B.Sc. Part – III Semester (V)
Year: 2020-21

Organic Chemistry
(Paper: XIV)

Introduction

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03rd May 2021

Shivaji University, Kolhapur: CBCS Syllabus Chemistry
B.Sc. Part – III Semester (V)
To be implemented from June - 2020

Nature of Syllabus

- **Paper – IX (XIII) : Inorganic Chemistry**
- **Paper – X (XIV) : Organic Chemistry**
- **Paper – XI (XV) : Physical Chemistry**
- **Paper – XII (XVI) : Analytical and Industrial Chemistry**

- **Theory : 400 (50+50 =100 marks for each paper)**
- **Practical : 200**
- **Total : 600 (Excluding English)**

Nature of Examination

Q. No	Details	Marks	Marks option
1	(A) Answer in one sentence (One mark each). (B) Multiple choice questions (One mark each)	04 04	
2.	Long answer type questions (2 out of 3)	20	10
3.	Short answer type questions (3 out of 5)	12	08
	Total	40	12

- **The duration of each theory paper : 2 hours**
- **Internal examination : 10 Marks: Oral/Seminar/Test/Home Assignment.**
- **Separate passing : (18/40 and 4/10)**

Practical Examination : Marks: 200 & duration: 3 days (6.5 hours per day)

1. **Physical Section : 60 marks**
2. **Inorganic Section : 65 marks**
3. **Organic Section : 60 marks**
4. **Project : 15 marks**

Unit 1. Reagents and Reactions in Organic Synthesis [10]

A] Reagents

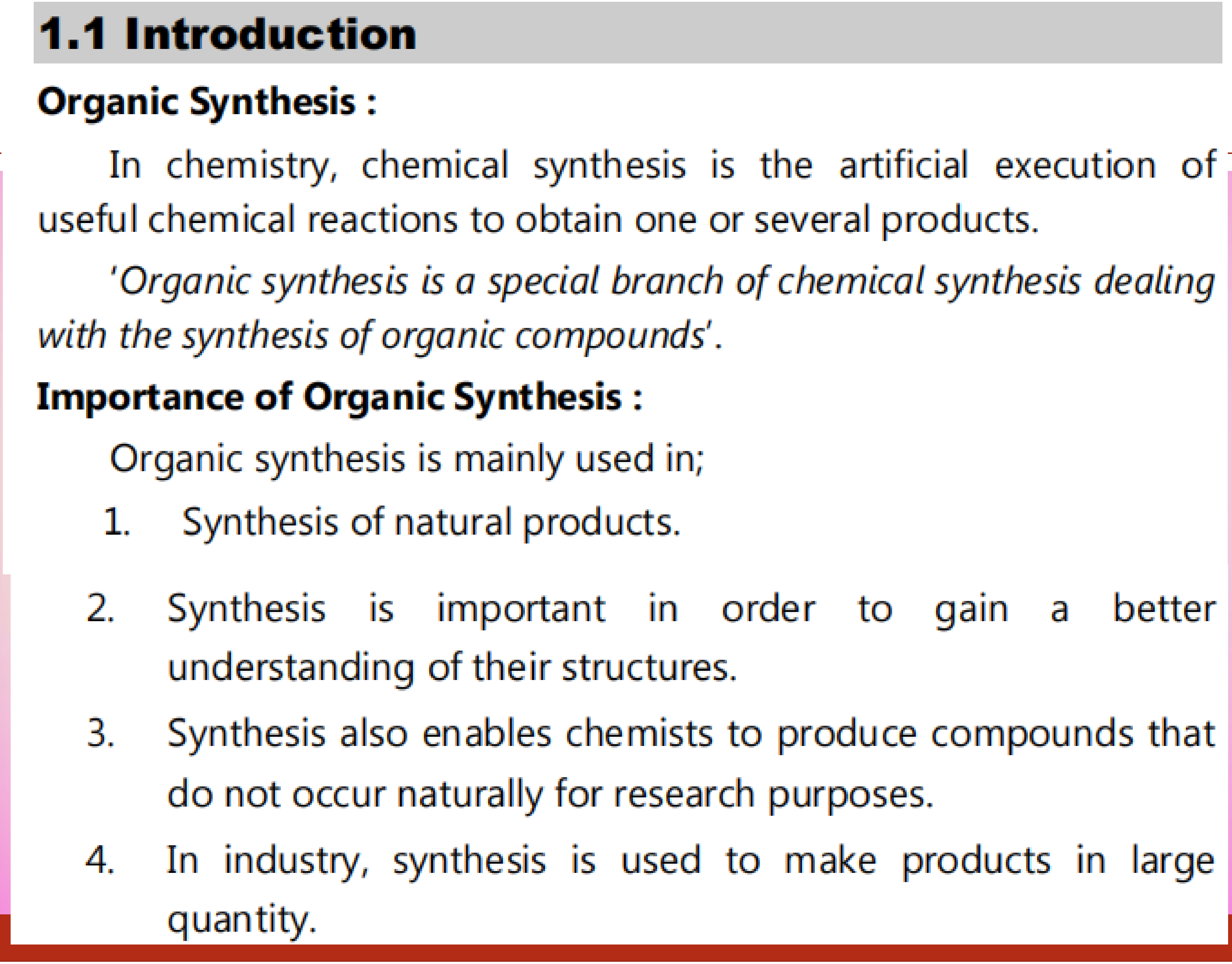
Preparation and Applications of following reagents.

1. Lithium aluminium hydride $LiAlH_4$.
2. Raney Nickel.
3. Osmium tetraoxide.
4. Selenium dioxide (SeO_2).
5. Dicyclohexyl Carbodiimide (DCC).
6. Diazomethane.

Reagents and Reactions in Organic Synthesis

Contents ...

(A) Reagents



1.1 Introduction

Organic Synthesis :

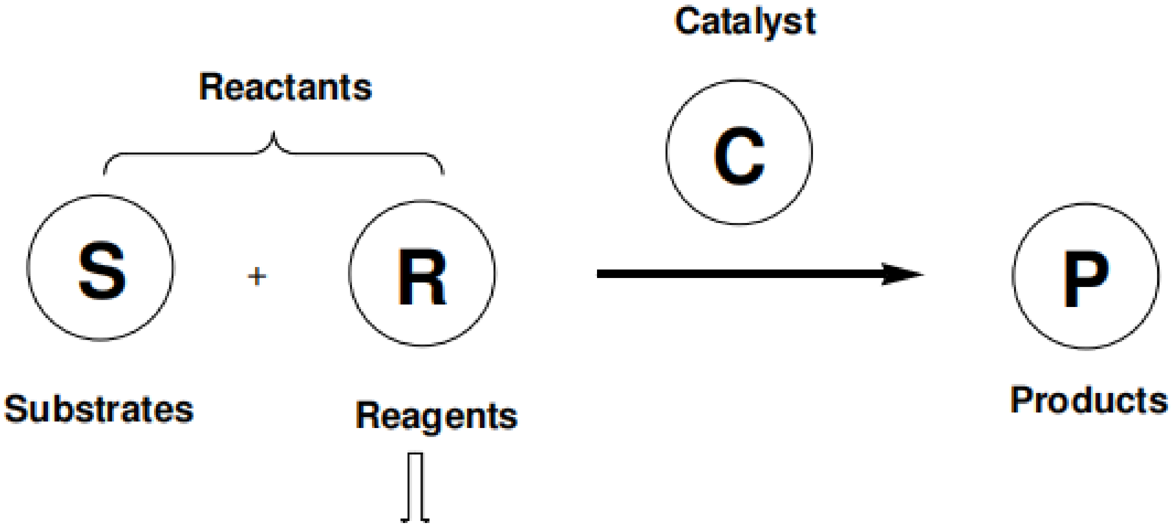
In chemistry, chemical synthesis is the artificial execution of useful chemical reactions to obtain one or several products.

'Organic synthesis is a special branch of chemical synthesis dealing with the synthesis of organic compounds'.

Importance of Organic Synthesis :

Organic synthesis is mainly used in;

1. Synthesis of natural products.
2. Synthesis is important in order to gain a better understanding of their structures.
3. Synthesis also enables chemists to produce compounds that do not occur naturally for research purposes.
4. In industry, synthesis is used to make products in large quantity.

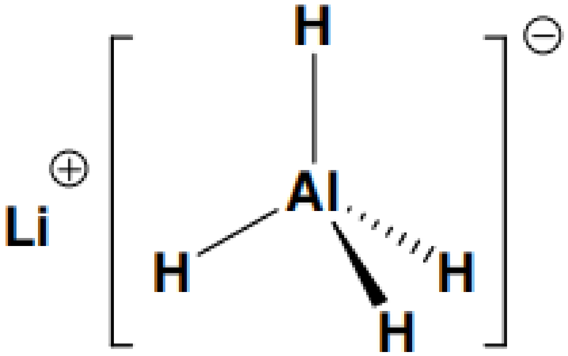


Reagents	Applications
1. LAH	Reducing agent: Reduction of carbonyl compounds.
2. Ra-Ni	Hydrogenating agent: Addition of hydrogen.
3. OsO_4	Oxidising agent: cis-1,2-Hydroxylation.
4. SeO_2	Oxidising agent: Oxidation of active $-CH_2$, $-CH_2-$, and $-CH-$.
5. Diazomethane	Methylating agent: Formation of methyl ethers, ester.

1.2 Preparation and Applications of Following Reagents

1.2.1 Lithium Aluminium Hydride/LAH ($LiAlH_4$)

Introduction : Lithium Aluminium Hydride (LAH) is a gray coloured solid mainly used for the reduction of carbonyl compounds. Its molecular formula is $LiAlH_4$ having the following structure.



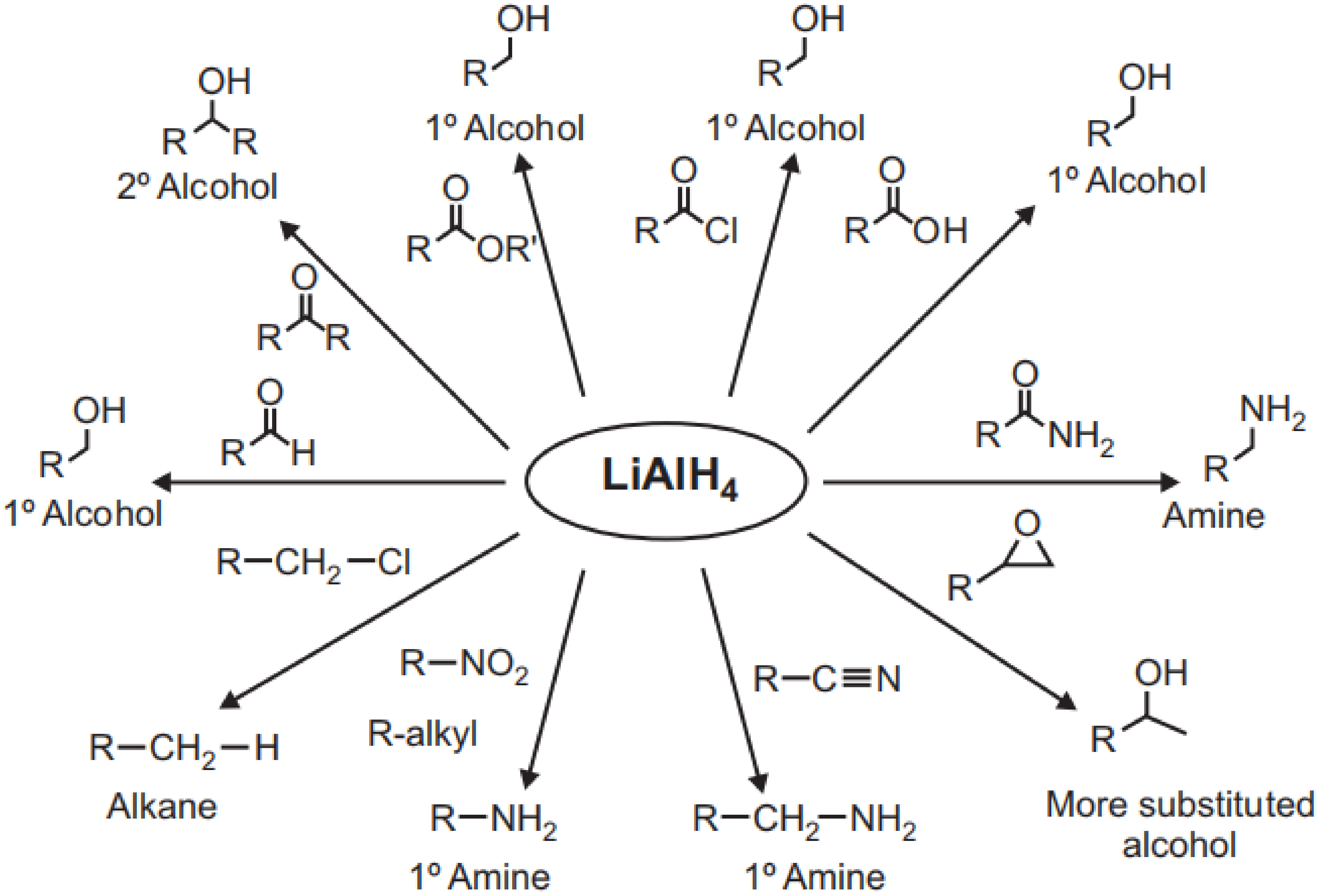
It was discovered by Finholt, Bond and Schlesinger in 1947. $LiAlH_4$ acts as a source of $4H^-$ (hydride ion).

