16th April, 2024

Alkenes

Alkanes are non reactive, and they are called paraffins, Par – affismus

Alkenes / Olefins → Addition reactions

① hydrogenation
② halogenation
③ hydration
④ hydrohalogenation

→ Oxidation reactions

⑤ hydroxylation
⑥ Ozonolysis

→ Polymerization

Combustion

(i) $C_xH_y + \alpha O_2 \rightarrow xCO_2 + \frac{y}{2}H_2O$

LHS = RHS

$2\alpha = 2x + \frac{y}{2}$

$\alpha = x + \frac{y}{4}$

$\therefore C_xH_y + \left(x + \frac{y}{4}\right)O_2 \rightarrow xCO_2 + \frac{y}{2}H_2O$

(ii) $C_nH_{2n+2} + \alpha O_2 \rightarrow nCO_2 + \frac{2n+2}{2}H_2O$

$2\alpha = 2n + \frac{2n+2}{2}$

$2\alpha = 2n + n + 1$

$2\alpha = 3n + 1$

$\alpha = \frac{3n+1}{2}$

$$\Rightarrow \boxed{C_nH_{2n+2} + \frac{3n+1}{2}O_2 \rightarrow nCO_2 + \frac{2n+2}{2}H_2O}$$

Classwork

(iii) $C_nH_{2n} + eO_2 \rightarrow fCO_2 + gH_2O$

$C_nH_{2n} + \alpha O_2 \rightarrow nCO_2 + \frac{2n}{2}H_2O$

$2\alpha = 2n + \frac{2n}{2}$

$2\alpha = 2n + n$

$\alpha = \frac{3n}{2}$

Class

$e = \frac{3n}{2}$, $f = n$, $g = n$

Assignment

(iv) $C_nH_{2n+1}OH + eO_2 \rightarrow fCO_2 + gH_2O$

(v) $C_nH_{2n+1}CHO + eO_2 \rightarrow fCO_2 + gH_2O$

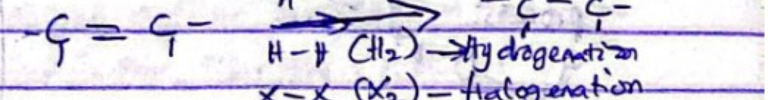
find e, f and g

(vi) $C_nH_{2n+1}COOH + eO_2 \rightarrow fCO_2 + gH_2O$

1st

Addition Reactions

Pi bonds break in addition reaction



$$-\overset{|}{\underset{|}{C}}=\overset{|}{\underset{|}{C}}- \xrightarrow{A-A} -\overset{A}{\underset{|}{C}}-\overset{A}{\underset{|}{C}}-$$

H–H (H_2) → Hydrogenation

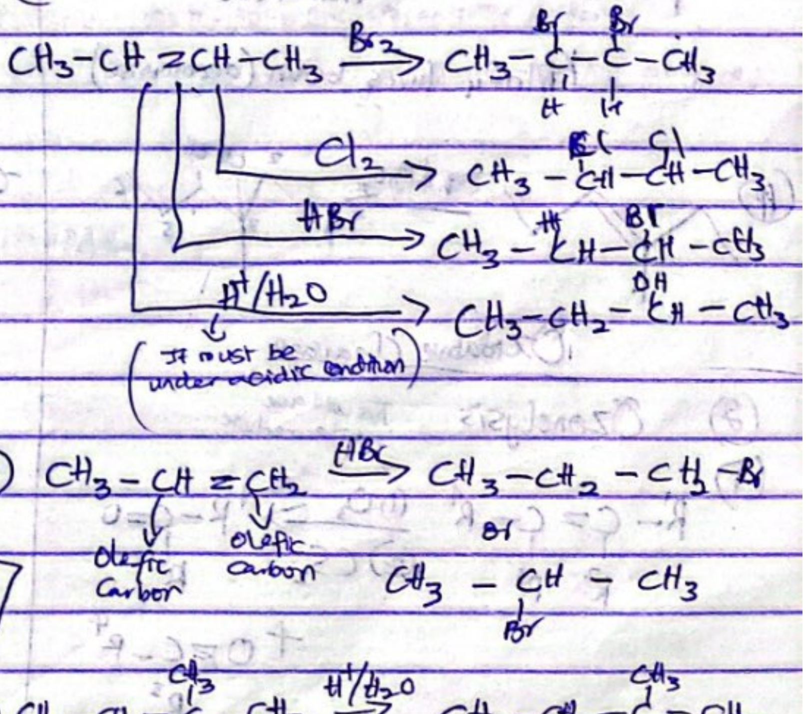
X–X (X_2) – Halogenation

H–X – Hydrohalogenation

A–OH – Hydration

(i) $CH_3-CH=CH-CH_3 \xrightarrow{H_2/Pt} CH_3-CH_2-CH_2-CH_3$

(Anytime there's is addition reaction, you use transition metal catalyst)



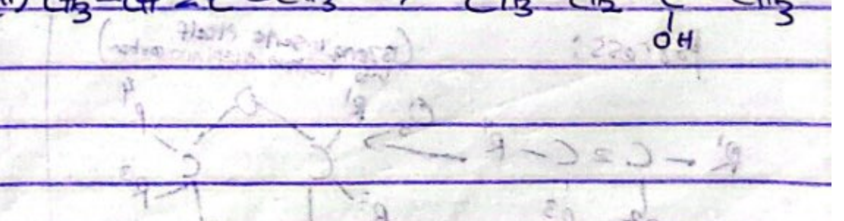
$$CH_3-CH=CH-CH_3 \xrightarrow{Br_2} CH_3-\overset{Br}{\underset{H}{C}}-\overset{Br}{\underset{H}{C}}-CH_3$$

$$\xrightarrow{Cl_2} CH_3-\overset{Cl}{CH}-\overset{Cl}{CH}-CH_3$$

$$\xrightarrow{HBr} CH_3-\overset{H}{CH}-\overset{Br}{CH}-CH_3$$

$$\xrightarrow{H^+/H_2O} CH_3-CH_2-\overset{OH}{CH}-CH_3$$

(It must be under acidic condition)



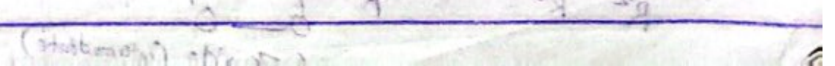
(ii) $CH_3-CH=CH_2 \xrightarrow{HBr} CH_3-CH_2-CH_2-Br$

olefic carbon

olefic carbon

Br

$CH_3-\underset{Br}{CH}-CH_3$

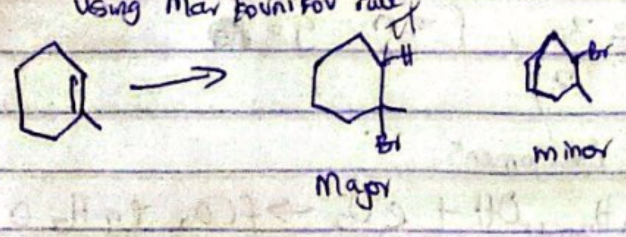


$$\text{(iii) } CH_3-CH=\overset{CH_3}{C}-CH_3 \xrightarrow{H^+/H_2O} CH_3-CH_2-\overset{CH_3}{\underset{OH}{C}}-CH_3$$

Class

18th April, 2024

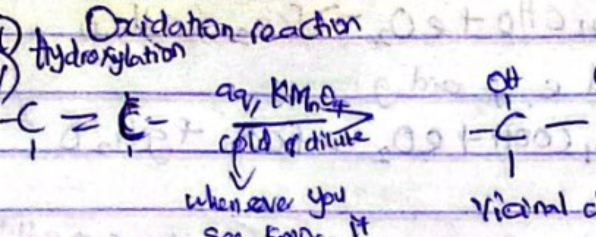
using Markovnikov rule



① Oxidation reaction

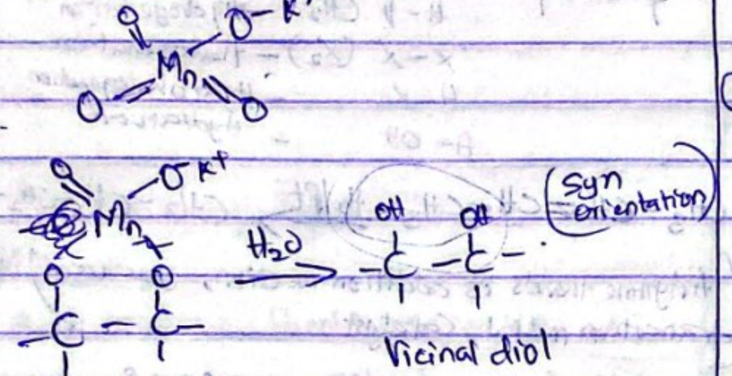
① Hydroxylation

(i)



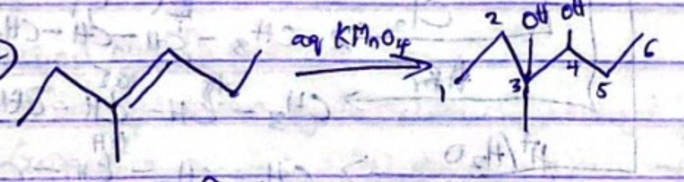
whenever you see KMnO4, it is called hydroxylation

Process:



$KMnO_4$ turns brown (decolourise)

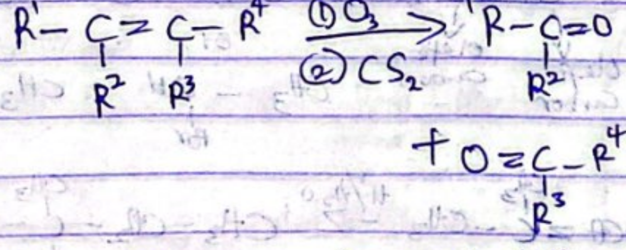
(ii)



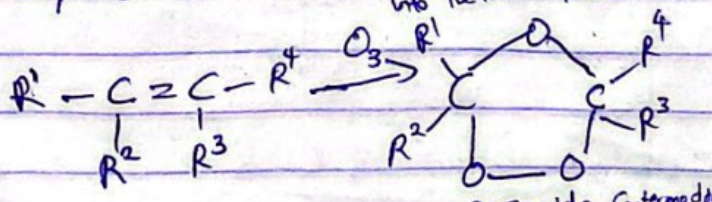
Oxidative Cleavage

② Ozonolysis

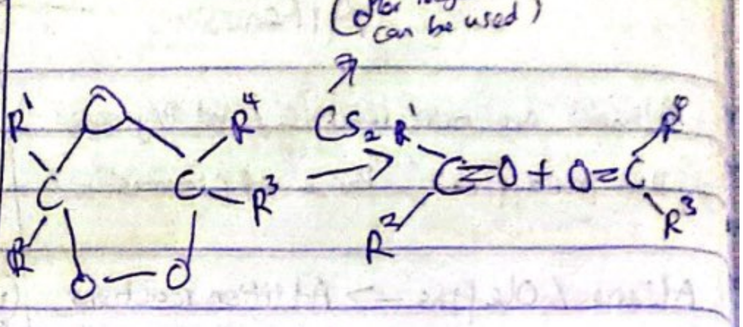
(i)



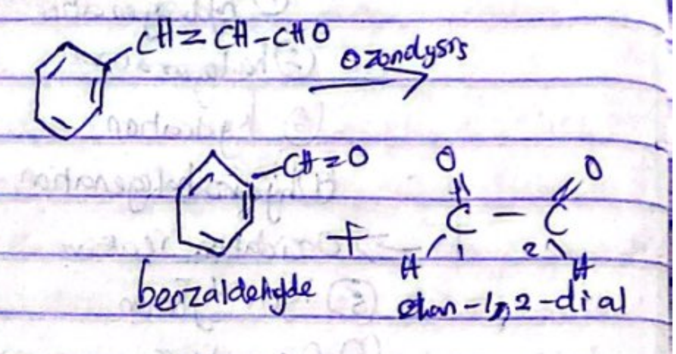
Process: (ozone inserts itself into the two olefinic carbon)



Ozonide (intermediate)

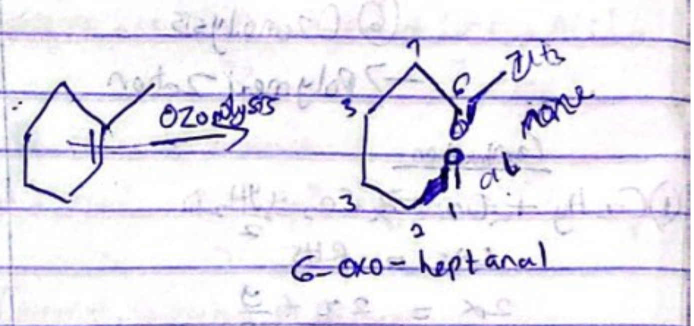


(ii)



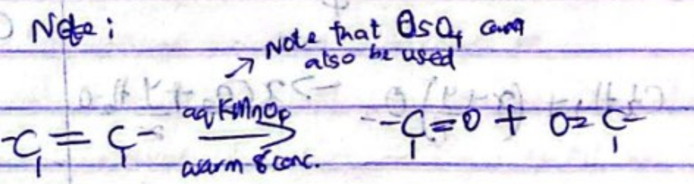
benzaldehyde + ethan-1,2-dial

(iii)



6-oxo-heptanal

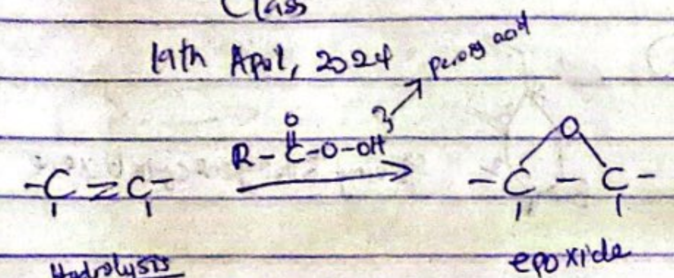
Note:

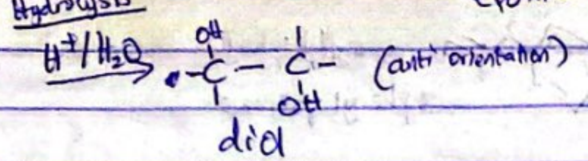


Carbonyls

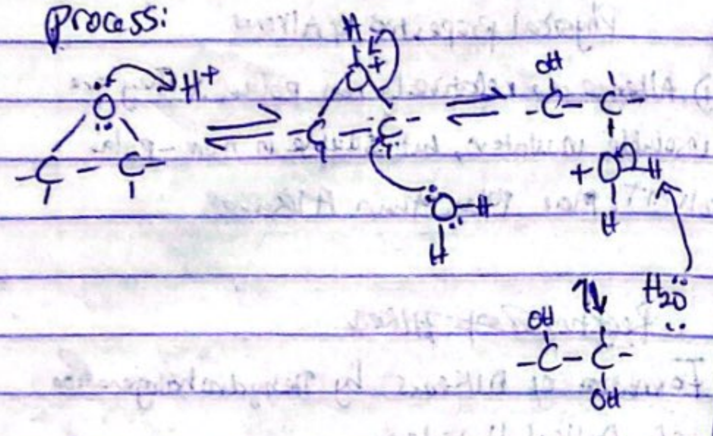
Class

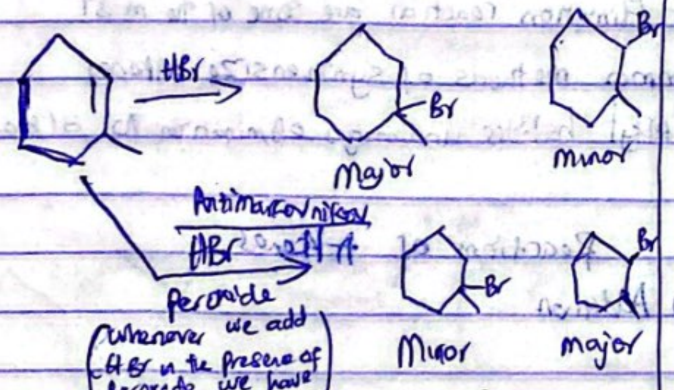
19th April, 2024



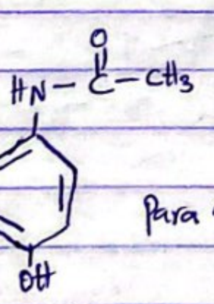


Process:



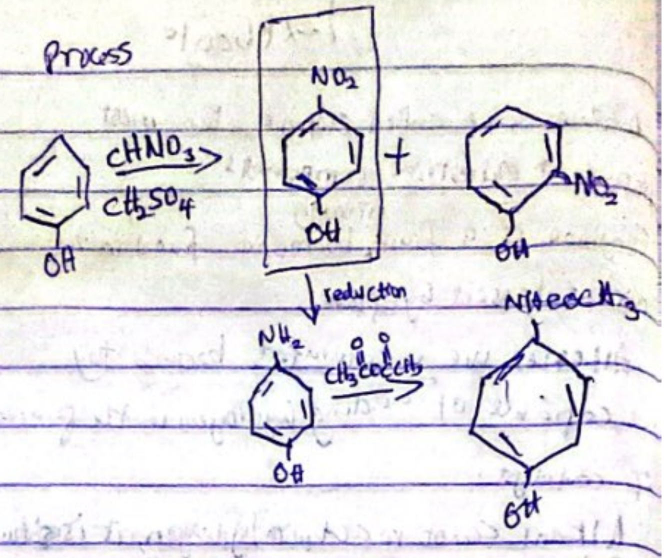


(whenever we add HBr in the presence of peroxide, we have antimarkovnikov)

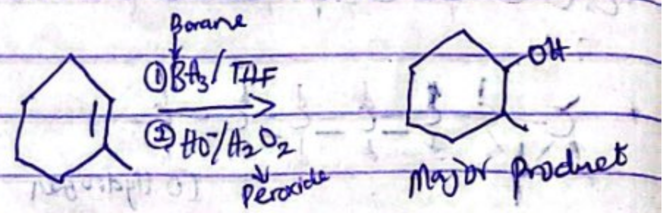


Para acetamido phenol

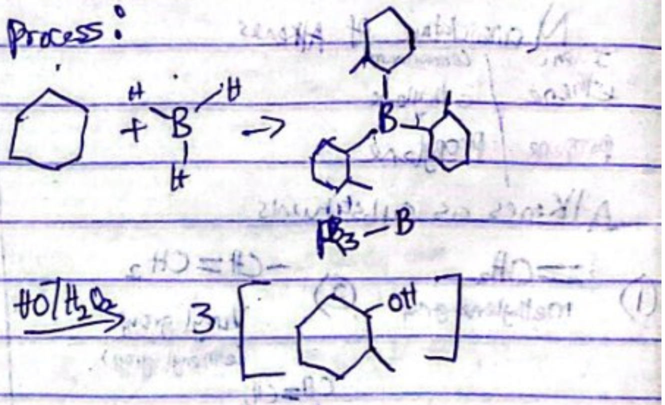
Process



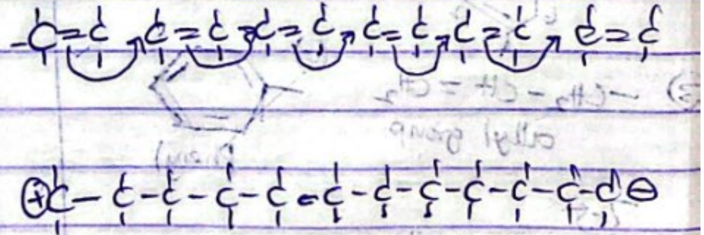
Contd. of Anti markovnikov



Process:



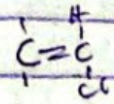
Polymerization of Alkenes



Polyethene

Initiators stabilize ⊕ and ⊖

PVC

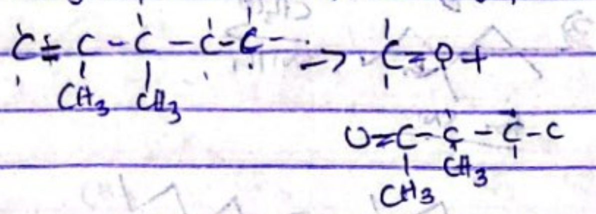


venyl chlorid

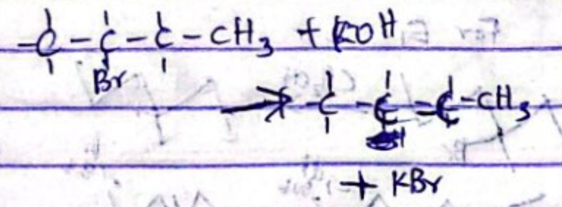
Styrene

Questions

(1) Ozonolysis products of 2, 3-dimethyl pentane



(2) Product when $CH_3CHBrCH_2CH_3$ reacts with KOH

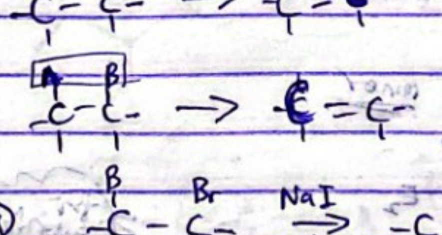


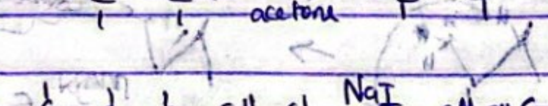
Class
22nd April, 2024

Preparation / Synthesis of Alkenes

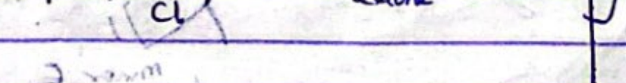
1. dehydrohalogenation
2. dehalogenation
3. dehydration

(A) dehalogenation



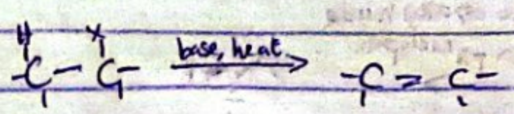


(i) NaI, acetone



(ii) NaI, acetone

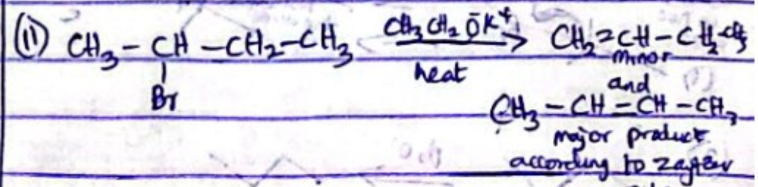
(2) dehydrohalogenation



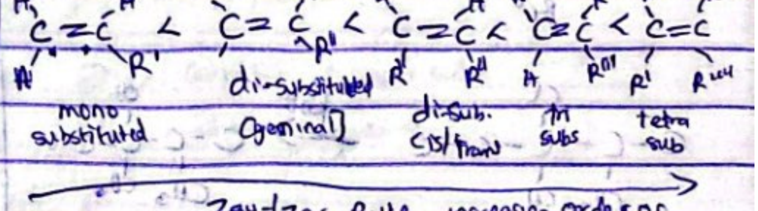
Examples

(i) $CH_3-CH_2-CH_2-Br \xrightarrow[heat]{CH_3O^-K^+} CH_3-CH=CH$

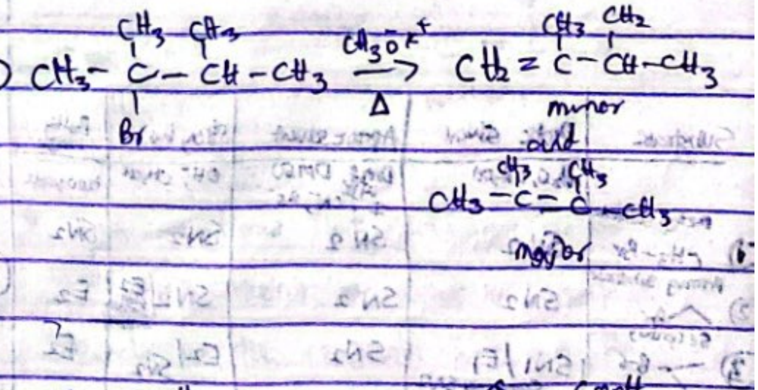
→methoxide



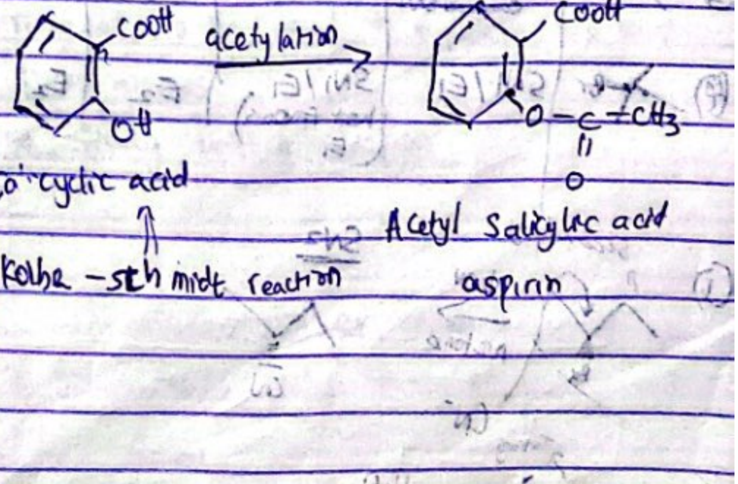
(ii) $CH_3-CH(Br)-CH_2-CH_3 \xrightarrow[heat]{CH_3CH_2O^-K^+} CH_2=CH-CH_2-CH_3$ minor and $CH_3-CH=CH-CH_3$ major product according to zaytzev rule



Zaytzev Rule increasing order of stability



(iii) $CH_3-C(CH_3)(Br)-CH(CH_3)-CH_3 \xrightarrow[\Delta]{CH_3O^-K^+} CH_2=C(CH_3)-CH(CH_3)-CH_3$ minor and $CH_3-C(CH_3)=C(CH_3)-CH_3$ major



Salicylic acid
⇑
Kolbe-Schmidt reaction

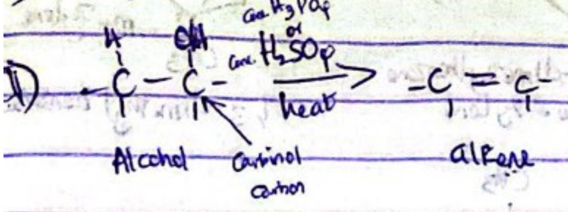
Acetyl Salicylic acid
aspirin

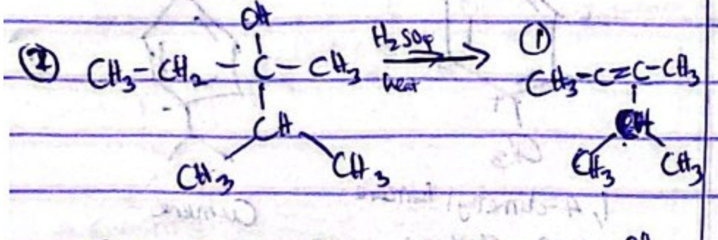
Class

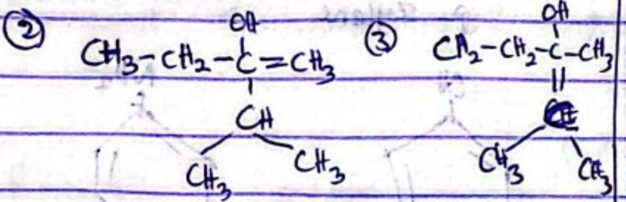
④ At what temp will you get alkene and what temp will you get ether?

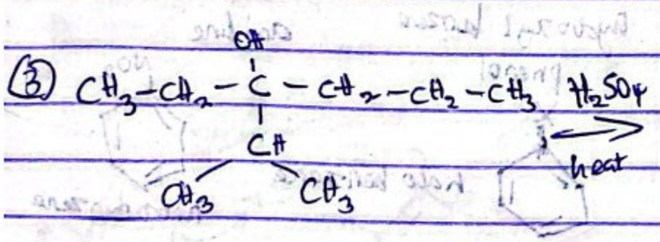
23rd April, 2024

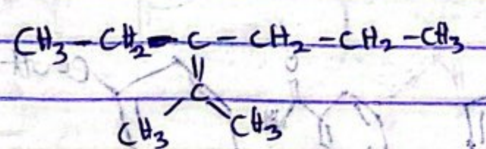
③ dehydration: Removal of water → E1 mechanism

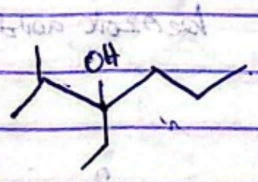
① 

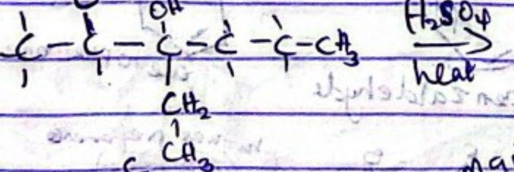


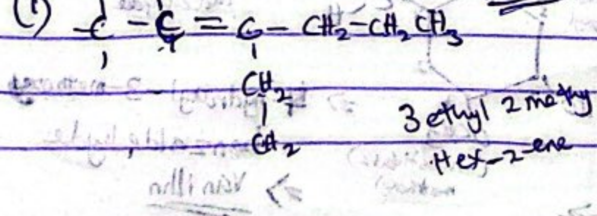




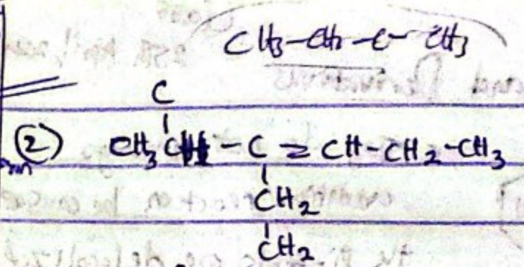


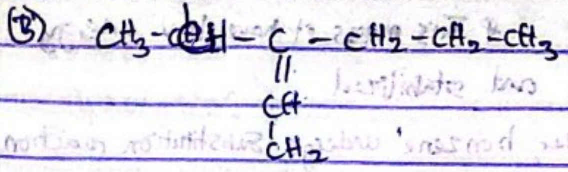


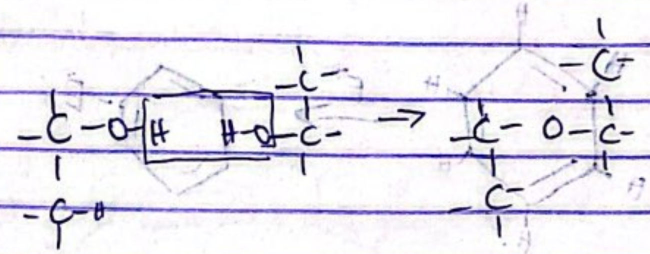




3 ethyl 2 methyl Hex-2-ene

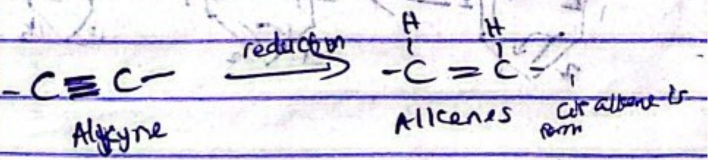






Ether can be formed under certain condition of temperature.

④ Reduction of alkynes



test question

* There are times that reduction of alkynes gives cis alkene or trans alkene, it depends on the reagent. Find out the reagent to be used to produce cis and trans alkenes.

* Study Wittig reaction

Stereo chemistry of Alkenes

* Cahn-Ingold-Prelog Convention

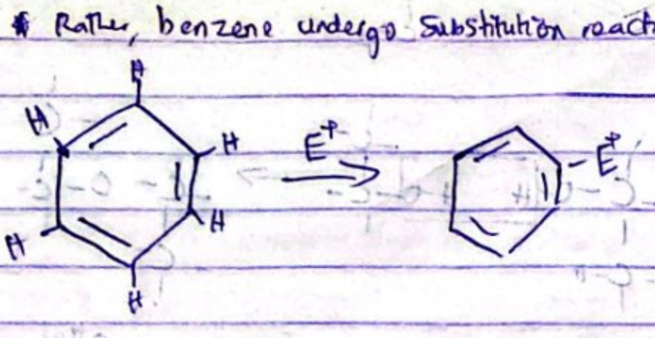
→ Cis alkene is formed when Pd/BaSO4 in the presence of quinoline is used as reagent
Trans alkene is formed when Na and liq NH3 is used as reagent

Class
25th April, 2024

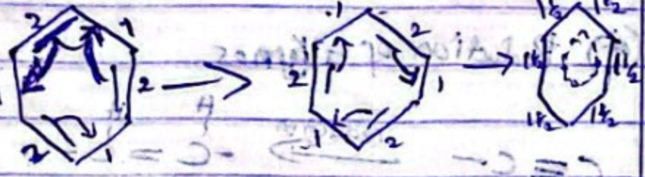
Benzene and Derivatives

- They do not undergo addition reaction because the pi-bonds are delocalized
- This makes it have low energy and stabilized

- Rather, benzene undergo substitution reaction

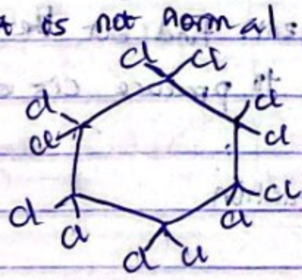


- The double bond are not really really, they are pseudo

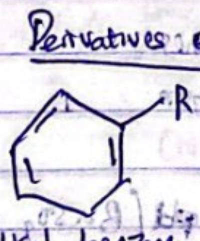


25th April, 2024

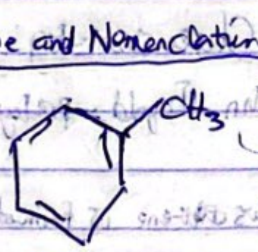
Benzene ~~may~~ undergo addition reaction but it is not normal:



Derivatives of Benzene and Nomenclature

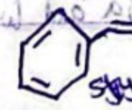


Alkyl benzene



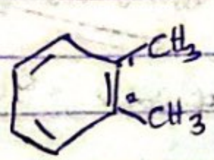
methyl benzene

Toluene

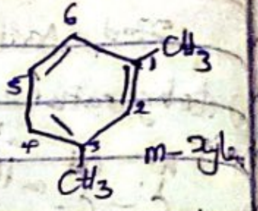


styrene/vinyl benzene

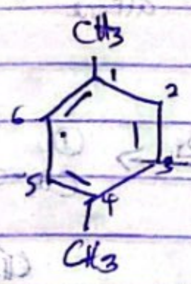
O = ortho, m = meta, p = para



1,2-dimethylbenzene
ortho-xylene



m-xylene
1,3-dimethyl benzene



1,4-dimethyl benzene
p-xylene

Cumene

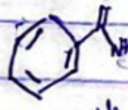
hydroxyl benzene
phenol

aniline

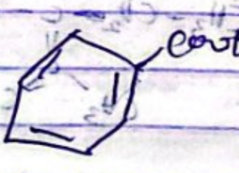
halo benzene

nitrobenzene

methoxybenzene
Anisole

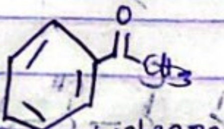


Benzamide

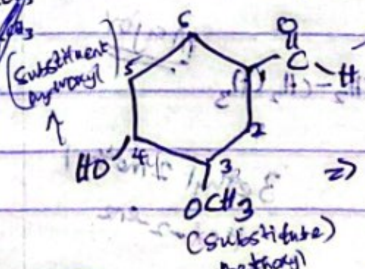


benzoic acid

benzaldehyde



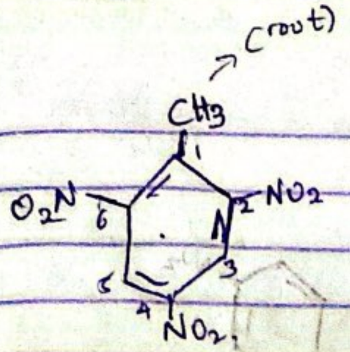
acetophenone



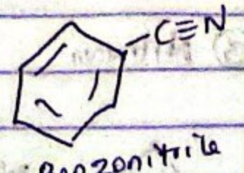
→ higher preference (root name) aldehyde

⇒ ~~4~~-hydroxyl-3-methoxy benzaldehyde

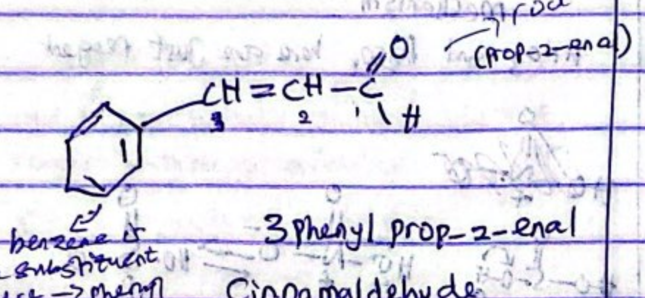
⇒ Vanillin



2, 4, 6-trinitro toluene



Benzonitrile



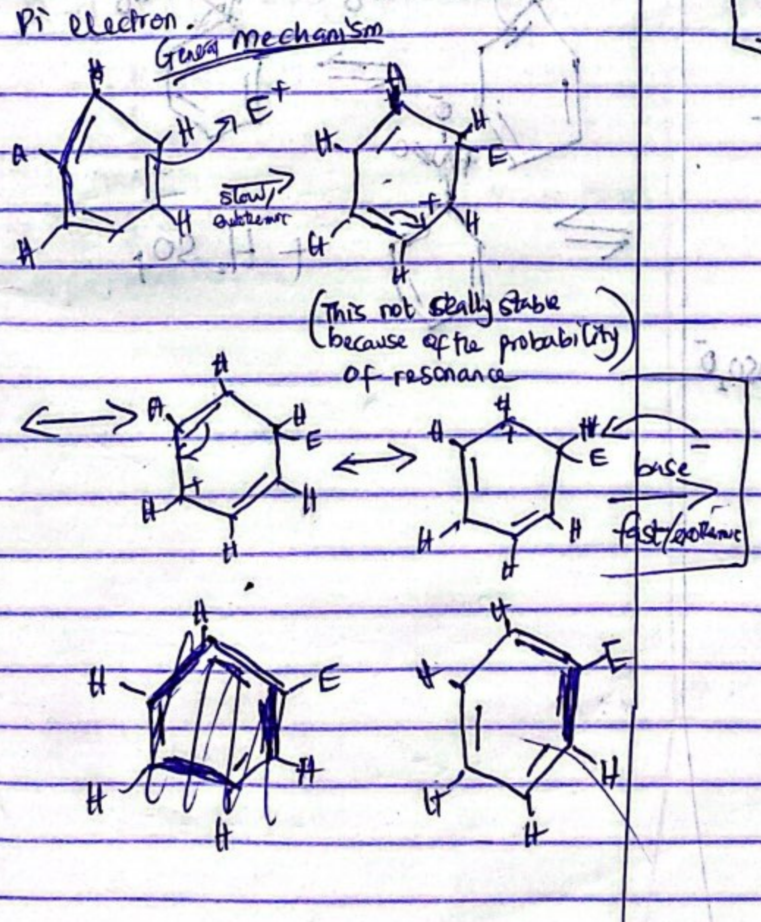
3phenyl prop-2-enal

Cinnamaldehyde

Reactions of Benzene

(1) Electrophilic substitution reaction: Benzene is as nucleophile, having 6 pi electron.

