Organic Chemistry II

Eugene de Silva

Organic Chemistry II

Contributing Authors

Eugene de Silva, Ocean County College

Original Publication Year 2023

Funding Statement

This material was funded by the Fund for the Improvement of Postsecondary Education (FIPSE) of the U.S. Department of Education for the Open Textbooks Pilot grant awarded to Middlesex College (Edison, NJ) for the Open Textbook Collaborative.

Open Textbook Collaborative

The Open Textbook Collaborative (OTC) project is a statewide project managed by Middlesex College along with assistance from Brookdale Community College, Ocean County College , Passaic County Community College, and Rowan University .

The project engages a consortium of New Jersey community colleges, four-year colleges and universities, and workforce partners to develop open educational resources (OER) in career and technical education STEM courses.

The courses align to career pathways in New Jersey's growth industries including health services, technology, energy, and global manufacturing and supply chain management as identified by the New Jersey Council of Community Colleges.

Organic Chemistry Book 2

Contents

Introduction

You have now embarked on a journey to study organic chemistry. I hope that by providing this open-source, free educational material, I have also assisted you on that journey.

I have written these two books, “Organic Chemistry 1” and “Organic Chemistry 2” in the format of lecture notes. The two books complement each other. The first book includes chapters 0 – 10. The second book includes chapters 11 – 21. The students are encouraged to read both books, although they could be studied independently.

Wherever possible, I have referred to common reactions and mechanisms that are used in most of the textbooks, websites, and OER materials. This should make it convenient for you to compare and comprehend the subject matter by relating it to what you have already read, seen, or studied. I have done my best to avoid including unnecessary descriptions and any other generic information that is not required to be successful in a taught course in organic chemistry. On some rare occasions, I have integrated some advanced reactions and mechanisms to provide you with more comprehensive information. This has been done intentionally to help you better understand the fundamentals. I have also included some questions, answers, and images from OpenStax.org and Chemistry LibreText.org websites, the material of which were available as OER under CC by NC-BY-NC.

The pedagogical approach to writing this book has been to first introduce you to broad, common, core facts in the first five chapters prior to discussing different reactions and mechanisms under different groups of organic compounds.

Chapter zero begins with an introduction to carbon atom, its bonding, structure, hybridization, oxidation and reduction, acidity and basicity, and molecular orbital theory, all of which are relevant to all organic compounds.

Chapter 1 introduces you to the classification of organic compounds, each of which you will study under separate chapters later.

We then progress into Chapter 2, which introduces you to the nomenclature of organic compounds. You will use the knowledge from this chapter to name different organic compounds you study in other chapters.

Moving into Chapter 3, you will learn about the isomers of organic compounds.

Chapter 4 elaborates on the different types of reactions. This chapter marks the final chapter wherein I present the vital foundational knowledge to you. By this point within the book, you should feel confident and prepared to tackle the reactions of different organic compounds discussed under different chapters.

The chapters 5 – 16 (transitioning to book 2 from book 1) take us on a path to explore different groups of organic compounds. The final five chapters (17 – 21) separately cover an introduction to spectroscopic methods, mass spectrometer, IR, UV/Vis, and NMR techniques. These are important analytical techniques used in the study of organic compounds.

Finally, I want to thank the team that made it possible for me to write these two books. Both books, which are Open Educational Resources (OER), were created through Open Textbooks Pilot Grant awarded to Middlesex College by the U.S. Department of Education Fund for the Improvement of Postsecondary Education (FIPSE) program.

The team members are,

Marilyn N. Ochoa, Open Textbook Collaborative PI and Project Director

Steven Chudnick, Project Coordinator

Joshua Gaul, Educational Technology Manager

Robert Hilliker, Curriculum Council Manager

Susan Scarangella, Health Services Curriculum Committee Chair

Next, I want to thank the team at Ocean County College:

Dean Vivian Lynn of e-Learning at Ocean County College for directing me to seek opportunities through the FIPSE program and her continuous encouragement for progress.

Dr. Eileen Garcia, Vice President for e-Learning and Learning Enterprises, for supporting scholarly work.

Dr. Jon H. Larson, The President of Ocean County College, for providing me with opportunities.

I want to especially thank Dr. Thilini Peramuna and Dr. Pramudi Abeydeera for drawing all the reaction mechanisms and equations for this book and my daughter Dr. Eugenie de Silva for providing all the other support to make these two books a success.

I hope to continuously improve this OER textbook as an ongoing project.

Finally, I want to dedicate this work to my mother, Latha, who taught me the importance of perseverance, resilience, and steadfastness through her exemplary life.

Chapter 11

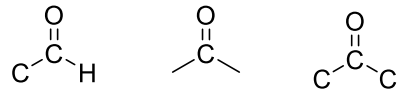
11.0 Aldehydes and Ketones

11.1 Objectives

1. Draw and interpret Lewis structures, line-bond structures and functional groups of aldehydes and ketones using IUPAC system of nomenclature.
2. Draw reaction mechanisms.
3. Describe reactions, predicting reactivity, and reaction products.
4. Devise syntheses including steps, reagents, and products including regiochemistry and stereochemistry

11.2 Introduction

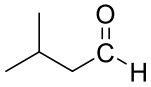
Aldehydes and ketones are used mostly as solvents in industry. These two classes of compounds play an important role in industry. Also, these compounds can be found in living systems as well. Both these compounds have a carbonyl group attached to the compound.

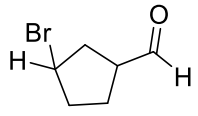


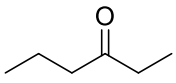
11.3 Nomenclature and Isomerism

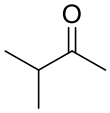
Please refer to the chapter on nomenclature and isomerism and answer the following questions:

1. **Naming Compounds – Give the IUPAC names for the following compounds.**

a) 

b) 

C) 

d) 

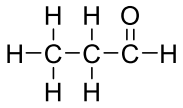
2. **Draw the structures of the following compounds**

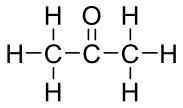
a) 1-phenylethanone

b) Benzenecarbaldehyde

3. **Questions on Isomers**

What types of isomers are the following two compounds?





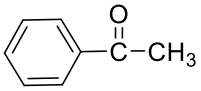
Solutions:

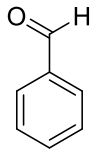
1. **Naming Compounds – Give the IUPAC names for the following compounds.**

a. 3- methylbutanal
b) 2,2,-dibromocyclopentanecarbaldehyde
c) 3-hexanone
d) 3-methyl-2-butanone

2. **Draw the structure of the following compounds.**

a)



b) 

3. **Questions on Isomers**

Both are constitutional (structural) isomers (specifically - functional isomers). One is a ketone and the other is an aldehyde.

11.4 Physical Properties

These two classes of compounds provide you with first introduction to the carbonyl group. The carbonyl functional group is planar and C=O bond is polar.

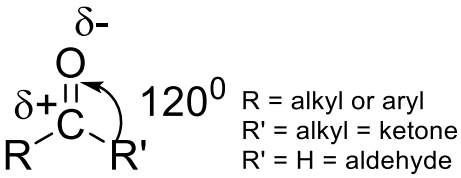


Figure 11.41: Bond angle of ketone or aldehyde compounds in a trigonal planar arrangement

The boiling points of ketones and aldehydes are higher than their corresponding alkanes. This is because carbonyl polarity enables the molecules to be connected weakly. Yet, ketones and aldehydes have lower boiling points than their corresponding alcohols, since alcohols make stronger H bonds. Except formaldehyde; the first aldehyde, all other aldehydes and ketones are liquids at room temperature. The bond length between C=O is shorter and stronger than C-O. The bond angle as shown above is 120 degrees. At room temperature, ketones and aldehydes undergo tautomerism. The common formular for aldehyde is C_nH_{2n}+1CHO. The common formula for ketone is $C_nH_{2n}O$.

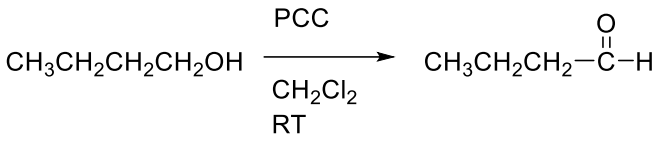
11.5 Preparation of Aldehydes and Ketones

11.5.1 Preparation of Aldehydes

Some of the preparation methods match previously studied reactions of other compounds.

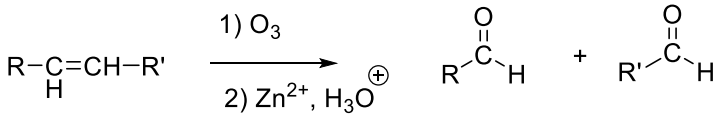
1. From alcohols:

Oxidation of primary alcohols using pyridinium chlorochromate (PCC) in the presence of dichloromethane at room temperature.

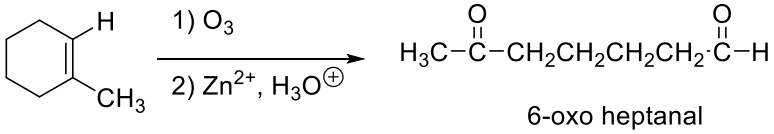


2. From alkenes:

An alkene with at least one proton (vinylic proton) in the presence of O_3, Zn ions, and acid undergoes oxidative cleavage to produce aldehydes.

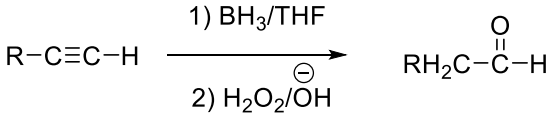


When the above reaction is carried out using a cyclic alkene, dicarbonyl compounds will be formed.



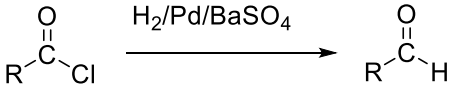
3. From alkynes:

In this reaction, terminal alkynes undergo hydroboration-oxidation to provide aldehydes.



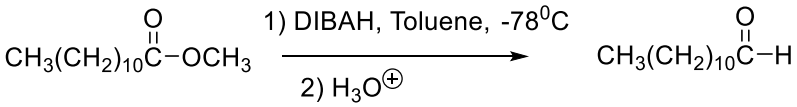
4. From acid chlorides:

Rosenmund Reduction: An acid chloride can be partially reduced by catalytically hydrogenating to produce an aldehyde. This is a cheap method used in a laboratory.

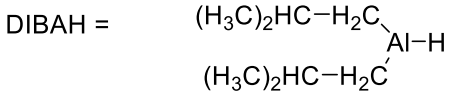


5. From esters:

An ester is partially reduced using diisobutylaluminum hydride (DIBAH) at -78^{0}C (dry ice) in a toluene solution. This is an expensive method.



The structure of DIBAH:

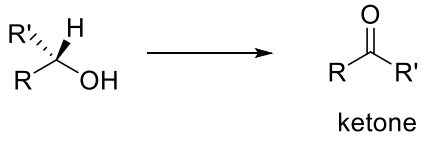


11.5.2 Preparation of Ketones

1. From alcohols

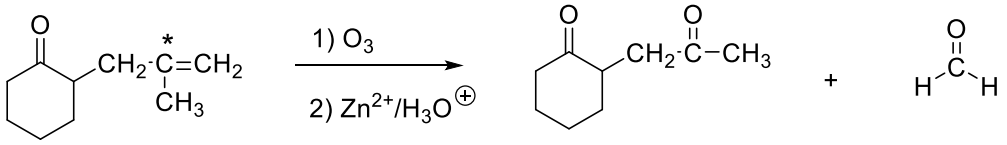
The oxidation of secondary alcohols produces ketones in the presence of any of the following oxidizing agents:

a) CrO_3/aqueous H_2SO_4
b) $Na_2Cr_2O_7$/aqueous CH_3COOH
c) Pyridinium chloro chromate



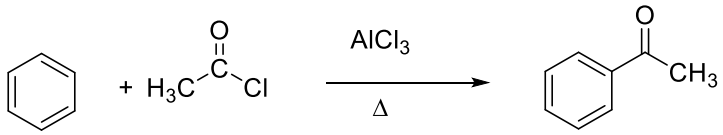
2. From alkenes:

Ozonolysis of alkenes with a disubstituted unsaturated carbon atoms produces ketones.

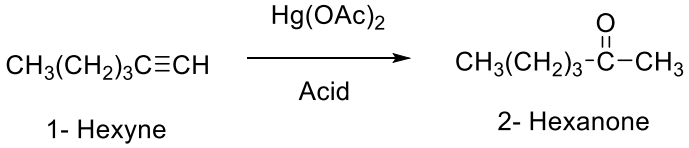


* = disubstituted unsaturated carbon atom

3) From acyl chlorides and benzene (Friedel-Crafts reaction):

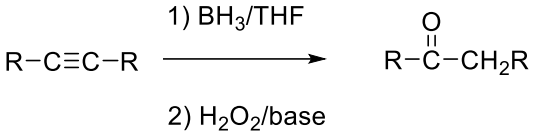


4) From terminal alkynes:



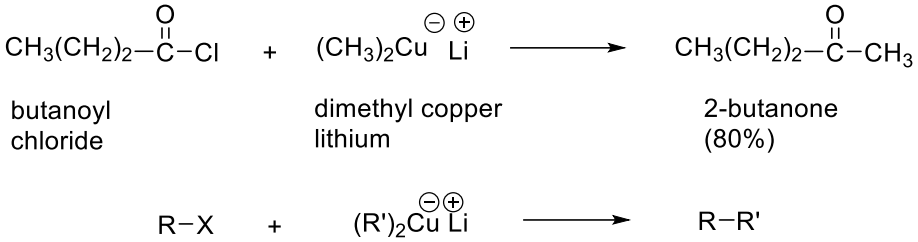
Hg acts as a catalyst.

5) From internal alkynes:



This is a hydroboration-oxidation reaction.

6) From acid chloride:



11.6 Reactions of Aldehydes

Aldehydes and ketones undergo three types of reactions:

1. Nucleophilic addition
2. α – substitution
3. Carbonyl condensation

11.6.1 Nucleophilic addition

In a nucleophilic addition reaction, the electron pair of the nucleophile attacks the C of C=O. As a result, a pair of electrons from the double bond has to move toward the electronegative O. This leads to an alkoxide ion leading to a tetrahedral geometry.

Aldehydes undergo nucleophilic addition reactions easily than ketones due to steric hindrance and electronic stabilizing. Since ketones have two bulky groups (R groups) surrounding the C=O bond, nucleophile finds it difficult to attack. Another steric hindrance factor of ketones to be less reactive than aldehydes is the tetrahedral intermediate being crowded.

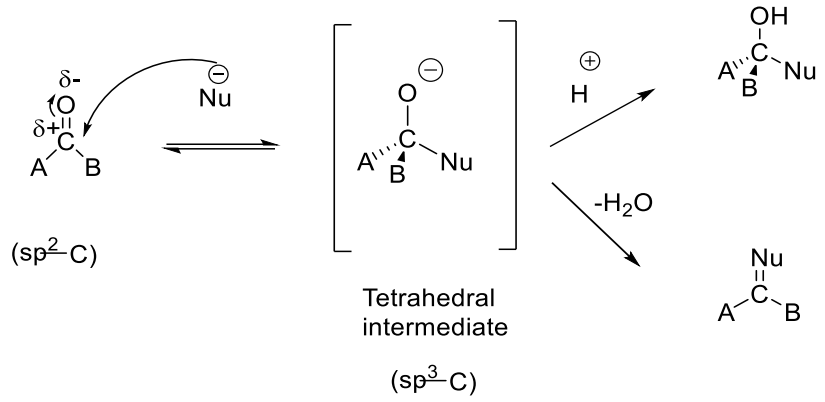


Figure 11.6.1.1: Tetrahedral intermediate of ketones leading to two possible paths. In the presence of two R groups, ketone intermediate appears crowded.

As shown below, when there are two R groups, they will inductively stabilize the partial positive charge on C=O group as opposed to one R group in aldehydes.

As a result, a ketone will be less reactive than aldehyde.

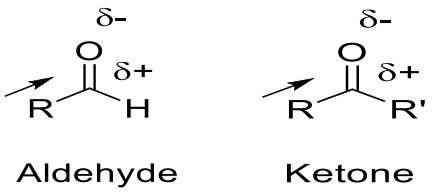


Figure 11.6.1.2: Inductive effect of R on the positive charge on C of C=O

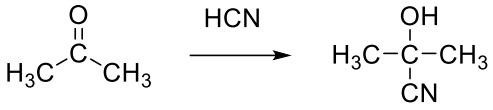
Types of Addition Reactions

1. Addition of HCN

Both aldehydes and unhindered ketones will undergo an addition reaction with HCN. This reaction is slow in the presence of pure HCN, since this is a weak acid. Nevertheless, this reaction is rapid with -CN.

Ethanal

2-hydroxypropanenitrile

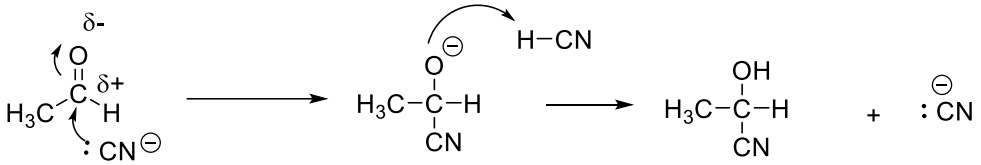


Propanone

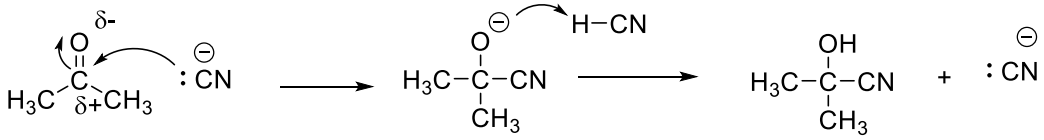
2-hydroxy-2-methylpropanenitrile

Generally, this reaction is performed using a carbonyl compound and sodium or potassium cyanide in water with the addition of some sulfuric acid. At pH of 4-5, the reaction happens fast.

Mechanism for an aldehyde:

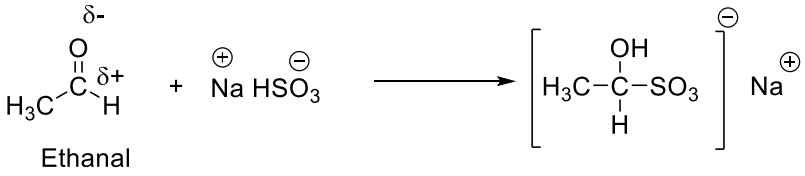


Mechanism for a ketone:

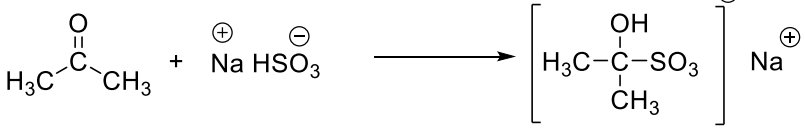


2. Addition of sodium hydrogen sulfite

This reaction happens easily with aldehydes. But with ketones, the reaction works well only if the attached R groups are methyl.



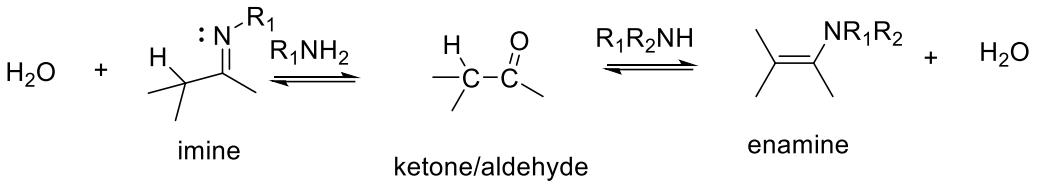
Ethanal



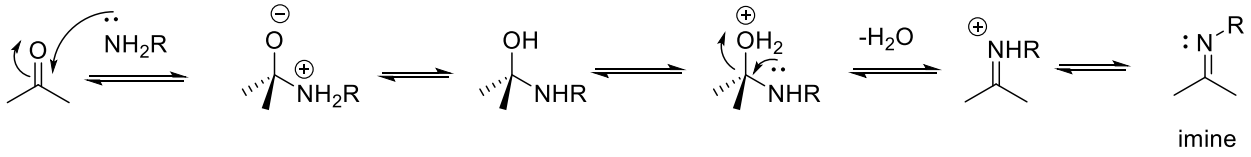
3. Addition of amines

Amines could be primary or secondary with alkyl or aryl groups attached to the structure.

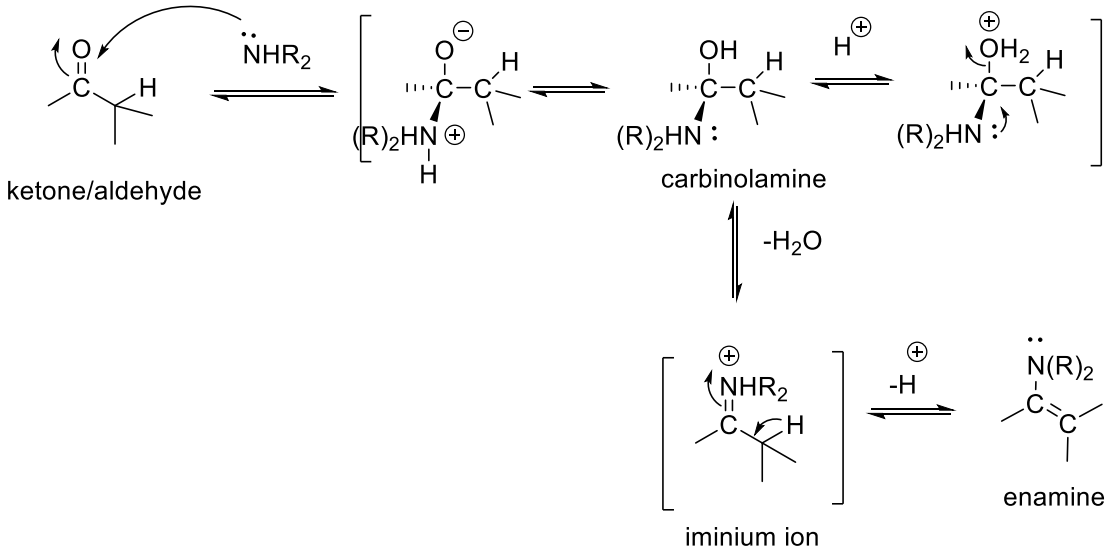
In this reaction, primary amines react with aldehydes and ketones to produce imines, while secondary amines yield enamines.



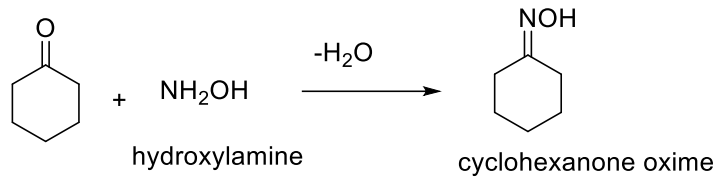
Mechanism for imine formation:

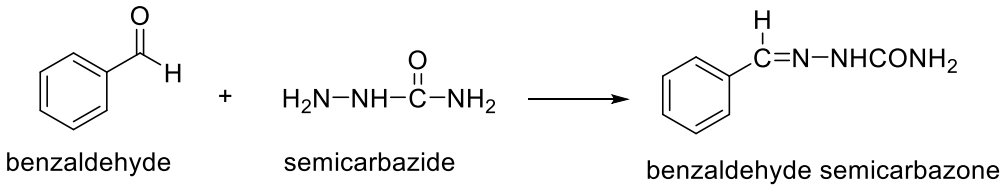


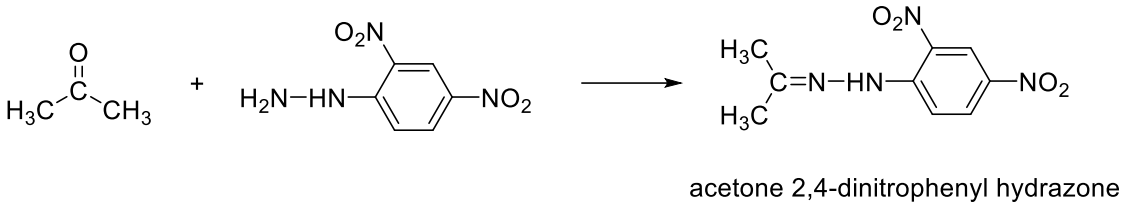
Mechanism for enamine formation:



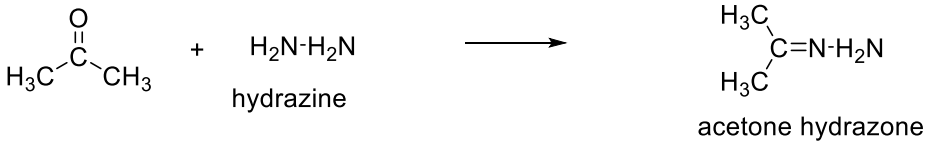
Other similar reactions:

- 

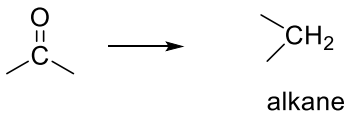
- 

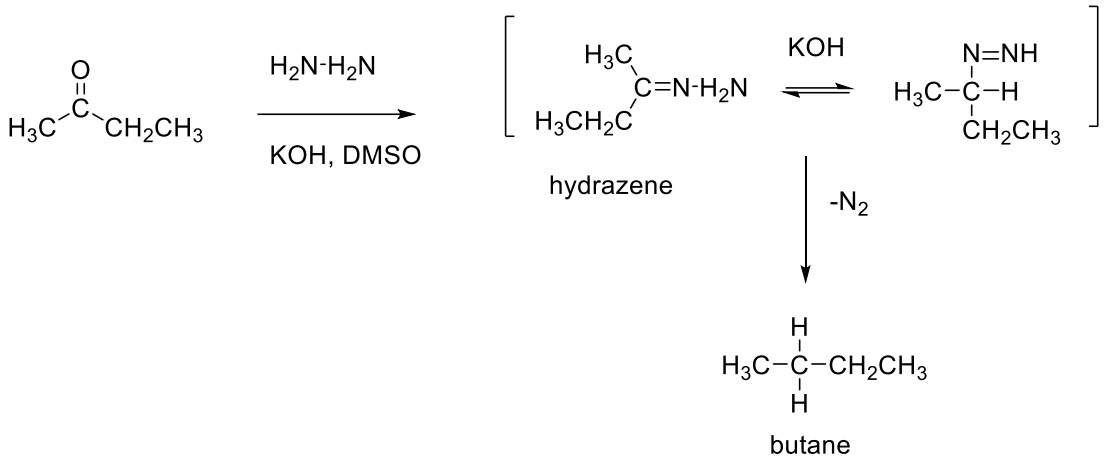
- 

2,4 dinitrophenylhydrazine

- 

4) Wolff-Kishner reaction

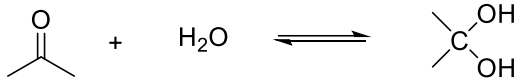




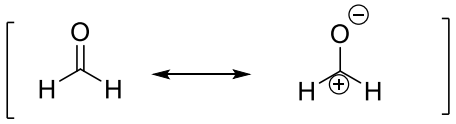
The above reaction is carried out by dissolving the reagents in DMSO and heated at 35^0C or refluxed at 240^0C in diethylene glycol. This reaction can be used to produce alkanes from carbonyl derivatives.

5) Reaction with water

Aldehydes and ketones react with water to produce gem-diols.

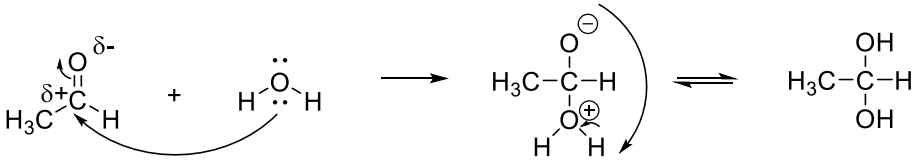


In order to understand the reactivity with water, it is important to understand the resonance dipole structure of the carbonyl compound.



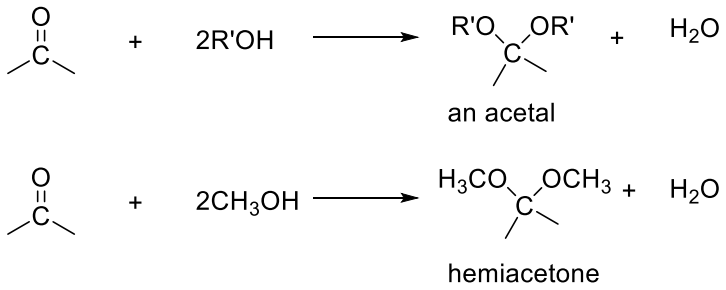
Acetone has the most stable carbocation. Therefore, acetone would be the least reactive compound with water.

Mechanism:

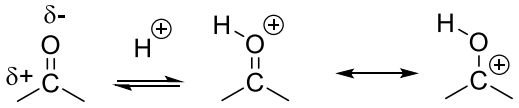


6. Reaction with alcohols and thiols

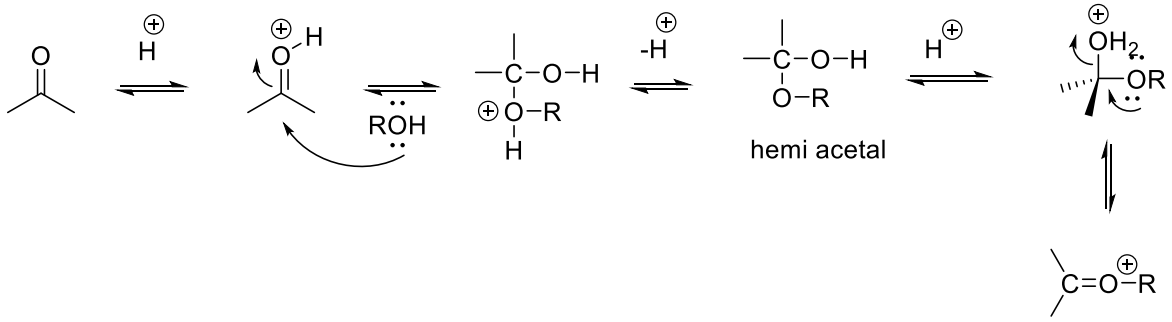
Aldehydes and ketones react with alcohol in the presence of an acid catalyst to produce acetals.

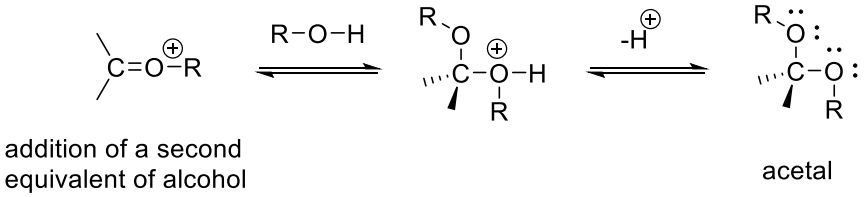


This addition reaction is initiated by an acid catalyst. The acid will protonate C=O, which is more active than the neutral C=O. Therefore, alcohol being a weak nucleophile undergoes the reaction efficiently when the reaction is catalyzed with an acid.



Mechanism

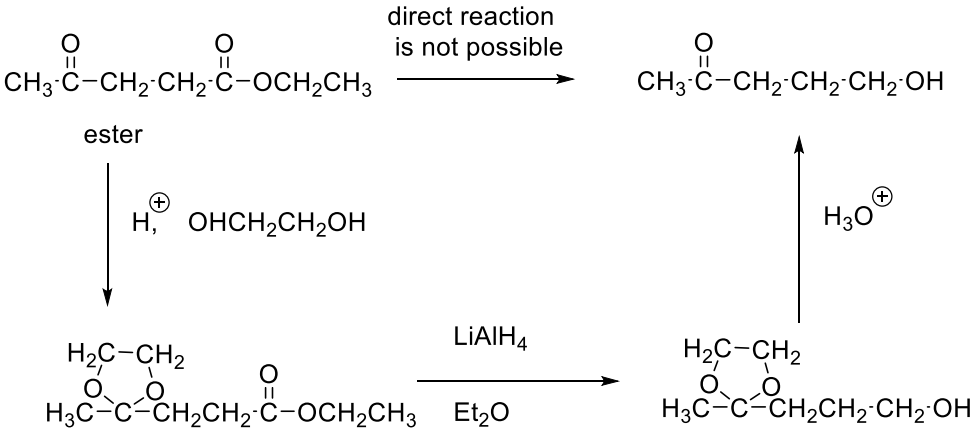




The above reaction is a reversible reaction. When water is removed from the reaction, the forward reaction becomes favorable. If aqueous mineral is added, then the reaction can be reversed.

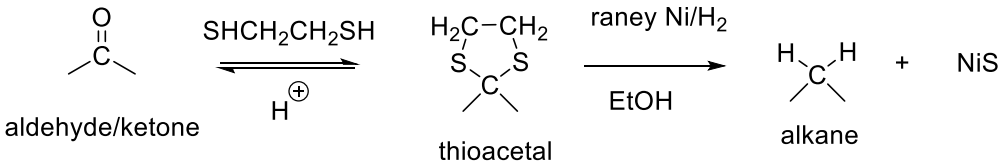
Acetals are used as protecting groups for carbonyl groups. When a reaction has to be carried out by first blocking a carbonyl group (to prevent that group from reacting), an acetal can be formed (carbonyl is prevented from reacting since an OR group is now connected) first, and then carry out the desired reaction.

After the desired reaction is over, the acetal formed can be reversed and the carbonyl group can be recovered.



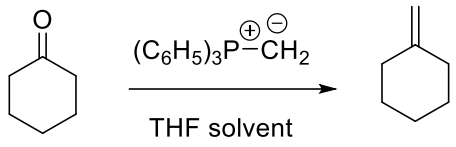
Similar to alcohols, thiols also follow a similar reaction.

Dithio acetal or ketal reduction:



The above reaction is an ideal method to prepare alkanes from a carbonyl compounds.

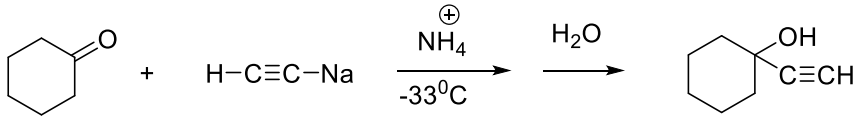
7. Reaction with phosphorus ylides – Wittig reaction:



8. Reaction with acetylide anions

Acetylide ions react with aldehydes and ketones to produce alkynylcarbinols. This reaction is carried out as follows:

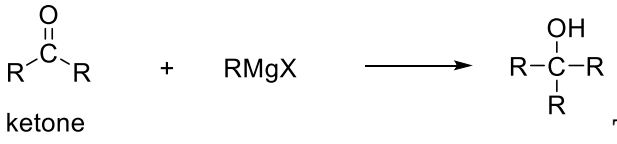
- Sodium amide in liquid ammonia is reacted with a terminal alkyne to obtain the sodium salt of the terminal alkyne.
- The product is then treated with a carbonyl compound.



1-ethynyl cyclohexanal

9. Reaction with the Grignard reagent

Grignard reagent (or organolithium reagents) react with formaldehyde to give a primary alcohol. Other aldehydes will react to produce secondary alcohols and ketones will produce tertiary alcohols.



ketone

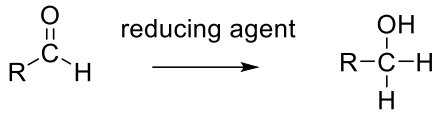
Tertiary alcohol

10. Reaction with a hydride

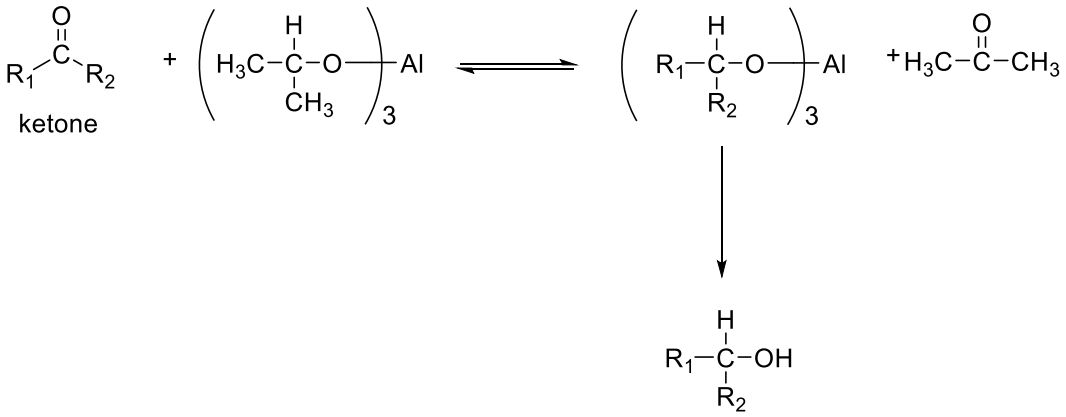
This leads to a reduction reaction. The common reducing agents are aluminum hydride and sodium borohydride.

Aldehyde will reduce to a primary alcohol.

Ketone will produce a secondary alcohol.



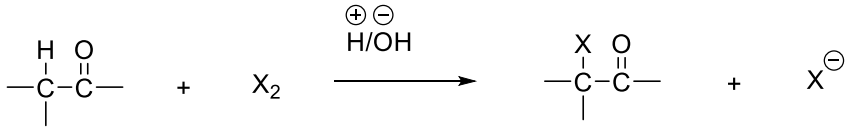
Another way to reduce aldehydes and ketones is by reacting a mixture of carbonyl compounds and aluminum isopropoxide in an isopropanol solvent.



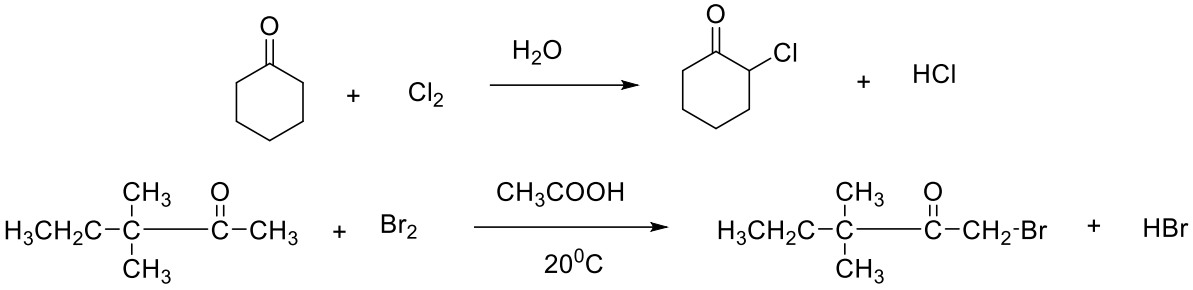
11.6.2 Alpha Substitution

Alpha substitution is another class of reactions that happens in compounds with C=O group. Alpha carbon is the carbon next to C=O group. The H atoms attached to this alpha carbon are known as alpha hydrogen atoms.

1. Acid or base catalyzed halogenation

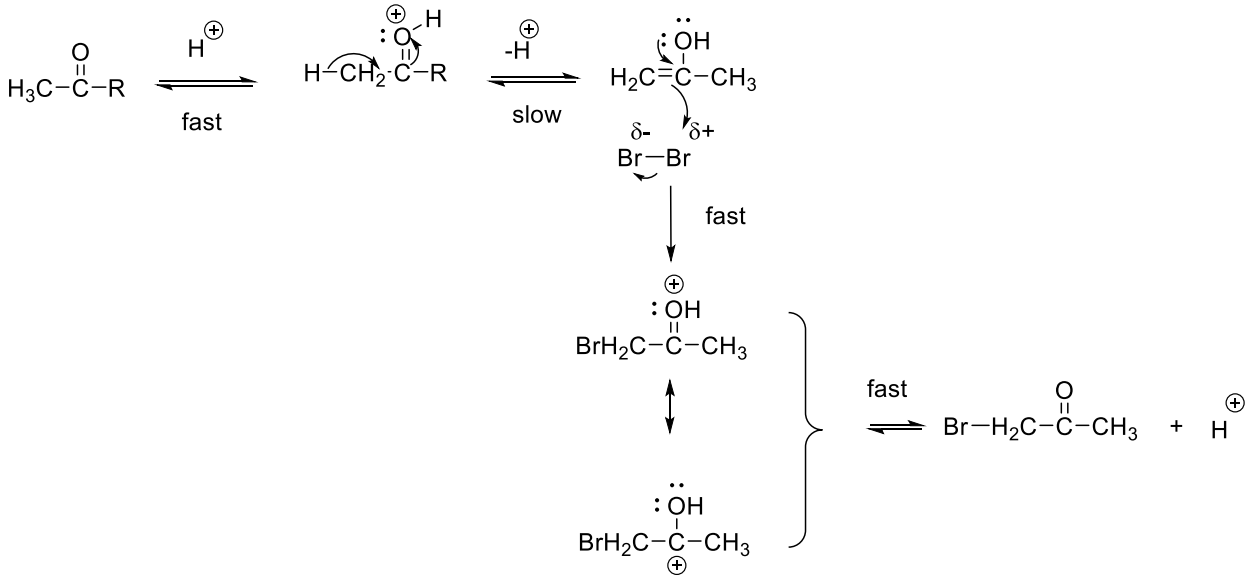


X_2 could be chlorine, bromine, or iodine.



At times the reaction is carried out without adding acid catalyst. During such instances, autocatalysis (catalyzed by one of the products) happens after a period of induction (the time where no reaction happens).

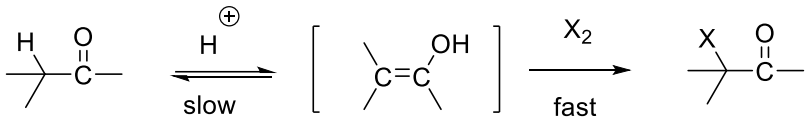
Mechanism



It is important to note the following:

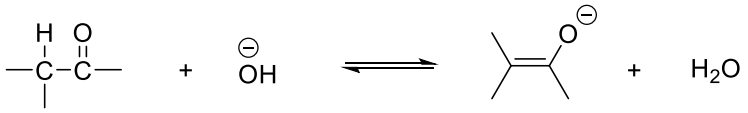
- Rate of halogenation reaction is independent of the halogen
- Chlorination, bromination, iodination for any ketone happens at the same rate
- This is a second order reaction. The rate includes the concentrations of ketone and acid only.
- Halogen is not a part of the rate limiting step.
- Enolate ion is considered the intermediate in base catalysis, while enol is the intermediate in an acid catalysis.

Acid catalysis

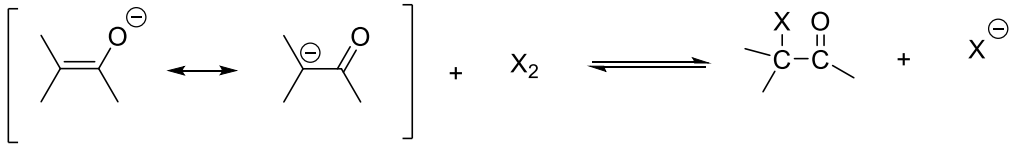


enol

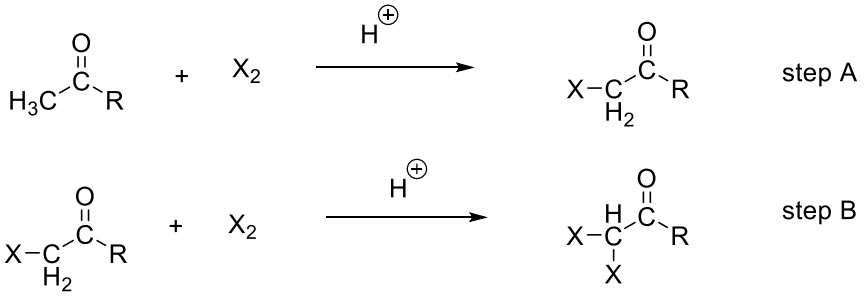
Base catalysis



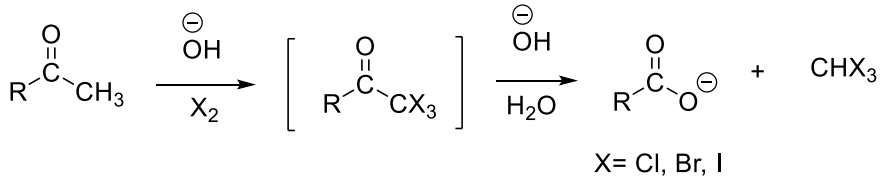
enolate anion



- When an acid catalyst is used instead of a base catalyst, the reaction proceeds to replace alpha hydrogens by halogens one by one, but each step is slower than the previous step. In a base catalyst, the subsequent reactions increase as the replacement continues.

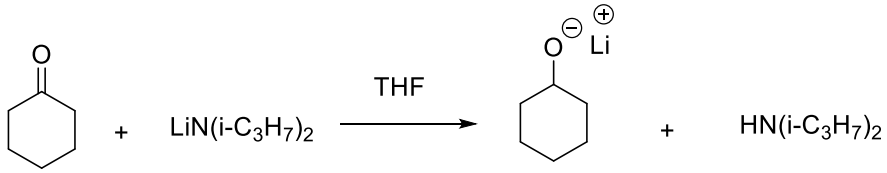


- The above reaction can be controlled by adding controlled amounts of X_2 to obtain mono/di/tri halogen bonded products.
- Methyl ketones undergo base catalyzed halogenation to provide a trihaloketone. This will react further with OH to give carboxylic salt and the corresponding trihalomethane (e.g. iodoform, chloroform, bromoform).

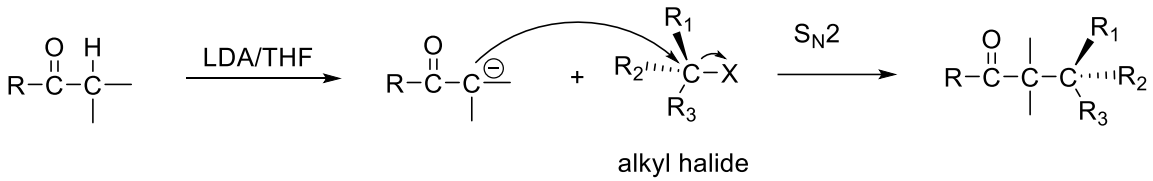


This is a good test for methyl ketones.
Methyl ketone dissolved in THF is reacted with aqueous NaOH and iodine, which forms a yellow precipitate known as iodoform.

Alpha H atoms are weakly acidic. If the compound is treated with a strong base such as NaH or $NaNH_2$ or lithium diisopropylamide, the carbonyl compound will be converted to its enolate compound.



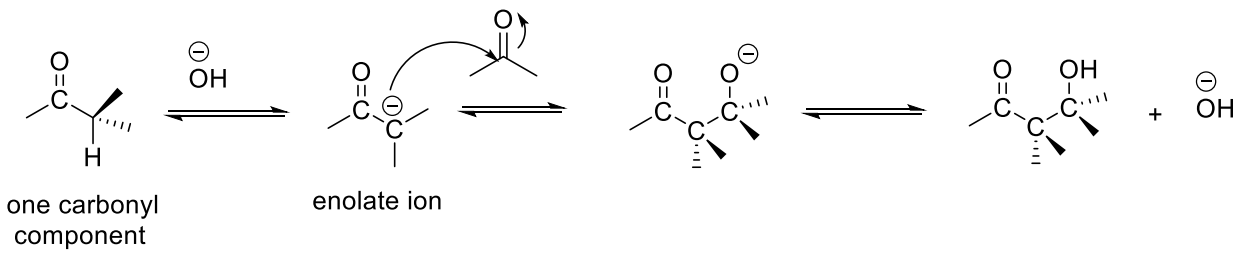
2. Alkylation of enolates



Alkylation of unsymmetrically substituted ketones will produce a mixture of products. This is due to the type of enolate that is produced during the reaction. Nevertheless, alkylation happens at the less hindered position due to easy accessibility.

11.6.3 Carbonyl condensation reactions

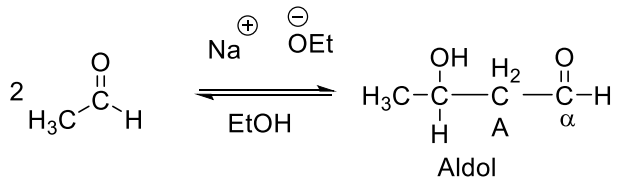
This class of reactions happens between two carbonyl compounds that include nucleophilic addition and alpha substitution. Out of the two carbonyl compounds, one will act as a nucleophilic electron donor and the other acts as an electrophilic electron acceptor.



In the above mechanism, the first carbonyl compound is converted by a base into an enolate anion. Then this enolate ion acts as a nucleophilic donor and adds to the electrophilic carbonyl group of the acceptor component.

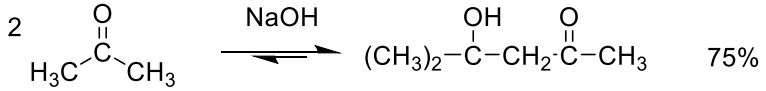
The donor component of a carbonyl condensation reaction undergoes an alpha-substitution process. The acceptor component undergoes a nucleophilic addition process. All types of carbonyl compounds such as aldehydes, ketones, esters, amides, acid anhydrides, thiol esters, and nitrile undergoes carbonyl condensation reactions.

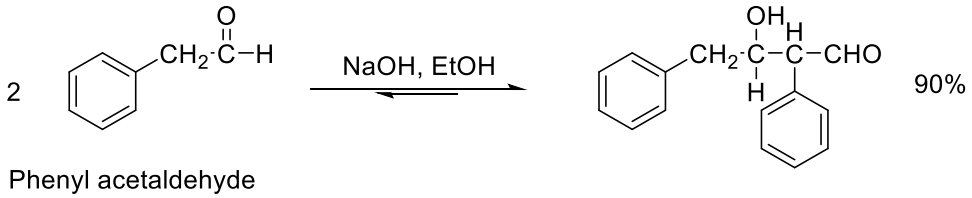
1. Aldol reaction = condensation of aldehydes and ketones.

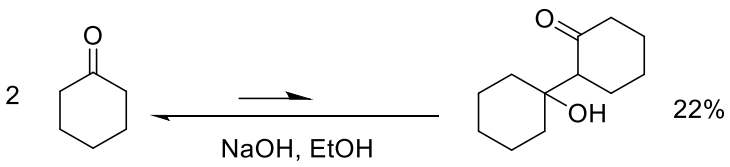


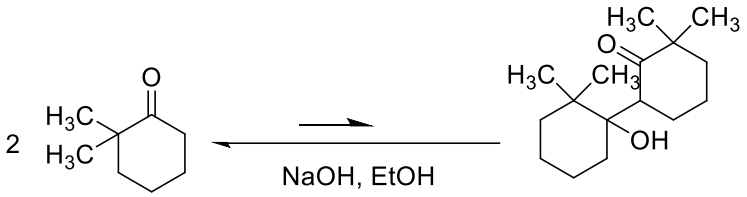
An acetaldehyde in a protic solvent in the presence of a basic catalyst (NaOET or NaOH) will undergo rapid condensation. The resulting product is a β- hydroxy aldehyde known as "aldol." Aldol term comes from aldehyde + alcohol. All aldehydes and ketones with alpha H atoms undergo dimerization. In the absence of alpha H atoms, these compounds do not undergo dimerization.

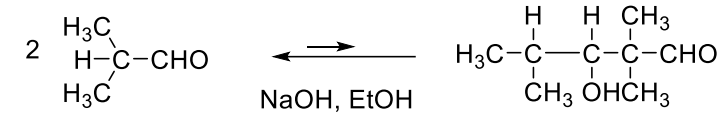
Aldol reactions being reversible reactions, favor the forward reaction providing condensed products in the case of monosubstituted acetaldehydes (RCH_2CHO). In the case of disubstituted aldols (R_2CHCHO) and most of the ketones, the reverse reaction is favored. This is due to the steric hindrance.



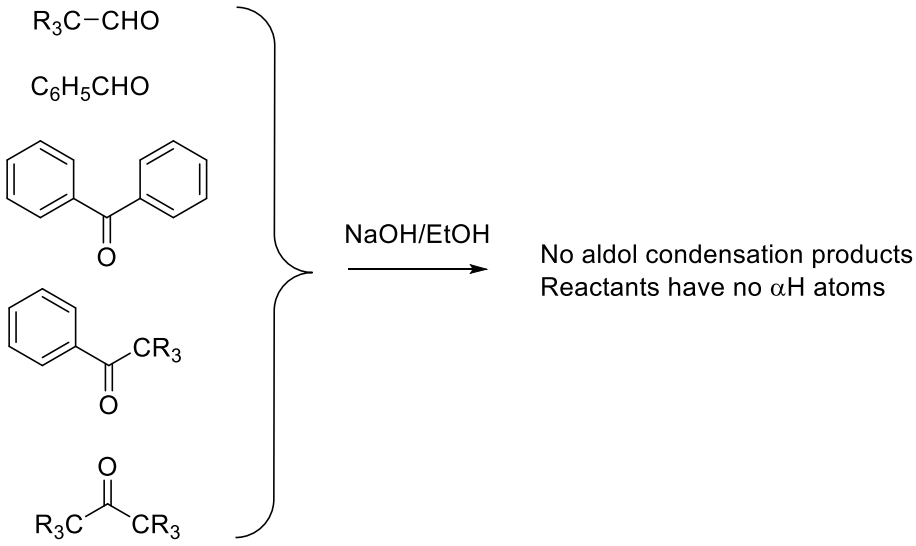






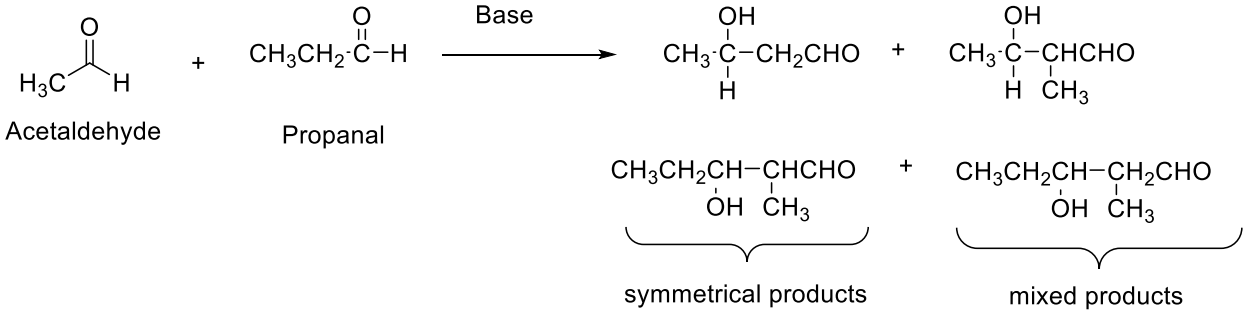


2-methyl propanal



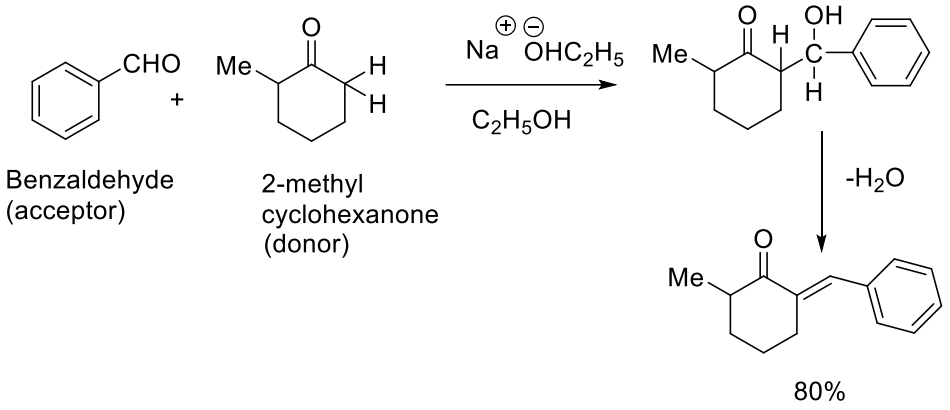
2. Mixed Aldol Reactions

When two different carbonyl compounds react, they will produce a mixed aldol reaction.



Mixed aldol reactions could produce a single product under the following two conditions:

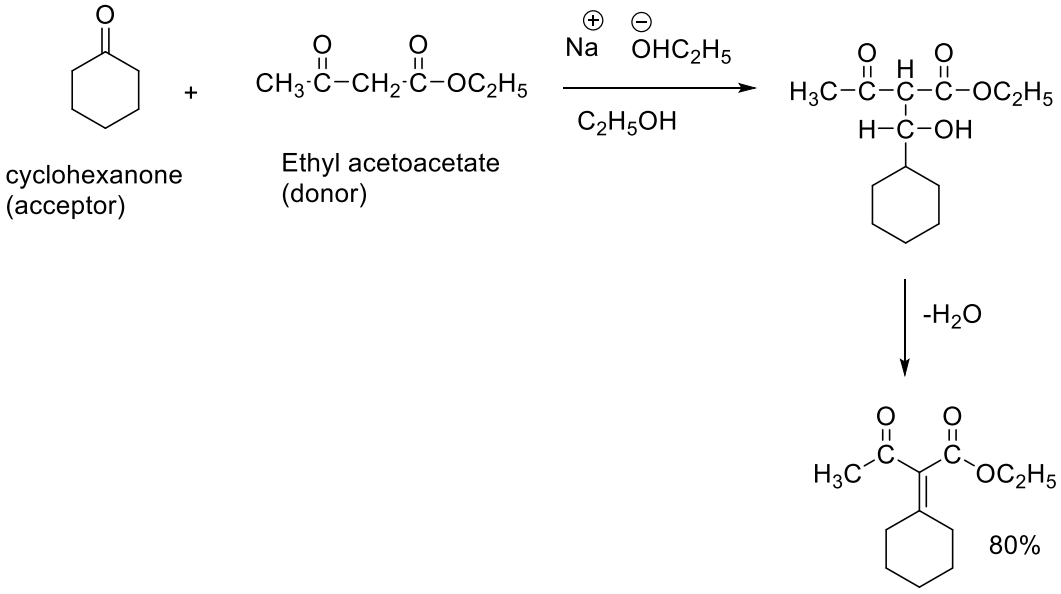
A. When the carbonyl group containing compound does not have alpha H atoms. e.g. benzaldehyde or formaldehyde. In this instance, the carbonyl group reacts as an acceptor producing a single product. The other compound joining will act as the donor.
e.g.



Benzaldehyde (acceptor)

2-methyl cyclohexanone (donor)

B. When one of the carbonyl compounds is unusually acidic and easily transformed into its enolate ion. e.g. ethyl acetoacetate converts to enolate ion in preference to the other carbonyl compound (e.g. cyclohexanone).

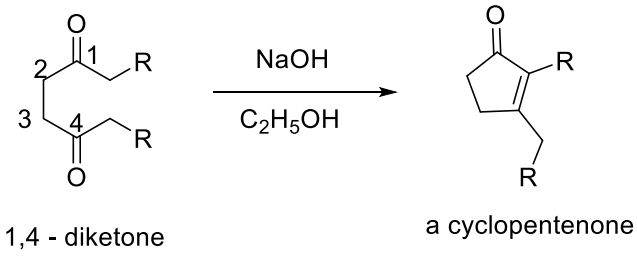


cyclohexanone (acceptor)

Ethyl acetoacetate (donor)

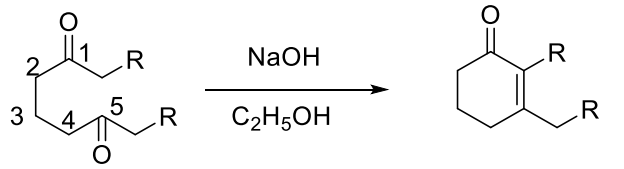
3. Internal Aldol Reaction

Using internal aldol reaction, 5- and 6- membered ring cyclic enones can be prepared by intramolecular aldol reactions of 1,4 or 1,5 diketones.



