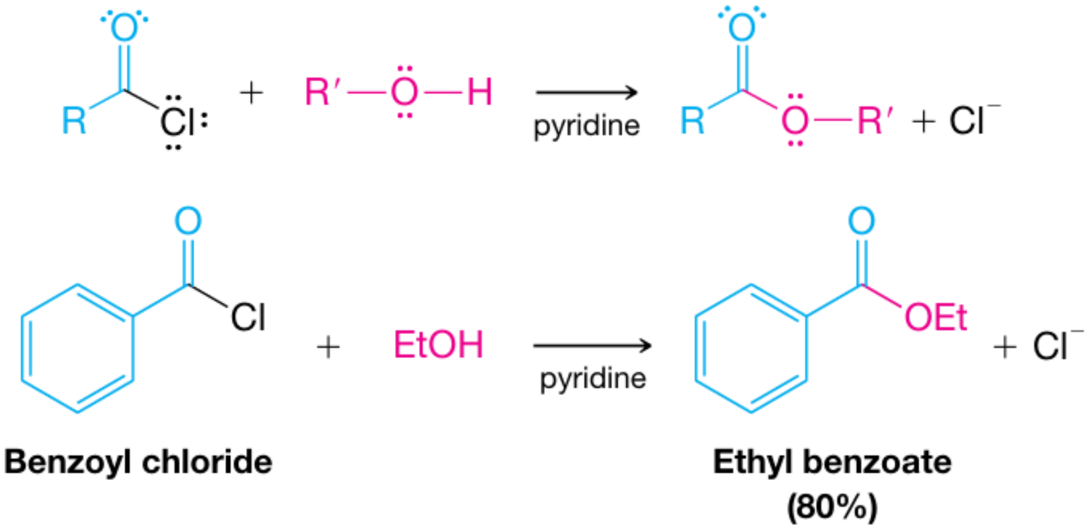
Esterification is the formation of an ester by reaction of a carboxylic acid, acid chloride, or carboxylic acid anhydride with an alcohol or phenol.

This method is often called Fischer esterification.



B) Esters from Acyl Chlorides:

The reaction of acyl chlorides with an alcohol or a phenol is one of the best ways to synthesize an ester.



Chapter 5: Organic Reactions

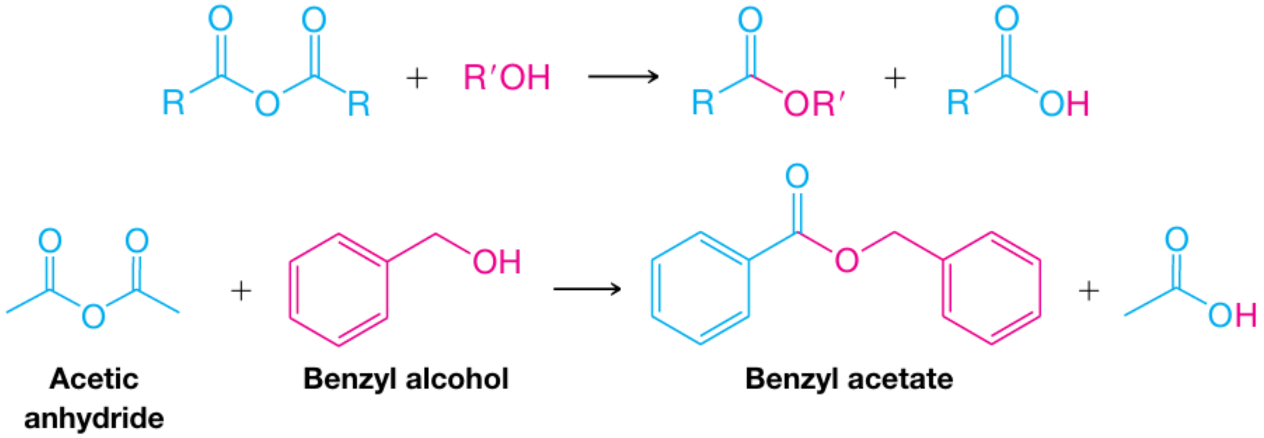
5. Nucleophilic Reactions

5.3 Substitution by Nucleophilic Addition-Elimination Reaction

5.3.5 Synthesis of Esters: Esterification

C) Esters from Carboxylic Acid Anhydrides

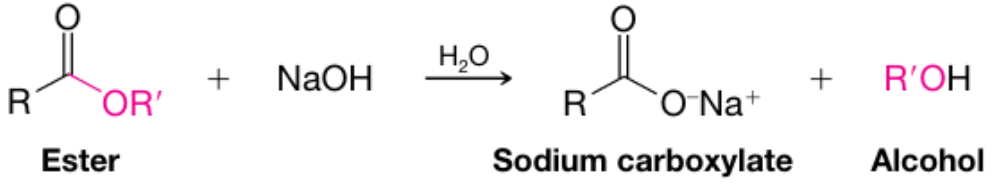
Carboxylic acid anhydrides react with alcohols and phenols to form esters in the absence of acid catalyst.