General mechanism



4 hydroxy 3 ne

Halogenation

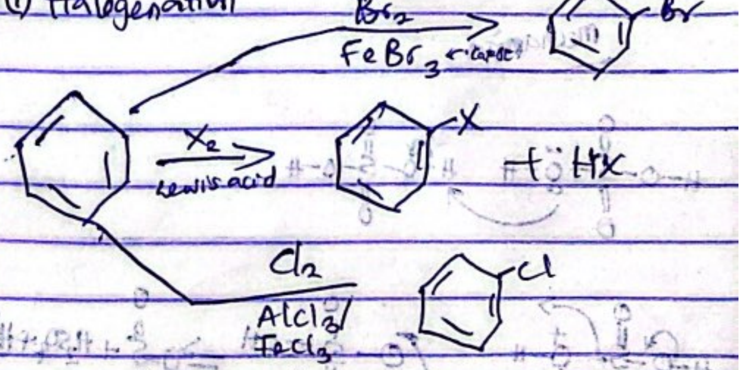
Alkylation (friedel-crafts)

Acylation (friedel-crafts)

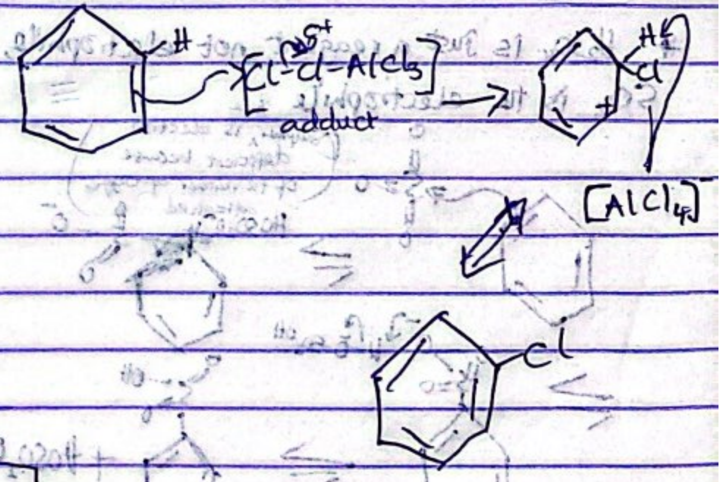
Nitration

Sulphonation

(1) Halogenation

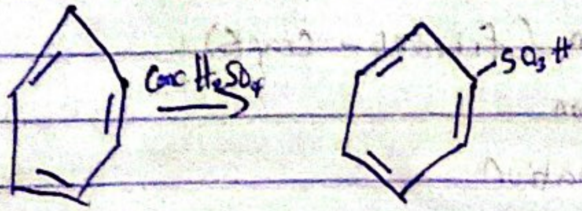


Mechanism:



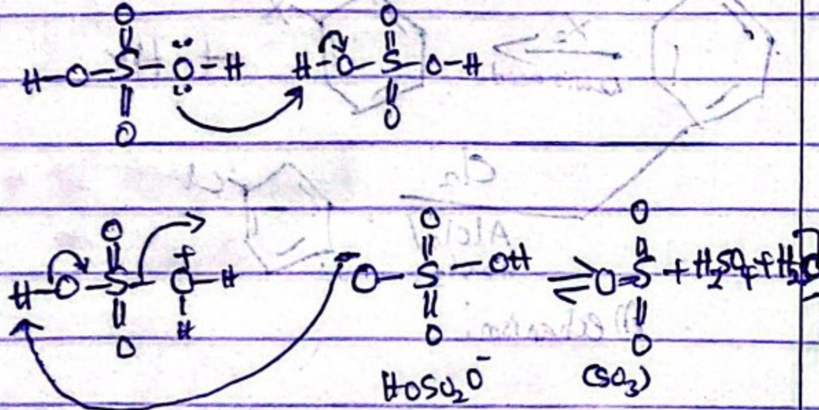
Class
26th April, 2024

② Sulphonation

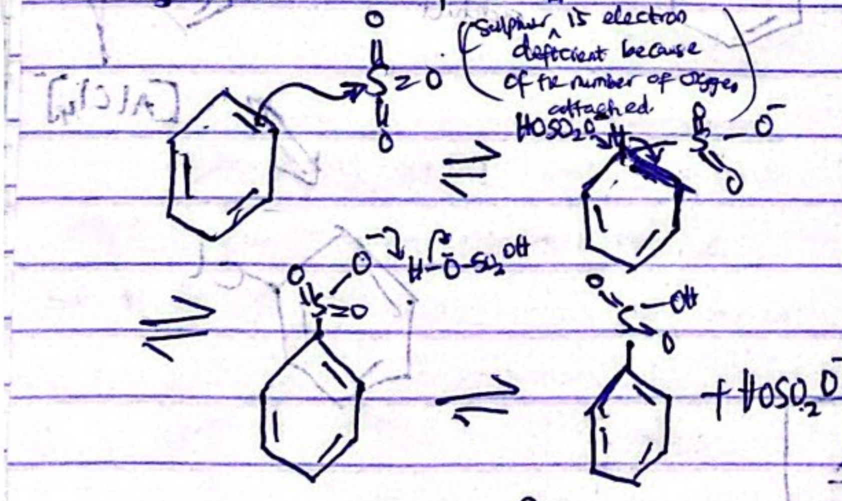


Benzene Sulfonic acid

mechanism



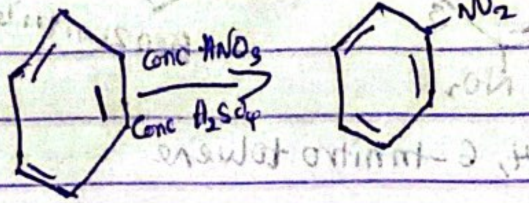
* H_2SO_4 is just a reagent not electrophile, SO_3 is the electrophile here



(sulphur here is electron deficient because of the number of oxygen attached)

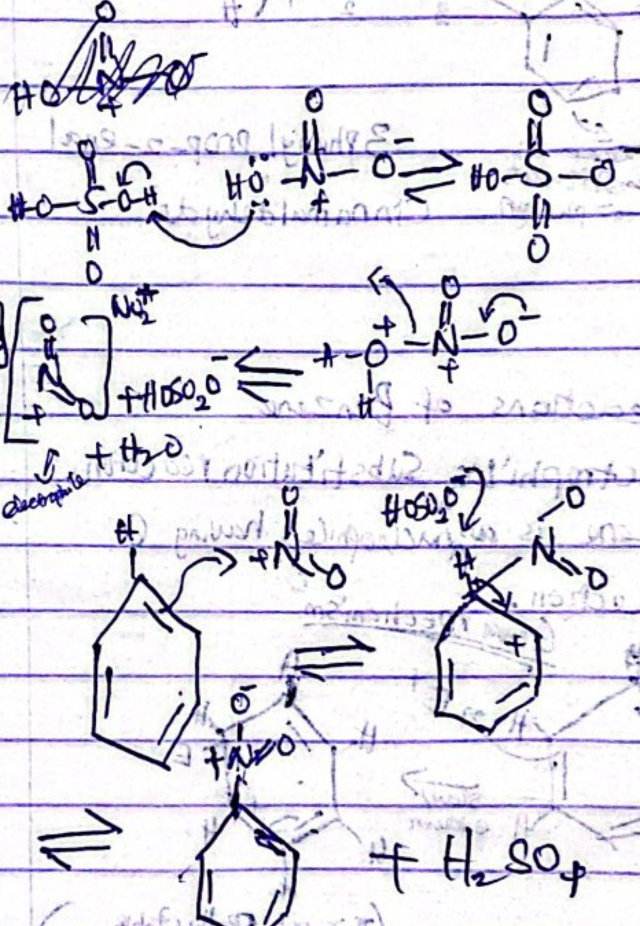
Benzene sulfonic acid

③ Nitration



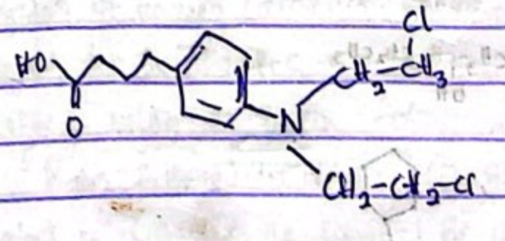
Mechanism

HNO_3 and H_2SO_4 here are just reagent



C_{on}

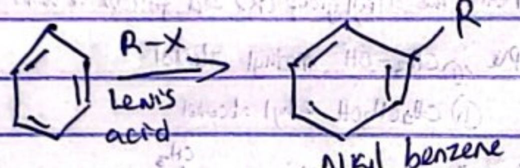
Why organic Chemistry is important



Chlorambucil

used in cancer patients. It undergoes SN2 reaction with the DNA/purine.

(ii) Friedal-crafts Alkylation



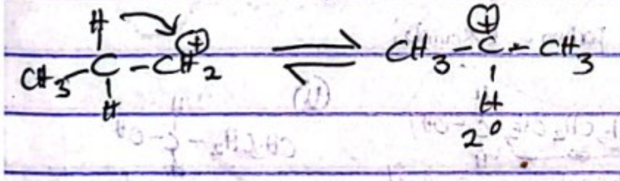
mechanic

$R-Cl + AlCl_3 \rightarrow [R-\overset{\delta+}{Cl}-AlCl_3]$

$\rightarrow \underset{\text{Carbocation/ electrophile}}{R^+} + [AlCl_4]^-$

If $R = CH_3$ or CH_3CH_2, it will not form a carbocation, it will be unstable

* An hydride shift



$CH_3-\overset{H}{\underset{H}{C}}-\overset{+}{C}H_2 \rightleftharpoons CH_3-\overset{+}{\underset{H}{C}}-CH_3$

2°

29th April 2024

Hydroxyl Compounds

Hydroxyl compounds are compounds with one or more hydroxyl functional groups (-OH) attached to a saturated carbon atom.

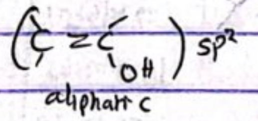
The Saturated carbon atom or a simple alkyl group

Alkanols (Alcohols)

Alkanol are hydroxyl compounds of general formular of R-OH. The -OH group is attached or bonded to a saturated carbon atom (sp³)

$-\overset{|}{\underset{|}{C}}-OH$ ~~so~~ sp^3

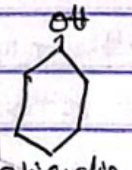
While there are some in which OH will attach to sp^2 hydridized carbon. carbon in which their OH group is attached to vinylic sp^2 is called "enol" while those in which the -OH is bonded to a benzene ring are referred to as phenols



$(\overset{|}{C}=\underset{OH}{C})\ sp^2$

aliphatic c

phenol

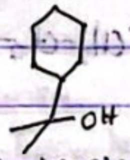


alicyclic (cyclohexanol)

However enols and phenols behave differently from alcohols

Classification

Alkanols are classified into 3 on the basis of which the OH group is bonded or attached to.

	Class	Gen. Formular	Functional group	Examples
must have 2 hydrogen	1°	$R-CH_2-OH$	$-CH_2OH$	$H-CH_2-OH$, CH_3CH_2OH
must have two hydrogen and 2 alkyl group	2°	$R-\underset{OH}{CH}-R'$	$-\underset{OH}{CH}-$	$CH_3\underset{OH}{CH}-CH_3$, $CH_3-\underset{OH}{CH}-CH_2CH_3$
No hydrogen, 3 alkyl group	3°	$R-\underset{OH}{\overset{R'}{C}}-R''$	$\rangle C-OH$	$CH_3-\underset{OH}{\overset{CH_3}{C}}-CH_3$,  α-terpineol

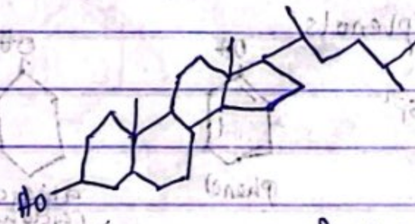
Alcohols can be further classified on the basis of the number of hydroxyl groups per molecule or attached to different carbon atoms:

(1) Monohydric: contain only one -OH per molecule

(2) Dihydric: contains two -OH per molecule. The Simplest form is Ethane-1-2-diol. (glycol) ← common name

$$\begin{matrix} CH_2-OH \\ | \\ CH_2\ OH \end{matrix}$$

Example of 2°



Cholesterol 2° alcohol

(3) Trihydric; contains 3-OH per molecule

Example: Propan-1,2,3-triol (glycerol)

$$\begin{matrix} {}_1CH_2-OH \\ {}_2CH_2-OH \\ {}_3CH_2-OH \end{matrix}$$

(4) Polyhydric: More than 3 or many -OH per molecule

Nomenclature

There are three important system used in name alcohols:

(1) Use of common names (systems) or functional class syst

This is good for simple alkanols

How? Name, the alkyl group (R) and follow the word alcohol

Example; (i) CH_3-OH methyl alcohol

(ii) CH_3CH_2OH ethyl alcohol

(iii) $CH_3-\underset{CH_3}{CH}-OH$ iso propyl alcohol

(v) $CH_3-\overset{CH_3}{C}-CH_3$ tet-butyl alcohol (t-butyl alcohol)

(iv) $CH_3-\overset{OH}{CH}-CH_2CH_2CH_2CH_3$. methyl pentyl alcohol

(2) CARBINOL SYSTEM ~~Carbinol system~~; This system of naming alcohol considers all alcohols to have been derived from methyl alcohol by the replacement of one or more hydrogen atom by other groups: RULES:

(1) Name the group(s) attached to the carbon bearing the OH group and then add the suffix carbinol to depict the C-OH portion. Example:

(i) $\underbrace{CH_3CH_2CH_2}_{\text{propyl}}-\underbrace{\underset{H}{\overset{H}{C}}-OH}_{\text{carbinol}}$

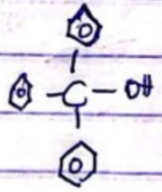
propyl carbinol

(ii) $CH_3CH_2-\underset{H}{\overset{H}{C}}-OH$

ethyl carbinol

(iii) $CH_3CH_2-\underset{CH_2CH_3}{\overset{H}{C}}-OH$

diethyl carbinol

(iv) 

Triphenyl carbinol

30th April, 2024

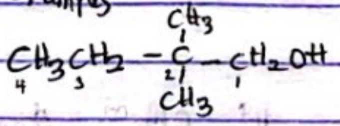
(3) IUPAC SYSTEM: This is the most versatile system of naming alcohols. Simple alcohols are named by the IUPAC as derivatives of parent alkane using the suffix -ol.

Rules Followed in Naming Using IUPAC

1) Select or consider the longest, or continuous carbon chain containing the -OH group in deriving the parent name

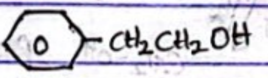
2) Number the alkane chain, beginning and the end nearer the -OH group so as to give carbon atom to which the -OH functional group is attached the lowest possible numbers.

Examples

(1) 

$\overset{4}{C}H_3\overset{3}{C}H_2-\underset{CH_3}{\overset{CH_3}{\overset{2}{C}}}-\overset{1}{C}H_2OH$

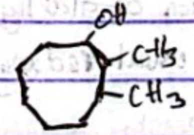
2, 2-dimethyl butanol

② 

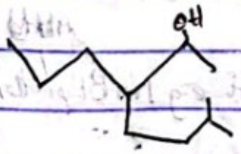
2 phenyl ethanol

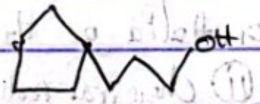
③ 

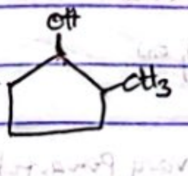
cyclopropanol

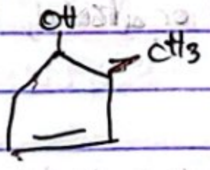
④  2,3-dimethylcyclooctanol

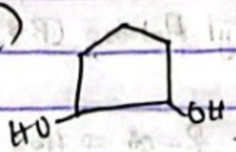
Questions

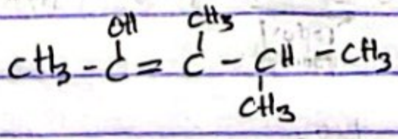
(1) 

(3) 

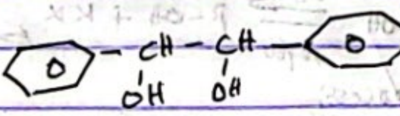
② 

(4) 

⑤ 

⑥ 

$CH_3-\overset{OH}{C}=\overset{CH_3}{C}-\underset{CH_3}{CH}-CH_3$

⑦ 

Physical Properties of Alkanols:

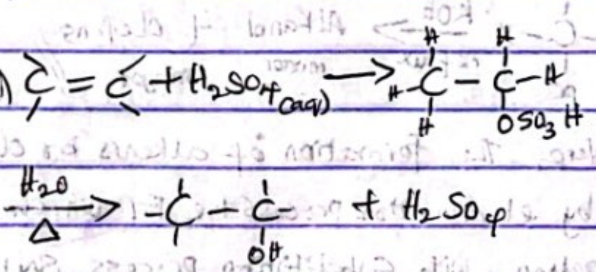
(1) Alkanols have high boiling points at room temperature

(2) They are miscible or soluble in water

All these physical properties can be explained in terms of intermolecular hydrogen bond

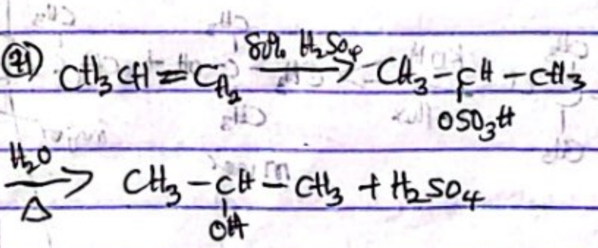
(3) Preparations of Alkanols

(1) Hydration of Olefins/Alkenes: This involves treatment of olefins or alkenes with cold H_2SO_4 followed by addition of water and heat.

(i) 

$>C=C< + H_2SO_{4(aq)} \longrightarrow H-\underset{H}{\overset{H}{C}}-\underset{OSO_3H}{\overset{H}{C}}-H$

$\xrightarrow[\Delta]{H_2O} -\overset{|}{\underset{|}{C}}-\underset{OH}{\overset{|}{C}}- + H_2SO_4$

(ii) 

$CH_3CH=CH_2 \xrightarrow{80\%\ H_2SO_4} CH_3-\underset{OSO_3H}{CH}-CH_3$

$\xrightarrow[\Delta]{H_2O} CH_3-\underset{OH}{CH}-CH_3 + H_2SO_4$

② Hydrolysis of Alkyl Halides (R-x) by SN

$$R-X + H_2O \underset{\text{reflux/ hydrolysis}}{\overset{Ag_2O}{\rightleftharpoons}} R-OH + HX$$

OR

$$R-X + KOH \underset{\text{reflux}}{\overset{H_2O}{\rightleftharpoons}} R-OH + KX$$ ← two steps are involved

Process:

① $R-X + \cancel{KH_2O} \rightleftharpoons R-OH + HX$

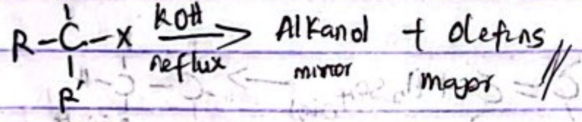
(ii) $\cancel{H}X + KOH \rightleftharpoons KX + H_2O$

Mechanism of Hydrolysis

The mechanism of alkaline hydrolysis can be SN1 or SN2

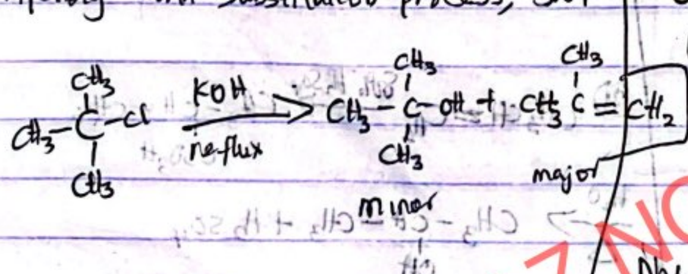
$$R-X \quad \overset{SN_1 \text{ increases}}{\underset{SN_2 \text{ increases}}{1^\circ, 2^\circ, 3^\circ}}$$

For tertiary alkyl halides, mixtures are often, mixtures are often found with the major product being alkenes



$$R-\overset{R''}{\underset{R'}{C}}-X \xrightarrow[\text{reflux}]{KOH} \underset{\text{minor}}{\text{Alkanol}} + \underset{\text{major}}{\text{olefins}}$$

Here, the formation of alkenes or olefins is by elimination process i.e E1 which is competing with substitution process, SN1

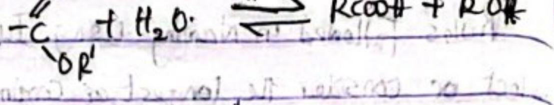


$$CH_3-\overset{CH_3}{\underset{CH_3}{C}}-Cl \xrightarrow[\text{reflux}]{KOH} \underset{\text{minor}}{CH_3-\overset{CH_3}{\underset{CH_3}{C}}-OH} + \underset{\text{major}}{\boxed{CH_3\overset{CH_3}{C}=CH_2}}$$

③ Hydrolysis of Esters:

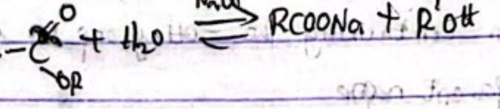
This hydrolysis can be acid catalyzed or alkaline catalyzed

(i)



$$R-\overset{O}{\underset{OR'}{C}} + H_2O \overset{H^+}{\rightleftharpoons} RCOOH + R'OH$$

(ii)



$$R-\overset{O}{\underset{OR}{C}} + H_2O \overset{NaOH}{\rightleftharpoons} RCOONa + R'OH$$

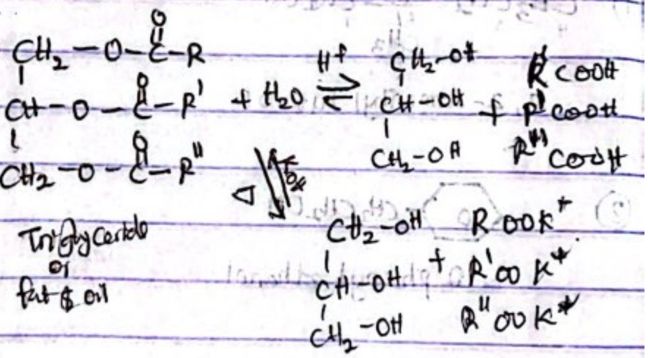
This also involves two steps

① $RCOOR + H_2O \rightleftharpoons RCOOH + R'OH$

② $RCOOH + NaOH \rightleftharpoons RCOONa + H_2O$

$\Rightarrow RCOOR + NaOH \rightleftharpoons RCOONa + R'OH$

Example



Triglyceride or fat & oil

$$\begin{matrix} CH_2-O-\overset{O}{C}-R \\ CH-O-\overset{O}{C}-R' \\ CH_2-O-\overset{O}{C}-R'' \end{matrix} + H_2O \overset{H^+}{\rightleftharpoons} \begin{matrix} CH_2-OH \\ CH-OH \\ CH_2-OH \end{matrix} + \begin{matrix} RCOOH \\ R'COOH \\ R''COOH \end{matrix}$$

$$\xrightarrow[\Delta]{KOH} \begin{matrix} CH_2-OH \\ CH-OH \\ CH_2-OH \end{matrix} + \begin{matrix} ROOK^+ \\ R'OOK^+ \\ R''OOK^+ \end{matrix}$$

Reduction of Carbonyl Compounds (Aldehydes and ketones):

The reduction of aldehydes and ketones involves the usual reducing agent such as

① H_2 with catalyst eg H_2/Pt or H_2/Pd or H_2/Ni

(ii) Chemical reducing agent e.g $NaBH_4$/ether or alcohol, $LiAlH_4$/ether

(stable; red: strictly and)

Note that $LiAlH_4$ is a very powerful reducing agent. It reduces $-CHO$ (aldehyde), $\overset{R}{\underset{R'}{>}}C=O$ (ketone),

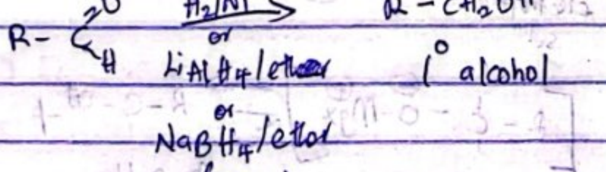
$RCOOR'$ and $\overset{|}{C}=\overset{|}{C}$.
ester — olefines

However, $NaBH_4$ is a milder than $LiAlH_4$ reduces $-CHO$ (aldehyde), $R_2C=O$ (ketone), but no effect on $ROOR'$ (ester) as well as $C=C$ (olefins)

2nd May, 2020

* ALDEHYDES:

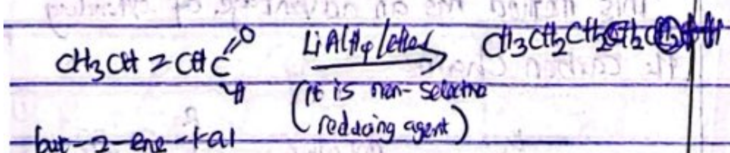
On reduction



$$R-\overset{O}{\overset{\|}{C}}-H \xrightarrow[\text{or } LiAlH_4/\text{ether} \text{ or } NaBH_4/\text{ether (methanol)}]{H_2/Ni} R-CH_2OH$$

1° alcohol

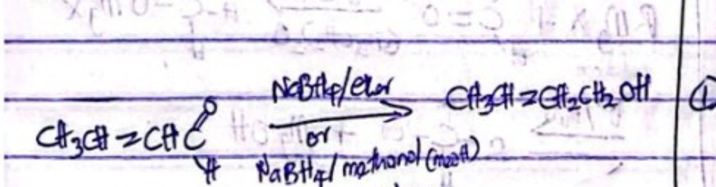
e.g



$$CH_3CH=CHCHO \xrightarrow{LiAlH_4/\text{ether}} CH_3CH_2CH_2CH_2OH$$

but-2-ene-al

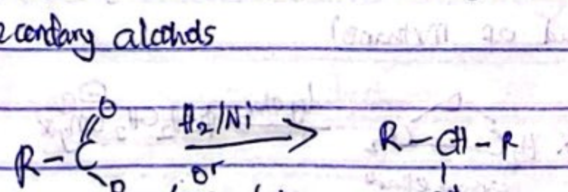
(It is non-selective reducing agent)



$$CH_3CH=CHCHO \xrightarrow[\text{or } NaBH_4/\text{methanol (meoH)}]{NaBH_4/\text{ether}} CH_3CH=CH_2CH_2OH$$

(selective reducing agent)

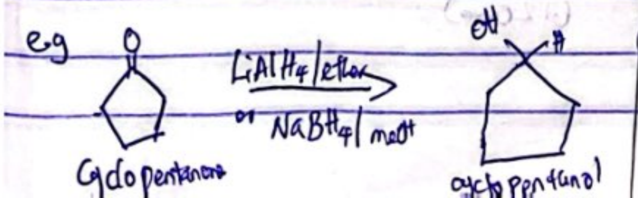
KETONES: Ketones on reduction will yield Secondary alcohols



$$R-\overset{O}{\overset{\|}{C}}-R \xrightarrow[\text{or } LiAlH_4/\text{ether or } NaBH_4/\text{meOH}]{H_2/Ni} R-\underset{OH}{\underset{|}{CH}}-R$$

2° alcohol

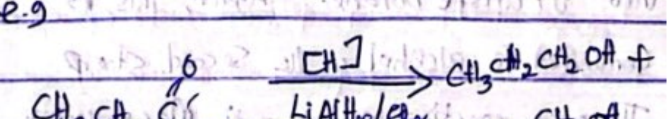
e.g



Esters: Esters will yield two types of alkanols will powerful reducing agents.

If ~~Sodium monohydride~~ $NaBH_4$ (a mild reducing agent is used. No reaction occurs or reduction may be very slow.

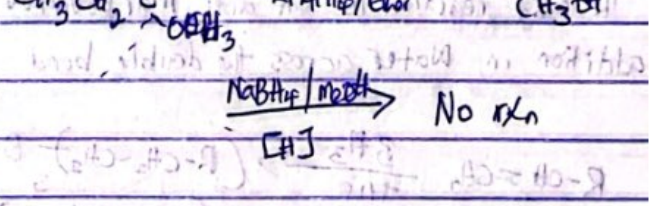
Hence, medium aluminium hydride is used



$$R\overset{O}{\overset{\|}{C}}OR' \xrightarrow[[H^+]]{LiAlH_4/\text{ether}} R-CH_2OH + R'-OH$$

Note that one of the products must be a primary alcohol, while the others depends on the nature of the R'

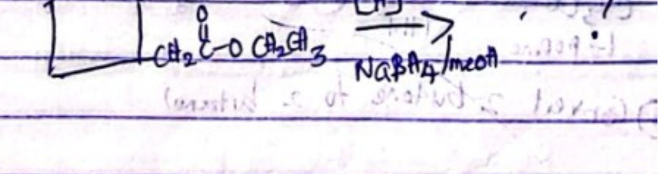
e.g

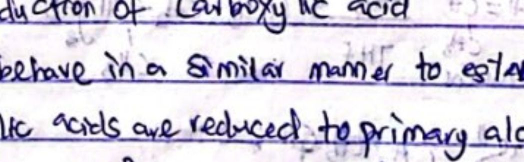


$$CH_3CH_2\overset{O}{\overset{\|}{C}}OCH_3 \xrightarrow[LiAlH_4/\text{ether}]{[H]} CH_3CH_2CH_2OH + CH_3OH$$

$$\xrightarrow[[H]]{NaBH_4/\text{meOH}} \text{No rxn}$$

Exercise

① 

(ii) 

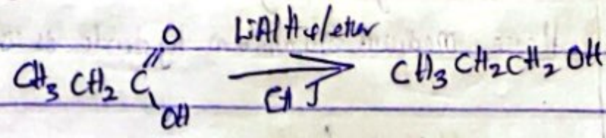
⑥ Reduction of Carboxylic acid

The behave in a similar manner to esters. Carboxylic acids are reduced to primary alcohols (a single product) with $LiAlH_4$ (in ether while there is no reaction $NaBH_4$ / in meOH

$$RCOOH \xrightarrow[LiAlH_4/ether]{[H]} RCH_2OH$$ (a single Product)

$$\xrightarrow[NaBH_4/MeOH]{[H]} \text{no rxn}$$

e.g



[illegible]

⑦ Hydroboration: This reaction is also used to convert alkene to alcohols.

It is a two step reaction process, in that the first step is conversion of alkene into trialkyle borane. Again, this is converted to alcohol in the second step

The next reaction is an anti Markovnikov addition in water across the double bond

$$R-CH=CH_2 \xrightarrow[THF]{BH_3} (R-CH_2-CH_2)_3B$$

(tetrahydrofuran, a solvent) (Trialkyl borane)

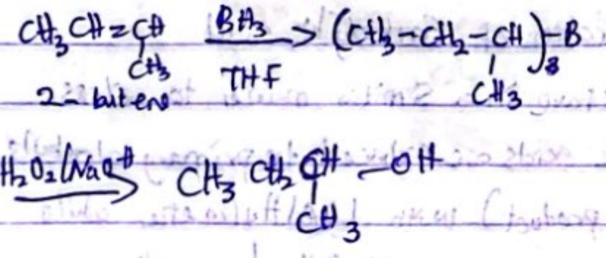
$$\xrightarrow{H_2O_2/NaOH} R-CH_2-CH_2-OH$$

alcohol

① Convert 1 propene to 1 propanol

$$\underset{\text{1-propene}}{CH_3CH=CH_2} \xrightarrow[THF]{BH_3} (CH_3CH_2CH_2)_3B \xrightarrow{H_2O_2/NaOH} CH_3CH_2CH_2-OH$$

② Convert 2 butene to 2 butanol

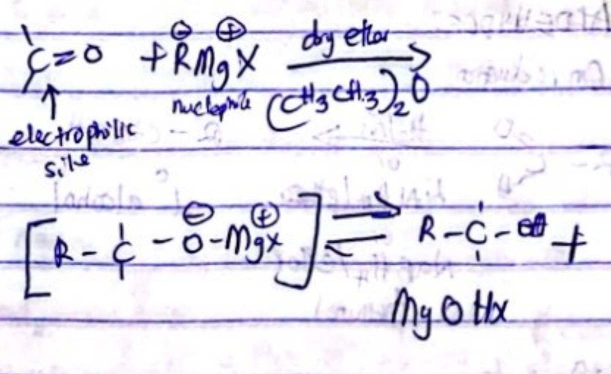


⑧

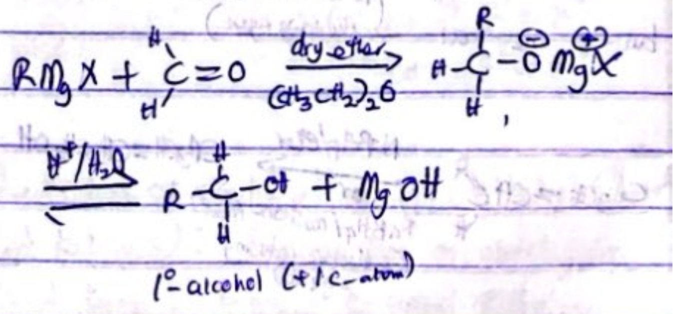
<u>Preparation of Alcohol From Grignard Reagent</u>: Grignard reagent is used in the synthesis in the preparation of all the three type of alcohols (1°, 2°, 3°)

The grignard reagent (RMgX) are reacted with carbonyl compound (aldehydes and ketones), esters, epoxide to for intermediate which are further hydrolyzed to alkanols

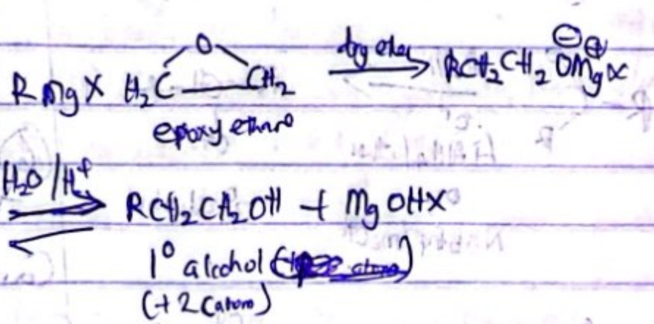
⑪ With aldehydes & ketones

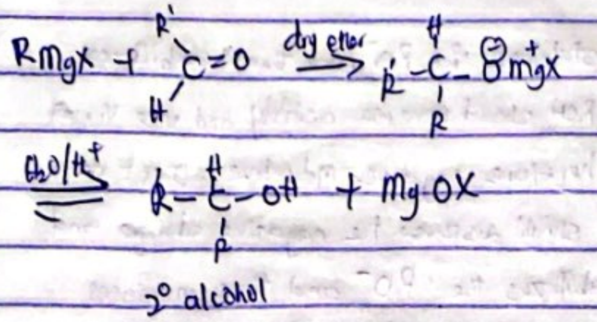


This method has an advantage of extending the carbon chain



Epoxy ethane (ethylene oxide) may be used instead of methanol





2° alcohol

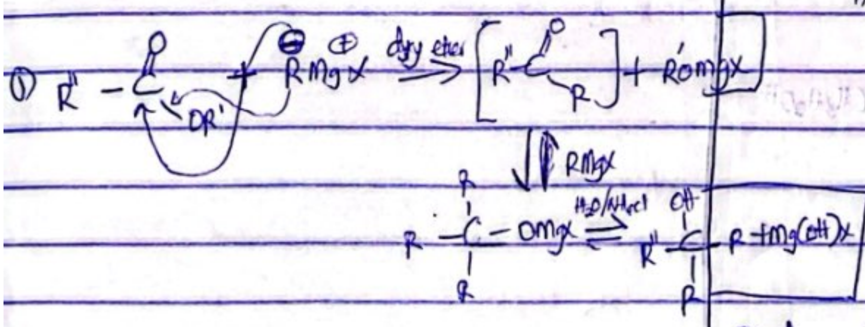
3rd May, 2024

In the preparation of tertiary alcohol, aqueous NH_4Cl is used for hydrolysis as dilute acid brings about dehydration (i.e H_2O/H^+) of the alcohol to alkene

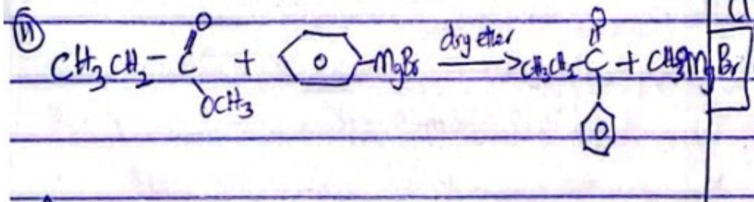
② With Esters

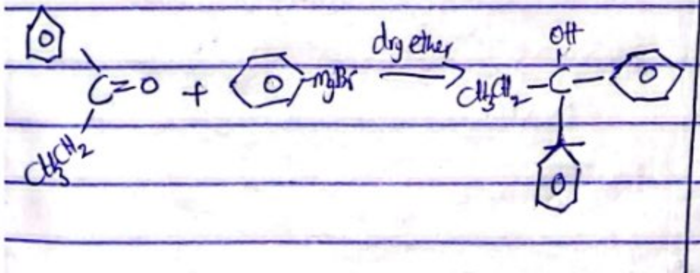
The reaction of grignard reagent and esters gives tertiary alcohol as the product. It is a two step reaction. The first step, gives ketone.

(i)

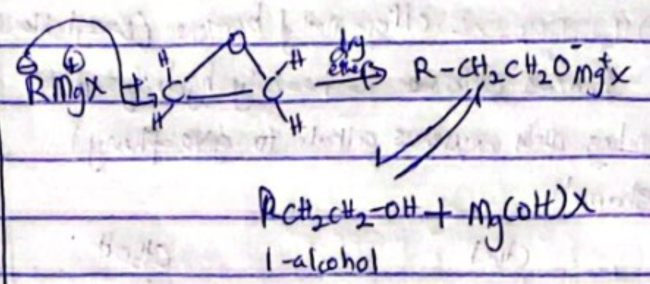


(ii)





With Epoxide: The reaction of grignard reagent and epoxide gives a primary alkanol with two carbon atoms added



1-alcohol

How do you prepare propanol from a named grignard reagent

In Summary:

Grignard Reagent + Methanal → 1° alcohol

" + other aldehyde → 2° alcohol

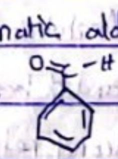
" + Ketone → 3° alcohol

" + esters → ketone → 3° alcohol

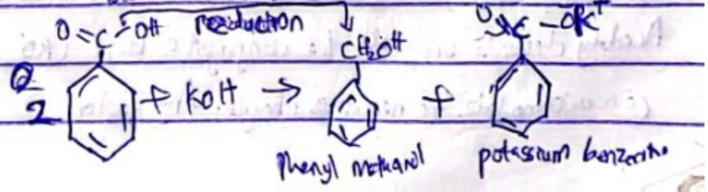
" epoxide → 1° alcohol

Preparation of Aromatic Alcohol

(1) Aromatic alcohol can be prepared by Cannizaro rxn. Aromatic aldehyde, such as benzaldehyde,



when shaken with aqueous KOH, it undergoes simultaneous oxidation and reduction (disproportionation reaction) yielding the potassium salt of the corresponding carboxylic acid together with the aromatic alcohol



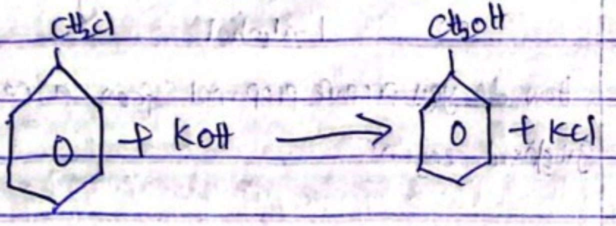
Phenyl methanol

potassium benzoate

The potassium salt is dissolved in water and the alcohol is extracted with ethoxyl ethane (ether) (diethylether) using seperating funnel.

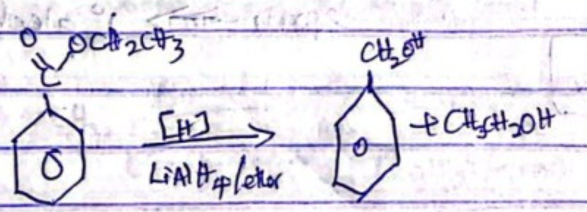
② Hydrolysis of chloromethyl benzene (Benzylchloride)

Benzide chloride is readily hydrolysed on boiling with aqueous alkali to give phenyl ethanol



③ By reduction of Benzene Carboxylate (Benzoate)

Benzenecarboxylic acid (benzoic acid) or ether benzoate can be reduced to the alcohol by using $LiAlH_4$ (reducing agent)



Chemical Reactivies of Alkanol

(1) Alkanols have Amphoteric behaviour. Alkanols can act as an acid and a base

(i) As an acid: An alcohol releases a proton

$$RO\text{-}H \rightleftharpoons \underbrace{RO^-}_{\substack{\text{Conjugate base}\\ \text{alkoxy}}} + H^+$$

acid

Order of acidity: $H_2O > CH_3OH >$ 1° alcohol > 2° alcohol > 3° alcohol

Acidity depends on well the conjugate base (RO^-) can accomodate the negative charge. Any factor that stabilizes the RO^- more than it stabilizes the ROH should increase acidity and vice versa

Therefore negative inductive effect in R should disperse the negative charge and stabilizes the ROH and thus increases acidity. On the other hand, positive inductive effect in R should intensify the negative charge on (RO^-), then stabilizes ~~Therefore~~ the anions (RO^-) and thus decreases acidity

6th may 2024

The acidity of alkanols is shown by their reaction with active metals to liberate H_2 gas and give the metal alkoxides

$$2Na + 2H_2O \rightarrow 2NaOH_{(aq)} + H_2$$

$$2Na + 2R\text{-}OH \rightarrow 2RO^-Na^+ + H_2$$

Example

$$RO\text{-}H + 2\underset{\text{metal}}{M} \rightarrow 2RO^{\ominus}M^{\oplus} + H_{2(g)}$$

Where M is metal

$$2CH_3CH_2OH + 2Na \rightarrow 2CH_3CH_2O^{\ominus}Na^{\oplus} + H_2$$

(ii) As a base. Alkanol accepts a proton using a lone pair of electron on oxygen atom.

$$R\text{-}OH + H^+ \rightarrow R\overset{+}{O}H_2 \rightarrow \text{oxonium}$$

The basicity of alkanol is shown by the reaction of hydrogen halides to give alkyl halides (RX)

$$\overset{\text{base}}{ROH} + \overset{\text{acid}}{HX} \rightarrow RX + H_2O$$

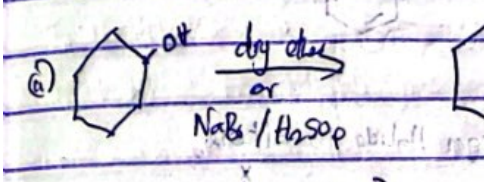
HI reacts most rapidly; while HCl ~~react~~ least rapidly and requires the presence of Zinc chloride for reaction with

* oily
* homogeneous
* layer

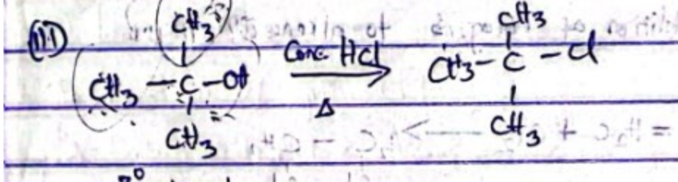
primary and secondary alkanol.