Preparation: Lithium Aluminium Hydride is prepared by slow addition of a calculated amount of anhydrous $AlCl_3$ to lithium hydride (LiH) in dry ether or THF.

$$4LiH + AlCl_3 \xrightarrow[\text{or THF}]{\text{Dry ether}} LiAlH_4 + 3LiCl$$

The precipitated lithium chloride (LiCl) is removed by filtration. The filtrate is evaporated in the absence of air and CO_2 to give LAH as a gray solid. LAH reacts violently with water and alcohol with the liberation of hydrogen, hence cannot be used in protic polar solvents.

Summary :


2° Alcohol
1° Alcohol
1° Alcohol
1° Alcohol
1° Alcohol
LiAlH$_4$
Amine
R−CH$_2$−Cl
R−NO$_2$
R-alkyl
R−C≡N
R−CH$_2$−H
Alkane
R−NH$_2$
1° Amine
R−CH$_2$−NH$_2$
1° Amine
More substituted alcohol

Applications of $LiAlH_4$: Lithium aluminium hydride is widely used in organic chemistry as a reducing agent. It is more reactive than $NaBH_4$ and normally reduces various polar functional groups except alkenes and alkynes.

1. It reduces aldehydes, ketones, esters, carboxylic acids, acid anhydrides, acid chlorides, and epoxides into the corresponding alcohols.
2. Amides, nitriles, and aliphatic nitro compounds are converted into corresponding amines.

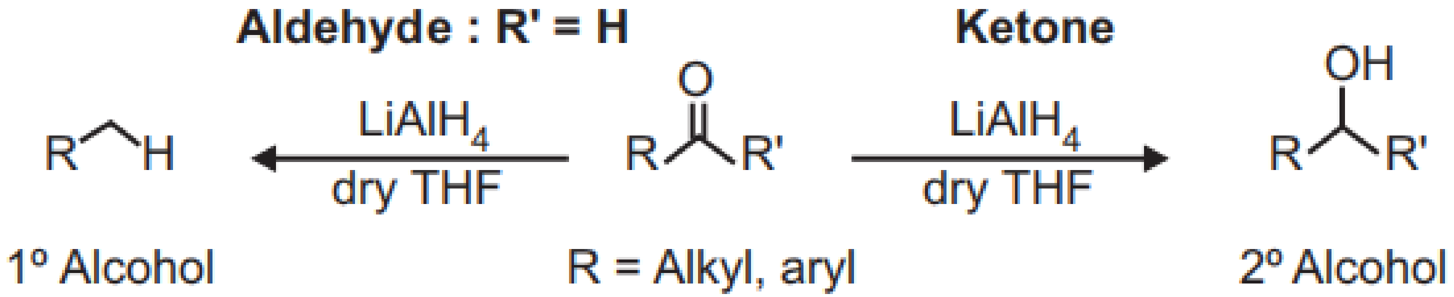
The high reactivity of the hydride ion (H^-) in $LiAlH_4$ makes it incompatible with protic solvents. For example, it reacts violently with water and therefore, $LiAlH_4$ reductions are carried out in dry (anhydrous) ether and THF.

(1) Reduction of carbonyl compounds : $LiAlH_4$ is one of the most powerful reducing agents efficiently working for any carbonyl compounds like aldehydes, ketones, esters, carboxylic acids, acid anhydrides, acid chlorides and amides.

(a) Reduction of aldehydes and ketones : Aldehydes and ketones are most readily reduced with $LiAlH_4$ to give alcohols.

(i) Reduction of aldehydes gives primary alcohols, while

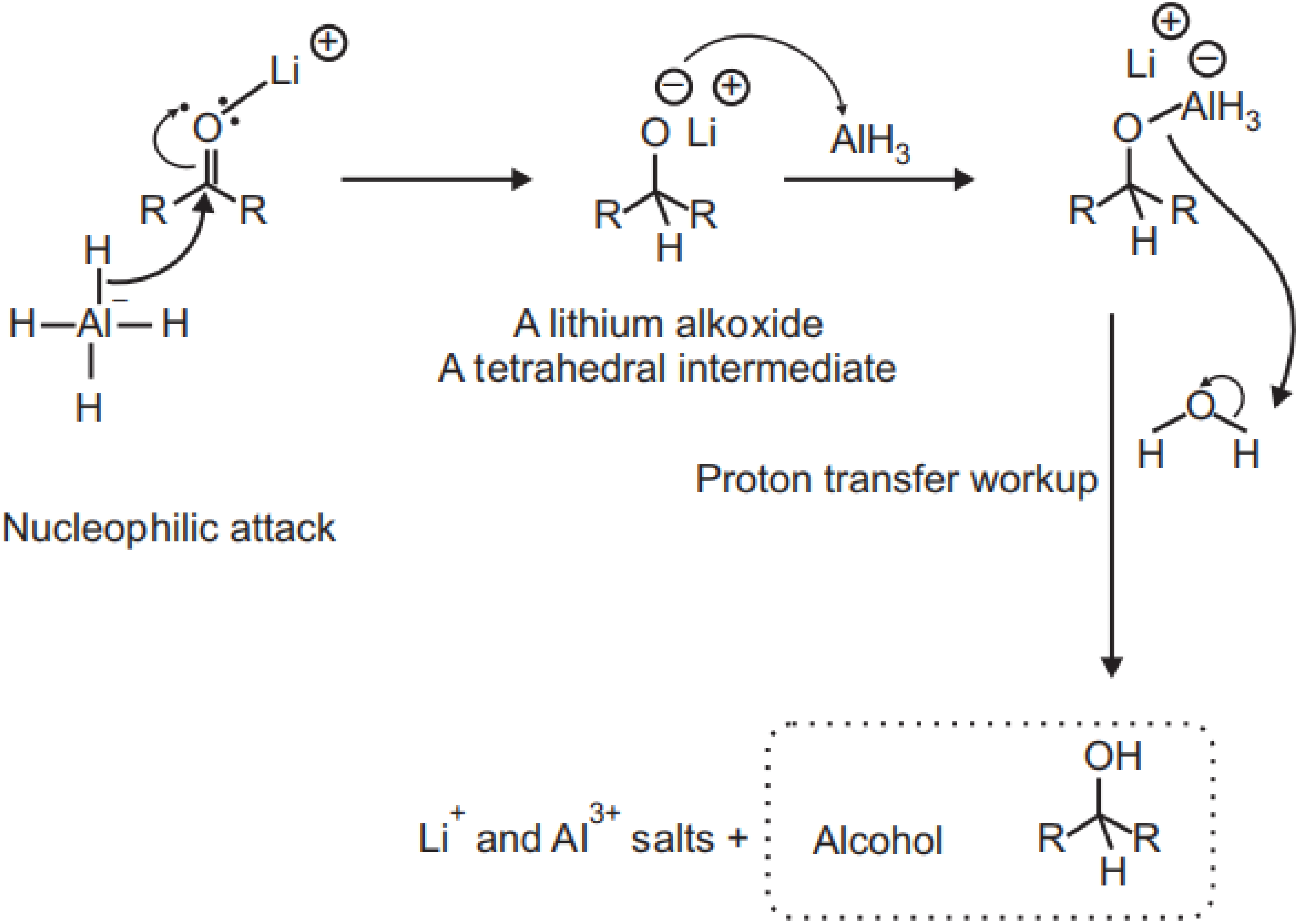
(ii) Reduction of ketones gives secondary alcohols.



Mechanism: The mechanism involves following main two steps.

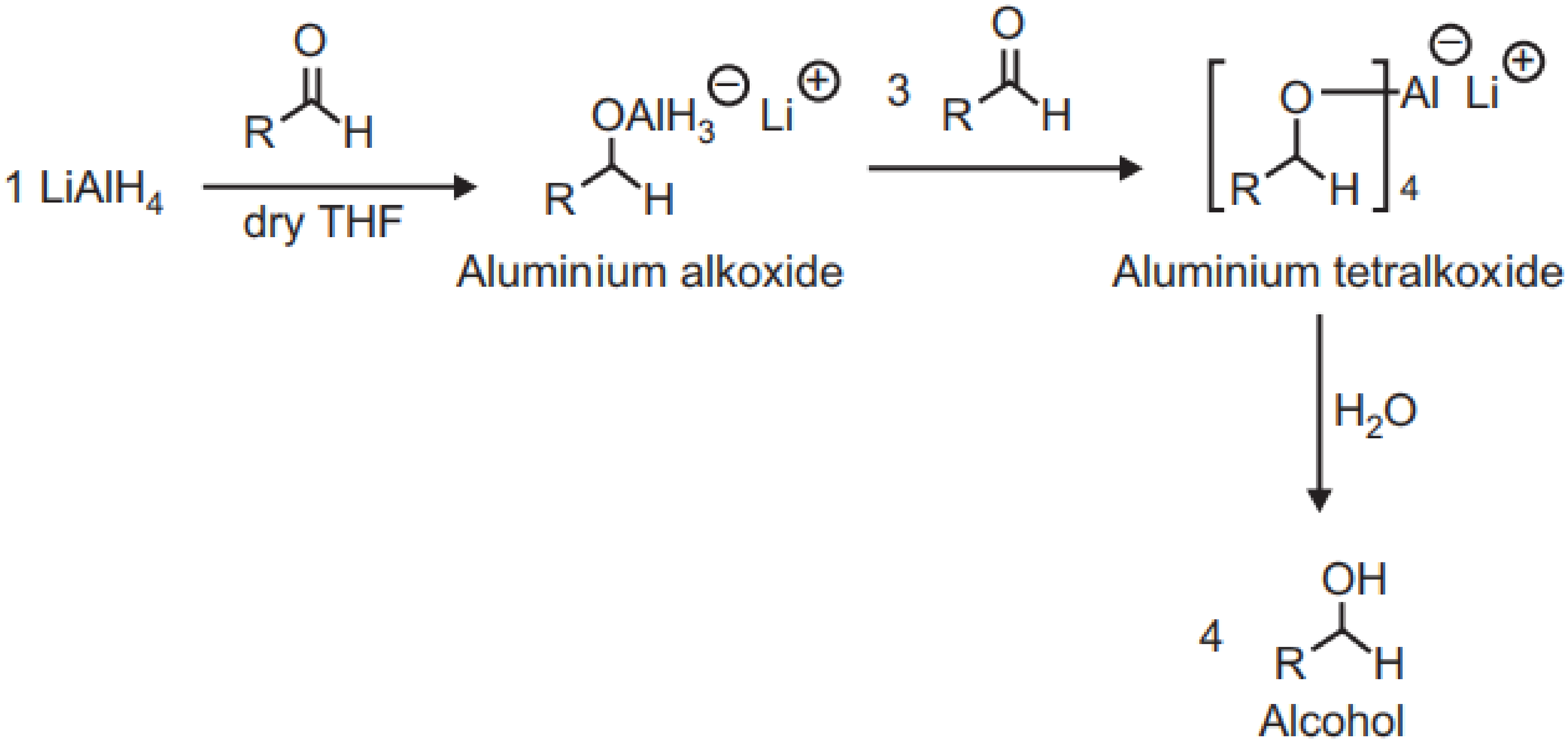
Step 1 : Nucleophilic addition : The nucleophile H^- in the LAH adds to the electrophilic carbonyl carbon (C=O) of aldehydes/ketones to form aluminium alkoxide intermediate.