5.3.6 Reactions of Esters

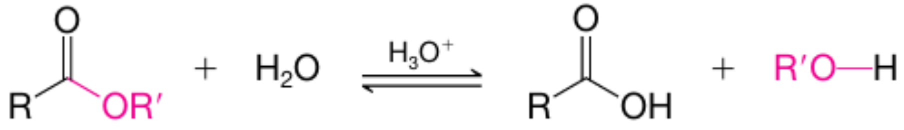
A) Base-Promoted Hydrolysis of Esters: Saponification

Reaction of an ester with sodium hydroxide results in the formation of a sodium carboxylate and an alcohol.



B) Acid-Catalyzed Ester Hydrolysis

Reaction of an ester with a large excess of water and dilute aqueous HCl or dilute aqueous H_2SO_4 results in the formation of a carboxylic acid and an alcohol.



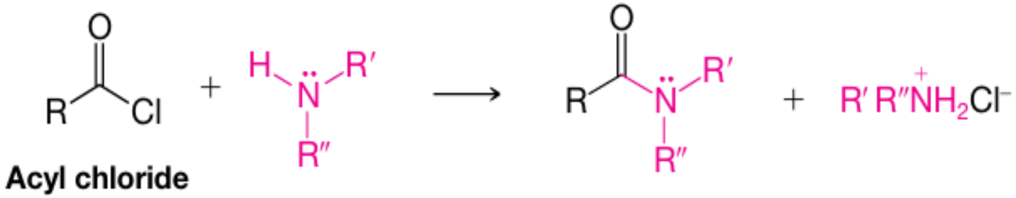
5. Nucleophilic Reactions

5.3 Substitution by Nucleophilic Addition-Elimination Reaction

5.3.7 Synthesis of Amides

A) From Acyl Chlorides

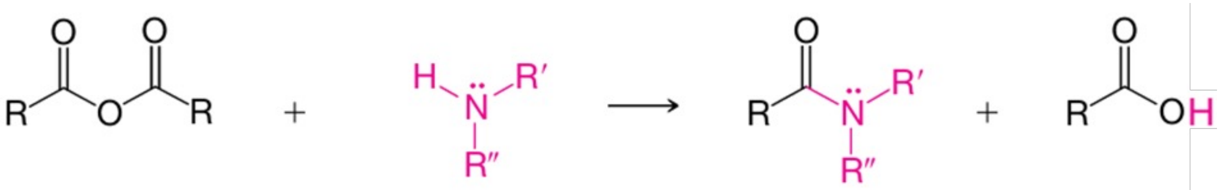
Ammonia, primary or secondary amines react with acid chlorides to form amides.



R′, R″ can be H, alkyl, or aryl.

B) From Carboxylic Anhydrides

Acid anhydrides react with amine to produce an amide and carboxylic acid.



R′, R″ can be H, alkyl, or aryl.

5. Nucleophilic Reactions

5.3 Substitution by Nucleophilic Addition-Elimination Reaction

5.3.7 Synthesis of Amides

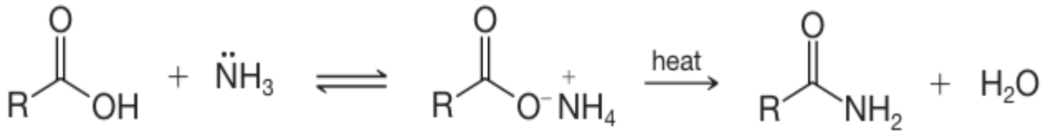
C) Amides from Esters

Esters react with ammonia (called ammonolysis) or with primary and secondary amines to produce an amide and an alcohol.

R′ and/or R″ may be H.

D) From Carboxylic Acids and Ammonium Carboxylates

Carboxylic acids react with aqueous ammonia to form ammonium salts. Some ammonium salts of carboxylic acids can be dehydrated to the amide at high temperatures



An ammonium carboxylate

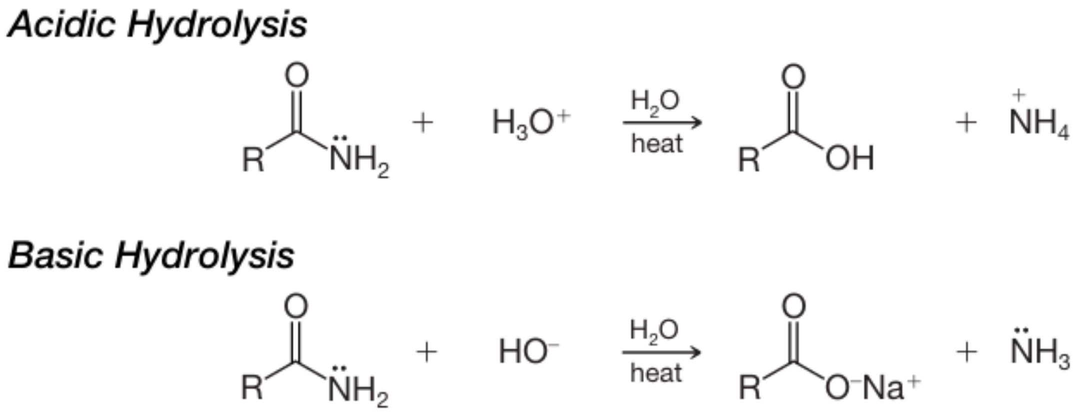
5. Nucleophilic Reactions

5.3 Substitution by Nucleophilic Addition-Elimination Reaction

5.3.8 Reactions of Amides

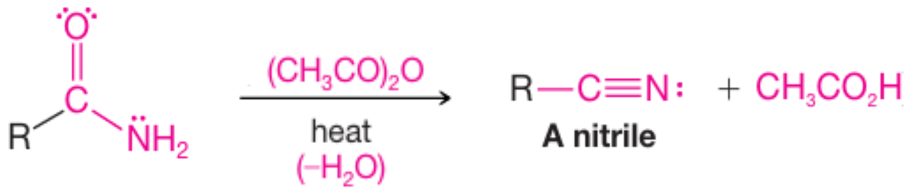
A) Hydrolysis of Amides

Amides undergo hydrolysis when they are heated with aqueous acid or aqueous base.