1,4 - diketone

a cyclopentenone

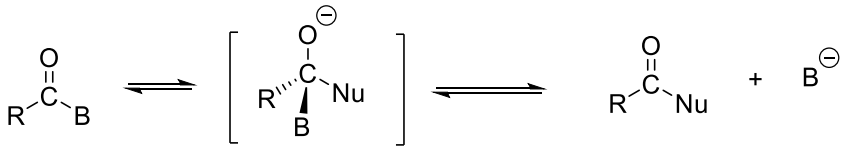


1,5 - diketone

a cyclohexenone

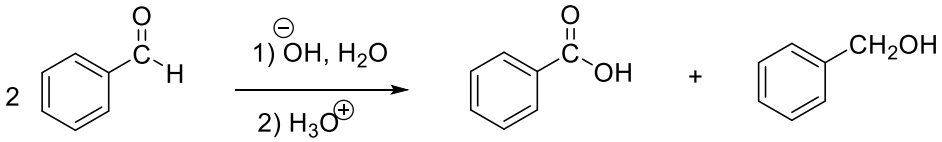
11.6.4 Nucleophilic Acyl Substitution

Carbonyl derivatives undergo these reactions, but not with aldehydes or ketones.



Not an aldehyde or ketone

When an aldehyde without alpha H atoms is reacted with OH^- and the mixture is heated, a disproportionation reaction happens. This will produce one equivalent of carboxylic acid and one equivalent of alcohol.



benzoic acid

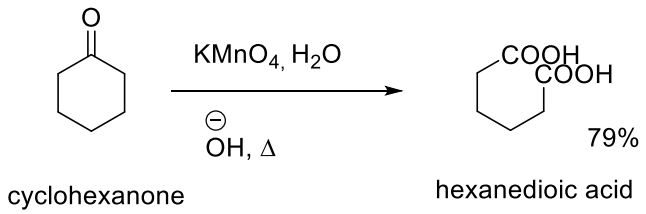
benzyl alcohol

11.6.5 Other Reactions

1. Oxidation

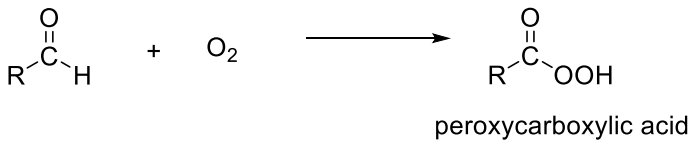
Aldehydes readily oxidizes to produce carboxylic acid. Ketones react only under vigorous conditions. The reason for this difference is the structure of aldehydes having – CHO proton. Common oxidizing agents used are,

- Hot HNO_3
- H_2O_2
- CH_3COOH
- $KMnO_4$
- Jones Reagent – CrO_3 in aqueous H_2SO_4
- Tollen's reagent – dilute ammonia solution of Ag_2O
- Hot alkaline $KMnO_4$ – Ketone's oxidation happens.
  e.g.

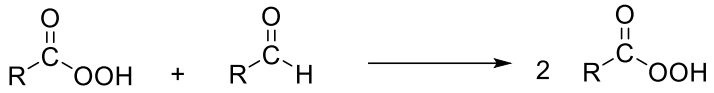


When the oxidation happens in air (auto oxidation), the following products are given out:

Step 1

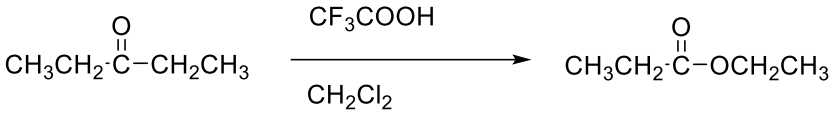


Step 2



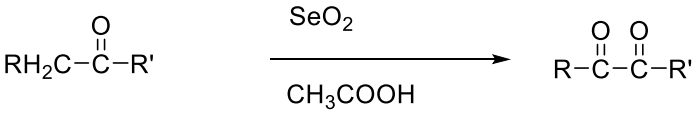
2.Beyer-Villiger Oxidation

In this reaction, ketone undergoes oxidation to produce an ester.



3.SeO_2 Oxidation

Aldehydes and ketones with a CH_3 or CH_2 group adjacent to C=O will undergo oxidation to produce alpha dicarbonyl compounds in the presence of SeO_2.

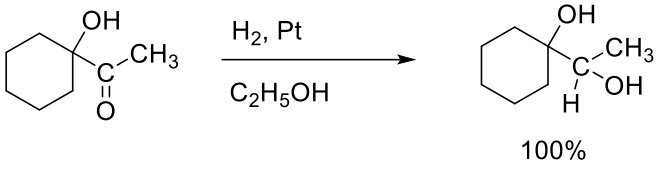


H_2SeO_3 (selenous acid) reagent is used in this reaction for SeO_2 component.

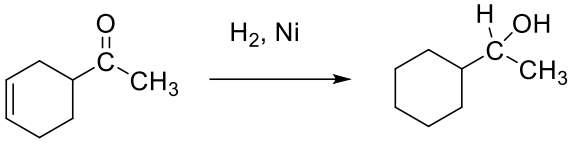
4. Reductions

Reduction happens under the following conditions:

A. Metal hydrides – nucleophilic addition reaction
B. Catalytic hydrogenation – some of the metal catalysts used are Pd, Pt, Ru, Rh, Ni, etc.



100%

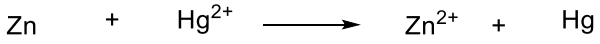


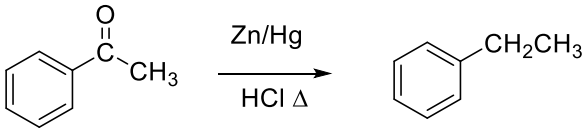
95%

C) Clemmensen Reduction

In this reduction, the carbonyl group of aldehyde or ketone will reduce to methylene group when the carbonyl group is refluxed with amalgamated zinc and HCl. This is suitable for compounds that can withstand hot acids – mainly for ketone reductions.

Amalgamation of Zn (Zn surface covered in Hg):





acetophenone

80%
ethyl benzene

D) Wolff-Kishner reduction – Discussed previously.

E) Dithio Ketals reduction – Discussed previously.

11.6 Tests of Aldehydes and Ketones

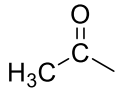
Test 1 – Brady's reagent

A yellow or orange crystalline precipitate with 2,4 – dinitrophenyl hydrazine (Brady's reagent) confirms the presence of a carbonyl group.

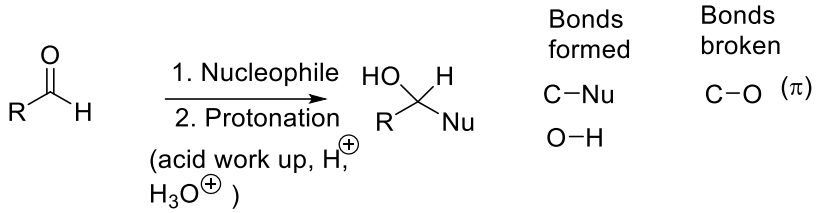
Test 2 – Ketones and Aldehydes differentiation

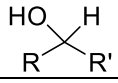
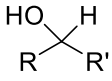
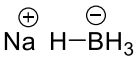
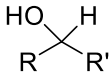
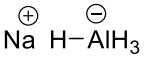
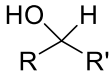
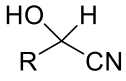
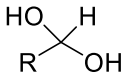
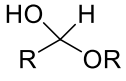
A) Fehling's test – by adding Fehling's A and B solutions and heating, aldehydes will undergo the following color changes:
Blue ⟶ Green ⟶ Brick Red (CuO_2)

B) Ag mirror test – aldehydes and other easily oxidizable compounds on warming with Tollen's reagent ($Ag(NH_3)_2$) gives a silver mirror.

C) Iodoform test – any compound with  group when reacted with CH_3I, a pale yellow crystalline precipitate will be given.

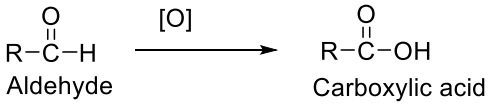
11.7 Summary of Reactions



Reaction	Nucleophile	Product
Grignard Reaction	R'—MgX	
Addition of organolithiums	R'—Li	
Reduction by sodium borohydride ($NaBH_4$)		
Reduction by lithium aluminium ($LiAlH_4$)		
Addition of cyanide ion to form cyanohydrins		
Addition of hydroxide ion to form hydrates		
Addition of alkoxide ion to form hemiacetals		

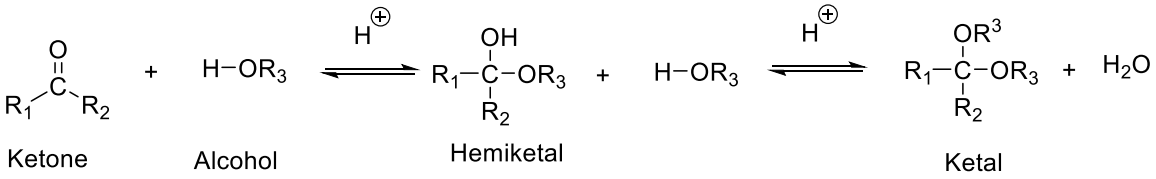
Aldehydes and Ketones

Oxidation of an aldehyde

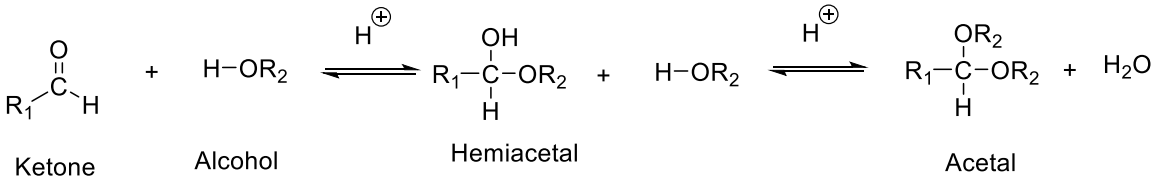


Addition Reactions

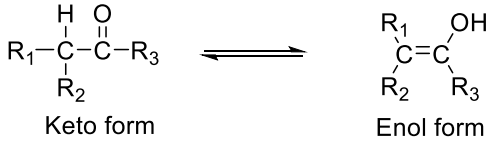
Addition of an alcohol to a ketone - ketal formation



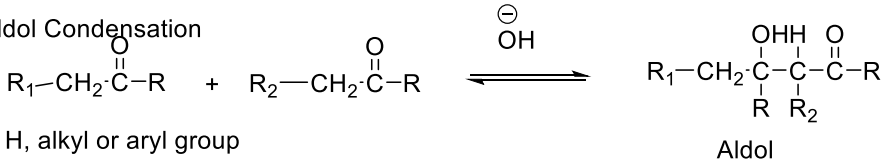
Addition of an alcohol to an aldehyde - acetal formation



Keto-enol Tautomerization

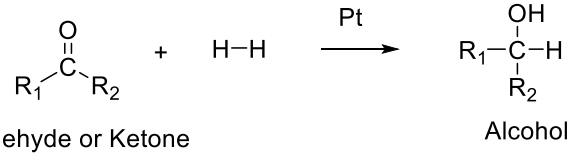


Aldol Condensation



R= H, alkyl or aryl group

Reduction of Aldehydes and Ketones



Chapter 12

12.0 Carboxylic Acids and Esters

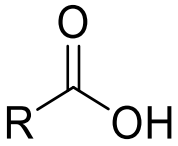
12.1 Objectives

1. Draw and interpret Lewis structures, line-bond structures and functional groups of carboxylic acids and esters using IUPAC system of nomenclature.
2. Draw reaction mechanisms.
3. Describe reactions, predicting reactivity, and reaction products.
4. Devise syntheses including steps, reagents, and products including regiochemistry and stereochemistry.

12.2 Introduction

12.2.1 Carboxylic acids

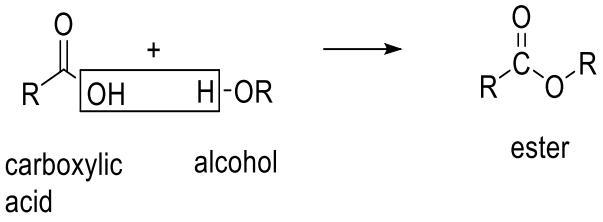
Carboxylic acids are also known as fatty acids since higher molecular weight compounds of acid group occur in natural fats. Simple carboxylic acids are also found in nature. The common functional group of carboxylic acids is -COOH (carboxylic) group. Vinegar is a diluted solution of acetic acid, which in turn a carboxylic acid.



The common formula of carboxylic acids is $C_nH_{2n}O_2$. It is also expressed as C_nH_{2n+1} COOH.

12.2.2 Esters

Esters are made by replacing the -OH bond of a carboxylic acid by and -OR group of an alcohol.



The general formula for esters is $C_nH_{2n}O_2$. This formula is the same as that of a carboxylic acid.

12.3 Nomenclature and Isomerism

Please refer to the chapter on nomenclature and isomerism and answer the following questions:

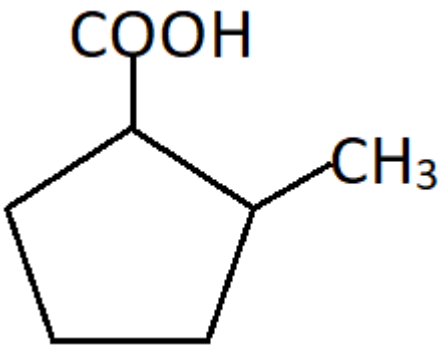
1. Naming Compounds – Give the IUPAC names for the following compounds

a) $CH_3CH=CHCH=CHCOOH$

b) $(C_6H_5)CH_2CH_2COOH$

c) $(CH_3)_3CCH_2COOH$

d)

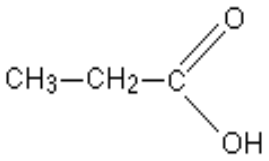


2. Draw the structures of the following compounds

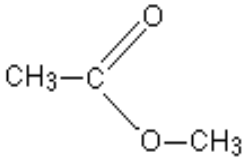
a) α-Methylpropionic acid
b) 4-Oxocyclohexan-1-carboxylic acid

3. **Questions on Isomers**

What type of an isomerism is displayed by the following two compounds?



propanoic acid



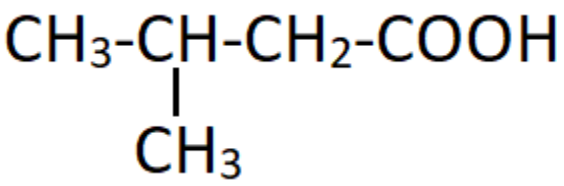
methyl ethanoate

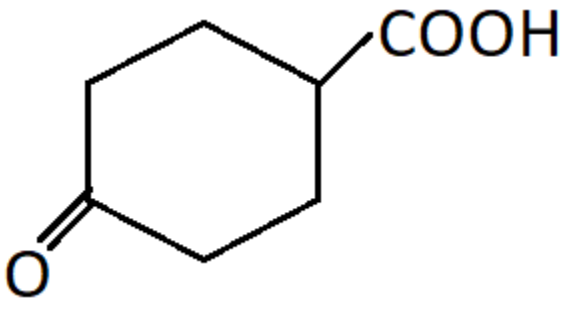
Solutions:

1. Naming Compounds – Give the IUPAC names for the following compounds.

a) Hexa-2,4-dienoic acid
b) 3-Phenylpropanoic acid
c) 3,3-Dimethylbutanoic acid
d) 2-Methylcyclopentanecarboxylic acid

2. Draw the structures of the following compounds

a) 

b) 

3. Questions on isomers

a) Functional isomerism

12.4 Physical Properties

12.4.1 Carboxylic Acids

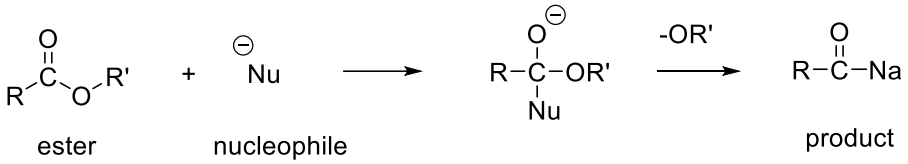
Formic, acetic, and propionic acids (the first three acids in this series) are colorless liquids with pungent smells. Butyric (C4) to nonanoic (C9) acids are oils. All the other acids above decanoic (C10) are odorless solids. The volatility of these compounds (mostly the low-molecular weight members of this class) is lower than the expected levels due to the hydrogen bonding. Lower members can exist as dimers in the vapor phase and in the aqueous state. In the liquid phase, they exist as polymers.

The carbonyl carbon atom is sp^2 hybridized and the C atom is also on the same plane as other atoms. The high electronegativity of oxygen makes that site an electron rich center. In the C=O bond, C is electron deficient in comparison to the oxygen. As a result, C of the carboxylic acids can react with a nucleophile, while O of the C=O can react with an electrophile.

12.4.2 Esters

Esters have a sweet or pleasant smell and are available in liquid or solid forms. The low molecular esters are soluble in water. These are useful as organic solvents. They are used in the manufacture of artificial flavors and perfumes.

Same as carboxylic acids, the carbonyl group of esters also react with a nucleophile (C of the C=O) and an electrophile (O of the C=O). In this regard, the chemistry of esters is similar to aldehydes and ketones. Yet, esters and other derivatives of carboxylic acids undergo cleavage in a reaction. This cleavage happens at the bond between the C of C=O and the group attached to that C.



This type of a cleavage is not observed with aldehydes and ketones. The mechanisms of the reactions undergone by esters is similar to the reactions of other acid derivatives.

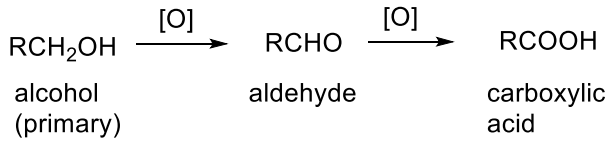
12.5 Preparation

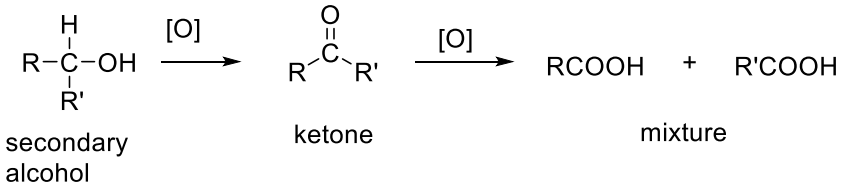
12.5.1 Carboxylic Acids

1. Oxidation of alcohols, aldehydes, and ketones.

Alcohol, aldehydes, and ketones can be oxidized by using the oxidizing agents such as dichromate or permanganate, to produce carboxylic acid.

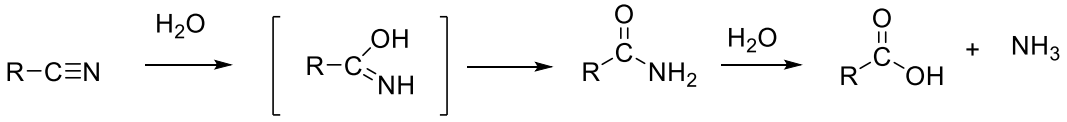
e.g.





2. Hydrolysis of alkyl cyanides (alkylnitriles)

Cyanides are hydrolyzed by using mild acids or bases to produce carboxylic acids.

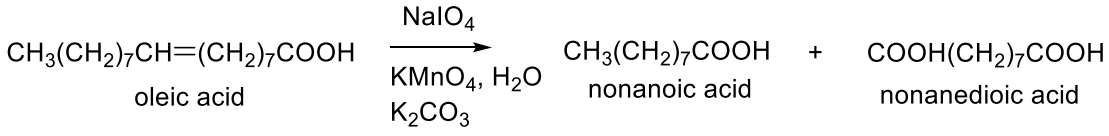


3. Using the Grignard reagent

When Grignard reagent (alkyl magnesium bromide) is allowed to react with dry carbon dioxide (in ether) at low temperatures with aqueous sulfuric acid, bromo magnesium salt is produced. This will readily hydrolyze to produce carboxylic acid.

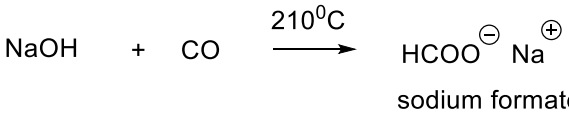
4. Oxidative cleavage of alkenes

Alkenes with at least one vinylic hydrogen undergoes oxidative cleavage to produce carboxylic acids. In this reaction, $KMnO_4$ or $Na_2Cr_2O_7$ or O_3 can be used as oxidizing agents. Another reagent used is in this reaction is a mixture of sodium periodate and a small amount of $KMnO_4$.



5. Preparation of formic acid

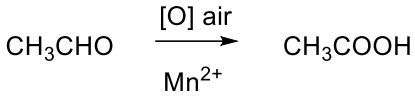
NaOH and carbon monoxide are heated at 210^0C and at a pressure of 6 -10 atm to obtain the salt of formic acid.



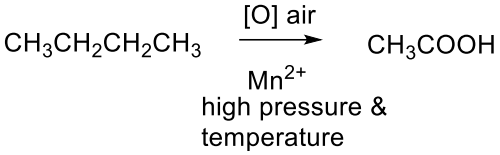
When sodium formate is distilled with dilute sulfuric acid, an aqueous solution of formic acid is produced.

6. Preparation of acetic acid

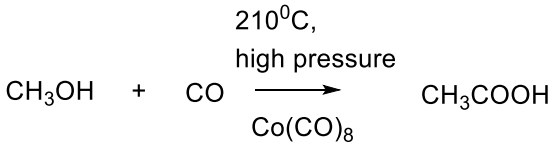
a) Oxidation of acetaldehyde in air in the presence of Mn ion catalyst gives acetic acid.



b) Oxidation of n-butane (liquid) in air under pressure at 130 – 230 ^{0}C in the presence of Mn catalyst gives acetic acid.



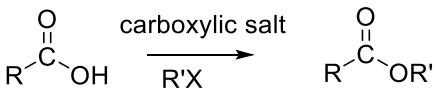
c) Under high pressure and temperature at 210^{0}C and in the presence of cobalt octa carbonyl, methanol can be converted to acetic acid.



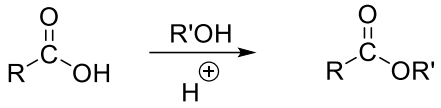
12.5.2 Esters

Esters are produced from carboxylic acids, acid chlorides, or acid anhydrides.

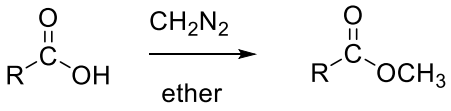
1. The direct conversion carboxylic acids to esters are as follows:
   a) Carboxylate salt undergoing a S_N2 reaction with a primary alkyl halide



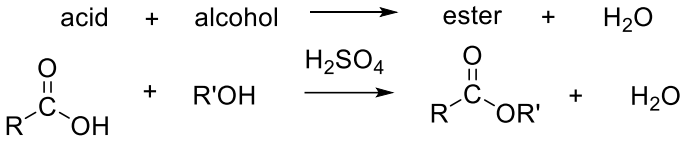
b) Fischer esterification of a carboxylic acid with an alcohol of low molecular weight in the presence of an acid catalyst.



c) Diazomethane reaction with an acid

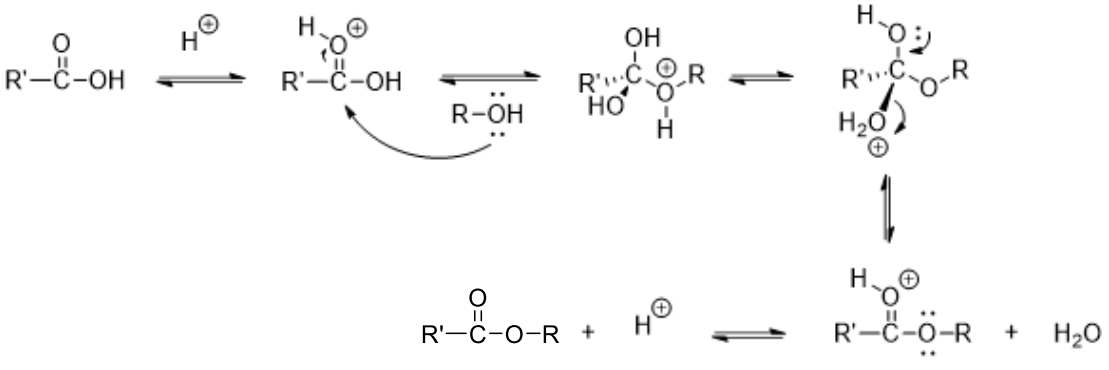


2. Esterification



Esterification happens when a carboxylic acid reacts with an alcohol in the presence of an inorganic acid. This is a reversible reaction. The forward reaction is esterification. The reverse reaction is hydrolysis.

Mechanism:



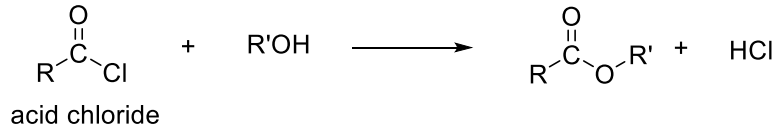
The mechanism can be described using the following steps:

1. Addition of H^+ to C=O and activation
2. Nucleophilic addition of alcohol producing a tetrahedral intermediate
3. Transfer of a proton from one oxygen to another. This generates another tetrahedral intermediate that converts the hydroxyl into a good leaving group
4. Water is lost giving a protonated ester
5. Loss of a proton (H^+) regenerates the used by H^+ from the acid catalyst.

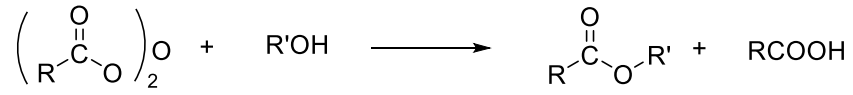
As mentioned earlier, the reactions are reversible. The formation of ester is favored when alcohol is used as a solvent. When water is used as a solvent, the formation of carboxylic acid is favored. The above mechanism where the oxygen of the leaving H_2O group comes from the acid has been confirmed by using radioactive O^{18} in the reaction.

3. From acid chlorides and acid anhydrides

Acid chlorides and acid anhydrides react rapidly with alcohol to form ester.



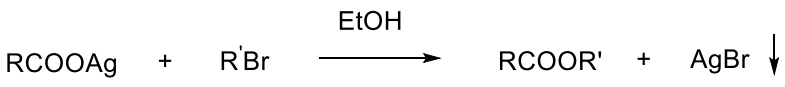
acid chloride



acid anhydride

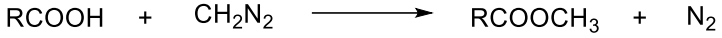
4. Using silver salt

By refluxing silver salt of an acid with an alkyl halide in ethanolic solution, and ester can be produced.



5) Methyl ester specific method

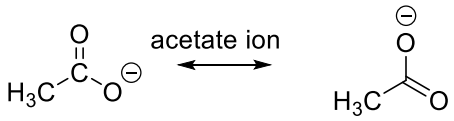
Methyl esters are prepared when carboxylic acid in ether is treated with diazomethane.



12.6 Reactions

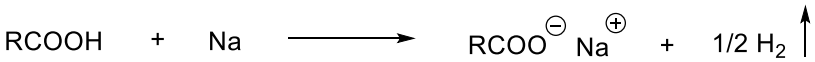
12.6.1 Carboxylic Acids

Carboxylic acids are weak acids than inorganic acids. Therefore, Ka values are smaller and pKa values are larger. The acidity of carboxylic acid is due to the resonance stabilization of carboxylate anion. Due to this resonance stabilization, negative charge on the carboxylic anion is spread equally over to two oxygen atoms (delocalization). The stabilization of the conjugate base increases the acid strength.



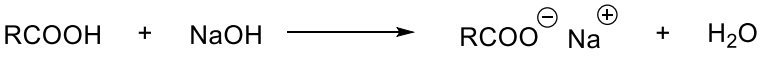
1. With electropositive metals

Electropositive metals such as alkali metals react with carboxylic acids to produce hydrogen and the metal salt.



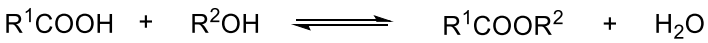
2. With a base

When carboxylic acid reacts with a base, a salt and water is given out. This is a neutralization reaction.



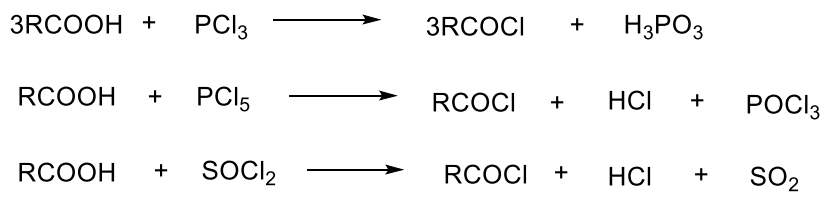
3. With alcohol

Monocarboxylic acids and alcohols produce ester and water in the presence of a dilute mineral acid catalyst.



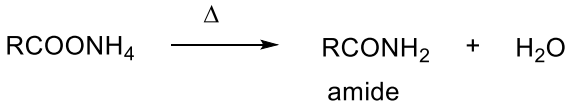
4. Acid Chloride formation

An acid chloride is obtained when carboxylic acid is treated with PCl_3 or PCl_5 or $SOCl_2$ (thionyl chloride).



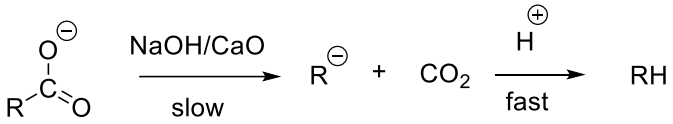
5. Amide formation

When the ammonium salt of carboxylic acid is vigorously heated, an amide is formed.

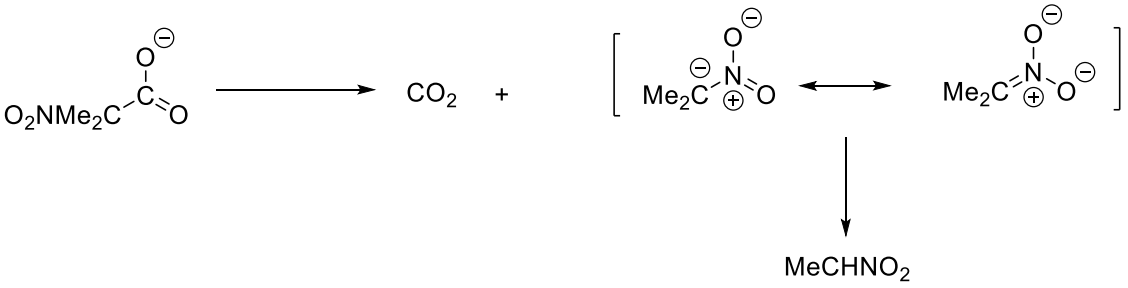


6. Decarboxylation

Decarboxylation happens when anhydrous sodium salt of a monocarboxylic acid is heated with sodium hydroxide. The result is an alkane.

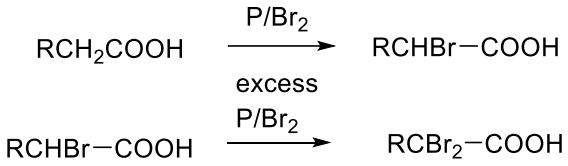


When a CO_2 is lost form a carboxylate anion, it forms a carbanion (R^-) intermediate, which will acquire an H atom. This process is promoted by electron withdrawing substituents attached to R, which will help to stabilize the carbanion intermediate. Therefore, NO_2 substituted carboxylate anion will undergo decarboxylation than the anion without NO_2.



7. Halogenation

A hydrogen attached to the alpha carbon atom of a carboxylic acid can be replaced by a chlorine or a bromine atom when reacted with an acid and a halogen in the presence of a small amount of phosphorous. At high temperature, the reaction proceeds to give an alpha halo acid.

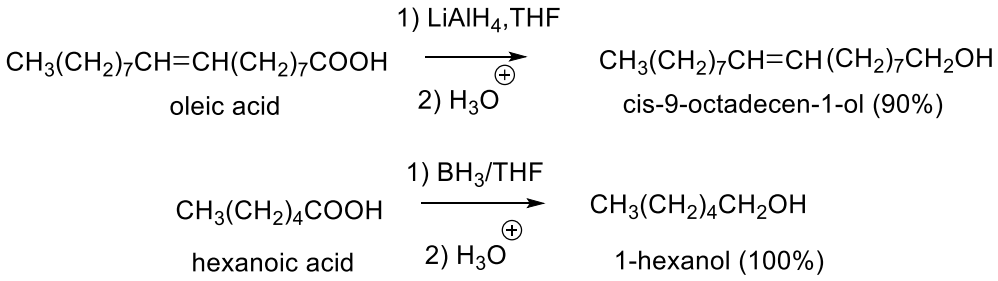


8. Oxidation

Other than formic acid, all the other acids are resistant to oxidation. When strong oxidizing agents are used, the acid will decompose to produce carbon dioxide and water. Formic acid is different from other monocarboxylic acids. It is a strong reducing agent. Formic acid reduces Tollen's reagent to metallic silver. Also, formic acid can convert mercuric chloride to mercurous chloride.

9. Reduction

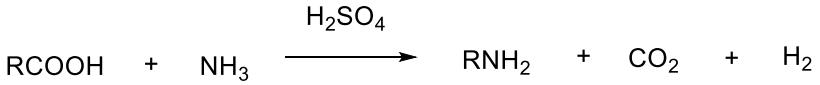
When $LiAlH_4$ (not $NaBH_4$) is reacted with carboxylic acid a primary alcohol can be obtained. This reaction needs to be refluxed in THF to reach completion.



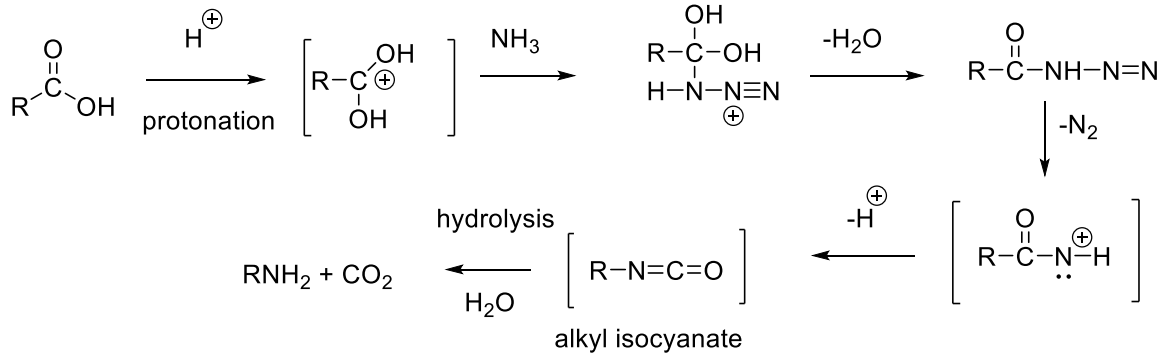
BH_3 can also be used to convert carboxylic acids to primary alcohols.

10. Schmidt reaction

The reaction of hydrazoic acid (HN_3) with carboxylic acid produces a primary amine. This Schmidt reaction is a modification of Curtius reaction.



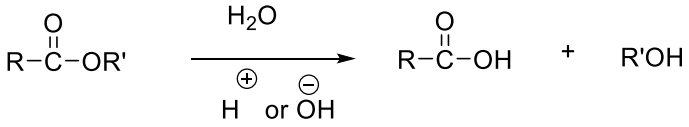
Mechanism



12.6.2 Esters

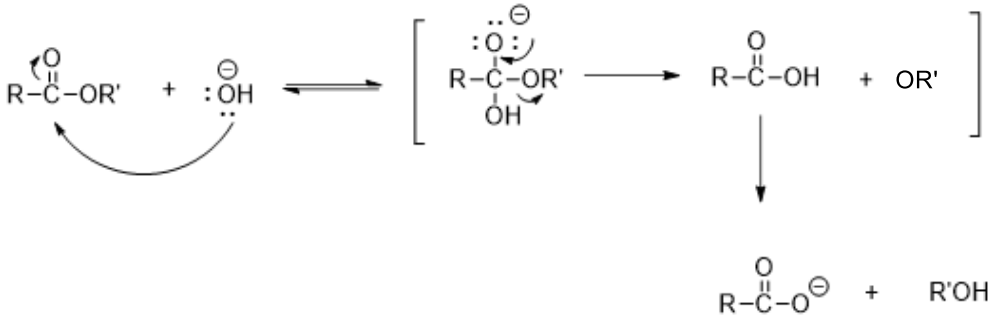
1. Hydrolysis

Hydrolysis of esters are done using an aqueous base or an aqueous acid. The resulting products are alcohol and acid.



- Base hydrolysis

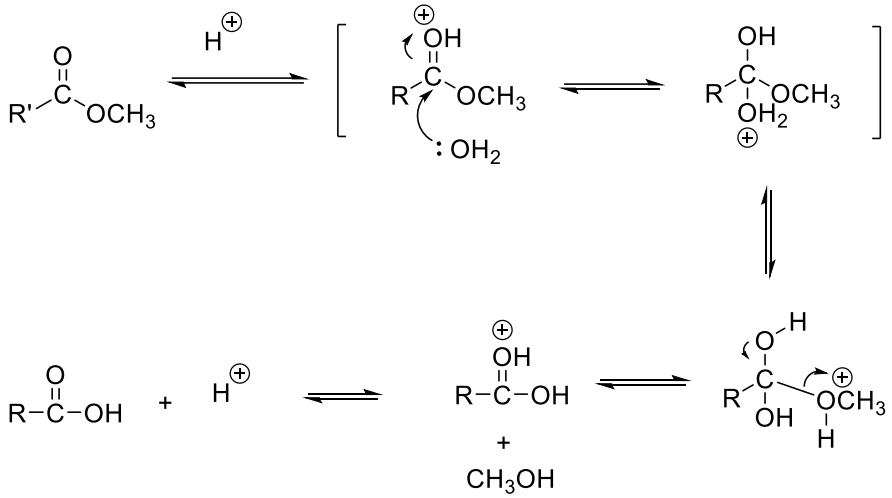
The hydrolysis using a base is known as saponification. The mechanism process for this reaction is a nucleophilic acyl substitution.



Quenching is used to stop the reaction by neutralizing the basic nature of the environment. The addition of an acid converts the carboxylic anion to carboxylic acid.

- Acid hydrolysis

The acid hydrolysis has more than one mechanism. The mechanism is dependent on the structure of the substrate. The most common path is the Fischer esterification.

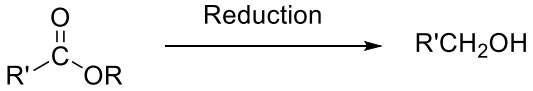


The above acid hydrolysis follows the steps below:

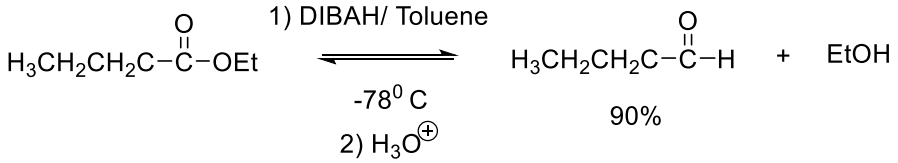
1. Protonation of carbonyl oxygen will lead to a nucleophilic attack on the ester molecule
2. Water will carry out a nucleophilic attack
3. Transfer of a proton
4. Elimination of alcohol will release the acid.

2. Reduction

Bouveault-Blanc reduction: Esters are reduced to alcohols by catalytic hydrogenation and by metallic hydrides (e.g., lithium aluminum hydride in ether, lithium borohydride in THF, diborane in THF).

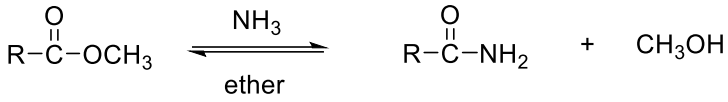


The above reduction process goes through an aldehyde intermediate. This aldehyde can be extracted by using one equivalent of DIBAH (di isobutyl aluminum hydride) in toluene solution. The reaction has to be carried out at -78^0C.



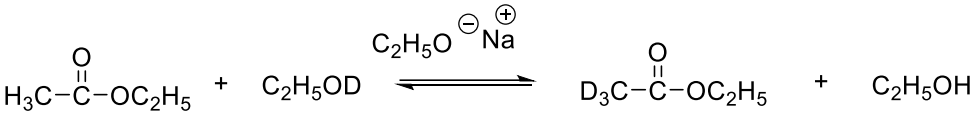
3. Aminolysis

Ammonia reacts with esters to produce amides. The reaction is a nucleophilic acyl substitution. When aminolysis is carried out using acid chlorides, the reaction will provide a high yield of amides.

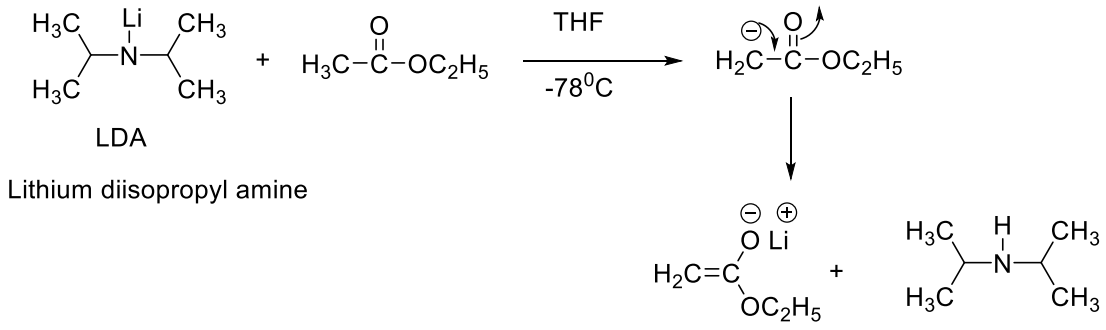


4. Alpha proton acidity

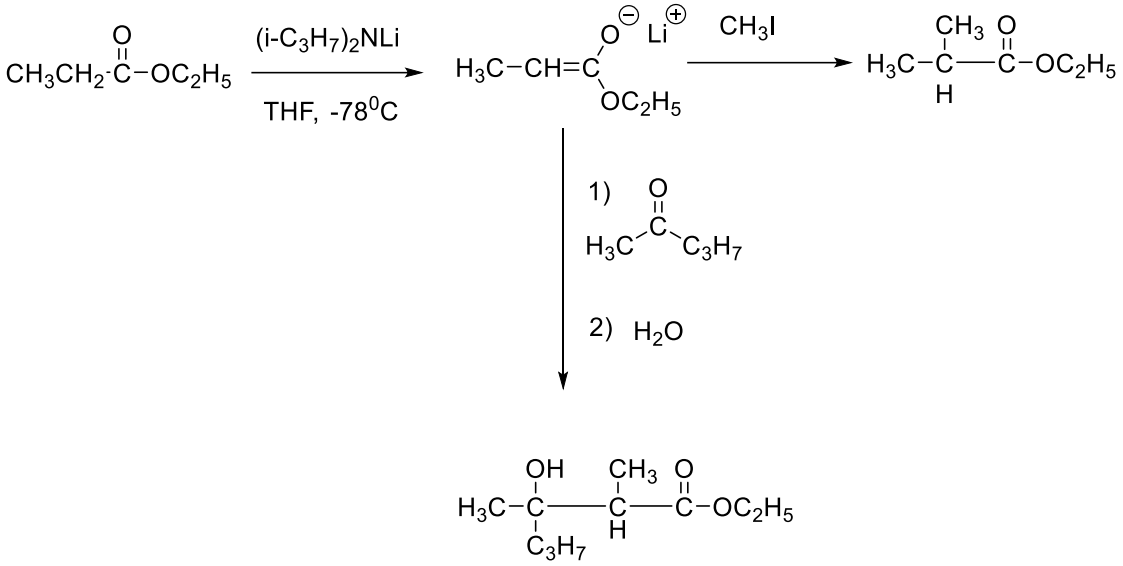
When ethyl acetate is dissolved in deuterio ethanol with a catalytic amount of NaOEt, alpha protons are exchanged with deuterium.



Since ethyl acetate is a weaker acid than ethanol, the above equilibrium is established only slowly. When ester reacts in the presence of a strong base, then the ester can be converted to the corresponding anion.

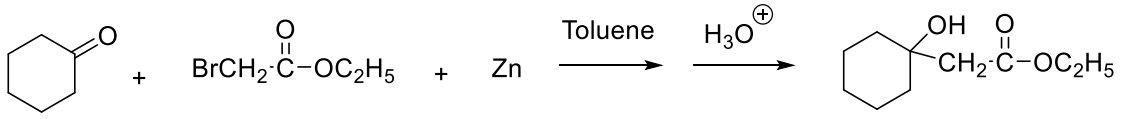


Anions of esters are strong bases and good nucleophiles.



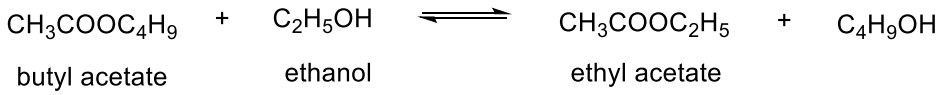
The above reactions show S_N2 displacements with primary alkyl halides and addition with aldehydes and ketones.

Reformatsky reaction: This reaction takes place when aldehydes or ketones are treated with alpha-halo ester and Zn in an inert solvent.



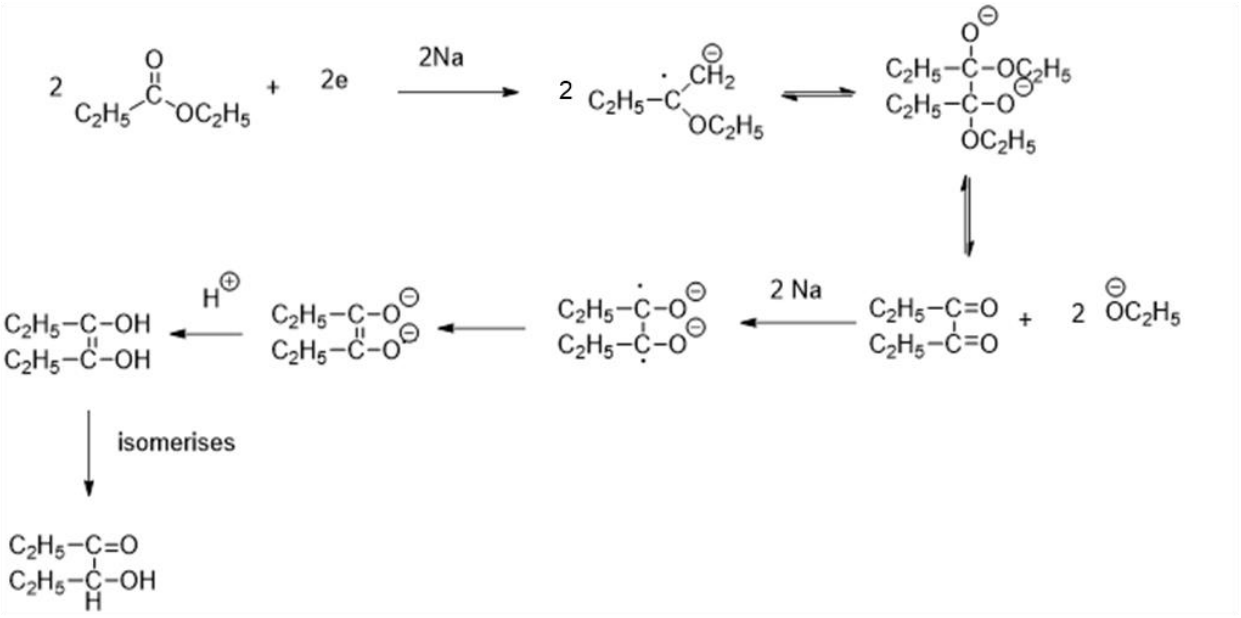
5) Trans-esterification

In this reaction, the alkoxy group of an ester can be replaced by another alcohol residue by refluxing the ester with a large excess of alcohol in the presence of a sodium alkoxide catalyst.



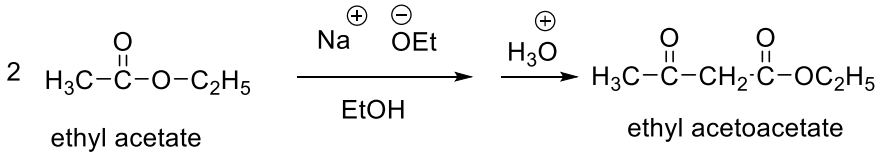
6) Acyloin reaction

An ethyl or methyl ester reacts with a piece of sodium in an inert solvent (such as ether, benzene, toluene) and then with a mild acid, the product is an acyloin. This reaction has to be carried out in the absence of any free alcohol. Acyloin can be reduced by Zn/Hg and HCl (Clemmensen method) to alkanes

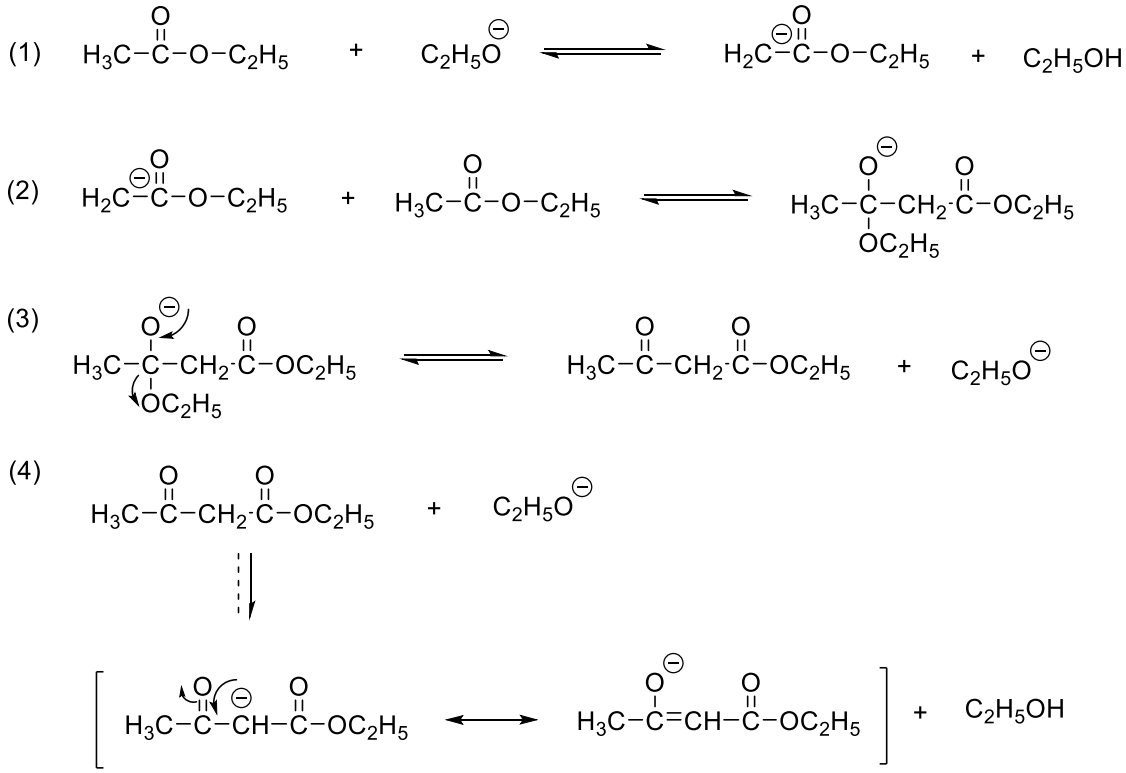


7) Claisen condensation

In this reaction, ester anion condenses with an un-ionised ester molecule to give a beta-keto ester.

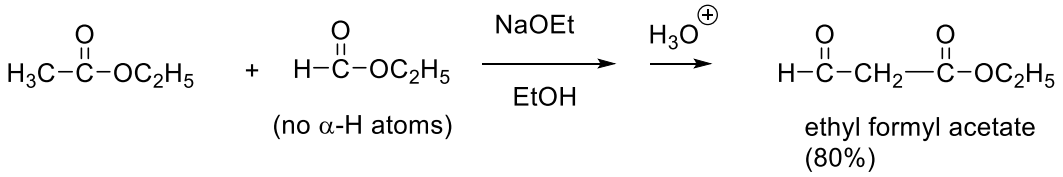


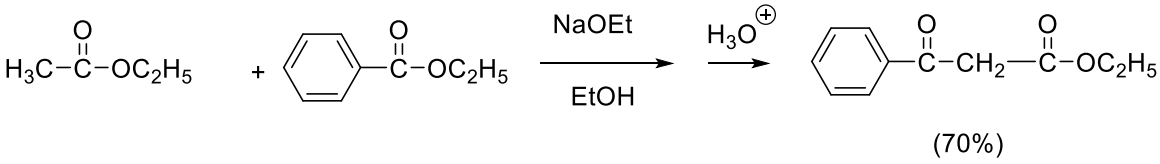
The mechanics of this reaction is similar to aldol condensation (because the conjugate base of the ester is a reactive intermediate).



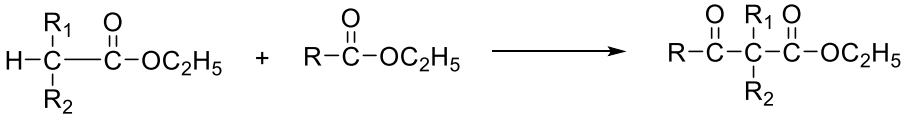
8) Mixed Claisen condensation

This is a reaction between two esters, when one ester has no alpha hydrogens.





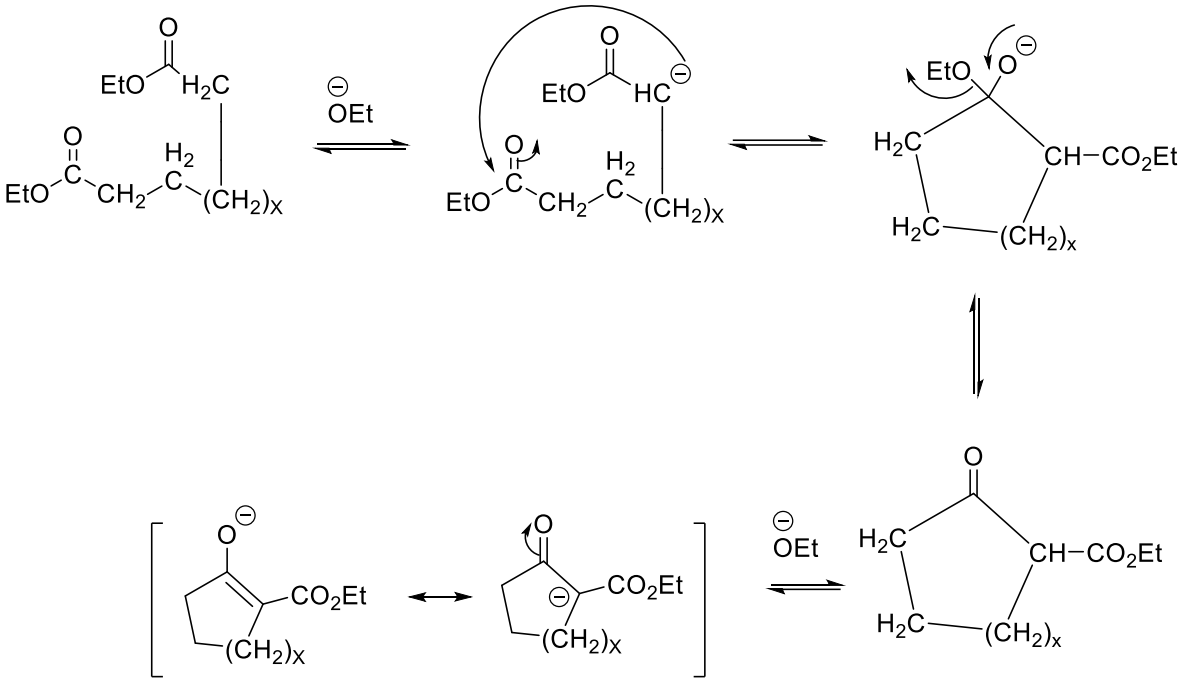
The overall mixed Claisen condensation is given below:



In the above reaction, R_1 and R_2 are H atoms and R has no alpha H atoms. In such a scenario, the reaction produces the best results.

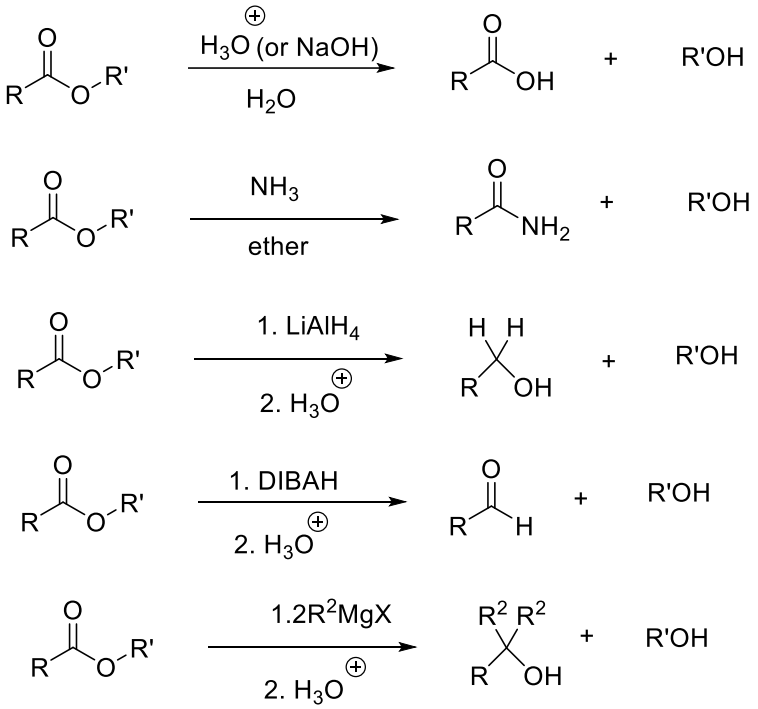
9) Dieckmann cyclisation

In this reaction, an intermolecular Claisen reaction happens where both ester groups are from the same molecule. This is a good reaction to produce 5, 6, or 7 member-cyclic beta keto esters.

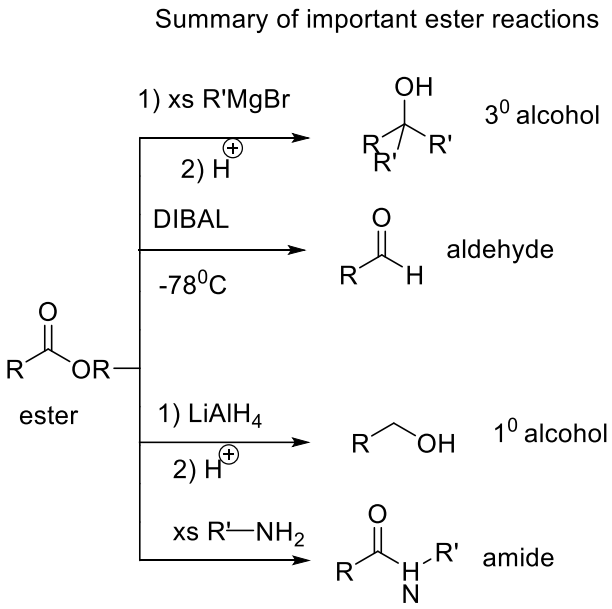


12.7 Summary

1.2.7.1 Carboxylic Acid Reactions



12.7.2 Ester Reactions



Chapter 13

13.0 Carboxylic Acid Derivatives

13.1 Objectives

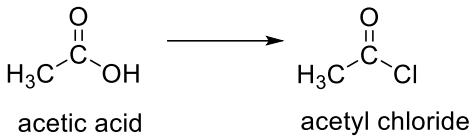
1. Draw and interpret Lewis structures, line-bond structures and functional groups of carboxylic acid derivatives using IUPAC system of nomenclature.
2. Draw reaction mechanisms.
3. Describe reactions, predicting reactivity, and reaction products.
4. Devise syntheses including steps, reagents, and products including regiochemistry and stereochemistry.