Step 2 : Work-up step : Protonation of aluminium alkoxide by the addition of water produces alcohol.

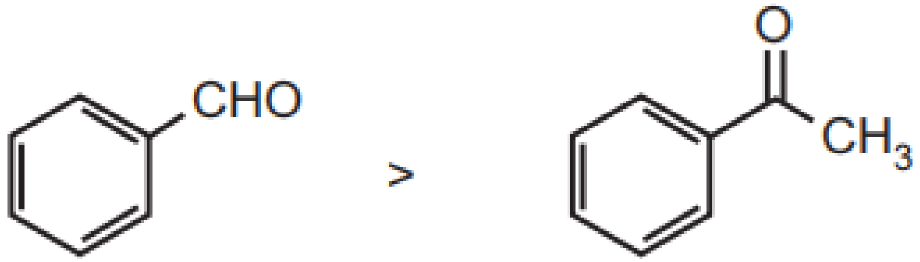


Characteristics :

1. All four hydride ions of LAH are added on four carbonyl compounds to produce aluminium tetralkoxides. Each subsequent step in which the transfer of H⁻ is slower than the previous one, due to the increased number of electronegative alkoxy substituents (-OR).



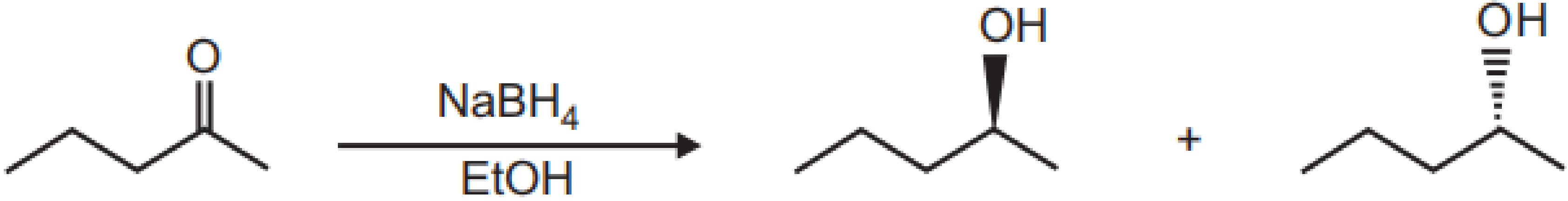
2. Aldehydes are more reactive than ketones as they are less hindered and the alkyl group in the ketone acts as a weak electron donor.



Aldehyde

Ketone

3. **Stereochemistry of reduction :** The reduction of unsymmetrical ketones with $LiAlH_4$ produces a pair of stereoisomers (racemic mixture), because H^- can attack either face of the planar carbonyl group.



Examples :

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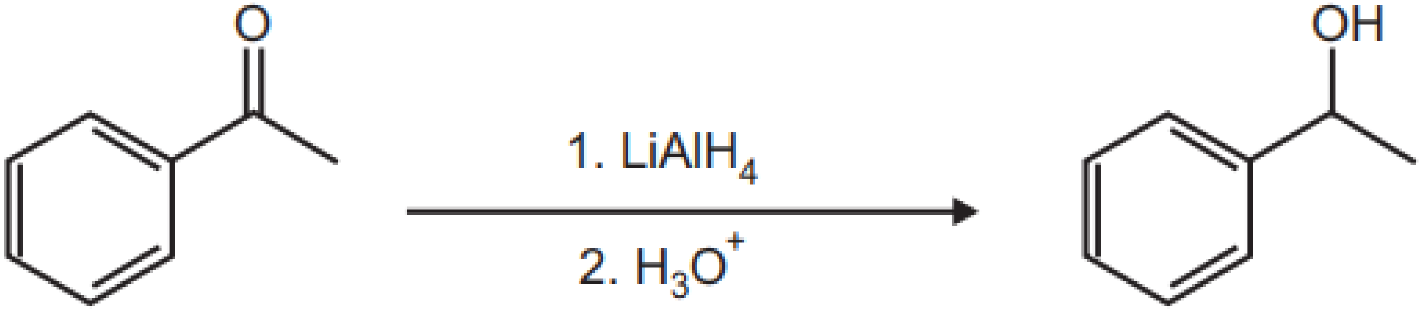

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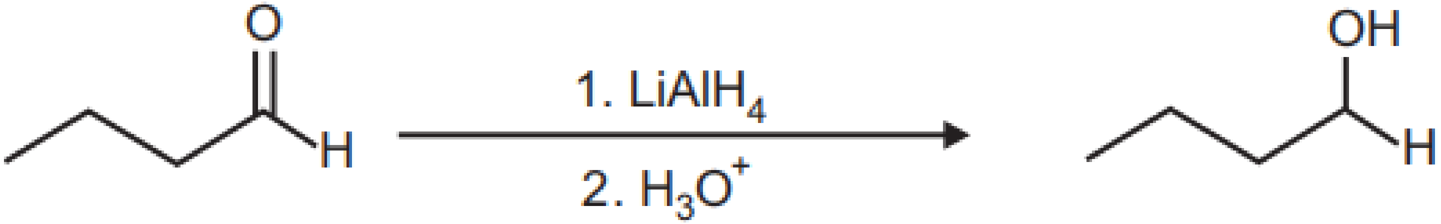

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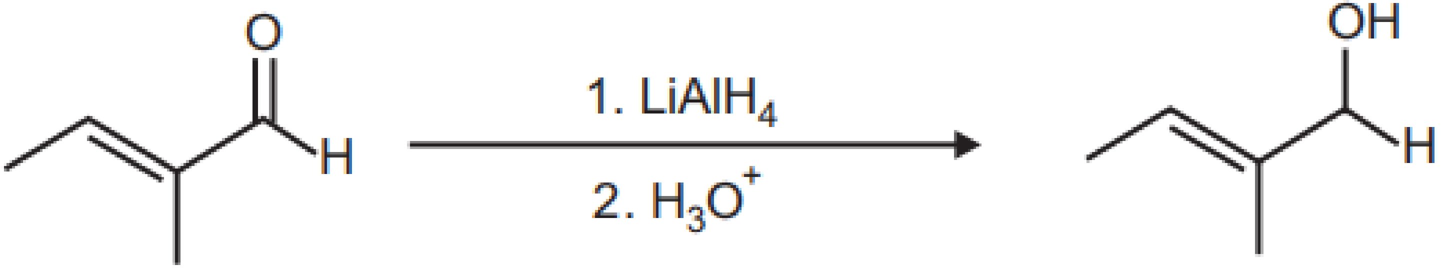
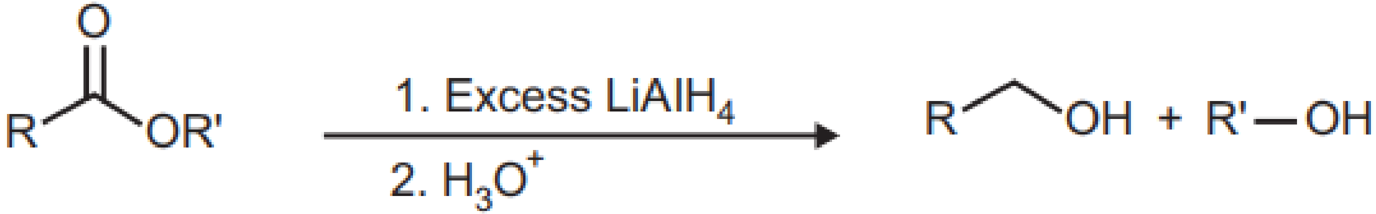


(b) Reduction of Esters : Esters are reduced to primary alcohols.



Characteristics :

1. **Excess of LAH :** The reduction of an ester to an alcohol requires two hydride additions to the carbonyl group and therefore, for reduction of esters, an excess of $LiAlH_4$ is used.

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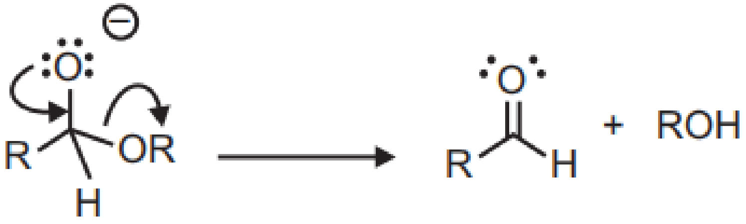
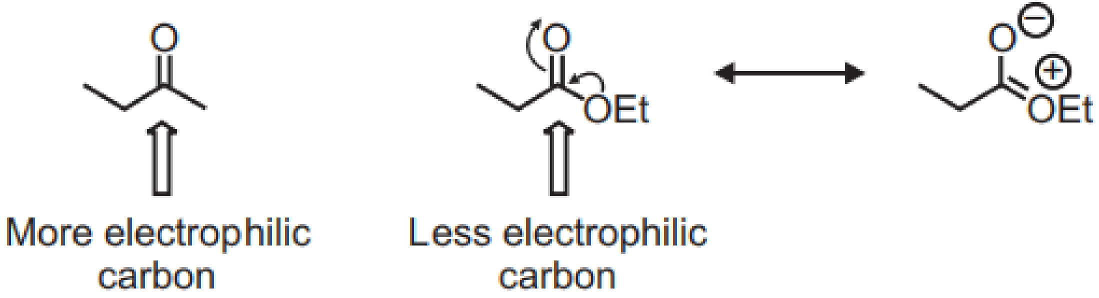
   This is because the tetrahedral intermediate formed after the first hydride addition form carbonyl group (aldehyde) which is more reactive than the ester and is attacked by one more time by $LiAlH_4$.



2. **Esters are less reactive than ketones and aldehydes :** Ester carbonyl is less electrophilic than aldehyde/ketone, since oxygen donates electrons to the carbonyl carbon (π-donation : mesomeric effect), hence less reactive as compared to aldehyde/ketone.