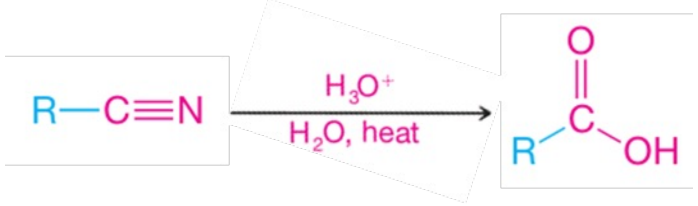
B) Nitriles from the Dehydration of Amides

Amides react with boiling acetic anhydride to form nitriles.



C) Hydrolysis of Nitriles

Complete hydrolysis of a nitrile produces a carboxylic acid.



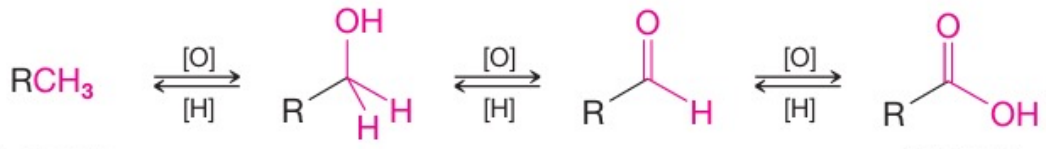
Oxidation and Reduction Reactions

6. Oxidation and Reduction Reactions

- Reduction; increasing the hydrogen content or decreasing the oxygen content of an organic molecule.
- A general symbol for reduction is [H].

- Oxidation; increasing the oxygen content of an organic molecule or decreasing its hydrogen content.
- A general symbol for oxidation is [O].
- Oxidation can also be defined as a reaction that increases the content of any element more electronegative than carbon.

- when an organic compound is reduced, something else the reducing agent must be oxidized.
- And when an organic compound is oxidized, something else the oxidizing agent is reduced.
- These oxidizing and reducing agents are often inorganic compounds.



Lowest oxidation state

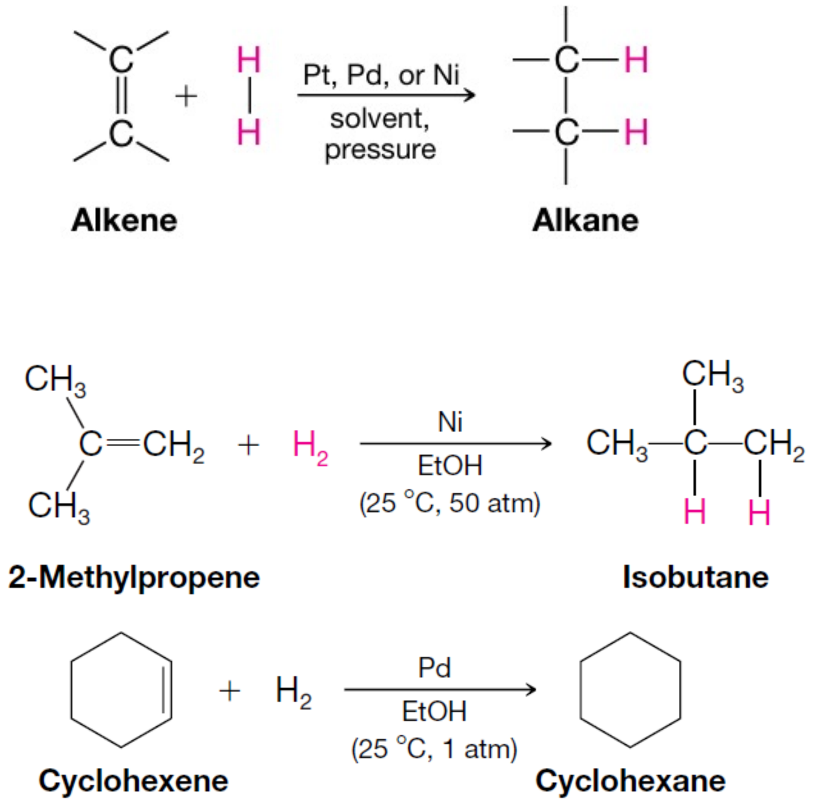
Highest oxidation state

$$Ar{-}CH_3 \underset{[H]}{\overset{[O]}{\rightleftharpoons}} Ar{-}CH_2Cl \underset{[H]}{\overset{[O]}{\rightleftharpoons}} Ar{-}CHCl_2 \underset{[H]}{\overset{[O]}{\rightleftharpoons}} Ar{-}CCl_3$$

6. Oxidation and Reduction Reactions

6.1 Hydrogenation of Alkenes: Synthesis of Alkanes and Cycloalkanes

- **Heterogeneous catalysts:** insoluble platinum, palladium or nickel catalysts that are not soluble in the reaction mixture.
- **Homogeneous catalysts:** soluble catalyst include rhodium or ruthenium complexes; Wilkinson's catalyst tris(triphenylphosphine) rhodium chloride ($Rh[(C_6H_5)_3P]_3Cl$).
- An unsaturated compound becomes a saturated (with hydrogen) compound.