But conc HCl at room temperature is right for tertiary alkanols. This test is called Lucas test for alkanols

(i) $CH_3CH_2CH_2OH + HCl \xrightarrow[\Delta]{ZnCl_2} CH_3CH_2CH_2Cl$

(ii)


$(2NaBr + H_2SO_4 \rightarrow 2HBr + Na_2SO_4)$

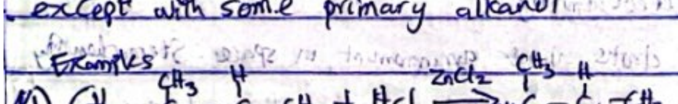
(iii)

$CH_3-\overset{CH_3}{\underset{CH_3}{C}}-OH \xrightarrow[\Delta]{Conc.\ HCl} CH_3-\overset{CH_3}{\underset{CH_3}{C}}-Cl$

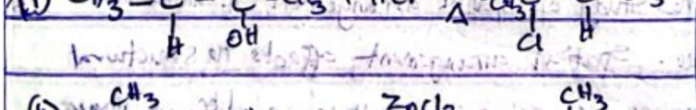
3° alkanol.

Note: (i) The reaction is catalyzed by acid. e.g Conc. H_2SO_4

(ii) Rearrangement of alkyl group may occur except with some primary alkanol

Examples


(1) $CH_3-\overset{CH_3}{\underset{H}{C}}-\overset{H}{\underset{OH}{C}}-CH_3 + HCl \xrightarrow[\Delta]{ZnCl_2} CH_3-\overset{CH_3}{\underset{Cl}{C}}-\overset{H}{\underset{H}{C}}-CH_3$


(ii) $CH_3-\overset{CH_3}{\underset{CH_3}{C}}-CH_3OH + HCl \xrightarrow[\Delta]{ZnCl_2} CH_3-\overset{CH_3}{\underset{Cl}{C}}-CH_2CH_3$

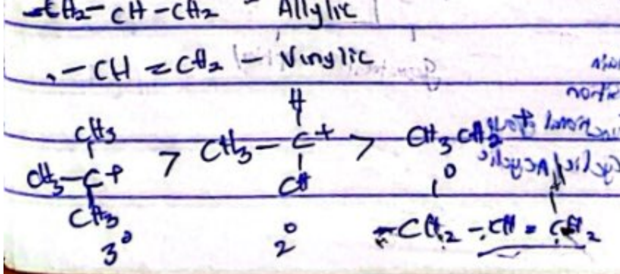
Order of Reactivity of Alkanol toward Hydrogen Halides

(Benzyl, Allyl > 3° > 2°) > 1° > CH₃OH

SN1 SN2

$-CH_2-CH-CH_2$ - Allylic

$-CH=CH_2$ - Vinylic


$CH_3-\overset{CH_3}{\underset{CH_3}{C^+}} > CH_3-\overset{H}{\underset{CH_3}{C^+}} > CH_3CH_2^+$

3° 2° 1°

$-CH_2-CH=CH_2$

Mechanism of Reaction

The mechanism of the reaction between and alkanol and HX is SN1 except for methanol and most primary alkanol where SN2 is preferred.

The SN1 mechanism involves 3 major steps;

(i) protonation of Alkanol to for oxonium ion (H_3O^+)

(ii) Dissociation of the protonated Alkanol into water and a carbocation

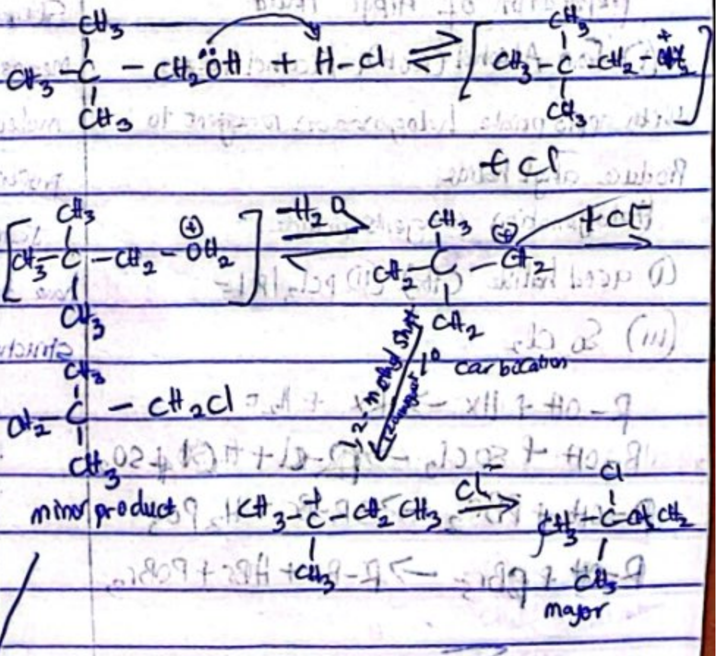
(iii) Combination of the carbocation or rearranged carbocation with halide ion (X^-) to form the alkyl halide

(i) $R\ddot{O}H + H-X \longrightarrow R\overset{+}{O}H_2 + X^-$

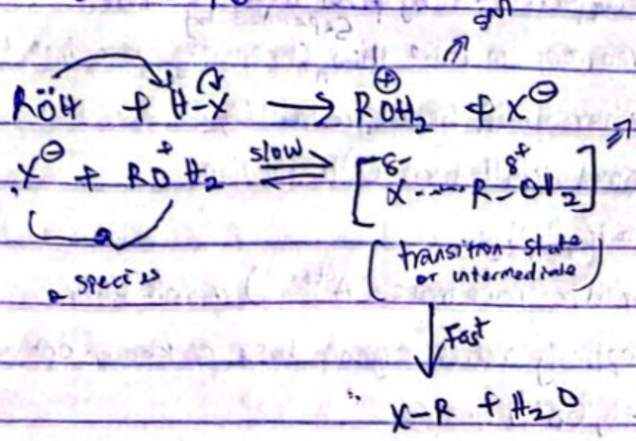
(ii) $R-\overset{\oplus}{O}H_2 \underset{}{\overset{slow}{\rightleftharpoons}} R^+ + H_2O$

(iii) $R^+ + X^- \xrightarrow{fast} RX$

The slow one is the rate determining step consisting of only one molecule i.e $R-\overset{+}{O}H_2$, therefore it is SN1 (unimolecular)



For most primary alcohol and methanol the formation of primary carbocation is very slow because of the poor accomodation of positive charges, Hence bimolecular attack is unhindered i.e SN2 is fast



$$R\ddot{O}H + H{-}X \longrightarrow R\overset{\oplus}{O}H_2 + X^{\ominus}$$

$$X^{\ominus} + R\overset{+}{O}H_2 \underset{}{\overset{slow}{\rightleftharpoons}} \left[\overset{\delta-}{X}\cdots R{-}\overset{\delta+}{O}H_2\right] \xrightarrow{Fast} X{-}R + H_2O$$

2 species in the slow step showing that the the mechanism is bimolecular.

7th May, 2024

Alkanol can also be converted to alkyl halides by reaction with thionyl chloride ($SOCl_2$) or phosphorus pentachloride (PCl_5) or PCl_3

$ROH + SOCl_2 \longrightarrow RCl + HCl_{(g)} + SO_{2(g)}$

$ROH + PCl_5 \longrightarrow RCl + HCl_{(g)} + POCl_3$

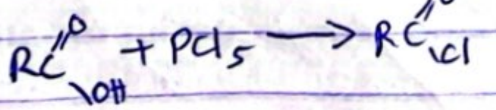
steamy white fume

$3ROH + PX_3 \longrightarrow R{-}X + P(OH)_3$

any of halide except flurine

The advantage of the ~~first~~ third reaction over others is that it does not contain contaminant as gases.

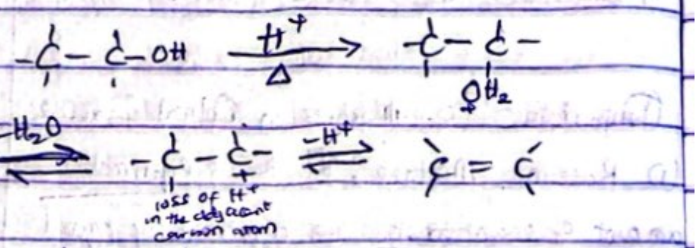
The steamy white fumes with PCl_5 ~~Contains~~ indicates presence of OH group in a compound, especially alkanols and alkanoic acid



$$RC\overset{O}{\underset{OH}{}} + PCl_5 \longrightarrow RC\overset{O}{\underset{Cl}{}}$$

② Dehydration of Alkanols : ~~[illegible]~~ It gives alkenes, if there is a total dehydration or alkoxyalkanes if there is partial dehydration

The common reagent for dehydration is conc. H_2SO_4 or H_3PO_4 (orthophosphoric acid or phosphoric acid). Also, alumina (Al_2O_2), with heat



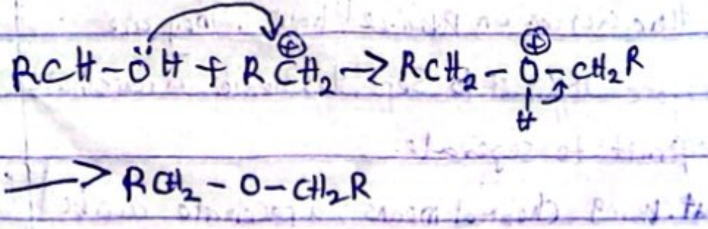
$$-\overset{|}{\underset{|}{C}}-\overset{|}{\underset{|}{C}}-OH \xrightarrow[\Delta]{H^+} -\overset{|}{\underset{|}{C}}-\overset{|}{\underset{\overset{|}{\overset{+}{O}H_2}}{C}}- \underset{}{\overset{-H_2O}{\rightleftharpoons}} -\overset{|}{\underset{|}{C}}-\overset{|}{\underset{+}{C}}- \overset{-H^+}{\rightleftharpoons} \rangle C=C\langle$$

* Order of dehydration

$3° > 2° > 1° > CH_3OH$

The reaction in the absence of a nucleophile (excess conc. H_2SO_4) gives olefin. The intermediate carbocation may rearrange to a more stable one in form of 1, 2 hydride shift or 1, 2, alkyl shift before losing a proton in the adjacent carbon atom to form olefin

The above carbocation is susceptible to attack by nucleophile, hence if excess alkanol is used, the alkanol may act as the nucleophile because of the excess lone pair of lone pair of electron on the oxygen atom



$$RCH{-}\ddot{O}H + R\overset{\oplus}{C}H_2 \longrightarrow RCH_2{-}\underset{H}{\overset{\oplus}{O}}{-}CH_2R \longrightarrow RCH_2{-}O{-}CH_2R$$

General Reaction

$R-OH + H^+ \longrightarrow R\overset{+}{O}H_2 \xrightarrow{-H_2O}$

$R^{\oplus} \xrightarrow[\text{No excess alkanol}]{-H^+}$ Alkene

with excess alkanol (ROH)

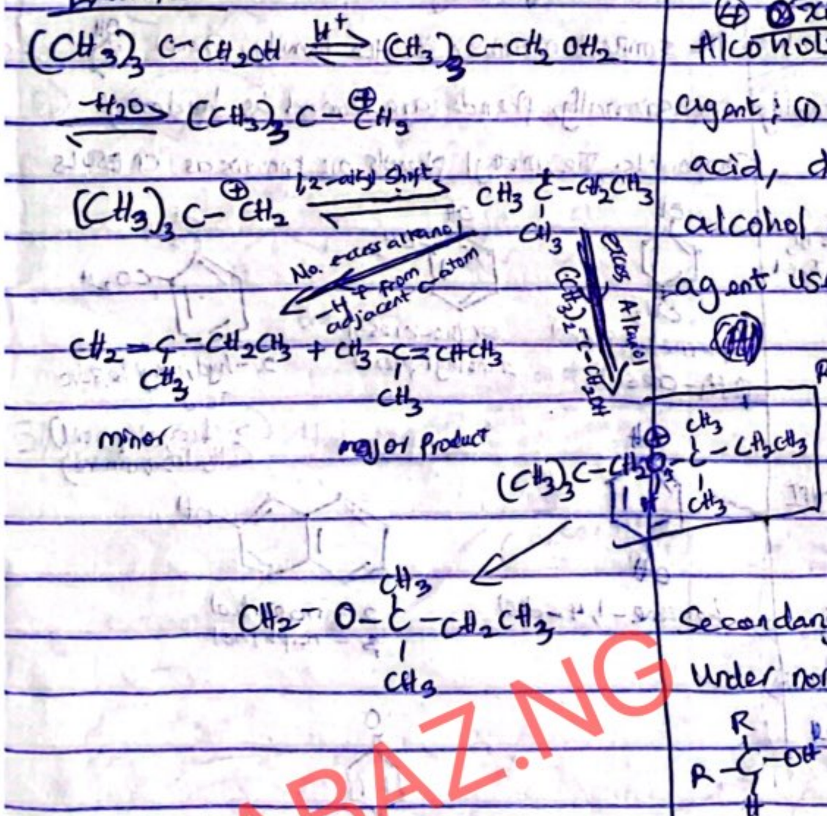
$R-O-R$ (ether)

Depending on the condition of dehydration, alkanols may give two types of product

(i) $ROH \xrightarrow[180^\circ C]{\text{excess Conc. } H_2SO_4}$ Alkene

(ii) $ROH \xrightarrow[145^\circ C]{\text{Conc. } H_2SO_4}$ Alkoxyalkane (ether)

Examples



(3) Formation of Esters (esterification)

Alcohols and carboxylic acid reacts in the presence of mineral acid e.g Conc. H_2SO_4 as a catalyst to give esters

① $R'-OH + R-C\overset{O}{\underset{OH}{\lessgtr}} \xrightarrow[\text{reflax}]{H^+} R-C\overset{O}{\underset{OR}{\lessgtr}} + H_2O$

Alcohol an also react with acid chloride

(ii) $R-C\overset{O}{\underset{Cl}{\lessgtr}} + R'OH \rightleftharpoons R-C\overset{O}{\underset{OR}{\lessgtr}} + HCl$

acid chloride

(iii) $(R-CO)_2O + R'OH \rightleftharpoons R-C\overset{O}{\underset{OR}{\lessgtr}} + RCOOH$

acid anhydride

8th May 2024

(4) Oxidation

Alcohols can be oxidized by various oxidizing agent; (i) Aldehyde (ii) Ketone (iii) carboxylic acid, depending on the nature of the alcohol and the strength of the oxidizing agent used

(i) $R-\underset{H}{\overset{H}{C}}-OH \xrightarrow[PCC]{-[H]} R-C\overset{O}{\underset{H}{\lessgtr}}$

PCC mild oxidizing agent

Jonas reagent strong oxidizing agent

" $\xrightarrow[-[2H]]{K_2Cr_2O_7/H_2SO_4} R-C\overset{O}{\underset{H}{\lessgtr}} \xrightarrow[H^+]{K_2Cr_2O_7} R-C\overset{O}{\underset{OH}{\lessgtr}}$

Secondary alcohol are oxidized to ketone under normal condition

$R-\underset{H}{\overset{R}{C}}-OH \xrightarrow[-[2H]]{K_2Cr_2O_7/H^+} R-\overset{R}{C}=O$

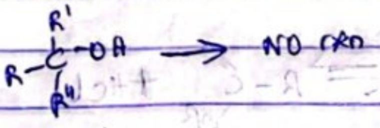
Ketone

$CH_3-\overset{CH_3}{CH}-OH \longrightarrow \underset{CH_3}{\overset{CH_3}{C}}=O \xrightarrow{[O]} CH_3-\underset{O}{\overset{}{C}}-OH + CO_2$

2-hydroxyl propane

The ketone formed has to undergo prolonged and drastic treatment because it can be broken down into acids with smaller number of carbon atoms

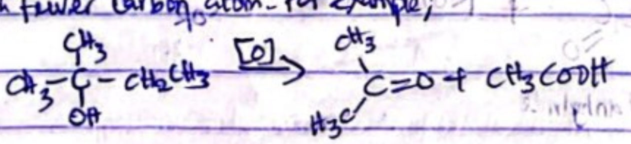
Tertiary alcohols are normally resistant to oxidation, in both neutral and alkaline medium because it will involve the breakage of the high energy C-C bonds in the alcohol



$$R-\overset{R'}{\underset{R''}{C}}-OH \longrightarrow \text{NO rxn}$$

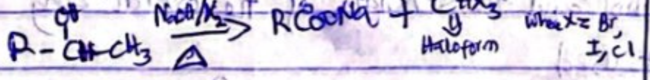
3° alcohol

However, in acidic solutions, tertiary alcohol can be oxidized to give a mixture of ketone and acids, both with fewer carbon atom. For example;



$$CH_3-\overset{CH_3}{\underset{OH}{C}}-CH_2CH_3 \xrightarrow{[O]} \overset{CH_3}{\underset{H_3C}{C}}=O + CH_3COOH$$

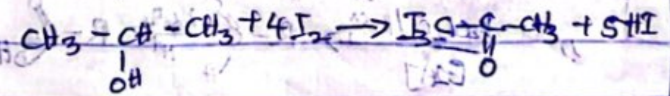
⑤ **Haloform Reaction**: ^expect in test^ Alcohols which contain the group $CH_3\underset{OH}{CH}$ can be oxidized under suitable conditions to CH_3-C^{O}. This group of alcohol will readily undergo haloform reaction.



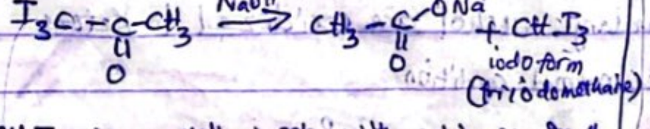
$$R-\overset{OH}{CH}-CH_3 \xrightarrow[\Delta]{NaOH/X_2} RCOONa + \underset{\text{Haloform}}{CHX_3} \quad \text{where } X = Br, I, Cl$$

Note that Flourine cannot be a reagent in haloform reaction

Example



$$CH_3-\underset{OH}{CH}-CH_3 + 4I_2 \longrightarrow I_3C-\underset{O}{\overset{\|}{C}}-CH_3 + 5HI$$



$$I_3C-\underset{O}{\overset{\|}{C}}-CH_3 \xrightarrow{NaOH} CH_3-\underset{O}{\overset{\|}{C}}-O^-Na^+ + \underset{\substack{\text{iodoform} \\ \text{(triiodomethane)}}}{CHI_3}$$

CHI_3 is a yellow ppt with antiseptic smell

The haloform reaction take place in step

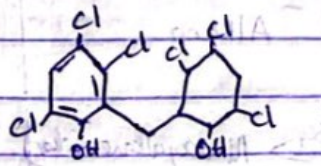
Steps;

① oxidation of the alcohol to an aldehyde or ketone
② Substitution of the halogen atom in the methyl group
③ Hydrolysis under alkaline condition to form the haloform.

Phenol

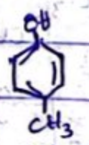
Phenols are hydroxyl compounds with general formular Ar-OH, where Ar is aryl or phenyl group. Phenols, differs from alkanols in having the -OH group directly attached to an aromatic ring. Like alcohols, they may be mono hydric or polyhydric, depending on the number of OH group that they contain.

The chemistry of phenol is very different from that of alcohols. A phenolic compound hexachlorophene is constituent of mouth washes, deodorant soap and medicinal skin cleanser

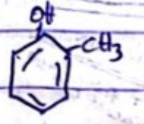


→ Acts on anti-bacteria activities

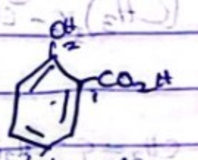
Phenols are generally named as derivatives of the simplest member of the family, Phenol  occasionally, phenols are named as hydroxy compounds. The methyl phenols are known as CRESOLS



4-methyl phenol
para-cresol

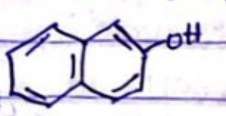


ortho-cresol
2 methyl phenol

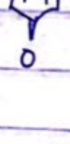


2-hydroxyl benzoic acid
(Salicyclic acid)
(Hydroquinone)

benzene-1,4-diol



2-naphthol
β-naphthol

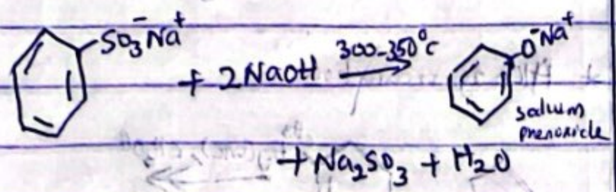


Class

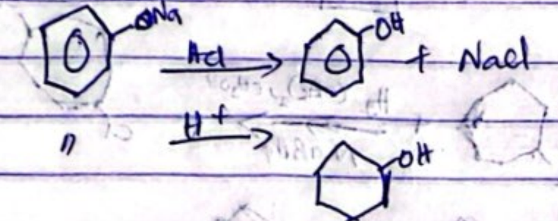
10th May, 2024

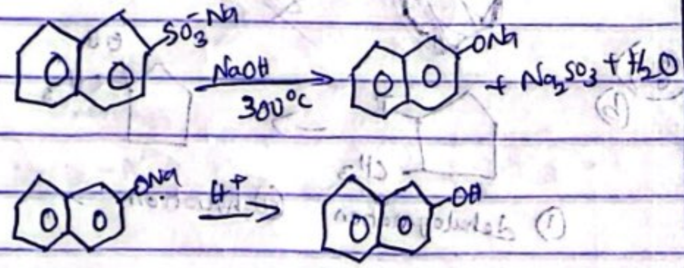
Preparation of Phenol

① By Diffusion of Aromatic sulphonic salt with an alkaline solution e.g NaOH



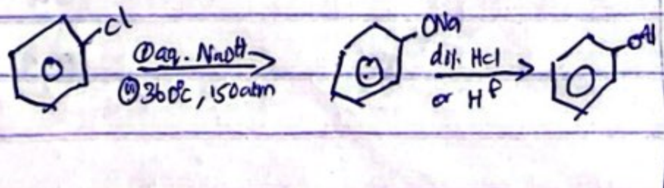
The phenol is obtained as an oily liquid by dissolving sodium phenoxide in acidified water and acidified.



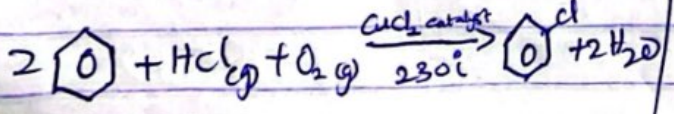


B-nepthol

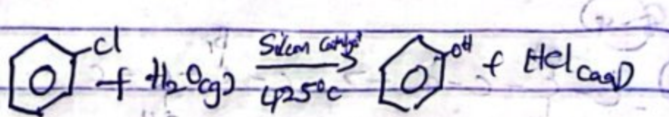
② By hydrolysis of chlorobenzene: Hydrolysis of chlorobenzene by aqueous NaOH at 360°C and 150 atm



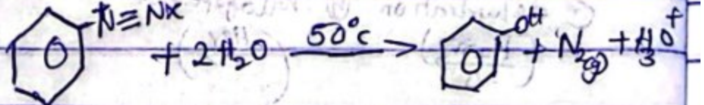
③ By rasching process: Here, benzene is chlorinenated by passing the vapour together with HCl gas and air over a heated $CuCl_2$ catalyst at 230°C



The cholobenzene formed is then catalytically hydrolysed by passing it with steady steam over silicon catalyst at 425°C



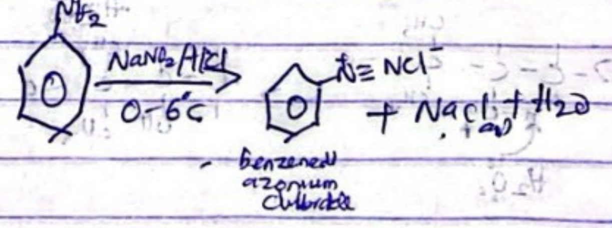
④ By hydrolysis of diazonium salt: In the Lab, heating of solution of benzene diazonium salt on a water bath at 50°C yields phenol



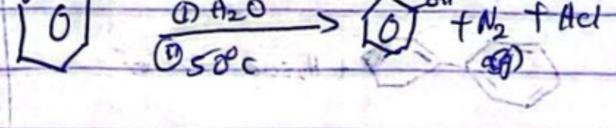
where x = Cl, Br, I.

The phenol is recovered by steam distillation and extracted with ethoxyethane (diethyl ether) using seperating funnel

Primary aromatic amine with cold nitrous acid in the presence of strong mineral acids to give diazonium salt. The process is known as diazotization



Reaction of diazonium salt with water will now give us phenol



Reactions of phenol

The reactions of phenol includes the following:

(i) Acidity of Phenol

(ii) Ether formation (williansm Synthesis)

(iii) Ester formation

(iv) Ring substitution reaction e.g Nitration, sulphonation, halogenation, friedal craft acylation, coupling with diazonium salt, carbonation, formylation.

Acidity of Phenol

Phenols are tremendiously more acidic than alkanol but carboxylic acid

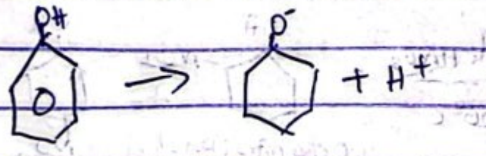
Order of acidity:

RCOOH > phenol > alkanols

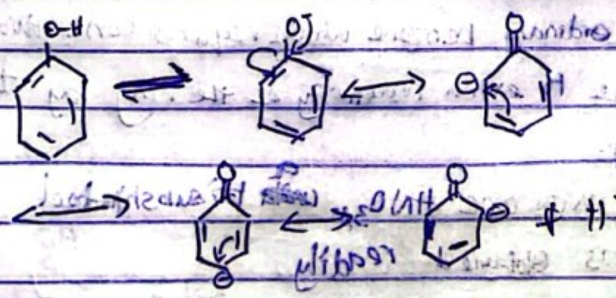
This shows that the OH group attached to an aromatic ring is so more acidic than that attached to an alkyl group

13th May, 2024

Phenol as an acid:



The reason why phenol is more acidic is because of stabilization of phenoxide ion

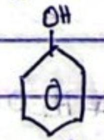


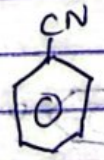
If compared with alcohol, $ROH \rightleftharpoons RO^- + H^+$ (not stabilized)

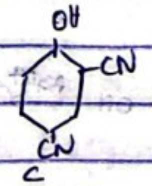
In the resonace stabilization of phenoxide ions, Position 2, 4 and 6 i.e orth and para position are more activated than other position, therefore electrophilic attack of the benzene ring will occur at ortho and para position.

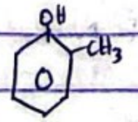
Electron withdrawing group such as CN^-, Cl^- CO, NO_2, attached to ortho and para position stabilizes the phenoxide and thus increase acidity.

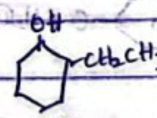
On the hand, electron donating group (R) attached to ortho and para position of phenol destabilizes the Phenoxide ion and therefore decreases acity


A


B


C

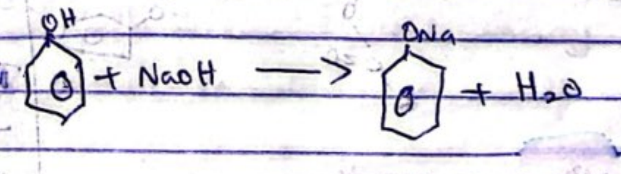

D


E

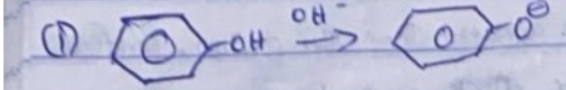
Order of acidity

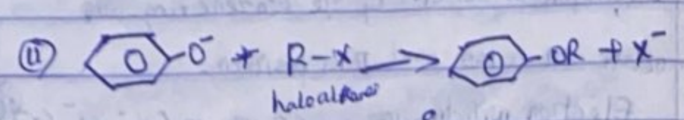
E < D < A < B < C

The acidity of Phenol is demonstrated by its ability to form salts with alkaline bases such as NaOH / KOH



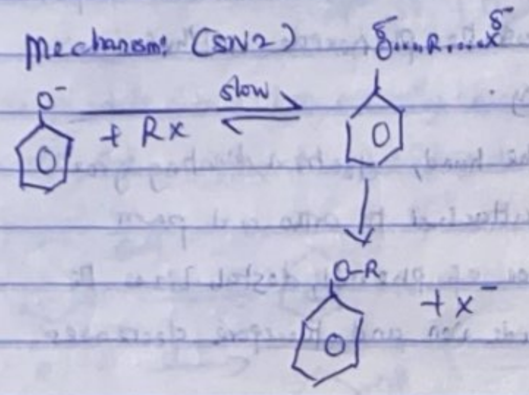
② Williamson's Synthesis (formation of ethers); Phenols in the presence of alkaline base (NaOH/KOH) reacts with haloalcane to form alkoxyethane/ether



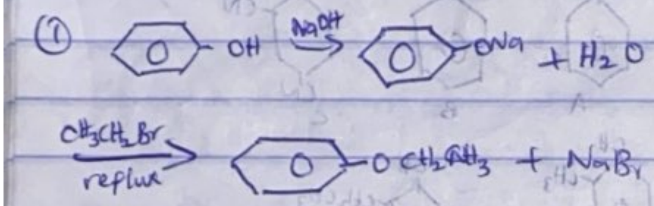


This is an SN2 reaction

Mechanism (SN2)



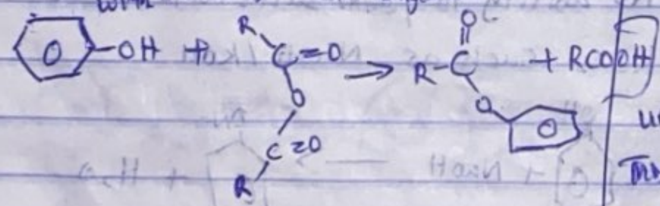
Example



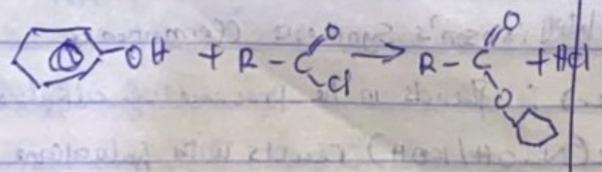
(5) Ester formation

Phenols reacts with carboxylic acid anhydride ($(RCO)_2O$), acetyl chloride $R\overset{O}{\overset{\|}{C}}-Cl$ to form esters

with carboxylic acid anhydride



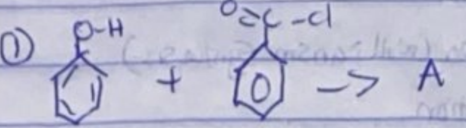
with acetyl chloride

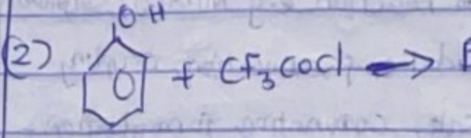


The second reaction is preferable because it does not need separation of products

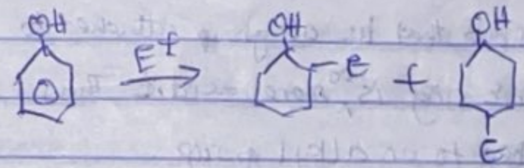
ortho ~~&~~ para position are active in Phenol

as HCl has been eliminated as a gas.

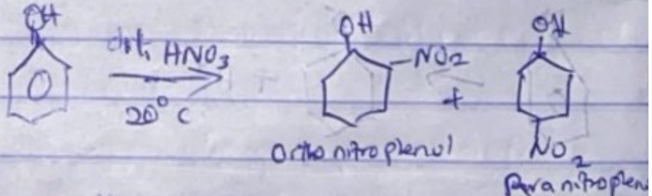




(4) Ring Substitution: The OH group attached to the benzene ring in phenol activate the ring powerfully and direct ortho and para in electrophilic aromatic substitution



(1) Nitration: Monosubstituted compound is obtained with dilute HNO_3 at room temperature

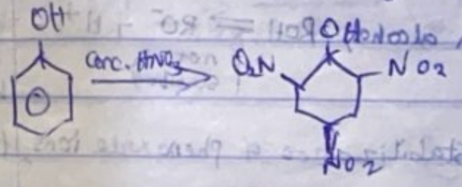


ortho nitrophenol

para nitrophenol

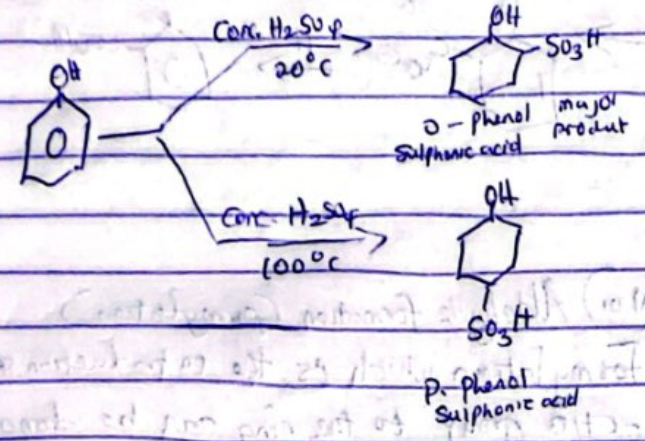
Dilute HNO_3 at 20°C will activate the reaction unlike ordinary benzene which requires conc. HNO_3. This is due to extra reactivity of the ring by the -OH group.

However, with conc HNO_3, ~~with~~ a trisubstituted product is obtained readily



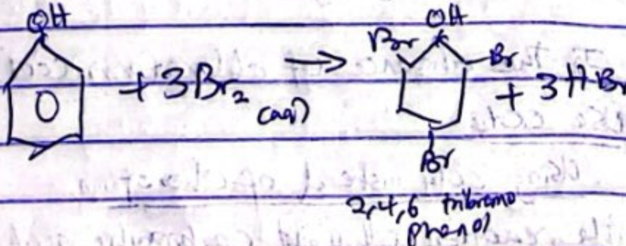
2, 4, 6 trinitrophenol

(ii) Sulphonation: When phenol is treated with conc. H_2SO_4. Different substituted product will be obtained depending on the reaction temperature.

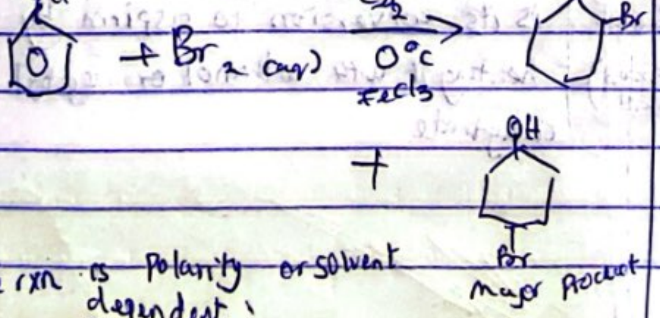


The product is temperature dependent. Raising the temperature of the ortho product to 100°C will yield the para product

(iii) Halogenation: Phenol reacts with aqueous solution of halogens to give polysubstituted product



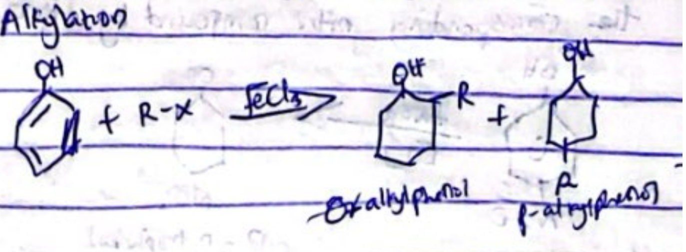
If the reaction is carried out in a solvent of low polarity such as CS_2, CCl_4 and chloroform ($CHCl_3$) the reaction can be limited to monohalogenation



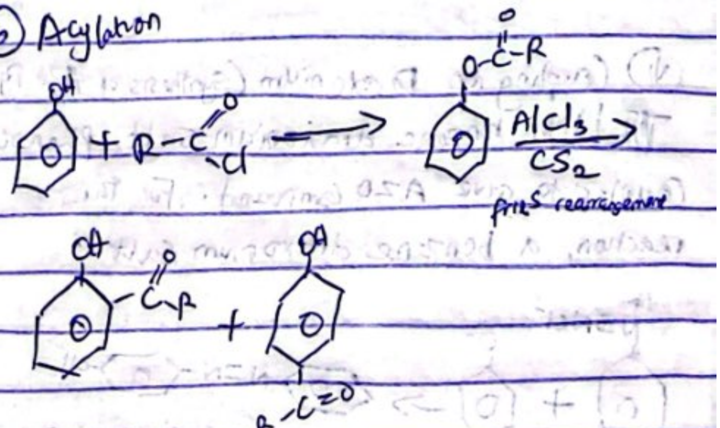
The rxn is Polarity or solvent dependent.

(iv) Friedal - Crafts Alkylation/Acylation

(a) Alkylation



(b) Acylation



Acylation is used for the preparation of phenolic ketones and this preparation occurs by means of fries rearrangement instead of direct substitution on the ring.

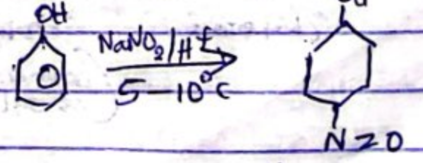
It goes through two steps;

① formation of ~~[illegible]~~ phenyl ester

(ii) migration of the acyl group from the phenolic ~~group to the~~ Oxygen to ortho and para position of the ring.

The rearrangement appears in involve generation of acylium ion $(R-\overset{O}{\overset{\|}{C}}+)$ which then attack the ring, as in ordinary friedal Craft reaction

(v) Nitrosation

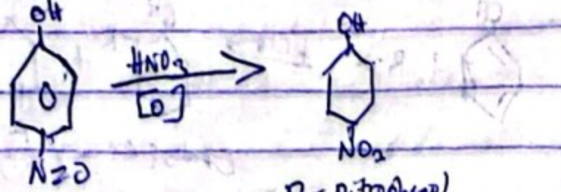


4 - nitrosophenol

The nitroso product is readily oxidized to

Asprin - Acetyl salicylic acid

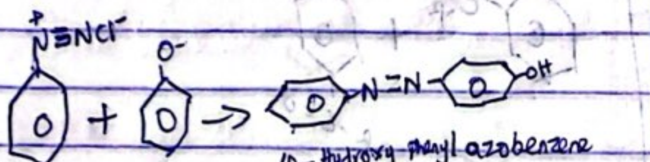
the corresponding nitro compound by HNO_3



p - nitrophenol

(VI) Coupling of Diazonium (Synthesis of Azo Dyes)

~~The~~ With benzene diazonium salt, Phenols couples to give AZO compound. For this reaction, a benzene diazonium salt

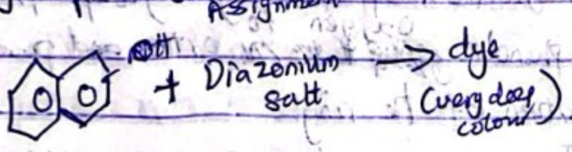


4 - hydroxy phenyl azobenzene (bright yellow precipitate) it is a dye.