13.2 Introduction

In this chapter, four types of carboxylic acid derivatives are discussed. They are,

1. Acid or acyl halides
   These compounds are formed by replacing the hydroxyl group of a carboxylic acid with a halide.

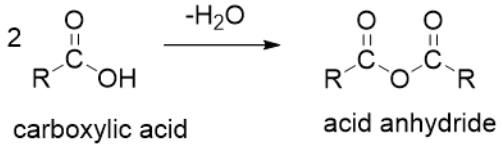
e.g.,



acetic acid acetyl chloride

2. Acid anhydrides
   These compounds are formed by the combination of two carboxylic acids while eliminating a water molecule.

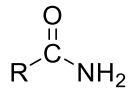
e.g.,



carboxylic acid acid anhydride

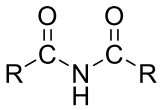
3. Acid amides
   These compounds are formed by replacing the hydroxyl group of a carboxylic acid with an amino group. There are three types of amides:

   Primary amides

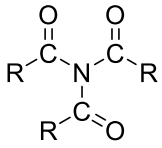


   This is the most important group.

   Secondary amides



   Tertiary amides



4. Alkyl cyanide (also known as alkyl nitriles or carbonitriles)

e.g., CH_3CN

Methyl cyanide or acetonitrile

$(CH_3)_2CN$

Isopropyl cyanide or Isobutyronitrile

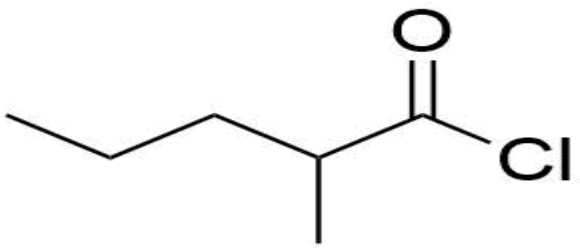
Since alkyl cyanides can be produced from carboxylic derivatives, this group of compounds are discussed in this chapter.

13.3 Nomenclature and Isomerism

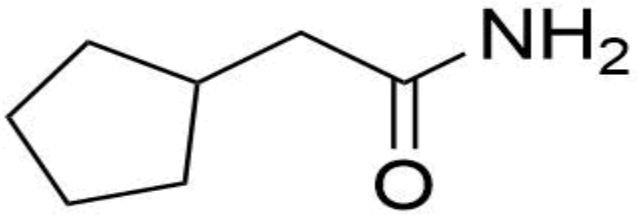
Please refer to the chapter on nomenclature and isomerism and answer the following questions:

1. **Naming Compounds – Give the IUPAC names for the following compounds**

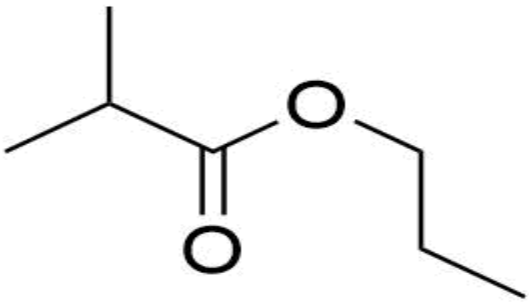
a)



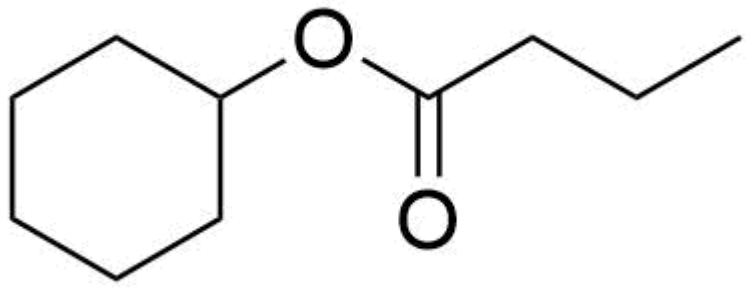
b)



c)



d)



2. **Draw the structures of the following compounds**

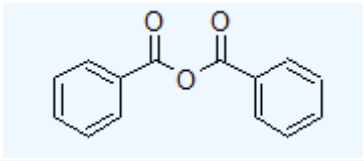
a) benzoic anhydride
b) phenyl hexanoate

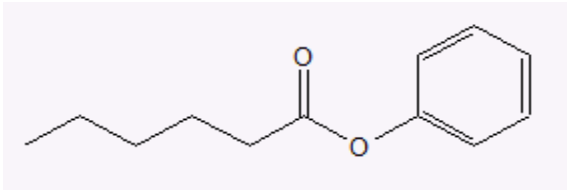
Solutions:

1. **Naming Compounds – Give the IUPAC names for the following compounds.**

a) 2-methylpentanoyl chloride
b) 2-cyclopentylacetamide
c) propyl 2-methylpropanoate
d) cyclohexylbutanoate

2) **Draw the structures of the following compounds.**

a) 

b) 

13.4 Physical Properties

13.4.1 Acyl halides

The lower molecular members of this group are colorless liquids with irritating odors. The higher molecular members are colorless solids.

13.4.2 Acid Anhydrides

Acetic anhydride is a colorless liquid with an irritating odor. This compound gets hydrolyzed slowly in water, except when an alkali that speeds up the reaction is present.

13.4.3 Acid Amides

All amides in this group, except formamide are colorless crystalline solids. The lower molecular weight members are soluble in water due to H-bonds. N-N dimethyl formamide (DMF) is an excellent solvent for polar and non-polar compounds.

13.4.4 Alkyl cyanides

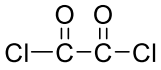
This group of compounds has a pleasant odor. They are stable neutral substances. The lower molecular weight members of this group are soluble in water and forms H-bonds. Their solubility decreases as the molecular weight increases. This group of members are more volatile than their corresponding acids, due to the lack of intermolecular H-bonds in cyanides.

13.5 Preparation of Carboxylic Acid Derivatives

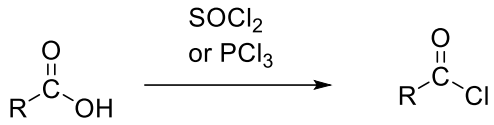
13.5.1 Acyl halides

Acyl chlorides can be prepared by allowing the carboxylic acid to react with any of the following reactants:

Thionyl Chloride – $SOCl_2$

Oxalyl Chloride - 

Phosphorous trichloride – PCl_3



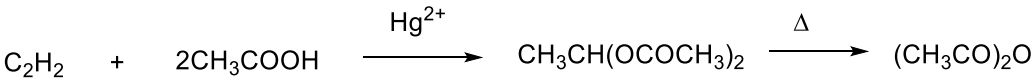
13.5.2 Acid Anhydrides

1. From acyl chloride

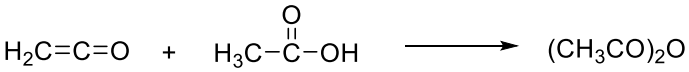
Check the section 13.6.1 – Reaction 4.

2. From acetylene – industrial preparation

a) In the presence of glacial acetic acid and mercuric ion catalyst, acetylene will react with carboxylic acid to produce ethylidene diacetate, which upon distillation will produce anhydride.



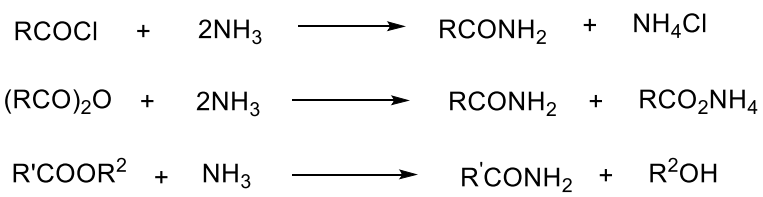
b) Similar to the above reaction, ketene reacts with glacial acetic acid to produce acetic anhydride.



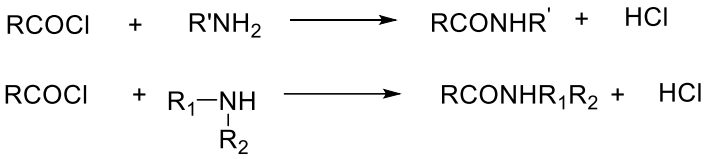
13.5.3 Acid Amides

1. From acyl chlorides, anhydrides, and esters.

When any of the above compounds are treated with concentrated ammonia, amides are produced.

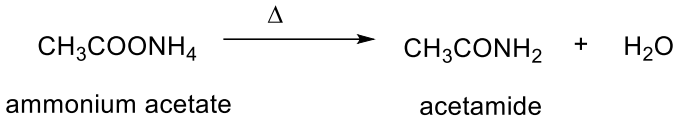


Other N-substituted amides can be obtained by reacting acyl chloride with primary or secondary amines.



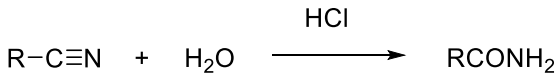
2. From ammonium salt of the carboxylic acid

When ammonium salt of carboxylic acid is heated in the presence of a small amount of free acid, an amide will be produced as the main product.



3. From alkyl cyanides

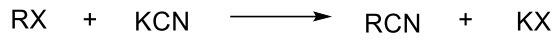
When alkyl cyanides undergo complete hydrolysis, they will produce carboxylic acids. Nevertheless, this reaction can be stopped at the amide stage by dissolving the cyanide in concentrated H_2SO_4 and then adding cold water into the solution.



13.5.4 Alkyl cyanides

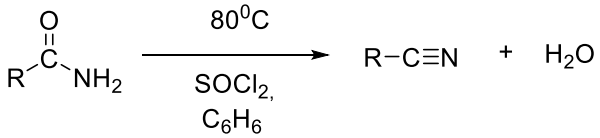
1. Form alkyl halides

When alkyl halides are reacted with potassium cyanide in aqueous solution, an alkyl cyanide can be obtained. Primary and secondary alkyl halides undergo this reaction while tertiary alkyl halides produce alkenes through elimination.



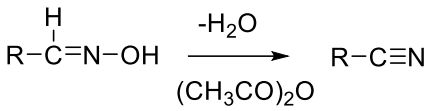
2. From acid amides

Amides undergo dehydration when treated with P_2O_5 or $POCl_3$ or $SOCl_2$ to provide corresponding cyanide. The higher molecular weight amides can be dehydrated using heat alone.



3. From aldoximes

When aldoximes are heated with P_2O_5 or with acetic anhydride, the corresponding cyanide is given.



4. From cyanogen chloride

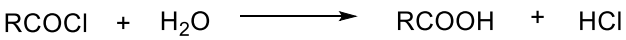
When cyanogen chloride (CNCl) reacts with alkyl Grignard reagent, the corresponding alkyl cyanides are formed. This is considered the best method for preparation of tertiary alkyl cyanides.

13.6 Reactions of Carboxylic Acid Derivatives

13.61 Acyl halides

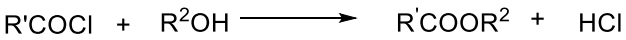
1. Hydrolysis

The low molecular compounds of acyl chlorides react vigorously with water. All chlorides are hydrolyzed to produce carboxylic acids.



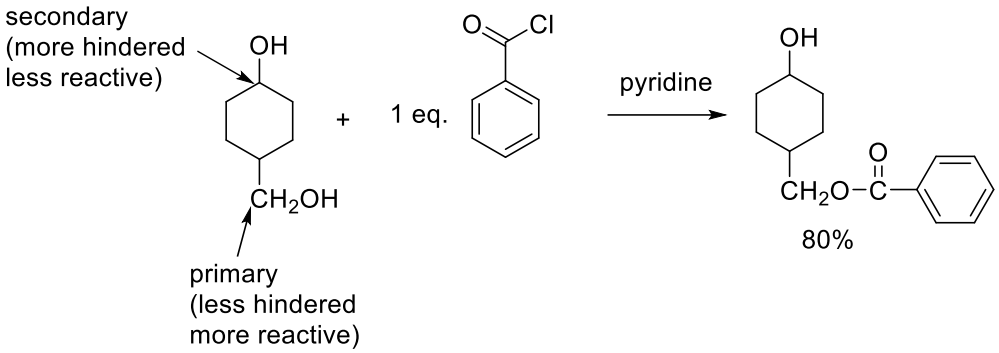
2. Formation of esters

Acyl chloride reacts with alcohols to form esters.



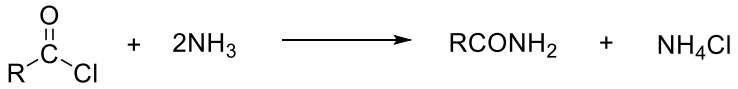
Due to the steric hindrance caused by large groups, the rate of reactions is high for primary alcohols, moderate for secondary alcohols, and slow for tertiary alcohols.

This steric hindrance can be used to selectively esterify certain alcohols while avoiding other hindered alcohols.



3. Formation of amides

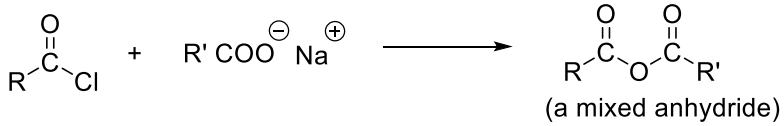
A reaction between ammonia and acyl chloride would provide amides. The stoichiometry of the reaction is 1:2 for acyl chloride to amide.



This reduction can also be conducted using $LiAlH_4$ or $NaBH_4$ or LiH.

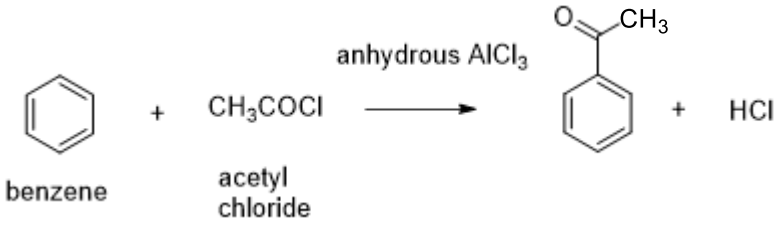
4. Formation to anhydrides

A reaction with salts of carboxylic acids will convert acyl chlorides to an anhydride.



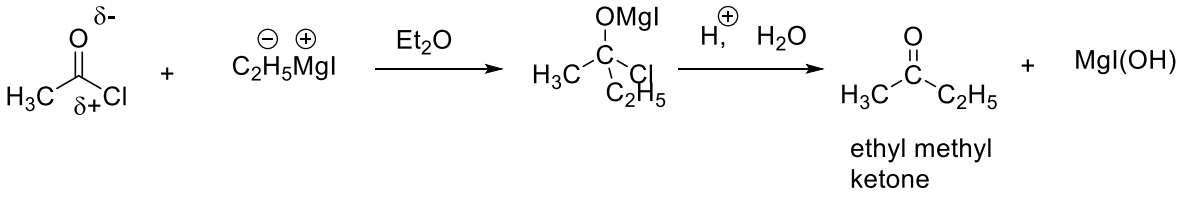
5. Formation of aromatic ketones – Friedel Crafts reaction

A reaction with benzene in the presence of a Lewis acid catalyst (anhydrous $AlCl_3$) will produce aromatic ketones. This is an electrophilic substitution.



6. Formation of ketones

When acyl chloride reacts with alkyl magnesium iodide in dry ether, ketones are produced.



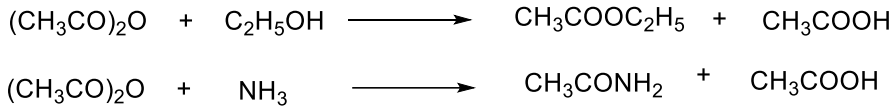
7. Reduction

A reduction of acyl chloride in the presence of H_2/Pd catalyst will produce alcohol via aldehyde.

13.6.2 Acid Anhydrides

1. Nucleophilic Reactions

The nucleophiles such as C_2H_5OH, H_2O, ^-OH, ^-OR, and NH_3 are less reactive with acetic anhydrides. Only half the molecule is used in the conversion as shown in the examples below:



2. Reduction

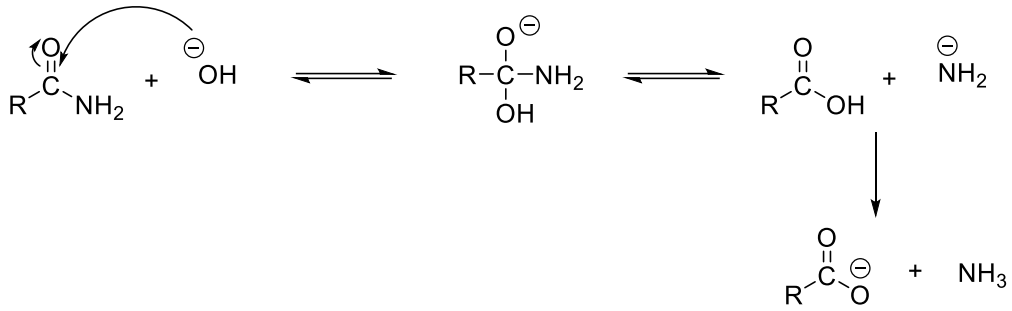
Acetic anhydrides upon reduction will produce ethanol. The reducing agents such as $LiAlH_4$, NaBH4, and B_2H_6 can be used in reduction reactions. The reduction can also be carried out in the presence of hydrogen with a catalyst.

13.6.3 Acid Amides

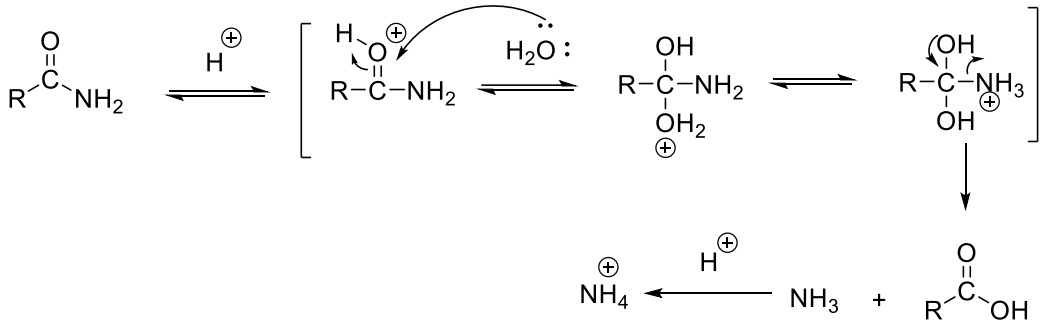
1. Hydrolysis

Amides undergo hydrolysis to produce carboxylic acids and ammonia. Whilst the reaction is slow in water, it is rapid when a base or an acid is added.

a) Base hydrolysis



b) Acid hydrolysis



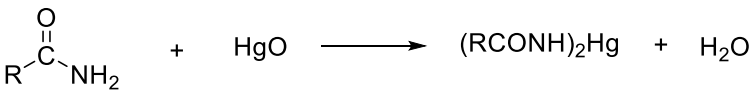
2. Formation of salts

Amides as weak bases when reacted with strong inorganic acids will form unstable salts.

e.g. $RCONH_2HCl$

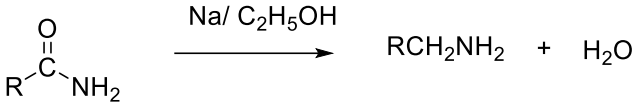
3. Formation of mercuric compounds

Amides also behave as weak acids. Amides produce covalent mercuric compounds when they are dissolved in mercuric oxides.



4. Formation of amines

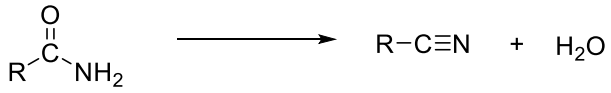
Amides undergo reduction to form amines in the presence of sodium and ethanol.



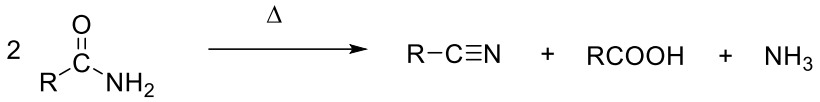
The reduction also could be done using $LiAlH_4$, B_2H_6, or with hydrogen in the presence of a catalyst.

5. Formation of alkyl cyanides

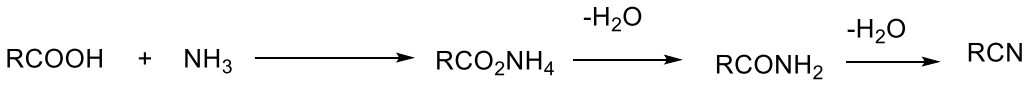
When amides are dehydrated using P_2O_5 or PCl_5, $SOCl_2$, they will produce alkyl cyanides.



When amides of higher acids are heated at high temperatures, they will give nitriles directly.

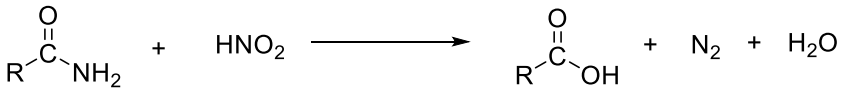


When this reaction is carried out in the presence of excess ammonia, amides will convert to cyanides.



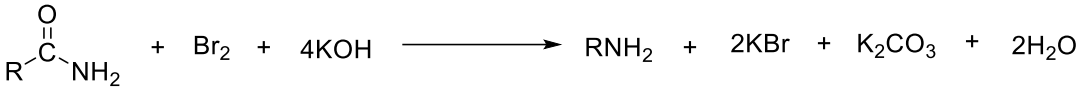
6. Formation of carboxylic acid and nitrogen

When amides react with nitrous acid, they will produce carboxylic acid and nitrogen.



7.Hofmann degradation of amides

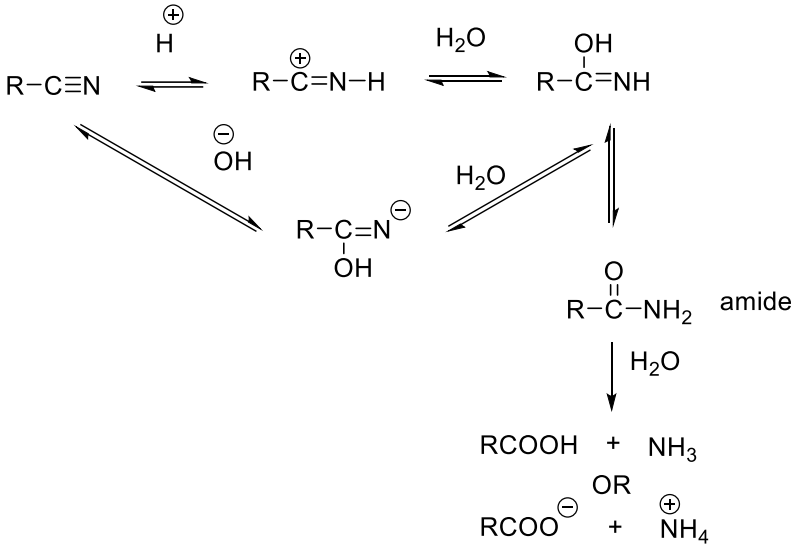
Amides can be converted to an amine with one carbon less than the original chain by treating with bromine or chlorine in the presence of a base.



13.6.4 Alkyl cyanides

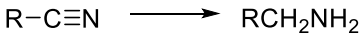
1. Hydrolysis

When alkyl cyanide undergoes complete hydrolysis in the presence of acids or bases, the reaction will produce a carboxylic acid (or its anion) via an amide.

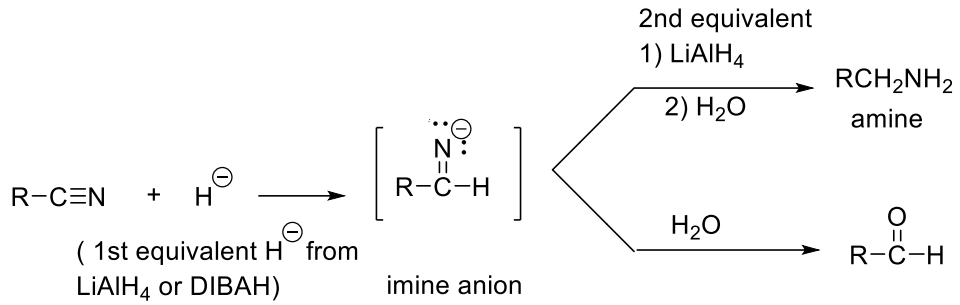


2. Reduction

Alkyl cyanide can be reduced (with $LiAlH_4$) to primary amines by reacting with sodium and ethanol or with metal hydrides.

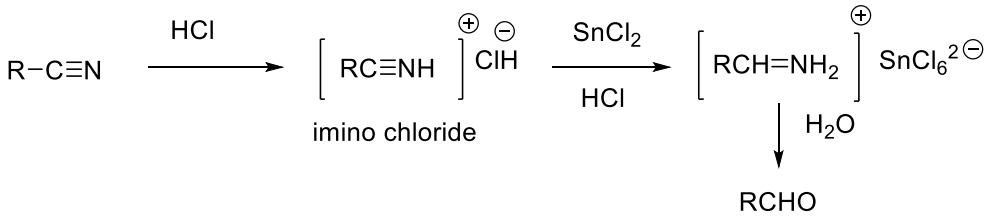


When the reduction is carried out using DIBAH, a partial reduction will happen and produce an aldehyde.



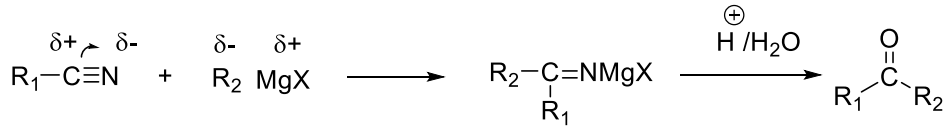
3) Stephens Reaction

In this reaction, an alkyl cyanide is dissolved in ethyl acetate and reduced with stannous chloride and hydrochloric acid followed by steam distillation.



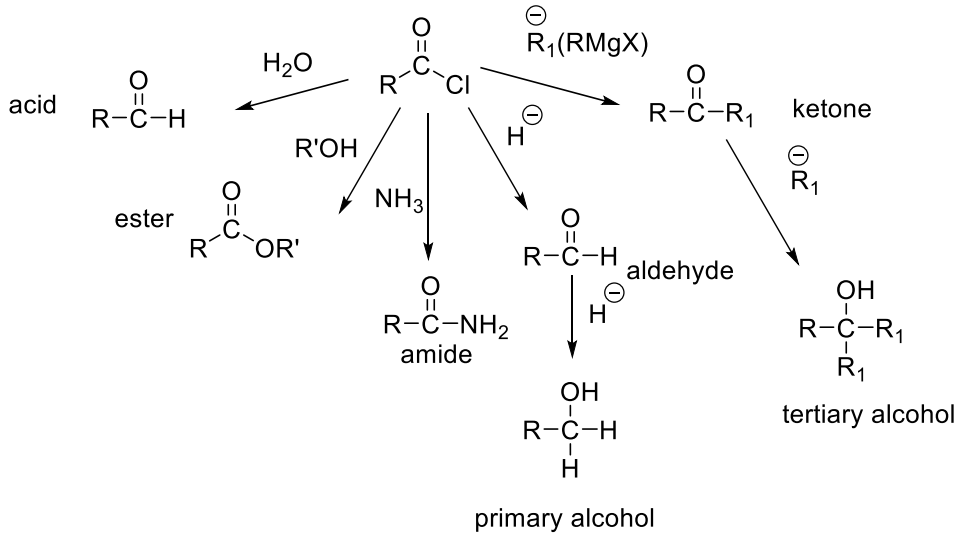
4) Grignard Reagent

Alkyl cyanide reacts with Grignard reagent to produce a ketone.

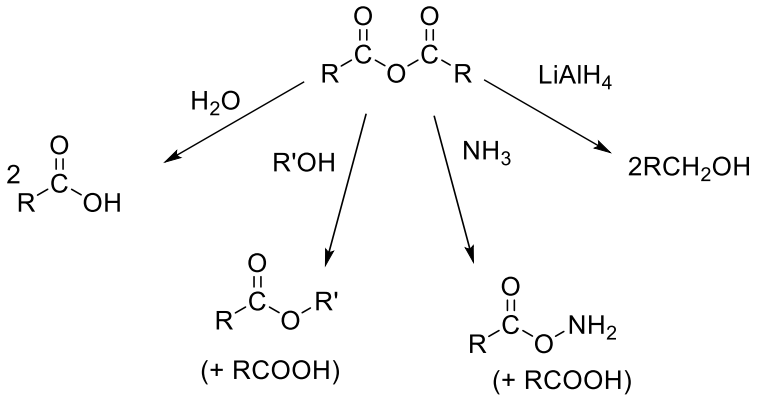


13.7 Summary of Reactions

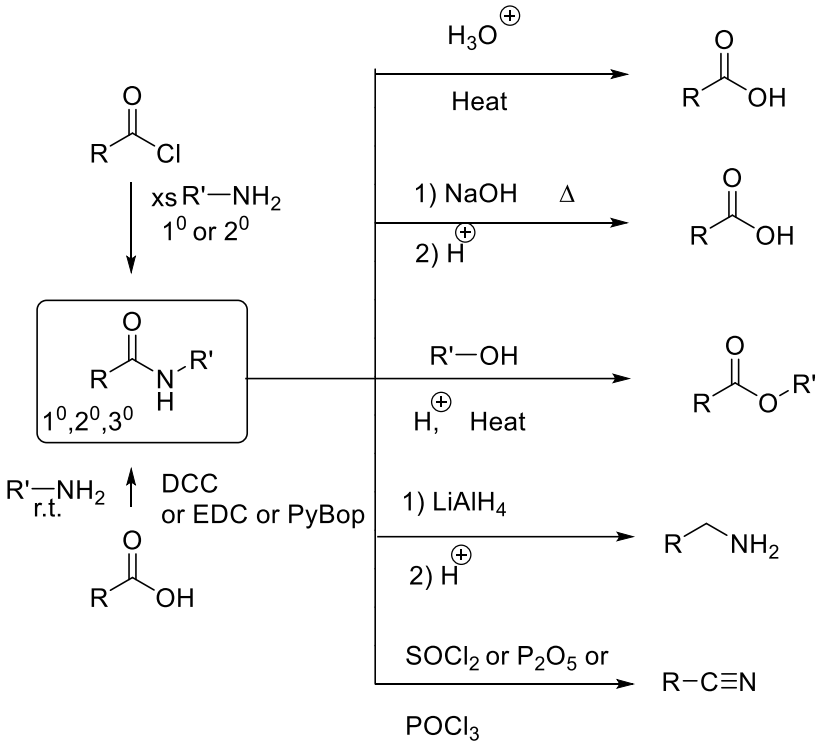
13.7.1 Acyl Chloride Reactions



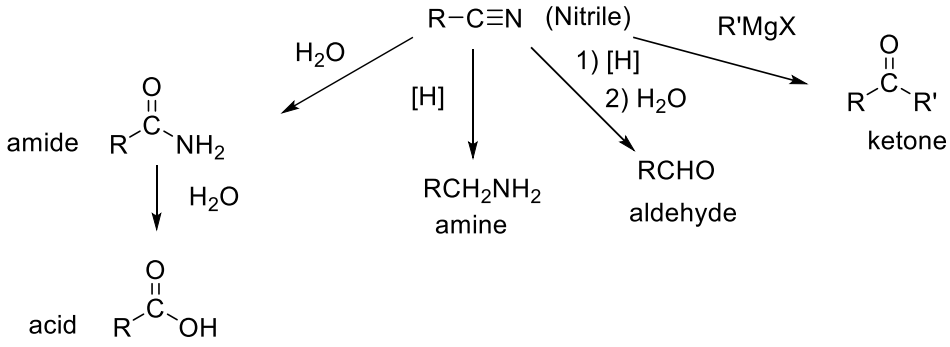
13.7.2 Acid Anhydrides



13.7.3 Acid Amides



13.7.4 Alkyl Cyanides



Chapter 14

14.0 Amines and Nitro Compounds

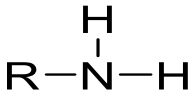
14. 1 Objectives

1. Draw and interpret Lewis structures, line-bond structures and functional groups of amines and nitro compounds using IUPAC system of nomenclature.
2. Draw reaction mechanisms.
3. Describe reactions, predicting reactivity, and reaction products.
4. Devise syntheses including steps, reagents, and products including regiochemistry and stereochemistry.

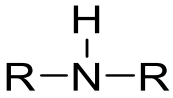
14.2 Introduction

14.2.1 Amines

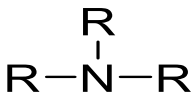
Amine is a group of organic compounds containing N atoms. They are derivatives of ammonia. These compounds can be broadly categorized as primary, secondary, and tertiary, yet the substitution here is at the N point.



1ry amine

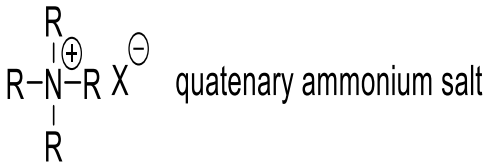


2ry amine



3ry amine

When four groups are attached to N, they are known as quaternary ammonium salts. N atom will then have a positive charge.



14.2.2 Nitro Compounds

This chapter covers only the simple nitroalkane compounds.

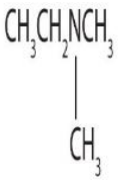
14.3 Nomenclature and Isomerism

Please refer to the chapter on nomenclature and isomerism and answer the following questions:

1. Naming Compounds – Give the IUPAC names for the following compounds

a) $CH_3CH_2CH_2NH_2$

b)



c) $CH_3CH_2NO_2$

d) $(CH_3)_3CNO_2$

2. Draw the structures of the following compounds

a) isopropyldimethylamine

b) dipropylamine

3. **Questions on Isomers**

a) What type isomers can amines exhibit?

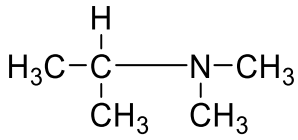
Solutions:

1. Naming Compounds – Give the IUPAC names for the following compounds.

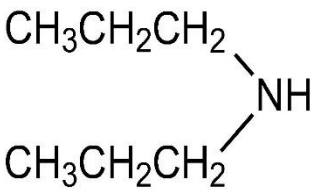
a) Propylamine
b) Ethyldimethylamine
c) Nitroethane
d) 2-methyl-2-nitropropane

2. Draw the structures of the following compounds

a)



b)



3) Questions on isomers

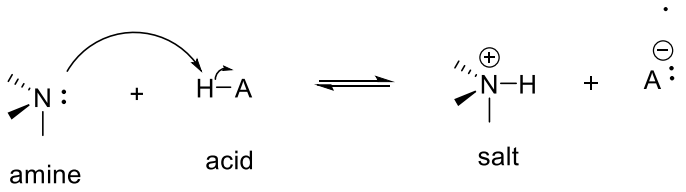
a) Chain isomerism, position isomerism, metamerism, functional isomerism, and stereo isomerism.

14.4 Physical Properties

14.4.1 Amines

Amines are highly polar compounds. Therefore, they have high boiling points than alkanes with the same molecular weight. Amines below 5 carbon atoms are generally water soluble. Primary and secondary amines form stronger H bonds.

The single lone pair of N makes amines basic and nucleophilic. Amines react with Lewis acids to form salts. A positive charge on the ion means they can react with electrophiles.



The basicity of amines can be used to separate amines from a mixture of organic compounds.
e.g.

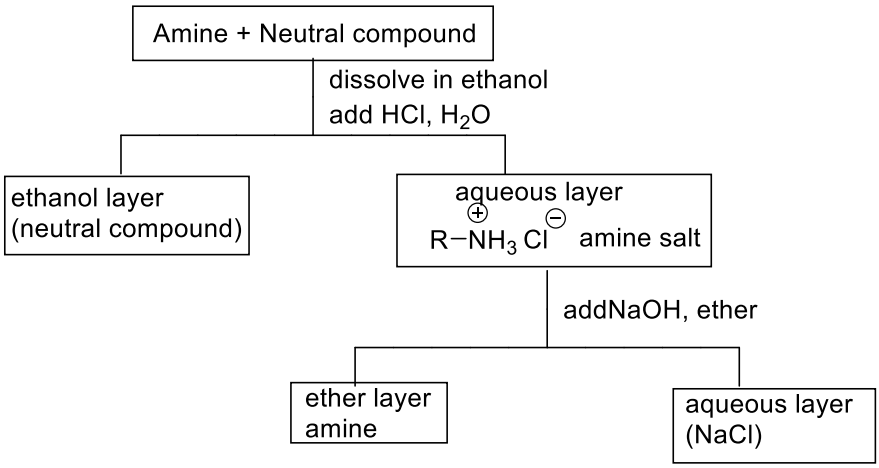


Table 14.4.1.1.: Separation of amines from a mixture

14.4.2 Nitro compounds

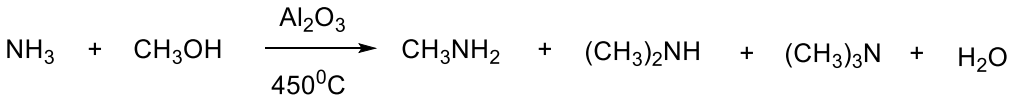
This group compounds are colorless liquids with a pleasant odor.

14.5 Preparation

14.5.1. Preparation of Amines

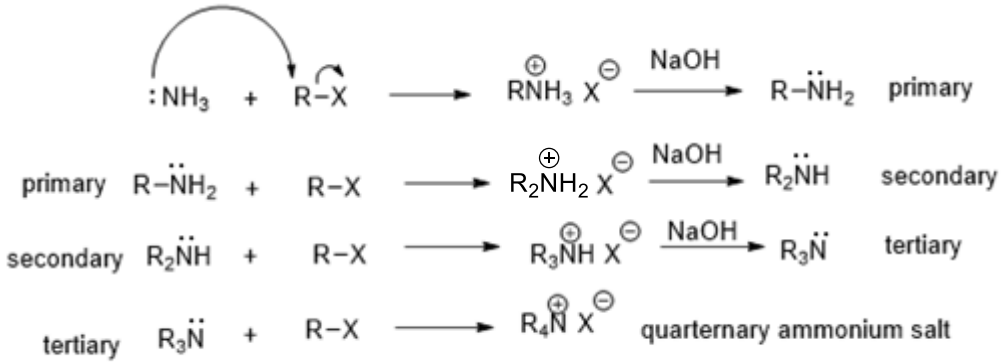
1. From ammonia and methanol

Methylated amines are prepared by reacting ammonia with methanol in the presence of alumina catalyst. The products yielded in this reaction are separated by distillation.



2. From alkyl halides

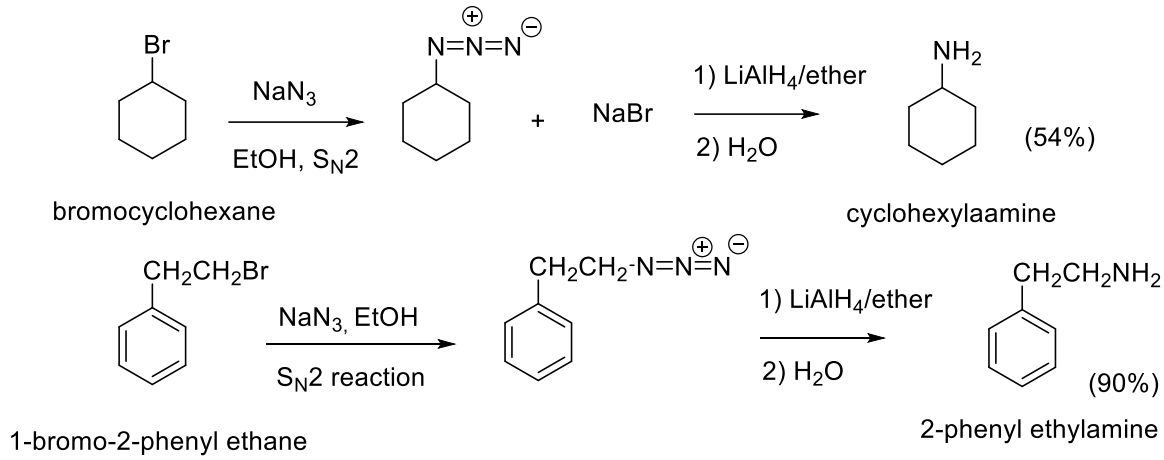
This reaction involves the alkylation of ammonia using alkyl halides. The mechanism path is S_N2. This reaction produces primary amines. Now primary amines in turn can react with alkyl halides to produce secondary amines. The secondary amines also can react with alkyl halides to produce tertiary amines. The tertiary amines will react with alkyl halides to produce quaternary ammonium salt.



3. From azide (N_3^-) synthesis

Azide is a non-basic, highly reactive nucleophile. In S_N2 reactions, azide displaces halides in primary or secondary alkyl halides to produce alkyl azides.

Alkyl azides are not nucleophiles; therefore, they will not undergo overalkylation. When alkyl azides are reduced with LiAlH4 or by catalytic hydrogenation using Pd, they will produce primary amines. This is considered an excellent method to produce primary amines.

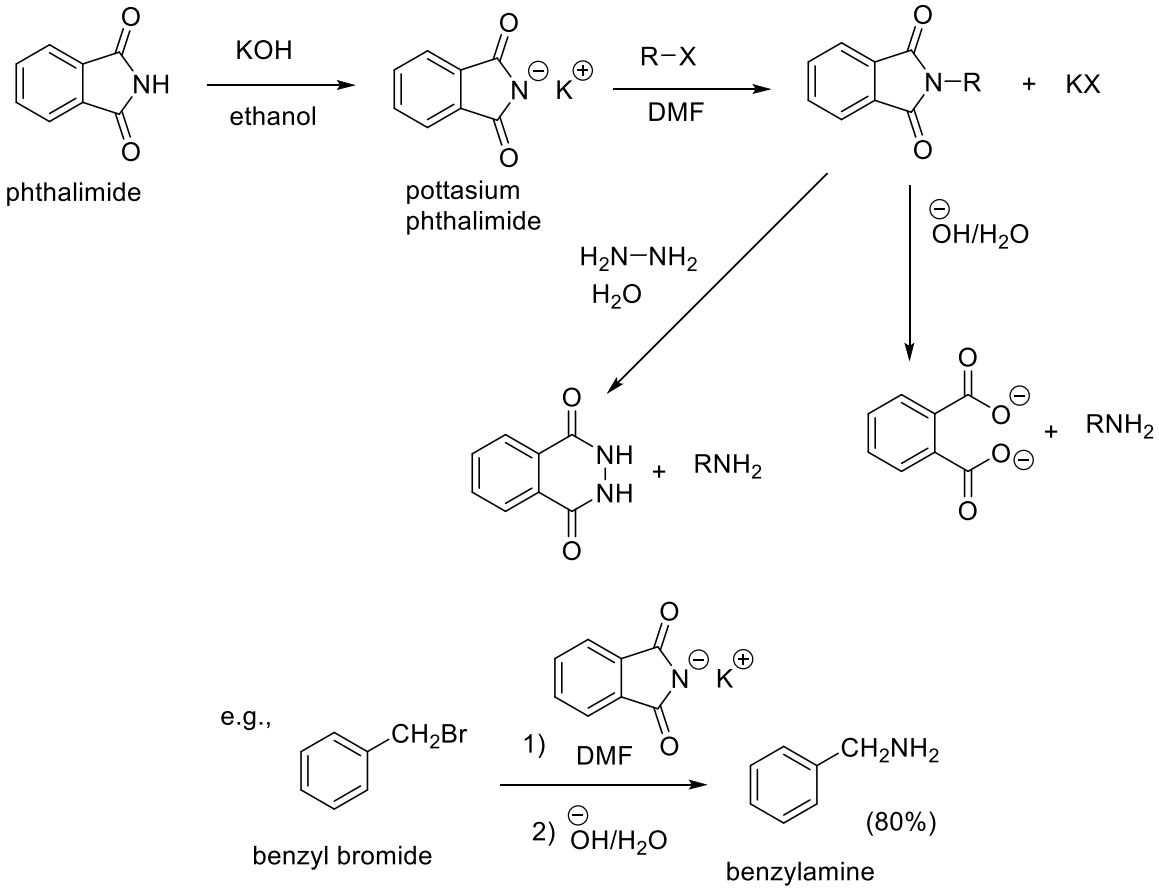


4. Gabriel Synthesis

When potassium phthalimide is alkylated with a primary alkyl halide, it will yield an N-alkyl phthalimide.

Imides (-CO-NH-CO-) contain a proton on nitrogen flanked by 2 acidifying carbonyl groups. Therefore, they can be quickly deprotonated using bases such as KOH. The anions formed after deprotonation can be readily alkylated.

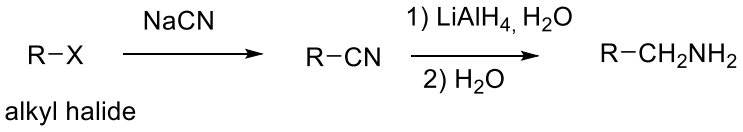
The hydrolysis of N-alkyl compounds using a base will produce a primary amine. The reaction is carried out in a highly polar solvent such as dimethyl formamide (DMF) ($HCON(CH_3)_2$).



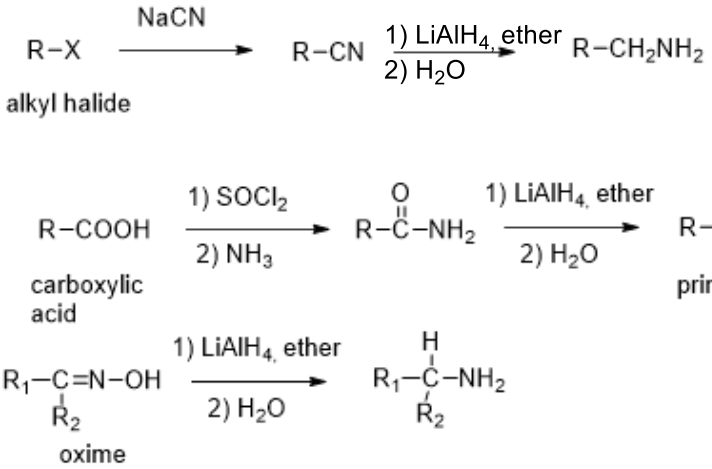
5. From reduction of nitrogen derivatives

a) Nitriles, oximes, and amides will be reduced to primary amines in the presence of $LiAlH_4$.

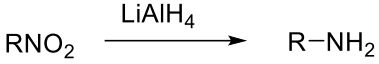
- The reduction of nitriles follows two steps. The first is the S_N2 displacement of halide by CN. The next is the reduction to produce a primary amine with one extra carbon than the original R.



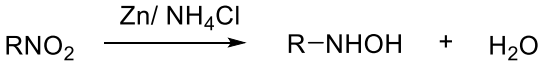
- The reduction of amides enables the conversion of carboxylic acids to primary amines.



b) The reduction of R-NO_2 a primary amine. This is done by using $LiAlH_4$ or metal/H+ (Sn/HCl) Solution.

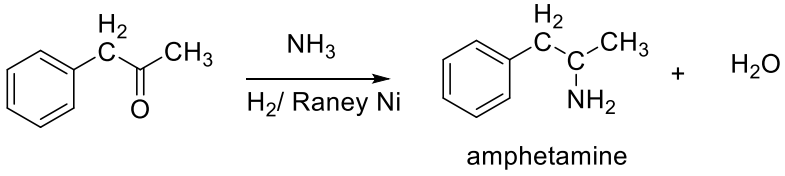


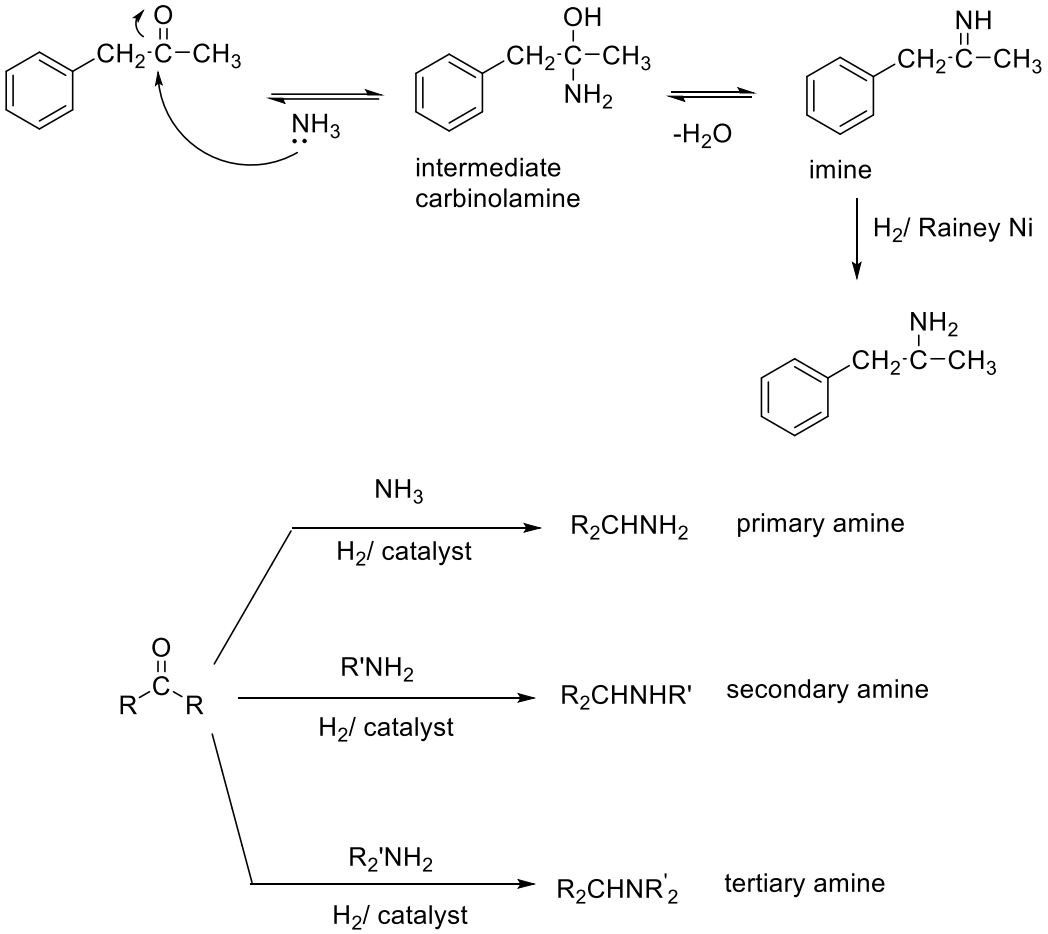
In neutral solutions, the following reaction is observed:



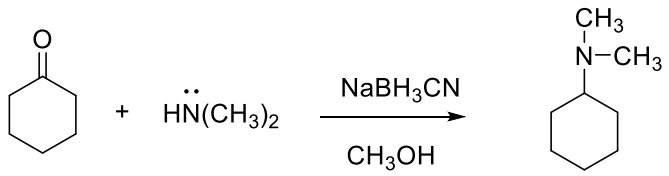
6. From reduction of aldehydes and ketones

In this method, aldehydes or ketones are reduced in the presence of ammonia or imine.





Another laboratory scale reduction is the following reaction:

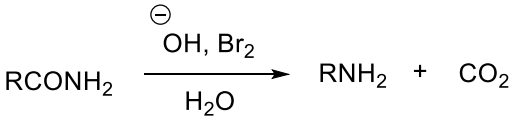


N,N-dimethyl-cyclohexamine

7. From the rearrangement of amides

Hofmann and Curtius rearrangements lead to the degradation of carboxylic acid derivatives to produce primary amines with one less carbon than the original R chain.

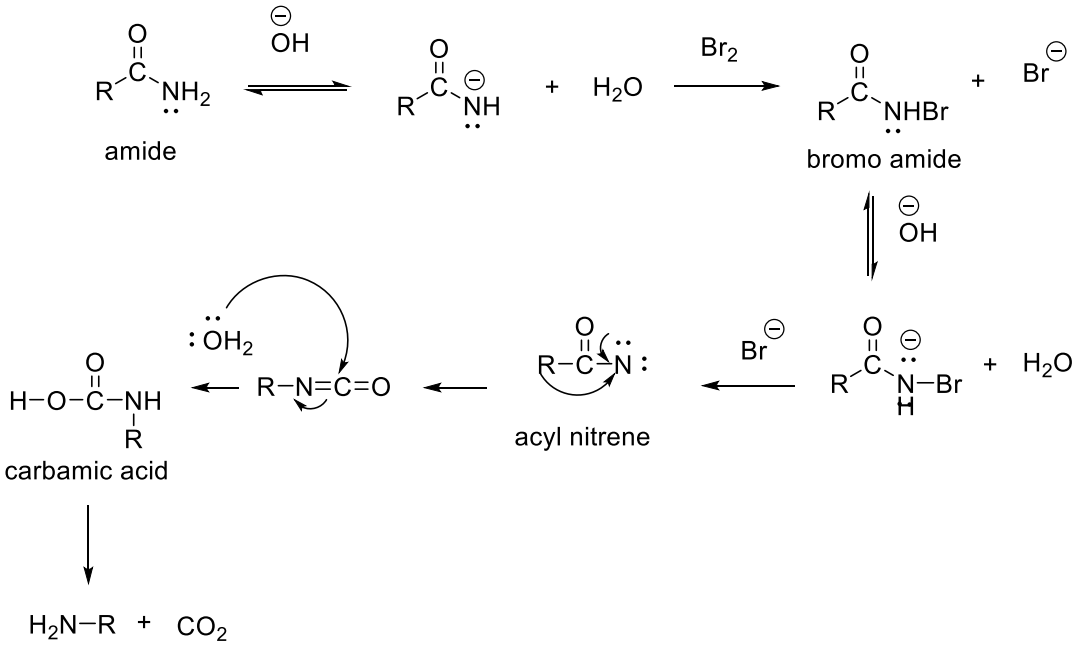
Hofmann rearrangement:



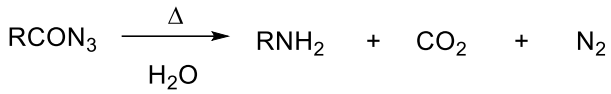
Mechanism of Hofmann rearrangement:

Steps:

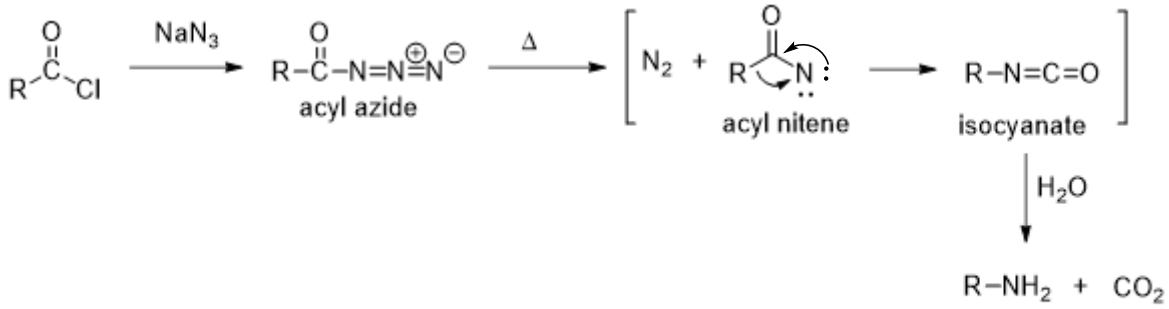
1. Acidic amide proton connects with the base to form water.
2. Amide anion combines with bromine to give N-bromoamide.
3. Base abstracts the remaining H from N to produce bromoamide anion.
4. The anion loses Br-, which is alpha elimination. This produces the intermediate nitrene.
5. R group now migrates from C to N (electron deficient) to give an isocyanate.
6. Isocyanate combines with water to produce carbamic acid.
7. Carbamic acid immediately loses CO_2 to give a primary amine.



Curtius rearrangement:



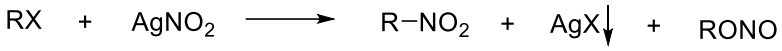
Mechanism of Curtius rearrangement:



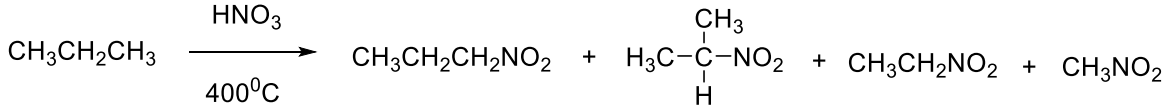
14.5.2. Preparation of Nitro Alkanes

1. From alkyl halide

When alkyl halides are heated with silver nitrite in aqueous solution, primary nitroalkanes are produced.



2. Direct nitration of alkanes



When alkanes are heated in vapor phase with HNO_3 or with oxides of nitrogen at optimal temperature, nitroalkanes are produced more efficiently.

4.6 Reactions

14.6.1 Reactions of Amines

1. Formation of salts

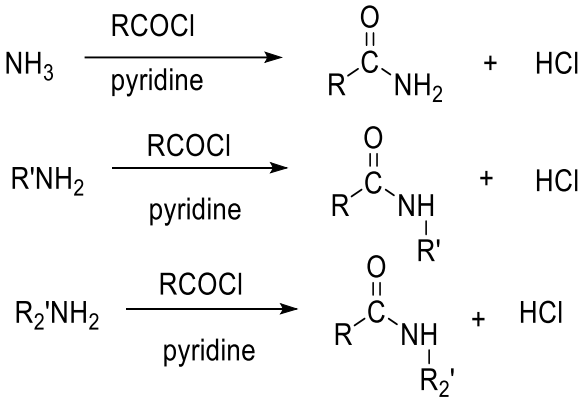
Described in 14.4.1.

2. Reaction with alkyl halides

Described in 14.5.1. reaction 2.

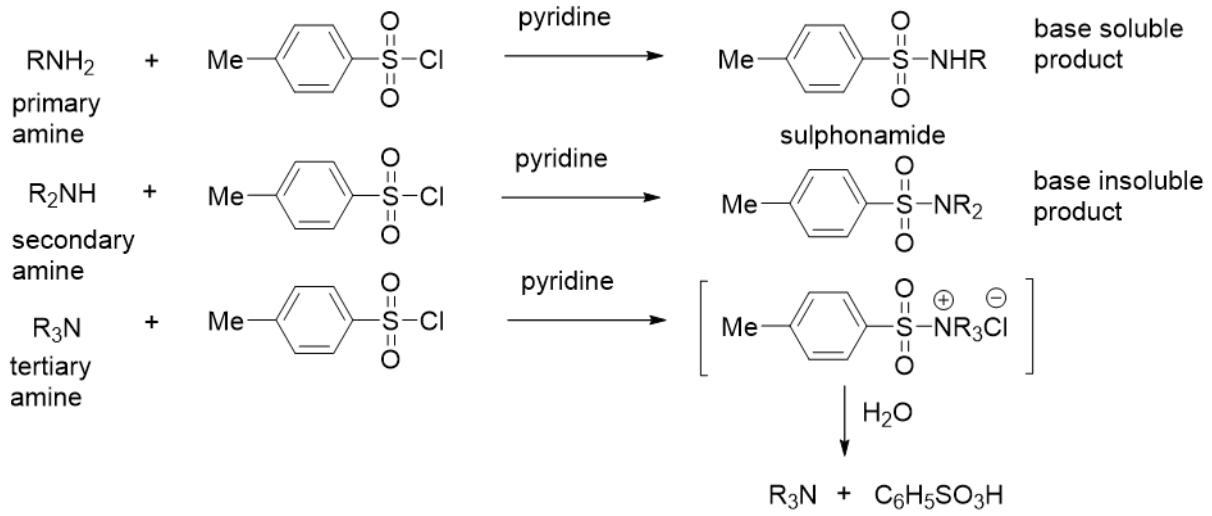
3. Reaction with acyl halides or acyl anhydrides

Primary and secondary amines will react with acyl chlorides to from amides. Tertiary amines will not react.