Chapter 5: Organic Reactions

6. Oxidation and Reduction Reactions

6.2 Hydrogenation of Alkynes: Synthesis of Alkanes and Cycloalkanes

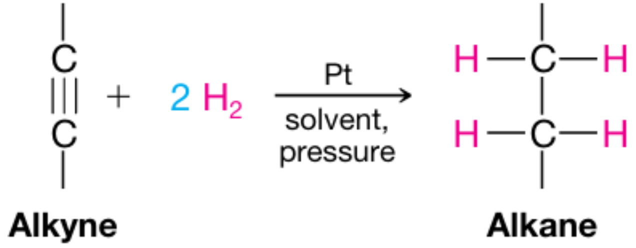
A) When a platinum catalyst is used, the alkyne reacts with two molar equivalents of hydrogen to give an alkane.

B) Syn Addition of Hydrogen: Synthesis of *cis*-Alkenes

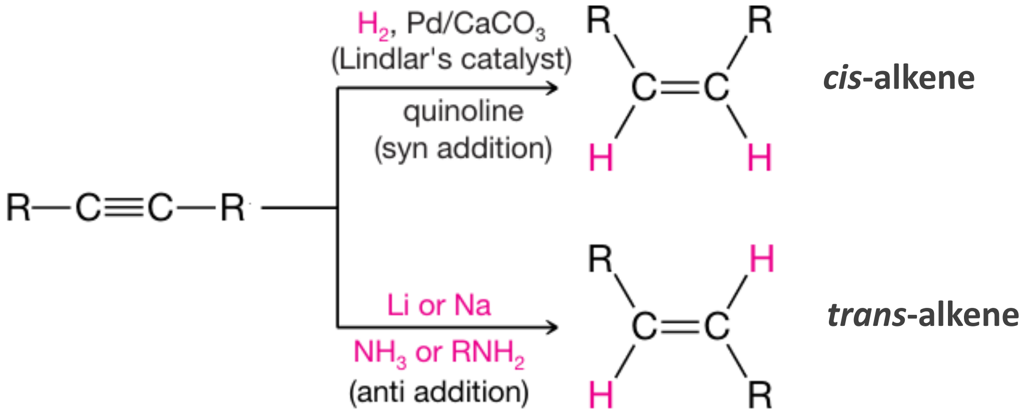
Metallic palladium deposited on calcium carbonate (Lindlar's catalyst) can be used to prepare *cis*-alkenes.

C) Anti Addition of Hydrogen: Synthesis of *trans*-Alkenes

Treatment of alkynes with lithium or sodium metal in ammonia or ethylamine at low temperatures prepare *trans*-alkene.



$$CH_3C\equiv CCH_3 \xrightarrow{Pt,\ H_2} [CH_3CH=CHCH_3] \xrightarrow{Pt,\ H_2} CH_3CH_2CH_2CH_3$$



6. Oxidation and Reduction Reactions

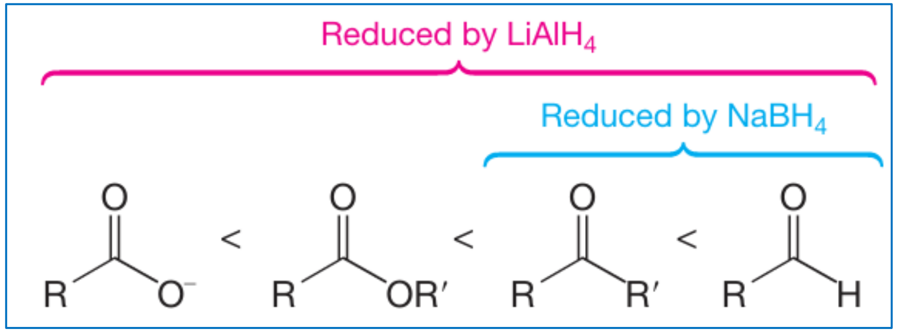
6.3 Reduction of Carbonyl Compounds; Synthesis of Alcohols