Note: In preparation of dye
Any phenol + Diazonium salt → dye

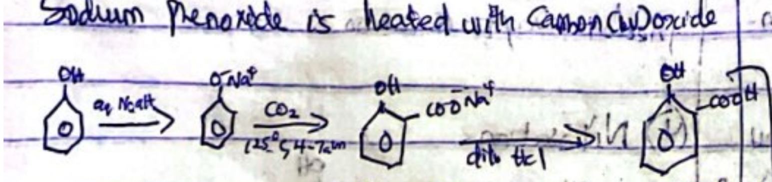
This reaction is very important in dye stuff industry because Azo compounds have very deep colours

Assignment



(VII) Carbonation (Kolbe Schmitt reaction)

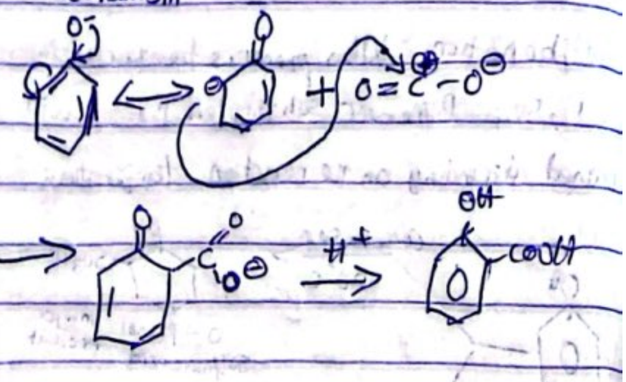
Sodium phenoxide is heated with carbon (IV) oxide



Chief product

2 hydroxyl benzoic acid (Commercially known as salicylic acid)

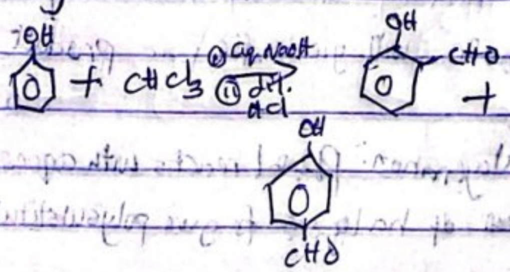
Mechanism



(VIII) Aldehyde formation (Formylation)

Formylation which is the introduction of -CHO group to the ring can be done in two ways

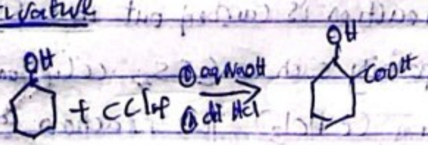
(a) By Reimer Tiemann reaction



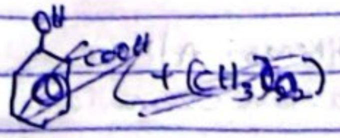
o- hydroxybenzene carbaldehyde

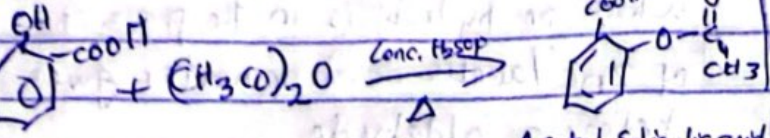
In the absence of chloroform (CCl_4) use CCl_4

Using CCl_4 instead of Chloroform, the reaction will yield carboxylic acid derivative



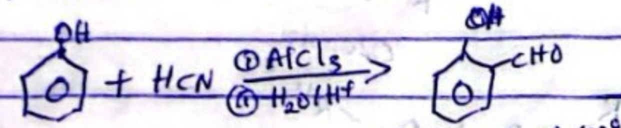
The main use of salicylic acid is its conversion to aspirin by heating it with ethanol or acetyl anhydride





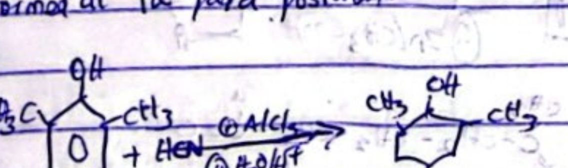
Acetyl Salicylic acid commonly known as aspirine

(b) Gattermann-Koch reaction



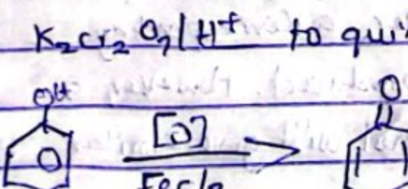
Ortho- almost 100%.

If the ortho position of phenol is blocked by a group, then, formylation may be caused to formed at the para position.



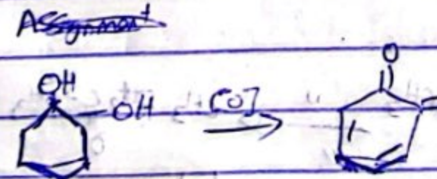
(12) Oxidation

Phenols are easily oxidized by $FeCl_3$ or $K_2Cr_2O_7/H^+$ to quinones



1, 4, benzoquinone

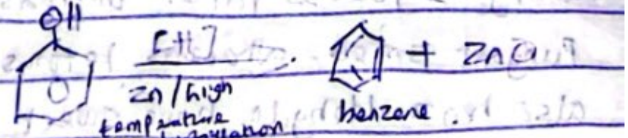
~~Assignment~~



1, 2 benzoquinone

Reduction

Phenols are reduced to the corresponding aromatic hydrocarbon by distilling it at high temperature



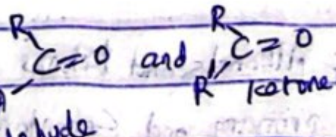
benzene.

16th May, 2020

Carbonyl Compounds

Carbonyl compounds consists of aldehydes and ketones as they both contain $>C=O$ functional group.

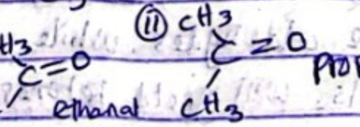
This carbonyl functional group in both aldehyde and ketone are sp^2 hybridized



where R or R' may be alkyl or allyl groups.

Aldehyde

(I) e.g



Propanone (acetone)

(iii)

cyclohexanone

Therefore, they have σ and π pi bond. They are generally very reactive because of the pie bond and the polarization of C=O bond. However, aldehydes are generally more reactive, being more easily oxidized and also more susceptible to nucleophilic addition reaction i.e electrophile

Physical properties of Aldehyde & Ketone

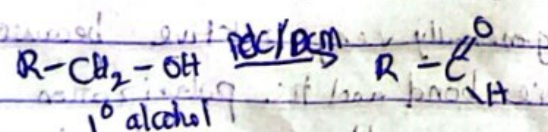
① They are mostly colourless liquid at room temperature, especially the simple aldehydes and ketone. The lower aldehydes poccess rather unpleasant pungent smell, whereas ketones and also benzaldehyde have sweet odours

② The lower aldehydes and ketones are appreciably soluble (miscible) in water due largely to their ability to form hydrogen bond with the water molecule

③ The lower aliphatic aldehyde and ketones have higher boiling point because of hydrogen bonding

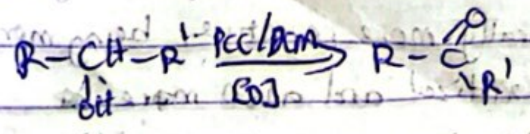
Preparations of Alkanals and ketones

① By mild oxidization of primary and secondary alcohols: Primary alkanols if mildly oxidized will give aldehydes while secondary alkanols will yield ketones. However, oxidation of primary alkanols often lead to carboxylic acid when strong oxidizing agent is used, PCC on DCM is a better oxidizing agent on the conversion of alcohols



$R-CH_2-OH \xrightarrow{PCC/DCM} R-\overset{O}{C}-H$

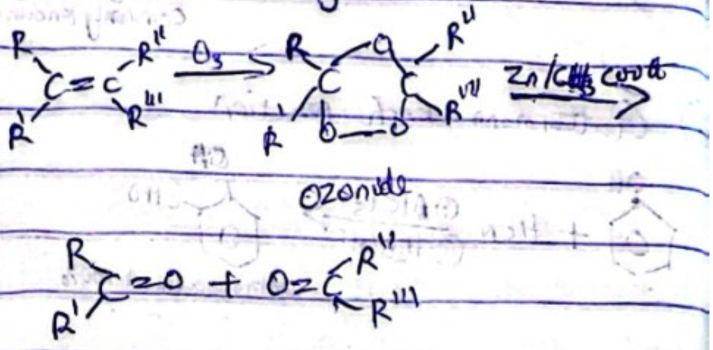
1° alcohol



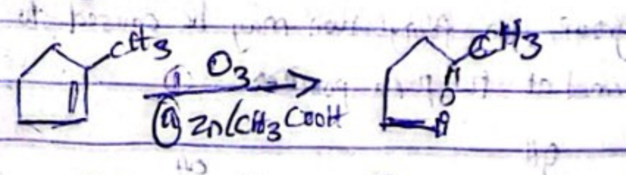
$R-\underset{OH}{CH}-R' \xrightarrow[{[O]}]{PCC/DCM} R-\overset{O}{C}-R'$

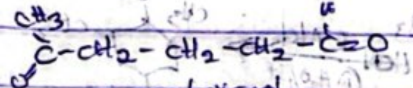
Note in test

② By ozonolysis of Alkenes: Alkenes reacts with ozone to form ozonide which on hydrolysis in the presence of zinc/acetic acid or water gives ketone or aldehyde



e.g

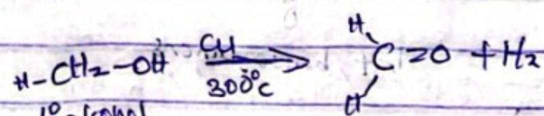




$\underset{O}{\overset{CH_3}{C}}-CH_2-CH_2-CH_2-\overset{H}{C}=O$

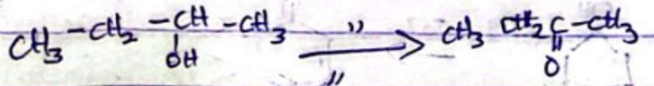
5-oxohexanal

3 Catalytic hydrogen of alkanol: When vapour of primary alcohol is passed over heated copper, a corresponding aldehyde is produced. However a secondary alcohol will give similar reaction.



$H-CH_2-OH \xrightarrow[300^{\circ}C]{Cu} \underset{H}{\overset{H}{>}}C=O + H_2$

1° alcohol



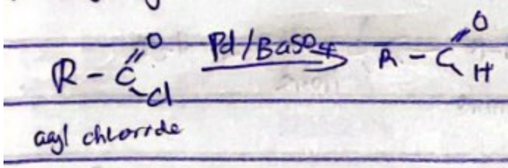
$CH_3-CH_2-\underset{OH}{CH}-CH_3 \xrightarrow[\text{''}]{\text{''}} CH_3\,CH_2\underset{O}{C}-CH_3$

2° alcohol

butan-2-ol

butanone
(ketone)

(4) Reduction of Acyl chloride (For aldehydes only): Ketones can not be prepared with this method. Acyl chloride is hydrogenated in the presence of pd Supported over $BaSO_4$. In practice, the pd catalyst is poisoned with sulphur to prevent the reduction process from going to alcohol.

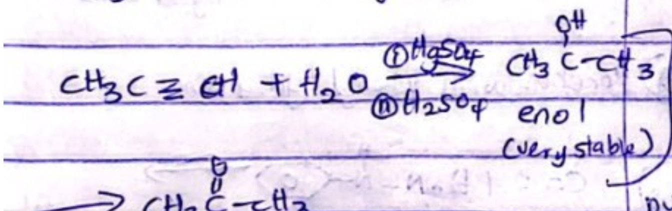


$$R-\overset{O}{\overset{\|}{C}}-Cl \xrightarrow{Pd/BaSO_4} R-\overset{O}{\overset{\|}{C}}-H$$

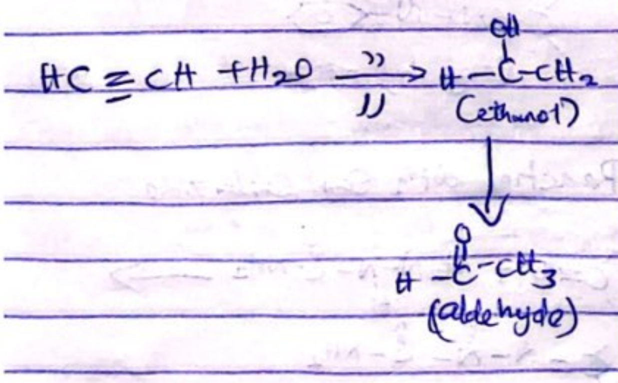
acyl chloride

This reaction is referred to Rosenmond reduction

(5) Hydration of Alkyne: Methyl Ketones Can be prepared by hydration of terminal alkynes in the presence of mercury salt as catalyst.



$$CH_3C\equiv CH + H_2O \xrightarrow[\text{(ii) } H_2SO_4]{\text{(i) } HgSO_4} CH_3\overset{OH}{C}-CH_3 \text{ enol (very stable)} \longrightarrow CH_3\overset{O}{\overset{\|}{C}}-CH_3$$

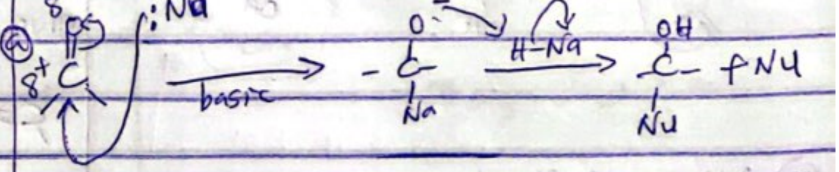


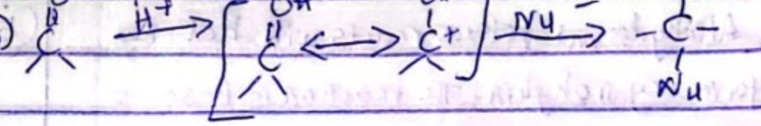
$$HC\equiv CH + H_2O \xrightarrow[\text{''}]{\text{''}} H-\overset{OH}{C}-CH_2 \text{ (ethanol)} \longrightarrow H-\overset{O}{\overset{\|}{C}}-CH_3 \text{ (aldehyde)}$$

17th May, 2023

Chemical Reactions of Aldehydes & Ketones

(1) Nucleophilic Addition: Aldehydes and ketones undergo mostly nucleophilic addition. This is the addition of nucleophile and proton across the polarized >C=O, the nucleophilic addition can occur in both basic and acidic medium

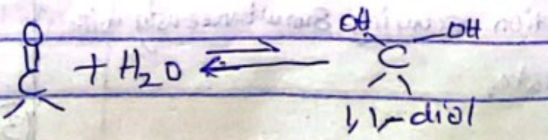




(a) Based catalyzed addition: Here, a strong nucleophile attacks the carbonyl to form an alkoxide which is then protonated.

(b) Acid catalyzed addition: Here, the acid protonates the carbonyl oxygen after which weak nucleophile attacks the carbonyl

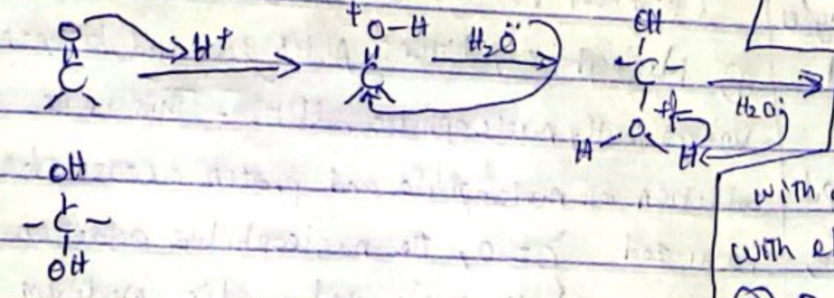
(2) Hydration of Aldehydes and Ketones: Aldehydes and ketones react with water in both acidic and basic medium to form 1,1 diol, i.e a geminal diol. The reaction is reversible and the backward reaction is more favoured.

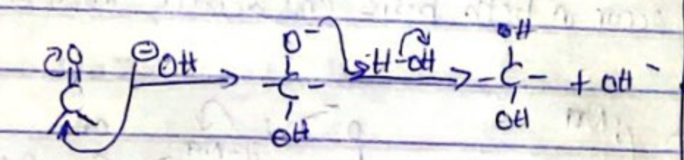


$$\overset{O}{\overset{\|}{C}} + H_2O \rightleftharpoons \overset{OH}{C}-OH$$

1,1-diol

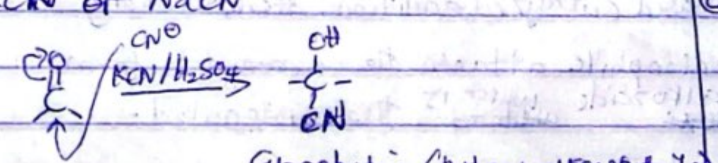
Mechanism





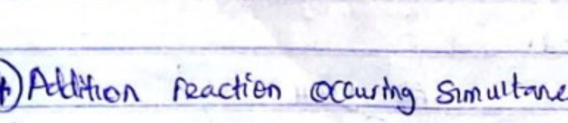
(ii) Addition of HCN

Aldehydes and ketones reacts with Hcl to form cyanohydrin. The reaction is base catalyzed, a poisonous gas is generated in situ by the action of dilute H_2SO_4 on KCN or NaCN



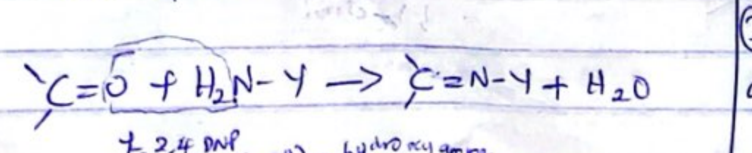
Cyanohydrin (hydroxyl alkanonitriles)

Like other nitriles, 2-hydroxyl alkanonitrile can be hydrolyzed to form the carboxylic acid derivative. In this case, the 2- or α-hydroxy acids.



$$R-\overset{OH}{\underset{R'}{C}}-CN \xrightarrow[\text{reflux, 50°C}]{\text{Conc. HCl}} R-\overset{OH}{\underset{R'}{C}}-COOH$$

To form 2-hydroxyl propanoic acid



$$CH_3-\overset{\overset{O}{\|}}{C}-H \xrightarrow{HCN} CH_3-\overset{OH}{\underset{H}{C}}-CN \xrightarrow{Conc.\,HCl} CH_3-\overset{OH}{C}-COOH$$

2-hydroxyl propanoic acid

(iii) Addition reaction occuring simultaneously with the loss of water

$$\rangle C=O + H_2N-Y \longrightarrow \rangle C=N-Y + H_2O$$

Y = 2,4 DNP
= OH (H_2N-OH) - hydroxy amine
= NH_2 (H_2N-NH_3) - Hydrazine

② Reaction of Ammonia Derivative

Some derivative of ammonia reacts with aldehyde and ketone to form compound with elimination of water molecule

ⓐ Reaction with Primary Amine: Primary amine reacts with aldehyde and ketone to give imine

$$\rangle C=O + \underset{1°\ amine}{H_2N-R} \longrightarrow \underset{imine}{\rangle C=N-R} + H_2O$$

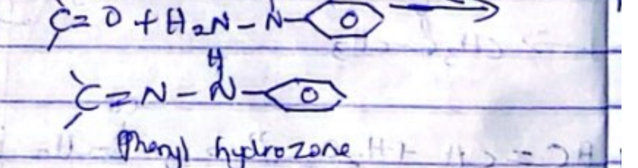
ⓑ Reaction with hydxylamine (H_2N-OH)

$$\rangle C=O + H_2N-OH \longrightarrow \underset{oxime}{\rangle C=N-OH} + H_2O$$

ⓒ Reaction with Hydrazine (H_2N-NH_2)

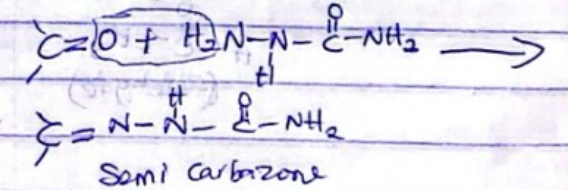
$$\rangle C=O + \underset{hydrazine}{H_2N-NH_2} \longrightarrow \underset{hydrazone}{\rangle C=N-NH_2}$$

ⓓ Reaction with Phenyl hydrazine



Phenyl hydrozone

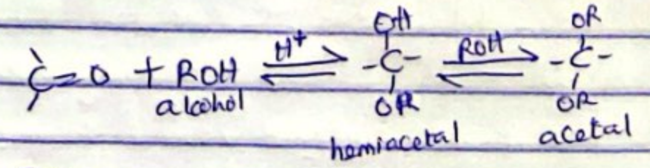
ⓔ Reaction with Semicarbazide



$$\rangle C=O + H_2N-\underset{H}{N}-\overset{O}{\overset{\|}{C}}-NH_2 \longrightarrow \rangle C=N-\overset{H}{N}-\overset{O}{\overset{\|}{C}}-NH_2$$

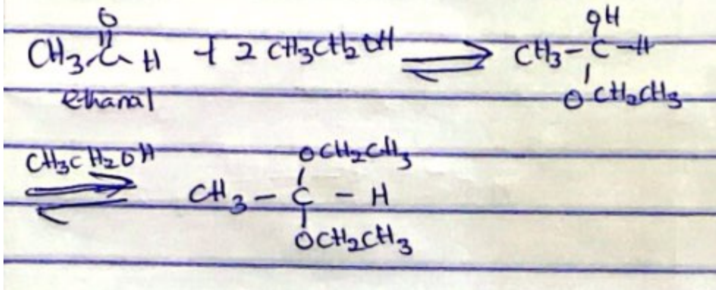
Semi carbazone

③ Reaction with Alcohol: Aldehyde and ketone react with equivalent alcohol to form acetals which are germinal di'ether



$$>C=O + ROH \underset{}{\overset{H^+}{\rightleftharpoons}} -\overset{OH}{\underset{OR}{C}}- \underset{}{\overset{ROH}{\rightleftharpoons}} -\overset{OR}{\underset{OR}{C}}-$$

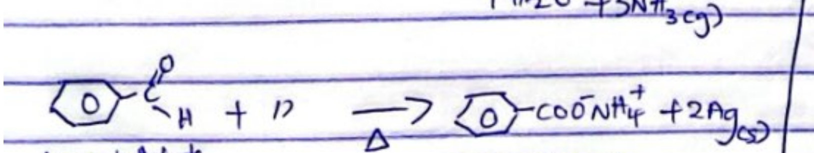
Exampre



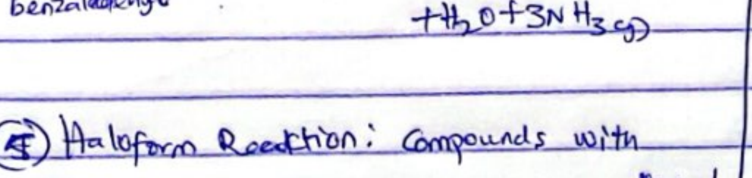
$$CH_3\overset{O}{\overset{\|}{C}}H + 2CH_3CH_2OH \rightleftharpoons CH_3-\overset{OH}{\underset{OCH_2CH_3}{C}}-H \overset{CH_3CH_2OH}{\rightleftharpoons} CH_3-\overset{OCH_2CH_3}{\underset{OCH_2CH_3}{C}}-H$$

④Reactrons with Tollen's Reagent: This reaction is for aldehydes only. Aldehydes reacts with tollen's reagent to give a deposit of silver (silver mirror test), to different between aldehydes and ketones. The reagent consists of a solution of Silver (I) nitrate in excess ammonia solution. Aldehydes reduce the Ag^+ to Ag, which is precipitated and forms a mirror effect in the bottom of a test tube.

Ethanal reacts almost immeddately, but with benzaldehyde, the reaction mixture requires warming, ~~but does not~~

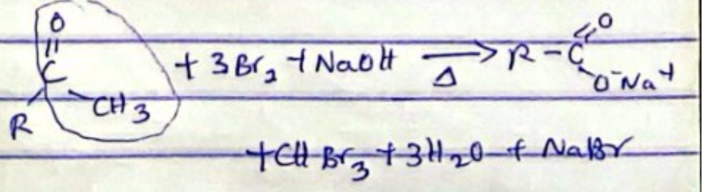


$$CH_3-C(=O)H + 2Ag(NH_3)_2OH \longrightarrow CH_3COO^-NH_4^+ + 2Ag + H_2O + 3NH_{3(g)}$$



$$C_6H_5-C(=O)H + " \xrightarrow[\Delta]{} C_6H_5-COO^-NH_4^+ + 2Ag_{(s)} + H_2O + 3NH_{3(g)}$$

⑤ Haloform Reaction: Compounds with methyl carbonyl group such as ethanal and Methyl ketones or any group that can be oxidized with alkanol will react rapidly with halagen (Cl, Br, I) to form haloform and a salt of carboxylic acid

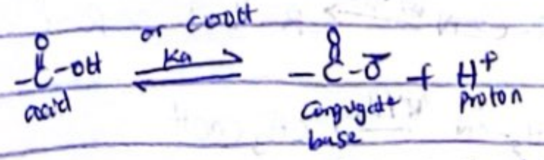


$$R-C(=O)-CH_3 + 3Br_2 + NaOH \xrightarrow[\Delta]{} R-C(=O)O^-Na^+ + CHBr_3 + 3H_2O + NaBr$$

If Iodine is used, it give yellow precipitate with a characteristic, ~~odour~~ and distinguishable odour. This is a diagonistic test for methyl carbonyl compound.

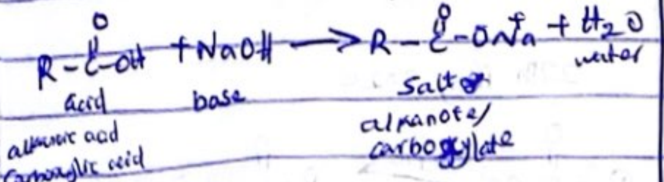
21st May, 2021

Carboxylic Acid



$$-\overset{O}{\overset{\|}{C}}-OH \underset{}{\overset{Ka}{\rightleftharpoons}} -\overset{O}{\overset{\|}{C}}-O^- + H^+$$

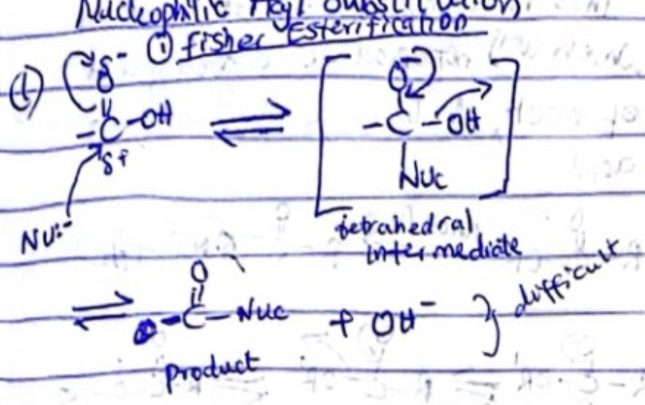
COOH can be involved in acid-base reaction

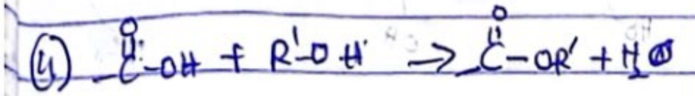


$$R-\overset{O}{\overset{\|}{C}}-OH + NaOH \longrightarrow R-\overset{O}{\overset{\|}{C}}-O^-Na^+ + H_2O$$

Nucleophilic Acyl Substitution

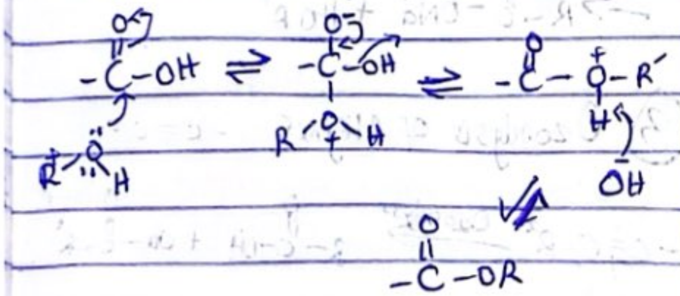
① Fisher Esterification



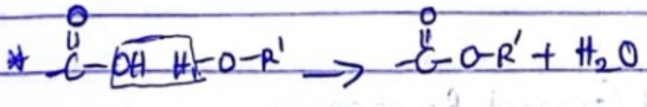


$$④\ -\overset{O}{\overset{\|}{C}}-OH + R'-OH \longrightarrow -\overset{O}{\overset{\|}{C}}-OR' + H_2O$$

Mechanism

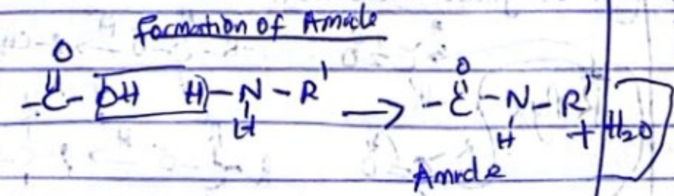


$$-\overset{O}{\overset{\|}{C}}-OH \rightleftharpoons -\overset{O^-}{\underset{R-\overset{+}{O}-H}{\overset{|}{\underset{|}{C}}}}-OH \rightleftharpoons -\overset{O}{\overset{\|}{C}}-\underset{H}{\overset{+}{O}}-R' \rightarrow -\overset{O}{\overset{\|}{C}}-OR$$



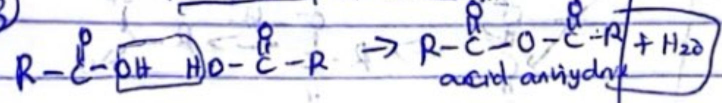
$$* -\overset{O}{\overset{\|}{C}}-\boxed{OH\ H}-O-R' \longrightarrow -\overset{O}{\overset{\|}{C}}-O-R' + H_2O$$

② Formation of Amide



$$-\overset{O}{\overset{\|}{C}}-\boxed{OH\ H}-\underset{H}{\underset{|}{N}}-R' \longrightarrow -\overset{O}{\overset{\|}{C}}-\underset{H}{\underset{|}{N}}-R' + H_2O$$

③ Formation of Acid anhydride



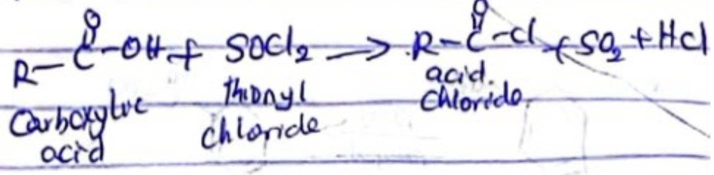
$$R-\overset{O}{\overset{\|}{C}}-\boxed{OH\ H}O-\overset{O}{\overset{\|}{C}}-R \rightarrow R-\overset{O}{\overset{\|}{C}}-O-\overset{O}{\overset{\|}{C}}-R + H_2O$$

Formation of Acid Chloride

④ Assignment

① Write the mechanism for the formation of acyl chloride.

$R\overset{O}{\overset{\|}{C}}Cl$ Reaction:



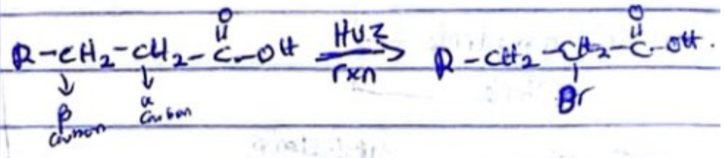
$$R-\overset{O}{\overset{\|}{C}}-OH + SOCl_2 \longrightarrow R-\overset{O}{\overset{\|}{C}}-Cl + SO_2 + HCl$$

Fisher esterification is difficult, this is easy

Carboxylic acid → acid chloride → ester

23rd May, 2021

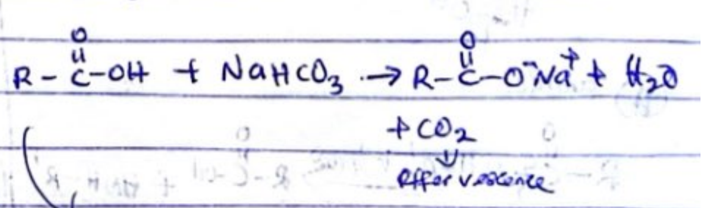
~~of~~ Hell – Volhard – Zelinsky Reaction



$$R-CH_2-CH_2-\overset{O}{\overset{\|}{C}}-OH \xrightarrow[rxn]{HVZ} R-CH_2-\underset{Br}{\underset{|}{CH}}-\overset{O}{\overset{\|}{C}}-OH$$

Assignment

Write the mechanism for Hell-Volhard-Zelinsky reaction



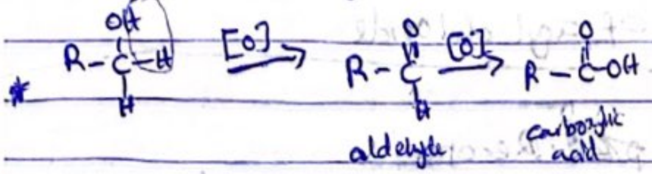
$$R-\overset{O}{\overset{\|}{C}}-OH + NaHCO_3 \rightarrow R-\overset{O}{\overset{\|}{C}}-O^-Na^+ + H_2O + CO_2$$

This reaction is used to test for Carboxylic acid.

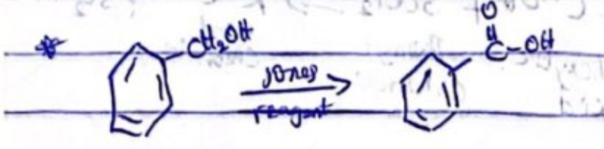
Synthesis

Preparation of Carboxylic Acid

① Oxidation of primary alcohol



$$R-\overset{OH}{\underset{H}{\overset{|}{C}}}-H \xrightarrow{[O]} R-\overset{O}{\overset{\|}{\underset{H}{C}}} \xrightarrow{[O]} R-\overset{O}{\overset{\|}{C}}-OH$$



$$CH_3CH_2CH_2CH_2-OH \xrightarrow[\text{acid}]{\text{chromic}} CH_3CH_2CH_2COOH$$

② Hydrolysis of carboxylic acid derivatives

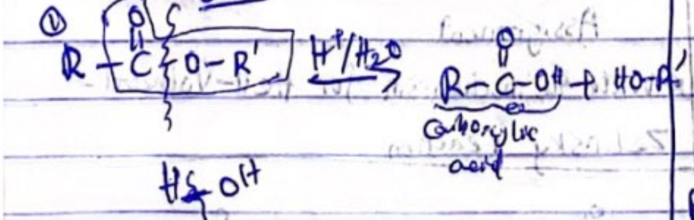
Carboxylic acid derivatives;

- ester
- amide
- acid chloride
- acid anhydride
- Nitrile

$\xrightarrow{\text{hydrolysis}} R-COOH$ using water to split

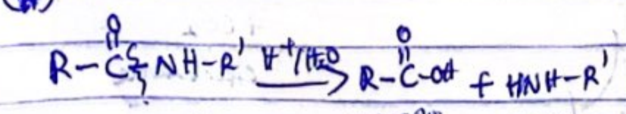
Examples ~~# hydrolys~~

① Ester



$$R-\overset{O}{\overset{\|}{C}}-O-R' \xrightarrow{H^+/H_2O} R-\overset{O}{\overset{\|}{C}}-OH + HO-R'$$

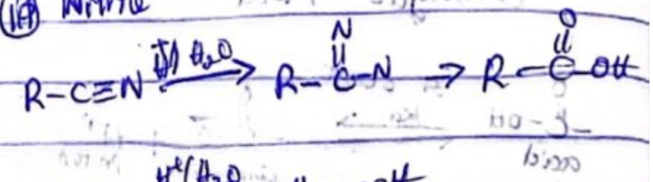
(1A) amide



$$R-\overset{O}{\overset{\|}{C}}-NH-R' \xrightarrow{H^+/H_2O} R-\overset{O}{\overset{\|}{C}}-OH + HNH-R'$$

* hydrolysis of esters happens faster than amides

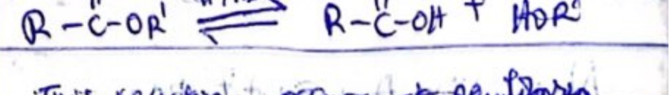
(1B) Nitrile



$$R-C\equiv N \xrightarrow{H^+/H_2O} R-\overset{N}{\overset{\|}{C}}-N \rightarrow R-\overset{O}{\overset{\|}{C}}-OH$$

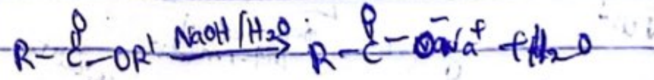
$$CH_3-CN \xrightarrow{H^+/H_2O} CH_3COOH$$

27th May, 2024

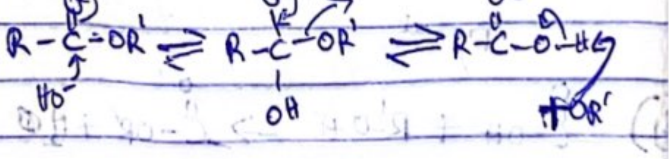


$$R-\overset{O}{\overset{\|}{C}}-OR' \underset{}{\overset{H^+/H_2O}{\rightleftharpoons}} R-\overset{O}{\overset{\|}{C}}-OH + HOR'$$

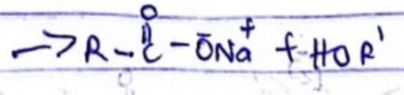
This reaction occurs at equilibrium which will not produce a good yield of RCOOH. A base is used instead of acid



$$R-\overset{O}{\overset{\|}{C}}-OR' \xrightarrow{NaOH/H_2O} R-\overset{O}{\overset{\|}{C}}-\bar{O}Na^+ + H_2O$$

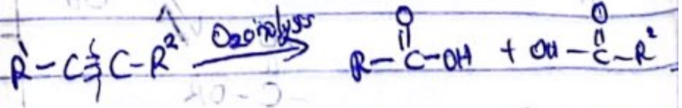


$$R-\overset{O}{\overset{\|}{C}}-OR' \rightleftharpoons R-\overset{O^-}{\underset{OH}{\overset{|}{\underset{|}{C}}}}-OR' \rightleftharpoons R-\overset{O}{\overset{\|}{C}}-O-H + \bar{O}R'$$



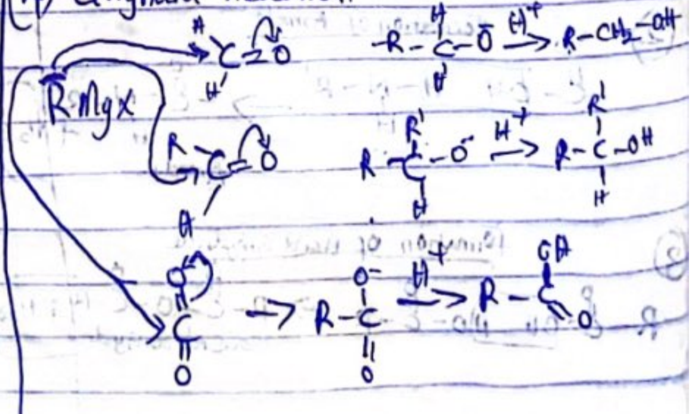
$$\rightarrow R-\overset{O}{\overset{\|}{C}}-\bar{O}Na^+ + HOR'$$

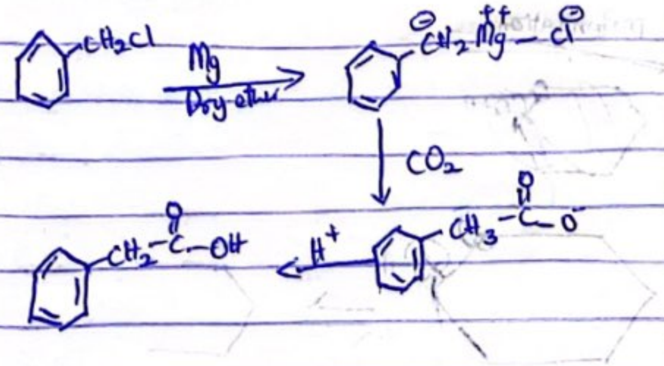
③ Ozonolysis of Alkynes $-C\equiv C-$



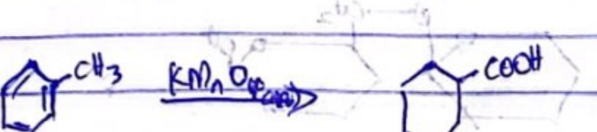
$$R^1-C\equiv C-R^2 \xrightarrow{\text{Ozonolysis}} R-\overset{O}{\overset{\|}{C}}-OH + OH-\overset{O}{\overset{\|}{C}}-R^2$$

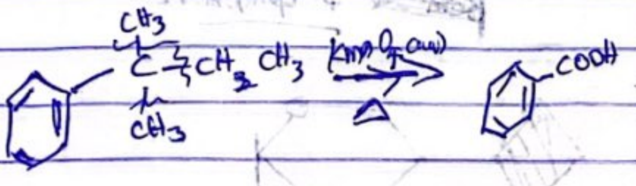
④ Grignard Reaction

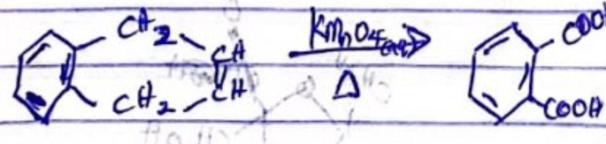




5) Oxidation of benzenes with Alkyl Substitution

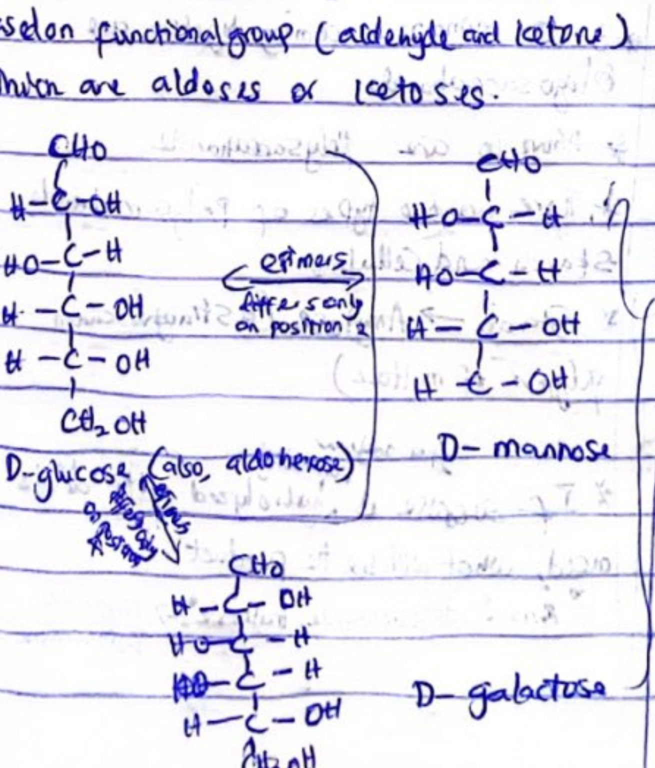
①


②


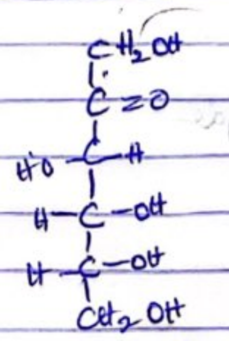
(iii)


Carbohydrates

Classification of carbohydrate can be based on functional group (aldehyde and ketone) which are aldoses or ketoses.