4. Reaction with sulfonyl chloride

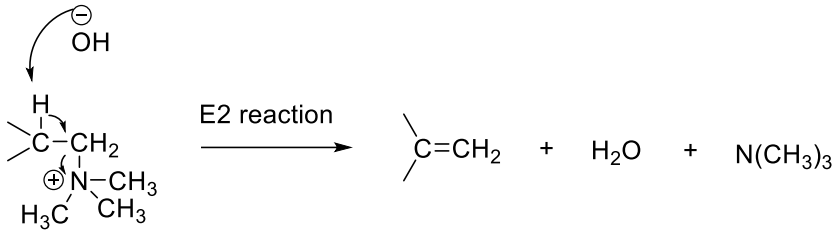
When amines (primary, secondary, and tertiary) react with sulphonyl chloride, a sulfonamide ($R_2N\text{-}SO_2R'$) is formed. This reaction is used in Hinsberg test to identify primary, secondary, and tertiary amines.



In the above reactions, only primary and secondary amines react irreversibly with p-toluene sulfonyl chloride. In the case of tertiary amines, it is easily identifiable since the product immediately hydrolyzes when water is added, and the reaction reproduces the free amine. A primary amine that produces sulfonamide shows solubility since it has one acidic N-H. This is a reaction to identify primary amines. When it comes to secondary amines, they produce sulfonamide with no acidic protons; therefore, they will not display base solubility.

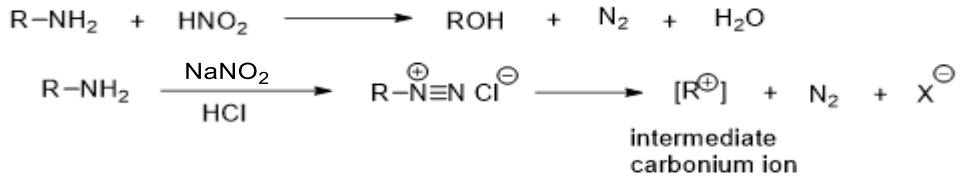
5. Hofmann Elimination

Amines undergo elimination under suitable conditions to produce alkenes.



6. Reaction with $HN0_2$

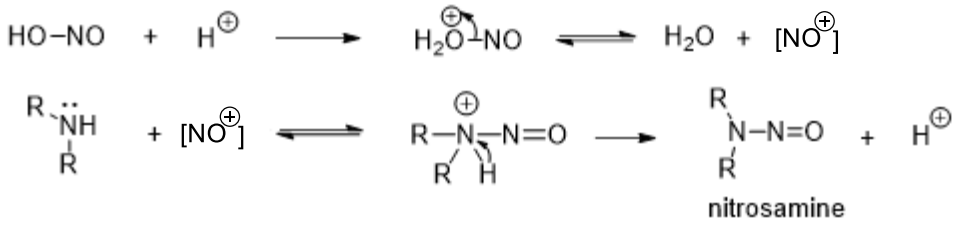
Primary aliphatic amines will react with nitrous acid to produce diazonium salt as an intermediate. This intermediate decomposes even at low temperature to produce the corresponding alcohol.



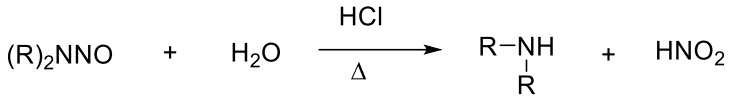
The product mixture could contain isomeric alcohols, isomeric alkenes, and other compounds depending on the type of R used in the above reaction.

In the above reaction, nitrogen is always produced. This is used as a test for primary amines.

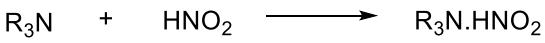
When HNO_2 reacts with secondary amines, insoluble, oily nitrosamines are produced. This reaction is known as Liebermann's nitroso reaction. Nitrogen is not produced in this reaction.



Nitrosamines can be easily hydrolyzed to produce amines when heated with dilute HCl.



Tertiary amines dissolve in cold HNO_2 to produce nitrite salt.

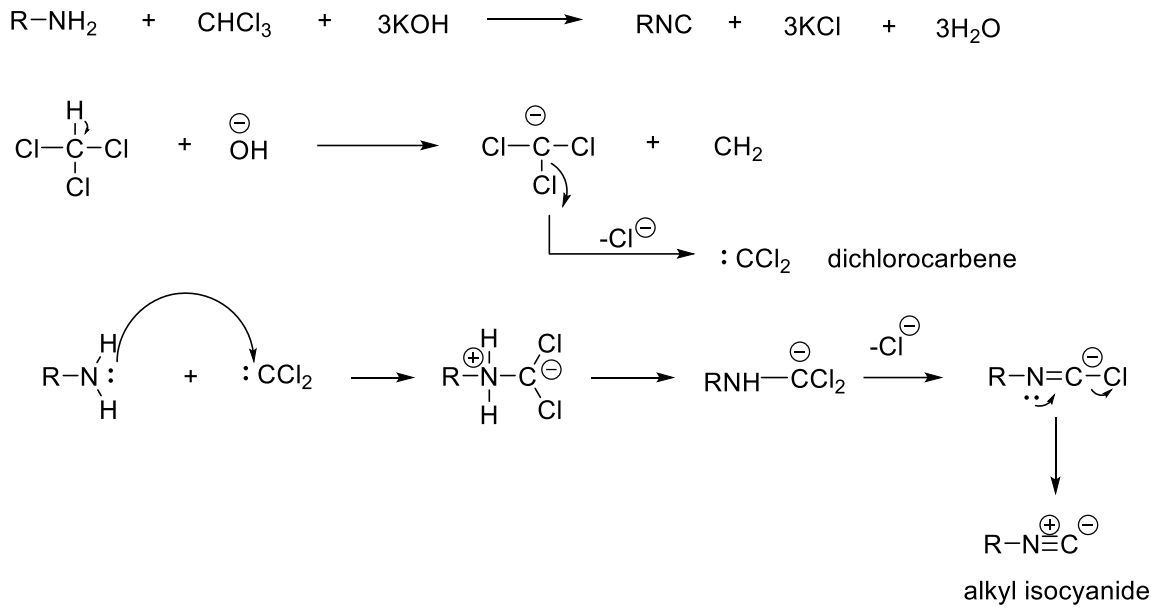


- When the amine is $R(CH_2)_3N$ type, and when the solution is warmed, it produces an aldehyde.
- When the amine is $(R_2CH)_3N$ type, and when the solution is warmed, it produces a ketone.
- Both cases also give nitrosamine and water.

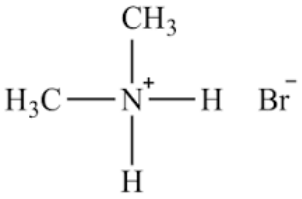
7. Reaction with chloroform

When primary amines are heated with chloroform in the ethanolic KOH, they will produce alkyl isocyanide (carbylamine). The strong smell of carbylamine is a test for identification. This is used as a test for primary amines. The test is known as carbylamine test.

The carbylamine is not produced by secondary or tertiary amines.



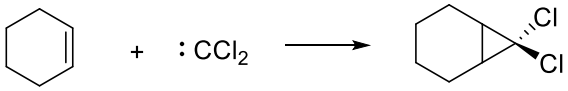
8. Tetra alkyl ammonium slats – phase transfer catalyst



Tetra alkyl ammonium bromide

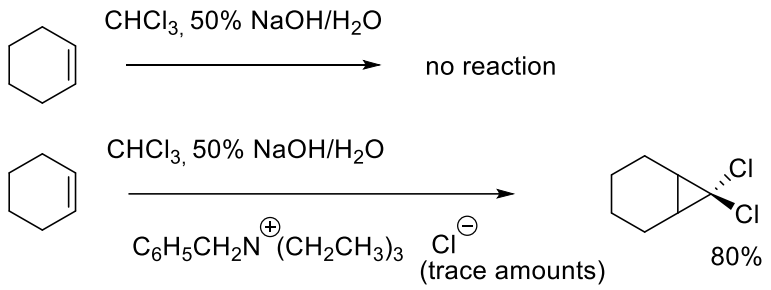
These salts are used as catalysts and also as phase transfer catalysts.

As explained in the previous reaction, chloroform reacts with a strong base such as NaOH to produce dichloro carbene ($:CCl_2$). This carbene adds to a carbon=carbon double bond to produce a dichloro cyclopropane addition.



Nevertheless, for the above reaction to take place the formation of carbene has to be initiated and allowed to be connected with cyclohexene. If cyclohexene is dissolved in chloroform and mixed with NaOH (50%), the two layers (inorganic NaOH and organic chloroform) will stay as separate media due to the immiscibility. Therefore, by adding a small amount of tetra alkyl ammonium salt

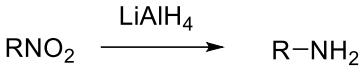
such as benzyl triethyl ammonium chloride the two phases can be mixed to produce dichlorocyclopropane.



14.6.2 Reactions of Nitro Alkanes

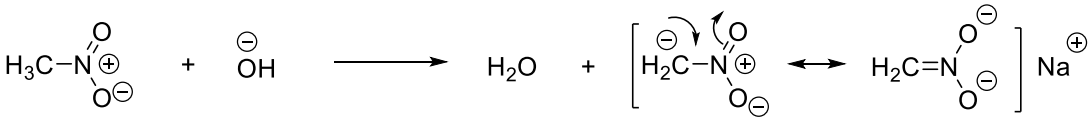
1. Reduction

Described under 14.5.1. – under the preparation method 5 (b).



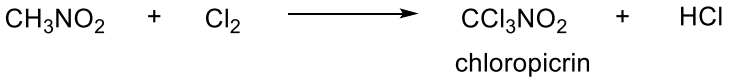
2. Formation of salts

Primary and secondary nitro compounds with alpha- H atoms will dissolve in NaOH to form salts.



3. Reaction with halogens

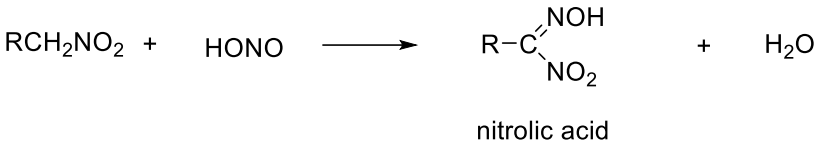
Primary and secondary nitro compounds react with halogens at alpha position. Primary nitro compounds produce mono and di halo derivatives. Secondary nitro compounds form only mono halo derivatives. In the case of nitromethane, it can form tribromo derivatives.



4. Reaction with HNO_2

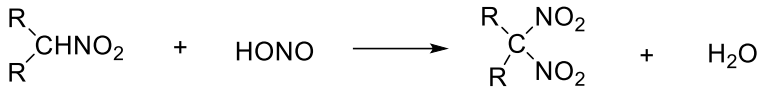
This reaction happens due the availability of alpha H atoms in nitro compounds.

Primary nitroalkanes react with nitrous acid to give nitrolic acid. When nitrolic acid crystals dissolve in NaOH, they produce a red solution.



nitrolic acid

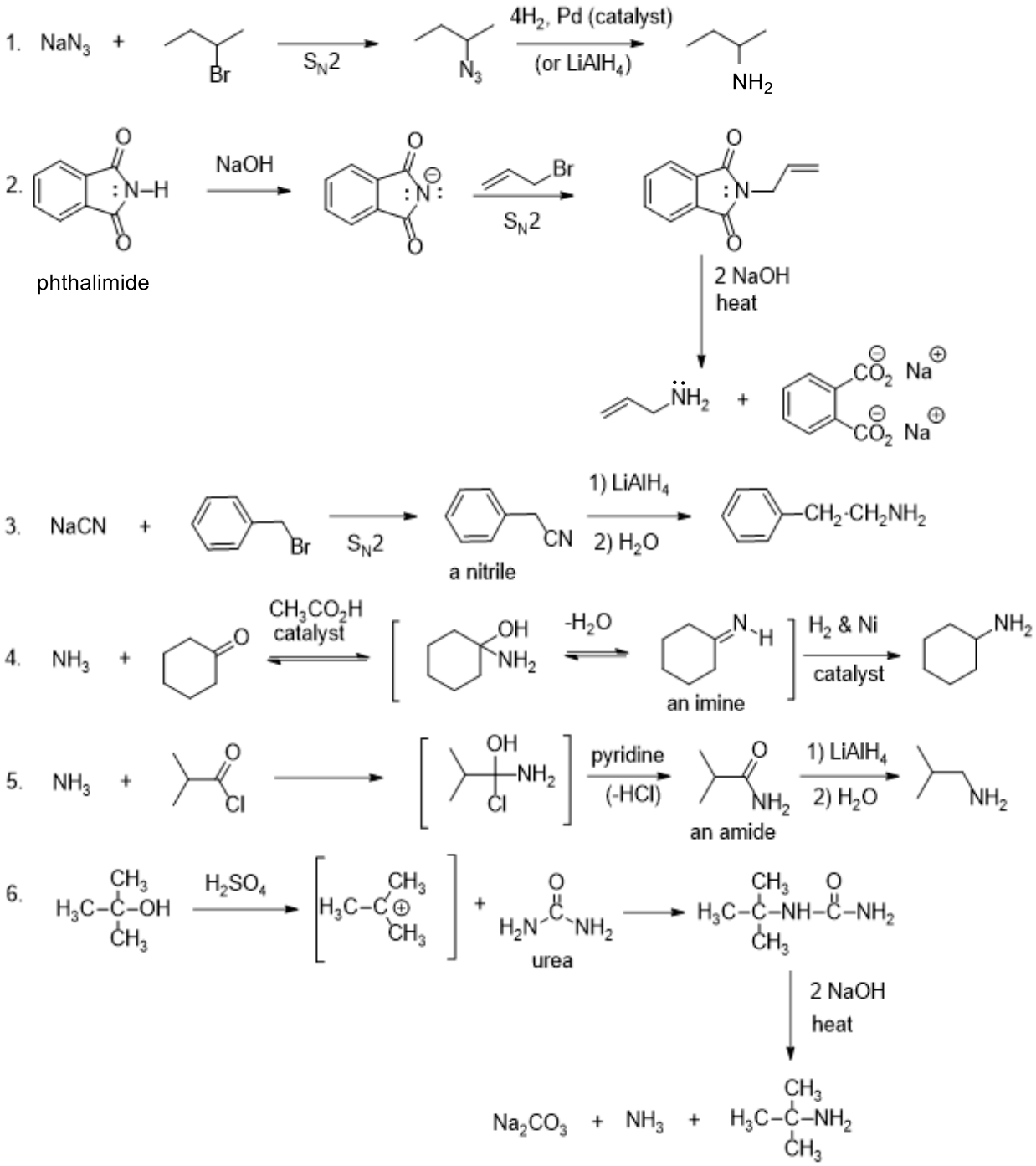
Secondary nitroalkanes from pseudo nitroles. These nitroles that are colorless crystalline when dissolve in NaOH produce a blue solution.



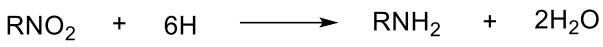
Tertiary nitro alkanes lack alpha H atoms. Therefore, they do not react with HNO_2.

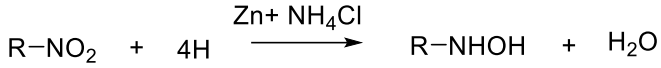
14.7 Summary of Reactions

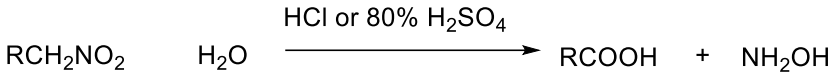
14.7.1 Summary of preparation of amines

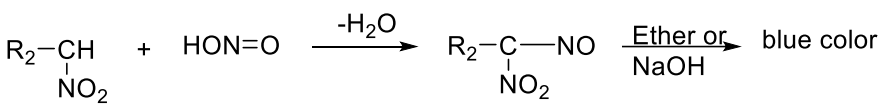


14.7.2 Summary of reactions of nitro compounds

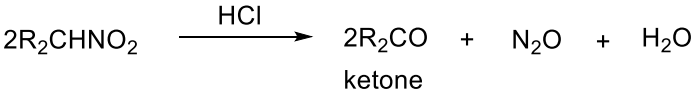




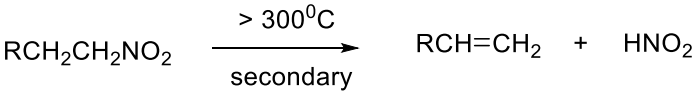




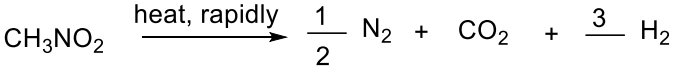
secondary

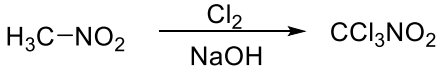


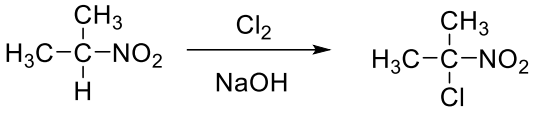
ketone

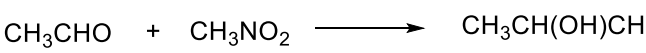


secondary

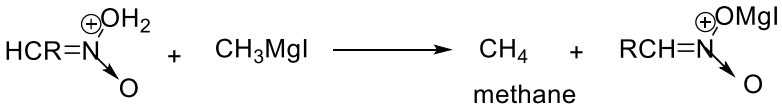




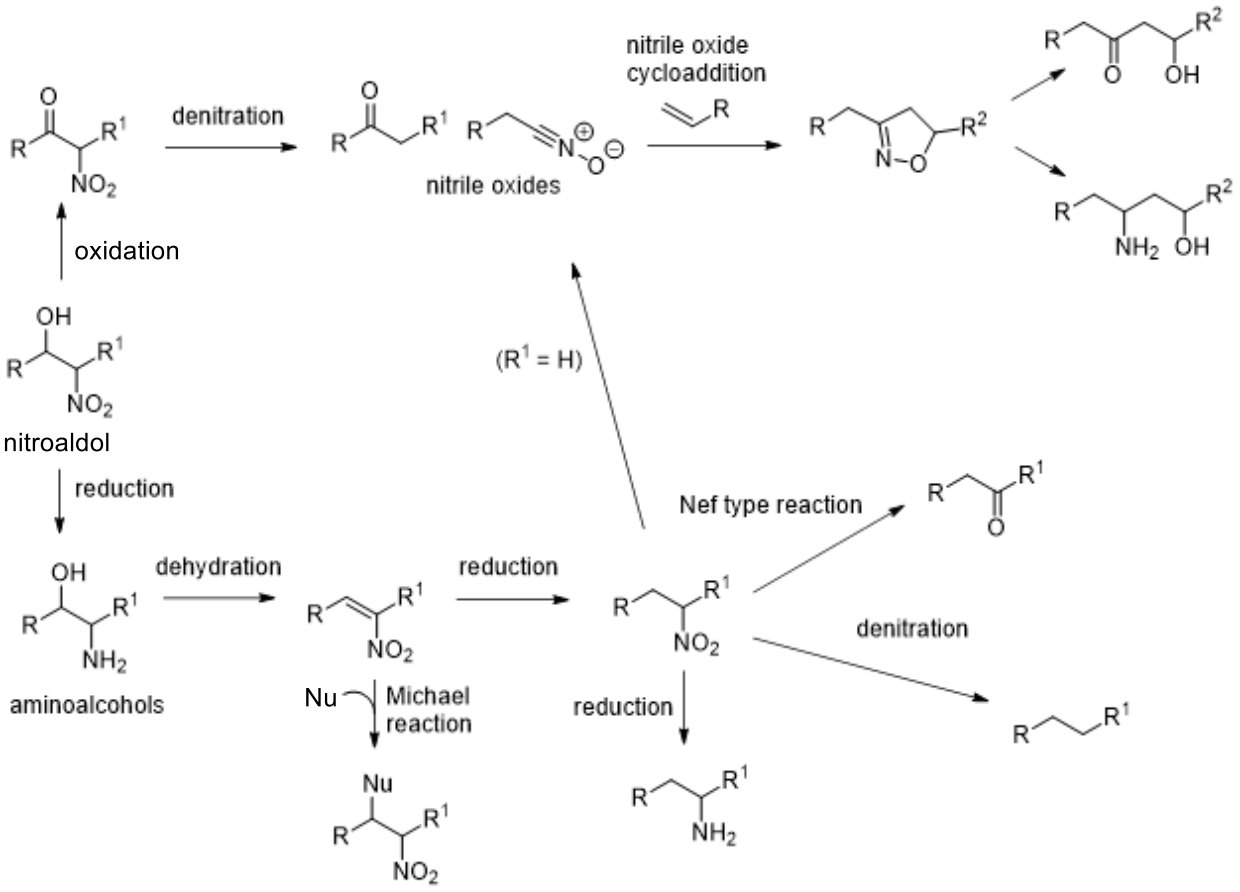




β hydroxynitropropane



methane


denitration
nitrile oxide
cycloaddition
nitrile oxides
oxidation
nitroaldol
reduction
dehydration
aminoalcohols
reduction
Nu
Michael
reaction
(R1 = H)
Nef type reaction
reduction
denitration

Chapter 15

15.0 Benzene and Alkyl Benzene

15.1 Objectives

1. Draw and interpret Lewis structures, line-bond structures and functional groups of benzene and alkyl benzene using IUPAC system of nomenclature.
2. Draw reaction mechanisms.
3. Describe reactions, predicting reactivity, and reaction products.
4. Devise syntheses including steps, reagents, and products including regiochemistry and stereochemistry.

15.2 Introduction

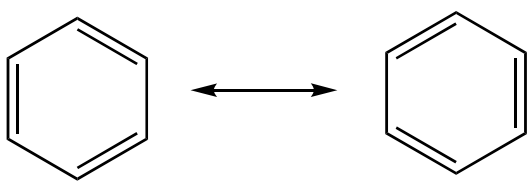
Benzene comes under the category of aromatic compounds. These compounds are different to aliphatic acyclic or cyclic compounds with or without saturation. Aromatic compounds are cyclic compounds with a special type of unsaturation.

Please read chapter 1, section 1.4.3.

Benzene has a molecular formula of C_6H_6. The carbon and hydrogen atoms lie on the same plane. The structure is a planar, regular hexagonal ring of six carbon atoms. The average distance between two adjacent C atoms is 0.1397 nm. This average value lies between the C-C bond length (0.147 nm) and the C=C bond length (0.134 nm), which confirms the existence of a resonance (alternating double and single bond) structure. The distance between C-H is 0.109 nm. All bond angles are 120^0. All C atoms are sp2 hybridized. There are three double bonds and three single bonds in benzene, and they show resonance. The bond order is 1.5.

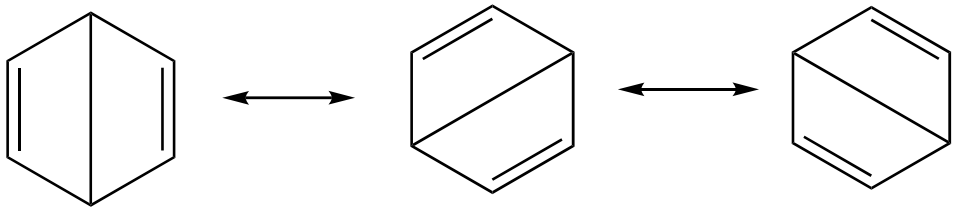
Kekulé formula

This formula suggests the existence of benzene's resonance structure and its stability.



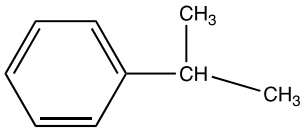
Dewar formula

This formula also suggested the existence of benzene resonance in a different way.



Out of the above two proposals, Kekulé is considered the closest to the actual benzene ring.

When an alkyl side chain is combined with a benzene, it is known as an alkyl benzene. This chapter also covers alkyl benzene preparation and reactons briefly.

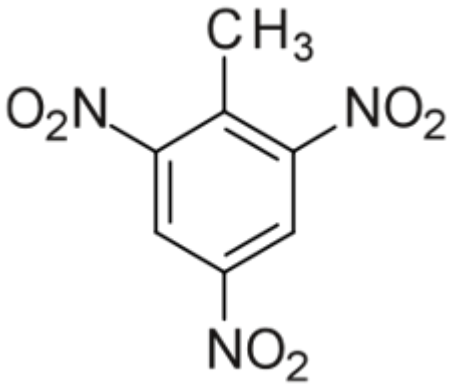


15.3 Nomenclature and Isomerism

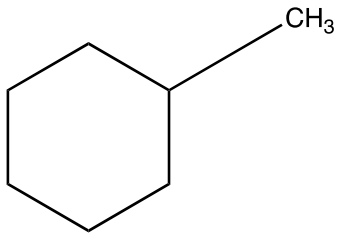
Please refer to the chapter on nomenclature and isomerism and answer the following questions:

1. Naming Compounds – Give the IUPAC names for the following compounds

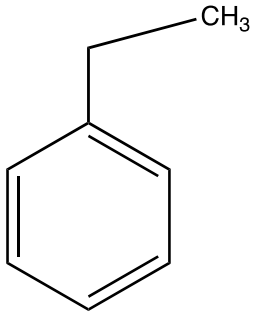
a)



b)



c)

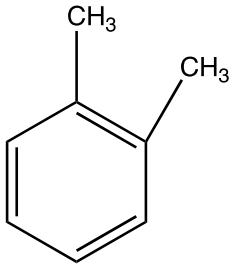


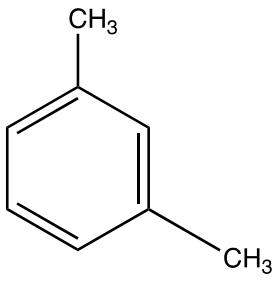
2. Draw the structures of the following compounds

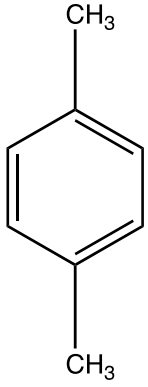
a) Toluene
b) m- xylene
c) m-xylene-4-sulfonic acid

3. **Questions on Isomers**

a) What isomers are the following three compounds?





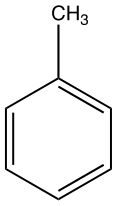


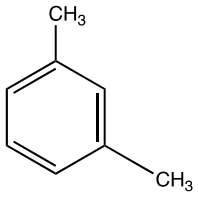
Solutions

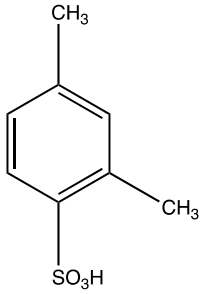
1. **Naming Compounds – Give the IUPAC names for the following compounds**

a) 2-methyl-1,3,5-trinitrobenzene
b) 1-methylbenzene
c) 1-ethylbenzene

2. Draw the structures of the following compounds

a. 

b. 

c. 

3. **Questions on Isomers**

a) They are ortho, meta, para structural isomers.

15.4 Physical Properties

15.4.1 Benzene

Benzene is a colorless, inflammable liquid. It burns with a luminous smoky flame due its high carbon content. Arenes (compounds with aromatic rings structure) are less dense than water. They are not soluble in water. Benzene and many of its derivatives are produced in large scale for uses in high octane gasolines, polymers, insecticides, detergents, dyes, etc.

According to the molecular orbital theory, the delocalized π bonds in benzene are cyclic, delocalized molecular orbitals. The following figure shows this arrangement.

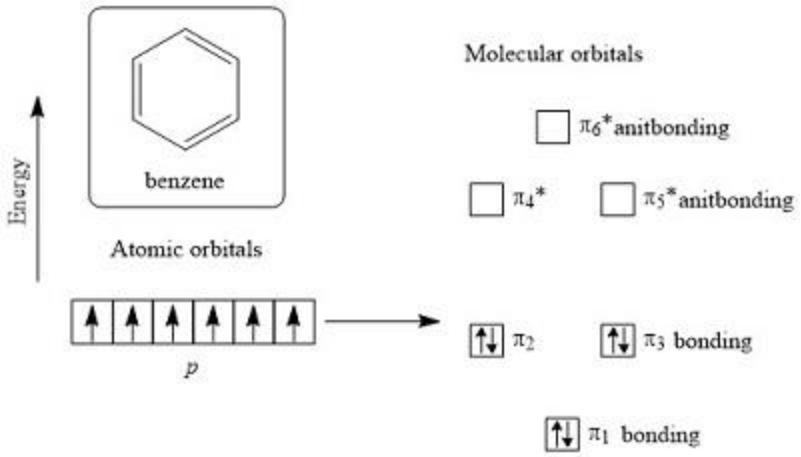


Figure 15.4.1.1: Delocalized π bond electrons in benzene

Hückel's Rule

The aromaticity of molecules is predicted using Hückel's rule. The presence of aromaticity is confirmed when the π electrons in the compound matches (4n+2)π electrons in a closed shell. n is always a positive integer including zero.

Therefore, benzene has one ring. n is one. Therefore, 4n+2 provides 6 π as the answer. Since there are 3 double bonds, the total number of π electrons is 6, thus confirming the aromaticity of benzene. 6 π electrons is known as the Hückel number.

Applying Hückel rule

When n = 0, the final number is 2. Therefore, a closed cycle with 2π electrons can be considered as aromatic. When n=1, the final number is 6. Therefore, a closed ring with 6 π electrons is aromatic like benzene.

15.4.2 Alkyl benzene

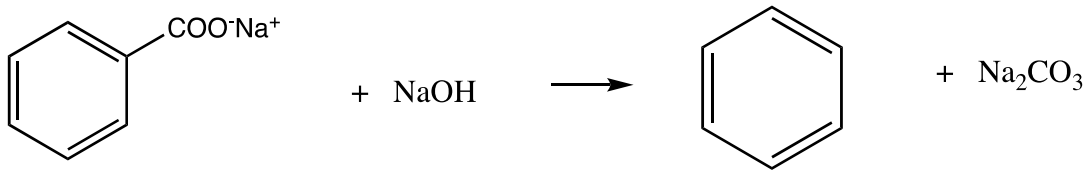
Alkyl benzenes have low polarity and are insoluble in water. They are soluble in organic solvents. The boiling point and the melting point of alkyl benzenes increase with increasing molecular weight. Melting point also depends on the structure of the compound.

15.5 Preparation

15.5. Preparation of benzene

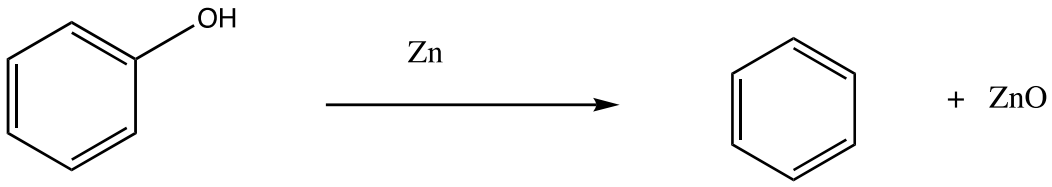
1. From sodium benzoate

When sodium benzoate (salts of benzoic) or benzoic acid is heated with soda lime, benzene is produced through decarboxylation.



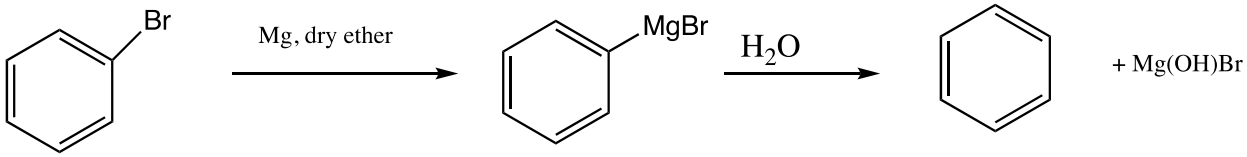
2. From phenol

When phenol vapor is passed over heated Zn dust, a reduction occurs, and benzene is produced.



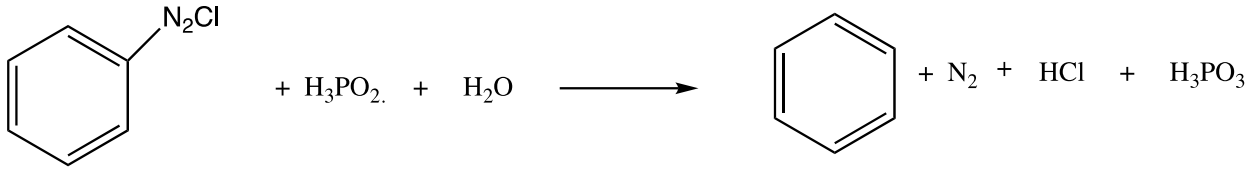
3. From phenyl magnesium bromide

Phenylmagnesium bromide undergoes an addition reaction with water to produce benzene.



4. From diazonium salt

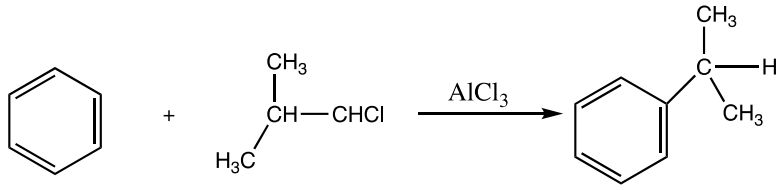
A reaction between benzene diazonium salt with hypophosphorous (H_3PO_2) undergoes reduction to yield benzene.



15.5.2 Preparation of alkyl benzene

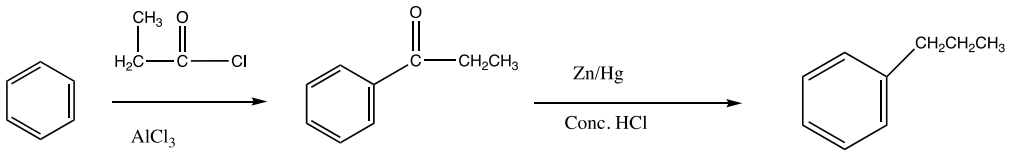
1. Friedel-Crafts reaction

Benzene rings undergo Friedel-Crafts reaction with an alkyl chloride in the presence of $AlCl_3$ catalyst to produce alkyl benzene.



2-chloro-propane isopropyl benzene

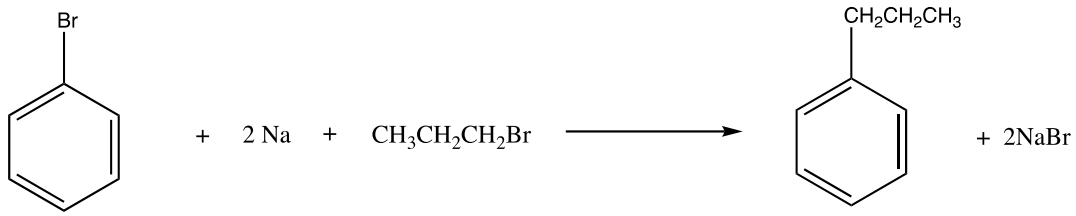
Benzene also undergoes Friedel-Crafts reaction with acyl chloride to produce alkyl benzene in the presence of Zn/Hg in concentrated HCl.



propiophenone propyl-benzene

2. Wurtz-Fittig reaction

A halogen derivative of benzene upon heating for several hours with alkyl halide and sodium will produce alkyl benzene and sodium halide.



15.6 Reactions

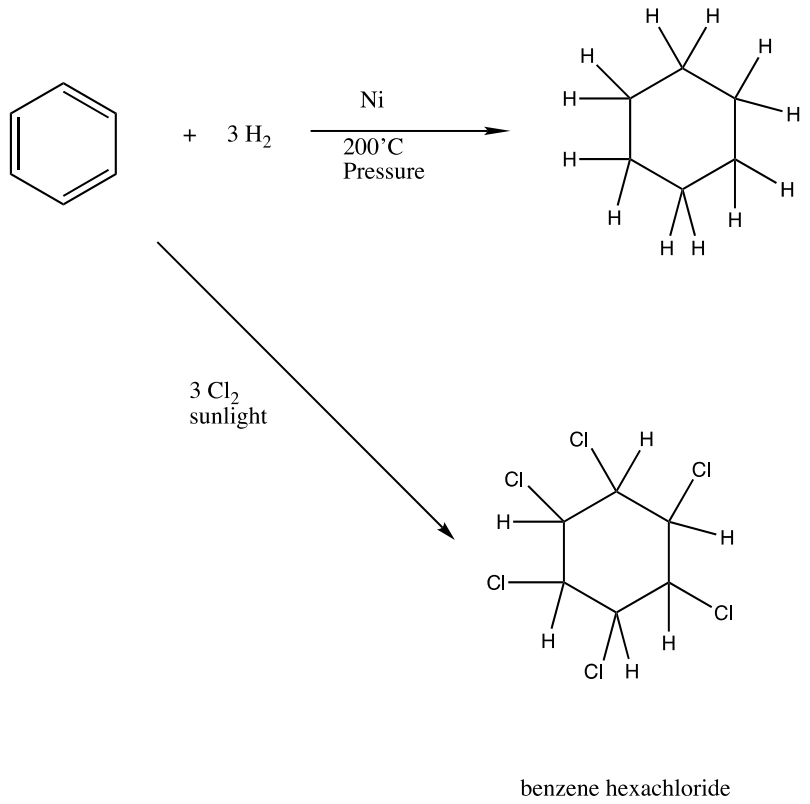
15.6.1 Reactions of benzene

Benzene does not undergo addition reactions easily. Such reactions need high temperatures and pressures.

1) Addition of hydrogen

Benzene undergoes hydrogenation in the presence of nickel at high temperatures to produce cyclohexane.

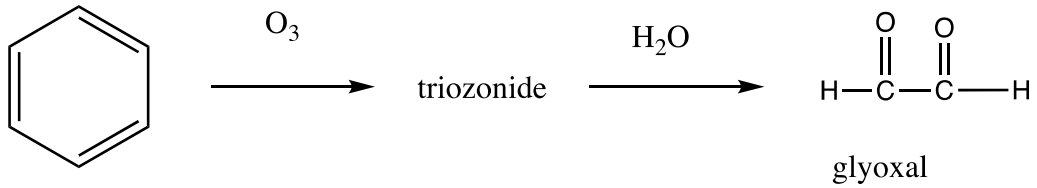
2) Addition of chlorineIn the presence of sunlight but in the absence of a catalyst, addition of chlorine to benzene produces benzene hexachloride.



benzene hexachloride

3) Addition of ozone

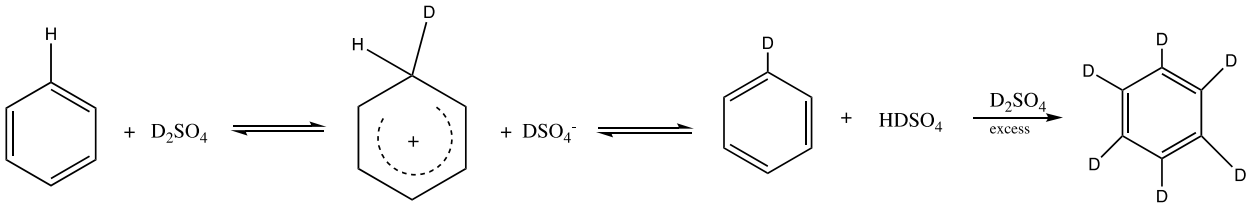
Ozone reacts slowly with benzene to produce triozonide, which in turn produces dialdehyde glyoxal on decomposition with water in the presence of Zn.



glyoxal

4) Substitution with deuterium atoms

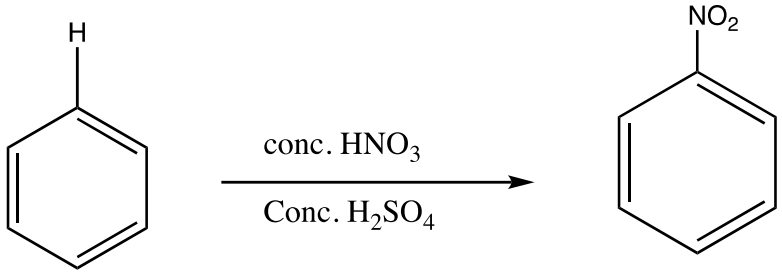
By reacting benzene with deuteriosulfuric acid, ring hydrogens can be replaced with deuterium ($_1H^2$) atoms. This substitution can be carried out for many aromatic compounds.



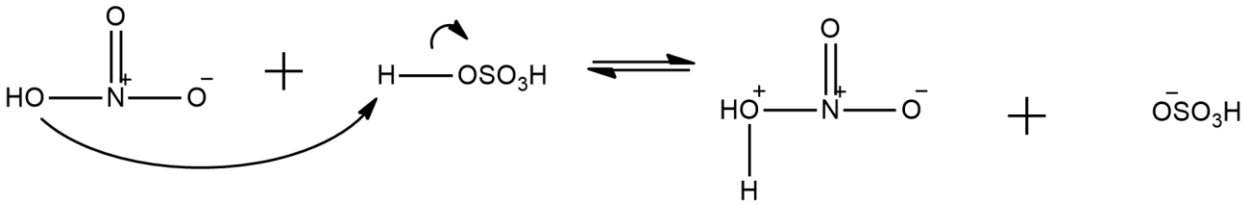
5. Substitution with NO_2

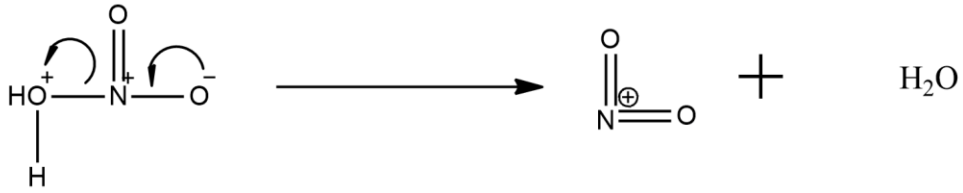
Nitration can be performed with many aromatic compounds irrespective of them being high or low reactive.

Benzene and other low reactive aromatic compounds are treated with concentrated nitric and sulfuric acids for nitration. For other highly reactive compounds nitric acid alone (or in water or in acetic acid) will produce nitration.



The NO_2^+ ion (nitronium ion) is the attacking group in this reaction.

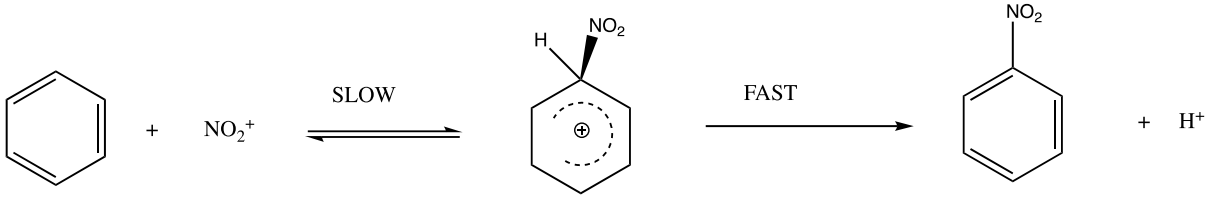




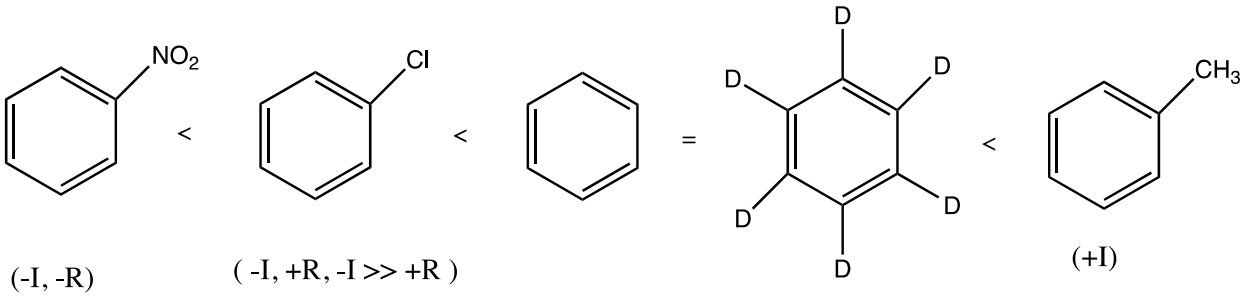
There is experimental evidence to confirm that nitronium ion is the attacking group. They are,

- Raman spectrum evidence (peak at 1400 cm^{-1} attributed to nitronium ion)
- Depression of freezing point of sulfuric acid confirming the production of ions including the nitronium ion
- X-ray studies showing the presence of nitronium salts making this nitronium ion available for attacking

- The rate of reaction dependency on nitronium ion and not on other ions
- The rate determining step is the formation of carbonium ion.



The order of increasing rate of nitration is,



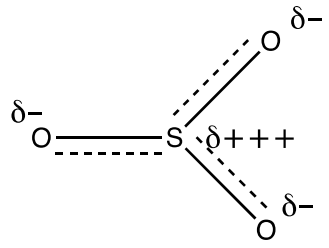
(-I, -R) (-I, +R, -I >> +R) (+I)

6. Substitution with SO_3H (sulfonic acid)

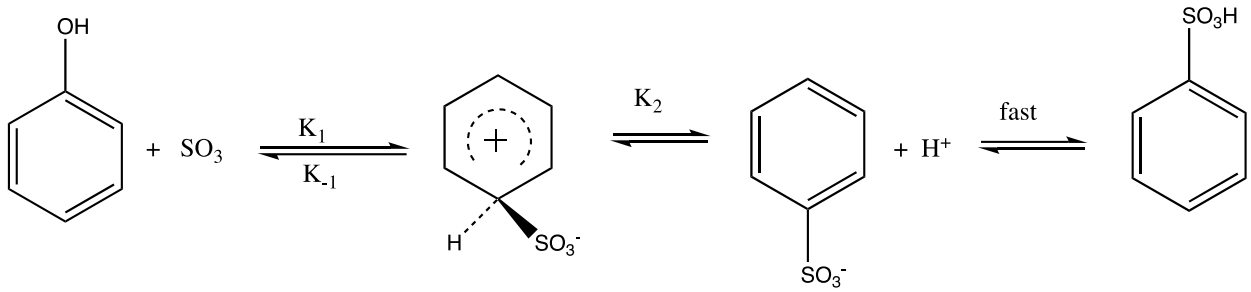
When benzene is reacted with fuming sulfuric acid, sulfonation happens.

$$2H_2SO_4 \rightleftharpoons SO_2 + H_3O^+ + HSO_4^-$$

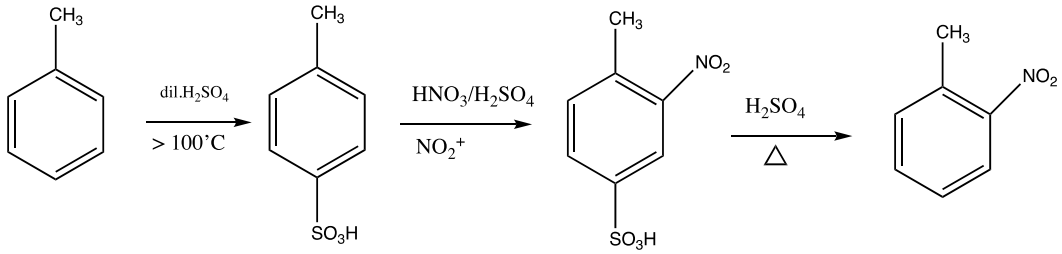
The attacking electrophile SO_3 gets attached to the ring from the S atom.



This reversible reaction pathway is as follows:



The reversibility of the above sulfonation reaction is used to block certain positions of the benzene ring in reactions and later HSO_3 is replaced with an H atom as shown below:

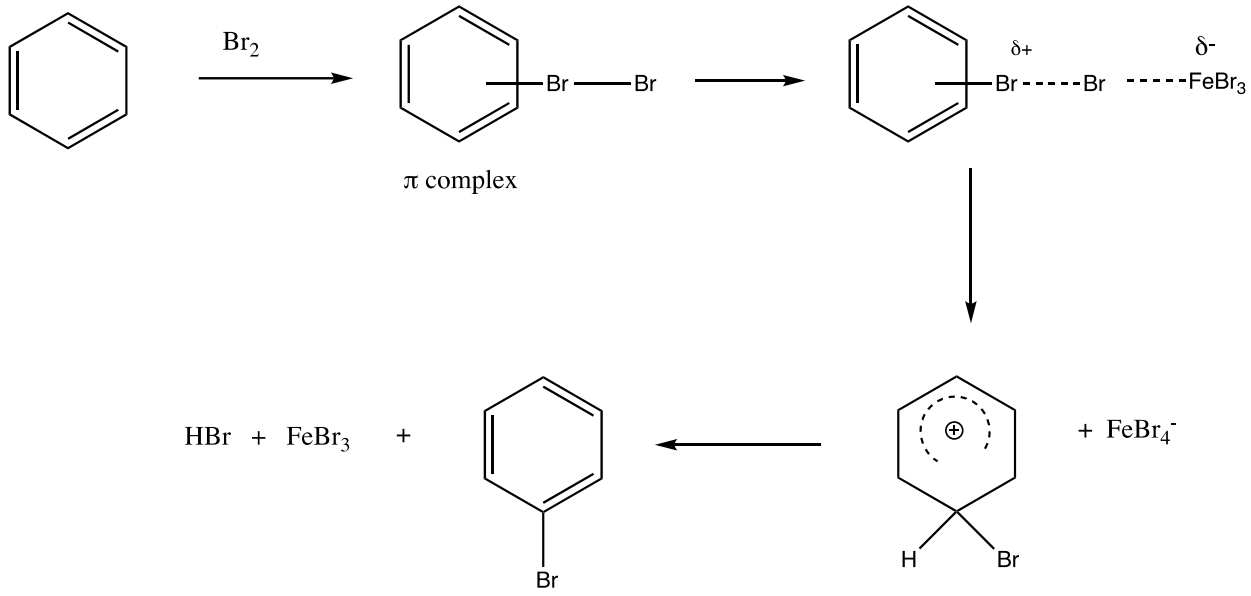


7. Substitution with halogens

In the presence of a Lewis acid such as $AlCl_3$ or $FeBr_3$, benzene undergoes substitution with halogens to produce the relevant halo benzene.

The order of the reactivity of halogens are as follows:

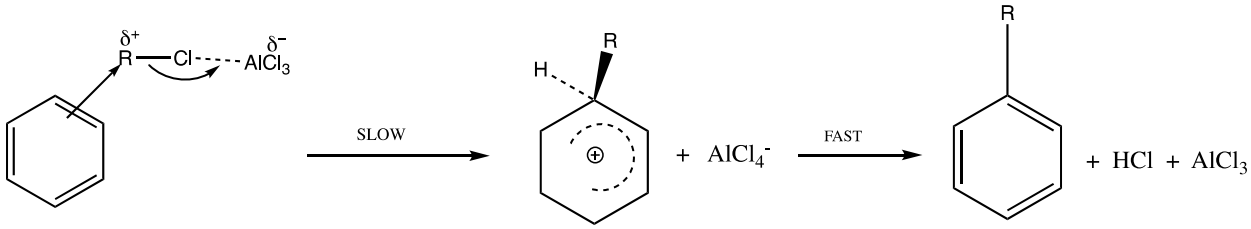
$$F_2 > Cl_2 > Br_2 > I_2$$



8. Substitution with an alkyl group – Friedel Crafts Alkylation

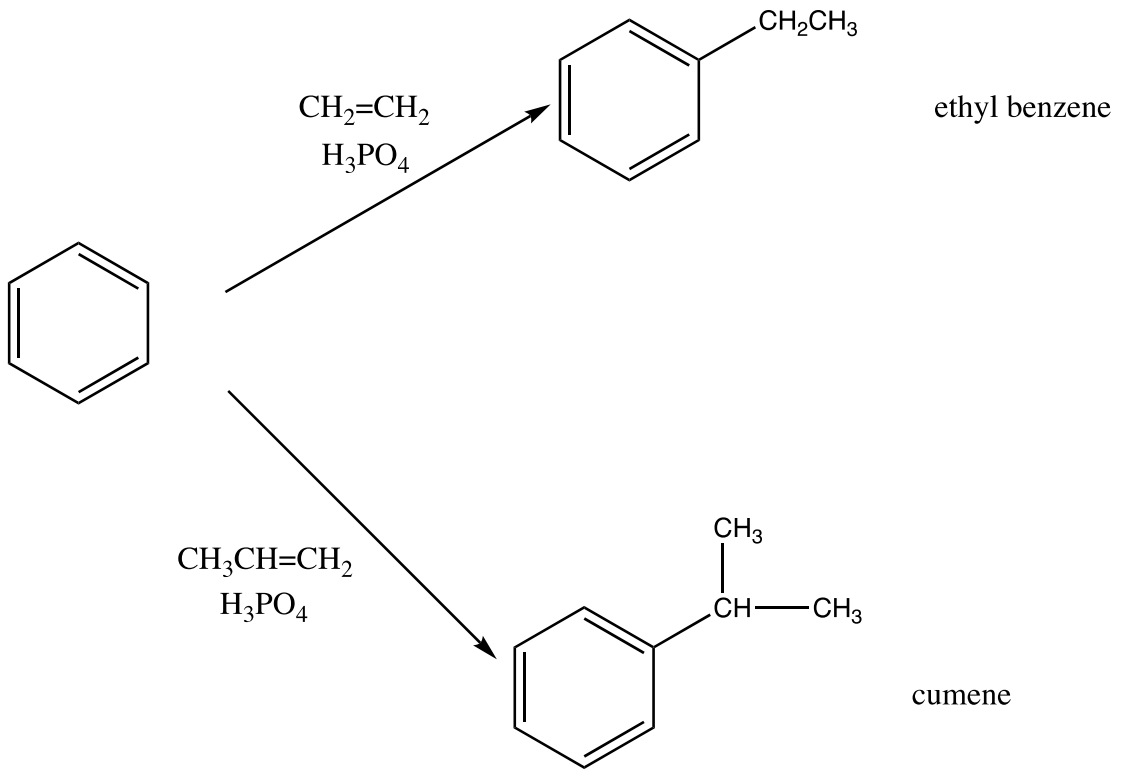
Described under 15.5.2 – Reaction 1.

Mechanism



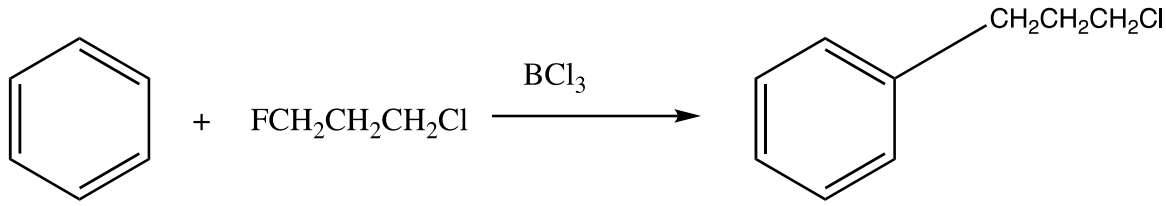
This reaction cannot be performed for nitrobenzene since -NO_2 group deactivates the ring.

Alkenes and alcohols also can be used in this reaction in lieu of alkyl halides for alkylating aromatic compounds. The presence of protic acids such as H_3PO_4, H_2SO_4, HF, BF_3 assist in protonating alkene or alcohol.

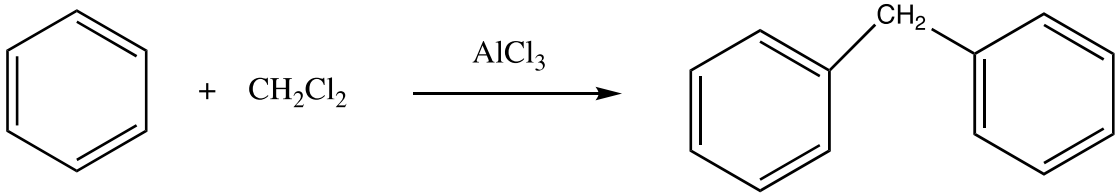


The order of the reaction when alkyl halides are used is as follows:

$$F > Cl > Br > I$$



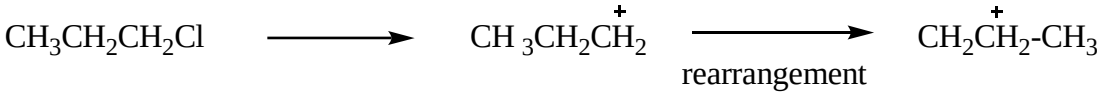
When di or tri halides are used and if all halides are the same, the reaction will proceed to produce a combination of more than one aromatic ring as follows:



Issues in using Friedel-Crafts reaction in alkylation:

1. Mostly di and poly products are yielded due to the activating nature of alkyl groups. In order to obtain monosubstituted products, excess arene may have to be used or promote the presence of electron-withdrawing substituents.
2. Rearrangement of the final product is a possibility in this reaction. Therefore, when n-propyl bromide is reacted with benzene, the predominant product is isopropyl benzene (cumene) because n-propyl benzene also has the tendency to rearrange and produce isopropyl benzene.

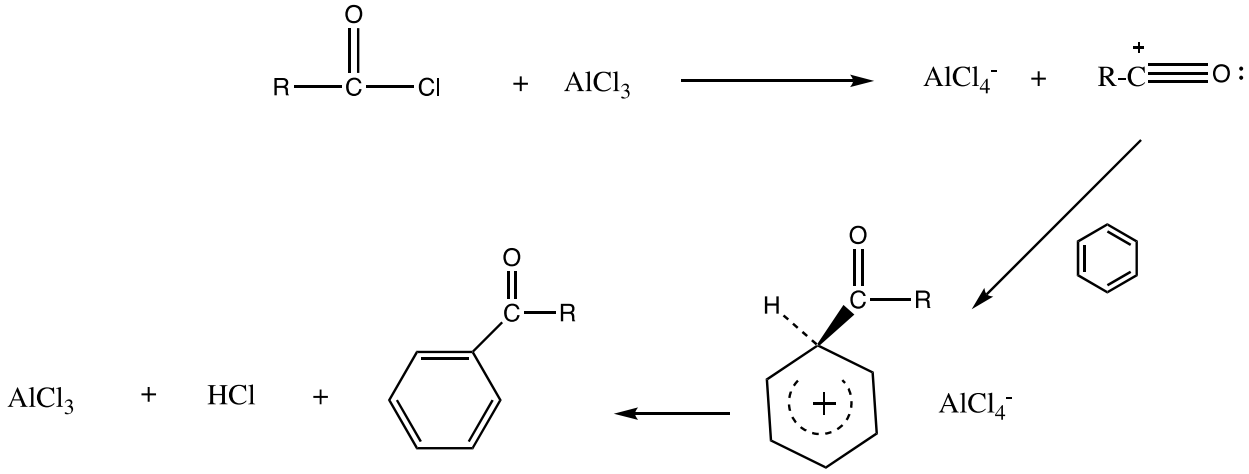
e.g.