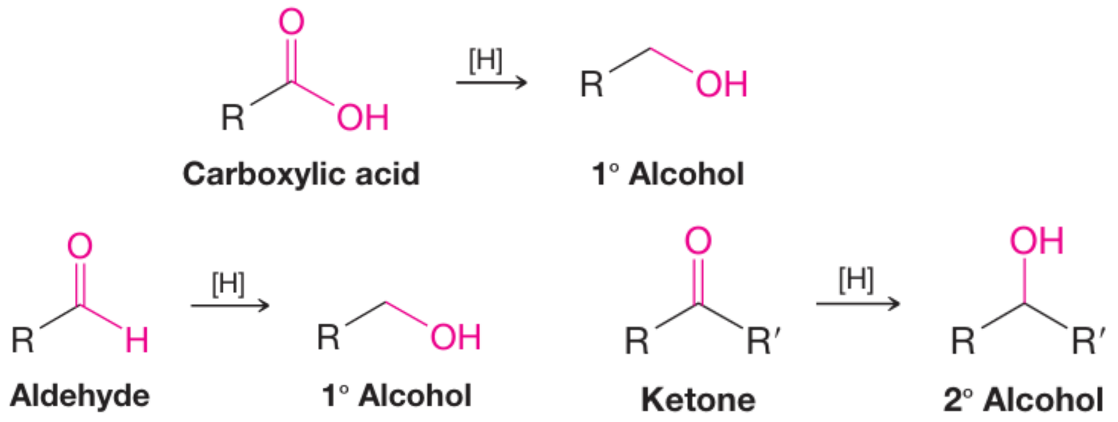
A) Lithium Aluminum Hydride ($LiAlH_4$)

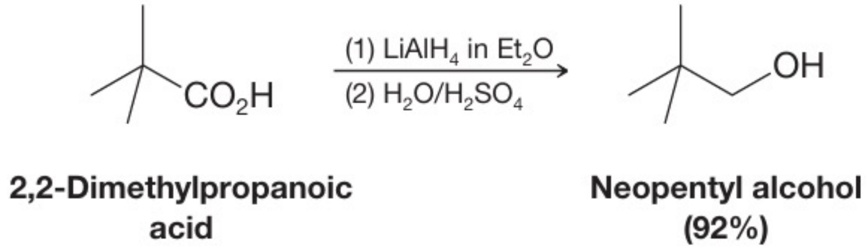
Carboxylic acids and esters can be reduced to primary alcohols.

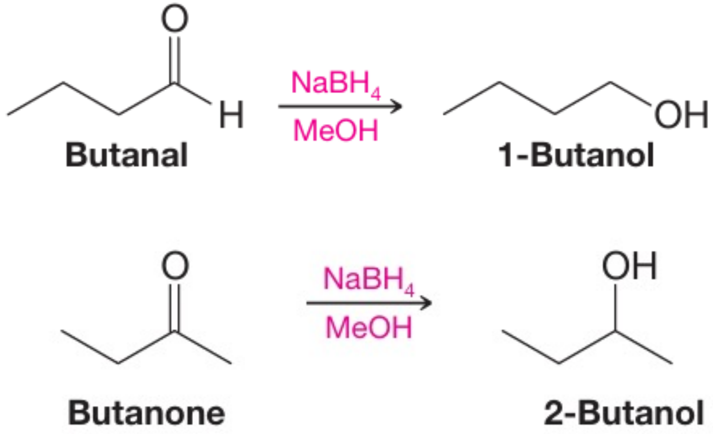
B) Sodium Borohydride ($NaBH_4$)

Aldehydes and ketones are reduced by mild reducing agent sodium borohydride ($NaBH_4$) to 1º and 2º alcohols, respectively.





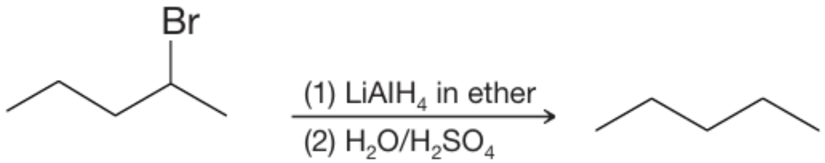




6. Oxidation and Reduction Reactions

6.4 Reduction of Alkyl Halides to Hydrocarbons: RX to RH

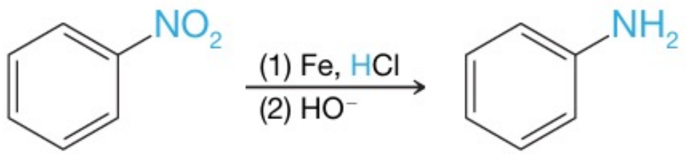
- Replacement of the halogen atom of an alkyl halide by hydrogen can be accomplished by treating the alkyl halide with lithium aluminum hydride.



6.5 Reduction of Nitro Compounds: Preparation of Aromatic Amines

- Aromatic amines can be synthesized by reduction of the corresponding nitro compound.

$$Ar{-}NO_2 \xrightarrow[\text{or (1) Fe, HCl (2) HO}^-]{H_2\text{, catalyst}} Ar{-}NH_2$$