Examples :

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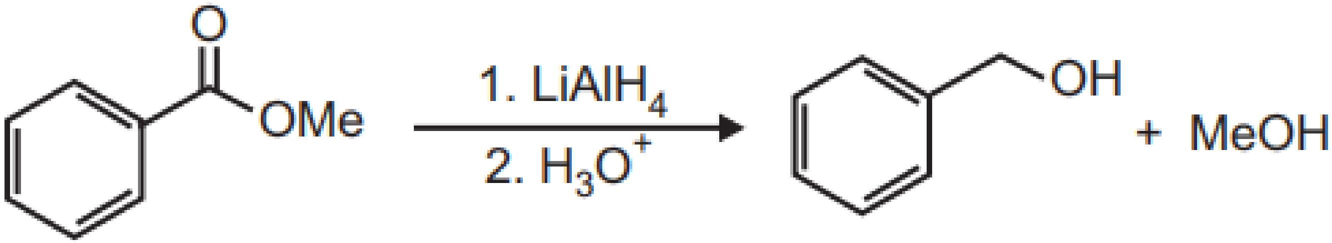

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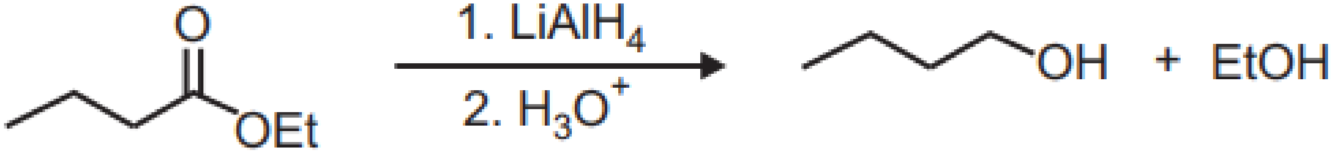

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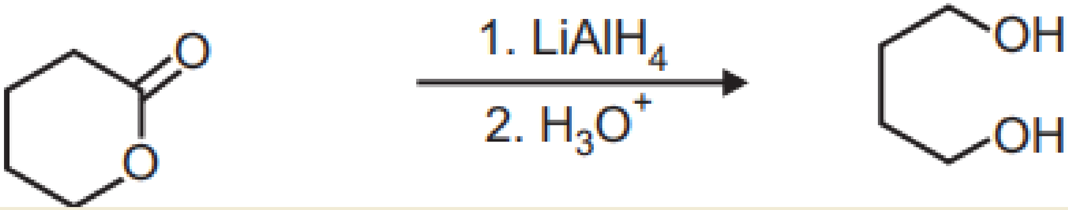
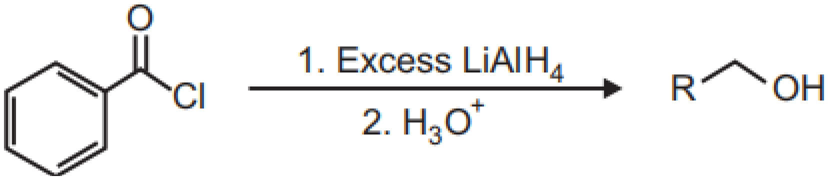


(c) Reduction of Acid Chlorides : $LiAlH_4$ reduces acid chlorides into primary alcohols. Here also there is an aldehyde intermediate formed and therefore, the reducing agent is used in excess to shift the reaction to completion.



Examples :

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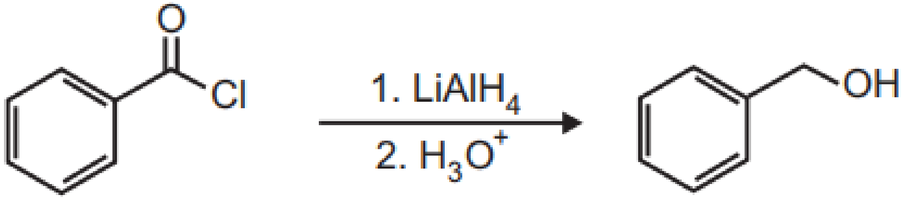

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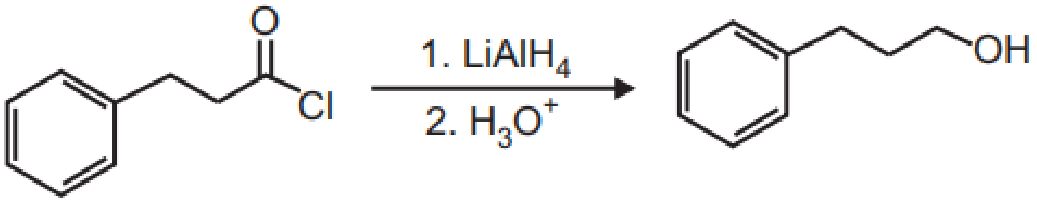

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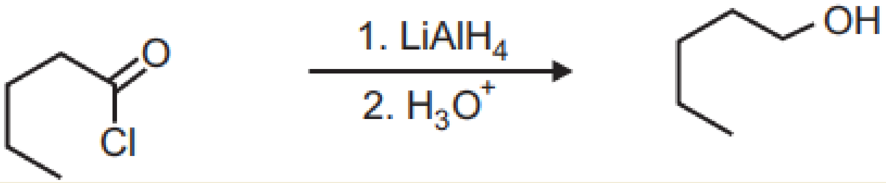
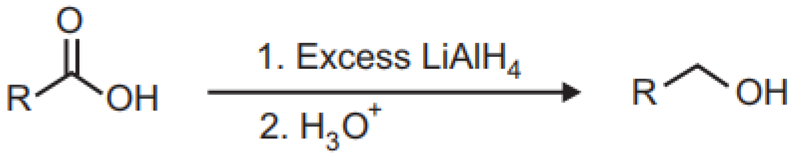


(d) Reduction of Acids : LAH reduces acids into primary alcohols.



Examples :

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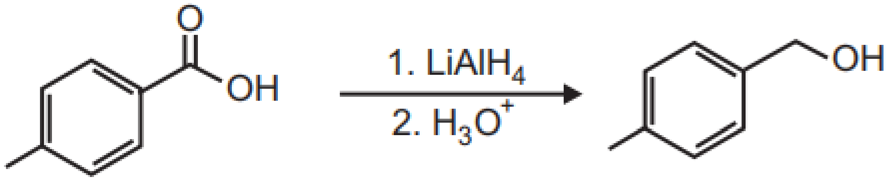

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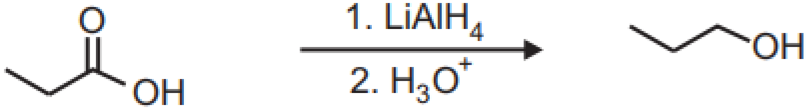

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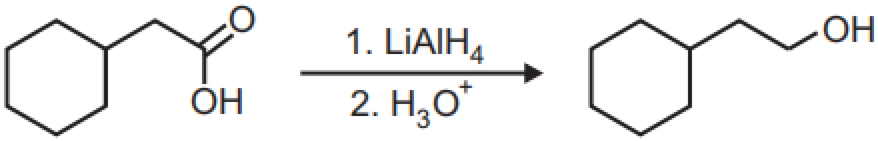

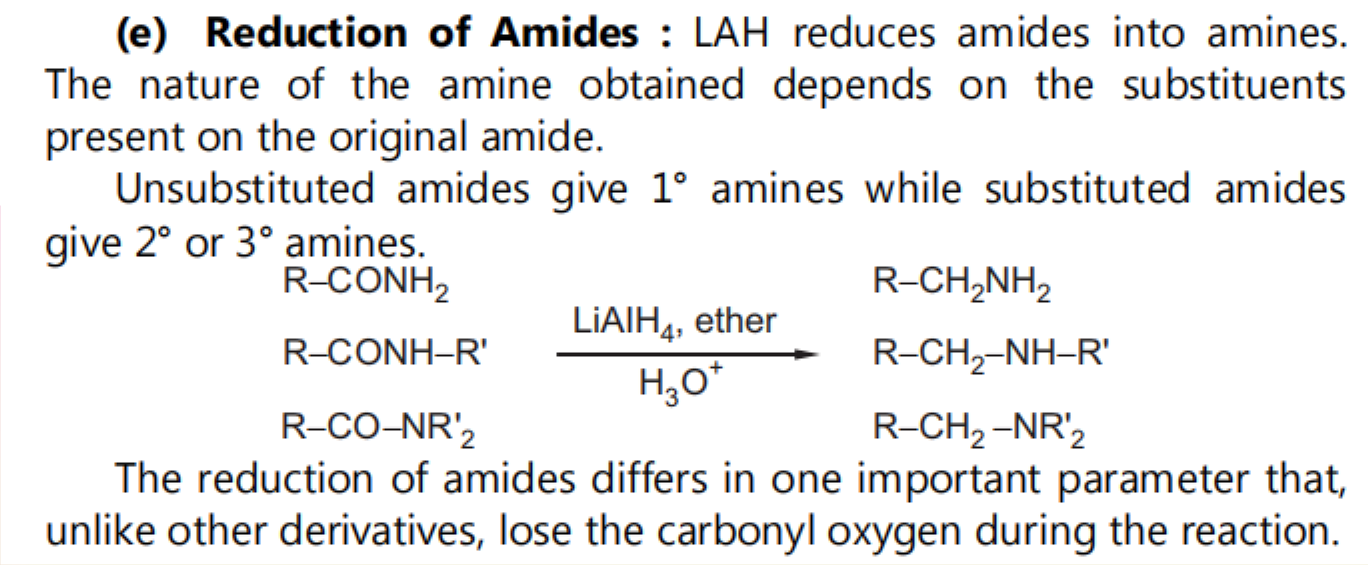

(e) Reduction of Amides : LAH reduces amides into amines. The nature of the amine obtained depends on the substituents present on the original amide.

Unsubstituted amides give 1° amines while substituted amides give 2° or 3° amines.

$$\begin{array}{c} R\text{–}CONH_2 \\ R\text{–}CONH\text{–}R' \\ R\text{–}CO\text{–}NR'_2 \end{array} \xrightarrow[H_3O^+]{LiAlH_4,\ ether} \begin{array}{c} R\text{–}CH_2NH_2 \\ R\text{–}CH_2\text{–}NH\text{–}R' \\ R\text{–}CH_2\text{–}NR'_2 \end{array}$$

The reduction of amides differs in one important parameter that, unlike other derivatives, lose the carbonyl oxygen during the reaction.

Examples :

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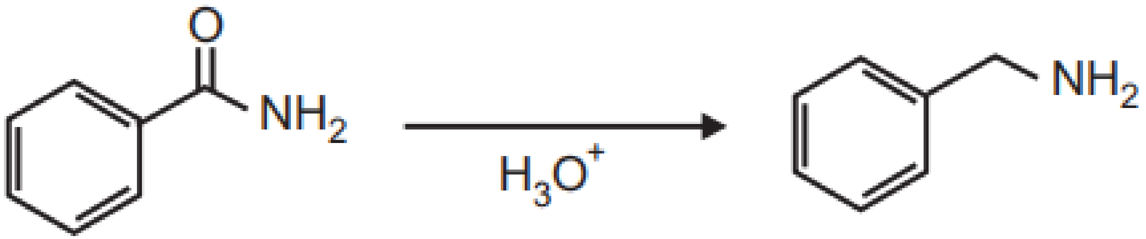

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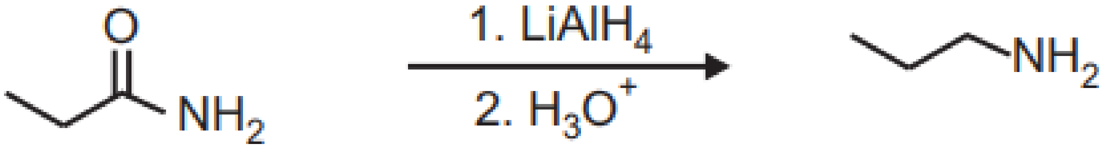