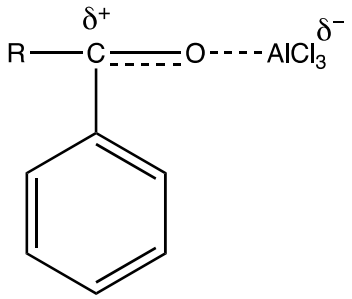
Therefore, n-alky benzenes are mostly prepared by acylation followed by Clemmensen or Wolff-Kishner reduction.

9. Substitution with an acyl group – Friedel-Carfts acylation

This reaction is similar to the previous alkylation. The effective electrophile is acylium ion ($RC^+=O$). The final product is an aryl ketone. Acylation reagents commonly used are acid halides, RCOCl, or anhydrides.



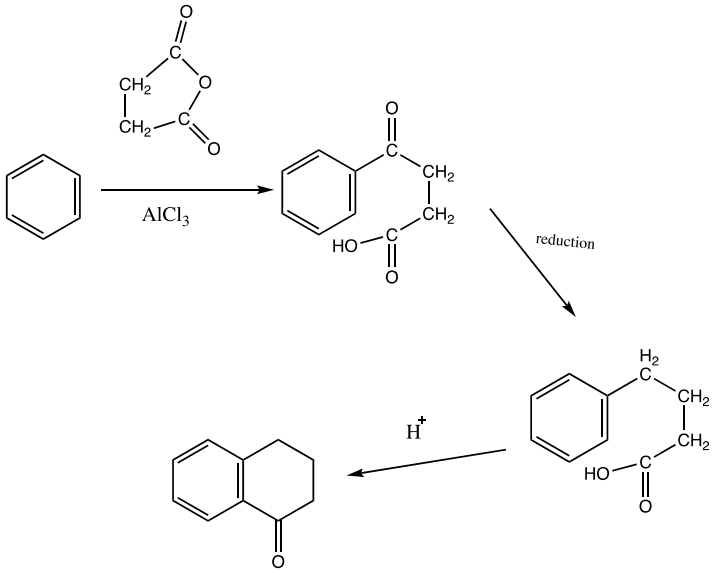
Unlike alkylation, acylation requires more than one mole of Lewis acid in the reaction. This is because much of the Lewis acid forms a complex with the product ketone.



Since the ketone product is less reactive, unlike alkylation, acylation will not lead to polyacylation.

This reaction is useful in preparing polycyclic compounds.

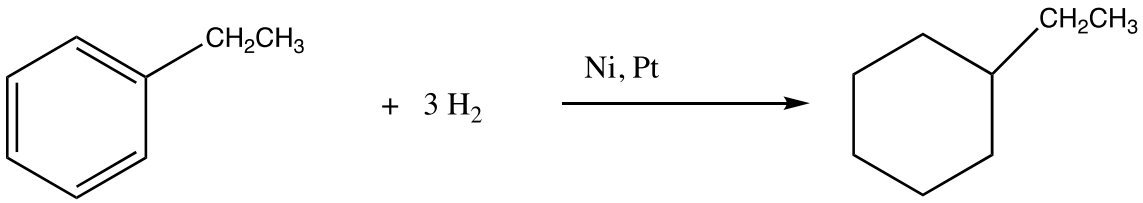
e.g.



15.6.2 Reactions of alky benzene

1. Hydrogenation

Alkyl benzenes undergo hydrogenation in the presence of a catalyst.

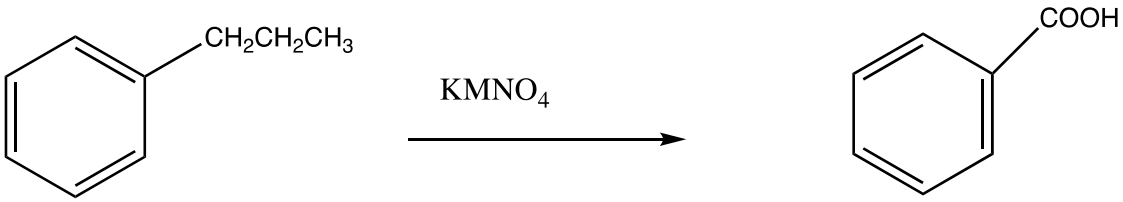


ethyl benzene

ethyl cyclohexane

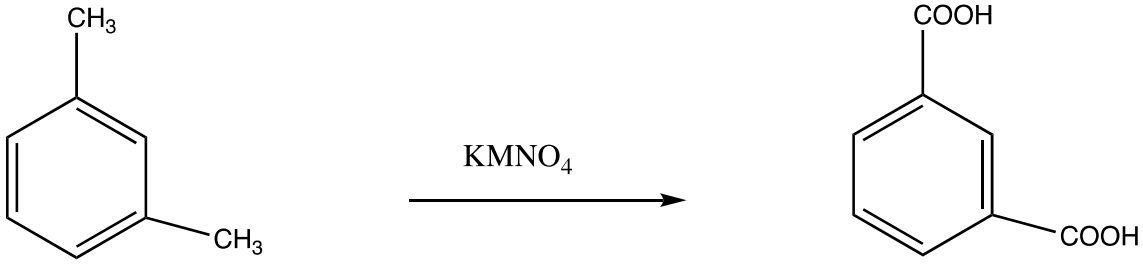
2. Oxidation

Alkyl benzene undergoes oxidation in the presence of generally used oxidizing agents such as $KMnO_4$, $K_2Cr_2O_7$, etc. The alkyl side chain will become COOH group when oxidized. This is a useful reaction to produce aromatic carboxylic acid. This reaction also can be used to identify alkyl benzenes.



propyl benzene

Benzoic acid

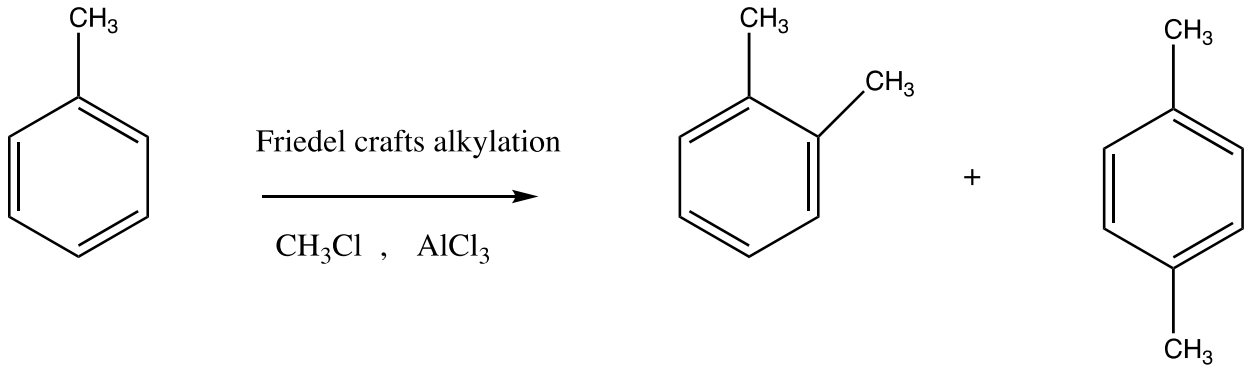


xylene

Isophthalic acid

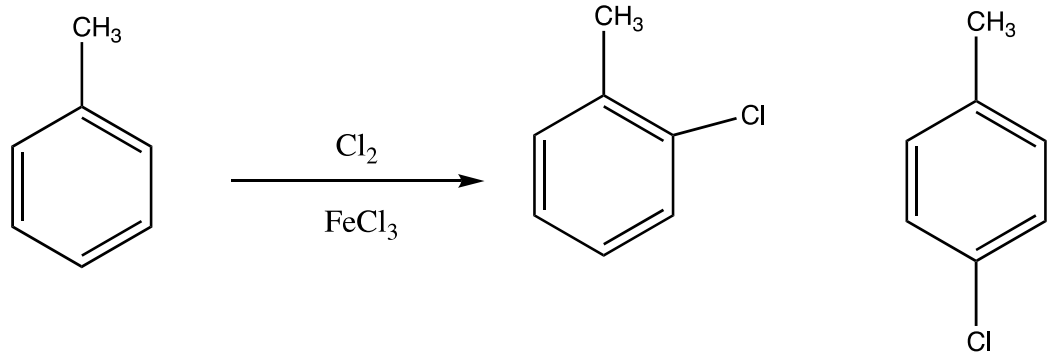
3. Electrophilic aromatic substitution

Due to the ring activating nature of the alkyl group, when it is attached to a benzene ring, ortho and para positions are activated for benzene to undergo another substitution (the first being the addition of the original alkyl group that replaced one H atom).



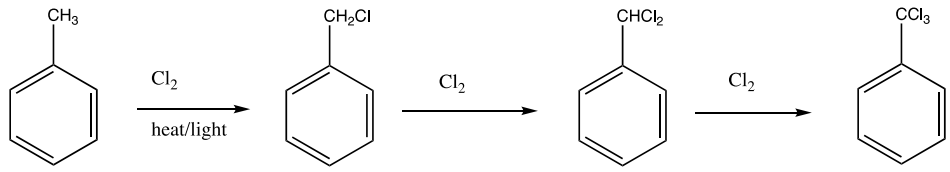
4. Catalytic substitution

In the absence of light and in the presence of Lewis acid catalyst, substitution of halogens occurs at ortho and para positions.



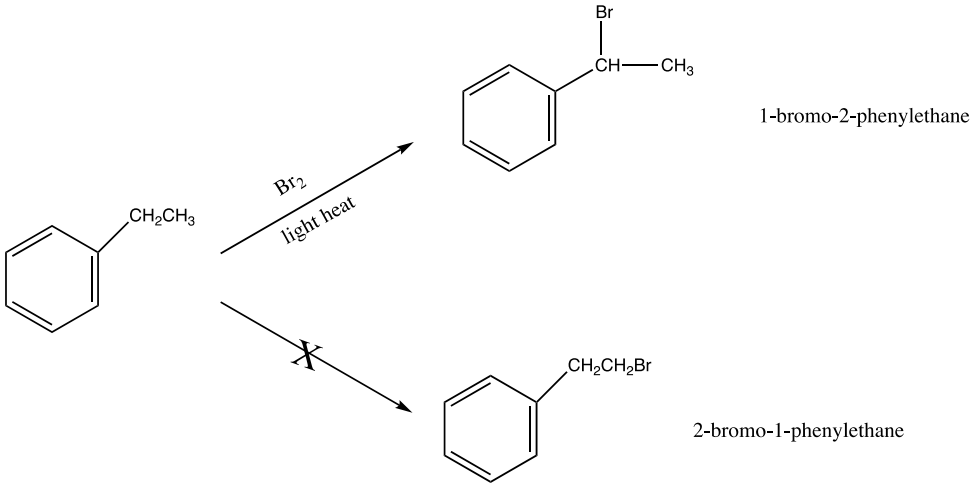
5. Side-chain halogenation

In the presence of heat and light, side-chain chlorination (substitution) happens. The following reaction shows halogenation of toluene.



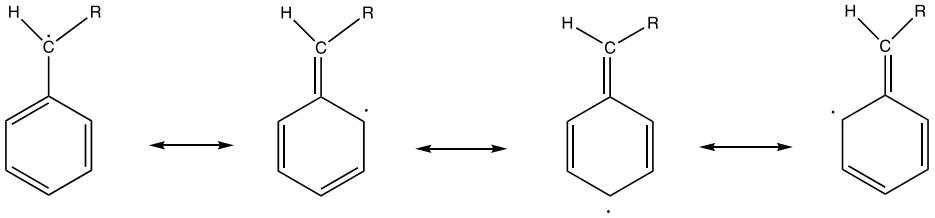
The mechanism of the above reaction is the same as the halogenation of alkanes.

When the chain is longer than one carbon atom, the chlorination happens only at the carbon immediately attached to the benzene (benzylic position).



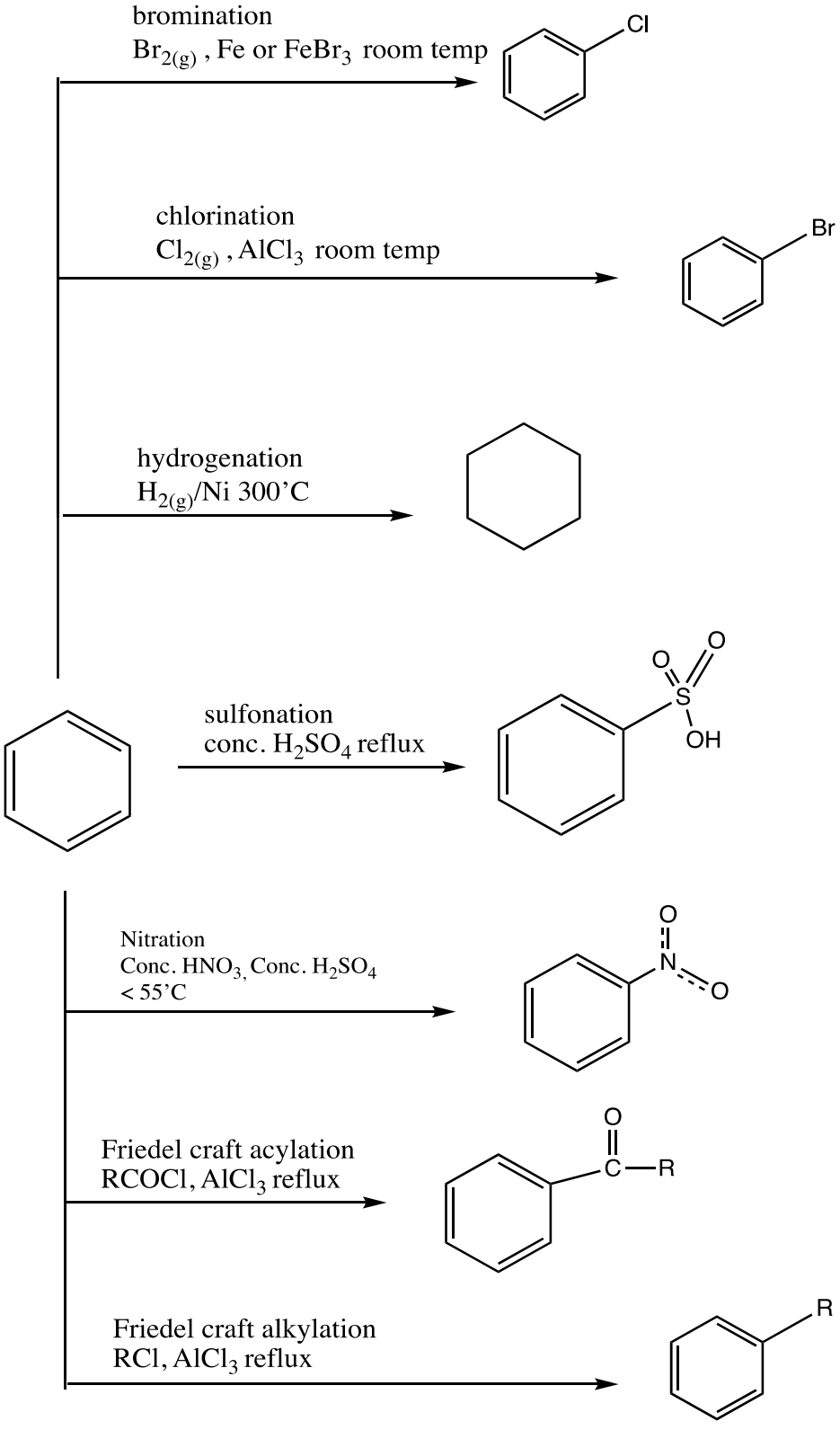
As indicated above, the only product formed is 1-bromo-1-phenyl ethane.

The reason for the reaction to occur only at the benzylic position is because of the resonance structure (highly stabilized) of the free radical (which is formed during the reaction process).



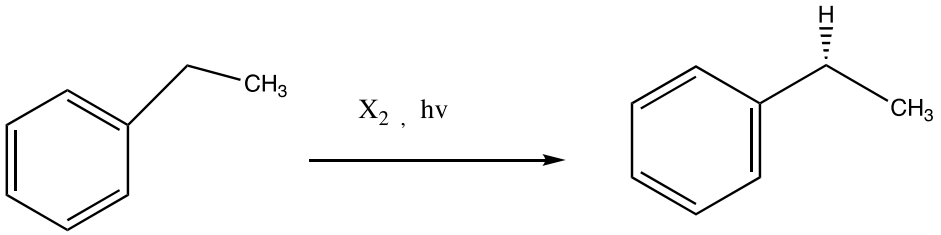
15.7 Summary of Reactions

15.7.1 Summary of benzene reactions

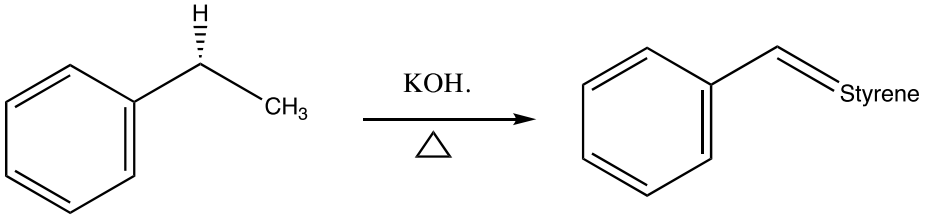


15.7.2 Summary of alkyl benzene reactions

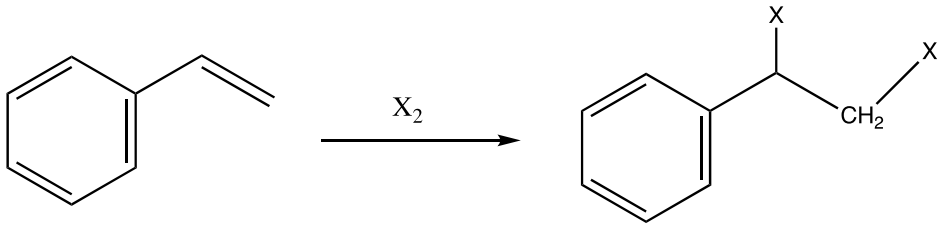
Reaction of Alkylbenzene Side Chain



Halogenation



Elimination



Additions to alkenylbenzenes

Chapter 16

16.0 Benzene Derivatives

16.1 Objectives

1. Draw and interpret Lewis structures, line-bond structures and functional groups of benzene derivatives using IUPAC system of nomenclature.
2. Draw reaction mechanisms.
3. Describe reactions, predicting reactivity, and reaction products.
4. Devise syntheses including steps, reagents, and products including regiochemistry and stereochemistry.

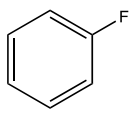
16.2 Introduction

The final chapter of this book covers only a selected number of benzene derivatives.

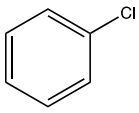
16.3 Nomenclature and Isomerism

The following is a list of most common benzene derivative compounds:

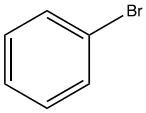
Halogen Containing



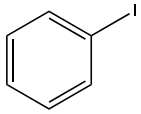
Flurobenzene



Chlorobenzene

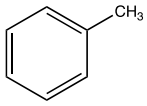


Bromobenzene

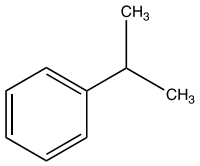


Iodobenzene

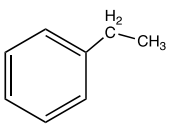
Hydrocarbon Derivatives



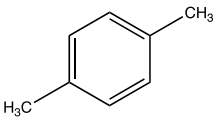
Toluene



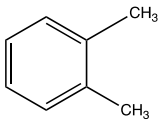
Cumene



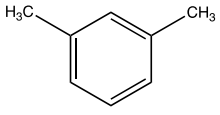
Ethylbenzene



para-xylene

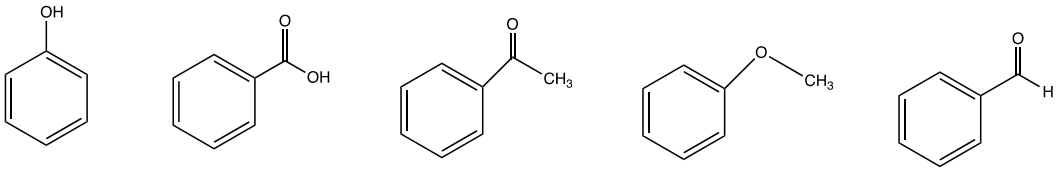


ortho-xylene



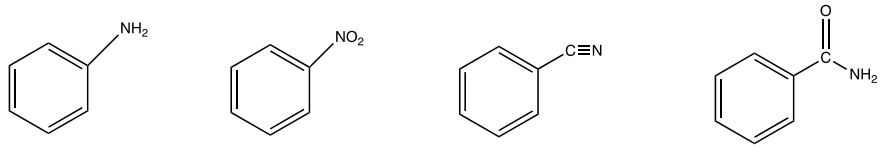
meta-xylene

Oxygen Containing



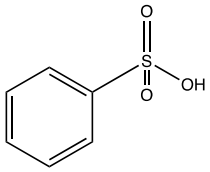
Phenol Benzoic acid Acetophenone Anisole Benzaldehyde

Nitrogen Containing



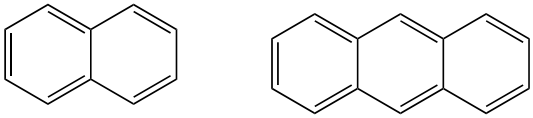
Aniline Nitrobenzene Benzonitrile Benzamide

Sulfur Containing



Benzenesulfonic acid

Polyaromatic



Naphthalene Anthracene

All benzene derivatives have one or more H atoms substituted by another atom, a group or a ring. The term phenyl group is used when one H atom is replaced by another atom or a group.

Therefore, if Ph denotes the phenyl group, benzene can be written as Ph – H, nitrobenzene as Ph – NO2, chlorobenzene as Ph-Cl, etc.

Most of these derivatives have a systematic name (IUPAC) and a common name.

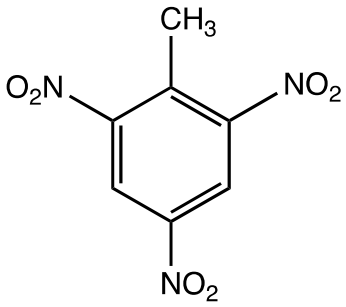
The naming of benzene is carried out according to the following formula:

The order of the names of benzene derivative:

1. Mention the position number of the substituent (e.g. 1, 2, 3, 4, etc.), followed by the name of the substituent
2. If there are more than one substituent of the same type, then mention the position number followed by di, tri, tetra, penta, etc., followed by the name of the substituent
3. Once the substituents are named with the correct numbering, end the name with benzene
4. If there are different substituents, follow the rules 1 and 2, but use the priority order discussed in the chapter on nomenclature to decide the parent name of the phenyl group. The order of naming the substituents must follow the alphabetical order. In such instances, the name will not end with benzene, but with the selected parent name.
5. Whilst the compounds are mostly named following the rules 1, 2, and 3, at times when more than one substituent is attached to the phenyl ring, the names carry ortho-, meta-, and para- prefixes to identify the position of the substituent groups.

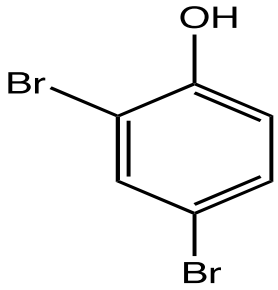
e.g.

1.



Systematic or IUPAC name for the above compound is 2-methyl-1,3,5-trinitrobenzene. The common name is 2,4,6-trinitrotoluene.

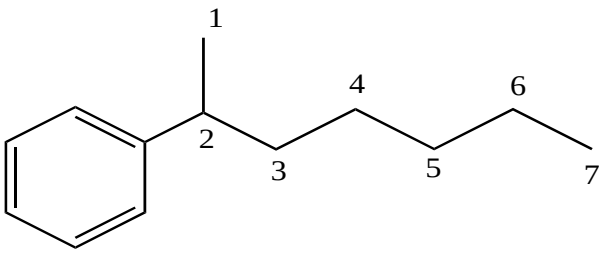
2.



The name of the above compound is 2,4 -dibromo phenol. This is used as the IUPAC name as well as the common name. Such sharing of the same terms is allowed for phenol, benzoic acid, and benzaldehyde.

N.B.: Whilst the term phenyl can be used in lieu of the term benzene (e.g. chlorobenzene can also be named as phenyl chloride), the phenyl term is used when the attached substituent has six or more carbons (more carbon atoms than benzene).

e.g.



2-phenylheptane – naming has been done following the longest chain. Phenyl is attached to the second position of the longest aliphatic chain.

Benzene group nomenclature is another way to name the derivatives of benzene. e.g. chlorobenzene can be named as benzyl chloride.
Please read the chapter on isomers to refresh your understanding of different types of isomers.
For a broader understanding on the isomers of benzene derivatives, please read the article titled, “Benzene and its Isomers - How many Structures can we Draw for C_6H_6 by visiting the following link:

https://www.ias.ac.in/article/fulltext/reso/016/12/1146-1151

16.4 Physical Properties

Aryl Halides – chlorobenzene, bromobenzene, iodobenzene

These are oily liquids. The boiling point increases with the increasing volume of the halide. These are insoluble in water and form a separate layer. These are also denser than water.

Nitrobenzene

Nitrobenzene is a yellowish, oil, aromatic compound. It gives out an almond-like odor. This is mainly used in the manufacture of aniline.

Phenol

Phenol is a white crystalline solid. It has the smell of disinfectants.

Aniline

Aniline is a colorless/brown, oily liquid. It turns dark on exposure to air and light. It has a distinct amine odor.

Toluene

Toluene is a colorless, flammable, toxic liquid with aromatic odor.

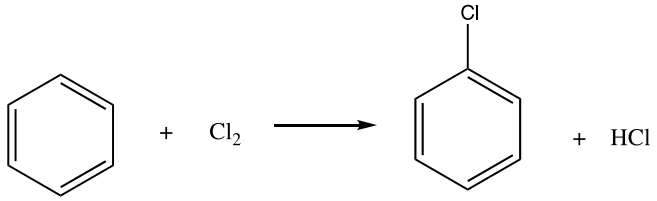
Xylene

Xylene is a clear/colorless, flammable liquid at room temperature. It has an aromatic odor similar to benzene or toluene.

16.5 Preparation of Benzene derivatives

Aryl halides

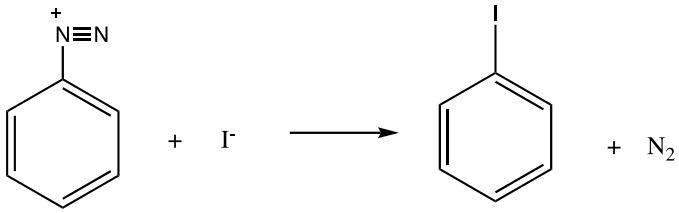
Benzene in the presence of aluminum chloride or iron (which gets converted to iron chloride during the reaction) at room temperature will undergo chlorination.



A similar reaction happens in the bromination of benzene in the presence of aluminum bromide or iron.

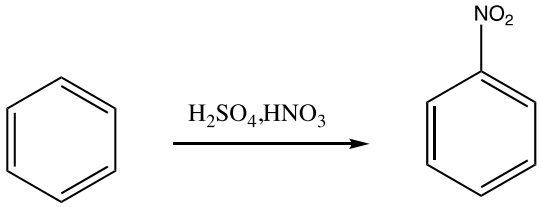
In order to form iodobenzene, benzene and iodine are heated under reflux in the presence of concentrated nitric acid.

Iodobenzene is normally made from benzenediazonium chloride solution.

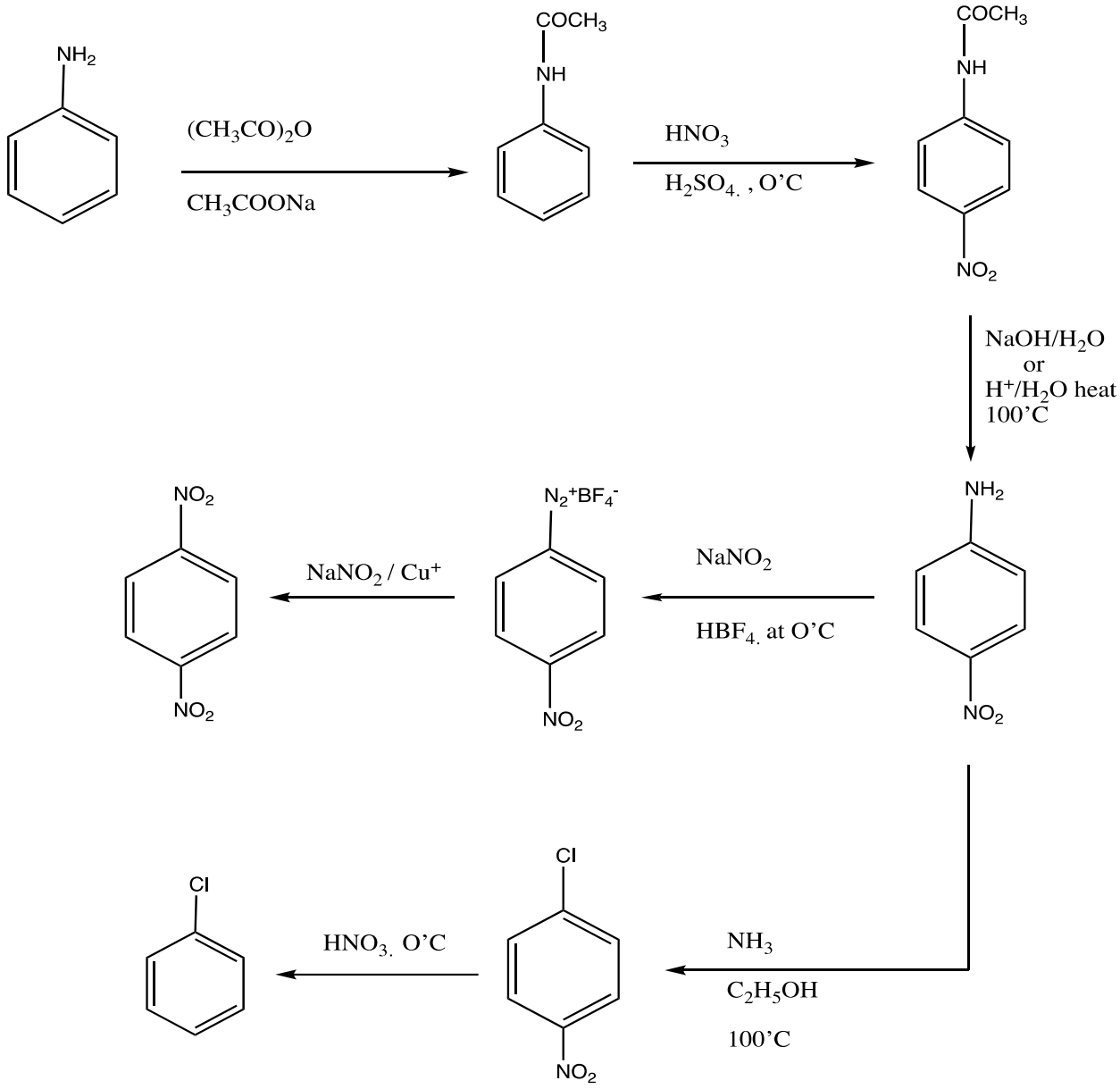


Nitrobenzene

Nitrobenzene is prepared by mixing with concentrated H2SO4 and concentrated HNO3.

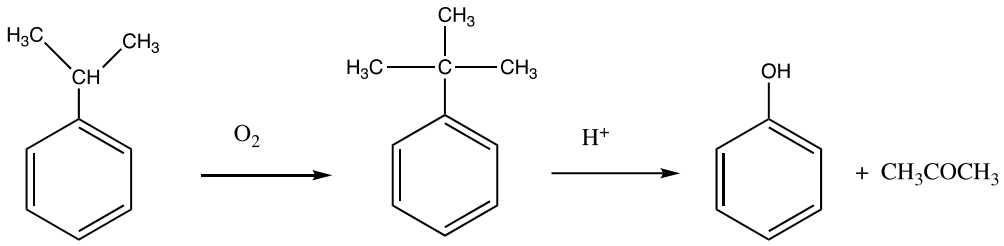


Other methods with benzene derivatives:

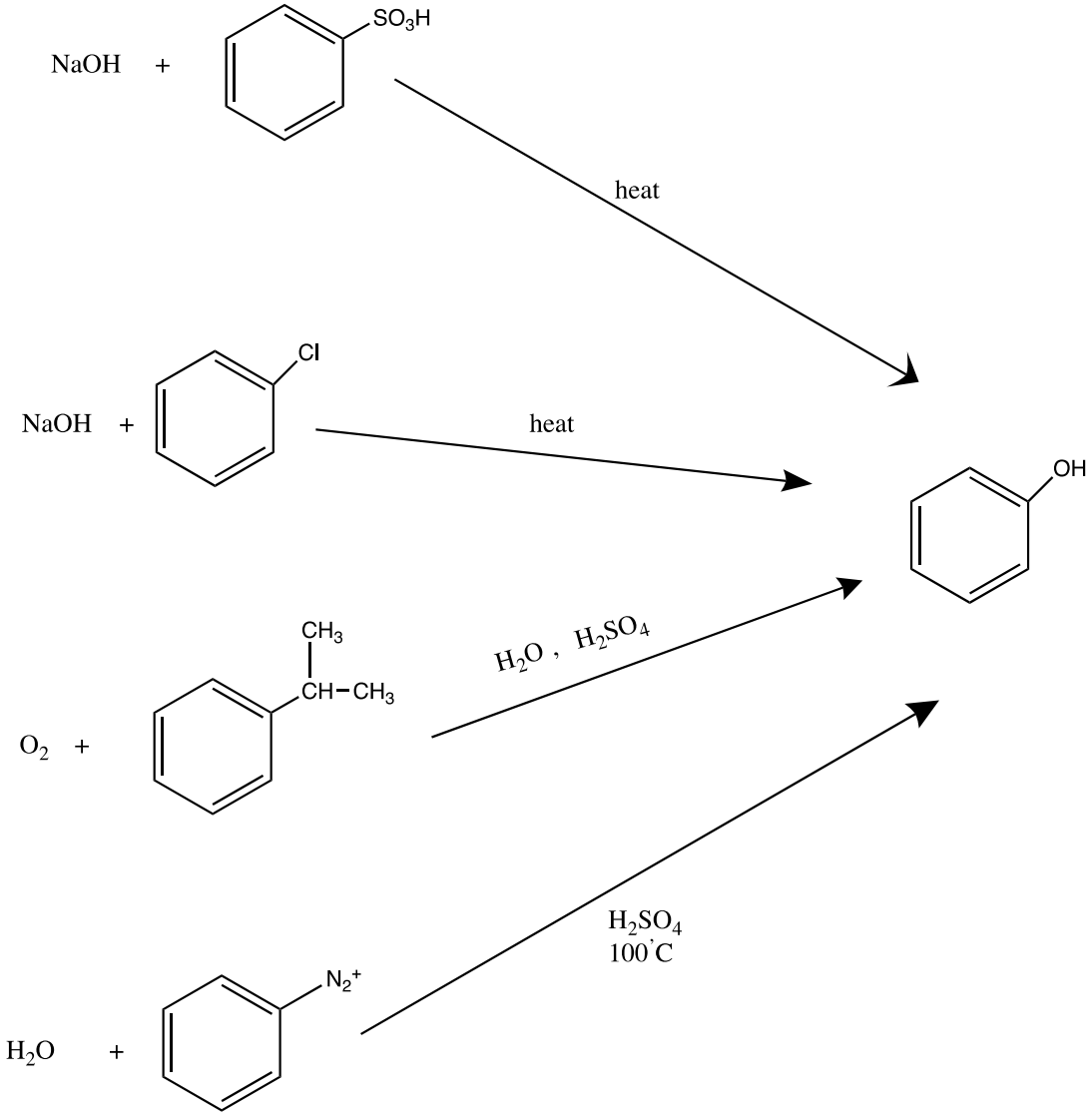


Phenol

A commercial method of preparing phenol is by oxidizing cumene to its hydroperoxide, which on reaction with acid decomposes to phenol and acetone.



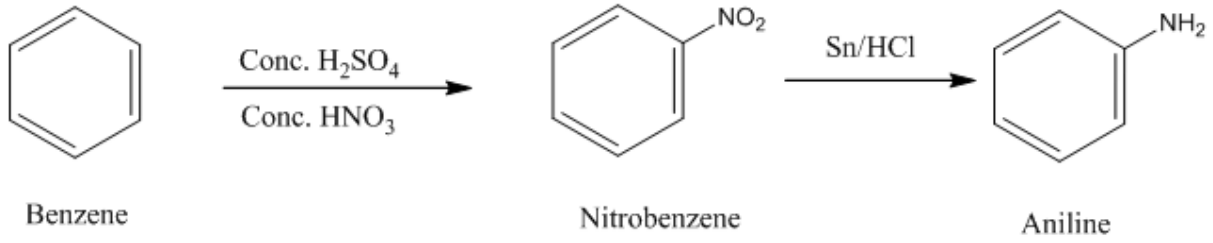
The following is summary of phenol preparatory methods:



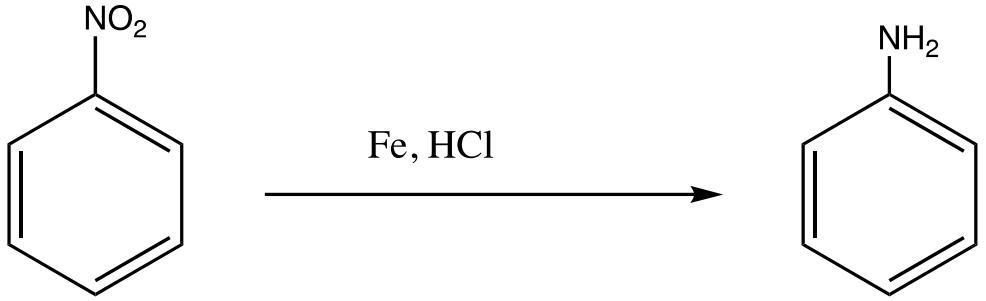
Aniline

Some preparation methods are given below:

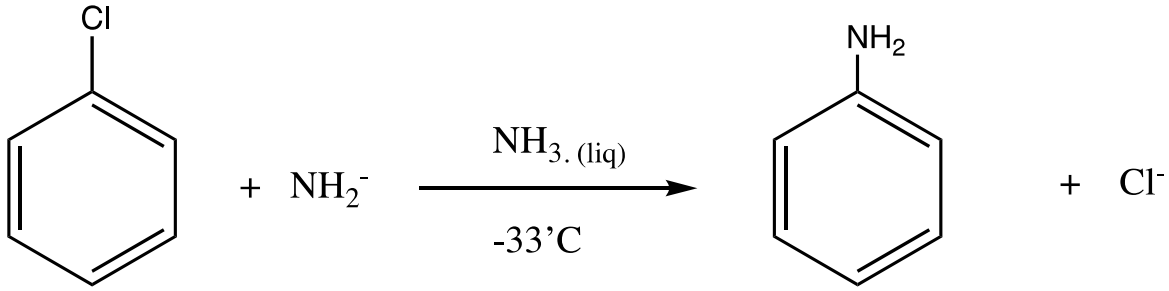
1. With concentrated sulfuric and concentrated nitric acid followed by Sn/HCl.



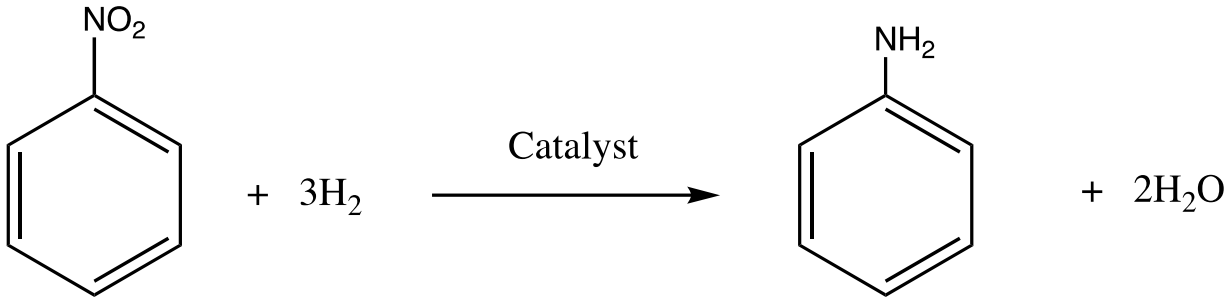
2. With Fe/HCl

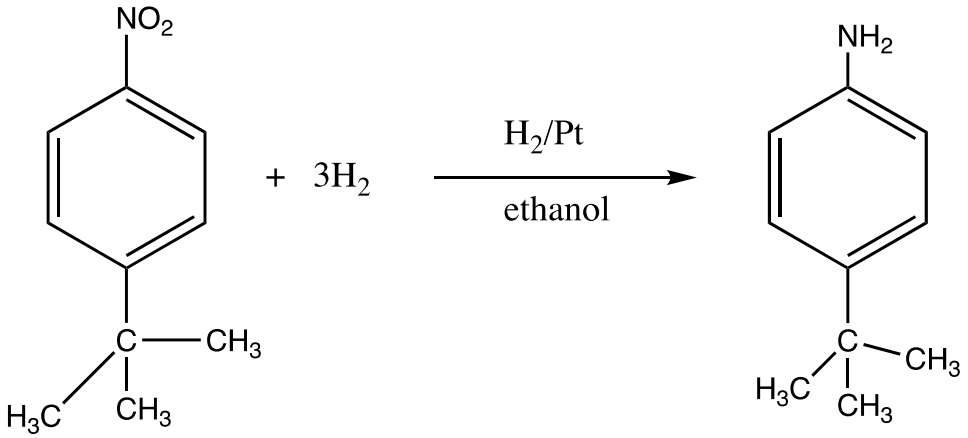


3. With liq. NH3 at low temperature



4. Hydrogenation with a catalyst

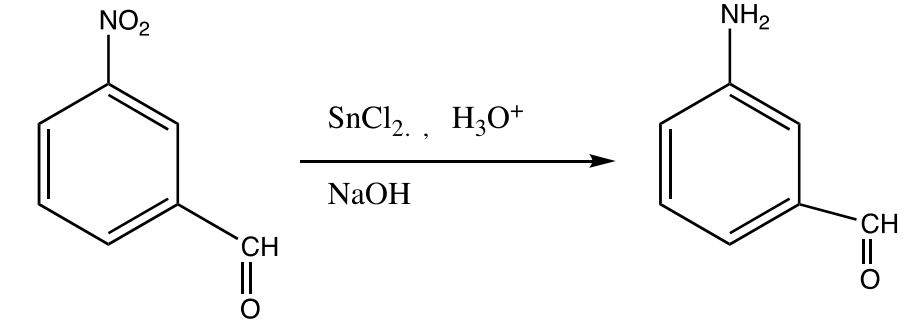




p-tert-butyl nitro benzene

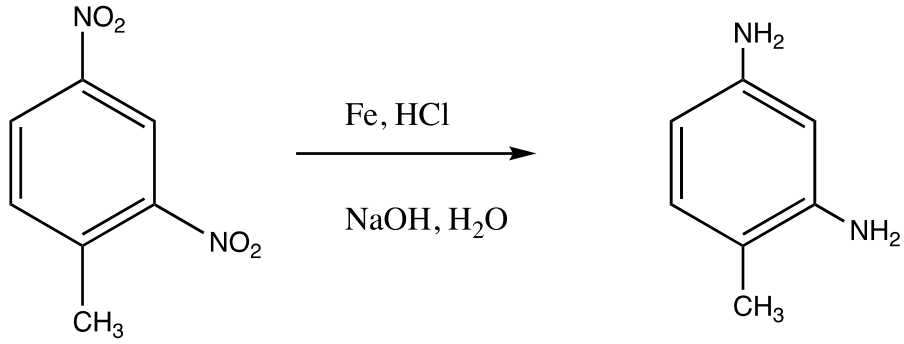
p-tert-butyl nitro aniline

5. With $SnCl_2$/acid and NaOH



p-nitro benzaldehyde

p-amino benzaldehyde

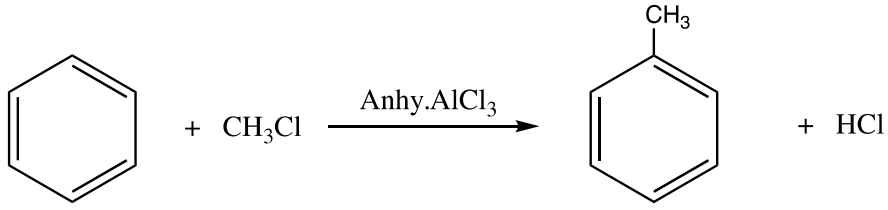


2,4 dinitro toluene

2,4 diamine toluene

Toluene

1. Friedel-Crafts Synthesis

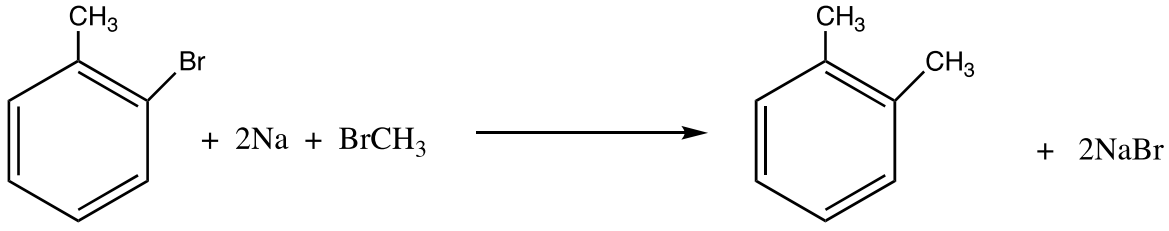


benzene

Toluene

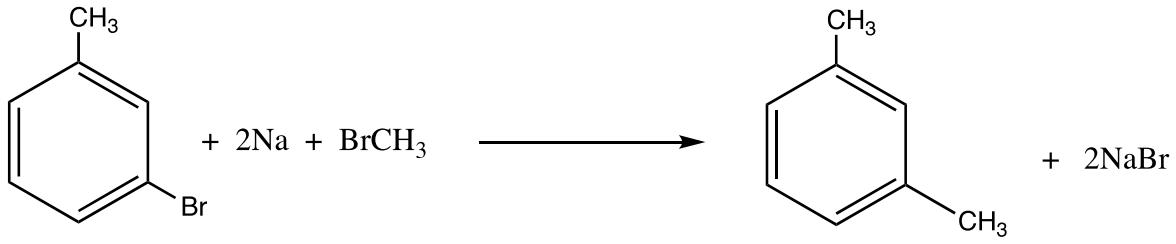
Xylene

1. With sodium and CH_3Br

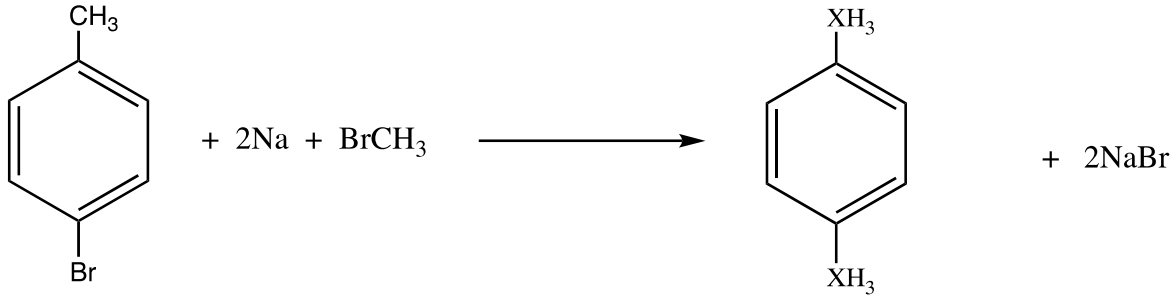


o-bromotoluene

o-Xylene



m-bromotoluene m-Xylene



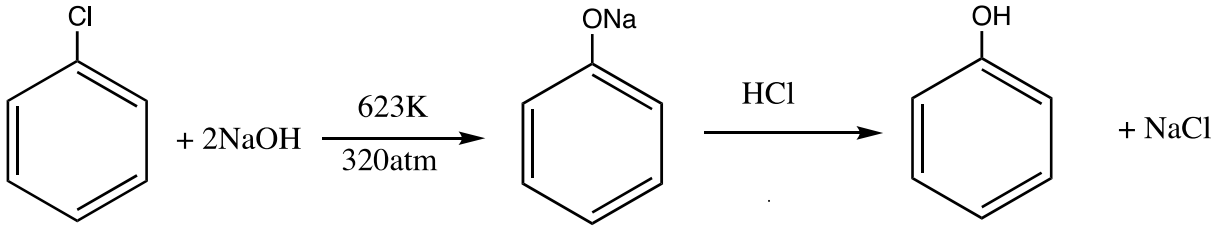
ρ-bromotoluene ρ-Xylene

16.6 Reactions of Benzene derivatives

Aryl halides

1. Formation of phenol

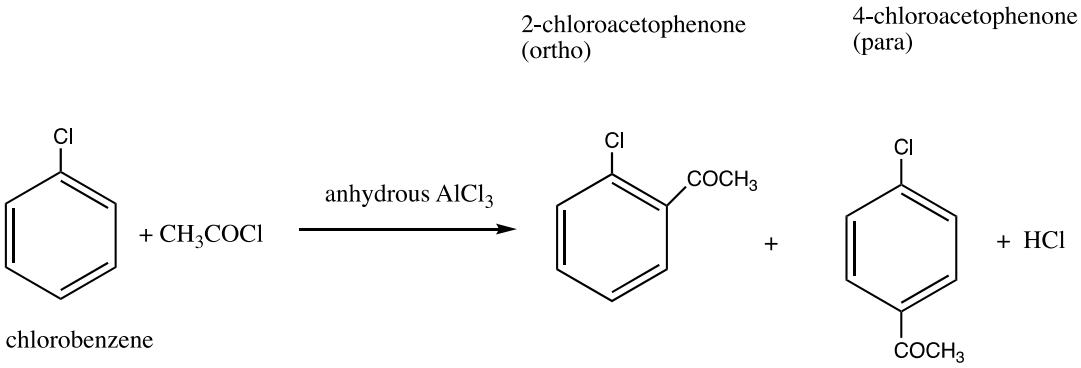
This is a nucleophilic substitution reaction.



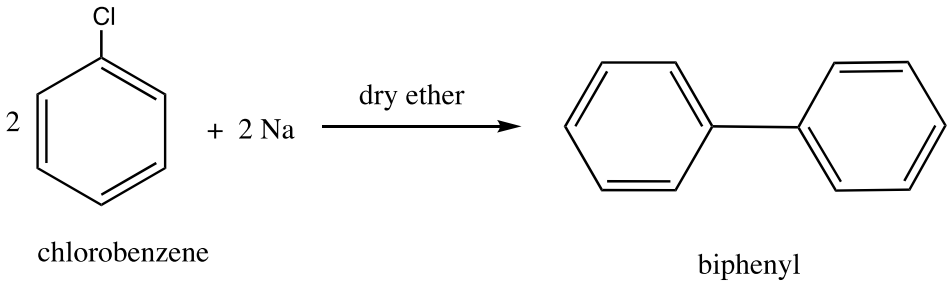
chlorobenzene sodium phenoxide phenol

+ NaCl + H_2O

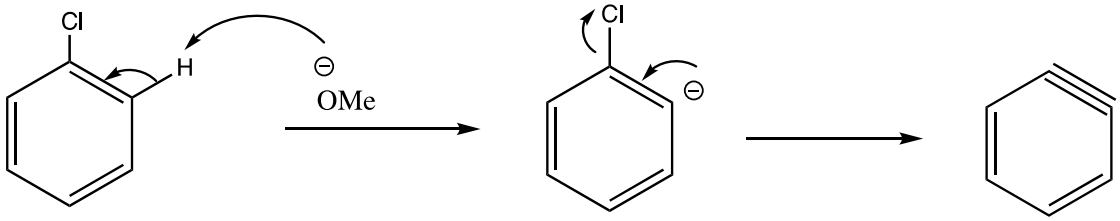
2. Formation of 4-chloroacetophenone – Friedel-Crafts acylation



3. Formation of biphenyl – Fittig reaction



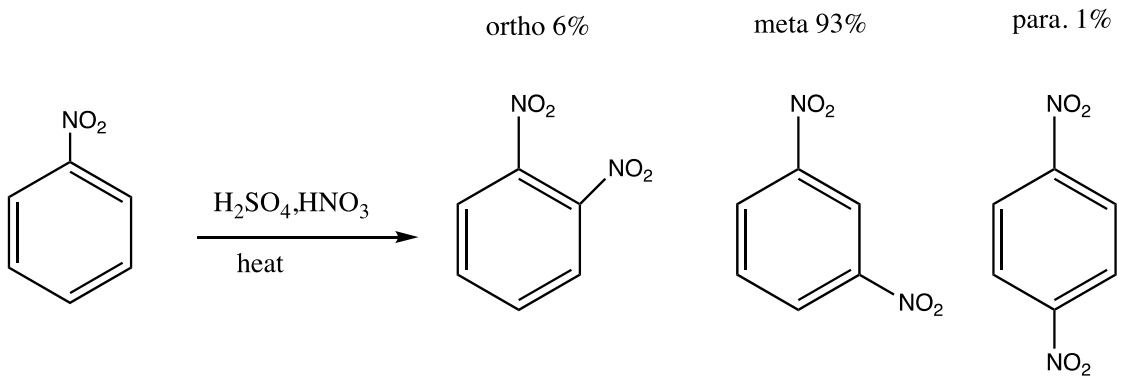
4. Formation of benzene



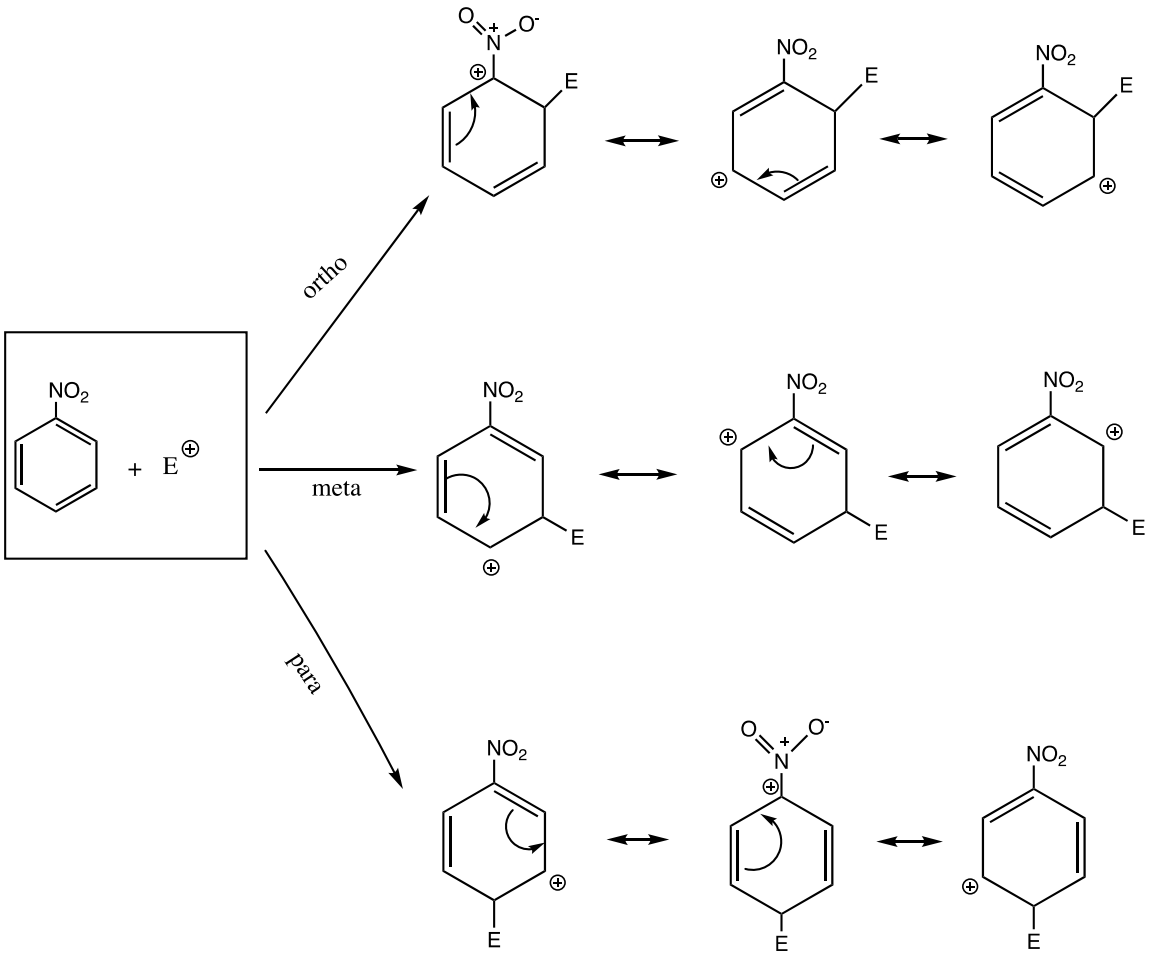
Nitrobenzene

1. With concentrated H_2SO_4 and concentrated HNO_3

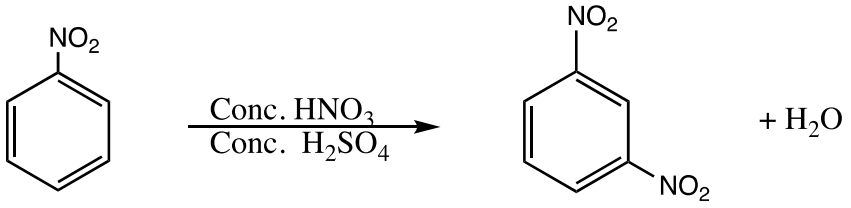
This is an electrophilic aromatic substitution. The nitro group direct the electrophile to meta position.