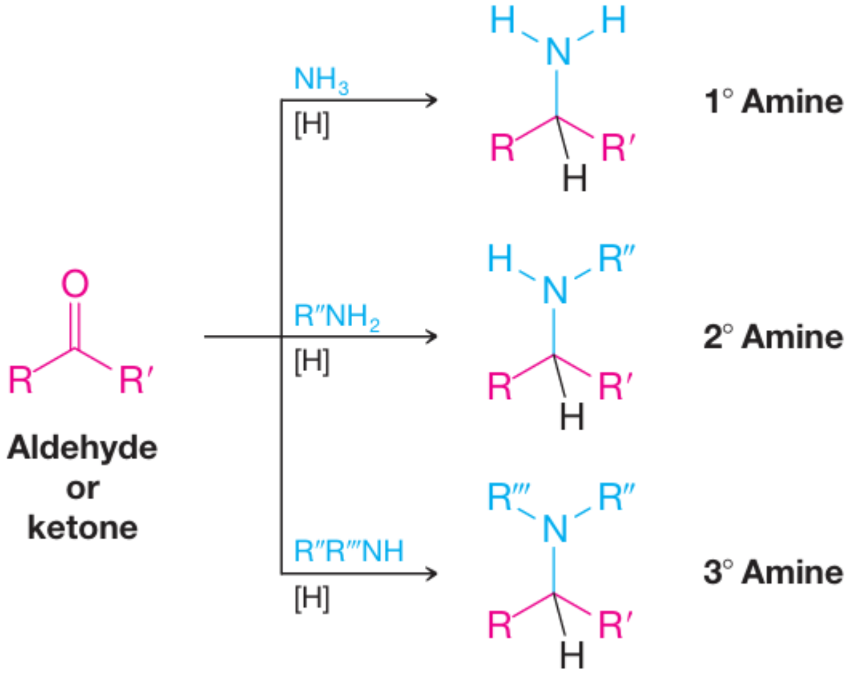


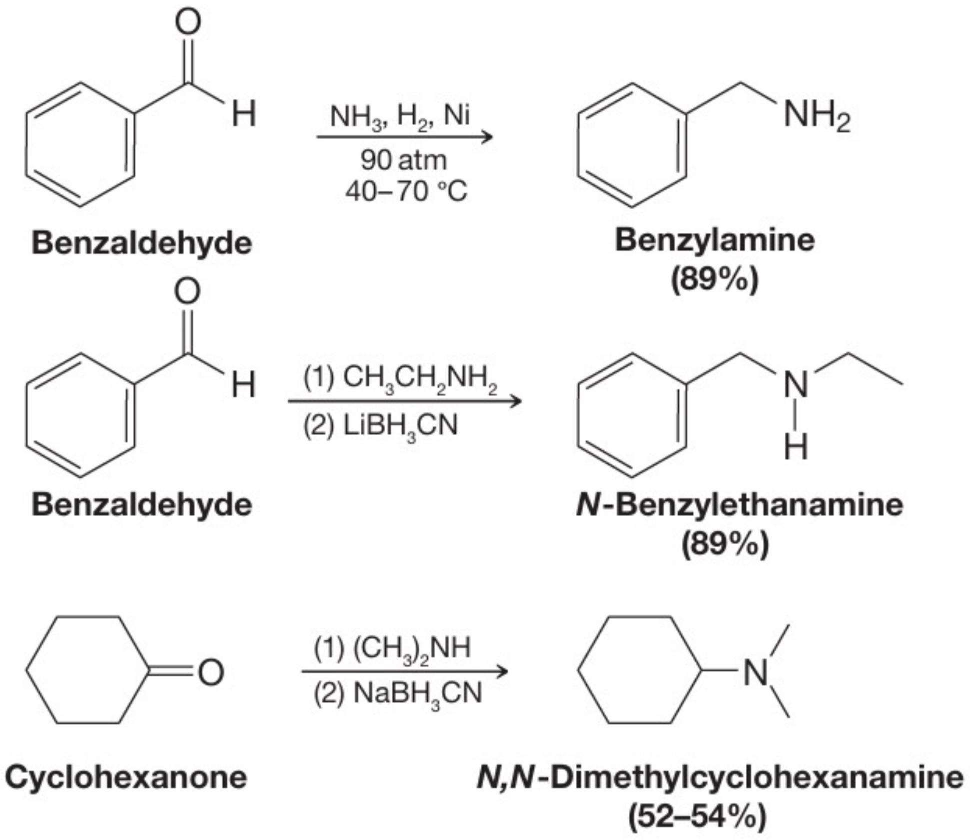
97%

6. Oxidation and Reduction Reactions

6.6 Reductive Amination of aldehyde or ketone: Preparation of Primary, Secondary, and Tertiary Amines

- Aldehydes and ketones can be converted to amines through catalytic or chemical reduction in the presence of ammonia or an amine.