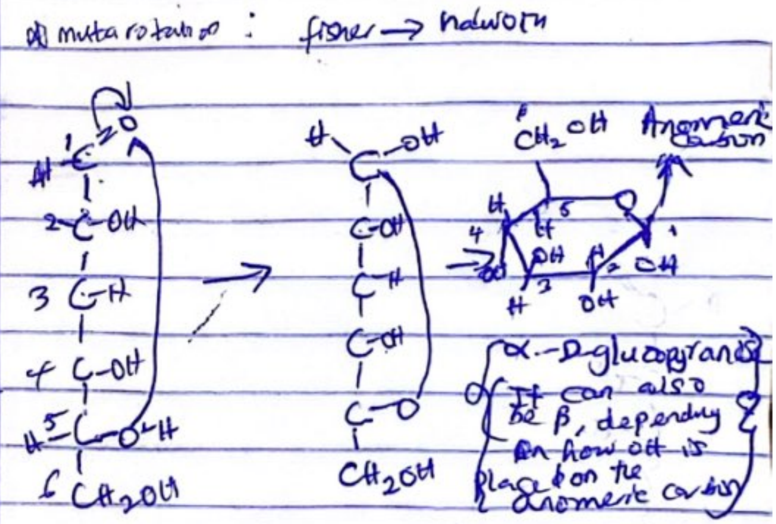


Keto-hexose



D-fructose

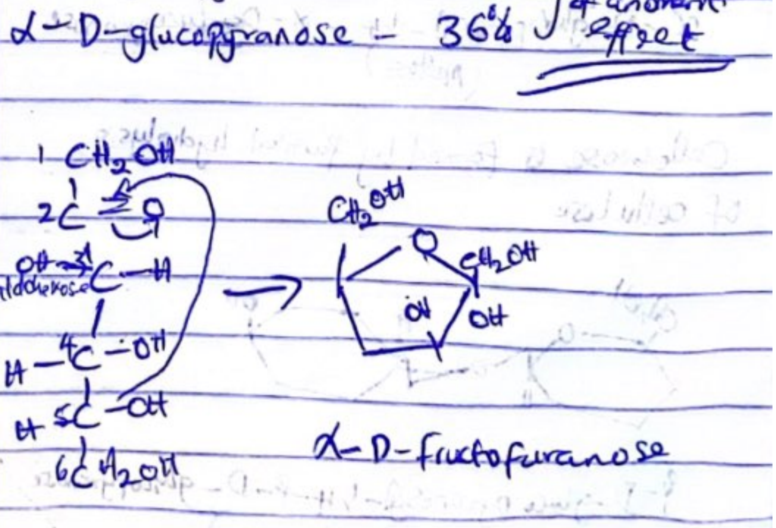
mutarotation : fisher → haworth



α-D-glucopyranose or It can also be β, depending on how OH is placed on the anomeric carbon

Anomeric reaction or hemiacetal reaction

β-D-glucopyranose – 64%
α-D-glucopyranose – 36%
} because of anomeric effect



α-D-fructofuranose

1.0 CHEMISTRY OF CARBOHYDRATES (SECTION ONE)

This section gives a simple treatment of the Chemistry of Carbohydrates. It provides concise information on this class of Chemistry and suitable for beginners.

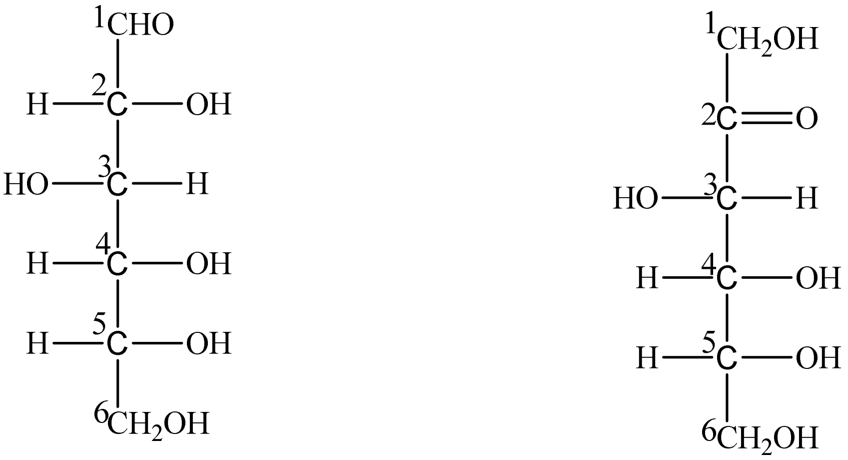
Carbohydrates are natural products with general a formula $Cn(H_2O)n$. Other names for carbohydrates are also saccharides. This very large family includes monomers - called simple sugars or monosaccharides up to very large molecules (complex) called polymers which are made up of these simple sugars. The polymers are also called polysaccharides such as starch, cellulose, dextrin and glycogen.

1.1 *Classification and nomenclature of monosaccharide*

1.1.1 *Monosaccharides*

Monosaccharides are chiral polyhydroxyalkanals or polyhydroxyalkanones which are the cylic hemiacetal forms of these sugars. This class of saccharide is divided into two major groups depending on whether their acyclic forms contain an aldehyde functional group or a keto functional group which are aldoses or ketoses, respectively.

Aldoses and Ketoses: All monosaccharides have their names end with ***"ose"*** hence, they are divided into aldoses that is aldehyde plus ose) and ketoses (ketone plus ose). For example, glucose is an, aldose while fructose is a ketose (Figures 1.0 a & b).



Glucose "a" (an aldose)
Fructose "b" (a ketose)

Figure 1.1 a & b: Structures of D-glucose and D-fructose

The above structures are the ***Fischer projections*** of these monosaccharides. The aldehyde functional group (carboxaldehyde carbon) of an aldose is assigned number 1 and the primary alcohol group (-CH_2OH) assigned the last number.

The simple sugars can also be classified according to the number of carbons that they contain. Both glucose and fructose given in Figure 1.1 a & b above contain six carbons each, hence they are both **hexoses**. If both classifications (functional groups and number of carbons) are combined, then glucose will become an **aldohexose** and fructose a **ketohexose**.

1.2 *Glyceraldehyde and dihydroxyacetone*

The simplest carbohydrates - glyceraldehyde and dihydroxyacetone, which are **aldotriose** and a **ketotriose**, respectively (Figure 1.2 a & b). All series of aldoses and ketoses are built from glyceraldehyde and dihydroxyacetone, respectively.

glyceraldehyde "a"

(an aldotriose)

dihydroxyacetone "b"

(a ketotriose)

Figure 1.2 a & b: Structures of a glyceraldehyde and dihydroxyacetone

1.3 *D - and L - Monosaccharides*

Using Fischer projection, the first carbon is a carbonyl carbon for aldose and the second carbon is carbonyl for ketose. If the last **chiral carbon** has its hydroxyl group on the right, the sugar is designated **D - sugar** but if it is on the left, it is a **L - sugar**. See Figure 1.3.1 a & b below:

(+) - D - glyceraldehyde "a"

(+) - (R) - glyceraldehyde

(-) - L - glyceraldehyde "b"

(-) - (S) - glyceraldehyde

Fig 1.3.1 a & b: Structures of D- and L - glucose

The Figure 1.3 a & b shows that L - Glucose is an enantiomer of D - Glucose.

The simplest sugar is glyceraldehyde ($C_3H_6O_3$). Because it contains three carbons, it is a triose, and it is an aldotriose because its first carbon is an alkanal.

Emil Fischer assigned the configuration (**-**) - glyceraldehyde to glyceraldehyde drawn using Fischer projection if the hydroxyl group of the only chiral carbon is on the left which called **"L"** (*laevo*). When the hydroxyl group is on the right of the chiral carbon, he called it **"D"** (*dextro*).

These two enantiomers of glyceraldehyde were later assigned **“S”** (*sinister*) for L - configuration and **“R”** (*recutum*) for D - configutation.

Any molecule that contains n chiral centres will have 2^n stereoisomers provided no meso compounds are present. For example, if there two chiral centres, hence $2^2 = 4$, which means four carbon sugars (aldotetrose). Their structures are given in Figure 1.3.2 a, b, c & d below:

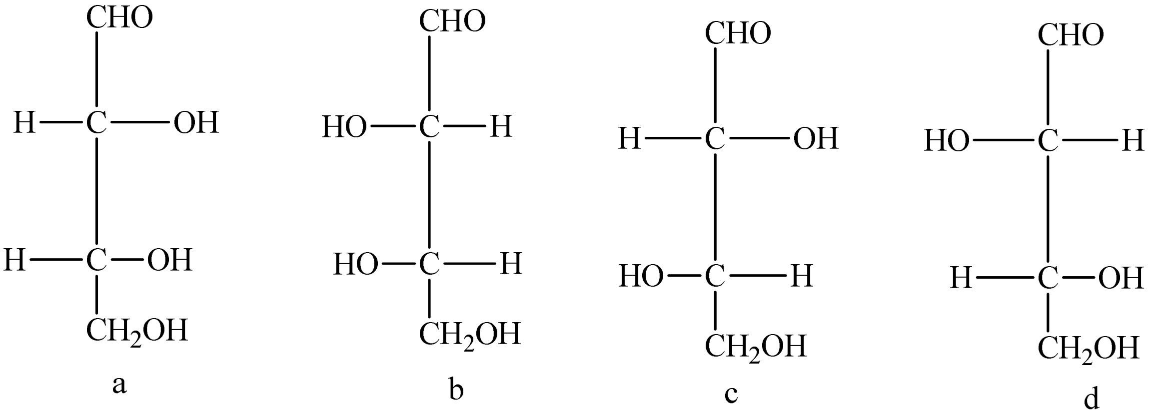
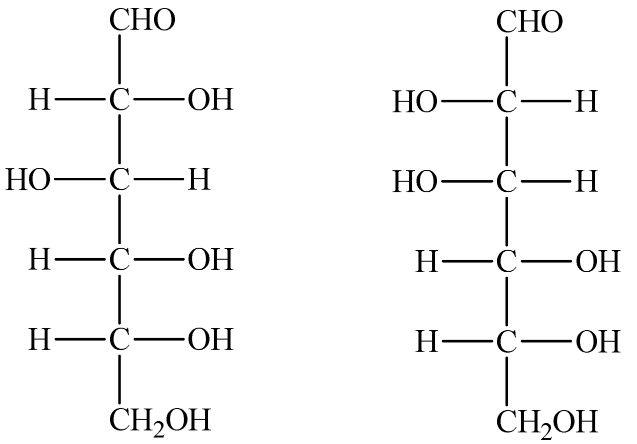


Figure 1.3.2 a, b, c & d: Structure of the stereoisomers of aldotetrose

These four aldotetroses were obtained by inserting **-HCOH-** between carbonyl carbon and the next chiral carbon of both L - glyceraldehyde and D - glyceraldehyde and the mirror image of each will give the other two compounds to make four aldotetroses given above.

1.3 *Epimers*

An epimer is one of a pair of **diastereomers.** Epimer occurs when two molecules have different configuration at only one chiral centre. That is all other chiral centres in the molecule are the same except one chiral centre. Examples are D - Glucose and D - Mannose (Figure 1.4 a & b).



D-glucose "a" D-mannose "b"

Figure 1.4 a & b: D-glucose and D-mannose

Diastereomer

This term is used to describe two molecules that are stereoisomers with the same formula, connectivity but different arrangement of atoms in space but are not enantiomers. That is the two molecules are not mirror images of each other or non-identical stereoisomers. They occur when two or more stereoisomers of compound for example sugar have different arrangement of atoms at one or more chiral centres but not at all centres which makes them not to be superimposable. If this different is at only one chiral centre, they are called ***epimers***.

The simplest ketose, dihydroxyacetone (Figure 1.5) lacks a chiral centre. Insertion of **-CH(OH)-** unit between the carbonyl carbon (carbon number 2) and the third carbon creates erythrulose (Figure 1.6). The D isomer of erythrulose is the bases of the D-ketose sugar series.

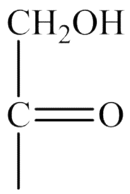


Figure 1.5: Dihydroxyacetone

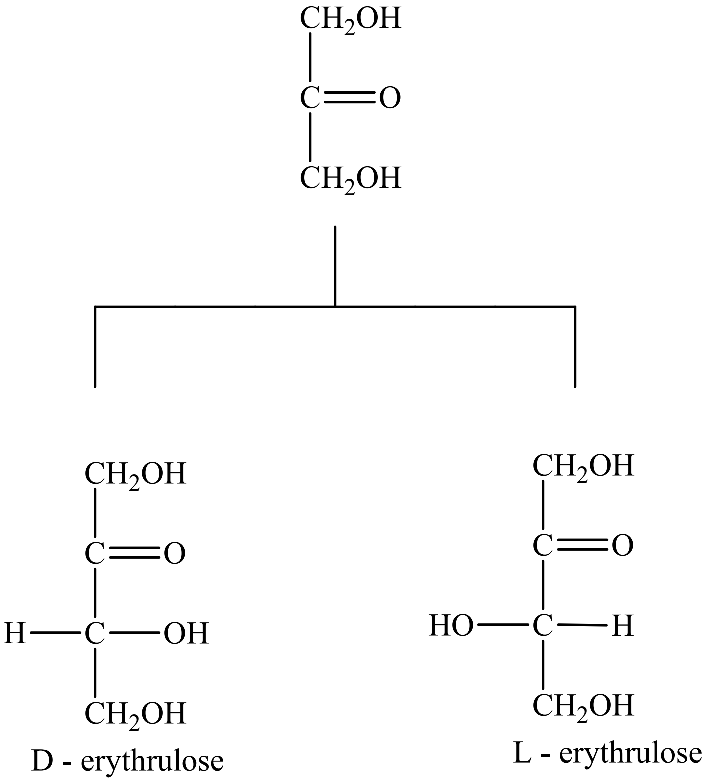


Figure 1.6: Formation of erythrulose from dihydroxyacetone

Ring structure of Monosaccharides

Glucose and other sugars can exist as cyclic hemiacetals or hemiketals. They are formed from intra-molecular reaction of a hydroxy group with a carboxyl group. Glucose and other aldohexoses form their most stable acetal by using the hydroxy group on carbon number 5, and the six-membered ring compound obtained is called the pyranose because it resembles tetrahydropyran (Figure 1.7). Hence, the cyclic form of D-glucose is called D-glucopyranose.

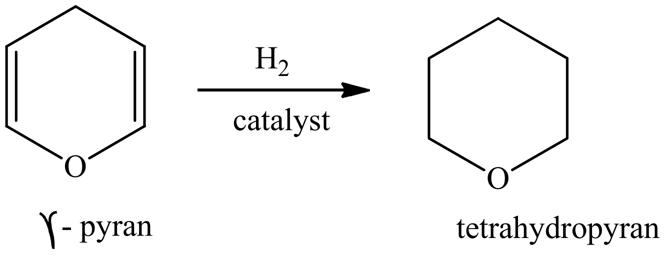


Figure 1.7: Terahydropyran from hydrogenation of γ-pyran

The hemiacetal formation or ***anomeric reaction*** creates a new chiral centre called ***anomeric carbon or anomeric centre*** that is carbon number one (Figure 1.8). This reaction results in two diastereomeric products that differed in configuration on the anomeric carbon. The two products are also called ***Anomers***. These anomers are designated – α or - β depending upon the relative configuration of the anomeric carbon (Figure 1.9 a and b).

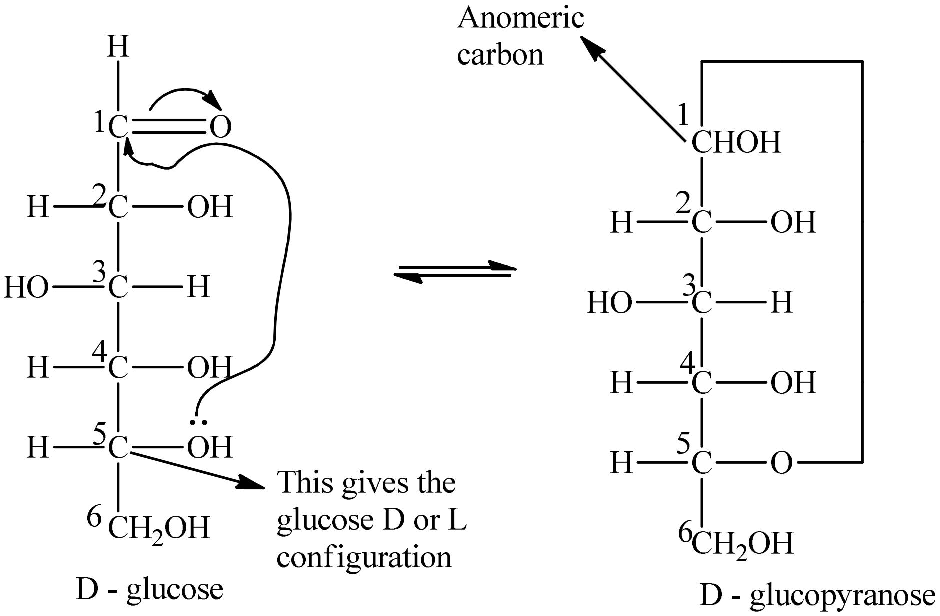
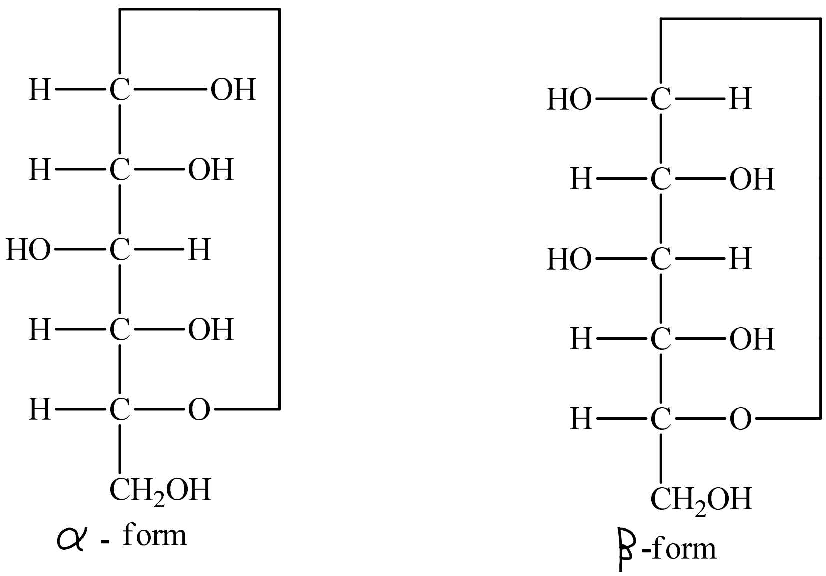


Figure 1.8: Anomeric reaction in D-Glucose (anomerization reaction)

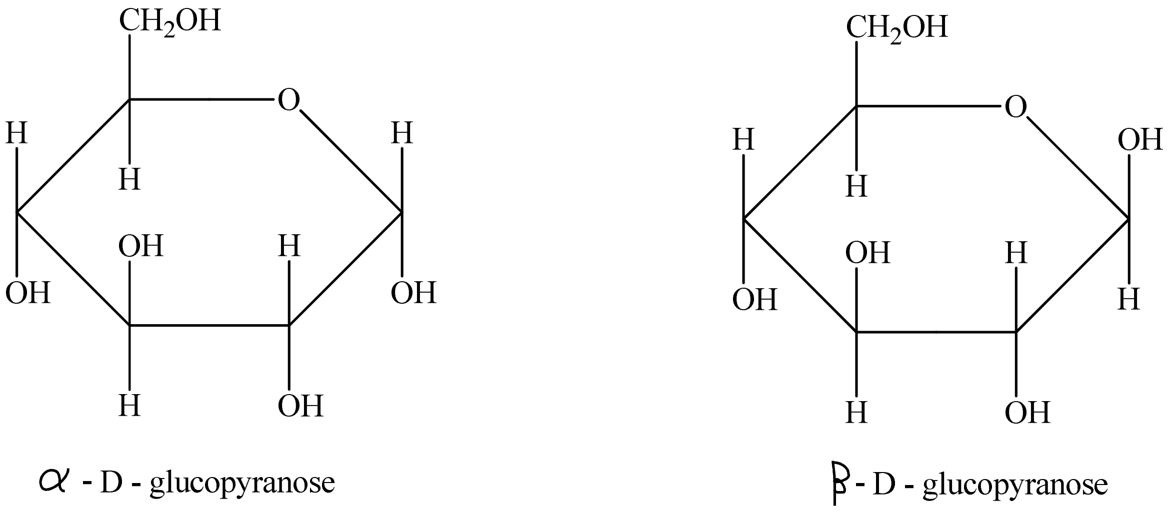


α - form

β -form

Figure 1.9: The α-form and the β-form of the glucose in ring forms

The structures in the Figure 1.9 above resemble the hydrogenated γ-Pyran (Figure 1.7) above, hence, D-glucose in ring form is named after pyran that is α- or β- D – glucopyranose (Figure 1.10 a and b).

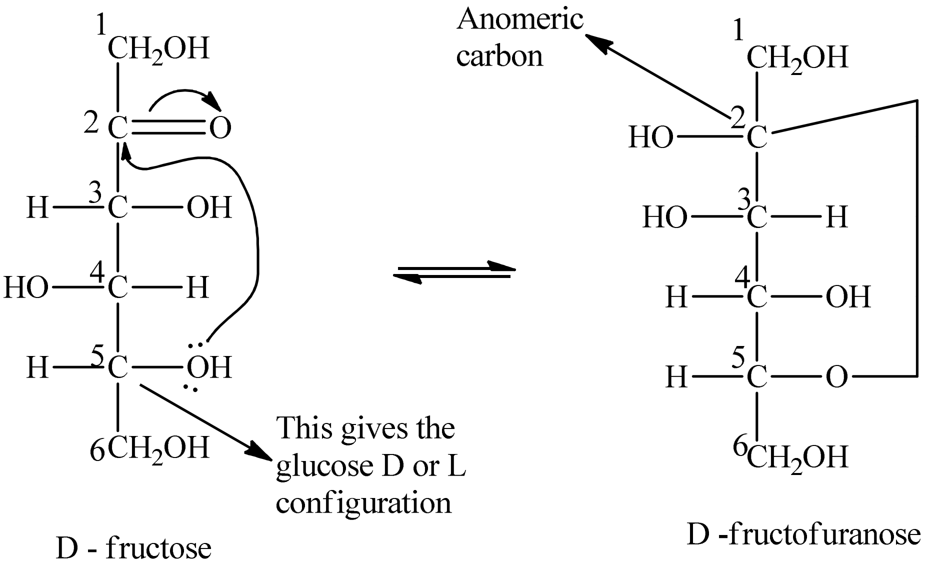


α - D - glucopyranose

β - D - glucopyranose

Figure 1.10 a & b: α- D – glucopyranose and β- D – glucopyranose

Ketohexoses also undergo the same intramolecular reaction described above for aldohexose using hydroxy on carbon number 5 (Figure 1.11). This anomeric reaction leads to the formation of five membered ring compound named after tetrahydrofuran because it resemblances hydrogenated Furan (Figure 1.12). The reaction leads to the formation of two products which are also called ***Anomers***. These anomers like glucopyranose are designated - α or - β depending upon the relative configuration of the anomeric carbon. The ring forms of D-Fructose resemble hydrogenated Furan (Figure 1.12), hence, the ring structure of D-Fructose is named after Furan that is α - or – β- D-Fructofuranose (Figure 1.13 a and b).



This gives the glucose D or L configuration

Figure 1.11: Anomeric reaction in D-Fructose (anomerization reaction)

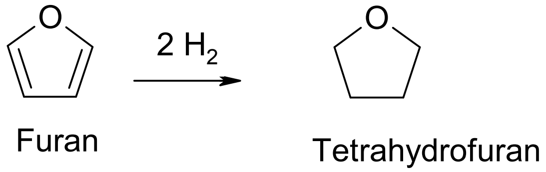
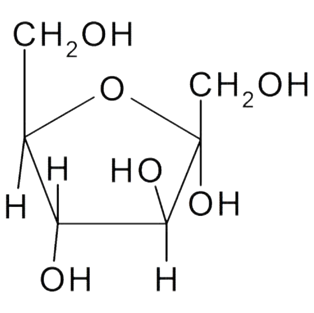
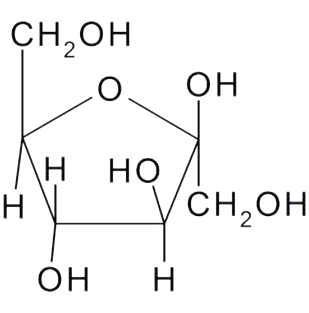


Figure 1.12: Hydrogenation of Furan





α - D-Fructofuranose (a) **β – Fructofuranose (b)**

Figure 1.13 a and b: α - or – β- D-Fructofuranose

The ratio of the α - D- glucopyranose to β - D- glucopyranose is 36 : 64% in nature. This is because the beta form is more stable than the alpha anomer. This stability can be explained using the ***anomeric effect***.

This effect arises from the orbital interaction between oxygen (heteroatom) and the anomeric carbon that is the CO bond. This reaction occurs when the anomeric hydroxy is in the ***axial position*** (Figure 1.14) that is **α-form** but this destabilizing reaction is not possible with the OH group in the ***equatorial position*** (Figure 1.15) that is **β-form**.

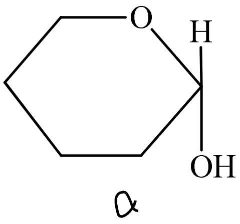


Figure 1.14: Figure showing OH group drawn in the axial position

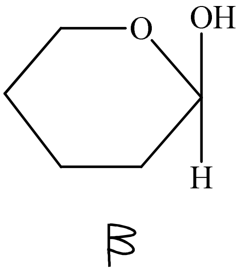
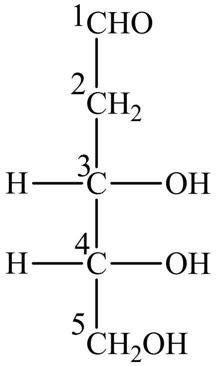


Figure 1.15: Figure showing OH group drawn in the equatorial position

Any ring substituents that are drawn perpendicularly to this axis of symmetry are called ***equatorial*** while those drawn parallel are referred to as ***axial***. For example, the OH group and other substituents on the β - D - glucopyranose are perpendicular to this axis. This reduces steric hindrance, hence, the β - form is more stable than the α - form. This is another explanation for the reason why β - and α - forms are 64 and 36 % in nature, respectively.

Deoxy and Amino Sugars

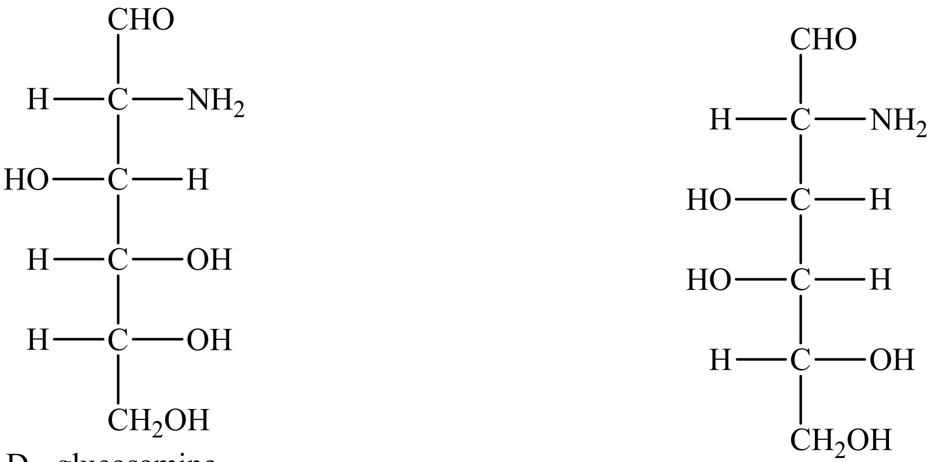
In nature, sugars can have one or more of their OH group(s) replaced by some substituents. Of these, substituents, H and -NH_2 are the most common. A Deoxy sugar has - CH_2 - group is place of a - CH(OH) - group. The most common deoxy sugar in nature is 2-deoxy—D—ribose (Figure 1.16) which is the sugar moiety of deoxyribonucleic acid (DNA).



2 - deoxy - D - ribose

Figure 1.16: 2–deoxy-D-ribose

Amino sugar on the other hand has a – $CH(NH_2)$ – group replacing a - CH (OH) - group. Examples of important amino sugars are D - galactosamine and D - glucosamine (Figure 1.17 a & b).



D - glucosamine
(2 - amino - 2 - deoxy - D - glucose)

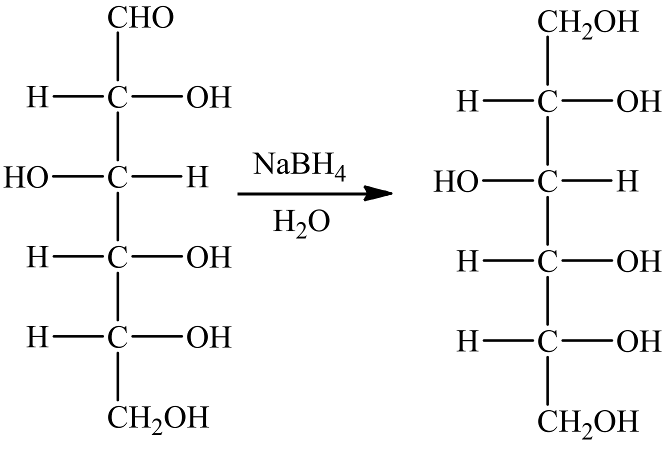
D - galactosamine
(2 - amino - 2 - deoxy - D - galactose)

Figure 1.17 a & b: D-glucosamine and D-galactosamine

1.3 *SOME REACTIONS OF MONOSACCARIDES*

1.3.1 *Reduction to glucitols*

Aldose monosaccharides such as D-glucose can be reduced glycitols. For example, D-glucose can be reduced to D-glucitol (Sorbitol) using a reducing agent such as Sodium borohydride in water ($NaBH_4/H_2O$) (Figure 1.18).



D - glucose

D - glucitol (sorbitol)

Figure 1.18: Reduction of D-glucose to D-Glucitol

1.3.2 *Oxidation to gluconic acids*

Aldoses are oxidized to glyconic acids using mild oxidants such as bromine water. For example, D-glucose is oxidized to D-gluconic acid (Figure 1.19).

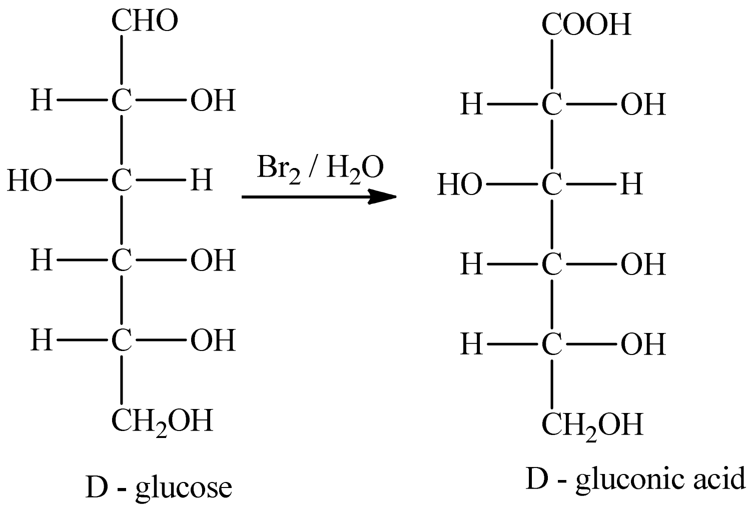


Figure 1.19: Oxidation of D-glucosewith mild oxidant to D-gluconic acid

1.3.3 *Oxidation to glucaric acids*

The oxidation of aldoses to glucaric acids can only be carried out using strong oxidants such as HNO_3. If D-glucose is oxidized with strong oxidant, it will give D-glucaric acid (Figure 1.20).

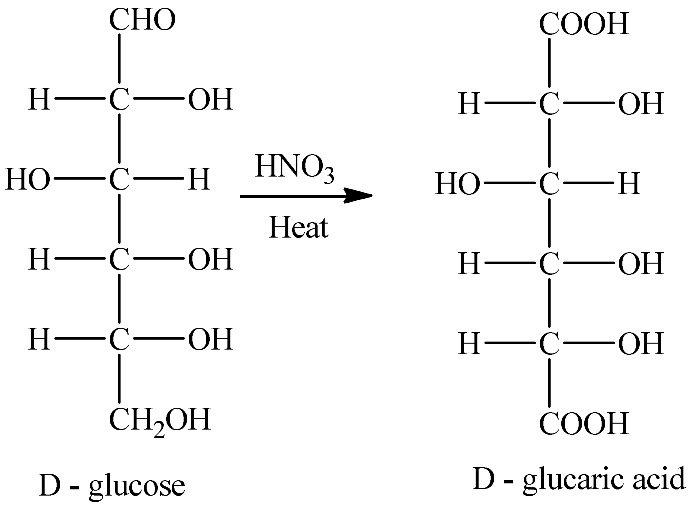


Figure 1.20: Oxidation of D-glucosewith strong oxidant to D-glucaric acid

1.3.4 (i) ***Reaction with Tollens' reagent***

The Tollens' reagent is prepared according the chemical equations (1 & 2) given below:

$2\ AgNO_3 + 2\ NaOH \longrightarrow Ag_2O\ (s) + 2\ NaNO_3 + H_2O$ ---------- (1)

The brown Silver (I) oxide precipitate formed is then dissolved in excess aqueous ammonia to give a clear solution of diammoniasilver (I) complex according to equation 2 given below:

$Ag_2O\ (s) + 4\ NH_3 + 2\ NaNO_3 + H_2O \longrightarrow 2[Ag(NH_3)_2]NO_3 + 2\ NaOH$ -----. (2)

The reaction between D-glucose and Tollens' reagent is given in equation 3 below:

$Ag(NH_3)_2^+ + \text{D-glucose} \longrightarrow \text{D-gluconic acid} + Ag\ (s)$

This reaction is the popular mirror image test used for the confirmation of alkanal.

1.3.4 (ii) ***Reaction with Fehling's and Benedict's Solutions***

Fehling's solution is made up of the following reagents: copper (II) ions complexed with tartrate ions. Both reagents are prepared in NaOH solution. On the other hand, Benedict's solution contains copper (II) ions with citrate ions instead of tartrate ions. It is prepared with Na_2CO_3 solution as against NaOH solution used for the Fehling's solution.

Both Fehling's and Benedict's solutions provide hydroxy ions that reacts with Cu^{2+} in complex form (equation 1). These hydroxy ions are provide by the NaOH and Na_2CO_3 used in the preparation Fehling's and Benedict's solutions, respectively. In the case of Benedict's solution, OH^- is obtained when CO_3^{2-} reversibly reacts with H_2O as follows:

$$CO_3^{2-} + H_2O \rightarrow HCO_3^- + OH^-$$

$$2Cu^{2+} + 2OH^- + 2e^- \rightarrow Cu_2O + H_2O \quad \text{..............................} (1)$$

$$RCHO + 3OH^- \rightarrow RCOO^- + 2H_2O + 2e^- \quad \text{...............................} (2)$$

(1) + (2) gives the overall chemical equation for the oxidation of the alkanal

$RCHO + 5OH^- + 2Cu^{2+} \rightarrow RCOO^- + 3H_2O + Cu_2O\ (red\ ppt)$

Only reducing sugars (aldoses) like D-glucose can be positive to Tollens', Fehling's and Benedict's tests. But it was observed that Fructose, a non-reducing sugar gives positive Tollens' test. This was made possible because a base catalyzed equilibrium takes place between glucose, mannose and fructose. The alkaline nature of this reagent provides this base catalyst and the rearrangement is called ***Lobry de Bruyn-Van Ekenstein rearrangment***. The mechanism for the conversation is given by the following chemical equations (Figure 1.21).

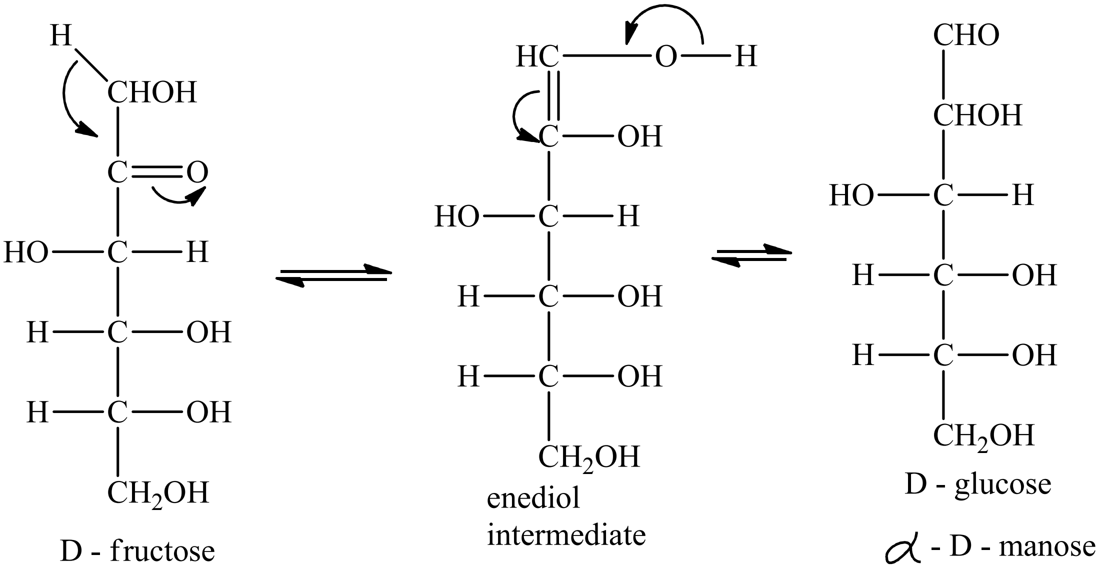


Figure 1.21: The base catalyzed equilibrium between glucose, mannose and fructose

1.3.5 *Reaction with hydrogen cyanide (HCN)*

Hydrogen cyanide reacts with reducing sugars the same way it reacts with alkanals (aldehydes) by attacking the carbonyl carbon to give a hydroxynitrile compound. An example of this reaction is given below (Figure 1.22):

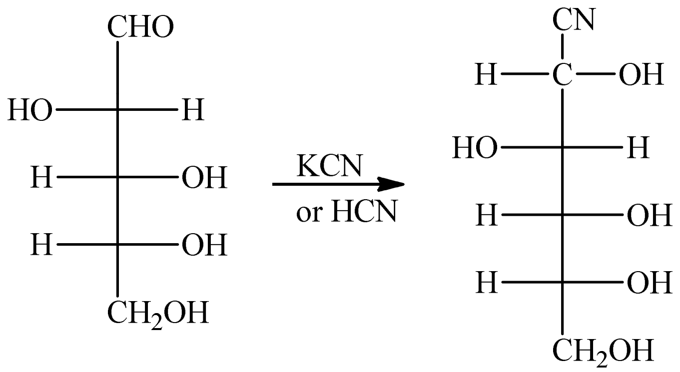


Figure 1.22: Reaction of reducing sugar with Cyanide to form hydroxynitrile compound

It should be noted that hydrogen cyanide is extremely poisonous gas; hence, it is not used directly. The aldehyde / ketone is reacted with a solution of sodium or potassium salt of cyanide in water along with little sulphuric acid to give a solution with a pH of between 4 and 5.