Mechanism

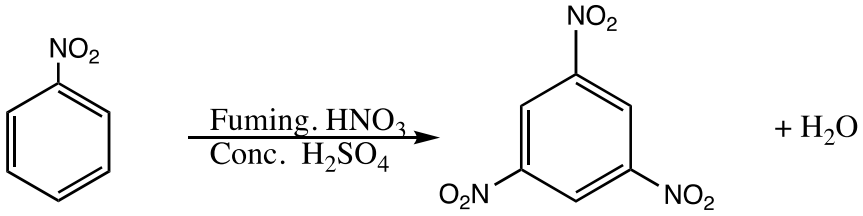


1. With H_2SO_4/HNO_3



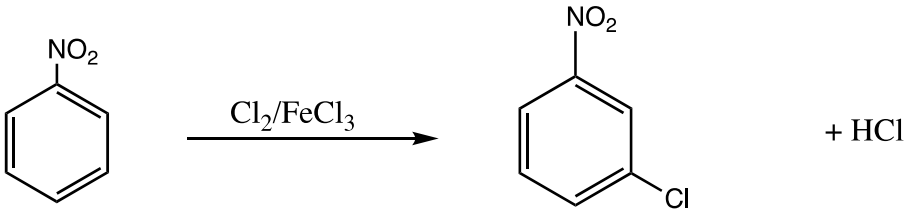
m-nitrobenzene

2. With fuming HNO_3 and Concentrated H_2SO_4



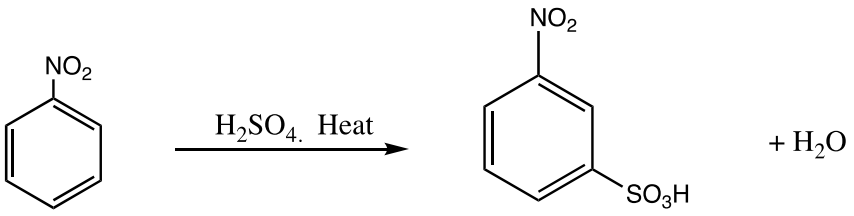
1,3,5 trinitrobenzene

3. With Cl_2 and $FeCl_3$



m-chloro-nitrobenzene

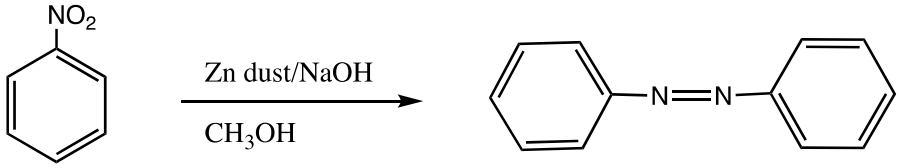
4. With H_2SO_4



m-nitrobenzene sulphonic acid

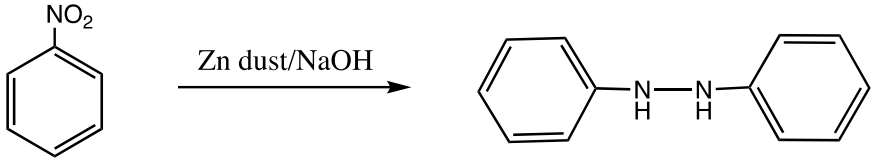
5. With Sn-HCl, Fe-HCl

6. With Zn dust/NaOH/CH_3OH



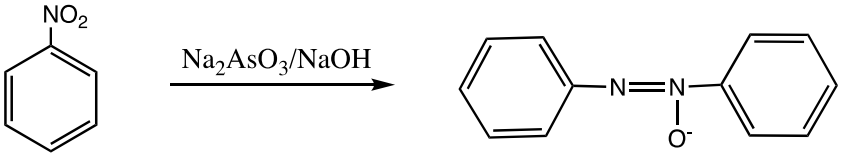
Azo benzene

7. With Zn dust/NaOH



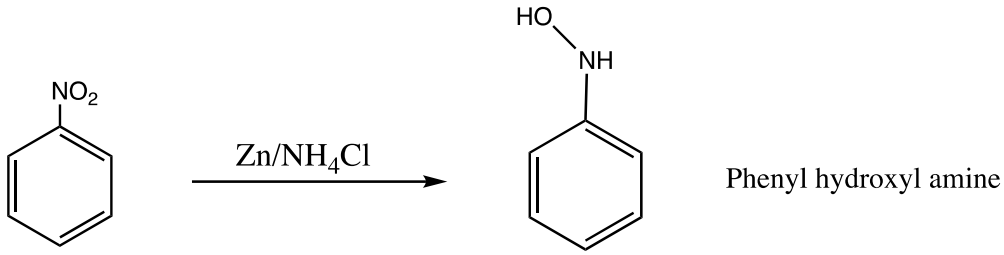
Hydrazo benzene

8. With Na_2ASO_3/NaOH



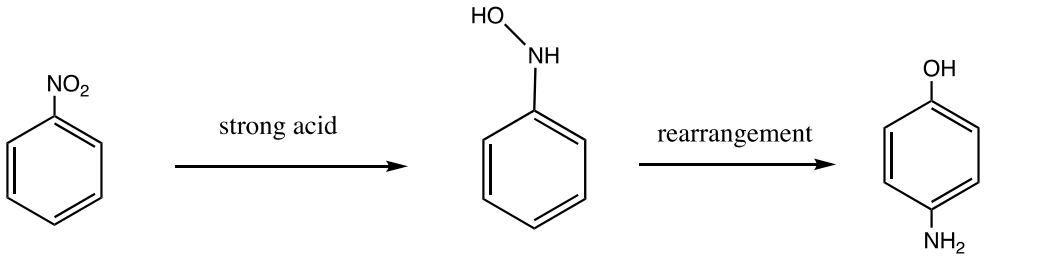
Azoxy benzene

9. With Zn/NH_4Cl

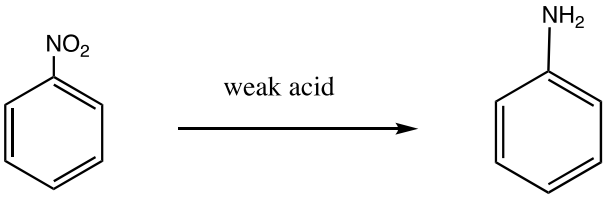


Phenyl hydroxyl amine

10. Electrolytic reduction



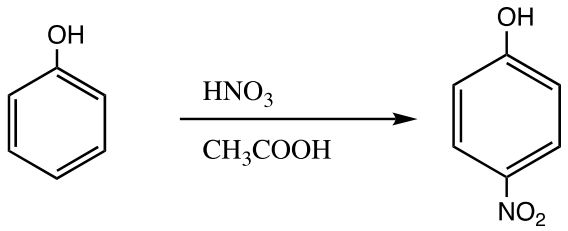
p-amino phenol



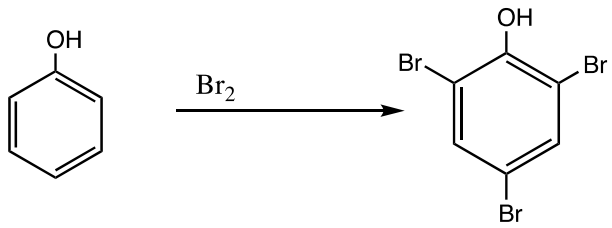
Phenol

In the following reactions the phenol act as the nucleophile, either through the aromatic ring or at the oxygen atom:

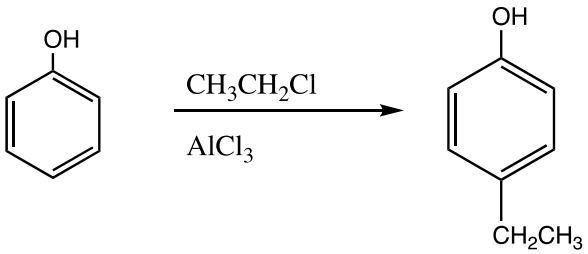
1. With HNO_3/CH_3COOH



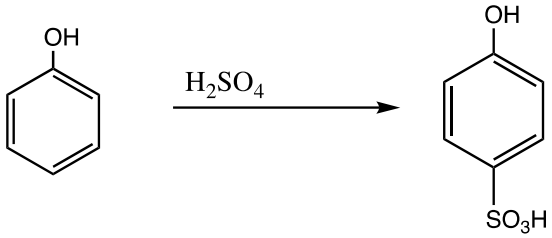
2. With Br_2



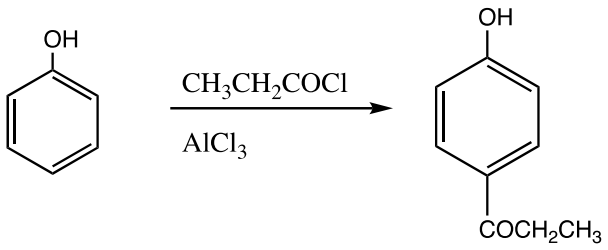
3. With $CH_3CH_2Cl/AlCl_3$



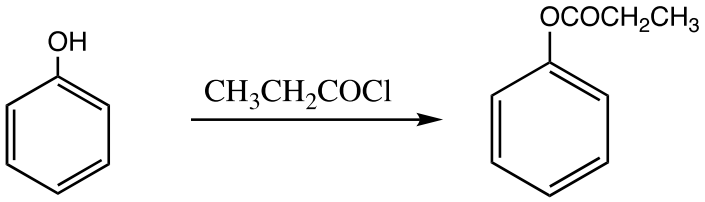
4. With H_2SO_4



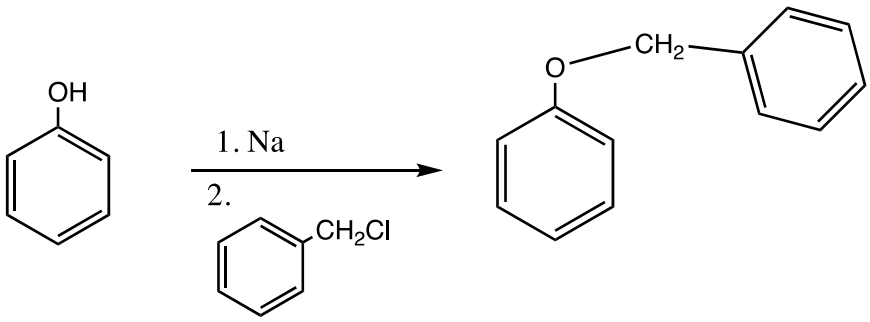
5. With $CH_3CH_2COCl/AlCl_3$



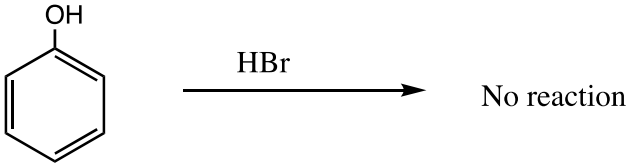
6. With CH3CH3COOCl



7. With Na and the with Ph-CH2Cl

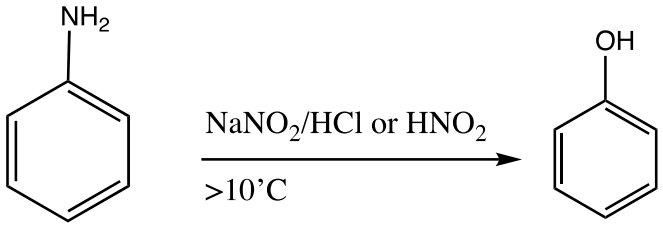


8. With HBr

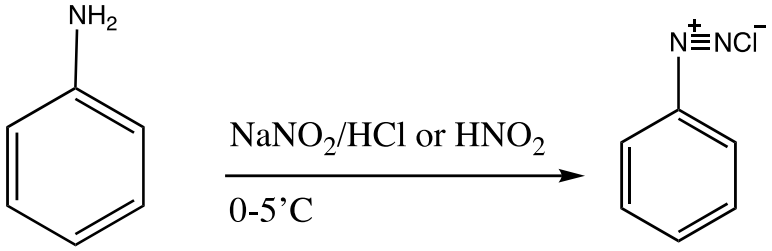


Aniline

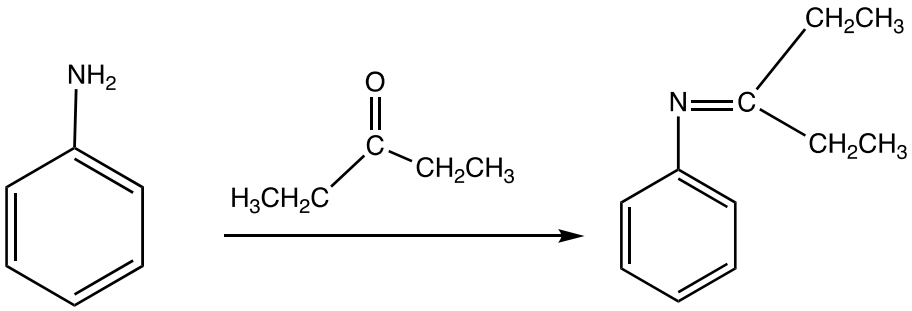
1. With $NaNO_2$/HCl or HNO_2 below >10^0C



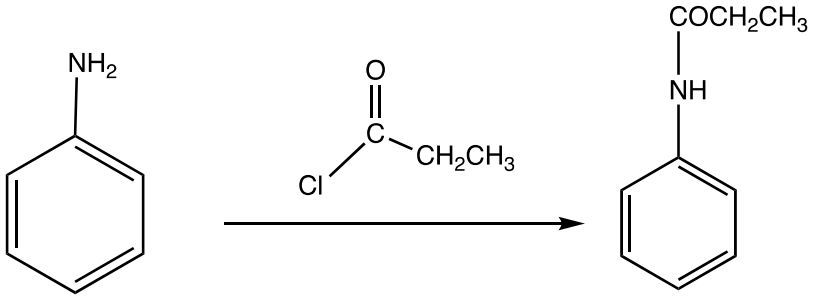
2. With $NaNO_2$/HCl or HNO_2 between 0 – 5 ^{0}C



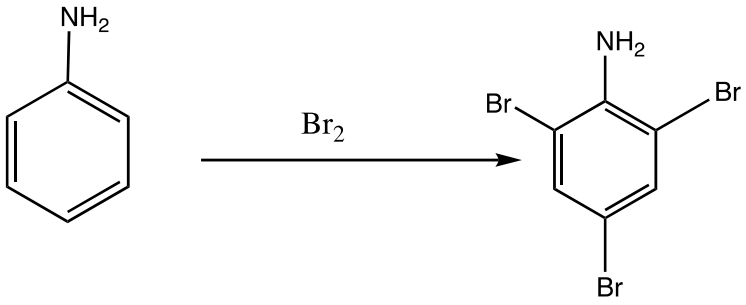
3. With diethyl ketone



4. With an acyl chloride

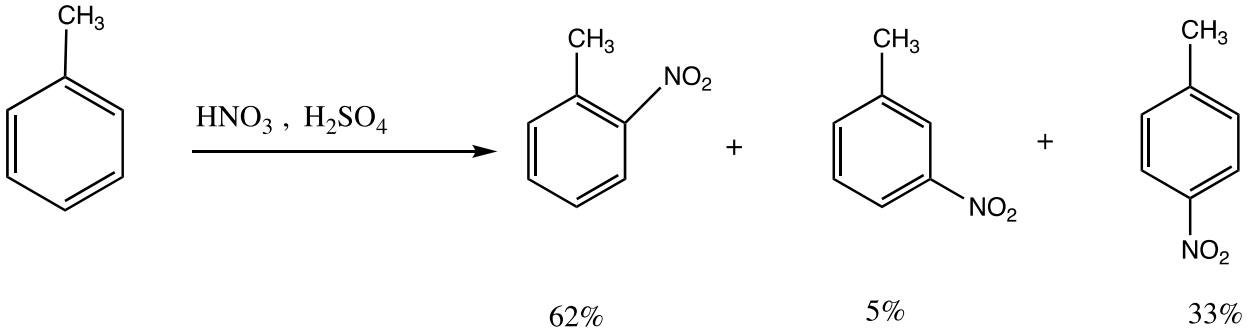


5. With bromine



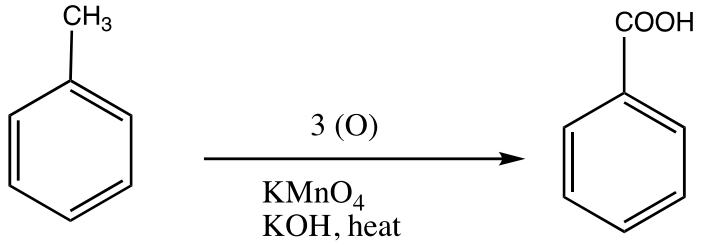
Toluene

1. With HNO_3 and $H2SO_4$

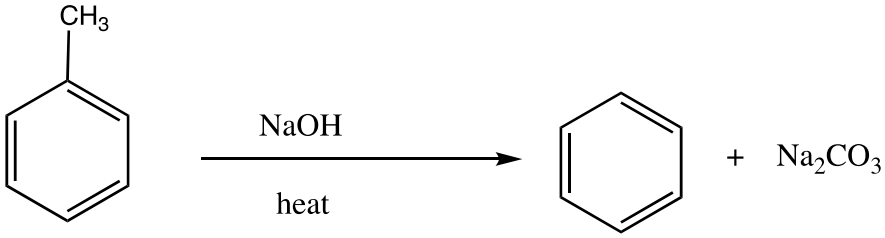


62% 5% 33%

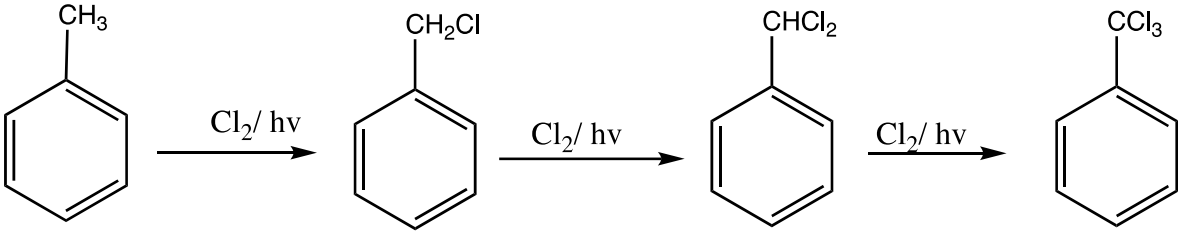
2. With $KMnO_4$ and KOH



3. With NaOH

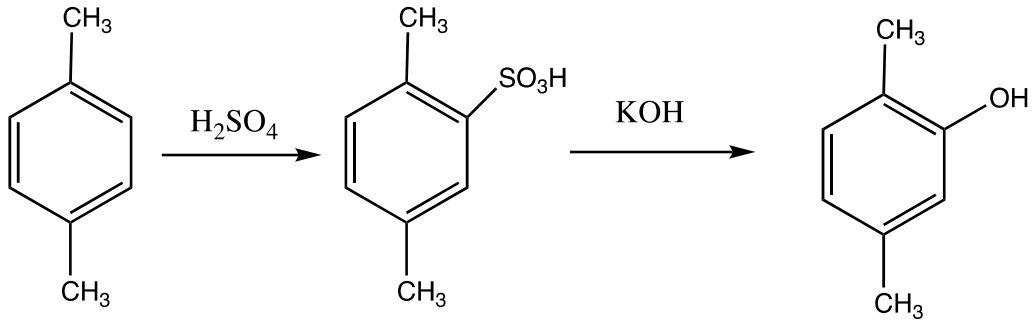


4. With chlorine/light

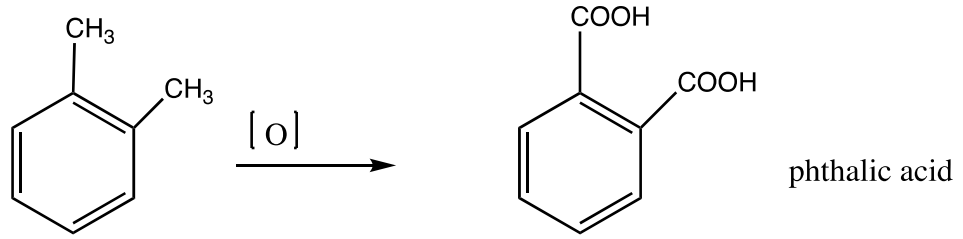


Xylene

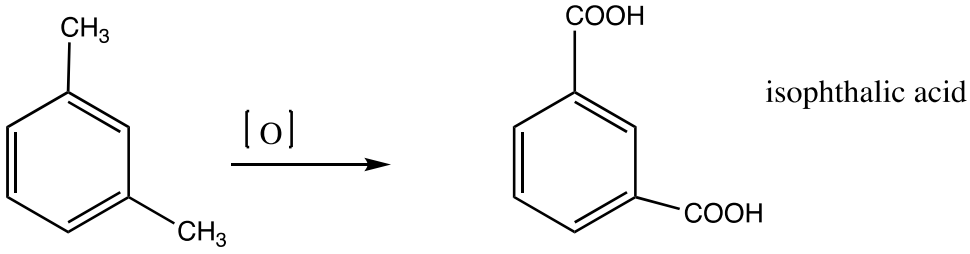
1. With concentrated H_2SO_4 followed by KOH



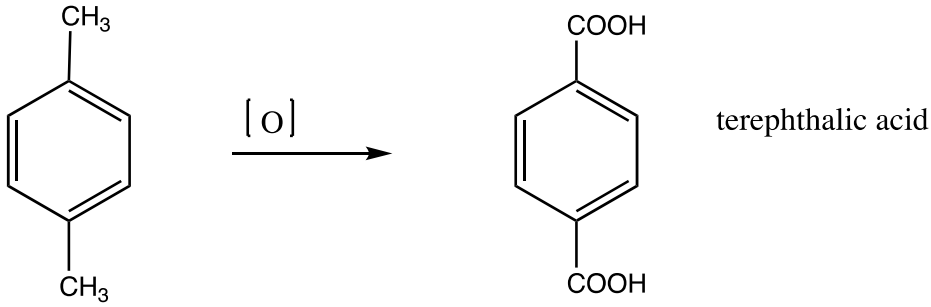
2. Oxidation with acidic $KMnO_4$



phthalic acid



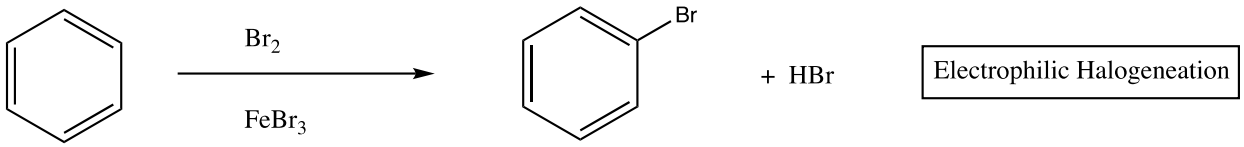
isophthalic acid



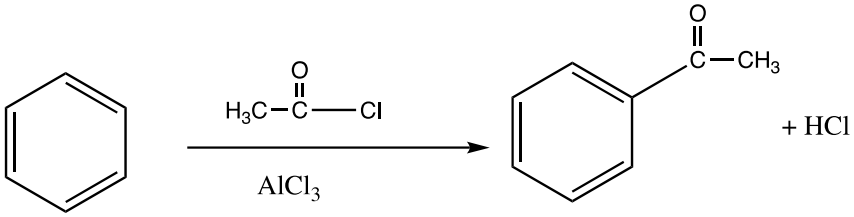
terephthalic acid

16.7 Summary

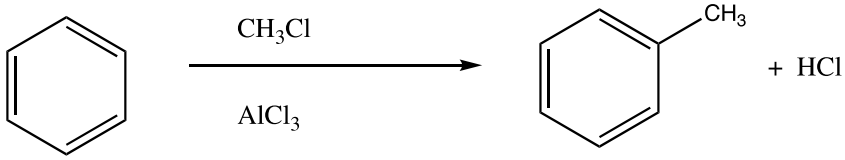
This section provides you with several important information relevant to aromatic compounds.



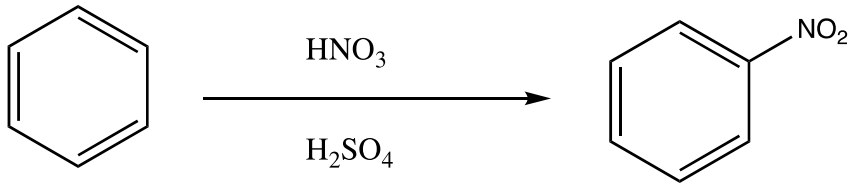
Electrophilic Halogeneation



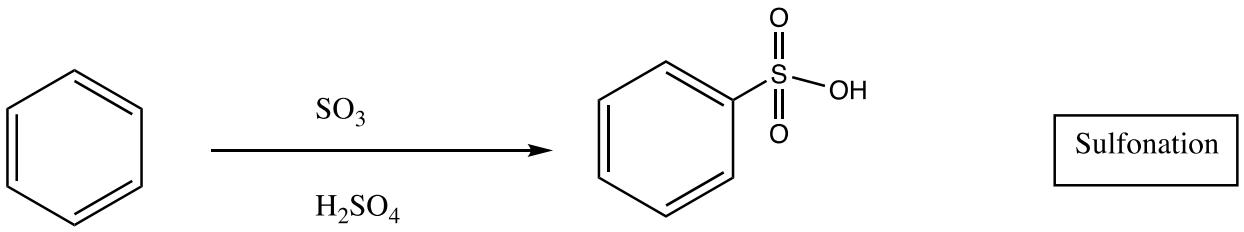
Friedel-Craft Acylation



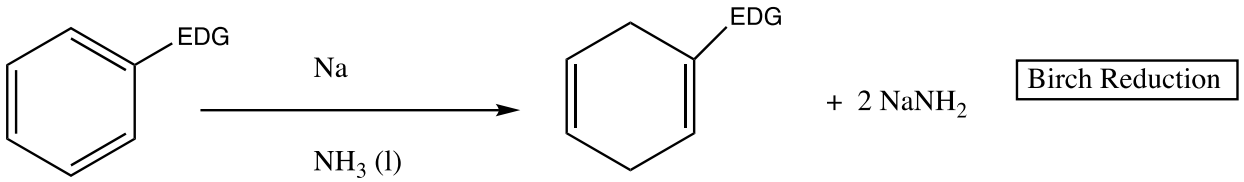
Friedel-craft Alkylation



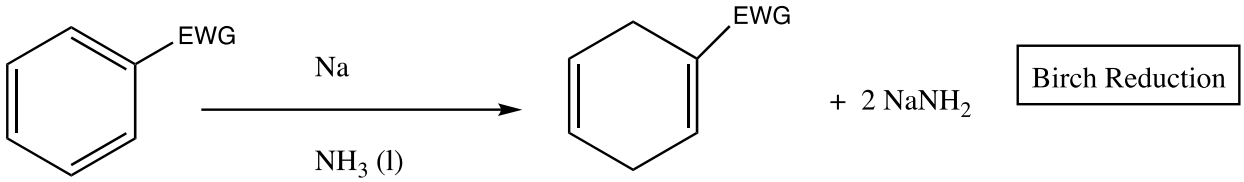
Nitration



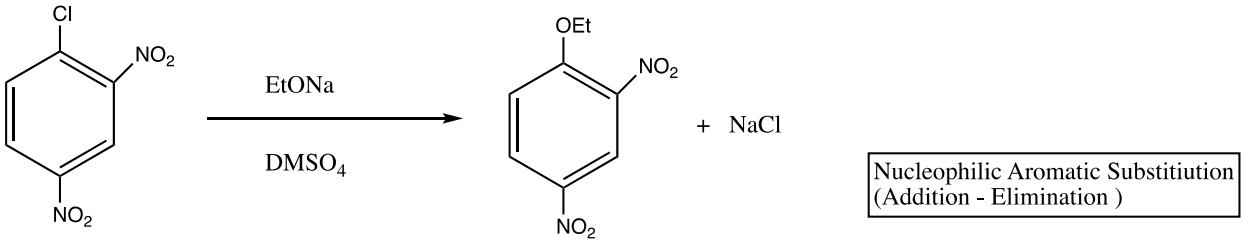
Sulfonation



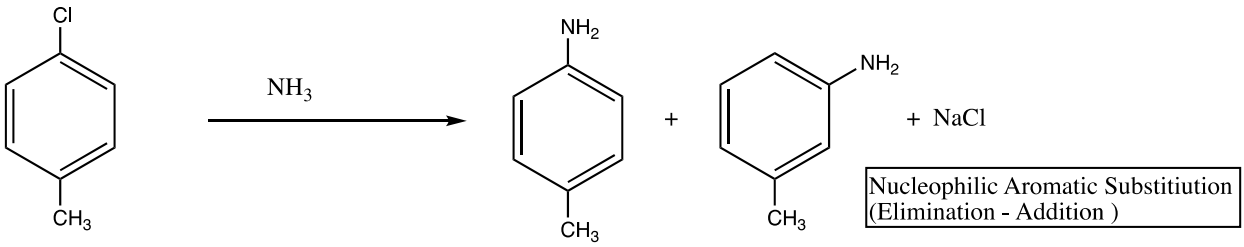
Birch Reduction



Birch Reduction



Nucleophilic Aromatic Substitiution
(Addition - Elimination)



Nucleophilic Aromatic Substitiution
(Elimination - Addition)

Ortho, para, and meta directing groups

When monosubstituted benzene reacts with an electrophile and undergoes substitution (electrophilic substitution) reactions, the substituent of the benzene ring may direct the incoming electrophile to attach to ortho, para, or meta positions. Generally, the direction by the substituents is ortho and para together or meta. When these substituent groups increase the rate of the electrophilic substitution reaction (faster than the reaction with benzene without any substituent), these groups are called activating groups. If these substituents slow down the reaction than that of a benzene without a substituent, they are called deactivating groups. Whilst activating groups are mostly ortho and para directing groups, in the case of halogens, while they being deactivating group, they also act as ortho and para directives. When it comes to other deactivating groups, they are meta directors.

	Activating Groups	Deactivating Groups
Ortho, Para – Directing Groups	Hydroxyl (-OH) - -I and +M effect Alkoxy (-OR R can be H, alkyl, aryl, acyl) – I and +M effect Amino (-NH2, -NR2 R can be H, alkyl, aryl, acyl or any other combinations) -I and +M effect Alkyl or Aryl -I and +M effect	Halogens – F (para), Cl, Br, I -I and + M weak effect

	Thio (-SH, -SR) a weak +M	
Meta Directing Groups	No groups	Nitro ($-NO_2$) -I and +M for dimer and -M for monomer Carbonyls (-COR - The R attached to this carbonyl carbon could be H, alkyl, aryl, hydroxy, alkoxy, phenoxy, or NH_2) -I and -M effect Cyano (-CN) -I and -M effect $-CX_3$ (X is any halogen group) – I effect Sulfonyl (-SO3H) -I and -M effect NR^+_3 (R can be H, alky, aryl or any other combinations) – -I effect

Table 16.7.1: Activating and deactivating groups and relevant ortho, para, and meta directives

When the substituent group is an electron donating group (EDG) (also known as electron releasing group -ERG), it sends its electron density into a conjugated pi system (such as the ones in benzene) through resonance (known as mesomerism or +M) or inductive effect or induction (+I). These groups are also known as activating groups. As a result, benzene ring will have more electronegativity on ortho and para positions. These are ortho and para directing groups.

If the EDG group is large, then steric effects may determine where the incoming second substituent group will combine in the ring.

When electron withdrawing groups (EWG) are attached to the benzene ring, the electron density from the pi system will be removed (-I or -M effect). These groups are known deactivating groups. As a result, these are meta directing groups. The exception is when halogens are connected to a benzene ring. Although, halogens are EWG, the lone pairs on halogens are shared with the benzene. As a result, halogens are ortho/para directing groups.

It is important to understand that +M effect shown by activating groups are stronger. Therefore, in cases where compounds have +M and – I effect, + M effect dominates, except in halogens.

The nitro group is withdrawing electron density through resonance. The incoming electrophile joins meta position since it has more negative charge than ortho and para positions which shows positive charges.

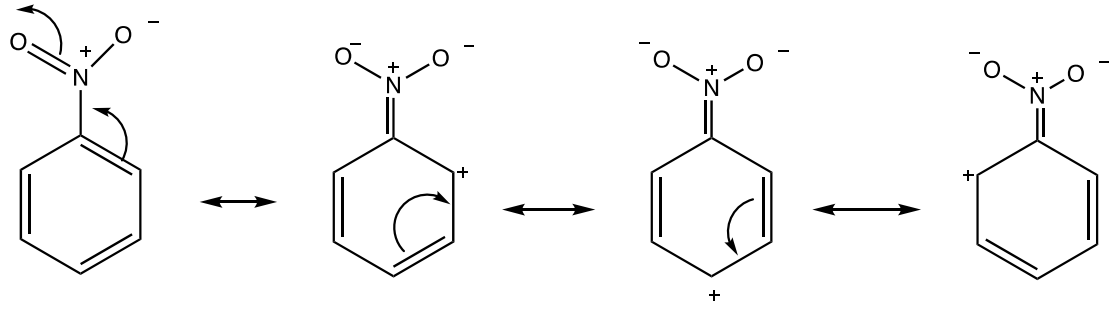


Figure 16.7.1: -M effect of NO2. This compound also has -I effect, since there is a full or partial charge on the element directly attached to the ring.

The EDG creating negative charges at ortho and para positions, thus making them ortho and para directing groups. The incoming electrophile joins ortho and para positions.

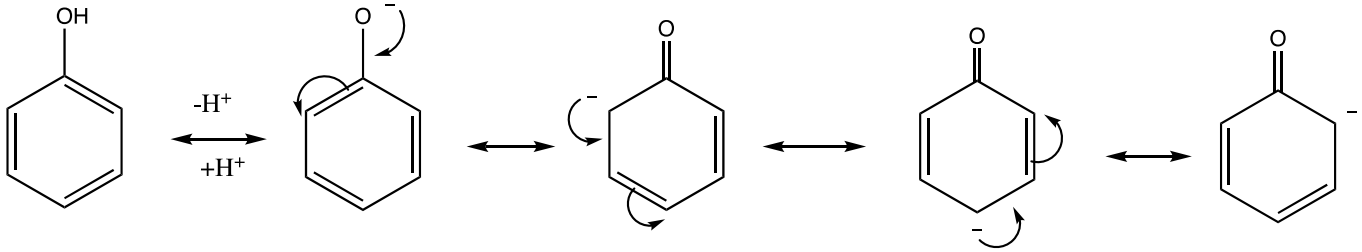


Figure 16.7.2: +M and +I effect of phenolate ion

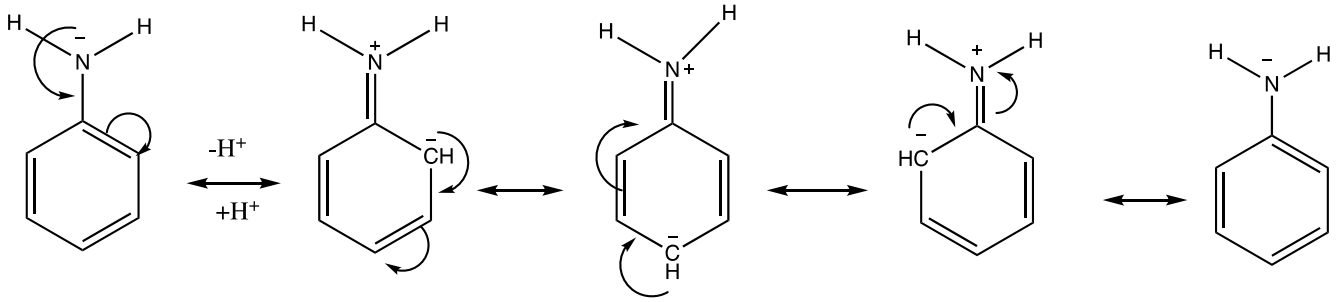


Figure 16.7.3: Amino EWG effect via +M effect

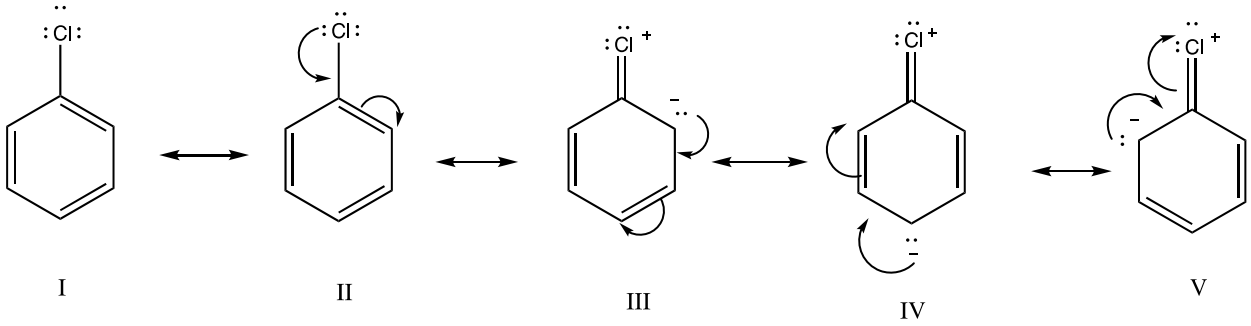


Figure 16.7.3: The ortho and para directing nature of chlorine (halogens) due to the availability of lone pairs (+M effect) although halogens also have -I effect.

Chapter 17

17.0 Spectroscopic Methods in Organic Chemistry

17.1 Objectives

1. Explain the use spectroscopic methods
2. Explain frequency, wavelength, and wave number
3. Apply Einstein-Planck equation
4. Describe the type of energies involved in NMR, UV/Vis, and IR analytical techniques

17.2 Introduction

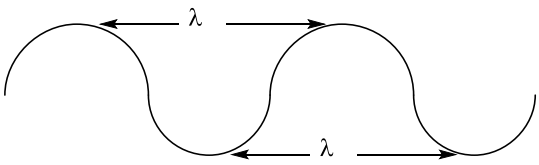
Spectroscopic methods are used to determine the structure of organic compounds. Compared to the traditional chemical analysis used in the past, spectroscopic methods are faster and more definitive. Also, spectroscopic methods use small samples; the samples used are non-destructive unlike in chemical analysis where the samples are chemically destroyed or undergoes modification.

In spectroscopic techniques, the amount of energy absorbed (or emitted) by organic matter sample is used as an indication of the structure of the organic compound.

17.3 Electromagnetic Radiation

Electromagnetic radiation (emr) exhibits dual nature – wave and particle nature. It can be described as a wave or as a collection of particles known as quanta or photons. Depending on the experiment, these two forms are seen separately.

The basic properties of a wave are given below before we begin to discuss various methods in spectroscopy:



The above diagram is a simple wave. λ is the wavelength measured from crest to crest or trough to trough of a wave. The wavelength is expressed as meters (m), centimeters (cm), millimeters (mm), micrometers (μm), or in nanometers (nm).

The frequency of a wave denoted as f or ν (pronounced as nu) is expressed as cycles per second (cps) or Hertz (Hz). Therefore, frequency is the number of cycles that passes a given point per second.

Wave number (ν) is another unit used to define wave number.

Wave number = 1/ wavelength

When wavelength is given in cm, the wave number is the number of cycles in each cm of the beam. The unit of wave number is cm^{-1}. The wavenumber is used to express frequency of absorption banks in infrared spectroscopy.

The relationship among the speed of light (c) (3×10^8 m s^{-1}), frequency, and the wavelength is given as follows:

$$f = \frac{c}{\lambda}$$

OR

$$\lambda = \frac{c}{f}$$

Since C is a constant, frequency and wavelength are inversely proportional. This means, when the wavelength is high the frequency is small; when the wavelength is small the frequency is high.

Since electromagnetic (emr) radiation also exhibits the particle nature, the energy in emr is expressed in photons. A photon is a discrete bundle or quantum of emr energy. Photons have the speed of light and are always in motion. They can travel in a vacuum. The relationship between the energy of a photon and the frequency is given by the Einstein-Planck equation:

$$E = hf$$

h = Planck's constant = 6.26×10^{-34} Js

f = frequency

E = Energy of a photon

The above equation can be written in terms of C and λ as follows:

$$E = \frac{hc}{\lambda}$$

Therefore, lower the wavelength, higher the energy of radiation or higher the wavelength, lower the energy of radiation.

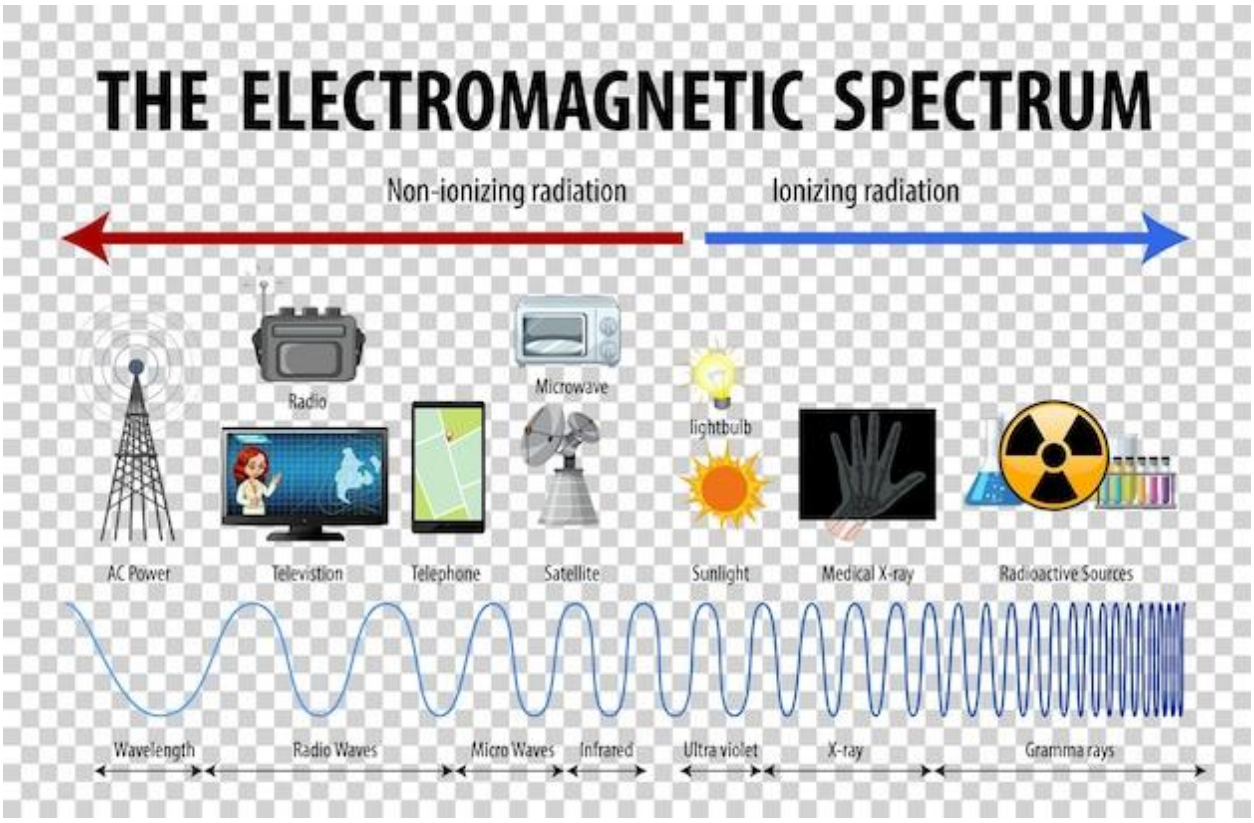


Figure 17.3.1 Electromagnetic spectrum with wavelengths and frequencies image

Copyrights: Electromagnetic vector created by brgfx - www.freepik.com

	Wavelength (m)	Frequency (Hz)	Energy (J)
Radio	$> 1 \times 10^{-1}$	$< 3 \times 10^{9}$	$< 2 \times 10^{-24}$
Microwave	1×10^{-3} - 1×10^{-1}	3×10^{9} - 3×10^{11}	2×10^{-24}- 2×10^{-22}
Infrared	7×10^{-7} - 1×10^{-3}	3×10^{11} - 4×10^{14}	2×10^{-22} - 3×10^{-19}
Optical	4×10^{-7} - 7×10^{-7}	4×10^{14} - 7.5×10^{14}	3×10^{-19} - 5×10^{-19}
UV	1×10^{-8} - 4×10^{-7}	7.5×10^{14} - 3×10^{16}	5×10^{-19} - 2×10^{-17}
X-ray	1×10^{-11} - 1×10^{-8}	3×10^{16} - 3×10^{19}	2×10^{-17} - 2×10^{-14}
Gamma-ray	$< 1 \times 10^{-11}$	$> 3 \times 10^{19}$	$> 2 \times 10^{-14}$

Table 17.3.1: Electromagnetic spectrum with wavelengths and frequencies

17.4 UV/Visible, IR, and NMR

When matter is exposed to emr, depending on the amount of energy of the radiation, there will be certain changes happening within the molecule. The energy related to the movement of a molecule as a whole is known as the translational energy. In addition to the translational energy, a molecule possesses vibrational, rotational, and electronic energy. All these three types of energies are quantized. This means that these three types can have only certain discrete values. When it comes to the translational energy, it is not quantized; the energy value depends on the temperature.

Depending on the amount of energy absorbed by the matter, vibrations, rotations, or electronic transitions can happen. When energy is absorbed, the electrons will move from a lower energy level to a higher energy level.

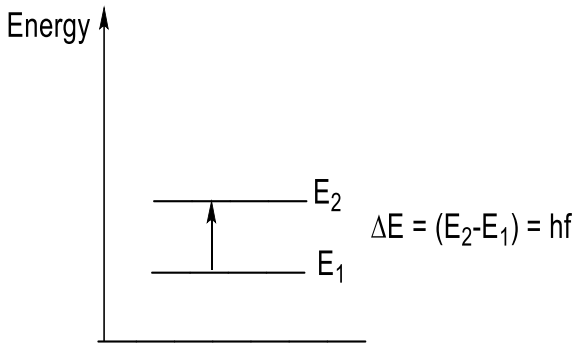


Figure 17.4.1: The energy difference between two levels

As shown in the above diagram, an electron in E1 energy level will transfer to E2 higher energy level, by absorbing E2 – E1 amount of energy. This energy is equal to hf.

h = Planck's constant

f = frequency

This type of an electronic transition needs the high energy (high frequency) part of the emr. This quantity of energy is provided by ultraviolet (U.V.)/visible region of the emr. UV-Vis Spectroscopy (or Spectrophotometry) is a quantitative technique used to measure the amount of energy absorbed my chemical compounds.

The energy required to move an electron from a lower level of vibration energy to a higher level is less than the energy required for electronic transitions. Therefore, the study of infrared energy is done using an Infrared Spectroscopy.

The energy required for rotations is lower than the energy required for vibrational movements. Therefore, this energy is known as microwave energy. Please note the frequency, energy, and wavelength values of these different regions of emr. The study of this type of energy is not covered in this text.

Similarly, there are transitions between energy levels of nuclei of certain elements as a result of the absorption of radio frequency waves. The analytical technique used here is known as the Nuclear Magnetic Resonance Spectroscopy.

Please note that spectroscopy is the study of a particular type of energy when it is absorbed by a compound. Spectrometer of that particular energy (i.e. UV/Vis spectrometer, IR spectrometer) is the instrument used to measure the changes as a result of the absorption by compounds. A spectrometer determines which wavelength range of that emr is absorbed and reflected. A spectrophotometer measures the relative intensity of light absorbed and reflected at a particular wavelength of the emr.

Chapter 18

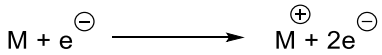
18.0 Mass Spectrometry

18.1 Objectives

1. Describe the theory of mass spectrometry
2. Explain the structure of the instrument
3. Apply the knowledge to find the structure of compounds

18.2 Introduction

This is an analytical method used mainly in organic chemistry. Unlike any other type of spectroscopic techniques where absorption or emission of electromagnetic radiation of molecules are used as an identification method, in mass spectrometry, the compound is bombarded with high energy particles (usually an electrons). As a result of the collisions of electrons with molecules of the compound being analyzed, the molecules will eject electrons and become positively charged molecular ions. When electrons are used to bombard a compound, such a mass spectrometry is known as Electron Impact Mass Spectrometry or EIMS. The molecule with an ejected electron will have an odd number or even number of electrons in the fragments, but the radicals formed will always have an odd number of electrons.



M = Molecule of the compound being analyzed

M+ = Positively charged molecule after the ejection of an electron after the collision with another electron.

M+ here is known as the radical cation. This radical cation is an unstable, high-energy species. This radical-cation will breakdown further to smaller radical-cations, neutral molecules, neutral radicals, and cations. The positively charged fragments are detected by the mass spectrometer according to the mass to charge (shown as m/e or m/z) ratio of the fragments. The resulting mass spectrum is a graph of abundance (or relative intensity) of positively charged fragments against m/e ratio. Since almost all the positively charged fragments have a charge of +1,

the mass to charge ratio is practically the mass values. Therefore, the spectrum is a record of fragment mass against the relative abundance of that fragment. If these fragments can be studied carefully and methodically, the structure of the original compound can be identified. The fragmentation of the compound happens according to the carbon skeleton and the functional groups present in the compound. The fragmented molecular ions aid in determining the molecular formula and the molecule mass of the original compound.

18.3 Structure of the instrument

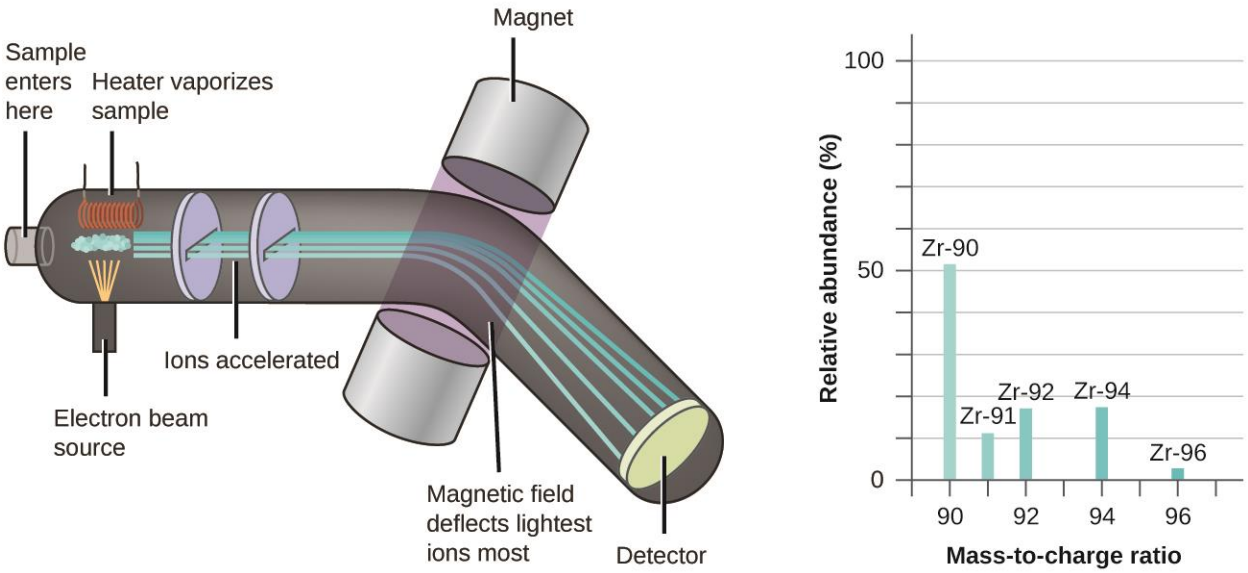


Figure 18.3.1: Mass Spectrometer Diagram

Image credit: "Atomic Structure and Symbolism: Figure 5(Opens in a new window)" by OpenStax Chemistry, CC BY 4.0.

The amount of sample introduced for analysis is generally one microgram. This sample is introduced, vaporized, and facilitated to flow in a continuous stream into the ionization chamber. The entire instrument including the ionization chamber is kept under a vacuum to minimize collisions and reactions between radicals, ions, and sample molecules.

The main points of this instrument are as follows:

- The compound to be analyzed in introduced to the instrument. Only a small amount is needed.
- Since the compound is neutral, the electron beam is used to bombard the compound and ionize them to smaller positively charged fragments. The beam of high energy (about 70 eV) is emitted from a filament that is heated to a high temperature. Positively charged fragments are known as molecular ions. The unstable molecular ions will breakdown or rearrange further into smaller charged ions.
- The repeller plate has a positive charge, so this plate will repel positively charged fragments toward the accelerating plates.
- The accelerator plate has a potential difference between 1 kV to 10kV. The plates have slits in the middle. These plates will accelerate the fragments of different masses (in general, most of these fragments have +1 charge) as a uniform beam.
- When these fragments go through the magnetic field in a curved path, the fragments with lower masses will get deflected more while the fragments with higher masses will get deflected less. The fragments that are not ionized will be removed by the vacuum. The fragments that are negatively charged will be attracted to the accelerator plates. Finally, only the positively charged particles will flow as an ion beam.
- After the ionization chamber the beam of ions passes through a short field-free region and enter the mass analyzer. The ions are separated here according to m/e ratio. If all ions have only +1 charge, then they are separated according to the masses of each ion.
- The radius of the curved path is given by the following equation:

$$\frac{m}{e} = \frac{B^2 r^2}{2V}$$

Mass of the ion = m

Charge of the ion = e

Potential difference of the ion accelerating plates = V

Radius of the curved path = r

Strength of the magnetic field = B

According to the above equation, when the magnetic field strength and the voltage are kept constant, the higher the mass, the higher the radius will be. The fragments with smaller masses will be easily deflected toward the magnetic field; therefore, the radius of the curved path will be small. The magnetic field pushes the lighter fragments to the ion collector easily thereby reducing their curved path.

- It is possible to change the path of the heavier particles by decreasing the accelerating voltage. Therefore, by changing the accelerating voltage, the detector can be allowed to detect heavier molecules. This technique can be used to collect the information about molecules with varying masses. Similar effect can be obtained by increasing the strength of the magnetic field. Decreasing the magnetic field will have the same effect as increasing the accelerating voltage.
- The detector, which is the ion collector of this instrument, has a counter that produces a current that is proportional to the number of ions that strike it. Therefore, this current can be measured accurately using electron multiplier circuits. The signal from the detector is fed to a recorder that produces mass spectrum. The accuracy of this instrument is very high that even the current caused by one ion can be detected.

18.4 Mass Spectrum

A mass spectrum is a very sensitive graph. It provides separate signals for particles differing in 1.0 mass unit. The peaks are arranged in the increasing order of m/e from left to right in the spectrum. The intensities of the peaks are proportional to the relative abundance of each particle. The abundance is related to the stability of the species.

The convention is that the tallest peak is called the base peak and it is assigned the intensity value of 100%.

e.g.

Mass spectrum of CH_3OH (methanol)

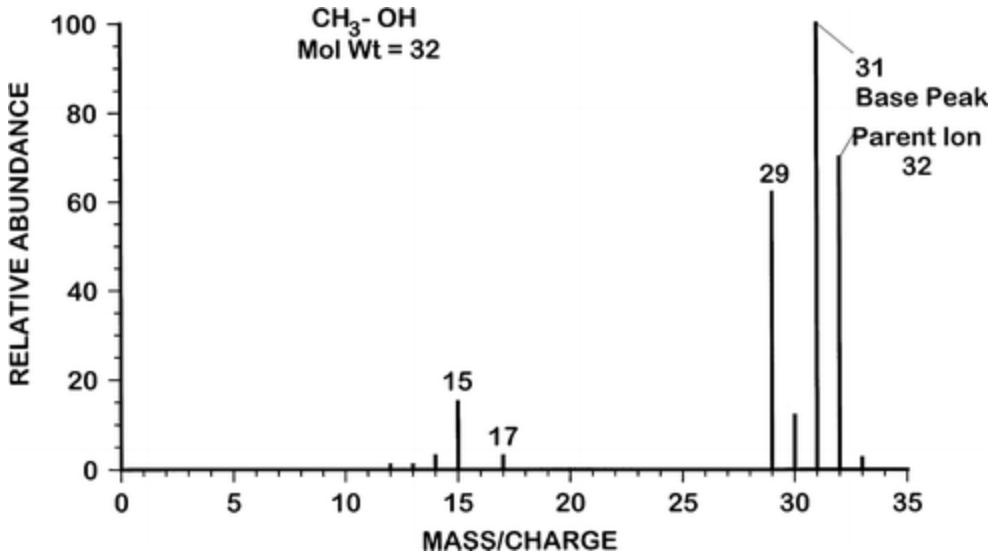


Figure 18.4.1: Mass spectrum of CH_3OH (methanol)

The tallest peak is at m/e 31. This is the base peak with a given intensity value of 100%. The molecular ion methanol is at m/e 32 and has an abundance of 65%.

If a compound with isotopes is run in a mass spectrometer, then depending on the number of isotopes, there will be peaks corresponding to that number of isotopes.

e.g. Br has two isotopes: ^{79}Br and ^{81}Br.

When these two bromine isotopes bond with CH_3 to form CH_3Br, then there will be two peaks corresponding to the compound CH_3Br for ^{79}Br and ^{81}Br isotopes at m/e 94 and 96. The average molecular weight of CH_3Br is 94.9 (the mass spectra will not show a peak at 94.9). In calculating this molecular weight, Br mass is taken as the average weight of the two isotopes (please refer to your general chemistry notes on calculating average mass of isotopes). Yet, in the mass spectrometer, the two compounds formed by the two isotopes are separated distinctly. Also, the peak 94 will be slightly higher. This is because the ratio of ^{79}Br to ^{81}Br is 100 to 98. This is the relative abundance in nature. The peaks intensities can be predicted by knowing the natural abundance of isotopes, because the peak intensity values directly correspond to the natural abundance. The two peaks that appear are more or less of equal intensity (100 to 98 ratio) and the two peaks will be two mass units apart. Therefore, the lower-mass isotope is considered the molecular ion and the other peak is known as M^{+2} peak.

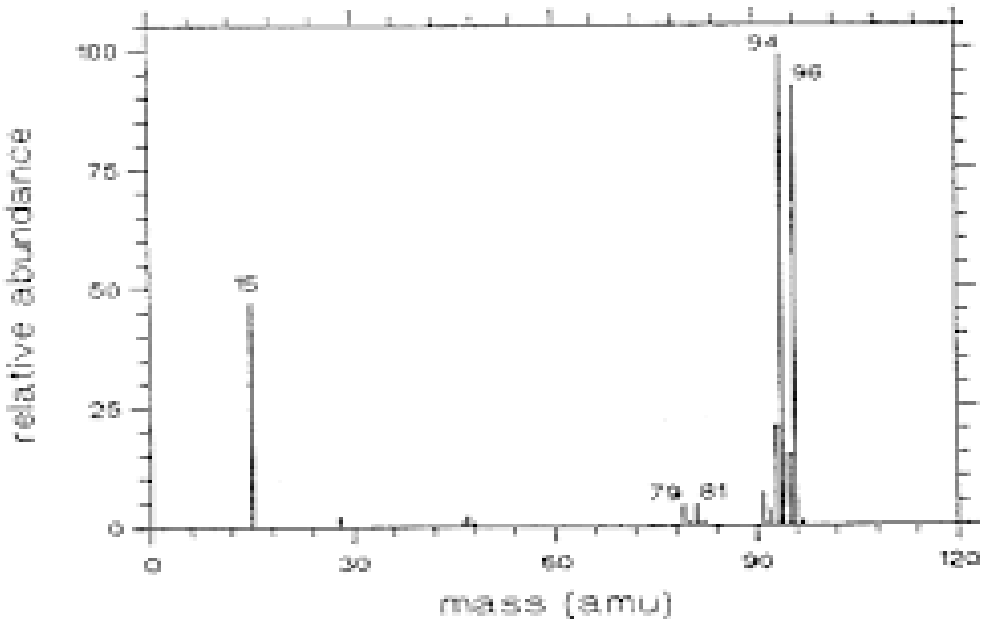


Figure 18.4.2: Mass spectrum of CH_3Br with two isotopes

18.5 Fragmentation Process

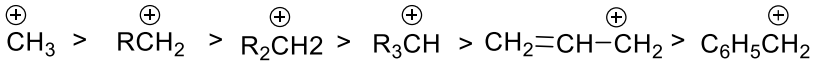
The fragmentation happens as a result of electron bombardment. The original molecule will gain a positive charge as a result of ejecting an electron from the molecule once it is bombarded with electrons. This M^+ (molecular ion) formed will absorb high energy as a result of its collision with higher electrons. Since this state is unstable, M+ will break down into different fragments. If the lifetime of molecular ion is greater than 10^{-5} seconds, then the molecule will be detected by the spectrometer. If the lifetime is less than 10^{-5}, then it will not be detected since it breaks down into fragments before it reaches the detector. As a result, in such situations, only the fragments with a positively charged ions will appear as peaks in the mass spectrum. In general, the spectrum will show the peaks corresponding to M^+ and its fragments. At times, M^+ may be absent in the spectrum due to shorter lifetime.

During the formation of M^+, there is an order in which an electron is ejected. The ejection of the electron with the highest energy (the most loosely connected electron) happens in this process. Therefore, non-bonding electrons are ejected

first. In the absence of non-bonding electrons, π electrons are ejected. In the absence of non-bonding and π electrons, σ electrons are ejected.