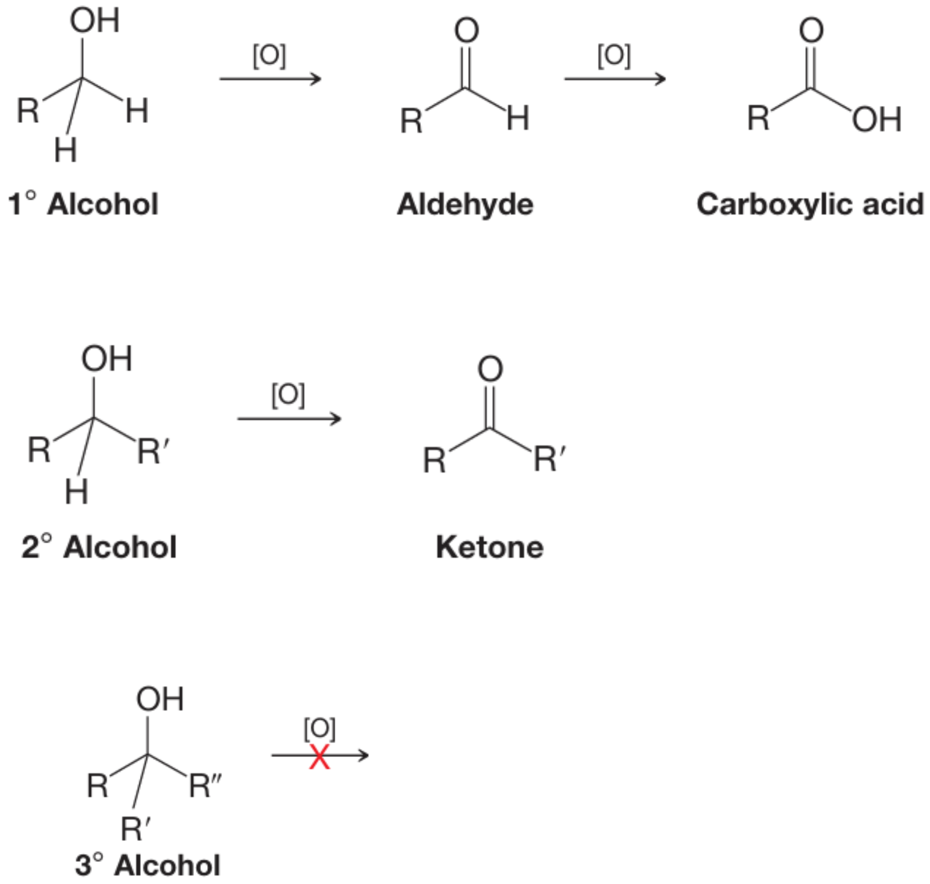




6. Oxidation and Reduction Reactions

6.7 Oxidation of Alcohols: *Preparation of Aldehydes, Ketones, and Carboxylic Acids*

- **Primary alcohols can be oxidized to aldehydes, and aldehydes can be oxidized to carboxylic acids.**
- **Secondary alcohols can be oxidized to ketones.**
- **Tertiary alcohols cannot be oxidized to carbonyl compounds.**



6. Oxidation and Reduction Reactions

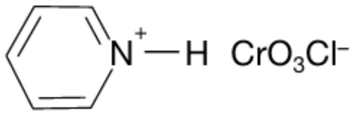
6.7 Oxidation of Alcohols: *Preparation of Aldehydes, Ketones, and Carboxylic Acids*

A) Oxidation by Chromic acid (H_2CrO_4)

- **Oxidations involving chromium (VI) reagents such as Jones reagent H_2CrO_4 (CrO_3 in H_2SO_4).**
- **Primary alcohols are oxidized to carboxylic acids.**
- **Secondary alcohols are oxidized to ketones.**

B) Oxidation by Pyridinium Chlorochromate (PCC)

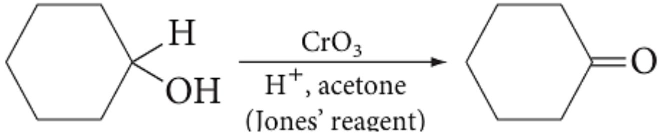
Pyridinium chlorochromate (PCC) is formed between pyridine (C_6N_5N), HCl, and CrO_3. PCC is soluble in dichloromethane. Thus, it can be used under conditions that exclude water, allowing for the oxidization of primary alcohols to aldehydes and secondary alcohols to ketones.



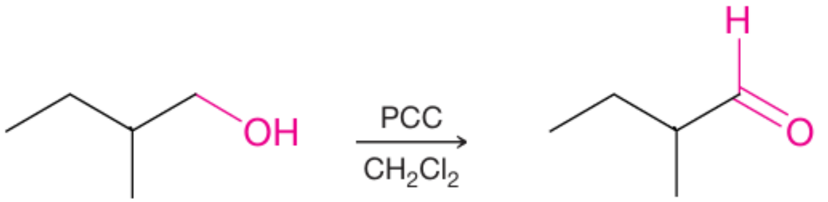
Pyridinium chlorochromate (PCC)

$$CH_3(CH_2)_6CH_2OH \xrightarrow[\text{reagent}]{\text{Jones'}} CH_3(CH_2)_6CO_2H$$

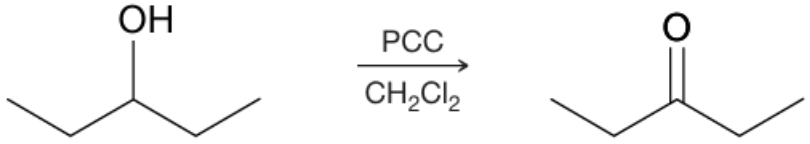
1-Octanol **Octanoic acid**



Cyclohexanol **Cyclohexanone**



2-Methylbutanol **2-Methylbutanal**



3-Pentanol **3-Pentanone**

6. Oxidation and Reduction Reactions

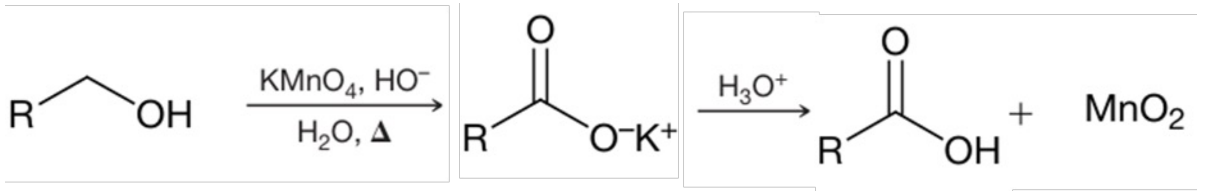
6.7 Oxidation of Alcohols; *Preparation of Aldehydes, Ketones, and Carboxylic Acids*