The Mechanisms of the Reaction

The mechanism is through nucleophilic addition. The mechanism is given below (Figure 1.23):

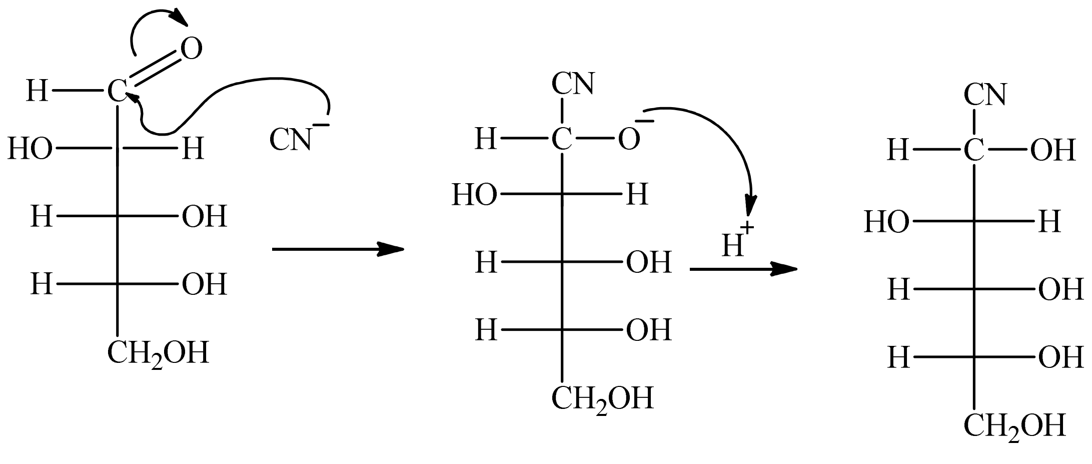


Figure 1.23: Mechanism for the reaction of reducing sugar with Cyanide

A typical example of this reaction is the reaction of D-arabinose with the solution of sodium cyanide given below. The reaction is called ***cyanohydrin***. This reaction is also used in carbohydrate synthesis for increasing the chain length of a sugar by one carbon for example the mixture of D-glucose and D-mannose from D-arabonise (Figure 1.24).

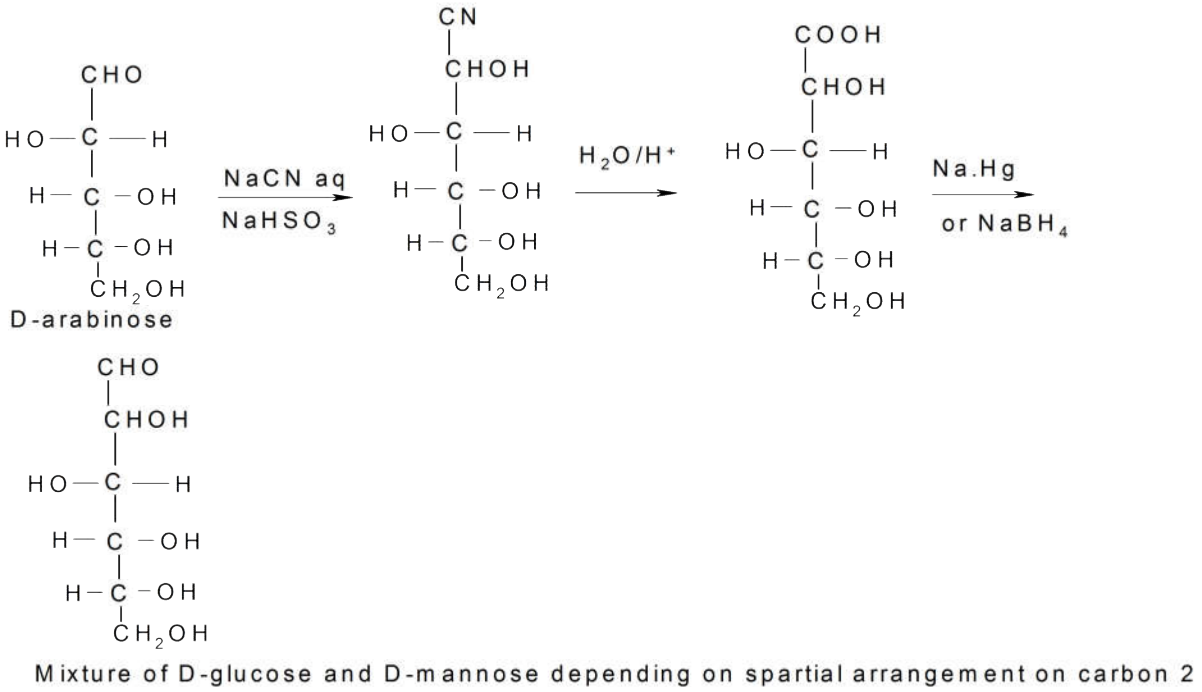


Figure 1.24: Synthesis of D-glucose and D-mannose from D-arabinose

1.3.6 *Ruff Degradation*

Ruff degradation is a method used for reducing the chain length of a carbohydrate by one carbon. In this method, the sugar to be shortened is first converted to gluconic acid using bromine water followed by decarboxylation (removal of CO_2) using ferric salt. Example is the conversion of D-glucose to D-arabinose (Figure 1.25)

Questions

1. Show using a suitable chemical equations how D-fructose forms hemiacetal.
2. Draw the structures of the following sugars: (a) D-ribose, (b) D–arabinose (c) D-mannose and (d) D-galactose.

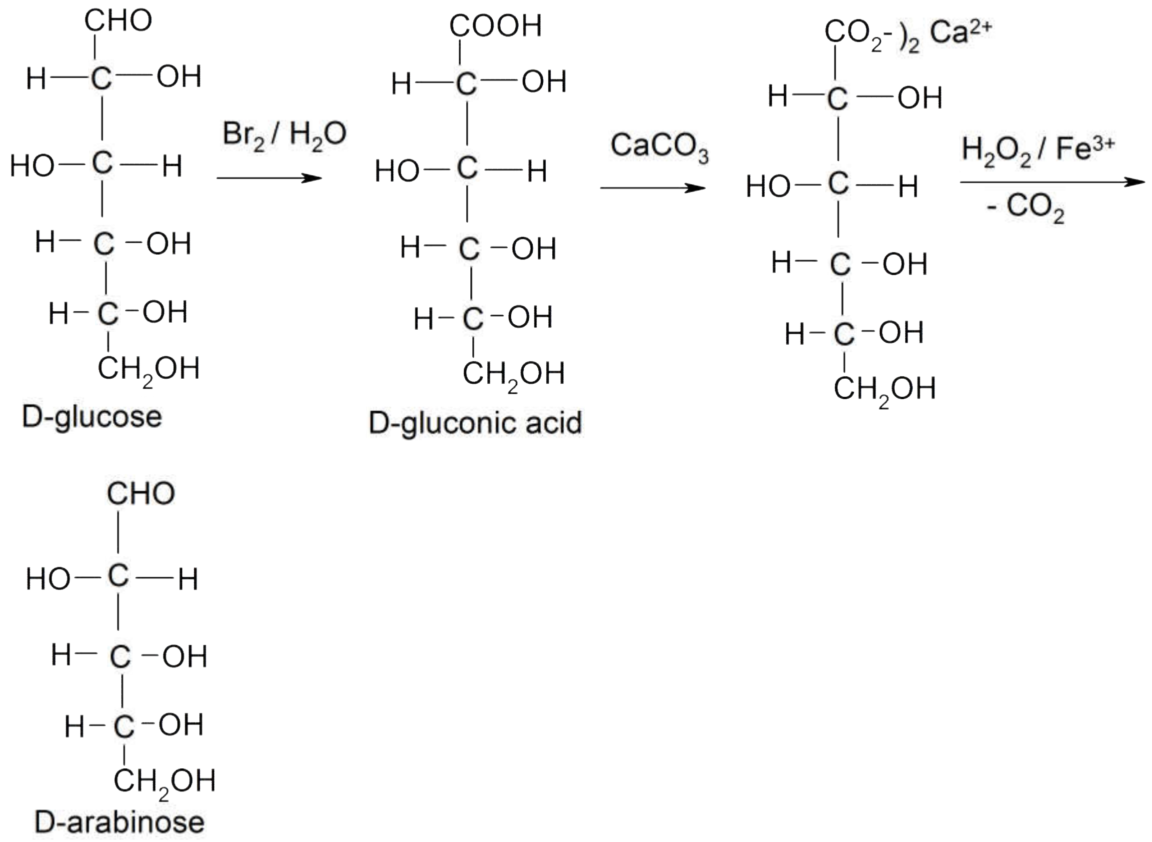


Figure: 1.25: Ruff degradation reaction for converting D-glucose to D-arabinose

1.3.7 Periodic acid oxidation

This is another method for determining the ring size of glycosides. It proceeds stoichiometrically and is a measure of the number of adjacent free hydroxyl groups. In this method, the moles of periodic acid (or sodium metaperiodate) consumed and the moles of formaldehyde and formic acid produced during the oxidation of a known weight of the saccharide under investigation are determined. One mole of the oxidant is reduced (consumed when two adjacent OH groups are oxidized with cleavage of the C-C bond joining them to yield two aldehyde groups. Terminal hydroxyl group yields formaldehyde while secondary hydroxyl group yields another aldehyde or form C acid if the 2^{0-} hydroxyl group is flanked on both sides by hydroxy groups (i.e. is oxidized twice). From the results, it is possible to determine the number and type (1^0 or z^0) of adjacent hydroxyl groups present in a molecule. The general reactions are given below (Figures 2.6 A to F)

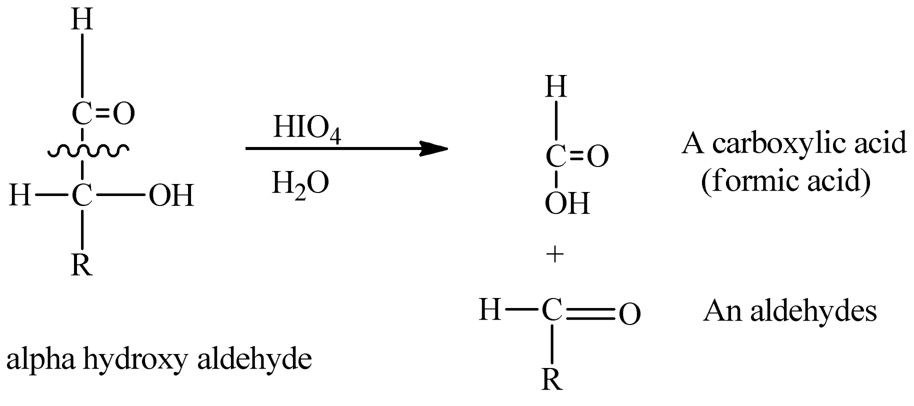


Figure 2.6 A

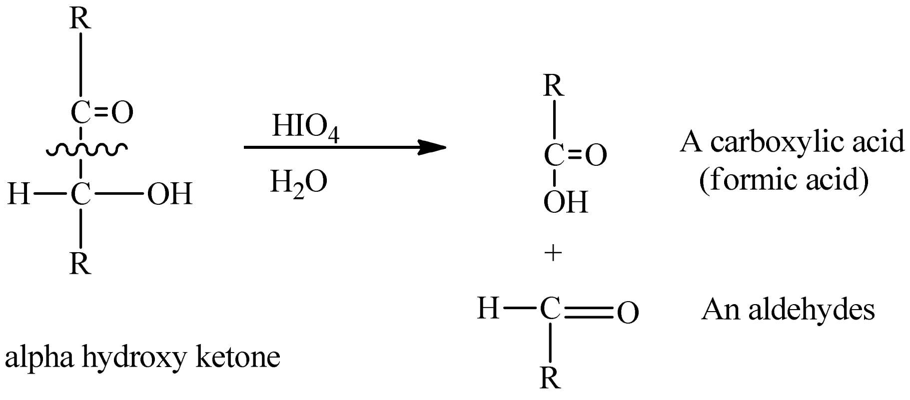


Figure 2.6 B

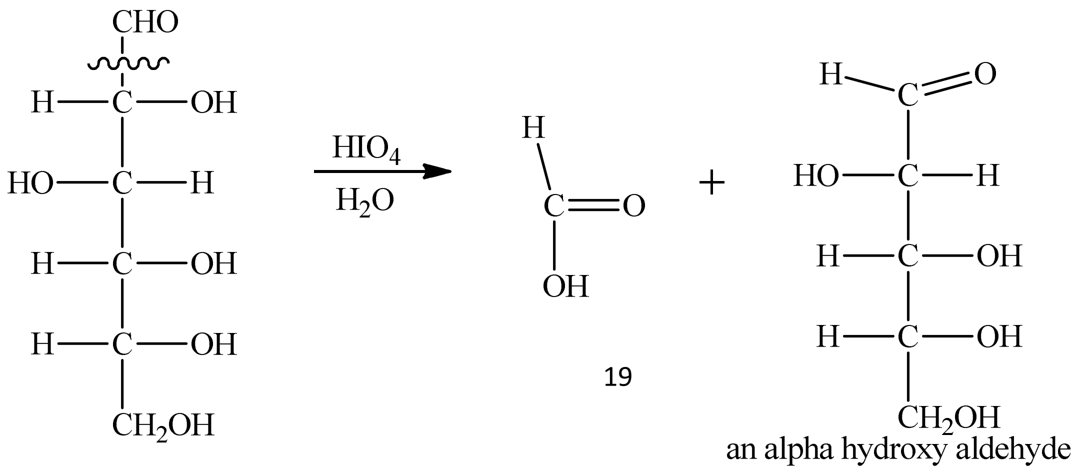


Figure 2.6 C

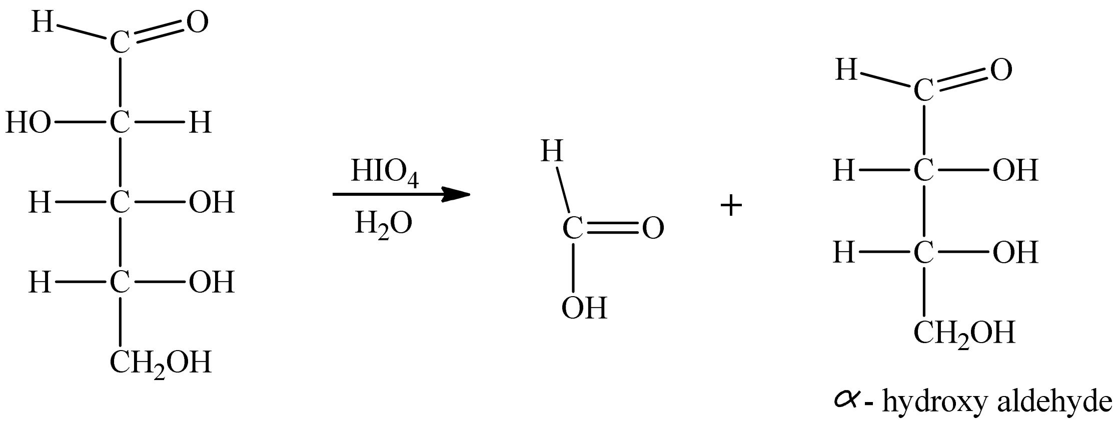


Figure 2.6 D

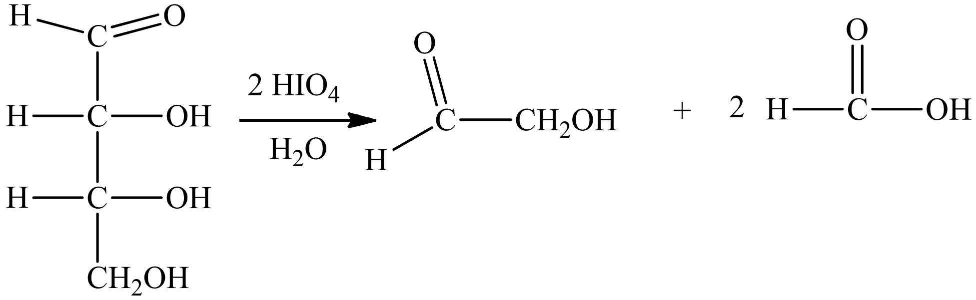


Figure 2.6 E

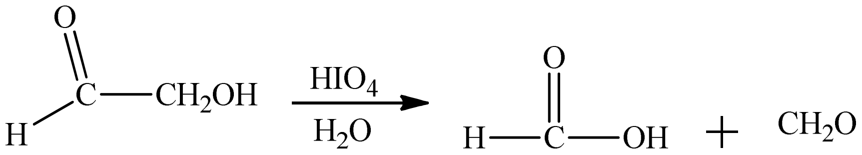


Figure 2.6 F

When all the steps are added up glucose will produce five times as much methanoic acid as methanal.

This type of degradation has played a vital role in understanding the structures of many carbohydrates. The degradation of α-D-glucopyranose by periodic acid is given below (Figure 2.7).

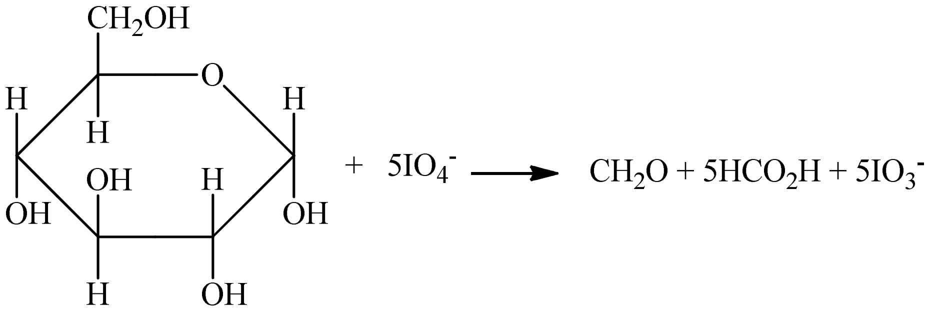
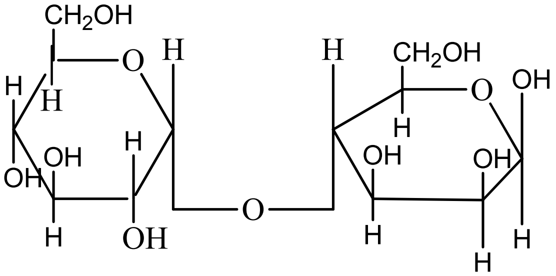


Figure 2.7: The degradation of Alpha - D - glucopyranose by periodic acid

1.4 *Disaccharides*

According to the name, they all consist of two simple sugars held together by ***a glycosidic bond***. Like monosaccharides, disaccharides are also simple sugars which are water soluble. Some typical examples of disaccharide are maltose, sucrose, lactose, cellobiose, getiobiose etc.

They have two simple sugars held together by a glycosidic bond. The most common involves the anomeric carbon of one sugar and non – anomeric carbon of the other (Compound Y)..



Y

MALTOSE

β – Maltose carries the impressive systematic name O – α – glucopyranosyl – (1,4) – β – D – glucopyranose. The disaccharide contains two latent carbonyl carbons. The one in the ring at the upper left is tied up in the glycosidic linkage. The other is in the ring at the lower right and is still a hemiacetal. The position of the free hemiacetal hydroxy group determines if it is β or α, which must appear in any name of the compound.

See the structure given in the class

Note, the structure of maltose is compound Y above.

Cellobiose and Gentiobiose

These are disaccharides that contains β – D glucopyranose bonded to a second β – D glucopyranose residue via a glycosidic bond. Cellobiose possesses a glycosidic bond between C1 and C4 of two simple sugars, while gentiobiose has a glycosidic between C1 and C6 of two simple sugars.

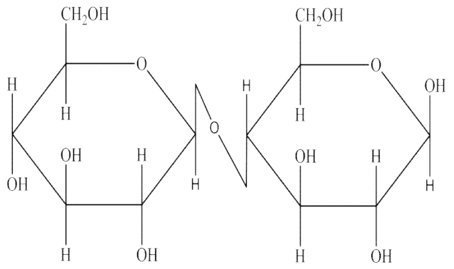


Figure 3.4: β - D - glucopyranosyl-1,4β- D - glucopyranose(β - Cellobiose)

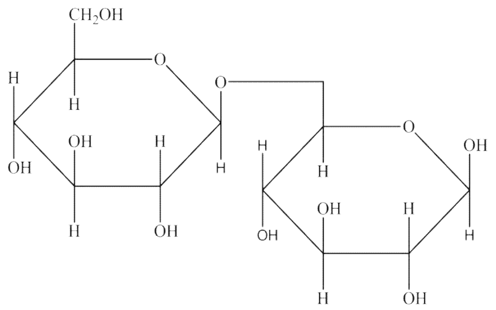
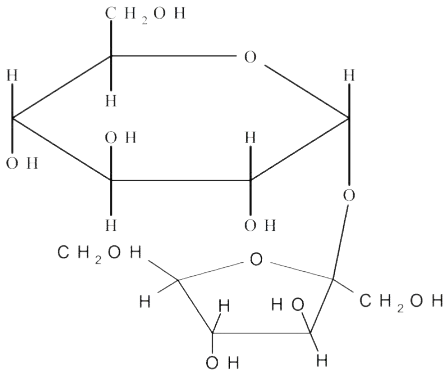


Figure 3.5: β - D - glucopyranosyl-1,6β- D - glucopyranose(β - Gentiobiose)

SUCROSE

The alternative names of sucrose are cane sugar or beet sugar. It is the common table sugar, o – α – D – glucopyranosyl – (1,2) – β – D – fructofuranoside. This sugar is different from other disaccharides, thus, far studied because its glycoside linkage involves the anomeric centre of both sugars.



Alpha-D-glucophyranosyl-1,2-beta-D-fructofuranoside [Sucrose]

Sucrose, unlike maltose, Lactose, Cellobiose, and gentiobiose, doesn't exist as readily – inter – converted α and β – forms.

The fructose position of the name ends in "oside" in order to indicate that C2 of fructose is involved in the glycoside bond,

Because both anomeric carbons are involved in acetal formation, sucrose is a non-reducing sugar. It is negative to Tollen's reagent and Fehling's solution or Benedict's solution. Moreover, sucrose does not form an osazone, does not exist on anomeric forms and does not show mutarotation in solution. All these facts indicate that sucrose does not contain a "free" aldehyde or ketone group. When sucrose is hydrolysed by dilute aqueous acid or enzyme invertase (from yeast), equal amounts of α – D glucopyranose and β - D – fructofuranose are produced.

POLYSACCHARIDES

Polysaccharides are polymers containing as many as several thousands monosaccharide unit per molecule. As with other saccharides, it is important to know the following:

(a) Which specific monomer are involved in the polymer formation
(b) The method of linkage between the monomer
(c) The gross structure of the polymer.

If the polymer contains more than one type of monosaccharides, then the sequence of the sugars is also important.

Of all the naturally occurring polysaccharides, starch and cellulose are the most important. Both are products of photosynthesis. Cellulose play a tremendous role in our society. As wood, cellulose provides shelter, as pulp, it is the major constituent of cotton which is a natural fibre. Starch is the mainstay of many diets since it is the major compound in rice, potatoes, wheat and corn.

STARCH

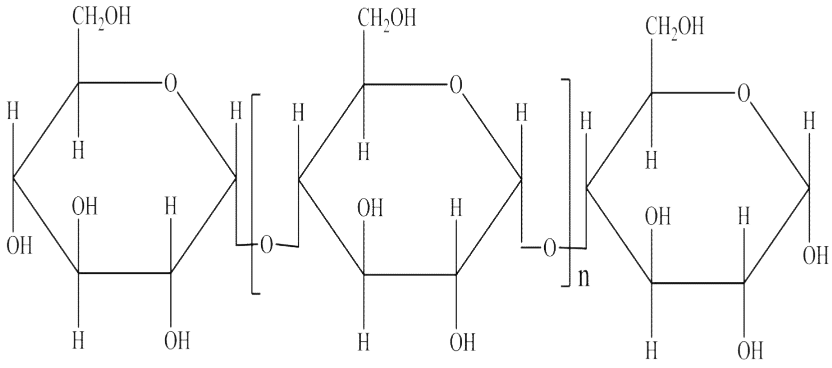
This is the major source of energy in plant cells. When intact, starch granules are insoluble in cold water; if the outer membrane has been broken by grinding, the granules swell in cold water and for a gel. When the intact granule is treated with warm water, a soluble portion of the starch diffuse through the granule wall, in hot water the granules swell and then burst

Starch contains two major fractions: amylose ($\approx 20\%$) and amylopectin ($\approx 80\%$). Both can be hydrolysed in acidic medium to give on D – glucose, since both polymer contains the same monomer, the important differences between them must exist in the bonding within these polymers.

AMYLOSE

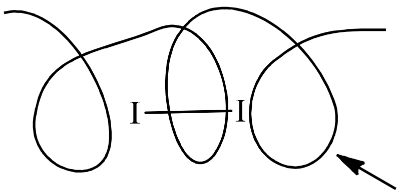
Maltose is the only disaccharide produced upon hydrolysis of amylose. The absence of cellobiose suggests that amylose is a linear polymer of D – glucose molecule, each bonded by an α – glycosidic linkage to C 4 of the adjacent glucose unit. If cellobiose had been produced, the β – glycosidic linkage would have been produced.

Amylose then is believed to be made up of long chains, each containing 1000 or more α – D glucopyranose units joined together by α – linkage as in maltose.



Amylose

α – Amylose is the fraction of starch that gives the intense blue colour with iodine. X – ray analysis shows that the chain coiled in the form of helix (spiral staircase) inside which is just enough to accommodate iodine molecule; the blue colour is due to entrapped iodine molecules.



Blue amylose iodine complex

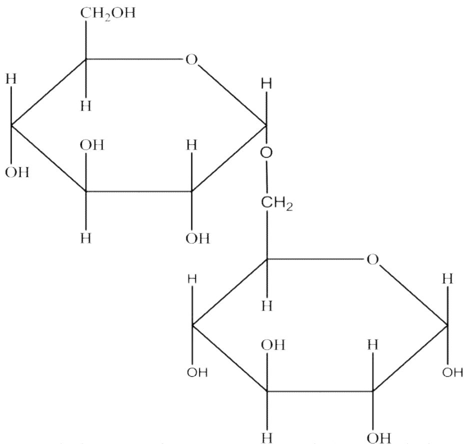
amylose chain

AMYLOPECTIN

Amylopectin is a branched polymer containing about 1000 D – glucose units. The main chain consists of an α – 1, 4 – D glycosidic linkage while branching occurs with an α – 1, 6 – D glycosidic bond. Branching is moderate with perhaps twenty five α – D glucopyranose units occurring between branching points.

The partial hydrolysis of amylopectin produces large molecules called dextrins. Dextrins are used to prepare mucilage, pastes and fabric sizing. (sizes are materials used to fill pores in cloth, paper; etc.). printing inks is often thickened by the addition of dextrins.

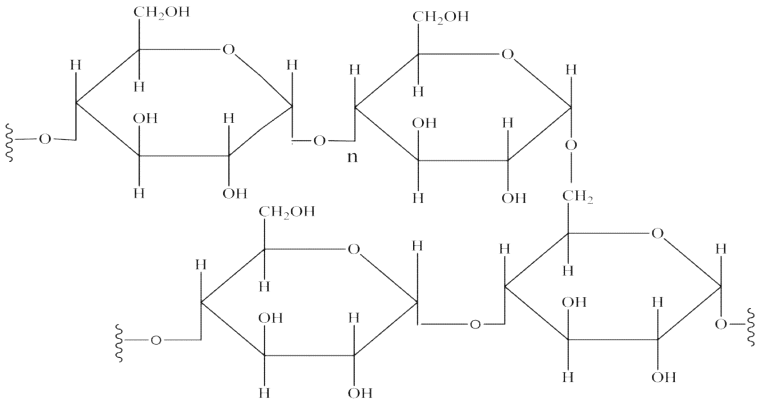
The major disaccharide produced by the hydrolysis of amylopectin is maltose, the glucose unit at each point has C – 1 and C – 6 – OH groups involved in glycosidic linkages. This leads to small amount of isomaltose upon hydrolysis.



Alpha-D-glucopyranosyl-(1,6)-alpha-D-glucopyranose (Alpha Isomaltose)

Structure of amylopectin

Amylopectin is hydrolysed to a single disaccharide maltose; the sequence of methylation and hydrolysis yields chiefly 2,3,6 – tri – o – methyl – D – glucose. Like amylose, amylopectin is made up of chains of α – D glucopyranose units, each unit joined by alpha – glucosidic linkage to C – 4 of the next one. However, its structure is more complex than that of amylose.

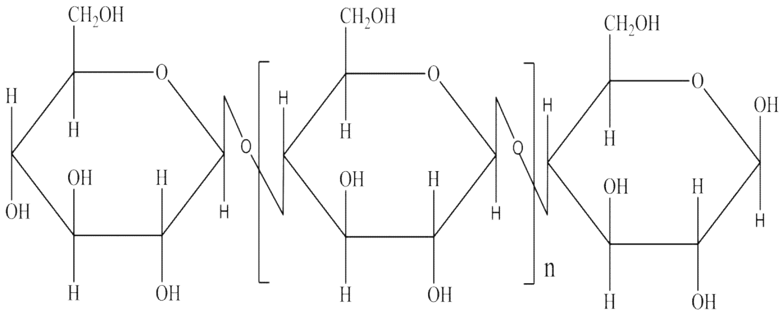


Amylopectin

CELLULOSE

Cellulose is an unbranched polymer of β – D – glucose which occurs in most plants. Most animals, including man and cattle, cannot hydrolyse the β – glycosidic link in cellulose

Cotton which is the most important natural fibre, is about 98% cellulose. Acetal linkage in cellulose are hydrolysed by acids but not by bases.



β-Cellulose

PROTEINS

Proteins are naturally occurring Polymers formed by condensation ~~of polymers~~ of α-amino acids. Hydrolysis of proteins with acids, bases or enzymes produces a mixture of α-amino acids. In proteins the amino acid units are linked by peptide linkages (–CO–NH–).

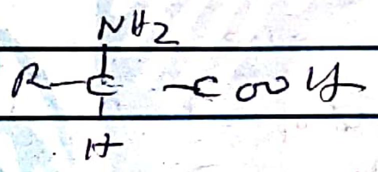
Amino acids

There are twenty three amino acids of general occurrence in all proteins.

Structures of amino acids

~~Some~~

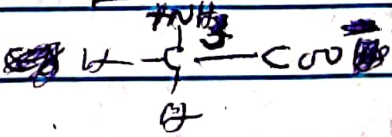
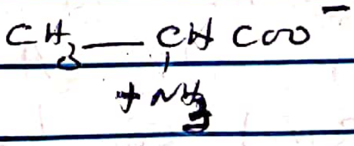
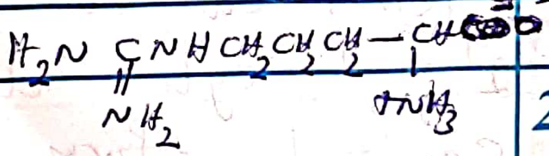
The general structure is given below:

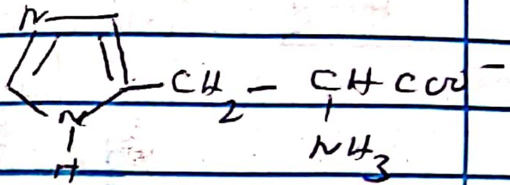
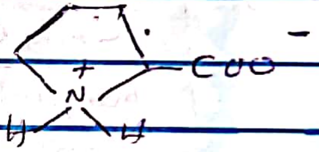
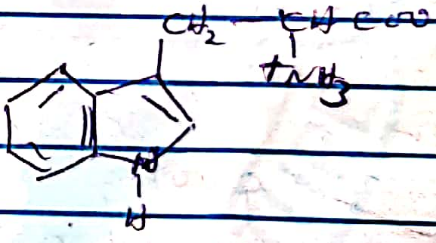


$$R-\overset{NH_2}{\underset{H}{C}}-COOH$$

~~Some of these~~

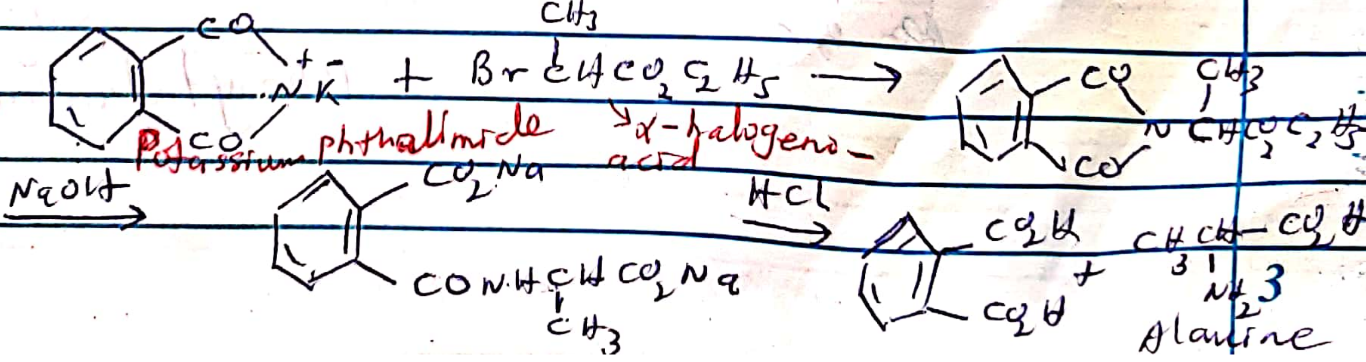
The structures of some of these amino acids are given below:

	Name	Abbreviation	Formula
1	Glycine	Gly (G)	 $H-\overset{{}^{+}NH_3}{\underset{H}{C}}-COO^-$
2	Alanine	Ala (A)	 $CH_3-\underset{{}^{+}NH_3}{CH}COO^-$
3	Arginine	Arg (R)	 $H_2N\underset{\overset{\|}{NH_2}}{C}NHCH_2CH_2CH_2-\underset{{}^{+}NH_3}{CH}COO^-$

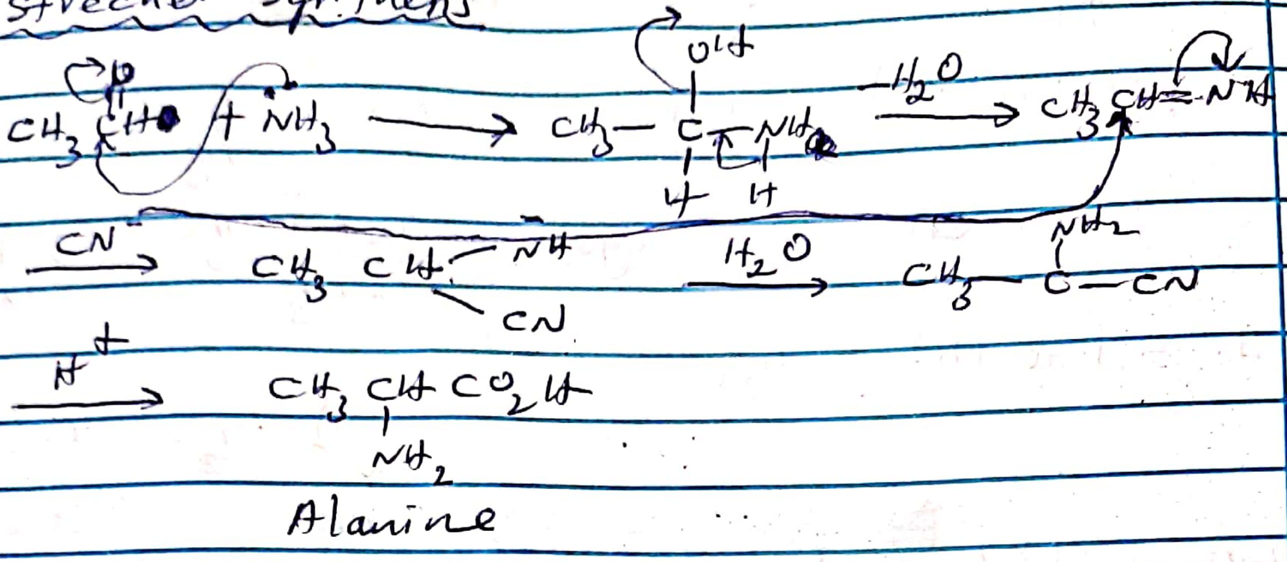
	Name	Abbr.	Formula
4	Aspartic acid (D)	Asp	$HOOCCH_2-\underset{+NH_3}{CH}COO^-$
5	Cysteine (C)	Cys	$HSCH_2-\underset{NH_3}{CH}COO^-$
6	Cystine	Cys - Cys	$OOC\underset{+NH_3}{CH}CH_2S-SCH_2-\underset{+NH_3}{CH}COO^-$
7	Histidine (H)	His	
8	Lysine (K)	Lys	$H_3\overset{+}{N}-(CH_2)_4-\underset{+NH_3}{CH}COO^-$
9	Methionine (M)	Met	$CH_3SCH_2CH_2-\underset{+NH_3}{CH}COO^-$
10	Proline (P)	Pro	
11	Tryptophan (W)	Try	

Preparation of Amino Acids

(I) Gabriel's Phthalimide Synthesis



(ii) strecker Synthesis



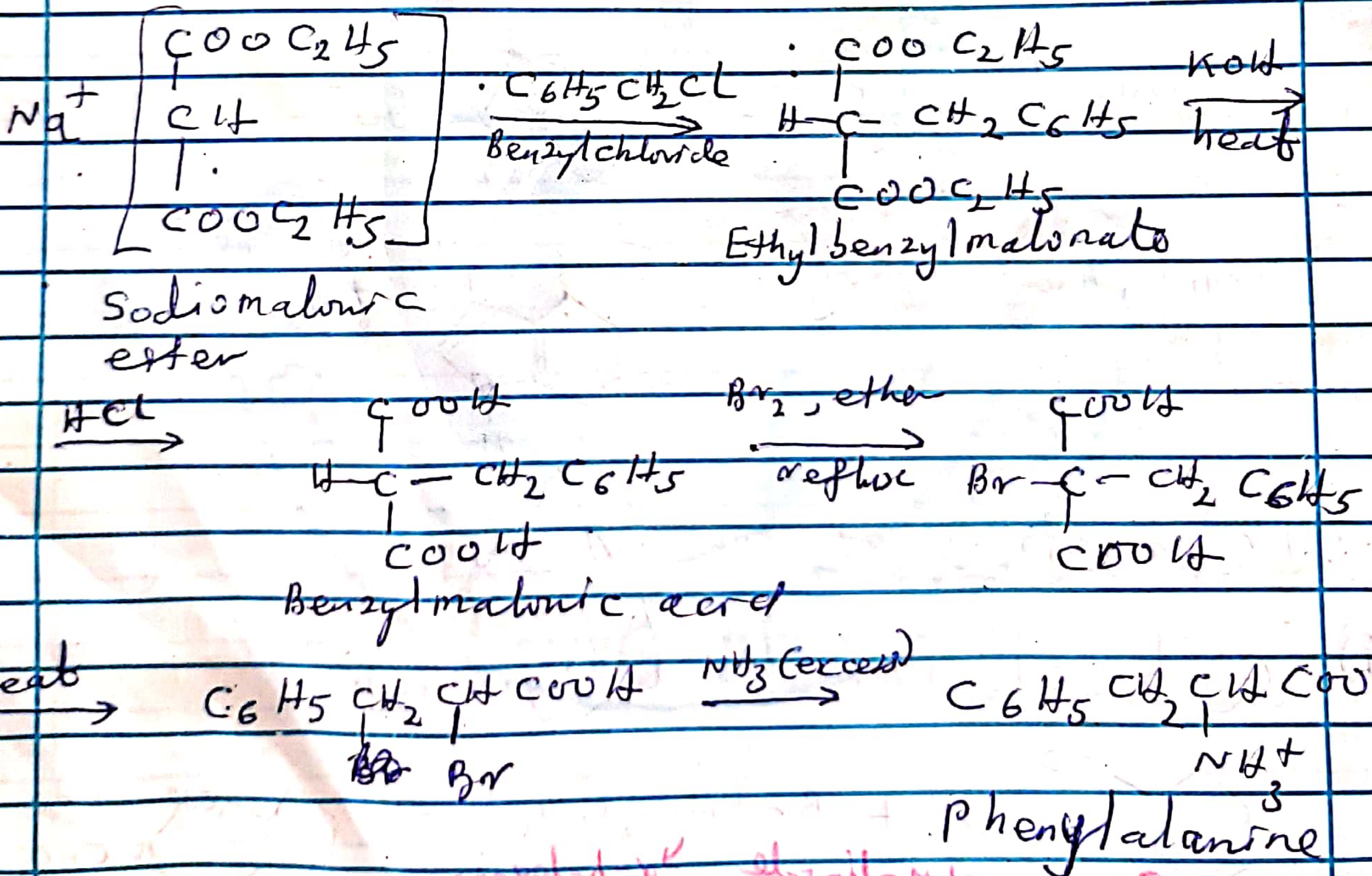
$CH_3CHO + NH_3 \longrightarrow CH_3-\overset{OH}{\underset{H}{C}}-\underset{H}{N}H \xrightarrow{-H_2O} CH_3CH=NH$