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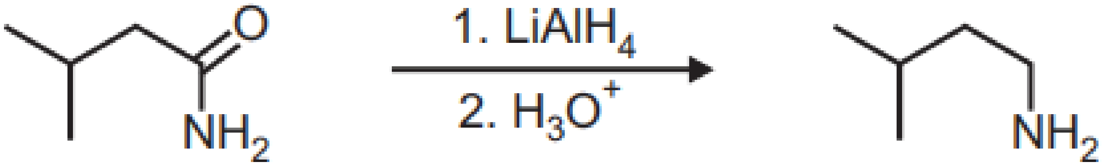
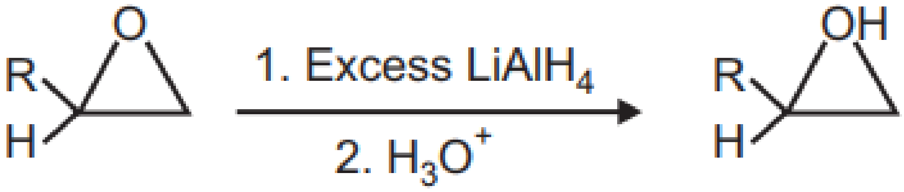
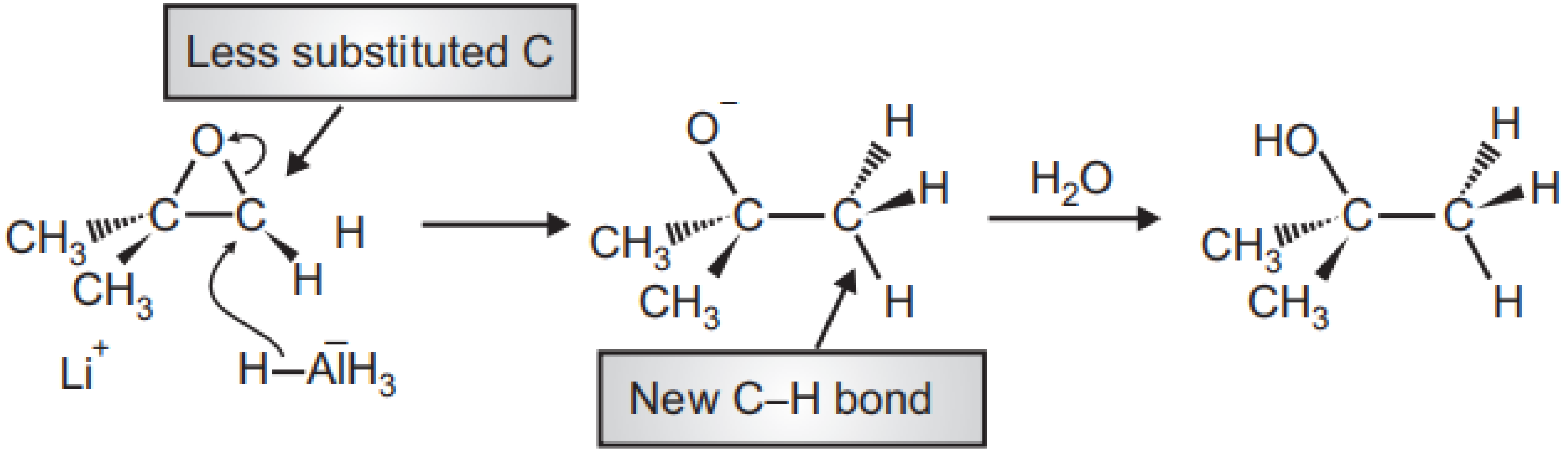
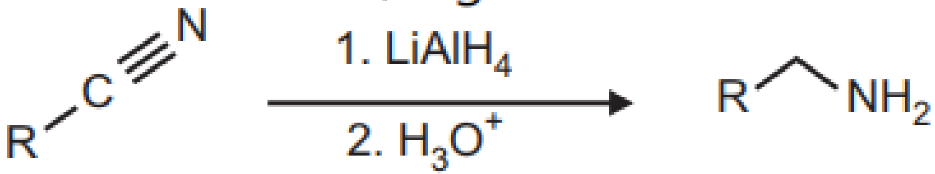


(2) Reduction of Epoxides : Epoxides are reduced to more substituted alcohol by LAH. This reaction is opposite to hydroboration-oxidation reaction, which gives less substituted alcohol.





(3) Reduction of Nitriles : When a solution of nitrile is added to the solution of LAH in the ether, it gives amines.



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Examples :

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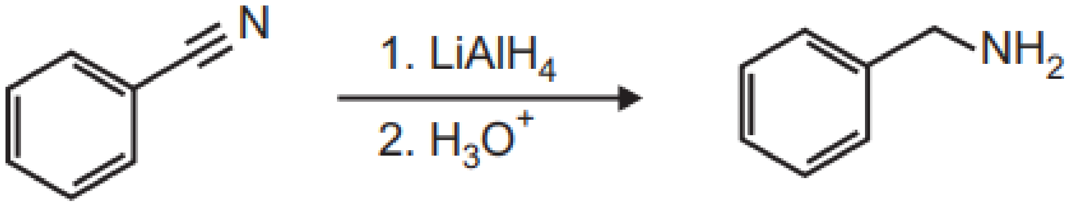

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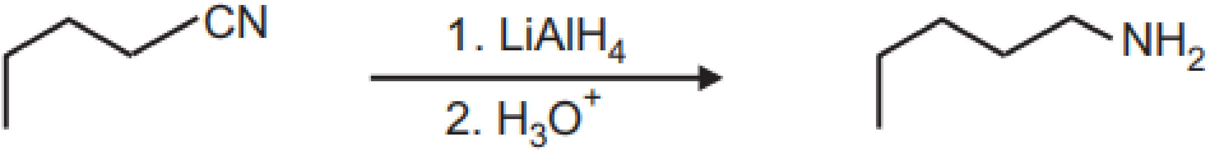

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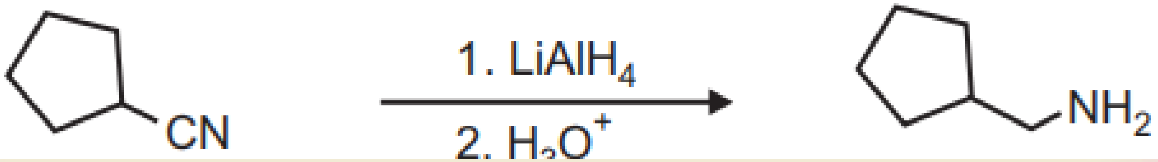
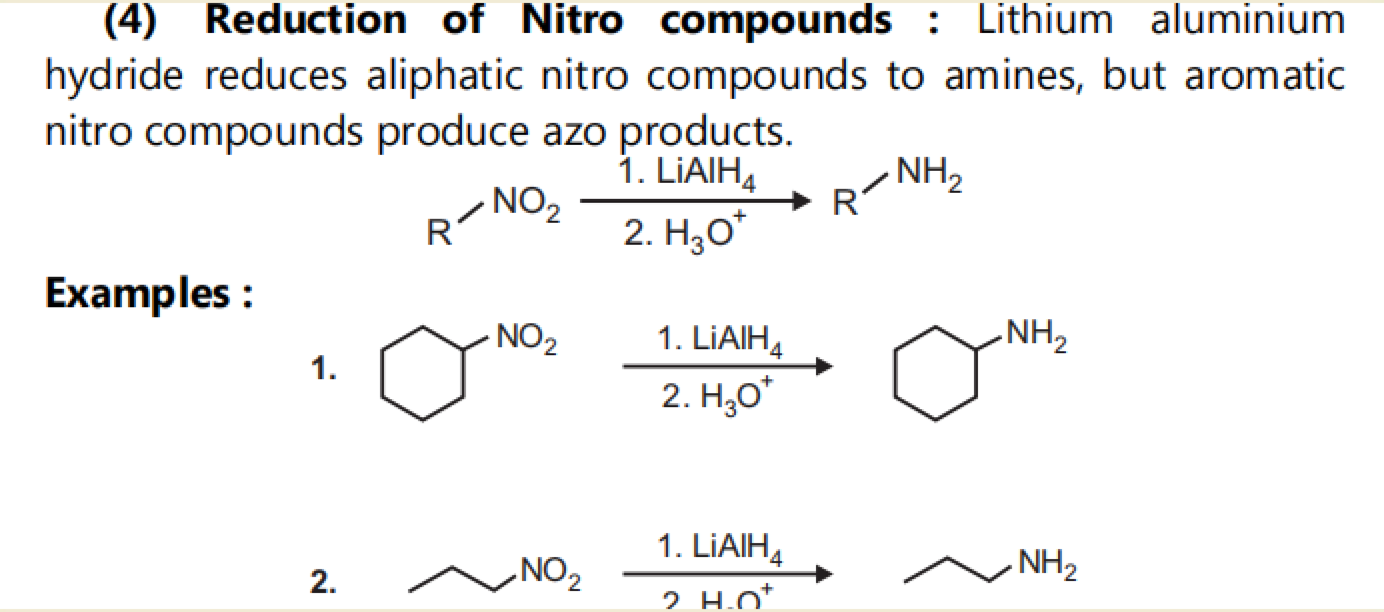




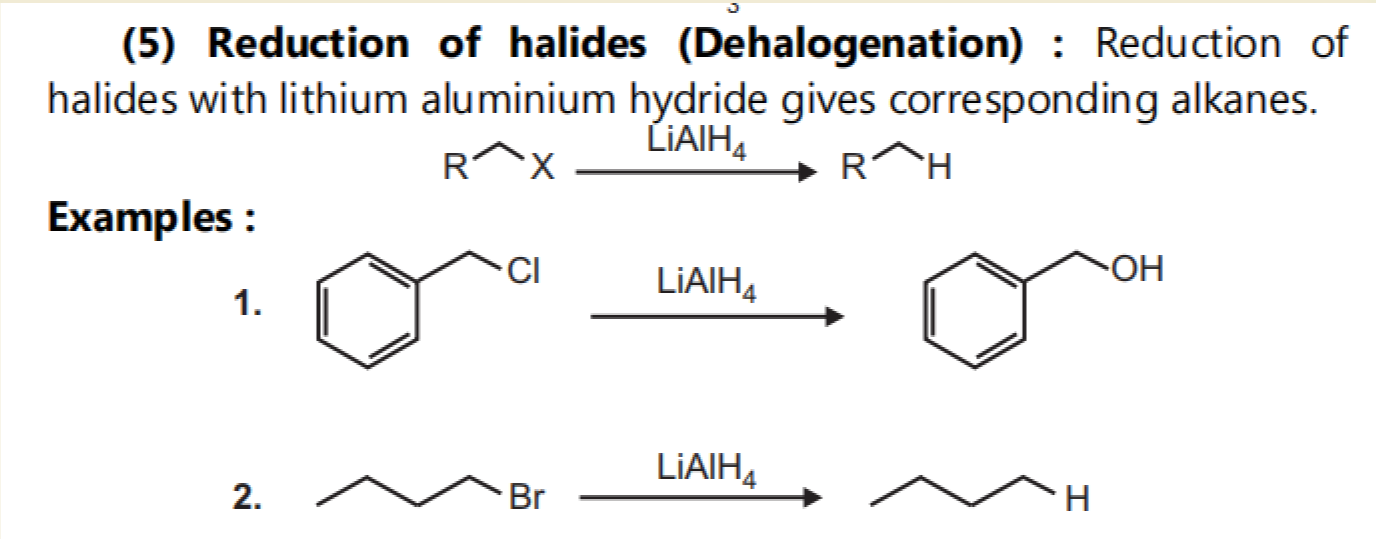
(4) Reduction of Nitro compounds : Lithium aluminium hydride reduces aliphatic nitro compounds to amines, but aromatic nitro compounds produce azo products.

$$R{-}NO_2 \xrightarrow[2.\ H_3O^+]{1.\ LiAlH_4} R{-}NH_2$$

Examples :

1.

2.



(5) Reduction of halides (Dehalogenation) : Reduction of halides with lithium aluminium hydride gives corresponding alkanes.

Examples :

1.2.2 Raney Nickel (Ra-Ni)

Introduction : Raney nickel, also known as spongy nickel, is a solid substance which is made up of nickel that is obtained from an alloy of nickel and aluminium.

Raney nickel is a fine-grained solid composed mostly of nickel derived from a nickel–aluminium alloy.

It was developed in 1926 by American engineer Murray Raney for the hydrogenation of vegetable oils.

Raney Nickel is used for hydrogenation of all types of C=C bonds. In Raney Nickel, hydrogen is bound to the surface of the catalyst by a weak nickel-hydrogen bonds.