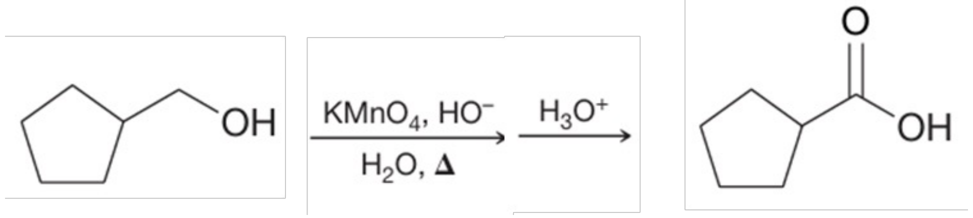
C) Oxidation by Potassium Permanganate ($KMnO_4$)

Primary alcohols and aldehydes can be oxidized by potassium permanganate ($KMnO_4$) to the corresponding carboxylic acids.

Secondary alcohols can be oxidized to ketones.

The reaction is usually carried out in basic aqueous solution.



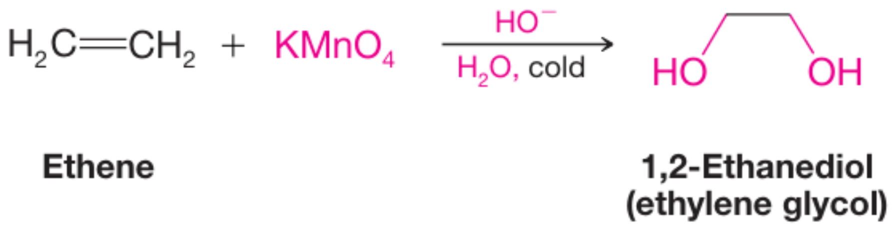


6. Oxidation and Reduction Reactions

6.8 Oxidation of Alkenes

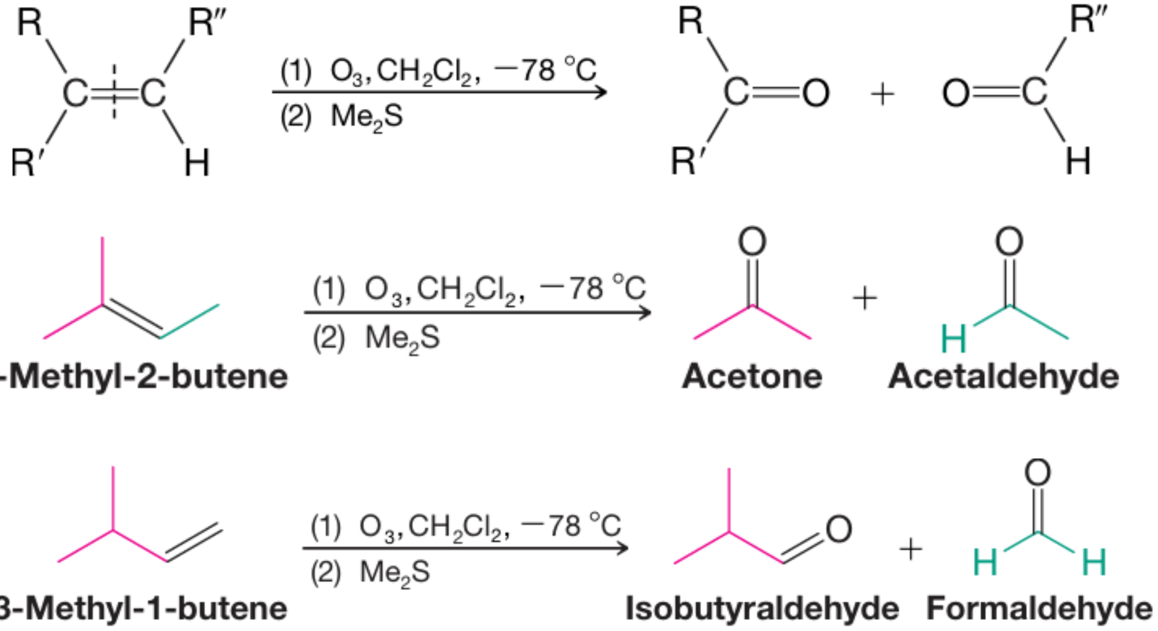
A) Oxidation of Alkenes: Syn 1,2-Dihydroxylation with Cold Basic Potassium Permanganate

Alkenes can be dihydroxylated using dilute solution of potassium permanganate under basic conditions with a cold to form a *cis*-diol (glycol).



B) Oxidative Cleavage OF Alkenes: Cleavage with Ozone

The most useful method for cleaving alkenes is to use ozone (O_3). Unsubstituted carbons are oxidized to formaldehyde, monosubstituted carbons are oxidized to aldehydes and disubstituted carbons are oxidized to ketones.



6. Oxidation and Reduction Reactions

6.9 Oxidation of the Side Chain of Aromatic Compounds

- Alkyl and unsaturated side chains of aromatic rings can be oxidized to the carboxylic acid using hot $KMnO_4$.