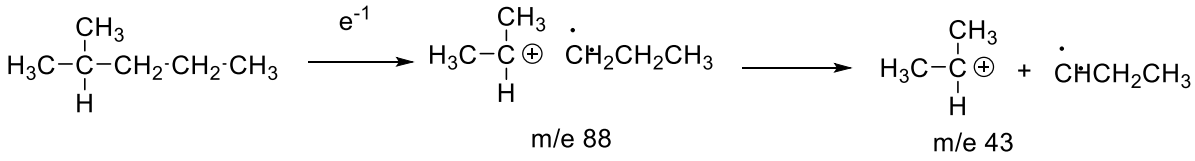
18.5.1 Main Types of Fragmentations

1) Simple cleavage of a σ bond in an alkane. In the cleavage, the formation of a more stable positive carbon ion (carbocation) is favored. The ease of fragmentation to form ions increase in the following order:

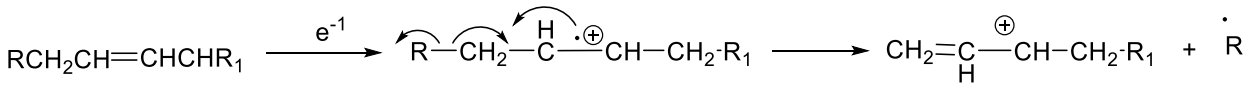


Also, when cleaving, always a radical and a carbocation are formed. In this process, more stable radical is favored as same as more stable carbocation is favored.

e.g.



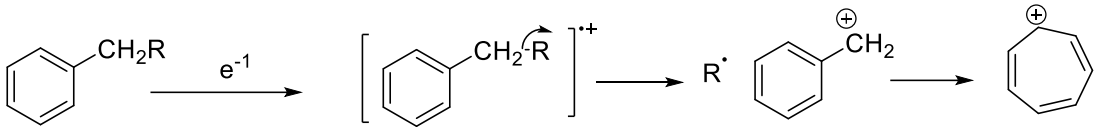
2) In an alkene, the cleaving happens at the allylic position.
e.g.



Alkynes also show similar cleaving at the triple bond.

3) Arenes cleave at benzylic position

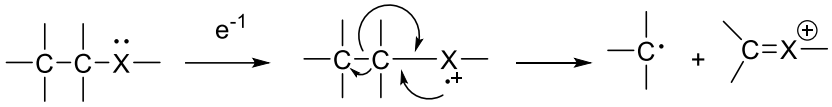
e.g.



Rearrangement

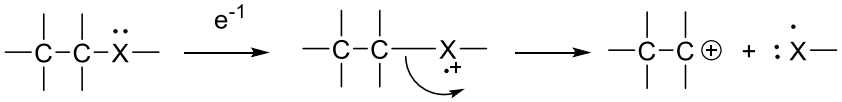
4) Alcohols, halides, ethers, and amines, and sulfides show two main types of cleavages.

- α cleavage



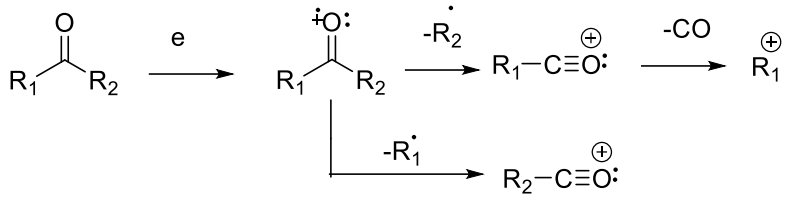
X = Halogen, OH, OR, NR_2, SR

- Cleavage of the C-X bond



5) Compounds with carbonyl groups undergo two types of cleavage

- α cleavage

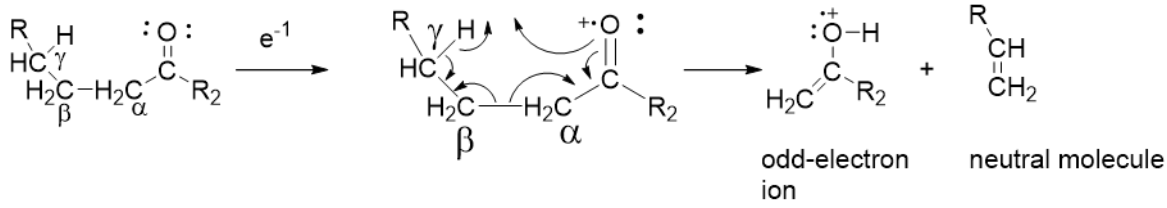


R_2 could be H in an aldehyde, alkyl in a ketone, OR form in an ester, NR_2 in an amide, or OH in an acid.

6) McLafferty rearrangement

This rearrangement takes place when there is a hydrogen atom present at γ carbon.

e.g.



Carbonyl compound with γ hydrogen

The six membered transition state produces a positively charged odd-electron ion and a neutral molecule.

18.6 Nitrogen Rule

The nitrogen rule states that if a compound has an even number of nitrogen atoms or no nitrogen atoms, its molecular ion will appear at an even mass. If a compound has an odd number of nitrogen atoms, then its molecular ion will appear at an odd mass. The nitrogen rule can also be applied to any odd-electron ions other than the molecular ions. This happens because the molecular ions are made up of the most abundant isotopes. Only in nitrogen isotope the mass (14) is even, and the valence

(5) is odd (In O, C, and H, the mass and the valence values are even numbers). This leads to the above nitrogen rule.

e.g.

$$[C_2H_5-NH_2]^{\bullet+}$$

The above compound has one nitrogen. This is an odd number. The mass of the compound is 45. This is an odd number as well.

18.7 Determination of Molecular Formula

Mass spectroscopy can be used to determine the molecular formular of an unknown compound. Once the molecular formular is found, the structure can be determined with the help of other analytical methods. Once the molecular formula is known, then the degree of unsaturation can be calculated. The number of unsaturated sites is known as the degree of unsaturation.

The following table shows the number of sites of unsaturation against the bonds:

C=C	1 site of unsaturation
C≡C	2 sites of unsaturation
Ring	1 site of unsaturation
C=O	1 site of unsaturation
C≡N	2 sites of unsaturation

Table: 18.7.1: The number of sites of unsaturation against the bonds

The degree of unsaturation can be calculated as follows:

- If the molecular formula shows the presence of maximum number of H atoms, then the molecule is saturated, and the degree of unsaturation is zero.

- If the formular has two hydrogens less than the maximum possible, then the degree of unsaturation is one.
- If the formular has four hydrogens less than the maximum number possible, then it has two degrees of unsaturation.
- In order to calculate the maximum number of unsaturation, first calculate the maximum number of hydrogen atoms theoretically possible.

H max = (C X 2) + (NX1) +2

C = number of tetravalent atoms

N = number of trivalent atoms

Number of divalent atoms are not included in the equation.

- The next step is to find the actual monovalent atoms such as H, Cl, Br present in the molecule. Consider this as Hx. If Hx is equal to Hmax, then there is no unsaturation.

  Otherwise, use the following formula:

Degree of unsaturation (U) = (Hmax – Hx)/2

It is important to note that the above mass spectroscopic discussions relate to simple low-resolution mass spectrometer. There are high resolution mass spectrometers used to determine the atomic masses precisely. These instruments take into consideration the nuclear packing fraction; the mass of each atom actually differs from a whole number by an amount known as the nuclear packing fraction. These high-resolution mass spectrometers are known as double focusing mass spectrometers. These instruments make the beam of ions passes through an electric field before entering the magnetic field to provide equal velocity to all the ions. This addition of equal velocity improves the resolution of the measurements.

Chapter 19

19.0 Ultraviolet-Visible Spectroscopy

19.1 Objectives

1. Describe the theory of uv/visible spectroscopy
2. Explain the structure of the instrument
3. Determine the functional groups and the structure of compounds

19.2 Introduction

This chapters covers the absorption of ultraviolet (UV) and visible light by organic molecules and the information that can be derived from those spectra.

The range used in uv and visible part of emr spectrum is expressed in nanometers (1 nm = 10^{-7} cm =10^{-9} m). The visible light range begins from 800 nm (long wavelength end, which is red) and ends at 400 nm (short wavelength, which is violet). The colors within the visible region are red, orange, yellow, green, blue, indigo, violet.

Approximate values of wavelengths for each color within the visible region of emr:

1. **Violet** - 400 - 420 nm
2. **Indigo** - 420 - 440 nm
3. **Blue** - 440 - 490 nm
4. **Green** - 490 - 570 nm
5. **Yellow** - 570 - 585 nm
6. **Orange** - 585 - 620 nm
7. **Red** - 620 – 800 nm

The ultraviolet range begins from 100 nm and ends at 400 nm. Nevertheless, in spectroscopic studies, the region from 200 nm to 400 nm is routinely used. The reason for not using the range between 100 nm – 200 nm is that atmospheric gases such as CO_2 also absorb UV light in this range. The absorption of UV or Visible light by molecules lead to electronic excitations from lower-energy ground state orbitals to higher-energy excited state orbitals.

Since visible light has a longer wavelength, they have low frequency and low energy. Therefore, the absorption of the visible range of emr promotes only the electrons that need low energy for excitations. All color compounds will absorb energy from the visible region (400 nm – 800 nm), since they have more electrons that require low energy for excitement. The colorless compounds absorb from the UV region (100 nm – 400 nm) since they have more electrons that require higher energy for excitement.

At this stage, it is important for you to review the Molecular Orbital Theory you have studied under general chemistry.

In organic molecules there are different types of molecular orbitals:

1. Sigma (σ) molecular orbitals
2. Pi (π) molecular orbitals
3. Non-bonding (n) molecular orbitals.

Each non-bonding orbital (n) contains an unshared pair (a lone pair) of electrons. They do not have any anti-bonding orbitals. The anti-bonding orbitals are formed when there is an overlap of two atomic orbitals. Therefore, sigma and pi orbitals, which are formed as a result of overlapping of atomic orbitals, have equal numbers of sigma and pi anti-bonding orbitals (σ* and π*). The σ and π are bonding orbitals are at the ground state level, and each of them has a pair of electrons. The σ bonds correspond to single bonds. These bonds are the lowest energy occupied molecular orbitals. The π orbitals are present in unsaturated molecules and are placed at a level higher than σ orbitals. The non-bonding level is higher than π orbitals. Then comes the antibonding orbitals of π and σ. In general, these antibonding orbitals σ* and π* are unoccupied.

When compounds are irradiated with UV or visible light, the energy absorbed will excite electrons from an occupied orbital to an unoccupied orbital of higher energy. The energy absorbed will later be dissipated as heat or light (phenomenon known as fluorescence).

The following table shows a selected list of possible transitions depending on the type of compound.

e.g. Alkanes will have only σ to σ* transitions since they have only σ bonds.

Transition	Compound
σ to σ*	Alkanes
π to π*	Alkenes, Carbonyl compounds, Alkynes, Azo compounds, etc.
n to σ*	Oxygen, Nitrogen, Sulfur, Halogen compounds
n to π*	Carbonyl compounds

Table 19.2.1: A selected list of possible transitions

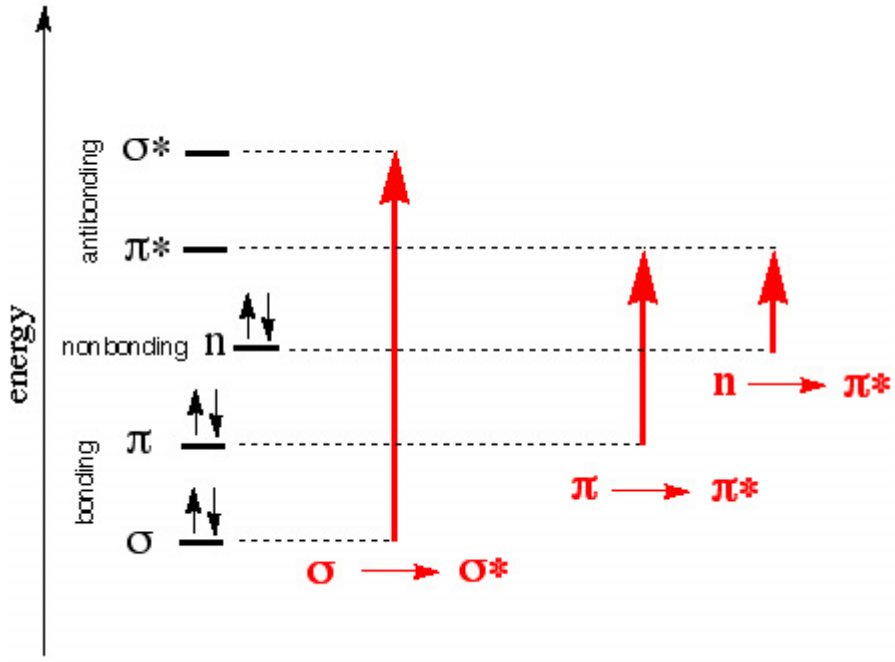


Figure 19.2.1: Energy needed for different transitions.

As shown in the above figure, the energy needed for a transition between the Highest Occupied Molecular Orbital (HOMO) also known as the highest occupied energy level and the Lowest Unoccupied Molecular Orbital (LUMO) also known as the lowest unoccupied energy level is less than the energy needed for a

transition between a lower occupied molecular orbital and a higher unoccupied molecular orbital. e.g. For a transition between n to π* requires less energy than a transition from π to π*.

It is important to note that these electronic transitions follow certain selection rules.

1. Spin selection rule - An electronic transition that leads to a change in its spin quantum number (spin multiplicity) is **not allowed**. This is a forbidden transition. This means $\Delta S = 0$ needs to be observed. Therefore, the transition between the states with the same total intrinsic spin or the same spin multiplicity **is allowed**.
2. Laporte (orbital) selection rule applies to the molecules with symmetry. According to this rule, the transitions between the states with the same symmetry (parity) (or transitions between the states with the same unsymmetry) with respect to an inversion center is **not allowed**.
   Gerade (in German meaning even) is a term used to describe an atomic or molecular orbital that is symmetric with respect to the center of inversion.
   Ungerade (in German meaning odd) is a term used to describe an atomic or molecular orbital that is anti-symmetric with respect to the center of inversion.
   Therefore, the transitions between gerade and gerade orbitals or ungerade and underade orbitals are not allowed, but transitions between gerade and ungerade or ungerade and gerade orbitals are allowed.
   Therefore, during an electronic transition, the azimuthal quantum number can change only by + or – 1.

19.3 Components of the instrument

The basic components are as follows:

1. Light source
   The light source is normally a deuterium lamp. This lamp emits ultraviolet region of emr. A tungsten lamp is used for wavelengths in the visible region. In a typical UV/visible spectrophotometer, the beam from the light source is split into two halves; one of the halves is directed to go through the sample solution (the compound being analyzed) in a cuvette and the other half of the beam known as the reference beam passes through a solvent in a cuvette. The solvent is selected in a way that they do not absorb any radiation from

the UV/visible region being analyzed. In order to determine the best solvent, the cutoff wavelength points of the solvents are considered. The cutoff point is the wavelength below which the solvent itself absorbs the light. Therefore, the selected solvent should have a cutoff point below the region being used for the analysis.

e.g. acetone – cutoff point 330 nm, benzene - cutoff point 278 nm, N, N-dimethylformamide - cutoff point 268 nm, ethanol - cutoff point 210 nm, toluene - cutoff point 284 nm, water - cutoff point 190 nm, hexane – cutoff point 195 nm.

The material that is used to make the cuvette is also carefully selected to not absorb any radiation from the region being analyzed. The material generally used is quartz, which does not absorb radiation from UV/visible region. The intensity of the radiation coming out of the reference cell has to be the same intensity as the original intensity (Io) of the radiation, since no absorption takes place. The intensity of the radiation that comes out from the sample (let us call it I) will have a lesser intensity than the intensity of the incident light.

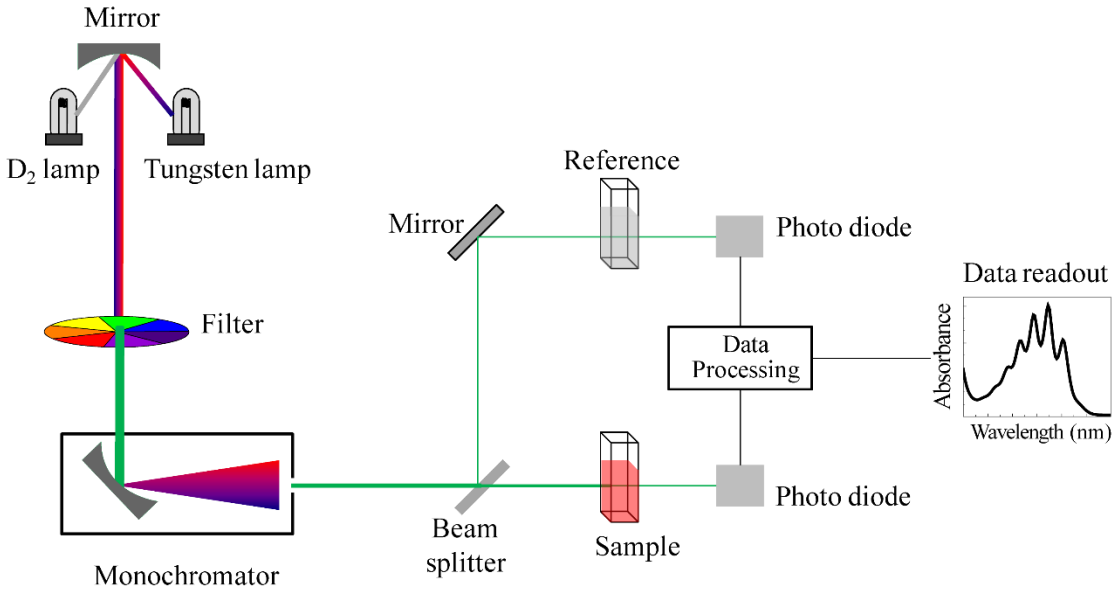


Figure 19.3.1: UV/Visible Spectrophotometer Diagram

This absorption wavelength is normally expressed as λmax.

The absorbance at a particular wavelength is defined as follows:

$$A = \log_{10}\left(\frac{I_0}{I}\right)$$

A = Absorbance
Io = Intensity of the incident radiation
I = Intensity of the radiation leaving the sample

The absorbance is different to optical density used in some measurements. The optical density is the degree to which a refractive medium retards the transmitted rays of light. The optical density considers both the absorbed and scattered light, whereas the absorbance considers only the absorbed light.
It is important to note that the absorption of radiation and transmittance of radiation have the following relationship:

$$A = \log_{10} T$$

T = Transmittance

Therefore,

$$T = \frac{I}{I_0}$$

$$T\% = \left(\frac{I}{I_0}\right) 100$$

The absorption of radiation by a compound at a given wavelength is dependent on the nature of the molecules and the number of molecules

present. The number of molecules is controlled by the concentration of the sample and the length of the cuvette. The Beer-Lambert law combines these factors in its expression:

$$A = \log_{10}\left(\frac{I_0}{I}\right) = \varepsilon C l$$

ε = molar absorptivity
C = concentration of the sample
l = length of the cuvette (sample cell)

The molar absorptivity also known as molar extinction coefficient is a property of the molecule undergoing electronic transition. This is not a function of the variable parameters included in the preparation of the solution. The probability of electronic transmission determines the absorptivity. This ranges from 0 – 10^6. Any value above 10^4 is considered high-intensity absorptions and any value below 10^3 is considered low-intensity absorptions. All forbidden transitions have absorptivity in the range of 0 – 100.

2. Monochromator
   This is a diffraction grating. The monochromator separates the beam of light into its component wavelengths. Without a monochromator, UV/visible instrument can measure only the intensity of one wavelength. By using a monochromator, different wavelengths can be directed to pass through the sample.
3. Detector
   The detector in a diode-array spectrophotometer consists of a series of photodiode detector positioned side by side on a silicon crystal. Each diode records a narrow band of the spectrum. Since the diodes are connected, the entire spectrum is recorded at once. This recording is displayed on a computer. The limitation of the number of diodes affects the resolution.

The following is an example of a UV spectrum of benzoic acid in cyclohexane:

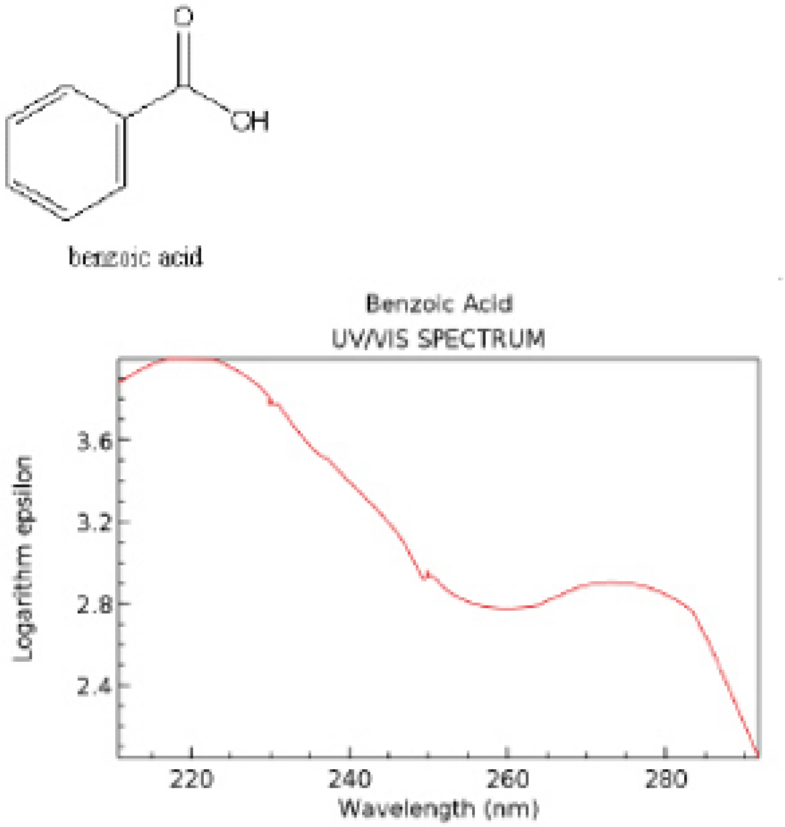


Figure 19.3.2: UV spectrum of benzoic acid in cyclohexane

The UV spectrum shows three peaks. Normally, the graph values are given as wavelengths of maximum absorption and it intensity.

For benzoic acid,

$\lambda max = 230$ nm

$\lambda max = 272$ nm

$\lambda max = 282$ nm

UV/Visible peaks are generally broad bands. The reason for this is that the electronic excitations have vibrational and rotational sub-levels. Therefore, the electronic transitions can happen from any one of the ground sub-levels to different sub-levels of the excited state. These various transitions differ slightly in energy. As a result, these wavelengths of absorption also differ slightly leading to broad bands.

19.4 Determining the Structure

Although the electronic excitations are promoted as a result of the absorption of energy from the UV/Visible region, the nuclei that hold these electrons control the energy difference between the ground and excited states. Therefore, the characteristic energy of a transition and the wavelength of radiation absorbed can be used to identify groups of atoms. Such groups of atoms in a compound (together with electrons) are known as chromophores. The changes in the structure of a chromophore will lead to changes in energy and intensity of absorptions. Therefore, there are empirical working rules that help to predict how the changes to the structures, change λmax of chromophores.

As discussed previously, in alkanes we can observe σ to σ* transitions. Other compounds such as alcohols, ethers, amines, etc, with atoms with non-bonding electrons will also display n to σ* transitions. The electrons of unsaturated compounds such as alkenes and alkynes will undergo π to π* transitions. The compounds with carbonyl group will display π to π* and n to π* transitions. The following is a table of absorption values for simple isolated chromophores:

Class of chromophore	**Transition**	**λmax nm**	**Log_{10} ε**
R-OH	n to σ*	180	2.5
R-O-R	n to σ*	180	3.5
R-NH_2	n to σ*	190	3.5
R-SH	n to σ*	210	3.0
$R_2C=CR_2$	π to π*	175	3.0
R−C≡C−R	π to π*	170	3.0
R−C≡N	n to π*	160	<1.0
R – N=N-R	n to π*	340	<1.0
R-NO_2	n to π*	271	<1.0
R-CHO	π to π*	190	2.0
	n to π*	290	1.0
R_2CO	π to π*	180	3.0
	n to π*	280	1.5
RCOOH	n to π*	205	1.5
RCOOR’	n to π*	205	1.5
$RCONH_2$	n to π*	210	1.5

Table 19.4.1: Absorption values for simple isolated chromophores

Therefore, when you observe the above λmax values on a graph of a UV/Visible spectrophotometer, you can predict the structure of the compound.

Most n to π* transitions absorb around 280 – 290 nm. Since these transitions are forbidden, they are of low intensity. A π to π* transition of an isolated carbonyl group absorbs at 188 nm. The above table shows that except for n to π*, all other chromophores absorb in the wavelength range of 160 - 210 nm.

From the above table, you should be able to understand that the suitability of a solvent depends on that solvents' λmax value. We can use any solvent as long as the λmax value of that solvent is below the absorption values of the compounds we are analyzing. Also, the presence of conjugation pushes λmax values to higher levels. Therefore, UV/Visible spectra also provide information about the existence of conjugation.

19.5 The Effect of Conjugation

When two double bonds are separated by a single bond, the two double bonds are known as conjugated bonds. If two double bonds are isolated by more than one single bond, then those double bonds are known as isolated double bonds. The energy required to promote a transition between HOMO and LUMO in a conjugated double bond is less than that is required in an isolated double bond. Since less energy means longer wavelength, λmax for a conjugate double bond is higher than that of an isolated double bond.

The conjugation of two chromophores normally has two effects:

1. A shift to longer wavelength
2. An increase in the intensity

The following table shows the effect of conjugation:

Alkenes	**λmax**	**ε**
Ethylene	175	15,000
1,3-butadiene	217	21,000
1,3,5-hexatriene	258	35,000
-carotene (this compound has 11 conjugated double bonds)	465	125,000
Ketones		
Acetone	189	900
	280	12
3-buten-2-one	213	7100
	320	27

Table 19.5.1: The effect of conjugation

The conjugation extends the pi bond character. As a result, the difference between HOMO and LUMO becomes smaller. Therefore, the energy needed for the transition becomes smaller. Consequently, λmax moves to longer wavelengths.

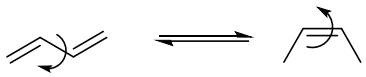
In addition to the changes we observe due to conjugation, when substituent groups replace hydrogen atoms in compounds, the position and the intensity of absorption changes for the main compound.

It is important to note that the substituent groups may not be absorbing high energy themselves, but the addition to other compounds lead to λmax and intensities. Such groups are known as auxochromes. e.g. methyl (CH_3 -), hydroxy (-OH), alkoxy (O-R), halogen (F, Br, Cl, I), amine (-NH_2). Although CH_3 group from the above example does not have unshared electrons as other auxochromes, the overlap of C-H bonding orbitals with the pi system of the compound with which it combines leads to an extension of the pi character. This is known as hyperconjugation. Therefore, the compound that combines with a methyl group will show a bathochromic shift. All other auxochromes mentioned above have unshared electrons.

In UV/Visible spectroscopy, these changes are known by the following terms:

1. Bathochromic shift (red shift) – a shift to lower energy or longer wavelength
2. Hypsochromic shift (blue shift) – a shift to higher energy or shorter wavelength
3. Hyperchromic effect – an increase in intensity (increase in molar absorptivity)
4. Hypochromic effect – a decrease in intensity (an decrease in molar absorptivity)

The dienes that show conjugation can exist in space as trans and cis form. In the example below, butadiene can exist as s-trans (transoid) or s-cis(cisoid) conformation:

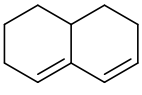


s-trans conformation (transoid) s-cis conformation (cisoid)

The above two forms can interconvert by the rotation around the connecting single bond. Most of simple acyclic conjugated dienes exist in a planer s-tran (transoid) conformation.

When the two double bonds of a conjugated system are in one ring, it is known as a homoannular diene. When the two double bonds are in two separate rings, it is known as a heteroannular diene.

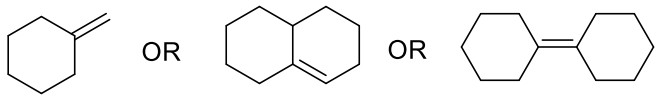
Homoannular (cisoid) – λmax – 273 nm, lower intensity



Heteroannular (transoid) – λmax – 234 nm, higher intensity

Homoannular diene has a cisoid conformation and absorb at a longer wavelength with lower intensity. The heteroannular has a transoid conformation and absorb at a shorter wavelength than the homoannular diene and has a higher intensity.

When a double bond is connected from the outside to a ring, it is known as an exocyclic double bond. This double bond could be a part of another ring or may be connected on its own.



The above figure shows three forms of exocyclic double bonds. The last compound has a double bond that is exocyclic to both rings

19.6 Woodward-Fieser Rules for Dienes

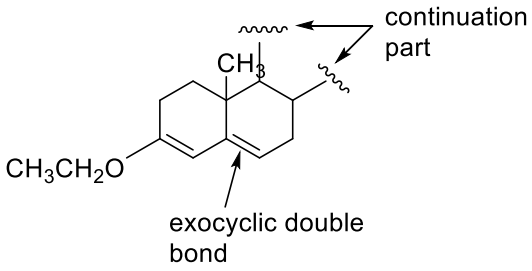
This rule helps to predict the total λmax values of dienes by adding individual λmax values of different components within a diene compound.

This rule works well for conjugated systems with 4 or less double bonds. The following table provides the values for calculations:

Core Chromophore - Base value for heteroannular or transoid diene	215 nm
Core Chromophore - Base value for homoannular or cisoid diene	253 nm (for cyclohexadiene – 260 nm)
Increment for double bond extending conjugation	+30
Increment for alkyl substituent or ring residue	+5_
Increment for exocyclic double bond	+5
Increment for polar grouping RCO_2- Acyl group	+0
Increment for polar grouping RO- Alkoxy groups	+6
Increment for polar grouping RS- Sulfide group	+30
Increment for polar grouping Cl, Br	+5
Increment for polar grouping R_2N- Amino group	+60
Further pi conjugation by C=C double bond	+30
Further pi conjugation by C_6H_5 Phenyl group	
Solvent correction	+0
Final λmax	Total

Table 19.6.1: Individual λmax values for selected components

e.g.



Base value for heteroannular diene = 215 nm

Ring residues – 3 X 5 = 15 nm

Exocyclic double bond = 5 nm

-OR = 6 nm

Total = 241 nm – Calculated value

Experimental value = 241 nm

19.6.1 Woodward-Fieser Rules for Carbonyl Compounds and Enones

Carbonyl compounds have two principal transitions:

1. Allowed - π to π* - high intensity – 190 nm
2. Forbidden - n to π* - low intensity – 280 nm

Since, π to π* is below 200 nm, only forbidden, weak n to π* transition is observed. As a result of the substitution on the carbonyl group by an auxochrome with a lone pair of electrons (-NR_2, -OH, -OR, -X giving amides, acids, esters, acid chlorides) will lead to a stronger hypsochromic shift on n to π* transition and lesser bathochromic shift on π to π* transition. The bathochromic shift is small and is not sufficient to shift the π to π* to useful UV region.

The following table provides hypsochromic shifts of lone pair auxochromes on the π to π* transition of a carbonyl group:

Compound with auxochrome	λmax nm	**εmax**	**Solvent**
CH_3-CHO	293	12	Hexane
CH_3-CO-CH_3	279	15	Hexane
CH_3-CO-Cl	235	53	Hexane
CH_3-CO-NH_2	214	-	Water
CH_3-CO-O-CH_2-CH_3	204	60	Water
CH_3-CO-OH	204	41	Ethanol

Table 19.6.1.: Hypsochromic shifts of lone pair auxochromes on the π to π* transition of a carbonyl group

The solvents selected have a cutoff point below λmax values.

The hypsochromic shift of n to π* transition is due to the inductive effect of oxygen, nitrogen, or halogen atoms. These atoms withdraw electrons from the carbonyl carbon. As a result, oxygen holds on to the electron pair firmly.

If the carbonyl compound is conjugated with double bonds, then both π to π* and n to π* will shift to longer wavelength. Nevertheless, the energy for n to π* transition will not decrease rapidly as π to π* transition. The π to π* transition is more intense than n to π*transition. If the conjugated chain becomes sufficiently long, then n to π* band will be masked (buried under) by π to π* transition.

The following values can be used to calculate λmax values for carbonyl compounds or enones:

α, β UNSATURATED CARBONYL COMPOUNDS OR KETONES:

1. Base value: a) Acyclic α, β unsaturated ketones = 214 nm

b) 6 membered cyclic α, β unsaturated ketones = 215 nm

c) 5 membered cyclic α, β unsaturated ketones = 202 nm

d) α, β unsaturated aldehydes = 210 nm

e) α, β unsaturated carboxylic acids & esters = 195 nm

2. Alkyl substituent or Ring residue in α position = 10 nm

3. Alkyl substituent or Ring residue in β position = 12 nm

4. Alkyl substituent or Ring residue in γ and higher positions = 18 nm

5. Double bond extending conjugation = 30 nm

6. Exocyclic double bonds = 5 nm

7. Homodiene compound = 39 nm

8. Polar groups: a) –OH in α position = 35 nm

–OH in β position = 30 nm

–OH in δ position = 50 nm

b) –OAc in α, β, γ, δ positions = 6 nm

c) –OMe in α position = 35 nm

–OMe in β position = 30 nm

–OMe in γ position = 17 nm

–OMe in δ position = 31 nm

d) –Cl in α position = 15 nm

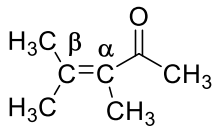
–Cl in β position = 12 nm

e) –Br in α position = 25 nm

–Br in β position = 30 nm

f) –NR2 in β position = 95 nm

e.g.



Acyclic enone = 215 nm

αCH_3 = 10 nm

βCH_3 = 24 nm

Total = 249 nm

Observed = 249 nm

Similarly, the following values can be used for aromatic compounds:

1) Base value: for a) ArCOR = 246 nm

b) ArCHO = 250 nm

c) ArCO2H = 230 nm

d) ArCO2R = 230 nm

2) Alkyl group or ring residue in ortho and meta position = 3 nm

3) Alkyl group or ring residue in para position =10 nm

4) Polar groups: a) –OH, –OCH3, –OAlkyl in o, m position = 7 nm

b) –OH, –OCH3, –OAlkyl p position = 25 nm

c) –O (oxonium) in o position = 11 nm

d) –O (oxonium) in m position = 20 nm

e) –O (oxonium) in p position = 78 nm

f) –Cl in o, m position = 0 nm

g) –Cl in p position = 10 nm

h) –Br in o, m position = 2 nm

i) –Br in p position = 15 nm

j) –NH2 in o, m position = 13 nm

k) –NH2 in p position = 58 nm

l) –NHCOCH3 in o, m position = 20 nm

m) –NHCOCH3 in p position = 45 nm

n) –NHCH3 in p position = 73 nm

o) –N(CH3)2 in o, m position = 20 nm

p) –N(CH3)2 in p position = 85 nm

Chapter 20

20.0 Infrared Spectroscopy

20.1 Objectives

1. Describe the theory of IR spectroscopy
2. Explain the structure of the instrument
3. Determine the functional groups and the structure of compounds

20.2 Introduction

This is another analytical method used to determine the structure of organic molecules. Almost any compound with covalent bonds, organic or inorganic, absorbs varying frequencies of infrared (IR) region. The narrow region of IR absorbed by a particular bond or functional group is unique for that bond or functional group. Therefore, this feature is used to analyze a compound.

In organic compounds, the bonds that connect atoms together undergo constant vibrations. These are known as molecular vibrations. In a diatomic molecule, the two atoms joined by a covalent bond can undergo stretching vibrations (atoms move back and forth) as shown below:

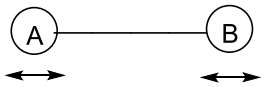
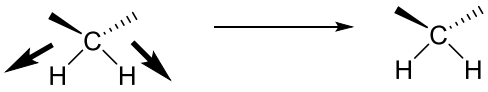


Figure 20.2.1: A stretching vibration – atoms move back and forth

The stretching vibrations change the bond length. Similarly, a polyatomic molecule will vibrate in many other ways. In addition to stretching, they display bending vibrations, too.

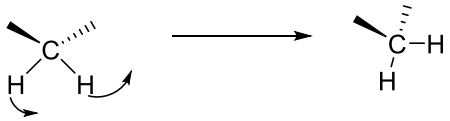
Symmetric Stretching



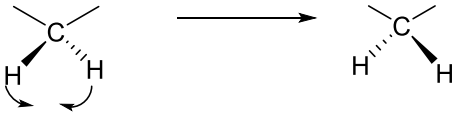
Asymmetric stretching

On the same plane bending - scissoring

On the same plane bending - rocking



Out of plane bending – twisting



Out of plane bending – wagging

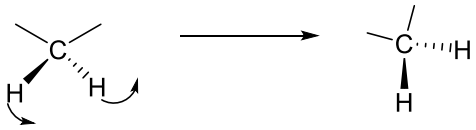


Figure 20.2.2: A stretching and bending vibrations of a polyatomic molecule

- Note the changes to the length of the bond in stretching. Also, the changes to the plane of the hydrogen atoms in twisting and not wagging. In scissoring the distance between H atoms reduces while in rocking that distance increases. As a result of vibrations, the bond angles change. Such different types of vibrations are called fundamental modes of vibrations of the molecule.

In a linear molecule, there are three translational degrees of freedom and two rotational degrees of freedom. The rest is vibrational. Therefore, the total number of fundamental vibrations for a given molecule is 3N-5. Similarly, in a non-linear molecule, there are three translational degrees of freedom and three rotational degrees of freedom. The rest is vibrational. Therefore, the total number of vibrations for a non-linear molecule is 3N-6. N is the number of atoms.

20.3 IR Spectrum

An infra spectrum of a compound is a graph where the percentage of transmittance is plotted against the wavenumber ($\tilde{\upsilon}$).

$$\tilde{v} = \frac{1}{\lambda}$$

Wavenumber is the number of complete wave cycles of an electromagnetic field per unit distance (normally expressed as cm^{-1}).

The transmittance (T) is given as follows:

T% = (Transmitted intensity/incident intensity) X 100

According to the above equation, if a compound does not absorb IR radiation, it will be noted as 100% transmittance. When a compound absorbs IR radiation, this will appear as a dip in the spectrum. The T% will then be less than 100.

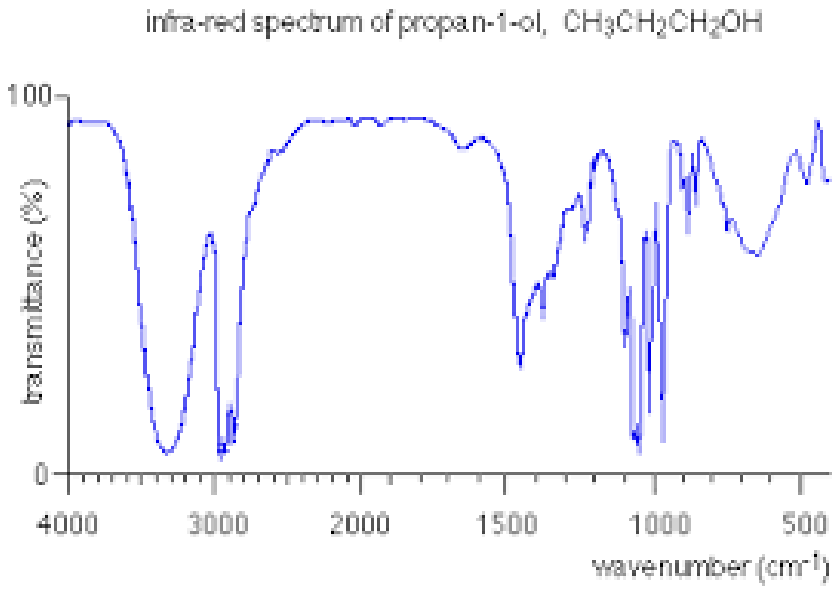


Figure 20.2.3: IR spectrum of propanol

20.4 IR Instrument

Infrared spectrophotometer is the instrument used to measure IR absorption by compounds.

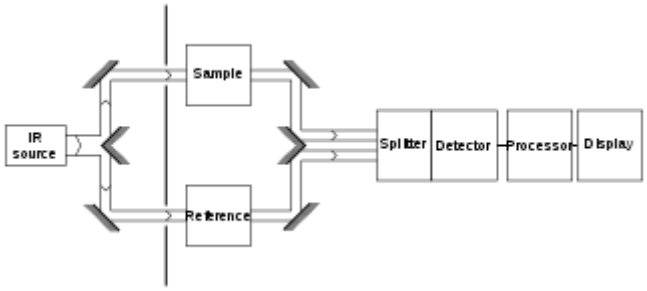


Figure 20.4.1: The basic structure of an IR Spectrophotometer

The IR source emits all wavelengths of IR radiation. The light is split using mirrors into two beams. One half of the beam will pass through the sample cell while the other half will pass through the reference cell. If the sample is dissolved in a solvent, then that pure solvent is used in the reference cell. If the sample is a pure compound, then the reference cell will be an empty cell.

After the beam passes through both cells, they go through the splitter, which controls and allows the two beams (reference and sample beams) to reach the detector alternatively. After the detector, the processor will compare the beams and the results are displayed on the screen.

Samples used could be solid, liquid, or gas. When the sample is a gas, a long pathlength (the length of the sample tube) is selected, since gas concentration is low. The glass tube is made of infrared-transparent windows at both ends.

When the sample is a liquid, the liquid is sandwiched between the two plates of a salt (sodium chloride). These two plates are infrared-transparent.

When the sample is a solid, one method of preparing the solid is by crushing the solid and mixing it with a mineral oil (Nujol brand) and apply a thin film on the two solid plates.

As shown in the sample spectrum below, the minimum points (which is the maximum absorption points) in the IR spectrum are noted (as the wavenumber values or frequency values or wavelength values) to identify different vibrational points and associated functional groups, bonded atoms, and types of bonds.

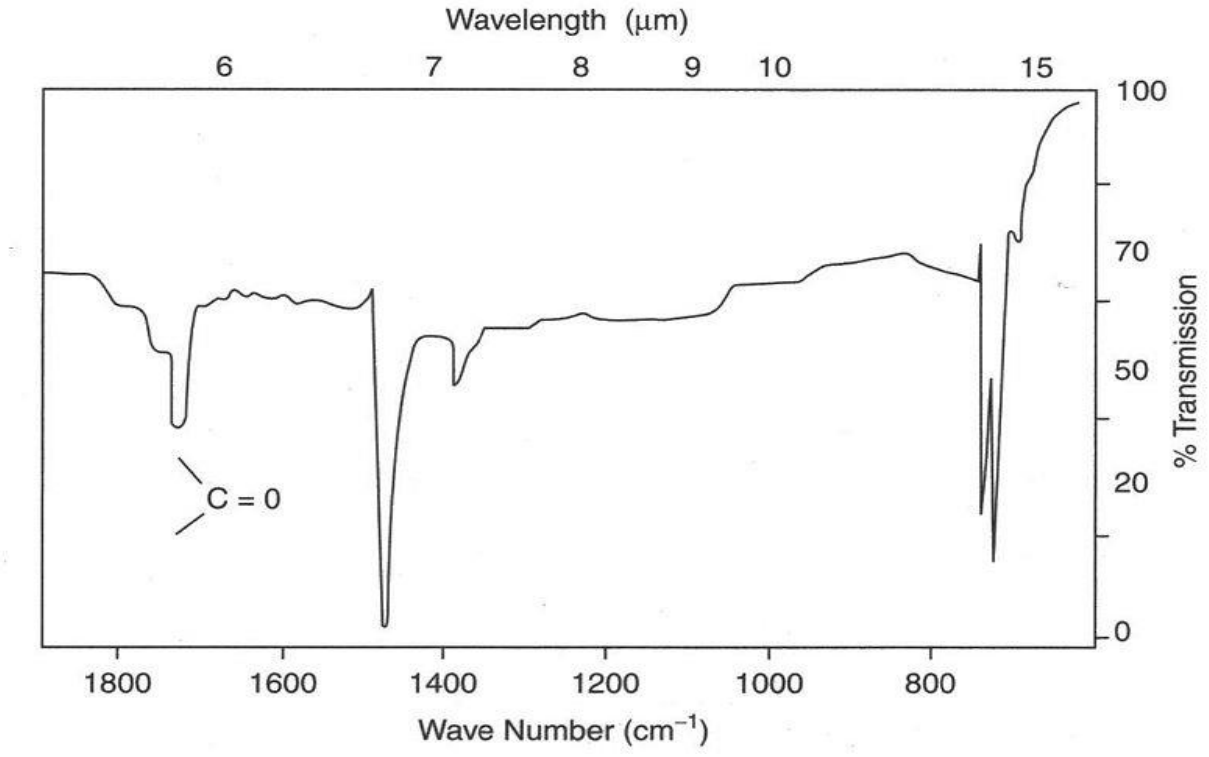


Figure 20.4.1. A sample IR spectrum

IR bands are also classified according to the intensity values as strong (s), medium (m), and weak (w). When a weak band overlaps a stronger band, it is called a shoulder (sh). The number of identical groups in a compound will increase the signal of a band (i.e. Two -CH bonds will produce a stronger band than one -CH group).

A strong band covers most of the y-axis and a weak band covers a small section of the y-axis as shown below:

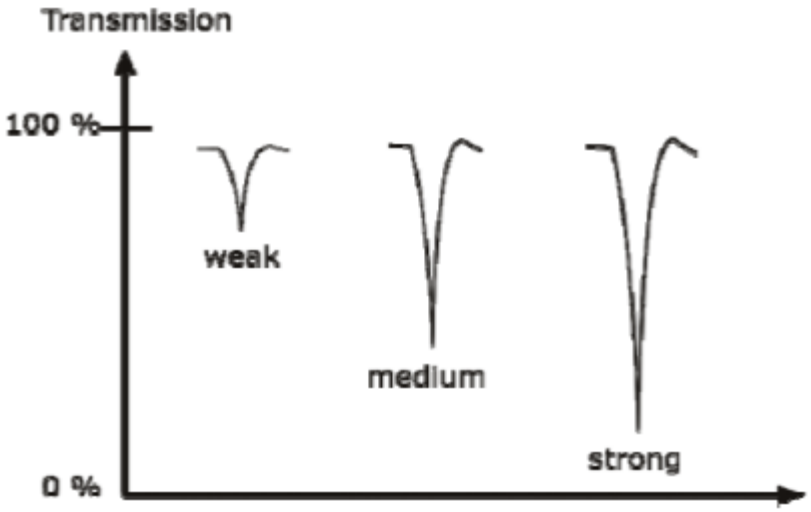


Figure 20.4.1. Examples of weak, medium, and strong IR bands

The intensity plays a vital role in identifying functional groups. A change in the dipole moment of a molecule leads to vibrations. Therefore, a large change in the dipole leads to a strong absorption of IR radiation. As a result, carbonyl groups absorb IR radiation strongly and produce strong peaks. When there is no change or a small change in the dipole, the band will be a weak band. Therefore, the stretching of carbon-carbon double or triple bonds give weak absorptions.

The IR spectrum in general has many bands. This is dependent on the number of atoms in the sample molecule. When you apply the degrees of freedom equation discussed under the introduction of this chapter (linear – 3N-5 and non-linear 3N-6), the number of vibrations can be determined.

e.g.

CH_4 has 9 fundamental modes of vibrations. N here is 5 and the molecule is non-linear.

Therefore,

3 X 5 – 6 = 9 fundamental modes of vibrations.

IR spectrum bands are useful to identify different types of bonds or functional groups, since these absorb IR at different wavelengths. The reason for different bonds or functional groups to have different IR absorption frequencies is because the stretching frequency is dependent on the masses of the atoms connected to a bond. The strength of the bond is related to its force constant.

The stretching frequency of a bond is given by the following equation:

$$\nu = \frac{1}{2\pi}\sqrt{\frac{f(m_1 \times m_2)}{m_1 m_2}}$$

$$\tilde{\nu} = \frac{1}{2\pi c}\sqrt{\frac{f(m_1 \times m_2)}{m_1 m_2}}$$

$\tilde{\upsilon}$ = wavenumber (expressed in cm^{-1})

m_1 and m_2 = masses of the two atoms connected by a bond (expressed in grams).

f = force constant (expressed in Nm^{-1})

c = velocity of light

The force constant for,

a single bond is about 5 X 10^{-1} Nm^{-1}

for a double bond it is 10 X 10^{-1} Nm^{-1}

for a triple bond it is 15 X 10^{-1} Nm^{-1}

Therefore, a triple bond has a higher stretching frequency since its force constant is high.

Since the stretching is also dependent on the mass of atoms, lighter atoms such H will have higher frequencies according to the equation.

20.5 Interpreting IR Spectra

In IR spectra, the mid-infrared region from 400 – 4000 cm^{-1} is the most useful region (the other two regions are near-infrared – 13000 – 4000 cm^{-1} and far-infrared – 400 – 10 cm^{-1}).

The region between 400 and 1400 cm^{-1} is known as the fingerprint region. This region is very complex and contains many absorption bands that include stretching and bending vibrations. Therefore, the bands present in this region can be directly correlated to functional groups. Additionally, since each compound has unique absorption patterns, these become useful in the identification of compounds by comparison. This is why this region is known as the fingerprint region.

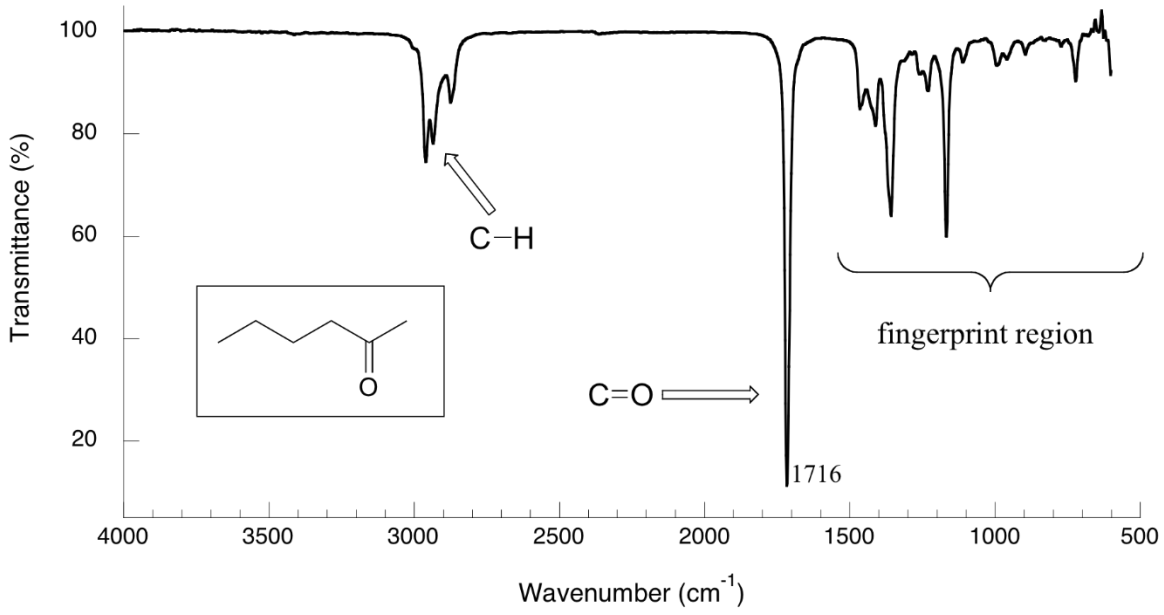


Figure 20.5.1: Fingerprint region

20.5.1 Absorption by Carbon-Carbon Bonds

Bonds between sp^3 hybridized carbon atoms display weak absorption bands in the IR spectrum. These are not useful in the structure identification. Bonds between sp^2 hybridized carbon atoms (C = C bonds) exhibit absorption between 1600 -1700 cm^{-1}. When it comes to symmetric alkenes, since they contain non-polar C=C bonds, they will not absorb IR radiation. Nevertheless, unsymmetrical alkenes that contain polar double bonds will show absorption in the range of 1600 – 1700 cm^{-1}. It is important to note that these stretching creates only a smaller change in the dipole moment. Therefore, these are weak absorptions.

Aryl C-C bonds (C-C bonds of aromatic compounds) display absorptions at lower frequencies. Carbon-carbon triple bonds (sp hybridized) show absorption between 2100-2260 cm. Except nitrile group ($C\equiv N$), there are no other functional groups that absorb in this region.

20.5.2 Absorption by C-H bonds

C-H stretchings are noted between 2700 – 3300 cm^{-1}. C-H stretching peaks are used to determine hybridization of carbon atoms.

Alkanes C-H bonds between saturated carbons and hydrogens are displayed in the region of 2850 – 2960 cm^{-1}. The stretching by alkenyl (vinylic) carbon -hydrogen bonds (=C-H) happens around 3020-3080 cm^{-1}. These alkenyl C-H bonds also display bending in the fingerprint region.

The $-C\equiv C-H$ stretching happens in 3300 cm^{-1} region.

The following graphs (figures 20.5.2.1, 20.5.2.2, 20.5.2.3) show the IR spectra for C-H, =C-H, and $\equiv C-H$ stretching.

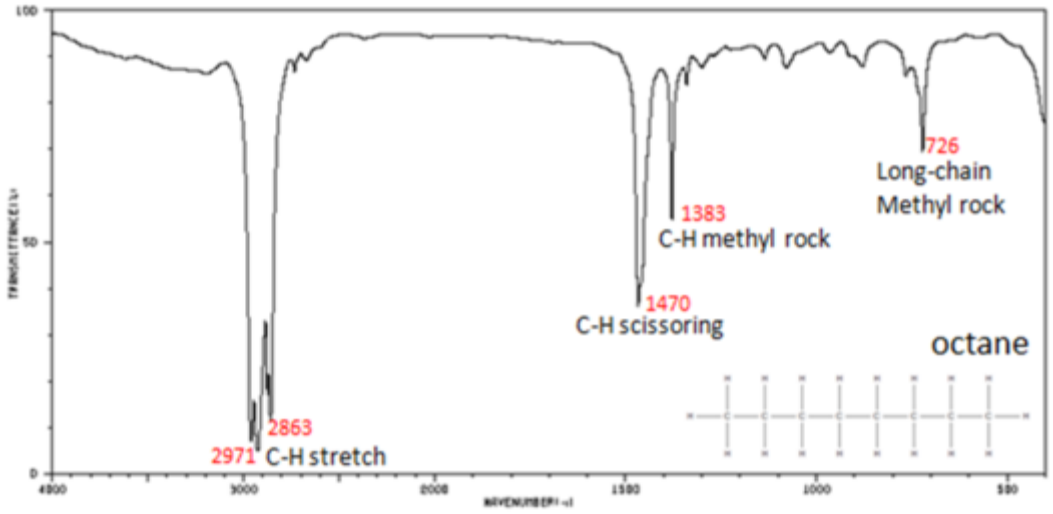


Figure 20.5.2.1: IR spectra for C-H Stretching

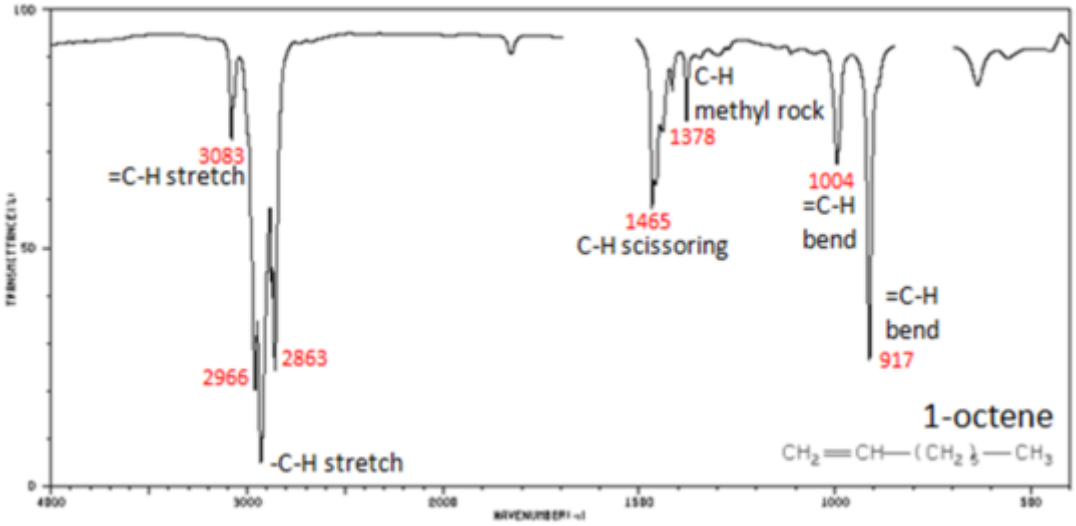


Figure 20.5.2.2: IR spectra for C=H Stretching

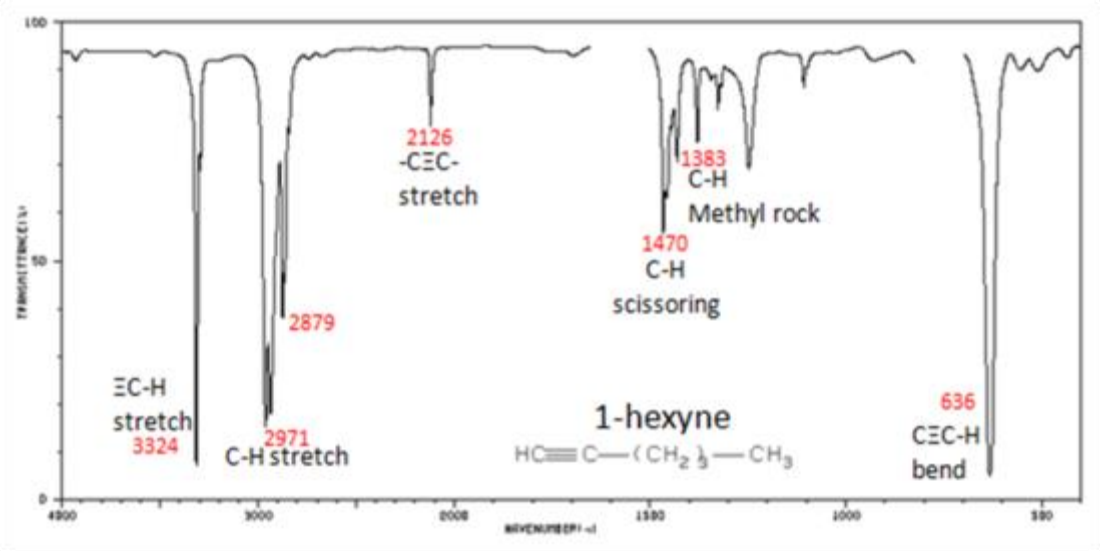


Figure 20.5.2.3: IR spectra for $\equiv C-H$ Stretching

20.5.3 Absorption by Haloalkanes (C-Cl, C-Br, C-I)

Carbon-Halogen stretching falls in the fingerprint region of 500-1430 cm^{-1}. It is important to note that the presence or absence of a band in this region alone cannot be related to the presence or absence of a halogen in the compound. Additional information is required for such confirmation.