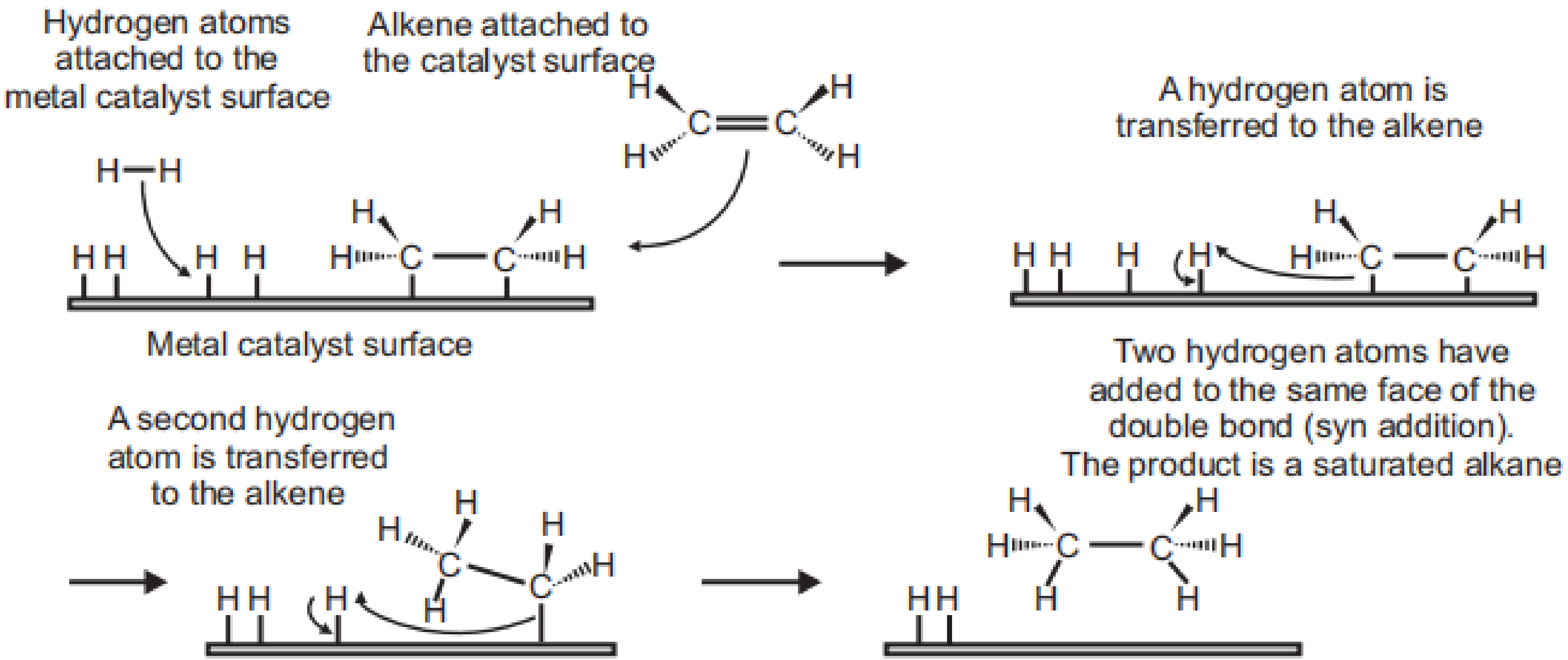
Preparation : Raney Nickel is prepared by adding Ni-Al alloy (1 : 1) over a period for 2-3 hours to an ice-cold solution of sodium hydroxide (25%). The mixture is heated to 115°-120°C with occasional stirring for about four hours. A further quantity of sodium hydroxide solution is added and the temperature is maintained at 115°-120°C till the evolution of hydrogen ceases. The alkali layer is decanted off and the residue (Ni-catalyst) is washed with water and then with alcohol. It is stored under absolute alcohol, ether or dioxon in a stoppered bottle.

$$\mathrm{Ni{-}Al + NaOH + H_2O \longrightarrow NaAlO_2 + \underset{\text{Raney Nickel}}{Ni{-}H} + H_2}$$

Applications : The primary application of Raney Nickel is its use as a reagent and catalyst for many hydrogenation reactions in the field of organic chemistry.

1. It is an extremely active form of Nickel.
2. Raney Nickel is very effective catalyst with which the hydrogenation can be generally carried out at room temperature and at atmospheric pressure.
3. It is widely used as a powerful reducing agent.
4. Most olefins are reduced at room temperature at about atmospheric pressure, while resistant compounds require higher temperature (110°C) and pressure (about 100 atm).
5. Double bonds, common to two rings are generally difficult to hydrogenate.

Catalytic hydrogenation mechanism



Hydrogen atoms attached to the metal catalyst surface

Alkene attached to the catalyst surface

A hydrogen atom is transferred to the alkene

Metal catalyst surface

A second hydrogen atom is transferred to the alkene

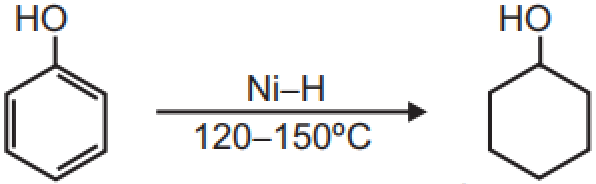
Two hydrogen atoms have added to the same face of the double bond (syn addition). The product is a saturated alkane

Examples :

1. $CH_2{=}CH_2$ Ethene

2. $HC \equiv CH$ Ethyne

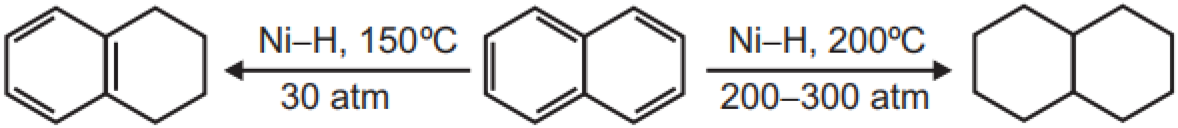
$\xrightarrow[\text{R.T.}]{\text{Ni – H}} CH_3-CH_3$ Ethane

3.


Phenol Cyclohexanol

4.


Benzene Cyclohexane

5.


Tetraline Decaline

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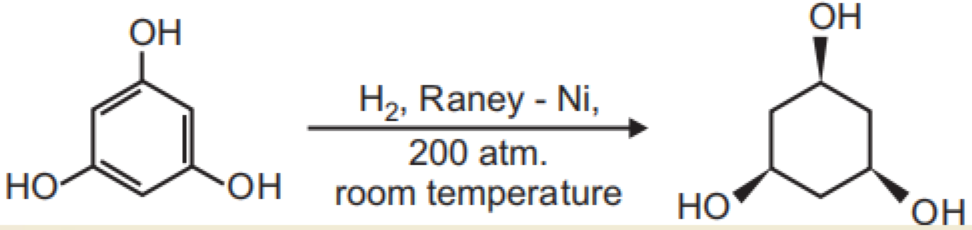

(2) Reduction of Nitro group to Amino group : Catalytic hydrogenation with Raney Nickel effectively reduces nitro groups. Raney Nickel is often used in place of Pd/C for substrates where dehalogenation of aromatic halides (I, Br, and Cl) is a concern.

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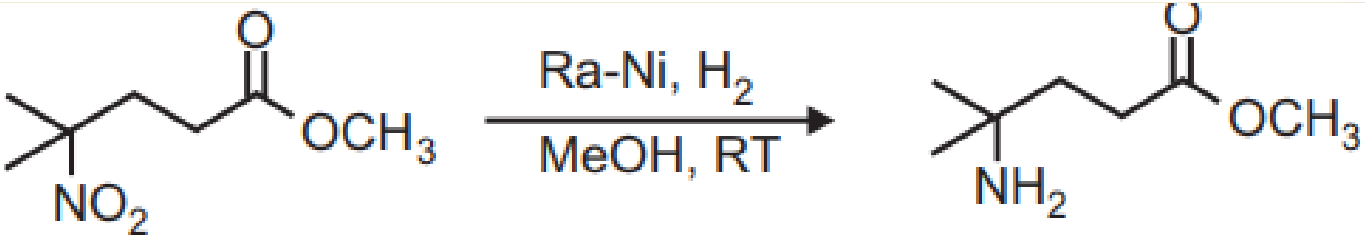

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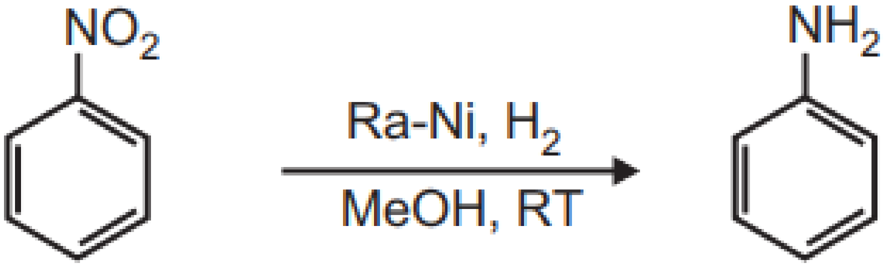

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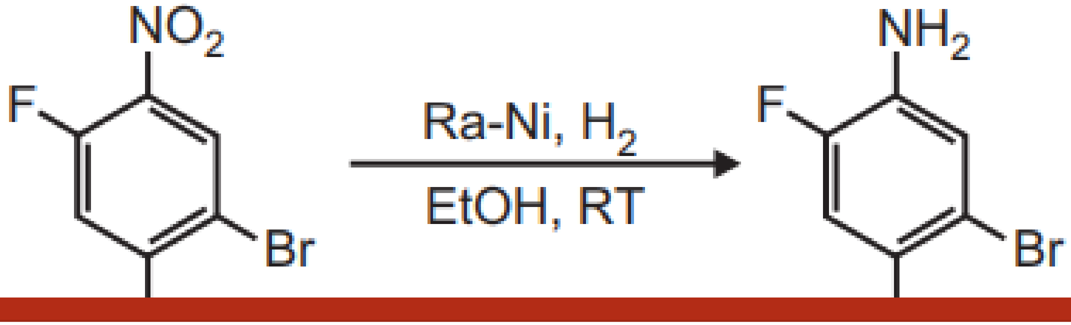
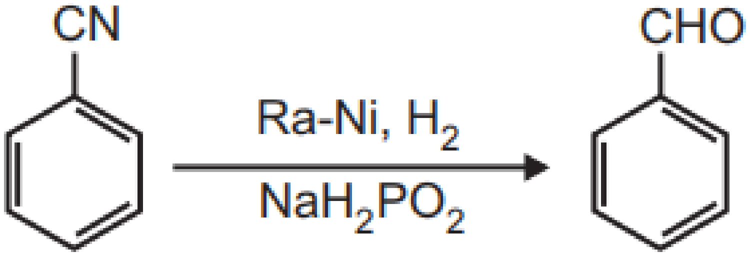
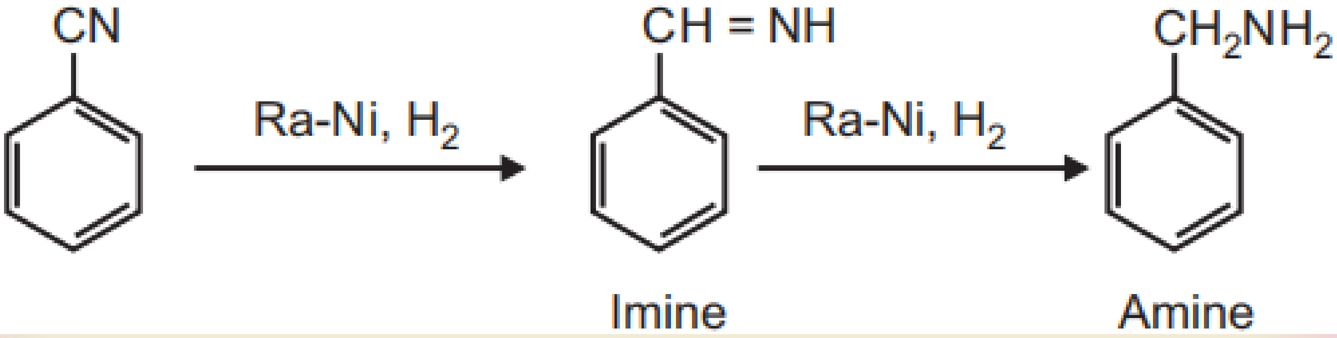


(3) Reduction of Nitriles : Nitriles are reduced to aldehydes or primary amines under different conditions.