$\xrightarrow{CN^-} CH_3CH\begin{smallmatrix}NH\\CN\end{smallmatrix} \xrightarrow{H_2O} CH_3-\overset{NH_2}{C}-CN$

$\xrightarrow{H^+} CH_3\underset{NH_2}{CH}CO_2H$

Alanine

(iii) Malonic ester Synthesis of Amino Acids



$Na^+\left[\begin{smallmatrix}COOC_2H_5\\CH\\COOC_2H_5\end{smallmatrix}\right]^- \xrightarrow[\text{Benzylchloride}]{C_6H_5CH_2Cl} H-\underset{COOC_2H_5}{\overset{COOC_2H_5}{C}}-CH_2C_6H_5 \xrightarrow[\text{heat}]{KOH}$

Sodiomalonic ester

Ethylbenzylmalonate

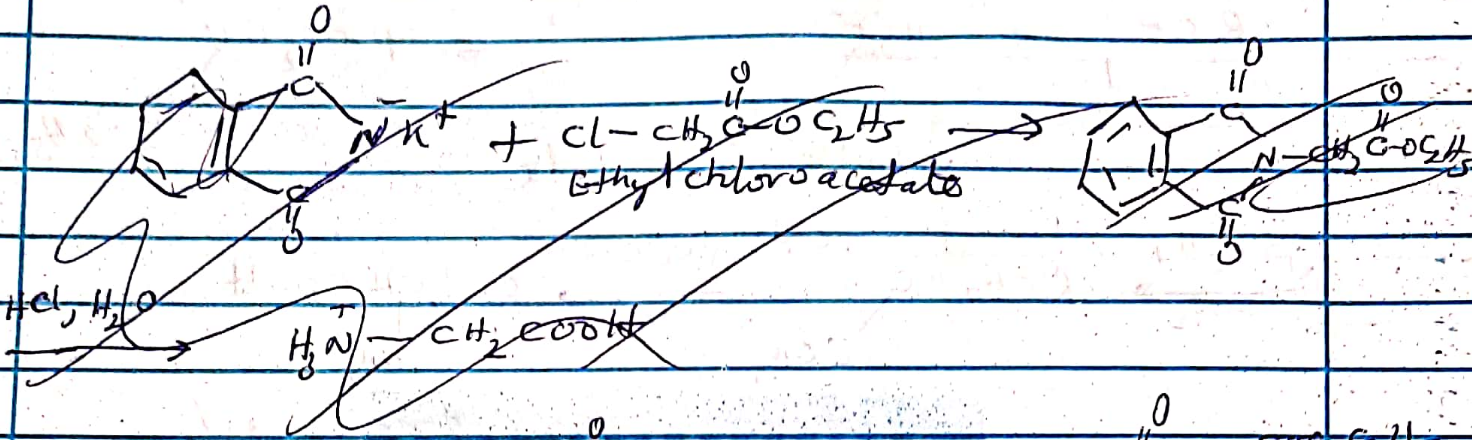
$\xrightarrow{HCl} H-\underset{COOH}{\overset{COOH}{C}}-CH_2C_6H_5 \xrightarrow[\text{reflux}]{Br_2,\ ether} Br-\underset{COOH}{\overset{COOH}{C}}-CH_2C_6H_5$

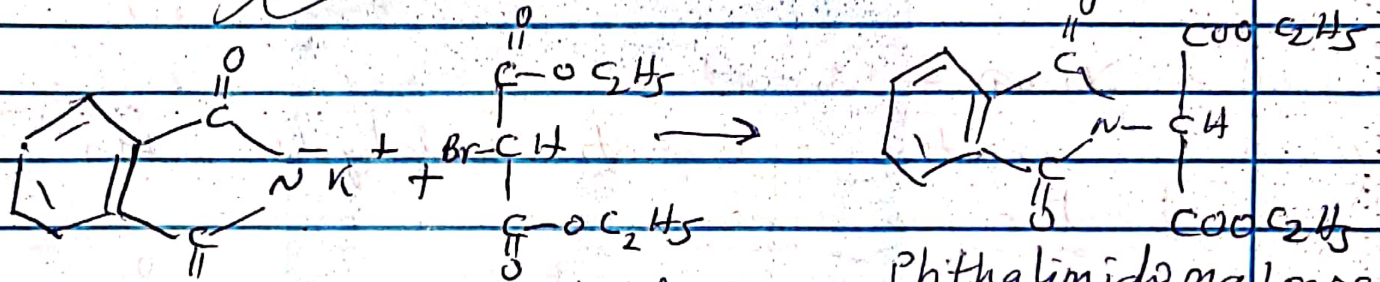
Benzylmalonic acid

$\xrightarrow{Heat} C_6H_5CH_2\underset{Br}{CH}COOH \xrightarrow{NH_3\ (excess)} C_6H_5CH_2\underset{NH_3^+}{CH}COO^-$

Phenylalanine

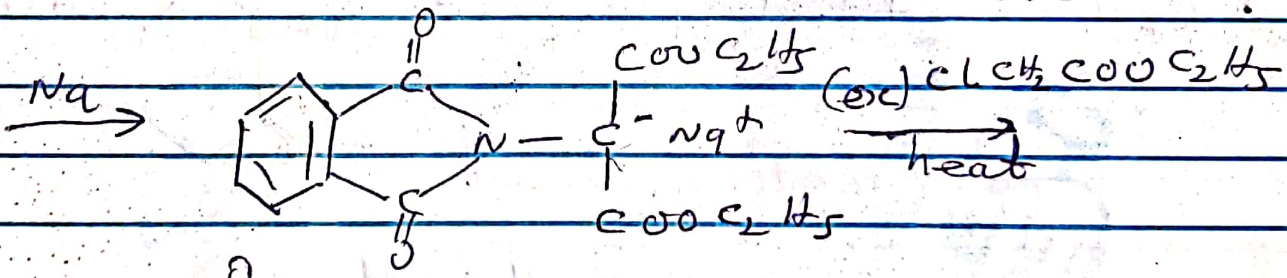
✓(IV) Synthesis of Aspartic acid (Gabriel phthalimide synthesis)

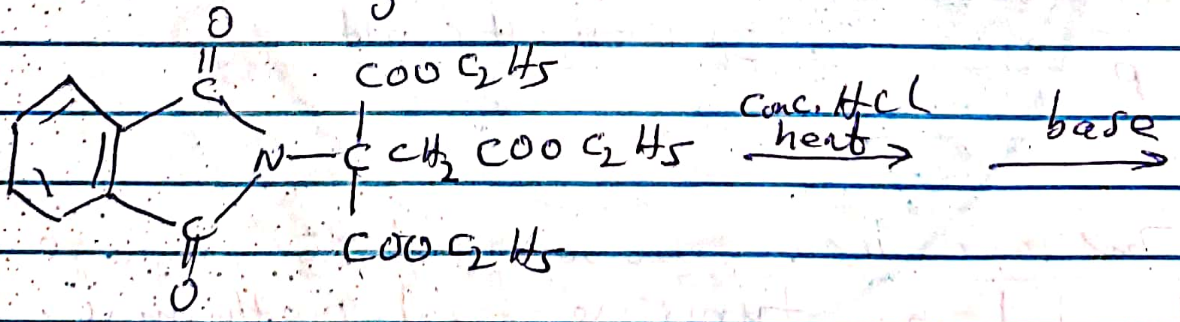


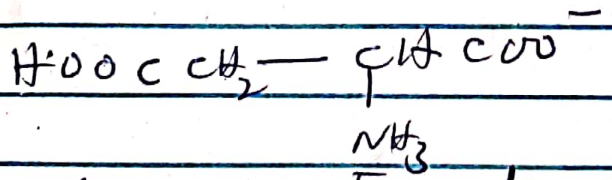


Bromomalonate

Phthalimidomalonic ester



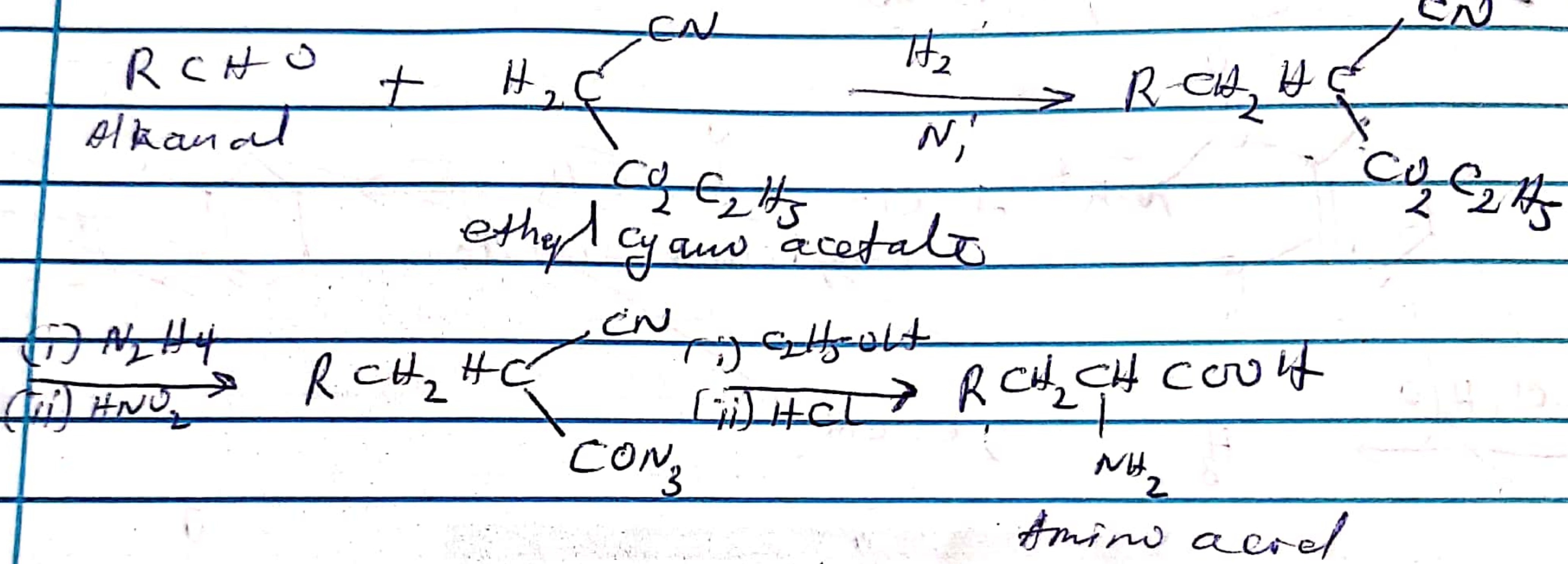




$$HOOC\,CH_2—\underset{\underset{\overset{+}{N}H_3}{|}}{C}H\,COO^-$$

Aspartic acid.

(v) Darapsky Synthesis



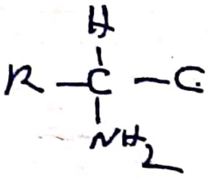
~~vi) Synthesis of Aromatic~~

Synthesis of amino acids

(2) Amination of α-Halo acid

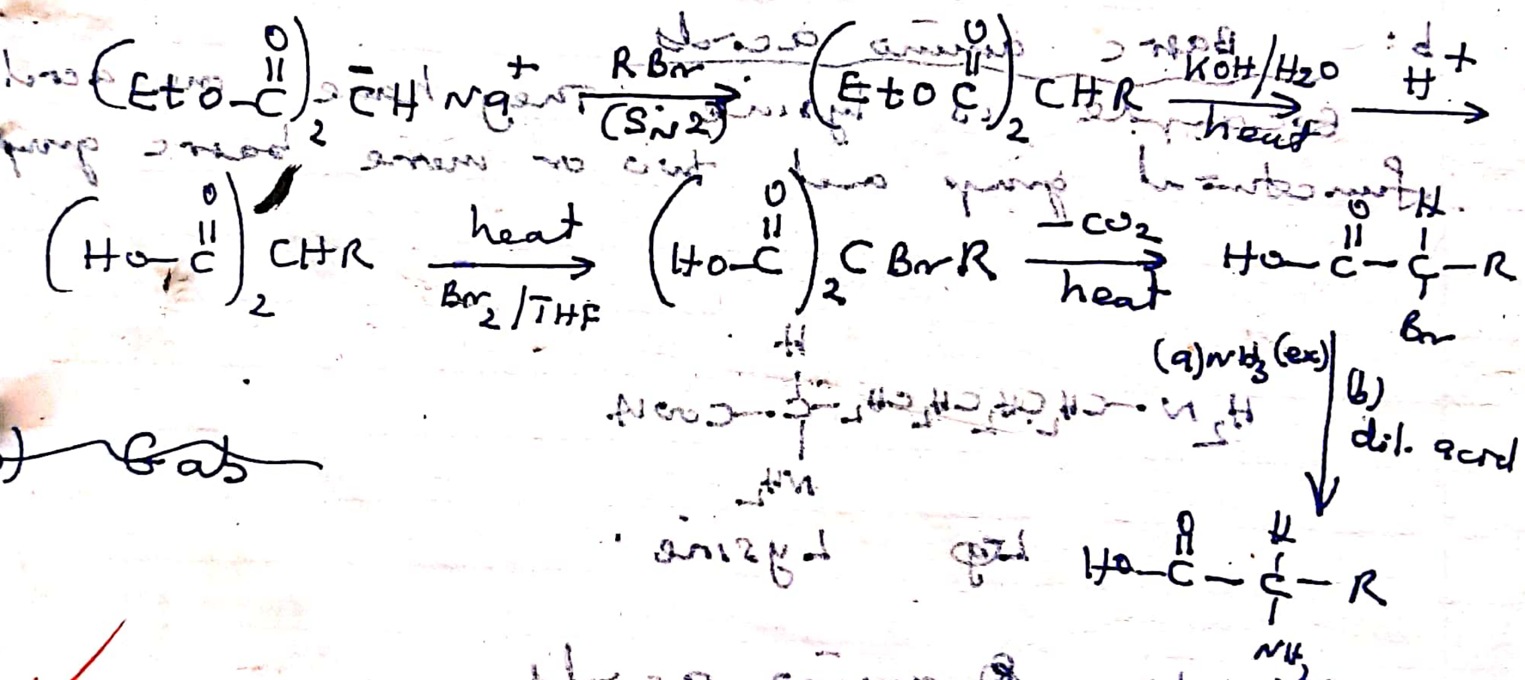
~~The halo acid is made by~~

$$RCH_2COOH + Br_2 \xrightarrow{PBr_3} RCHBrCOOH \xrightarrow[(b)\ dil.\ acid]{(a)\ NH_3\ (excess)}$$



$$R-\overset{H}{\underset{NH_2}{C}}-COOH$$

Bromination can also be accomplished using Malonic acid.



$$(EtO-\overset{O}{\overset{\|}{C}})_2\bar{C}H\ Na^+ \xrightarrow[(S_N2)]{RBr} (EtO\overset{O}{\overset{\|}{C}})_2CHR \xrightarrow[heat]{KOH/H_2O} \xrightarrow{H^+}$$

$$(HO-\overset{O}{\overset{\|}{C}})_2CHR \xrightarrow[Br_2/THF]{heat} (HO-\overset{O}{\overset{\|}{C}})_2CBrR \xrightarrow[heat]{-CO_2} HO-\overset{O}{\overset{\|}{C}}-\overset{H}{\underset{Br}{C}}-R$$

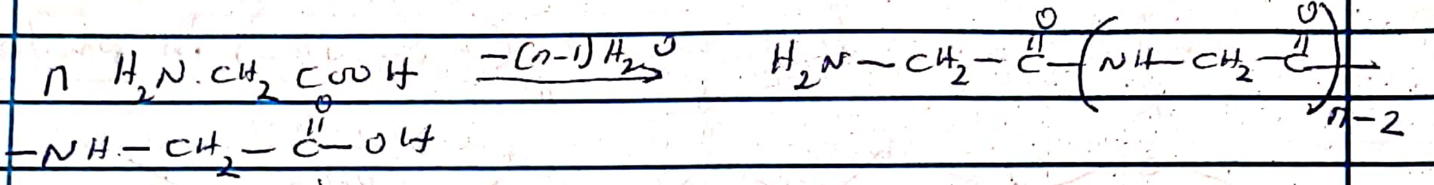
$$\xrightarrow[(b)\ dil.\ acid]{(a)\ NH_3\ (ex)} HO-\overset{O}{\overset{\|}{C}}-\overset{H}{\underset{NH_2}{C}}-R$$

~~(3) Gab~~

(4) Gabriel Synthesis

Peptides

When amino acids polymerized, they form polyamide. The polyamides derived from α-amino acids are called peptides or polypeptides.



$n\ H_2N.CH_2COOH \xrightarrow{-(n-1)H_2O} H_2N-CH_2-\overset{O}{\overset{\|}{C}}-\left(NH-CH_2-\overset{O}{\overset{\|}{C}}\right)_{n-2}-NH-CH_2-\overset{O}{\overset{\|}{C}}-OH$

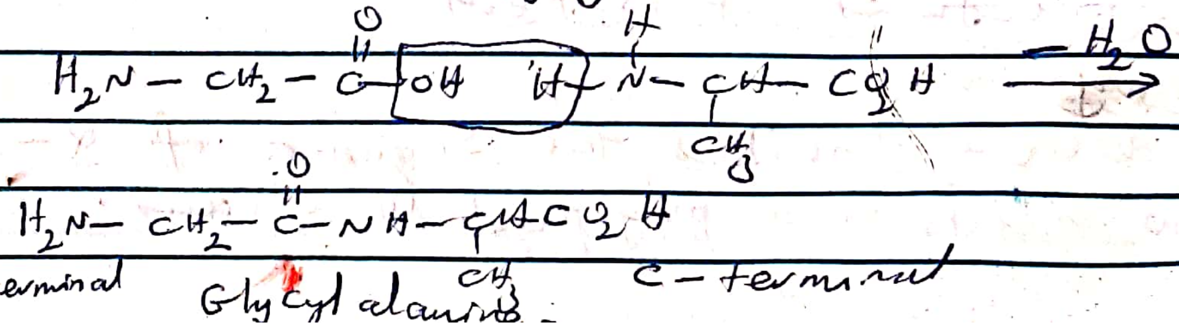
Polyglycine.

The amido linkage in the polymer is called peptide bond or peptide linkages.

In a heteropolyamide, the amino acid at the end of the polymer bearing a free NH_2- group is called the "N-terminal amino acid". The amino acid with free carboxyl group is called "C-terminal amino acid". Amino acid residue in a peptide are numbered starting from the N-terminal amino acid.

Polypeptides are named as derivatives of C-terminal amino acid, the N-terminal amino acid being listed first and the C-terminal last.

Example is glycylalanine

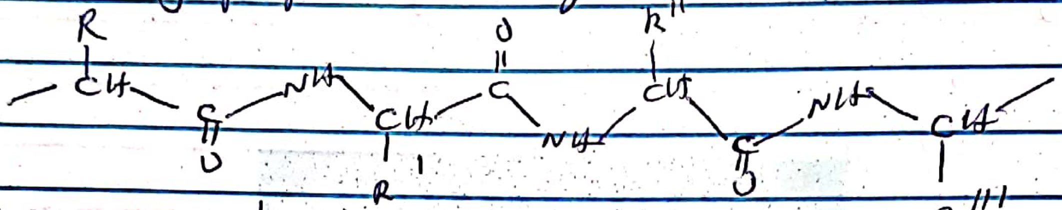


$H_2N-CH_2-\overset{O}{\overset{\|}{C}}-\boxed{OH\quad H}-\overset{H}{\overset{|}{N}}-\underset{CH_3}{\underset{|}{CH}}-CO_2H \xrightarrow{-H_2O} H_2N-CH_2-\overset{O}{\overset{\|}{C}}-NH-\underset{CH_3}{\underset{|}{CH}}CO_2H$

N-terminal Glycyl alanine C-terminal

PROTEINS

Proteins are the naturally occurring condensation polymers of α-amino acids. Hydrolysis of proteins with acids, bases or enzymes produces a mixture of α-amino acids. Amino acids units are ~~R~~ linked by peptide linkages $(-\overset{\|}{C}-NH-)$ in proteins.



where R, R', R'', etc can be either ~~by~~ Hydrogen or an organic group.

~~Structures of Proteins~~

Simple proteins can be divided into fibrous and globular proteins. Proteins with high intermolecular hydrogen bonding are fibrous and those with intramolecular hydrogen bonding are globular. The globular proteins become insoluble or denatured on heating. Examples are ~~the~~ egg albumins, globulins & glutelins while examples of fibrous proteins are silk, wool, hides and hooves.

glutelins

Structures of Protein

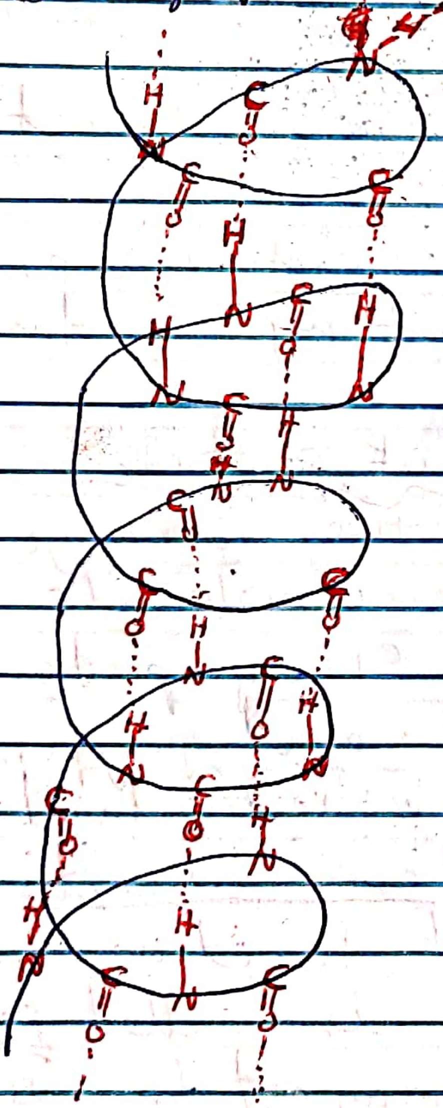
(i) Primary structure

This ~~describe~~ describes the sequence of α-amino acids in a polypeptide chain.

(ii) Secondary structure

~~It describes~~

It described its conformation or molecular shape. It has been proved that the polypeptide chains have helical conformations in their crystal lattices. The helices are stabilized by intramolecular hydrogen bonds involving $-NH\overset{O}{\overset{\|}{C}}-$ groups. The α– helix is ~~a~~ right handed.



α– Helix

(III) Tertiary structure

This term is used to describe the shape or folding resulting from the presence of Sulphur-sulphur cross-links between the polymer chains.

It is the three dimentional shape of a protein. The tertiary structure will have a single polypeptide chain backbone with one or more protein secondary structures, the protein domains.

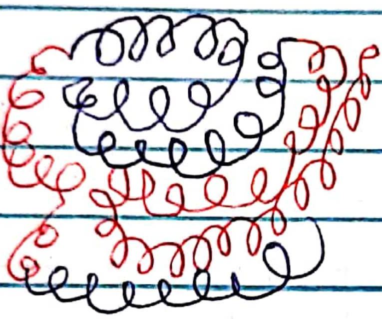
Amino acid side chains may interact and bond in a number of ways. The interactions and bonds of side chains within a particular protein determine its tertiary structure.

(IV) Quaternary structure of protein

Quaternary structure is the arrangement of more than one protein molecule in a multi-subunit complex. Many proteins are acutally comprised of several polypeptide chains. In this case, the individual peptide chains are called protein subunits, and each unit ~~cannot~~ cannot function on its own. These sub-units are also called protomers. These subunits may or may not be identical, and when they are held together by hydrogen bonds, they may be separated by e.g dissolving in water containing urea.

~~An example~~

The figure below is a ~~steech~~ sketch of the structure of quaternary proteins.



An example of a protein with quaternary structure is hemoglobin. In hemoglobin, one protein binds to oxygen while another binds carbon dioxide. This is how one protein can serve two functions. Another example is holoenzymes, proteins with several subunits. Each subunit of a holoenzyme has a different function. For example, one protein subunit may be the regulatory subunit. Another unit may be the catalytic subunit.

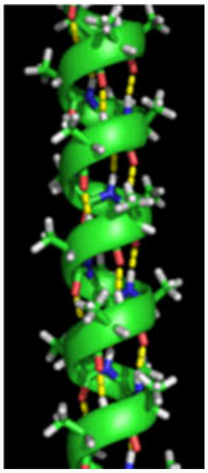
PROTEIN STRUCTURES

Protein primary structure is the linear sequence of amino acids in a peptide or protein. By convention, the primary structure of a protein is reported starting from the amino-terminal (N) end to the carboxyl-terminal (C) end. Protein biosynthesis is most commonly performed by ribosomes in cells. Peptides can also be synthesized in the laboratory.

Isomerisation

The chiral centers of a polypeptide chain can undergo racemization. Although it does not change the sequence, it does affect the chemical properties of the sequence. In particular, the L-amino acids normally found in proteins can spontaneously isomerize at the atom to form D-amino acids, which cannot be cleaved by most proteases. Additionally, proline can form stable trans-isomers at the peptide bond.

Secondary structure



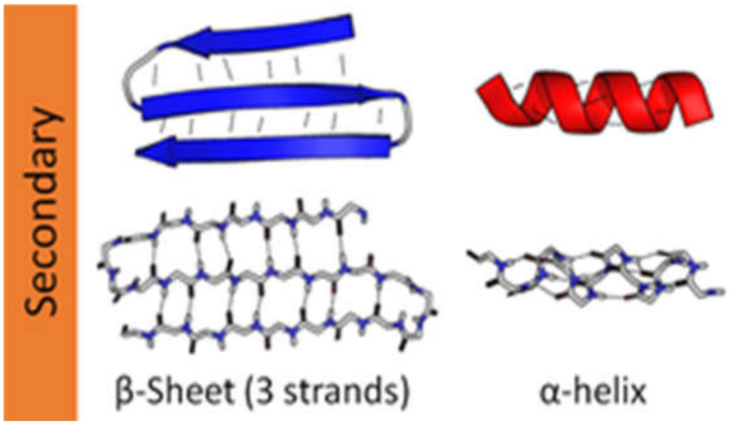
An α-helix with hydrogen bonds (yellow dots)

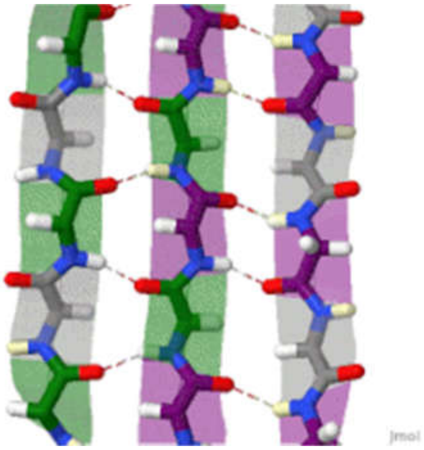
Secondary structure refers to highly regular local sub-structures on the actual polypeptide backbone chain. Two main types of secondary structure, the α-helix and the β-strand or β-sheets, were suggested in 1951 by Linus Pauling. These secondary structures are defined by patterns of hydrogen bonds between the main-chain peptide groups.

Secondary structure of protein refers to local folded structures that form within a polypeptide due to interactions between atoms of the backbone.

- The proteins do not exist in just simple chains of polypeptides.

- These polypeptide chains usually fold due to the interaction between the amine and carboxyl group of the peptide link.
- The structure refers to the shape in which a long polypeptide chain can exist.
- They are found to exist in two different types of structures α – helix and β – pleated sheet structures.
- This structure arises due to the regular folding of the backbone of the polypeptide chain due to hydrogen bonding between -CO group and -NH groups of the peptide bond.
- However, segments of the protein chain may acquire their own local fold, which is much simpler and usually takes the shape of a spiral an extended shape or a loop. These local folds are termed secondary elements and form the proteins secondary structure.





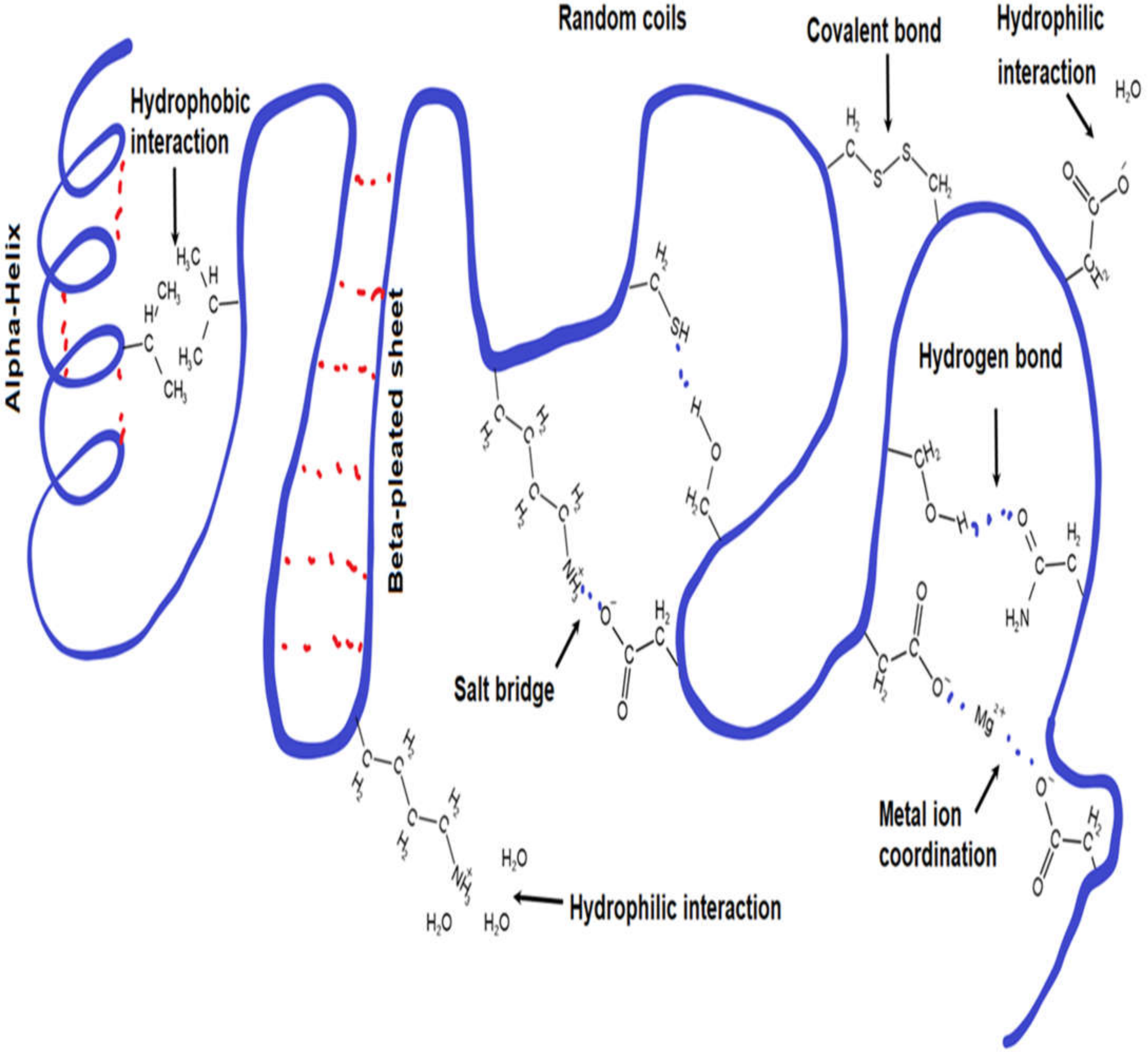
Three-dimensional structure of parts of a beta sheet in green fluorescent protein

Tertiary Structure of Protein

- This structure arises from further folding of the secondary structure of the protein.
- H-bonds, electrostatic forces, disulphide linkages, and Vander Waals forces stabilize this structure.
- The tertiary structure of proteins represents overall folding of the polypeptide chains, further folding of the secondary structure.
- It gives rise to two major molecular shapes called fibrous and globular.
- The main forces which stabilize the secondary and tertiary structures of proteins are hydrogen bonds, disulphide linkages, van der Waals and electrostatic forces of attraction.

The three-dimensional arrangement of all the atoms of a single polypeptide chain in space, held together by stabilizing interactions between groups on the side chains and between the side chain groups and the backbone groups is called the **tertiary structure of proteins**.

The stabilizing interactions involved in stabilizing the tertiary structure include disulfide linkage, salt bridge, coordinate bonds with metal ions, hydrogen bonding, and hydrophobic interaction, as shown in Fig. and explained below.



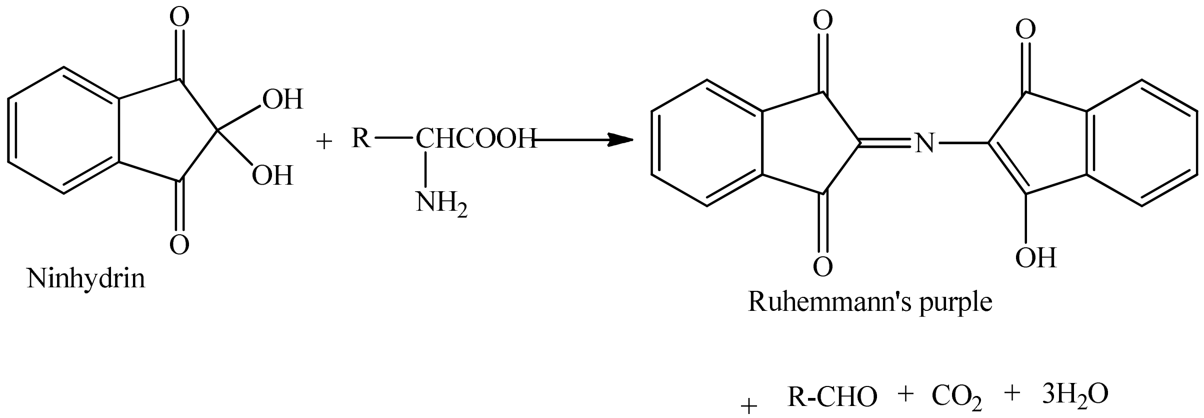
This figure illustration of disulfide linkage, salt bridge, coordinate bonds with metal ions, hydrogen bonding, and hydrophobic interaction that stabilize the tertiary structure of proteins.

Chemical reactions and interactions of Amino acids and proteins

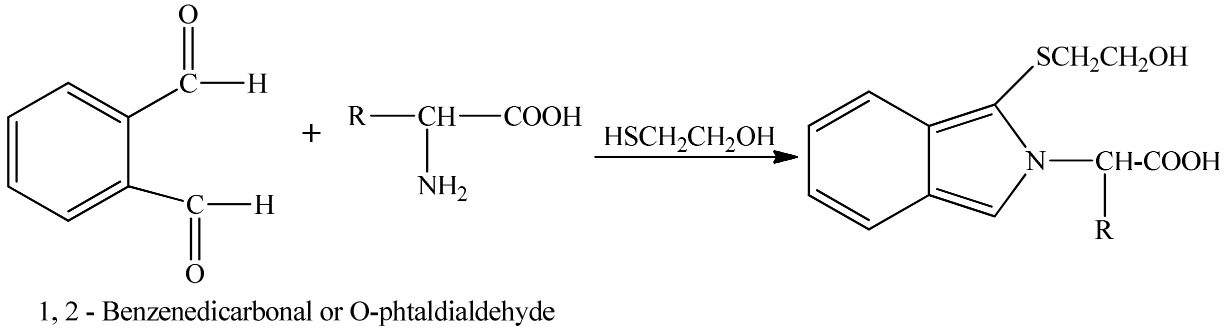
Reactions of various functional groups of amino acids and proteins are used for the chemical estimations.

(i) Reaction with ninhydrin(2,2,-D, hydroxyl-13-indasdione

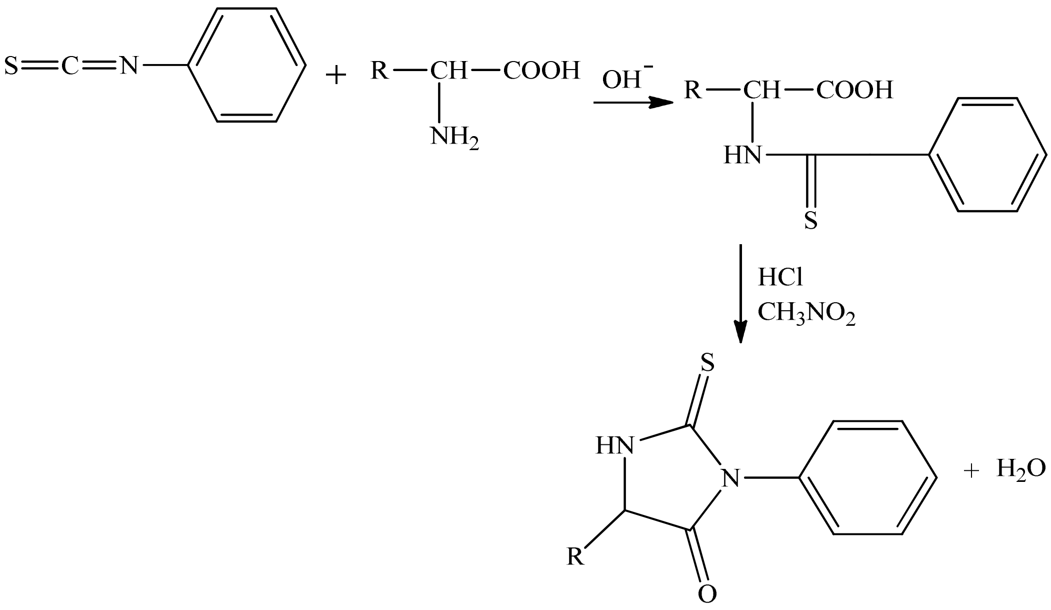
The reaction leads to the formation of coloured complex which is used for quantitative determination of amino acids.



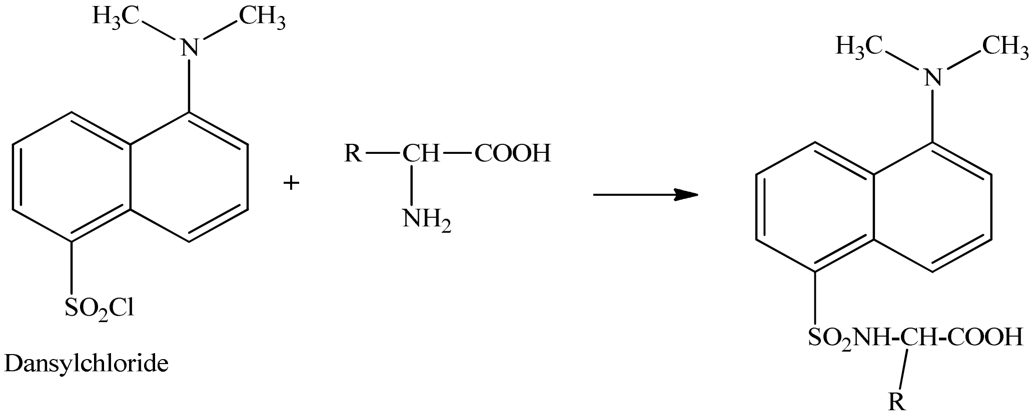
(ii) Reaction with 1,2- Benzene dicarbonal: 1,2- Benzene dicarbonal reacts with amino acids to give highly fluorescent isoindole derivatives.