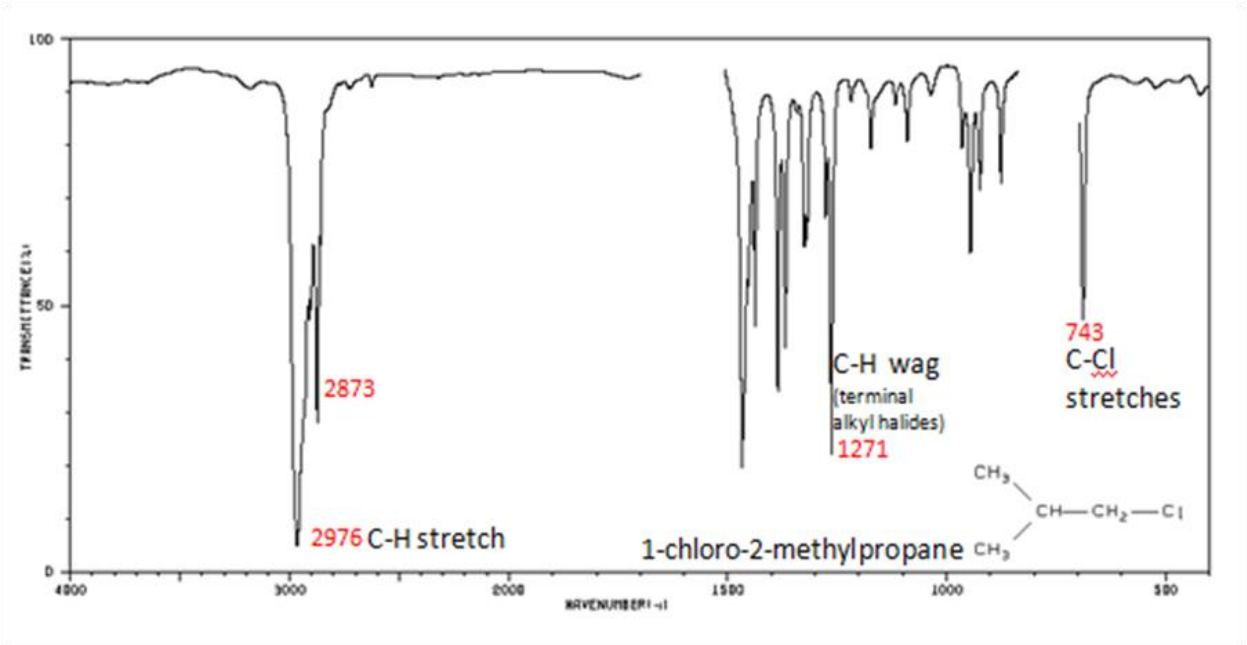


Figure 20.5.3.1: IR spectra for haloalkanes

20.5.4 Absorption by Alcohols and Amines

The O-H in alcohols and the N-H in amines show stretching absorptions in the region 3200 – 3650 cm^{-1}. When there are two hydrogens on an amine (a primary amine), then N-H absorption appears as a double peak. When only one N-H exists as in secondary amine, only one peak appears. A tertiary amine with no H atoms will not show any absorption in this region.

The O-H stretching band in alcohols is a prominent broad band centered around 3330 cm^{-1}. Alcohols and amines also exhibit C-O and C-N absorptions. These absorptions occur in the region 1000 -1360 cm^{-1}. Also, the existence of hydrogen bonds changes the position and appearance of IR bands. When H-bonds are widespread (in pure, liquid alcohol), a wide band around 3300 cm^{-1} appear. When H-bonds are not extensive (alcohol in vapor phase has no H-bonds), then sharper less intense peak is observed.

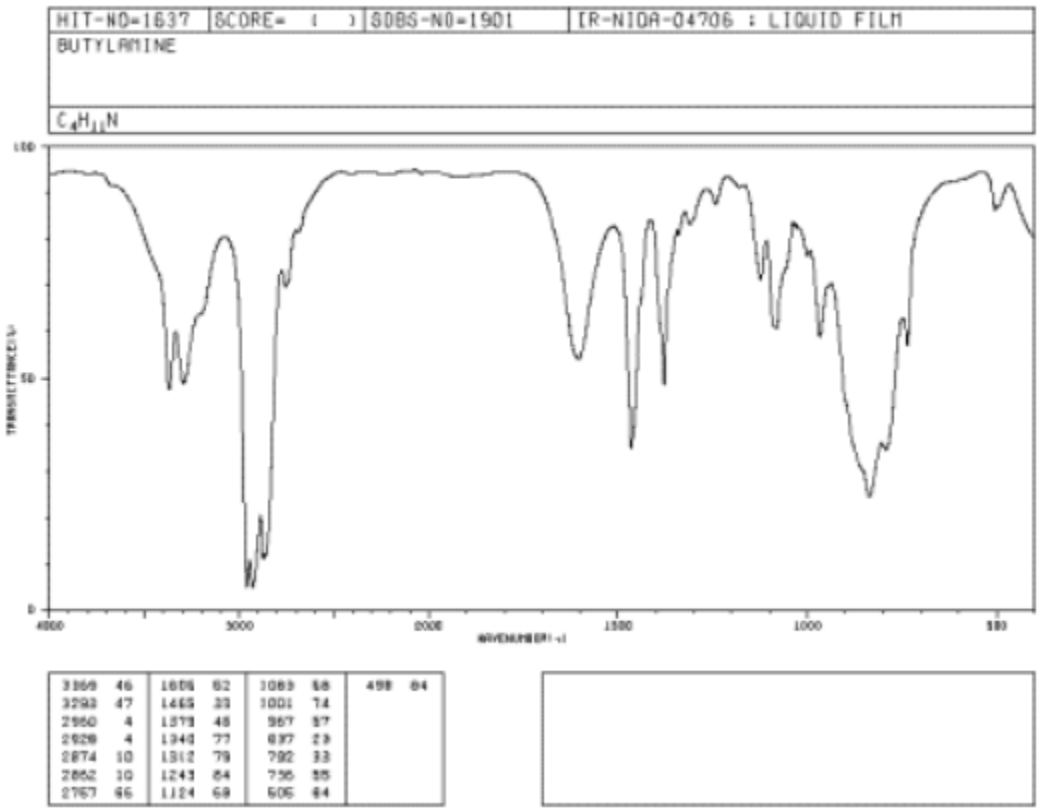


Figure 20.5.4.1: IR spectrum of primary amine N-H stretching – butylamine absorption- $H_3CH_2CH_2CH_2C-NH_2$

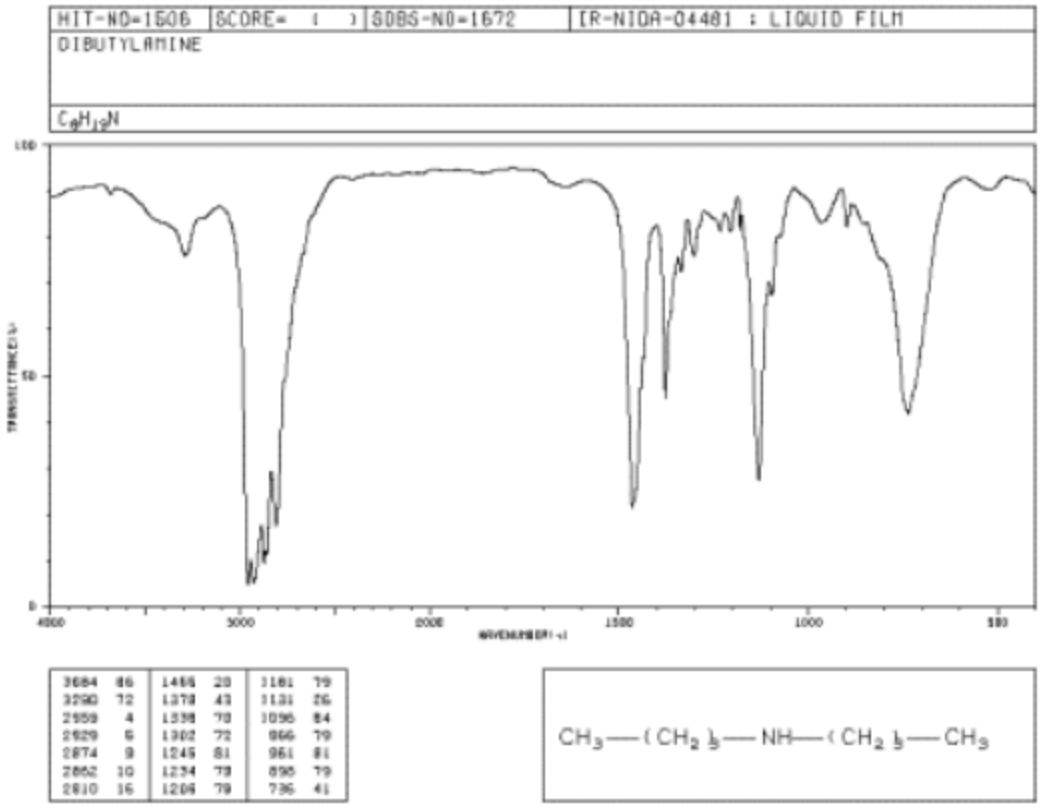


Figure 20.5.4.2: IR spectrum of secondary amine N-H stretching - dibutylamine

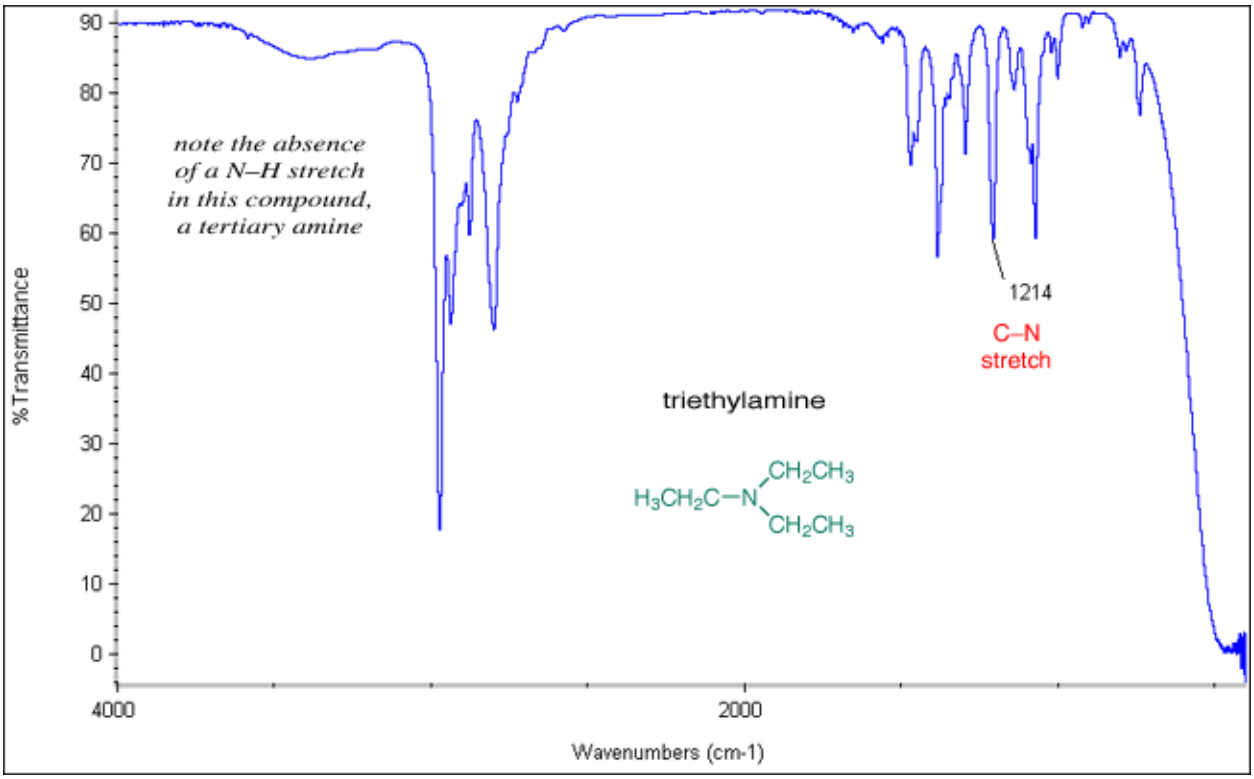


Figure 20.5.4.3: IR spectrum of tertiary amine – No N-H stretching – triethyl amine

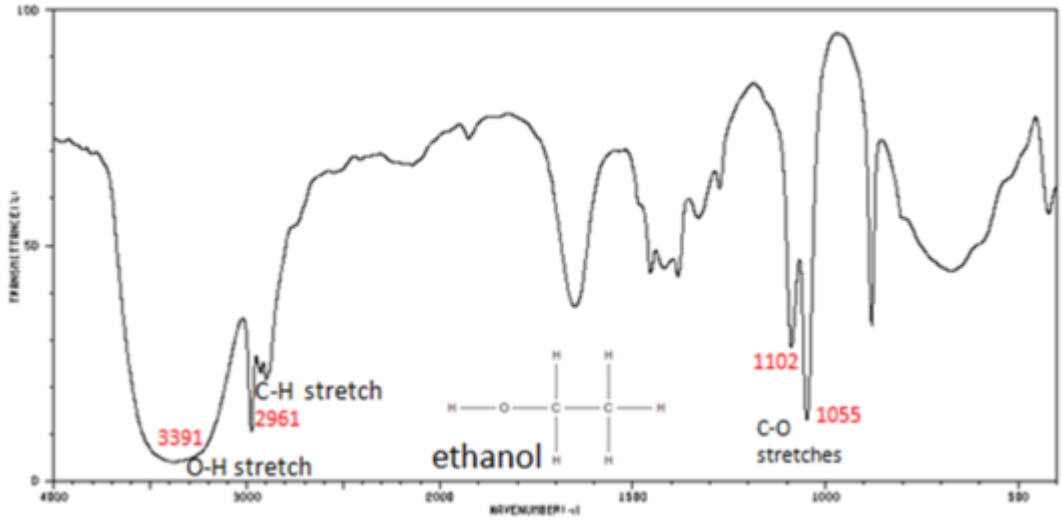


Figure 20.5.4.4: IR spectrum of alcohol O-H stretching

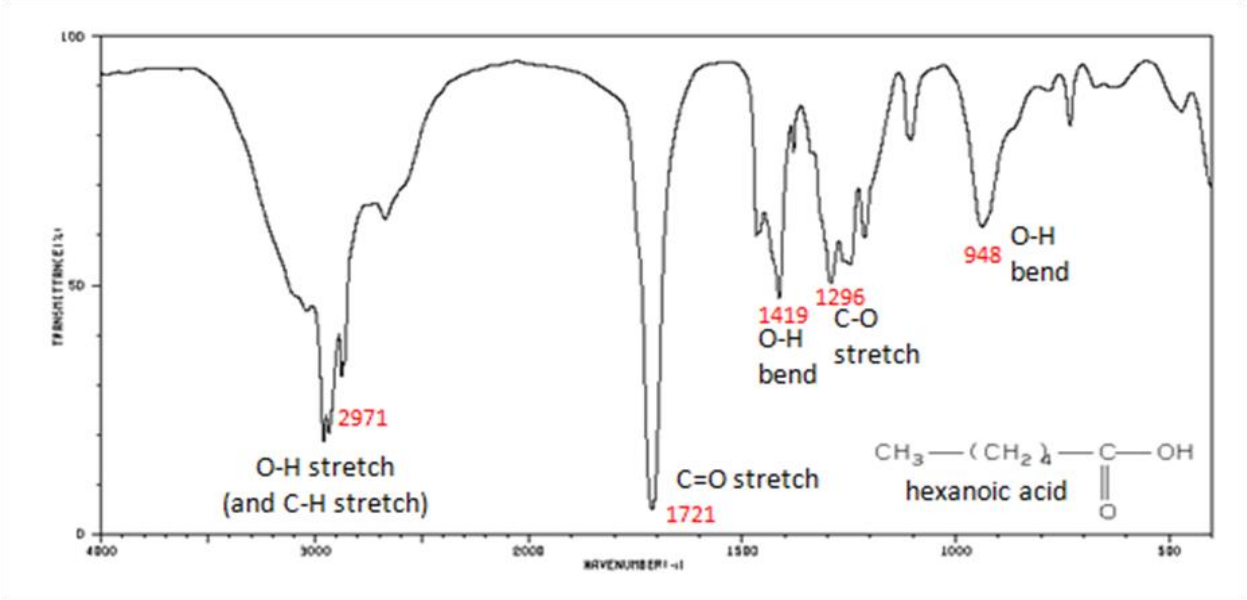


Figure 20.5.4.5: Infrared spectrum of some functional groups

20.5.5 Absorption by Ethers

Ethers show an absorption due to C-O in the region of 1000 cm^{-1} – 1300 cm^{-1}. Since oxygen is electronegative, the stretching causes a large change in the dipole moment. This C-O is quite intense. Alcohols, ethers, and other compounds with C-O show absorptions in this region.

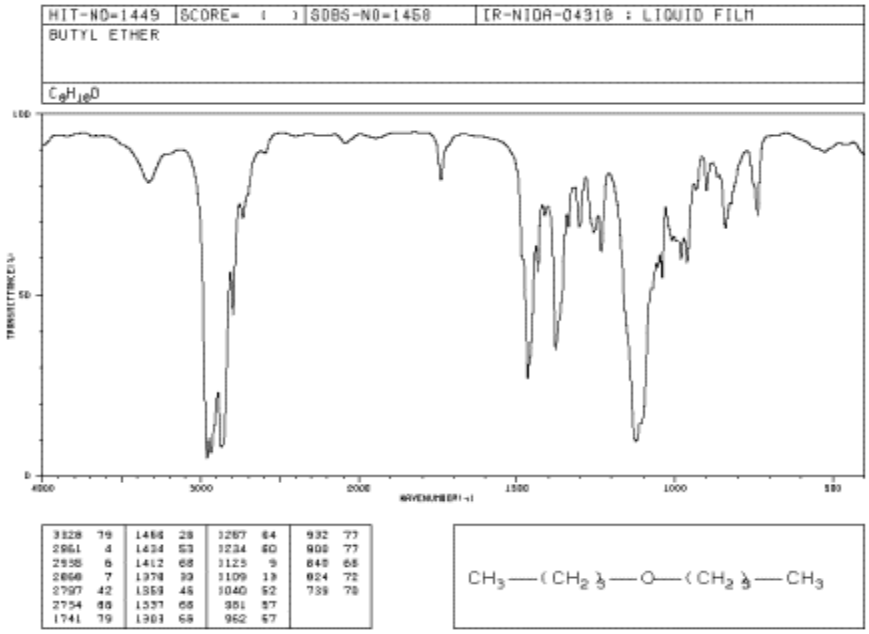


Figure 20.5.5.1: IR Spectrum of dibutyl ether

20.5.6 Absorption by Carbonyl Compounds

The compounds that come under this category are aldehydes, ketones, acids, esters, amides, acid anhydrides, and acid chlorides. Carbonyl group absorbs strongly and appears in the range 1850 -1650cm^{-1}.

A link to obtain a list of IR absorption values is given at the end of this chapter. The absorption by a carbonyl group is dependent on the functional group. Anhydrides absorb at the highest frequency and amides absorb at the lowest frequency.

The change in the absorption by a carbonyl group attached to different functional group/s can be explained as follows:

1. Electron Withdrawing Effect – Inductive Effect

When carbonyl carbon is attached to an electronegative group (e.g. Cl), that electronegative group will pull electrons from C and O bond toward the group. This increases the carbonyl frequency while C=O bond becomes stronger.

The electron withdrawing effect is clearly seen when ketones and aldehydes absorptions are considered. Since ketones have an additional alkyl group, which is electron-donating (relative to H) and provides electrons to C=O, this weakens C=O bond and reduces frequency.

2. Resonance Effect

The resonance effect increases the single bond character. An increase in single bond character will reduces the frequency of C=O.

The above two effects have a combined effect. When electron withdrawing effect is more important than the resonance effect, it will result in a net increase in the carbonyl absorption frequency. When resonance effect is more important than the electron withdrawing effect, then the carbonyl frequency will reduce.

3. Hydrogen Bonding Effect

Hydrogen bonds combine molecules. Therefore, the frequency of C=O will reduce.

4. Ring Size Effect

When a carbonyl group is attached to a ring structure, the frequency increases with increasing strain of the angle of the ring. The smaller the ring, the higher the angle strain. This means carbonyl groups attached to smaller rings will produce higher frequency bands.

5. Conjugation Effect

When conjugation happens, it increases the single bond character of C=O and C=C bonds. Therefore, the frequency reduces. In general, an introduction of a conjugated double bond reduces the frequency by 25 – 45 cm^{-1}.

I have given below a link where you can access two tables displayed on Sigma-Aldrich website. The two tables provide the IR values by the type of stretching (i.e. O-H, C-H, N-H, etc.) and by the compound class (i.e. aldehydes, alcohols, amines, etc.) You do not need to know all these values, but you can refer to them when needed.

The link:

https://www.sigmaaldrich.com/US/en/technical-documents/technical-article/analytical-chemistry/photometry-and-reflectometry/ir-spectrum-table.

Chapter 21

21.0 Nuclear Magnetic Resonance Spectroscopy

21.1 Objectives

1. Describe the theory behind NMR
2. Describe the main components of NMR instrument
3. Explain the uses of H-1 and C-13 NMR spectroscopy
4. Apply NMR as an analytical tool to determine the structure of organic compounds

21.2 Introduction

We have so far studied mass, UV/Vis, and IR spectroscopy.

In NMR, we measure the absorption of radio waves by some nuclei of atoms in organic or inorganic molecules, when placed in a strong magnetic field. An NMR spectrum is a plot of frequency of absorption versus peak intensities. The absorption of radio frequency leads to transitions between nuclear spin states.

From our previous lessons, we know that IR spectrum provides information about functional groups, UV/Vis provides information about conjugation systems present, in addition to other information. Similarly, NMR provides information about C and H atoms in an organic compound. This information assists in the structure determination.

21.3 Nuclear Spin

The nucleus of an atom carries protons (positive charges) and neutrons (zero charges). In some type of nuclei, this charge spins on the axis of the of the nucleus. This spin generates a weak magnetic field. As a result, they behave as small magnets. These magnetic fields are vector quantities. The magnetic field is described by nuclear magnetic moment (μ). The spin of a nucleus is expressed as I for the spin quantum number and m for the spin in a magnetic field.

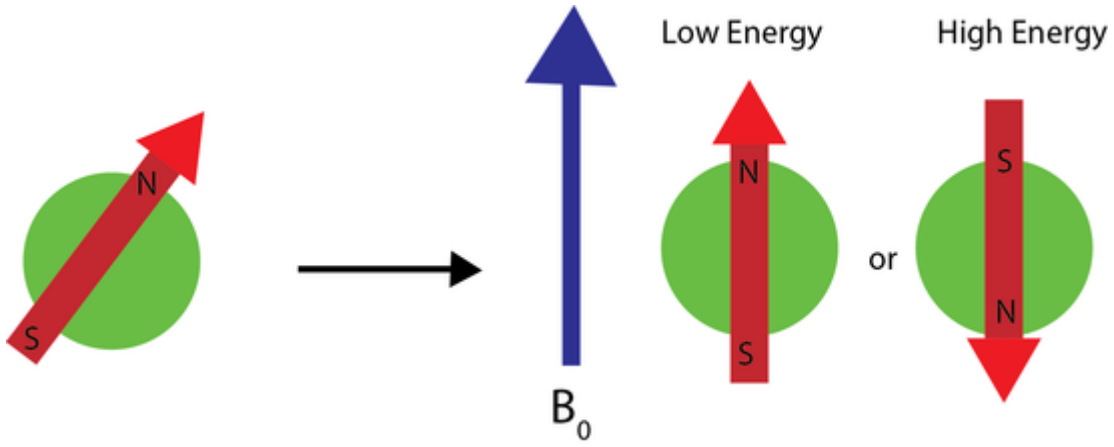


Figure 21.3.1: Nuclear magnetic reference in the absence of a magnetic field and in the presence of a magnetic field (randomly arranged). The arrows marked N and S show the magnetic moment of the nucleus. B_o is the magnetic field of the bar magnet (external magnetic field).

When the spin aligns with the external magnetic field, it is +1/2 (therefore, low energy level and is known as alpha state. At this state, H nucleus has a clockwise spin) and when the spin does not align, it is -1/2 (therefore, high energy level and is known as beta level. At this stage, H nucleus has a counterclockwise spin).

Only the nuclei with nuclear spin create NMR and produce a spectrum. It is important to note that not all nuclei have this nuclear spin.

- When even number of protons and even number of neutrons are in a nucleus, that nucleus will have a zero spin.
- When the number of protons plus the number of neutrons is an odd number, then the nucleus has a half-integer spin – 1/2, 3/2, 5/2.
- When the number of neutrons and the number of protons are both odd, then the nucleus has an integer spin – 1, 2, 3.
- All molecules with non-zero spin have a magnetic moment (μ).

  e.g. $^{1}H_{1}$ and $^{13}C_{6}$ have nuclear spins. $^{12}C_{6}$ and $^{16}O_{8}$ do not have nuclear spins.

The equation below shows the relationship between, the magnetic moment and the angular momentum (overall spin quantum number describes the angular

momentum). (There are two types of angular momenta – spin angular momentum and orbital angular momentum. In this case, we refer to the spin angular momentum.)

Magnetic Moment (μ) = Gyromagnetic Ratio of the nucleus (γ) X Angular Momentum (*I*)

The overall spin (*I*) will have 2I+1 possible orientations. Therefore, when *I* is 1/2, there are 2 possible orientations. In the absence of an external magnetic field, these orientations will have the same energy. When an external magnetic field is present, the energy levels split. Each level is identified by a magnetic quantum number (m).

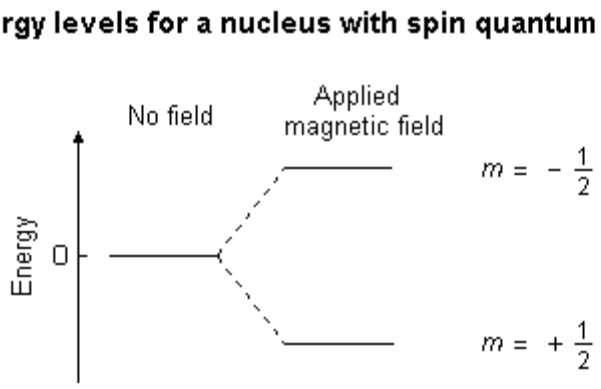


Figure 21.3.2: Energy levels for a nucleus with spin quantum number +/- 1/2

The lower energy level will contain slightly more nuclei than the higher level. These lower-level nuclei can be excited to a higher level with electromagnetic radiation. The difference in energy between the energy levels will determine the frequency of radiation required to excite nuclei from a lower-level to a higher level. Therefore, if a compound is irradiated with radio frequency, the nuclei in alpha state (+1/2) will absorb energy and change the spin to beta state (-1/2). This change is called spin flipping. The process of spin flipping is known as nuclear magnetic resonance phenomenon.

The absorbed energy ΔE is equal to hν as we have studied in earlier chapters. (h is Planck's constant and ν is the frequency. In general, this energy difference is a function of the applied magnetic field. The greater the magnetic field, the higher the energy difference between the two spin states (in the absence of a magnetic

field, there is no difference between the two states). Also, this difference varied depending on the type of the nuclei (i.e. 1H, 13C, etc.).

$$\Delta E = h\nu$$

$$\Delta E = \left(\frac{h}{2\pi}\right) \gamma B_0$$

$$\nu = \left(\frac{1}{2\pi}\right) \gamma B_0$$

The following table shows how magnetic field strength changes the frequencies for 1H-NMR.

Field Strength (B0) Tesla (T)	Frequency ν (MHz)
1.00	42.6
1.41	60.0
2.35	100.0
4.70	200.0
7.05	300.0

Table 21.3.1: Frequencies and field strength relationships for 1H nuclei resonance

21.4 The NMR Spectrometer – 1H-NMR and 13C-NMR

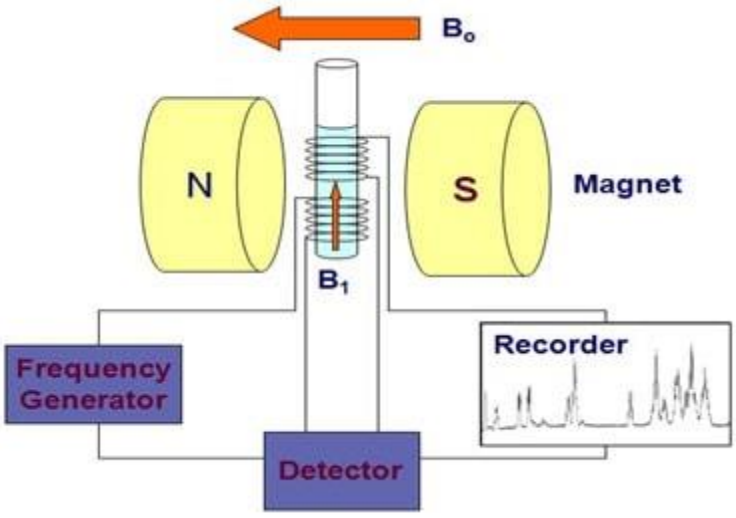


Figure 21.4.1: Schematic diagram of NMR Spectrophotometer

In this instrument, the sample is dissolved in a solvent that does not have $^{1}H_{1}$ isotope of hydrogen. Otherwise, H in the solvent will interfere with H in the sample in case of 1H-NMR.

e.g. Some solvents used in 1H-NMR - CCl4, CDCl3 – D here is deuterium ($^{2}H_{1}$ – isotope of hydrogen).

In NMR instrument, the sample is subject to a magnetic field strength by placing it between two poles of a magnet. The sample is irradiated with radio waves from a radiofrequency (RF) oscillator. The emitting RF frequency is captured by a detector placed perpendicular to the oscillator. The detector is connected to the recorder, and a graph is produced.

The NMR Spectrophotometer uses two methods to obtain RF spectrum:

1. The first type, which is easier to manipulate varies or sweeps the magnetic field strength, while keeping RF frequency constant. The varying of magnetic field strength is known as the Field Sweep Method.

2. The second type holds the magnetic field strength constant and varies the radio frequency. This is known as the frequency sweep method.

As can be seen by the Table 21.3.1, when the matching radio frequency and magnetic field strength are provided, the nuclear magnetic resonance takes place.

The resonance condition that happens when the absorption takes place is given by the following equation:

$$\nu = \left(\frac{\gamma}{2\pi} \right) B_0$$

This activity leads to the creation of a tiny current that flows in the detector coil. The instrument then amplifies the current, and is displayed as a signal in the graph in frequency units.

There are two types of NMR instruments: Continuous-wave spectrometer (The above description matches this kind of an instrument) and Pulsed Fourier Transform spectrometer (in this type a short burst of energy (pulse) in the radio frequency is used).

In NMR spectrum, we run the radiation at an applied magnetic field and change the applied RF frequency. When this RF frequency matches the proton resonance, we see peaks for those protons. So, by changing the RF frequency, we will be able to capture peaks for all types of resonating protons.

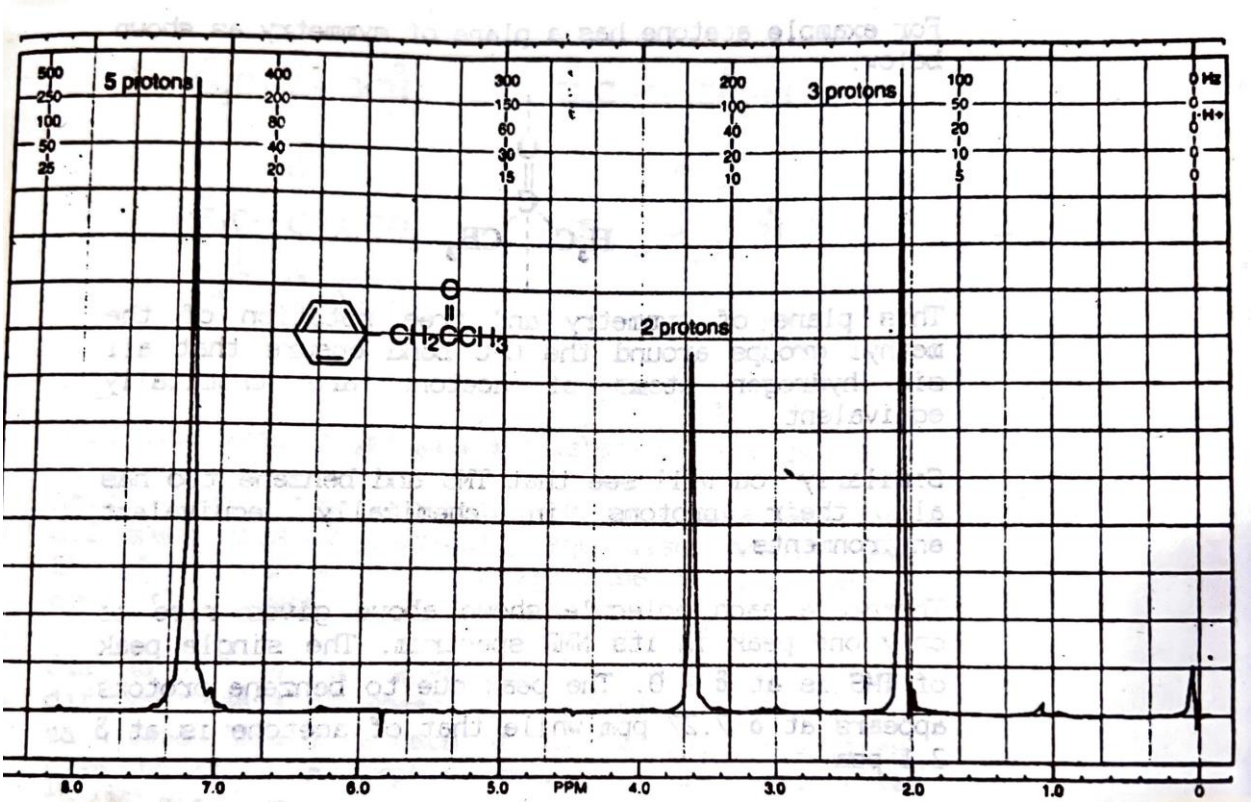


Figure 21. 4. 2: 1H- NMR spectrum of 1-phenylpropan-2-one (phenylacetone)

The small peak at δ =0 is TMS.

The NMR spectrum has 3 absorption peaks at,

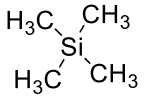
- δ = 2.1 ppm – due to CH_3 protons
- δ = 3.6 ppm – due to CH_2 protons
- δ = 7.3 ppm – due to aromatic protons

According to the spectrum, the peak at 2.1 ppm is the most shielded (upfield – toward the right side of the spectrum) peak. The more downfield a peak, lower the shielding.

Please note that depending on the solvent used, the position of the peaks may slightly change.

When protons are in a chemically identical environment within a molecule, they are known as chemically equivalent. These protons exhibit the same shift.

e.g.

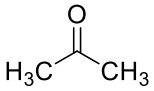


TMS molecule

All protons in CH_3 are chemically equivalent (they show symmetry).

Benzene

All protons in benzene are chemically equivalent (they show symmetry).



Acetone showing symmetry

In this case, the plane of symmetry shown above and free rotation of the methyl groups around C-C bond ensure that all protons of CH_3 are equivalent.

All three examples shown above will show only one peak in their respective 1H-NMR spectra due to chemically equivalent protons. Yet, their individual shift values will be different.

When there are chemically non-equivalent (distinct from each other) protons, they will give rise to more than one peak to match the number of chemically non-equivalent protons. From the number of peaks, we can predict how many different types of protons are present.

21.5 Shielding

According to the table 21.3.1, all 1H nuclei should resonate at the same combination of the applied magnetic field and radiofrequency. Nevertheless, this resonance is affected by the surrounding atoms since they have different electronic environment around them. These electrons of the atoms surrounding H nuclei vary. This variation happens according to the electronegativities of these atoms. Therefore, the structural arrangement within an organic molecule plays a role in the resonance frequencies of H nuclei (when it is 1H-NMR).

In an applied magnetic field, the valence electrons surrounding 1H nuclei (protons) will begin to circulate. This is known as the local diamagnetic current. This diamagnetic current will develop a counter magnetic field (opposite to the applied magnetic field) in the region of the nucleus. The strength of this induced magnetic field is dependent on the electron density around the nuclei. The higher the electron density, the greater the induced magnetic field. This induced magnetic field will shield each proton (H) from the applied magnetic field. Therefore, the actual magnetic field felt by any nucleus is given by the difference between the applied and the induced magnetic fields. This effect is called the diamagnetic shielding. This shielding increases with increasing electron density.

Diamagnetic Shielding = Applied Magnetic Field – Induced Magnetic Field

This means, because the induced magnetic field acts opposite to the applied magnetic field, the energy separation at alpha and beta states would be low. This leads to upfield peaks – peaks toward the right side of NMR spectrum. The process where the induced field reduces the effect of the applied magnetic field is shielding.

When the induced current also moves in the same direction as the applied field, then deshielding happens. Then the peaks move downfield.

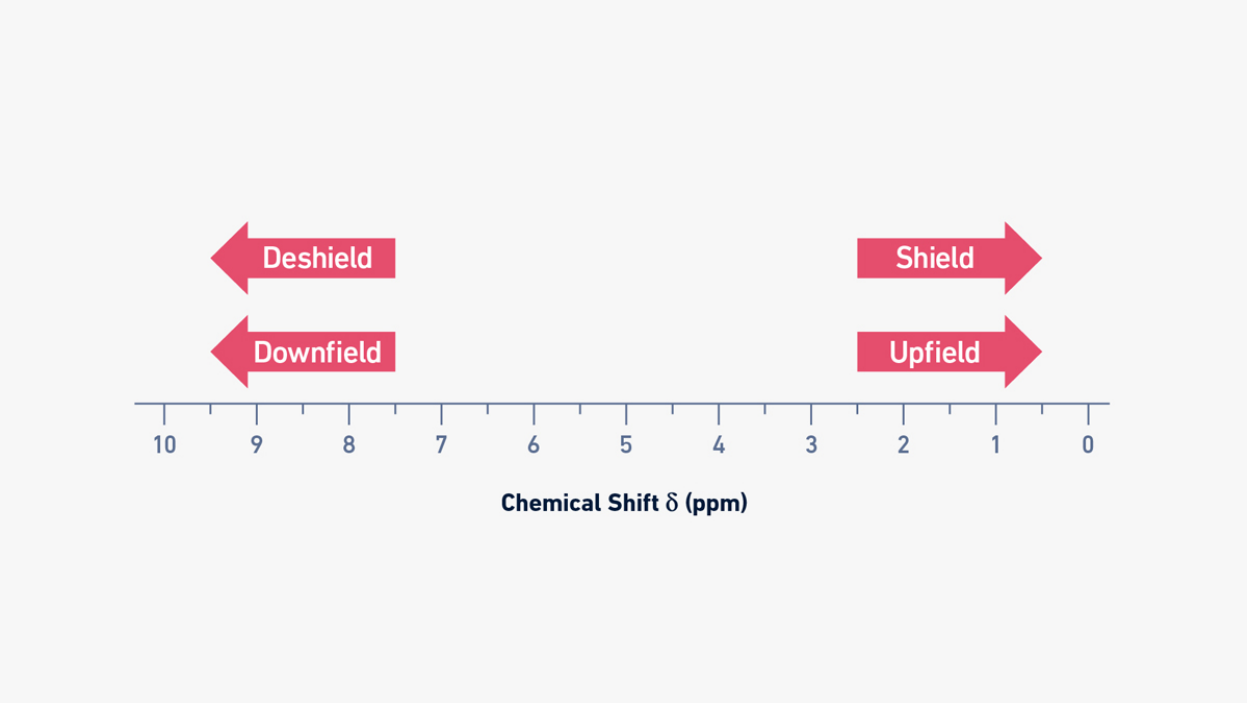


Figure 21.5.1 : Deshield/Downfield and shield/upfield – Left side is high frequency and right side is low frequency.

21.6 Chemical Shift δ (ppm)

As a result of the shielding, the difference between alpha and beta states become smaller. Therefore, the energy change also becomes smaller. This means the radio frequency wave required for spin flipping or nuclear magnetic resonance also decreases. Accordingly, different protons (H) will experience different magnetic fields. This difference is difficult to measure because it is very small. The solution to this problem is sought by running a standard reference compound and comparing its frequency against the sample frequency graph. The deviation from the standard is known as the chemical shift (δ).

A known standard used in 1H-NMR is tetramethylsilane (TMS) - $(CH_3)_4Si$.

Since all the protons (H nuclei) in methyl groups are more shielded than most of the other known compounds, TMS is used widely. When they are shielded, the effect of neighboring electrons will be less. As a result, these shielded protons resonate in higher frequencies.

There are other deuterated (replacing protium with deuterium atoms) compounds used in both 1-H and 13-C NMR. e.g. chloroform, dimethyl sulfoxide, heavy water

The signal from the TMS protons appear at one end of the spectrum. Therefore, the protons from the sample compound are measured by determining how far these signals are from the TMS protons, which are more shielded. This distance is expressed in terms of frequency units Hz. The position of a sample proton peak relative to the TMS (the standard used) is called the chemical shift. It is important to note that this shift is also dependent on the applied magnetic field. In order to avoid this, a definition was developed where chemical shift was defined independent of the field strength.

$$\delta_i = \frac{\nu_i - \nu_{TMS}}{\nu_0} \text{ ppm}$$

δ_i = Chemical shift of proton i expressed in ppm (parts per million).

ν_i = Resonance frequency of proton i in Hz

ν_{TMS} = Resonance frequency of protons of TMS in Hz

ν_o = Operating frequency of the spectrometer in MHz

This equation ensures that the value of the chemical shift for a given proton is always the same irrespective of the strength of the applied magnetic field. This is because the difference of the frequencies between TMS and the sample is divided by the applied magnetic field, which gives the same ratio irrespective of the applied field.

e.g. Consider the following values obtained from an experiment:

Applied Magnetic Field – 60 MHz. The difference at this field between TMS and a proton in CH_3Br is 162 MHz.

When you apply the above equation: 162/60 = 2.7 ppm

Applied Magnetic Field – 100 MHz. The difference at this field between TMS and a proton in CH3Br is 270 MHz.

When you apply the above equation: 270/100 = 2.7 ppm

Both calcualtions provide the same value for chemical shift.

Electronegativity of the neighboring atoms leads to deshielding, because electrons are withdrawn from the atoms near H atoms.

The following table shows the effect of electronegativity on the chemical shift:

Compound	Electronegativity	Chemical Shift ppm
CH_3F	4.0	4.26
CH_3OH	3.5	3.4
CH_3Cl	3.1	3.05
CH_3Br	2.8	2.68
CH_3I	2.5	2.16
CH_4	2.1	0.23
$(CH_3)_4Si$	1.8	0

Table 21.6.1: Electronegativity values and chemical shifts

When there is an electron withdrawing group (with high electronegativity values) attached, the electron density near H will reduce. This will lead to deshielding and larger chemical shift. When there are more than one electron withdrawing groups present, the total deshielding effect will increase. Therefore, the shift will be higher.

Compound	Chemical Shift ppm
CH_4	0.23
CH_3Cl	3.05
CH_2Cl_2	5.30
$CHCl_3$	7.27

Table 21.6.2: Electron Withdrawing Groups and Chemical Shiftss

In addition to the electronegativity, hybridization and the strain on the ring also affect the chemical shift.

- Hybridization leads to deshielding, which means downfield peaks. This happens because when there is hybridization sp^2 (or sp^3), it will hold electrons closer to the nucleus. Therefore, fewer electrons to shield the magnetic field effect. This will lead to deshielding.
- Strain on a ring also affects the chemical shift. The angle strain and torsional strain together is known as ring strain. Compounds with small rings will have more strain and their Hs will eclipse (shield) each other.

Other factors that affect chemical shift is acidic hydrogens and hydrogen bonding, and magnetic anisotropy (Anisotropy means non-uniform behavior in all directions).

- Acidic hydrogens do not appear in 1H-NMR, because they can exchange with NMR solvents such as methanol. Also, when acidic hydrogen is attached to compounds such as in the case of carboxylic acid, the oxygen withdraws electrons from the acidic hydrogen atoms. As a result, those H atoms will be extremely deshielded.
- Hydrogen bonding effect on protons varies depending on the solvation, acidity, concentration and temperature. In 1H-NMR, hydrogen bonding will lead to peaks in upfield due to shielding. Although, hydrogen bonding increases the electron density in the adjacent atoms, the shift happens is downfield due to deshielding. This seems contrast to what we have studied so far. It is important to understand that the electron shielding created by hydrogen bonding (intermolecular bonding) does not affect in the case of NMR to create the shielding effect (in addition, H bonding is controlled by the above mentioned factors i.e. solvation, acidity, concentration, etc.). Int his case, the predominant effect is the intramolecular boding. Therefore, deshielding happens.

- The magnetic anisotropy happens when pi electrons induce a magnetic field that are direction-dependent. This is called anisotropic effect. When an aromatic compound such as benzene is placed in a magnetic field, the pi electrons in the ring will get induced to circulate around the ring. This is called the ring current. This current induces a magnetic field, which is in the same direction as the applied magnetic field at the periphery (where H atoms

are attached to the ring). Therefore, these H atoms are deshielded. (The induced magnetic field at the center is in the opposite direction to the applied magnetic field.) This deshielding leads to downfield absorption around 7.27 ppm.

- It is important to note that if protons are in a position in a compound where the induced field circulates in the opposite direction, then shielding happens. The chemical shifts happen upfield.

Proton Type	Effect	Chemical Shift ppm
C_6H_5-H	Highly deshielded	6.5 - 8
C=C-H	Deshielded	4/5 - 6
C≡C-H	Shielded due to the location of H relative to pi electrons	2.5
O=C-H	Very highly deshielded	9 - 10

Table 21.6.3: Shielding due to pi electrons

21.7 Spin-Spin Splitting

The peaks that appear in 1H - NMR, sometimes could appear as a triplet, a doublet or some other splitting. This signal splitting is known as spin-spin splitting. The spin-spin splitting happens because of spin-spin coupling (multiplicity). The splitting tells us how many H atoms are on the neighboring carbon.

The number of Hs in the neighboring atom is calculated by the following equation:

Number of neighboring H atoms = Number of lines in a peak - 1

The distance between two adjacent peaks in a simple multiplet is known as the coupling constant (J). This is a measure of how strongly a proton is coupled to its neighbors. Also note that Pascal's triangle is used to verify the intensities of multiplets of 1H-NMR. Pascal's triangle is a mathematical device where each entry in the triangle is the sum of the two entries above it.

Number of lines	Ratio of lines – Pascal's Triangle	Name of the peak	Number of neighboring H atoms
1	1	Singlet	0
2	1:1	Doublet	1
3	1:2:1	Triplet	2
4	1:3:3:1	Quartet	3
5	1:4:6:4:1	Quintet	4

Table 21.7.1: Number of lines and peaks

Spin-spin coupling is not observed among chemically equivalent protons.

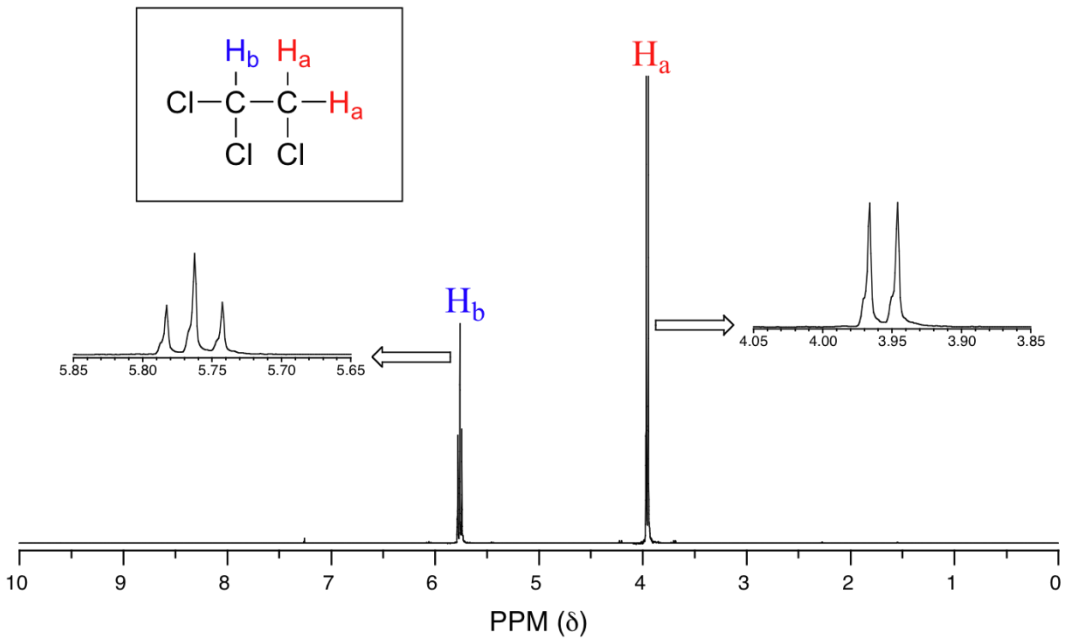


Figure 21.7.1: 1H-NMR spectrum of showing splitting of an organic compound

H_a has only one neighboring atom (H_b) – showing a doublet.

H_b has two neighboring atoms (H_a) – showing a triplet.

NMR spectrum not only express the types of protons that are present in a compound, but it also tells us how many protons of that type are present.

In the NMR spectrum, the area under each peak is proportional to the number of H atoms generating that peak. The NMR spectrometer has the ability to integrate the area electronically leaving above each peak a vertical line knows as the integral. The height of this line increases according to the number of H atoms of that particular type.

e.g.

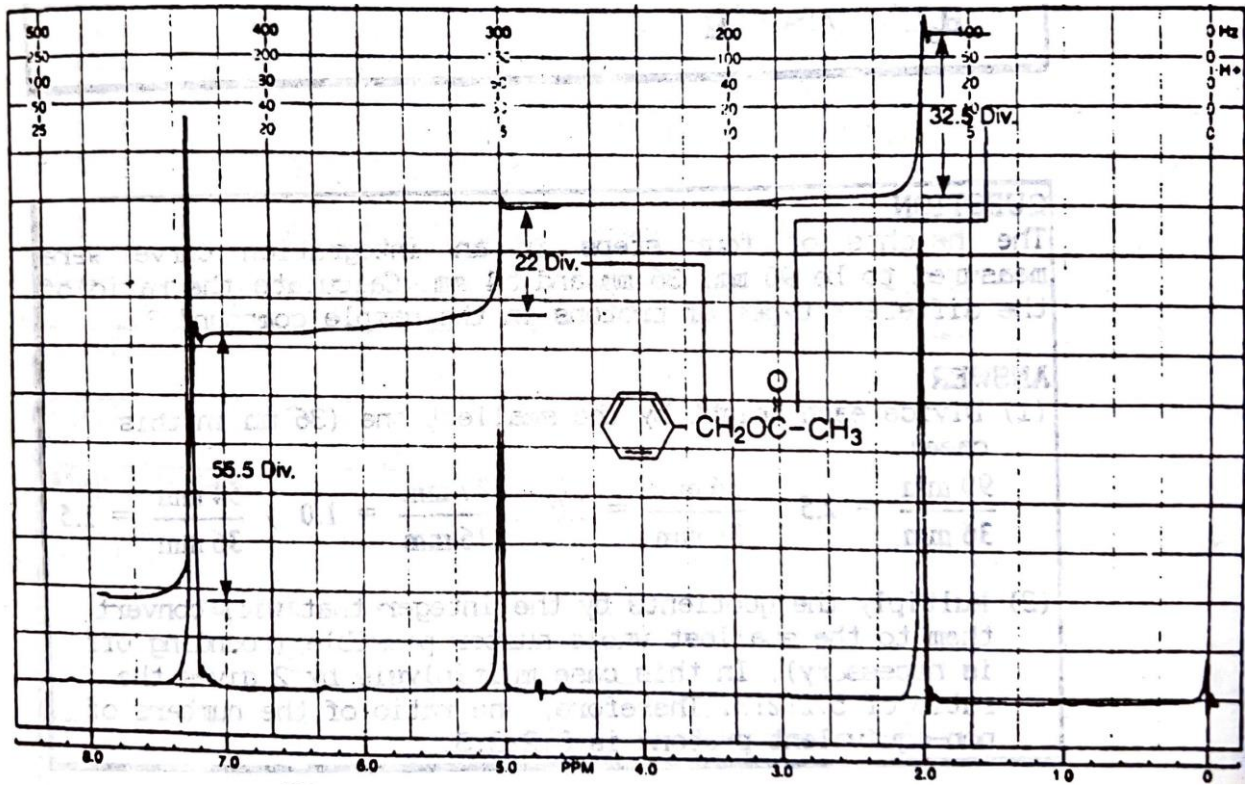


Figure 21.7.2 :1H-NMR graph for benzylacetate.

You will notice that the heights of the vertical lines do not give the number of protons. But the ratios of the three peaks will provide a relative number of each type of Hs in the compound.

The vertical lengths of the lines above the peaks are 55.5, 22, 32.5.

Therefore, the ratio is,

55.5/22 = 2.52

22/22 = 1

32.5/22 = 1.48

Therefore, the ratio is, 2.52:1:1.48. If we know the number of hydrogens of a particular type matches one of the given ratios, then we can multiply the ratio by that known number of Hs. If we know that the peak where the ratio is 1 due to two hydrogen atoms, then the ratios of H atoms will be, 5:2:3.

Once we have this information, we can assign the H atoms to different types within the compound.

5 H atoms are from the 5 Hs that directly attached to the ring. The 2 H atoms are from CH_2 and the 3 H atoms are form CH_3. Therefore, by comparing 1H-NMR spectra with standard known molecules, we can assign chemical shits to different functional groups and/or structural feature. When we are given the 1H-NMR of an unknown compound, we identify the type of H atoms by comparing the shift values of the standards at given frequencies and magnetic field strengths.

The following is a list of known chemical shifts for H atoms attached to different types of structures and functional groups:

Type of H	Chemical Shift ppm (approximations)
Alkyl $R\text{-}CH_3$	0.8 – 1.0
Alkyl $R\text{-}CH_2\text{-}R$	1.2 – 1.4
Alkyl R_3CH	1.4 – 1.7
Allylic	1.6 – 1.9
Benzylic $Ar\text{-}CH_3$	2.2 – 2.5
Alkyl chloride $R\text{-}CH_2\text{-}Cl$	3.6 – 3.8
Alkyl bromide $R\text{-}CH_2\text{-}Br$	3.4 – 3.6
Alkyl iodide $R\text{-}CH_2\text{-}I$	3.1 – 3.3
Ether $R\text{-}O\text{-}CH_2\text{-}R$	3.3 – 3.9
Alcohol $R\text{-}CH_2\text{-}OH$	3.3 – 4.0
Ketone	2.1 – 2.6
Aldehyde	9.5 – 9.6
Vinylic $R_2C{=}CH_2$	4.6 – 5.0
Vinylic	5.2 – 5.7
Aromatic Ar-H	6.5 – 8.5
Acetylenic RC	2.5 – 3.1
Alcohol Hydroxyl R-OH	0.5 – 6.0
Carboxylic	10.0 – 13.0
Phenolic Ar-OH	4.5 – 7.7
Amino $R\text{-}NH_2$	1.0 – 5.0

Table 21.7.2: The chemical shift v. types of H

21.8 13C – NMR

When it comes to 13C-NMR, similar chemical shifts happen due to shielding and deshielding. The high intensity of peaks is due to the overlapping of peaks that correspond to the same type of C atoms. The attachment of C to an electronegative atom leads to deshielding. Similarly aromatic Cs will show similar peaks due to orthro, para, and meta positions. Since 13C isotope is available on 1.1% in nature, the sensitivity of 13C-NMR is low. There is no peak integration in 13C-NMR. The unknown compound is identified by comparing the13C-NMR chart of the unknown with the 13C-NMR charts of the known compounds. During the comparison, the peaks are analyzed for any overlapping, and the labelling is done for different types of C atoms.

The following 13C-NMR spectrum explains how C atoms are identified:

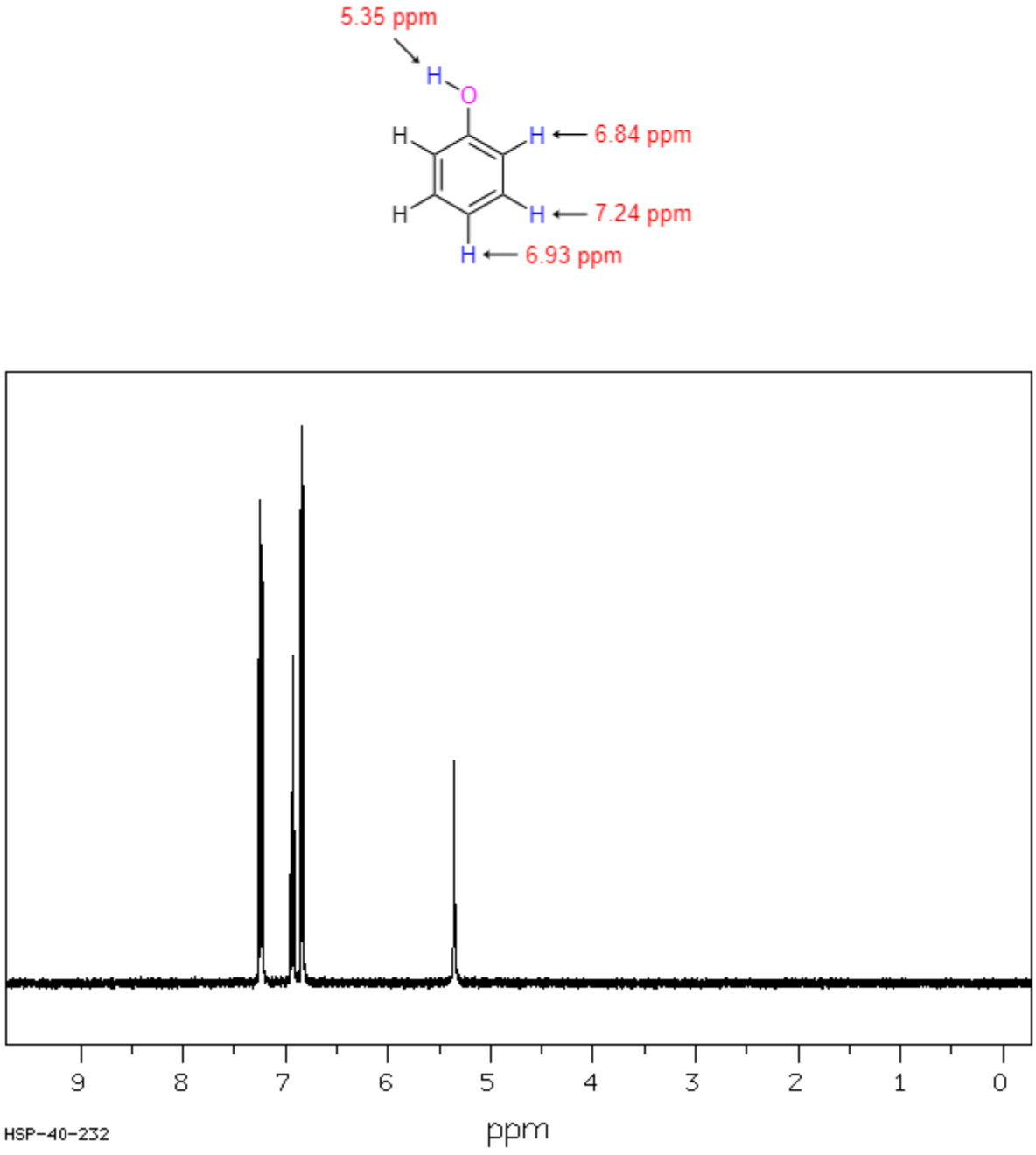


Figure 21.8.1: 13C NMR of Phenol

From the above explanation, you would see how four peaks are due to four different C atoms. Also, the intensity (the peak height) is high due to two ortho and two meta, C atoms.

Carbon Environment	Chemical Shift ppm
Ketone C=O	205-220
Aldehyde C=O	190-200
Acids and Esters C=O	170-185
Aromatic C	125-150
Alkenes C=C	115-140
RCH_2OH	50-65
RCH_2Cl	40-45
RCH_2NH_2	37-45
R_3CH	25-35
CH_3CO-	20-30
R_2CH_2	16-25
RCH_3	10-15
Grouping by Carbon Type	
C-C	0-50
C-O	50-100
C=C	100-150
C=O	150-200

Table 21.8.1: Carbon environment and chemical shifts