(a) Nitriles in aqueous acetic acid : Nitriles are reduced to aldehydes with Raney Nickel and sodium hypophosphite.



(b) When nitriles are treated with Raney Nickel under pressure, primary amines are formed.



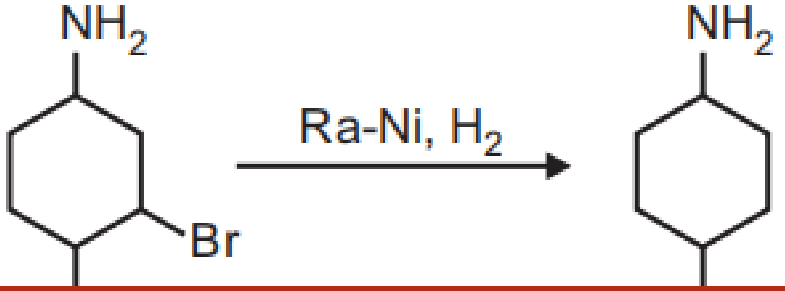
(4) Hydrogenolysis : Hydrogenolysis is a chemical reaction whereby a carbon–carbon or carbon–heteroatom single bond is cleaved or undergoes lysis (breakdown) by hydrogen.

(a) Reduction of Aromatic Ethers : Aromatic ethers are reductively cleaved on heating with Raney Nickel. Hydrogen comes from that normally contained in Raney Nickel and from the solvent.

$$\mathrm{Ar-O-R} \xrightarrow{\mathrm{Ni-H}} \mathrm{Ar-H+R-H}$$

(b) Dehalogenation of Halides : Dehalogenation of halides including fluorine using Raney Nickel is called dehalogenation.

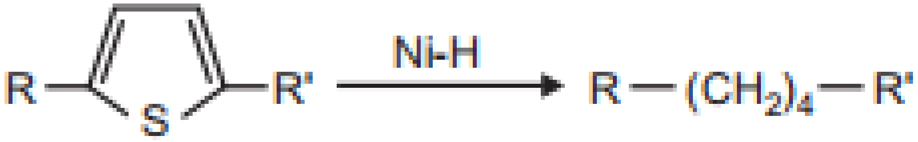
$$\mathrm{Ar-X} \xrightarrow[\mathrm{NaOH}]{\mathrm{Ni-H}} \mathrm{Ar-H} \text{ (where X = Cl, Br, I and F)}$$



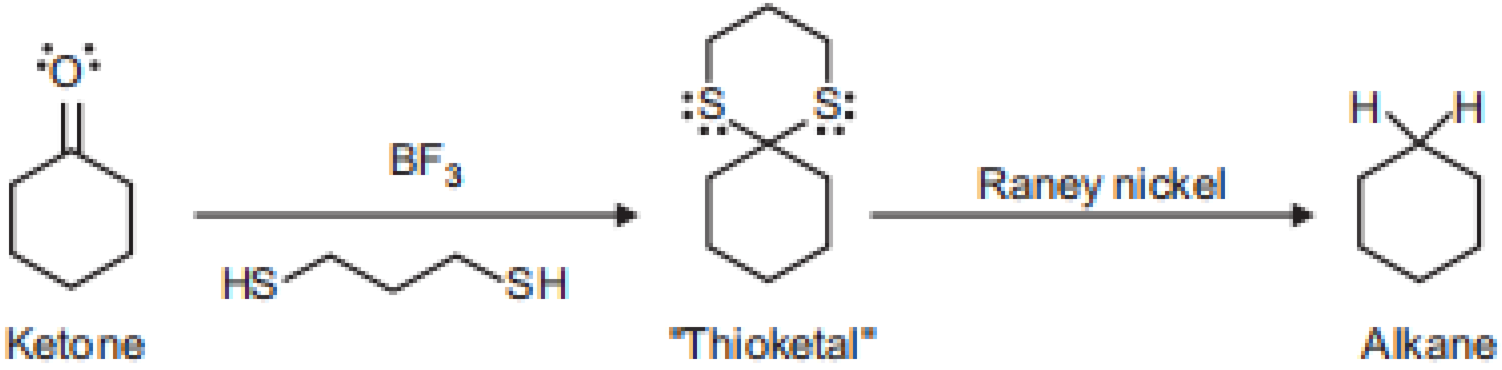
(d) Desulphurization : Thioalcohols, thioethers, disulphides, thioamides, sulphoxides and sulphones are desulphurized by hydrogenolysis with Raney Nickel.

(e) $R-S-R' \xrightarrow{Ni-H} R-H+R'-H$

Thiophene derivatives which may be considered as cyclic thioethers are desulphurized by accompanying reduction of double bonds.

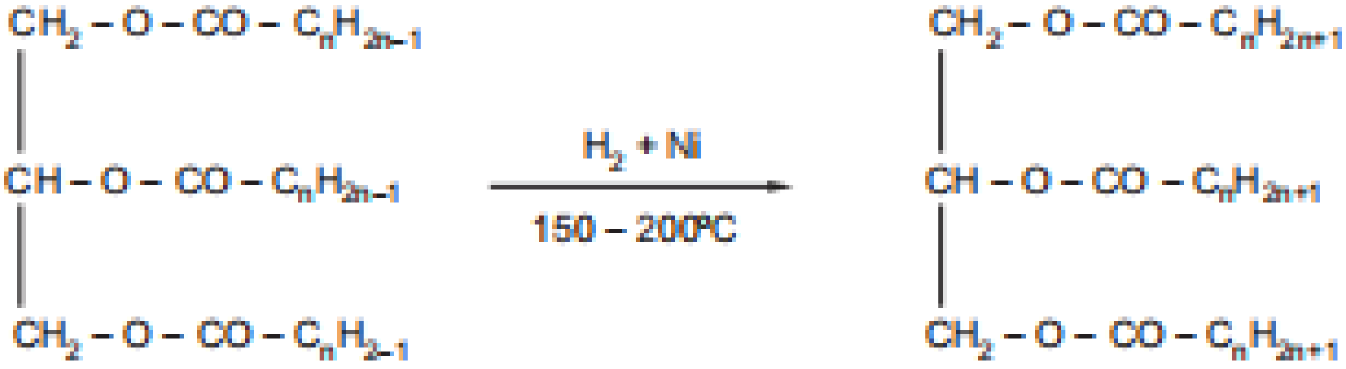


Desulphurization has been utilized for the conversion of a ketonic group to methylene group when the carbonyl compound to be reduced is sensitive and cannot be reduced by Clemmensen or Wolff-Kishner methods.



(5) Hardening of oils : Raney Nickel is employed in the industrial production of hydrogenated oils (Vegetable ghee).

Oils are glycerides of unsaturated fatty acids. The unsaturated hydrocarbon part of the fatty acid is partially hydrogenated with Raney-Nickel at 150-200°C under pressure to yield the hydrogenated oil.

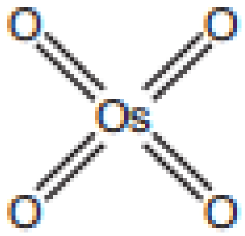


$$\begin{array}{l} CH_2-O-CO-C_nH_{2n-1} \\ | \\ CH-O-CO-C_nH_{2n-1} \\ | \\ CH_2-O-CO-C_nH_{2-1} \end{array} \xrightarrow[150-200°C]{H_2+Ni} \begin{array}{l} CH_2-O-CO-C_nH_{2n+1} \\ | \\ CH-O-CO-C_nH_{2n+1} \\ | \\ CH_2-O-CO-C_nH_{2n+1} \end{array}$$

Glyceride of unsaturated fatty aacids (oils)

Partially hydrogenated oil (vegetable ghee)

1.2.3 Osmium Tetraoxide (OsO_4)



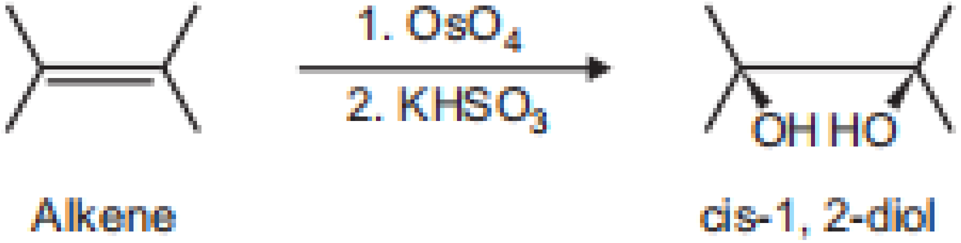
Introduction : Osmium tetraoxide is a yellow coloured highly toxic solid mainly used for syn-hydroxylation of alkenes having following structure. The OsO_4 was discovered in 1803 by Smithson Tennant.

Preparation : It is formed slowly when osmium powder reacts with O_2 at ambient temperature. The reaction of the bulk solid requires heating at 400°C.

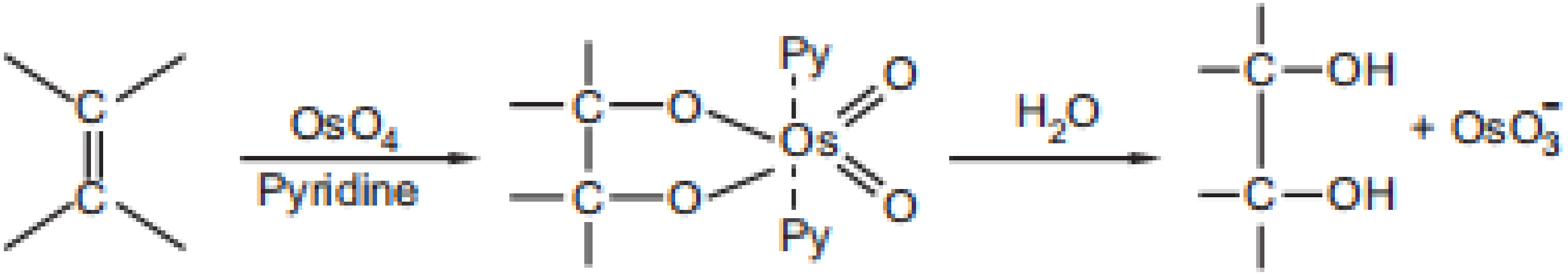
$$\underset{\text{Osmium}}{Os} + 2O_2 \xrightarrow{\Delta T} \underset{\substack{\text{Osmium}\\ \text{tetraoxide}}}{OsO_4}$$

Applications : It is an expensive and toxic substance used only for the synthesis of fine chemicals (pharmaceuticals) and degradative purposes in the structure elucidation.

(1) Hydroxylation of Alkenes and Cycloalkenes : It is used for syn/cis-hydroxylation of olefinic compounds to form corresponding cis-1, 2 diols, similar to alk. $KMnO_4$.



Pyridine catalyses the reaction by co-ordinating with the resulting osmic ester.