(iii) Reaction with phenylisothiocyanate

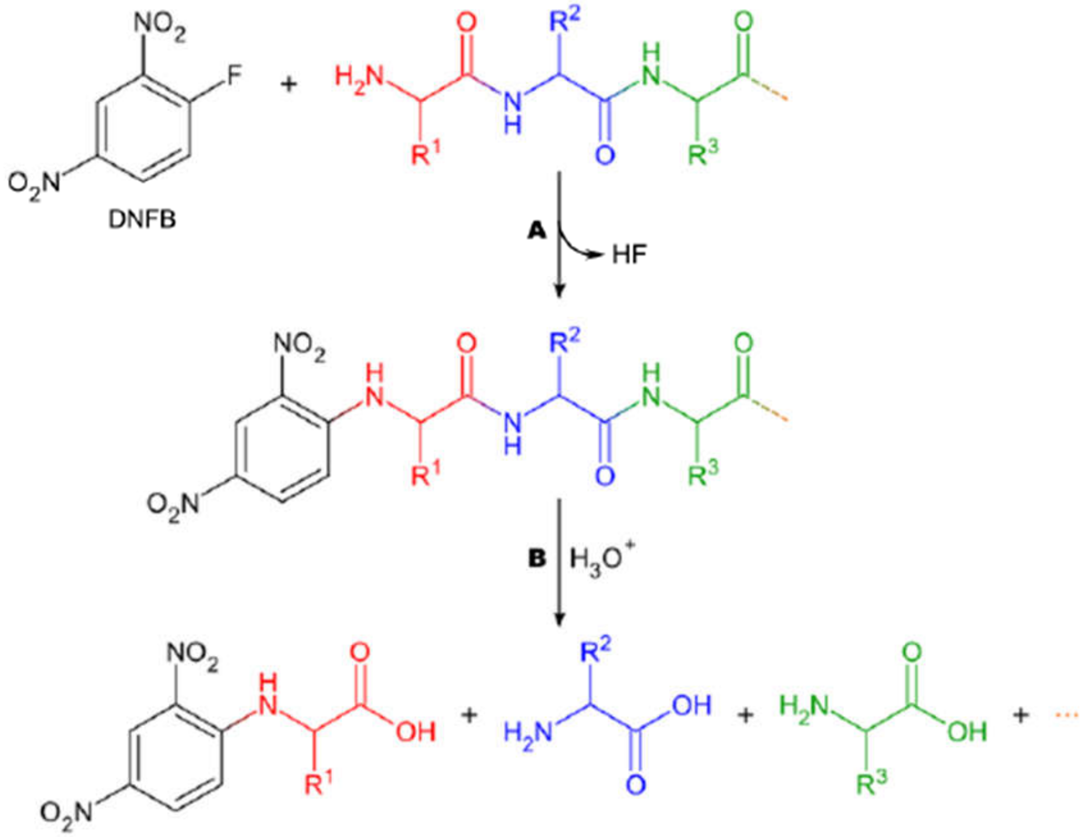


(iv) Reaction with Dansyl chloride (1, 1-Dimethy-aminonaphthalene-5-sulfonyl chloride)



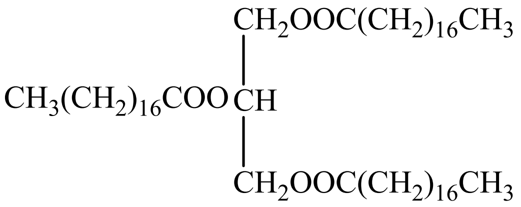
The following reactions are used for the N-terminal analysis of proteins:

A. Sanger's reagent, FDNB (fluorodinitrobenzene), modifies N-terminus for determination via amino acid analysis.



Acylglycerols

Neutral fats are mono -, di -, and triesters of glycerol with fatty acids, and are termed monoacylglycerol, diacylglycerol and triacylglycerols respectively. The use of old terms is discouraged



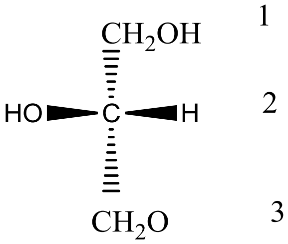
$$\begin{array}{rl} & CH_2OOC(CH_2)_{16}CH_3 \\ & | \\ CH_3(CH_2)_{16}COO & CH \\ & | \\ & CH_2OOC(CH_2)_{16}CH_3 \end{array}$$

It can be named any of the following:

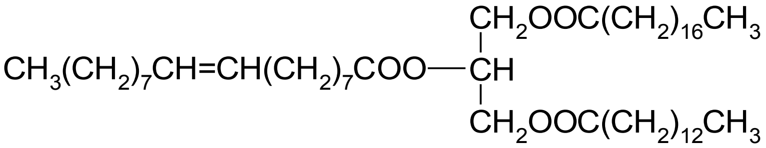
Tristearoylglycerol, glyceroltristearate, tristearin or St St St.

Stereospecific Number

The sn – system was proposed by Hiroschmann. The usual Fischer planar projection of glycerol is utilized with the middle hydroxyl group positioned on the left side of the central carbon. The carbon atoms are numbered 1 – 3 in the conventional top – to – bottom sequence.



For example, if stearic acid is esterified at sn – 1, oleic at sn – 2, and myristic at sn – 3, the acylglycerol would be



$$\begin{array}{rl} & CH_2OOC(CH_2)_{16}CH_3 \\ CH_3(CH_2)_7CH{=}CH(CH_2)_7COO— & CH \\ & CH_2OOC(CH_2)_{12}CH_3 \end{array}$$

And would be designated: 1 – stearoyl – 2 – oleoyl – 3 – myristoyl – sn – glycerol; sn – glycerol – 1 – stearate – 2 – oleate – 3 – myristate, ‘sn – STOM, or sn – 18:0. 18:1.14:0

The following prefixes are now widely used:

sn: if used immediately preceding the term “glycerol” indicates that sn – 1, sn – 2, and sn – 3 positions are linked in that order.

rac: racemic mixture of two enantiomers. The middle acid in the abbreviation is attached at the sn – 2 position, but the remaining two acids are equally divided between sn – 1 and sn – 3 (e.g. rac. StOM indicates equal amounts of sn – StOM and sn – MOst)

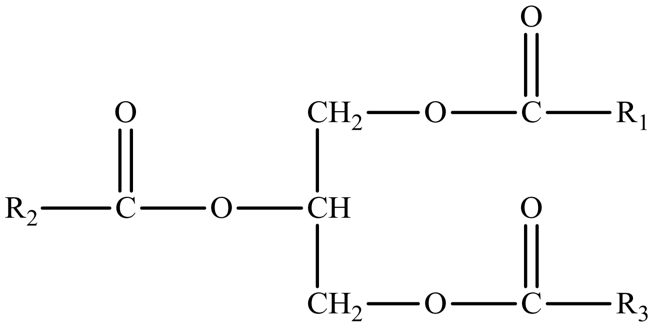
CLASSSIFICATION

Lipids are classified based on their structural components. Such a classification, however, may be rigid for a group of compounds so diverse as lipids and their classification should be used only as a guide

(a) *Simple lipids*

Examples of this class are neutral fat (i.e esters of fatty acids and glycerol) and waxes (esters of monohydric alcohols and fatty acid).

In neutral simple lipids, if the triglycerides (triacylglycerols) are liquid at room temperature, they are called oil, but if solid they are called fat.



(b) *Compound or Complex lipids*

This consists of esters of fatty acids with alcohols (glycerol) in addition to other groups. They are further divided as follows:

(i) Phospholipids: They contain in addition to fatty acids and an alcohol, a phosphoric acid residue. They may or may not contain nitrogen – containing bases and other substituents, e.g. in glycerophospholipids with glycerol as the alcohol and sphingophospholipids whose alcohol is sphingosine.

(ii) Glycolipids: These are lipids containing a fatty acid, sphingosine, and carbohydrate. They are also called cerebrosides

(iii) Sulphatides: These are lipids that contain sulphate residue.

(c) ***Precursor and derived lipids:*** This class is derived from both simple and compound lipids which still possesses lipid – like characteristics. They include long – chain fatty acids, aldehydes and ketones bodies, hydrocarbons, lipid – soluble vitamins (D, E and K) and hormones.

CHEMICAL REACTIONS OF LIPIDS

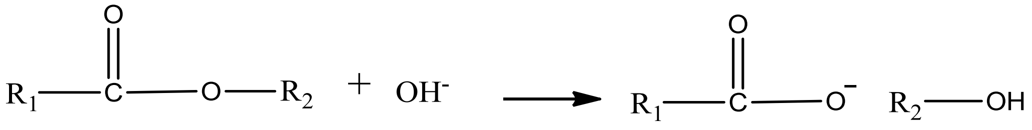
(i) Lipolysis:

Hydrolysis of ester bonds in lipids (Lipolysis) may occur by enzyme action or heat and moisture resulting in the liberation of free fatty acids. Free fatty acids are virtually absent in the fat of living animal tissue. They can be formed, however, by enzyme action after the animal is killed; hence rendering processes are necessary to inactivate the enzymes by heat treatment.

Base – catalyzed hydrolysis

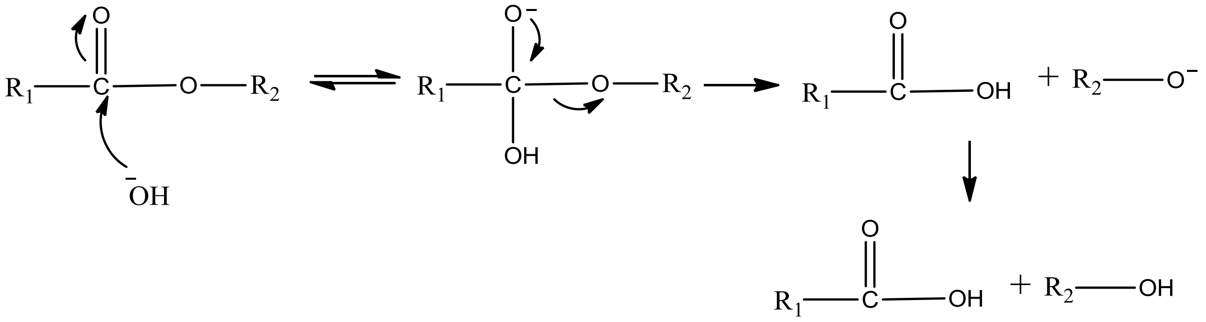
Saponification is the term used to designate base – catalysed ester hydrolysis. This reaction results in acyl – oxygen fission and involves an addition – elimination sequence.

Net reaction:



$$R_1-\overset{O}{\overset{\|}{C}}-O-R_2 + OH^- \longrightarrow R_1-\overset{O}{\overset{\|}{C}}-O^- \quad R_2-OH$$

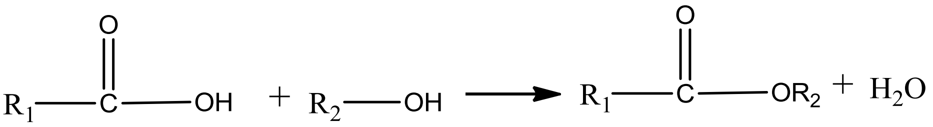
MECHANISM



The mechanism for the saponification is designated as **B$_{AC}$ 2** (Based catalysed; Acyl – fission; bimolecular).

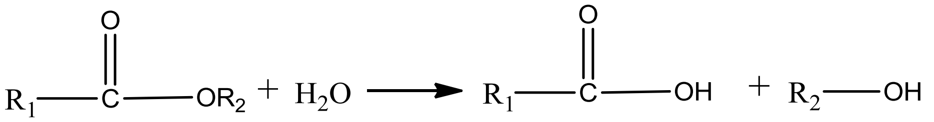
For the acid catalyzed

The mechanism of the acid – catalyzed hydrolysis of an ester is exactly the reverse of the mechanism of the formation of the ester by the Fischer esterification.



$$R_1\overset{O}{\overset{\|}{C}}-OH + R_2-OH \longrightarrow R_1\overset{O}{\overset{\|}{C}}-OR_2 + H_2O$$

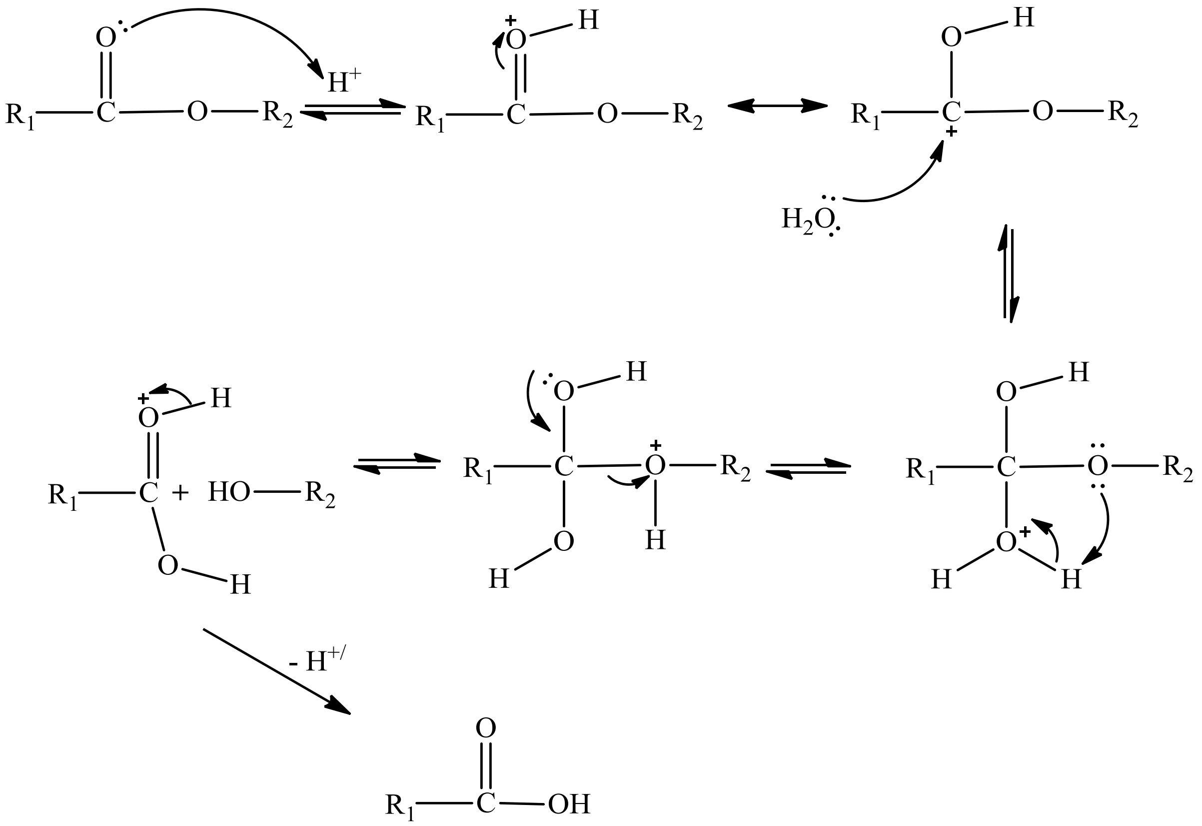
Acid catalyzed
ester formation



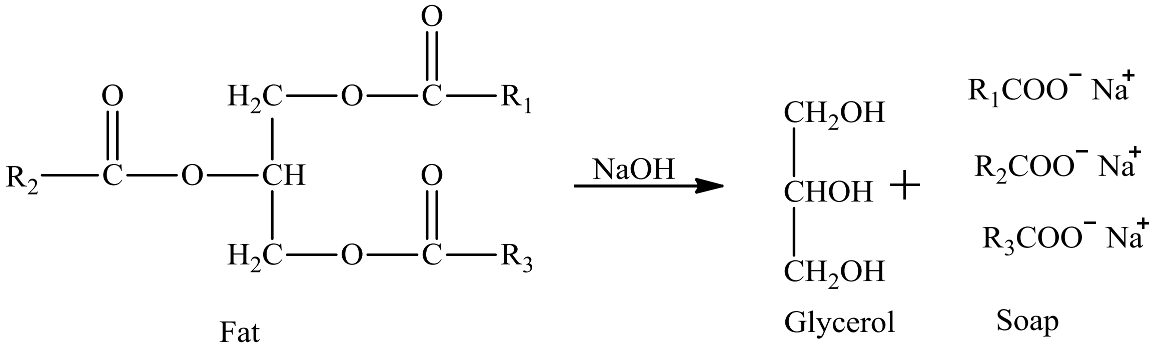
$$R_1\overset{O}{\overset{\|}{C}}-OR_2 + H_2O \longrightarrow R_1\overset{O}{\overset{\|}{C}}-OH + R_2-OH$$

Acid catalyzed
ester hydrolysis

The general mechanism for the acid catalyzed hydrolysis of esters is given below:



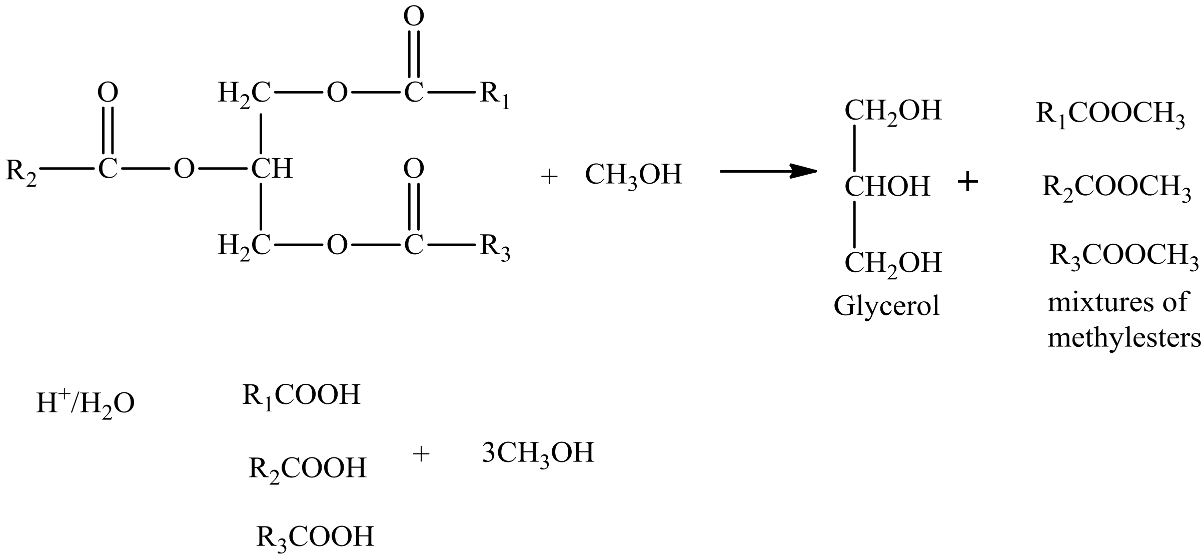
The reaction between fat or oil and NaOH or KOH leads to hydrolysis of the former leading to the formation of soap and glycerol.



Transesterification of fats

Fats can be converted by transesterication into methyl esters of carboxylic acids by allowing triacylglycerol to react with methanol in the presence of a basic or acidic catalyst. The mixture of the methylesters formed can be separated by fractional distillation which can be hydrolysed to individual carboxylic acids of high purity.

This is thus, the source of straight chain acids of even carbon number ranging from six to 18 carbons.



(ii) Lipid oxidation

(a) Autoxidation

Lipid oxidation is one of the major causes of food spoilage. It is of a great concern because it makes edible oils and fat containing food to develop various off – flavour and off – odours called *rancid*. In addition, it can also decrease the nutritional quality of food while some oxidation products are potentially toxic. On the other hand, some oxidation reactions are desirable because they lead to the production of aromas in some fried foods.

In foods, the lipids can be oxidized by both enzyme and nonenzymic mechanisms.

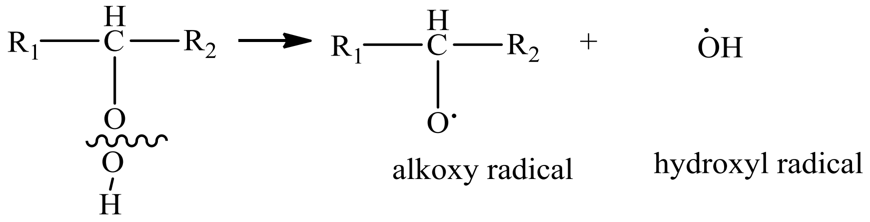
Hydroperoxides which are the primary initial products of lipid auto-oxidation are relatively unstable. They enter into numerous and complex breakdown and interaction mechanism responsible for the production of compounds which are of biological significant as well as impartation of flavour.

Decomposition of Hydroperoxides

Hydroperoxides break down in several steps leading to the production of varieties of decomposition products.

The products of decomposition themselves can undergo further oxidation and decomposition, thus, contributing to a large and varied free radical pool.

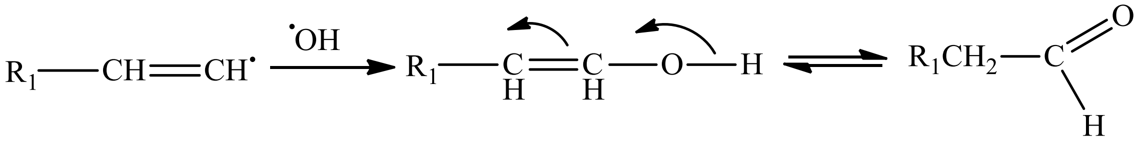
The first step in hydroperoxide decomposition is scission at the oxygen – oxygen bond of the hydroperoxide group, leading to an ***alkoxy radical*** and a ***hydroxyl radical***.



The second step is the carbon – carbon cleavage on either side of the alkoxy group.

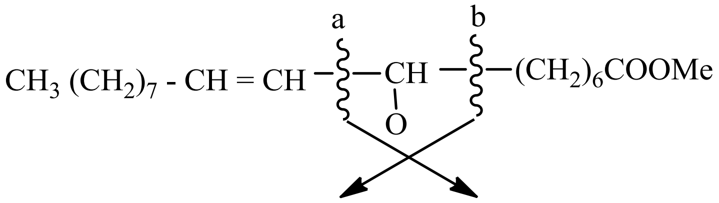
NOTE

- Cleavage on the side (i.e carboxyl or ester side) gives an aldehyde and acid (or ester)
- On the hydrocarbon (or methyl) side, hydrocarbon and an oxo acid (or oxo ester) are formed
- If a vinylic radical is formed, an aldehydic functional group is formed:



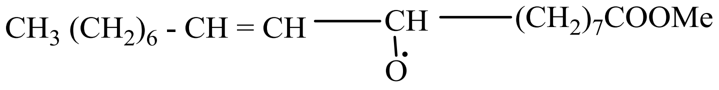
For example: (8 – hydroperoxide) of methyl oleate

Cleavage about (a) side produces decanal and methyl – 8 – oxooctanoate while cleavage on the ester side (b) gives 2 - undecenal and methyl heptanoate



$CH_3\,(CH_2)_7 - CH = CH - \underset{O}{CH} - (CH_2)_6COOMe$

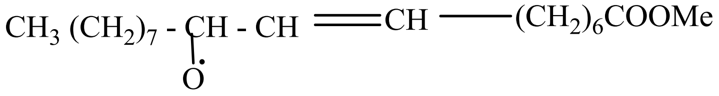
In the same manner, each of the remaining three oleate hydroperoxides would be expected to produce four typical products; for example, the 9 – hydroperoxide.



$CH_3\,(CH_2)_6 - CH = CH - \underset{\dot{O}}{CH} - (CH_2)_7COOMe$

Would give nonanal, methyl – 9 – oxononanoate, 2 – decenal and octanoate;

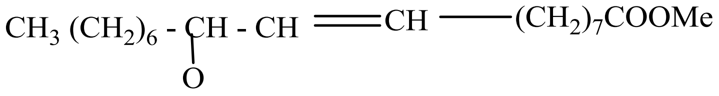
For 10 – hydroperoxide



$$CH_3\,(CH_2)_7 - \underset{\dot{O}}{\underset{|}{C}}H - CH = CH - (CH_2)_6COOMe$$

Gives octane, methyl – 10 – oxo – 8 – decanoate, nonanal and methyl – 9 – oxononanoate

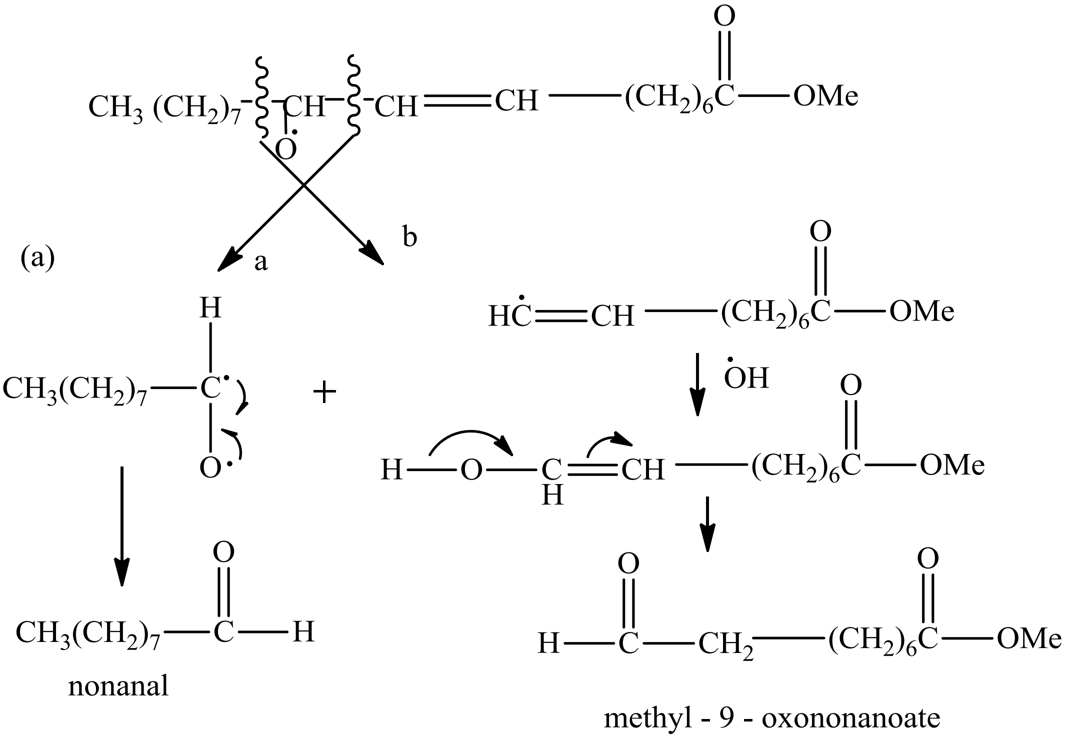
For 11 – hydroperoxide



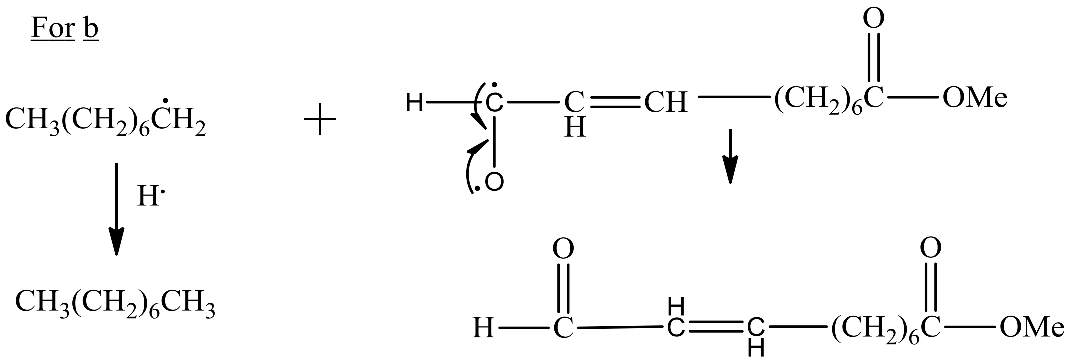
$$CH_3\,(CH_2)_6 - \underset{O}{\underset{|}{C}}H - CH = CH - (CH_2)_7COOMe$$

Gives heptane, methyl – 11 - oxo – 9 – undecanoate, octanal and methyl – 10 – oxodecanoate.

On 10 – hydroperoxide of oleate



For b

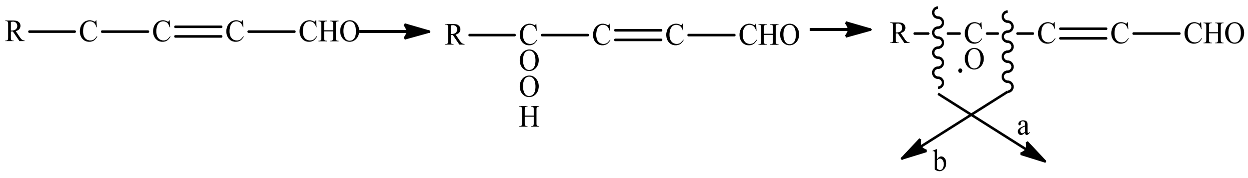


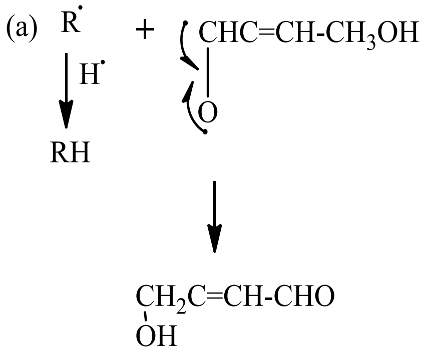
Octane

methyl - 10 - oxo - 8 - decenoate

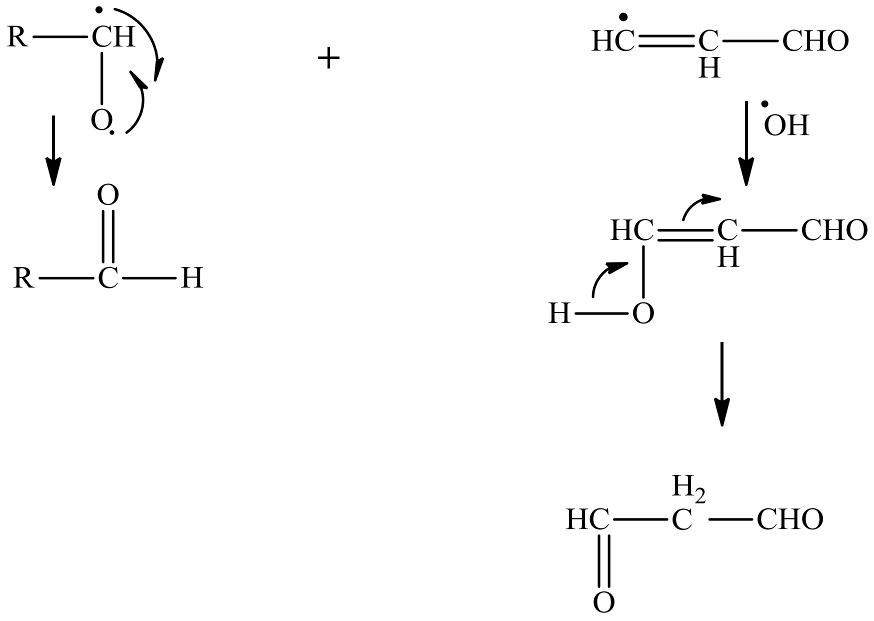
It should be noted that apart from all these compounds, other compounds can be formed like short chain aldehydes, epoxide, dimers etc.

Unsaturated aldehydes can undergo classic autoxidation with oxygen attack at a methylenic position giving rise to short – chain hydrocarbons, aldehydes and dialdehydes.



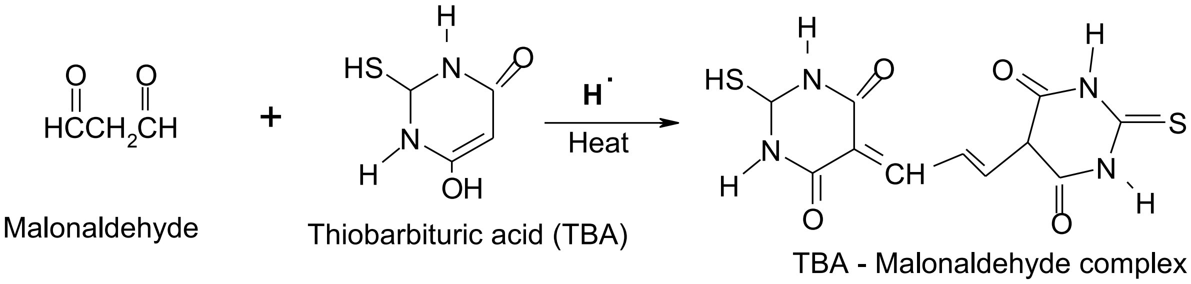


(b)



Malonaldehyde

Formation of malonaldehyde is the basis for the well-known TBA method used for measuring lipid oxidation. The formation of this compound is an indication that the vegetable oil has reached an advanced stage of deterioration.



Factors influencing the rate of Lipid oxidation in foods

(1) *Fatty Acid Composition*: The number, position and geometry of double bond affect the rate of oxidation. For example, the oxidation for arachidonic, linolenic, linoleic, and oleic are approximately 40: 20: 10: 1, respectively. ***Cis acids*** oxidize more readily than their ***trans isomers***, and conjugated double bonds are more reactive than non-conjugated. Oxidation of saturated fatty acids is extremely slow, at room temperature.

(2) *Free fatty acids versus the corresponding acyl glycerol*:

Fatty acids oxidize at a slightly greater rate than in triacylglycerol. Randomizing the fatty acid distribution of a natural fat reduces the rate of oxidation.

(3) *Oxygen concentration*: When the supply of oxygen is unlimited, the rate of lipid oxidation is independent of oxygen pressure, but in limited quantity, the higher the pressure, the higher the rate of oxidation i.e. rate of oxidation is directly proportional to oxygen pressure. The effect of oxygen pressure on the rate is influenced by other factors, such as temperature and surface area.

(4) *Temperature*: The rate of oxidation increases with increase in temperature. As temperature increases, the increase in rate with increasing oxygen concentration is insignificant, because oxygen becomes less soluble as the temperature is raised.

(5) *Surface Area*: The rate also increases with increase in the surface area of the lipid that is exposed to the air. However, as the surface – volume ratio increases, reducing the oxygen partial pressure because less effective in decreasing the rate of oxidation.

(6) *Moisture*: The rate of oxidation also depends on water activity. In dried foods with low moisture content i.e. $a_w < 0.1$, oxidation proceeds at rapid rate. If the a_w is about 0.3, the rate will be reduced to minimum. This also has to do with catalytic activity of metal catalyst, by quenching free radicals, by promoting non-enzymic browning which in turn produced compounds with antioxidant activities. At higher water activities ($a_w = 0.55 – 0.85$), the rate increases again, which was presumed to be due to increase in mobilization of the catalyst present.

(7) *Pro – oxidants*: The transition metals especially those with two or more valency states (e.g. cobalt, copper, iron, manganese and nickel) are major pro – oxidants even as low as 0.1ppm concentrations. They can decrease the length of the induction period and increase the rate of oxidation.

(8) Antioxidant: The presence of antioxidant compounds in lipid also affects the rate of lipid oxidation. This will be treated in detail. They delay the onset and slow rate of oxidation. This is treated in details below.

Saturated fatty acids

Saturated fatty acids have no C=C double bonds. They have the formula $CH_3(CH_2)_nCOOH$, for different *n*. An important saturated fatty acid is stearic acid (*n* = 16), which when neutralized with sodium hydroxide is the most common form of soap.

Examples of saturated fatty acids

Common name	Chemical structure	*C*:*D*
Caprylic acid	$CH_3(CH_2)_6COOH$	8:0
Capric acid	$CH_3(CH_2)_8COOH$	10:0
Lauric acid	$CH_3(CH_2)_{10}COOH$	12:0
Myristic acid	$CH_3(CH_2)_{12}COOH$	14:0
Palmitic acid	$CH_3(CH_2)_{14}COOH$	16:0
Stearic acid	$CH_3(CH_2)_{16}COOH$	18:0
Arachidic acid	$CH_3(CH_2)_{18}COOH$	20:0
Behenic acid	$CH_3(CH_2)_{20}COOH$	22:0
Lignoceric acid	$CH_3(CH_2)_{22}COOH$	24:0
Cerotic acid	$CH_3(CH_2)_{24}COOH$	26:0

***C*:*D* is the ratio of numbers of carbons to double bonds**

Examples of Unsaturated Fatty Acids

Common name	Chemical structure	Δ	*C*:*D*	IUPAC	*n*−*x*
Myristoleic acid	$\mathrm{CH_3(CH_2)_3}\mathbf{CH{=}CH}\mathrm{(CH_2)_7COOH}$	*cis*-Δ^9	14:1	14:1(9)	*n*−5
Palmitoleic acid	$\mathrm{CH_3(CH_2)_5}\mathbf{CH{=}CH}\mathrm{(CH_2)_7COOH}$	*cis*-Δ^9	16:1	16:1(9)	*n*−7
Sapienic acid	$\mathrm{CH_3(CH_2)_8}\mathbf{CH{=}CH}\mathrm{(CH_2)_4COOH}$	*cis*-Δ^6	16:1	16:1(6)	*n*−10
Oleic acid	$\mathrm{CH_3(CH_2)_7}\mathbf{CH{=}CH}\mathrm{(CH_2)_7COOH}$	*cis*-Δ^9	18:1	18:1(9)	*n*−9
Elaidic acid	$\mathrm{CH_3(CH_2)_7}\mathbf{CH{=}CH}\mathrm{(CH_2)_7COOH}$	*trans*-Δ^9	18:1	18:1(9t)	*n*−9
Vaccenic acid	$\mathrm{CH_3(CH_2)_5}\mathbf{CH{=}CH}\mathrm{(CH_2)_9COOH}$	*trans*-Δ^{11}	18:1	18:1(11t)	*n*−7
Linoleic acid	$\mathrm{CH_3(CH_2)_4}\mathbf{CH{=}CH}\mathrm{CH_2}\mathbf{CH{=}CH}\mathrm{(CH_2)_7COOH}$	*cis*,*cis*-Δ^9,Δ^{12}	18:2	18:2(9,12)	*n*−6
Linoelaidic acid	$\mathrm{CH_3(CH_2)_4}\mathbf{CH{=}CH}\mathrm{CH_2}\mathbf{CH{=}CH}\mathrm{(CH_2)_7COOH}$	*trans*,*trans*-Δ^9,Δ^{12}	18:2	18:2(9t,12t)	*n*−6
α-Linolenic acid	$\mathrm{CH_3CH_2}\mathbf{CH{=}CH}\mathrm{CH_2}\mathbf{CH{=}CH}\mathrm{CH_2}\mathbf{CH{=}CH}\mathrm{(CH_2)_7COOH}$	*cis*,*cis*,*cis*-$\Delta^9,\Delta^{12},\Delta^{15}$	18:3	18:3(9,12,15)	*n*−3
Arachidonic	$\mathrm{CH_3(CH_2)_4}\mathbf{CH{=}CH}\mathrm{CH_2}\mathbf{CH{=}CH}\mathrm{CH_2}\mathbf{CH{=}}$	*cis*,*cis*,*cis*,*cis*-	20:4	20:4(5,8,11,	*n*−6

acid	**CH**CH$_2$**CH=CH**(CH$_2$)$_3$COOH	$\Delta^5\Delta^8$,Δ^{11},Δ^{14}		14)	
Eicosapentaenoic acid	CH$_3$CH$_2$**CH=CH**CH$_2$**CH=CH**CH$_2$**CH=CH**CH$_2$**CH=CH**CH$_2$**CH=CH**(CH$_2$)$_3$COOH	*cis*,*cis*,*cis*,*cis*,*cis*-Δ^5,Δ^8,Δ^{11},Δ^{14},Δ^{17}	20:5	20:5(5,8,11,14,17)	*n*−3
Erucic acid	CH$_3$(CH$_2$)$_7$**CH=CH**(CH$_2$)$_{11}$COOH	*cis*-Δ^{13}	22:1	22:1(13)	*n*−9
Docosahexaenoic acid	CH$_3$CH$_3$**CH=CH**CH$_2$**CH=CH**CH$_2$**CH=CH**CH$_2$**CH=CH**CH$_2$**CH=CH**CH$_2$**CH=CH**(CH$_2$)$_2$COOH	*cis*,*cis*,*cis*,*cis*,*cis*,*cis*-Δ^4,Δ^7,Δ^{10},Δ^{13},Δ^{16},Δ^{19}	22:6	22:6(4,7,10,13,16,19)	

***n−x* is the position of double bonds when numbering from the methyl side, the n is also referred to as omega (ω)**

"Δ" This is used when numbering from the carboxyl (-COOH) side; cis and trans indicate the configuration around the carbons bearing the double bonds that is sp^2 carbons.