$[OsO_3 + H_2O \longrightarrow H_2OsO_4]$

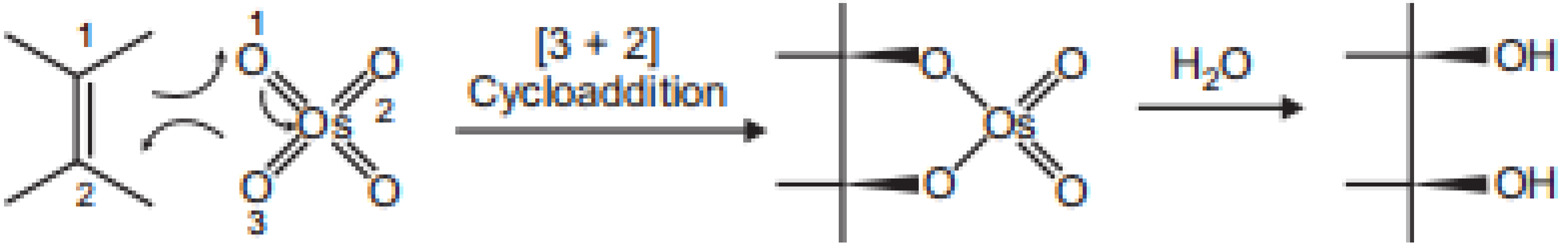
Osmic acid

Characteristics :

- It always gives vicinal-1,2-diols.
- Stereochemistry of addition is always syn.
- It can be used in catalytic amount in the presence of H_2O_2/NMO as a co-catalyst.

Mechanism :

The dihydroxylation proceeds through a concerted process *via* a [3+2] cycloaddition reaction between the OsO_4 and alkene. This results in a 5-membered ring called cyclic osmate ester and generates the syn stereochemistry. The osmate ester is broken up into 1,2-diol by the use of an aqueous solution of a reducing agent such as potassium bisulfite ($KHSO_3$).



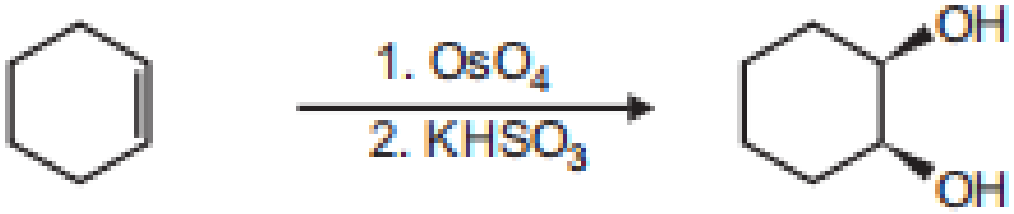
Os(VIII)

Cyclic osmate ester
Os(VI)

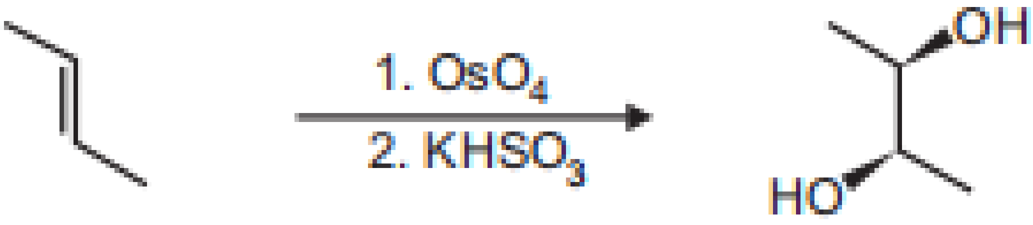
cis-1, 2-diol

Examples :

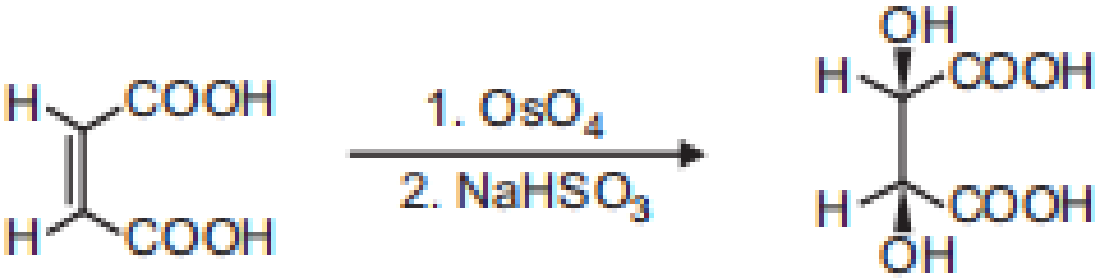
1.



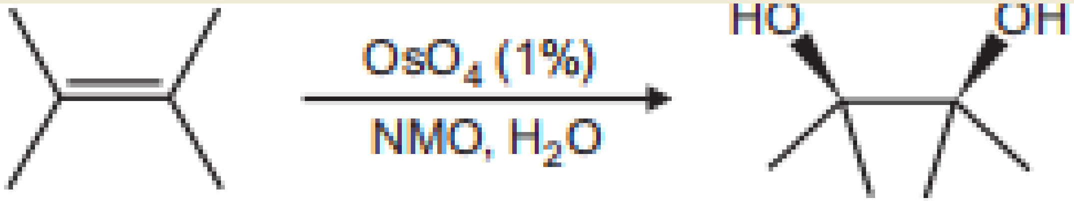
2.



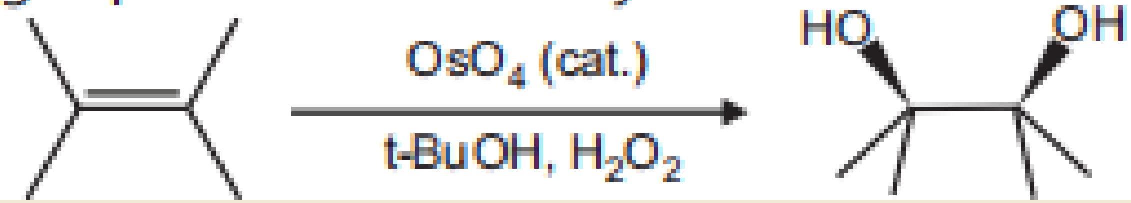
3.



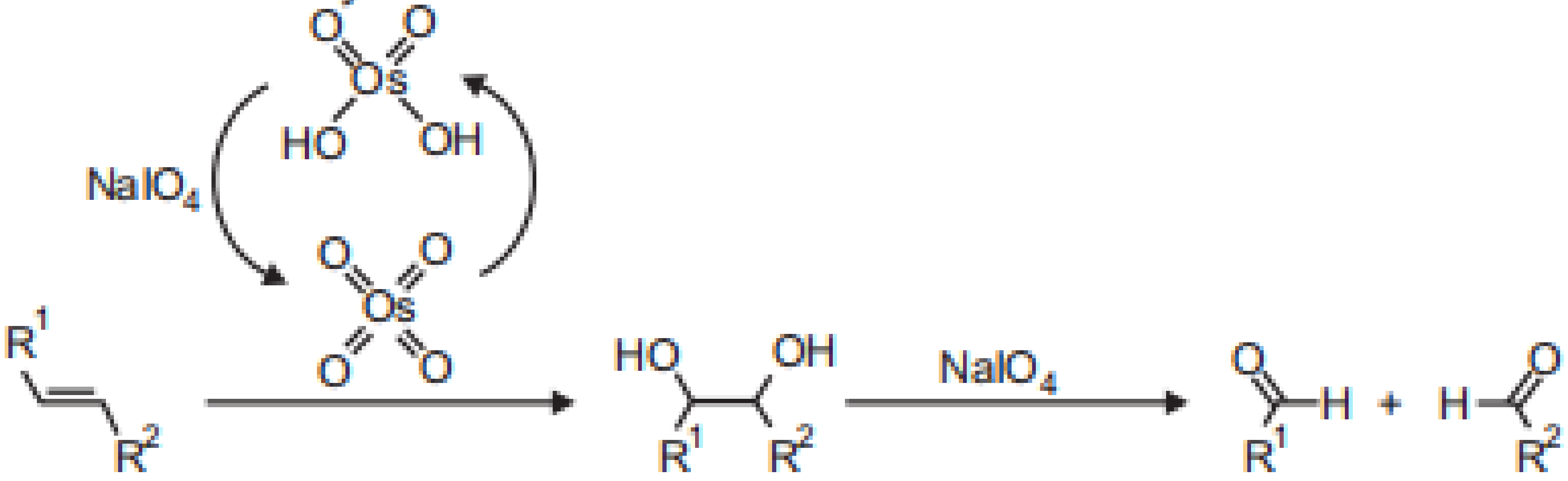
(2) Upjohn oxidation : The Upjohn dihydroxylation is an organic reaction which converts an alkene to cis vicinal diol, using N-methylmorpholine N-oxide (NMO) as a stoichiometric re-oxidant. NMO regenerates the osmium catalyst, allowing for catalytic amounts of osmium to be used. It is superior to previous catalytic methods.



(3) The Milas hydroxylation : It converts an alkene to vicinal diol, using hydrogen peroxide and a catalytic amount of osmium tetroxide.



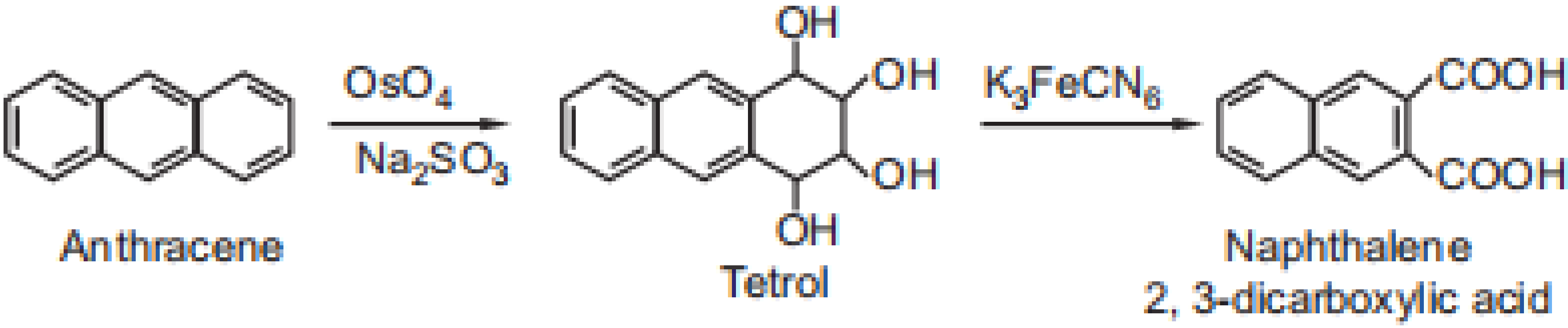
(4) Lemieux-Johnson oxidation (Formation of aldehydes/ ketones) : When OsO_4 is used in combination with $NaIO_4$, it is known as *Lemieux-Johnson reagent*. The Lemieux–Johnson or Malaprade–Lemieux–Johnson oxidation is a chemical reaction in which an olefin undergoes oxidative cleavage to form two aldehyde or ketone units. The reaction proceeds in a two step manner, beginning with dihydroxylation of the alkene by osmium tetroxide, followed by a Malaprade reaction to cleave the diol using periodate. Excess periodate is used to regenerate the osmium tetroxide, allowing it to be used in catalytic amounts.



(5) Formation of 1, 2-diketones : Acetylene reacts with OsO_4 in the presence of tertiary amines, such as pyridine or isoquinoline to give osmium (VI) ester complexes, which on hydrolysis with sodium sulphite yield the corresponding 1,2-diketones from non-terminal alkynes.

$$\underset{\text{Alkyne}}{R-C\equiv C-R'} \xrightarrow[\text{2. } Na_2SO_3]{\text{1. } OsO_4/\text{t-amine}} \underset{\text{Diketone}}{R'COCOR}$$

(6) Elucidation of structures of polynuclear hydrocarbons : Oxidation of anthracene by OsO_4 give tetrol, which on further oxidation with potassium ferricyanide gives naphthalene 2, 3-dicarboxylic acid. Carboxylic group at 2 and 3 position clearly indicate the ortho fusion of the third ring and also linear fusion of three rings.




Thank You!