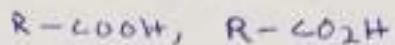


Carboxylic acids

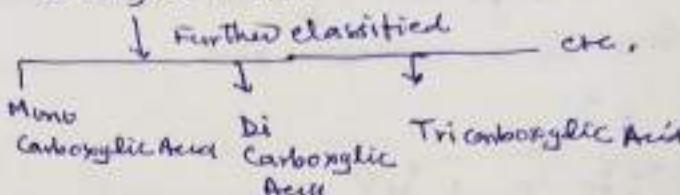
①

Organic compounds which contain carboxylic functional group ($-COOH$) are called the carboxylic Acids.

General formula $R-COOH$ where R is aliphatic group



Carboxylic Acids



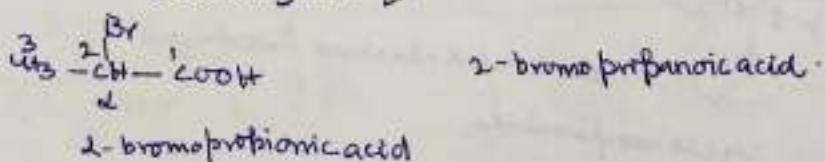
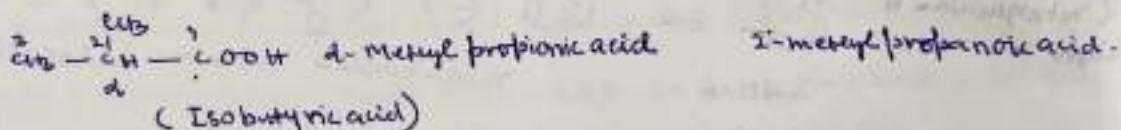
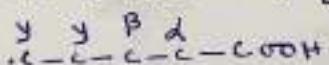
depending upon the number of carboxyl group

The long chain carboxylic acids are generally called Fatty acid.

Monocarboxylic acid

$H-COOH$	Formic Acid	IUPAC Methanoic Acid
CH_3-COOH	Acetic Acid	Ethanolic Acid
CH_3-CH_2-COOH	Propionic Acid	Propanoic Acid
$CH_3-CH_2-CH_2-COOH$	Butyric Acid.	Butanoic Acid

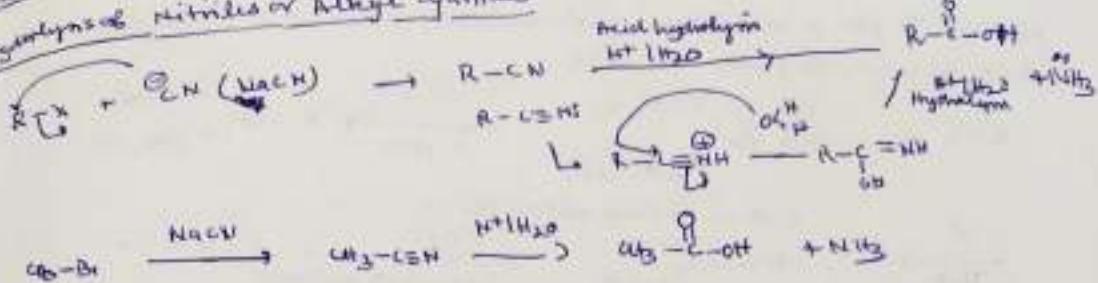
Position of Substituents by Greek Letters, $\alpha, \beta, \gamma, \delta$ etc.



Method of Preparation

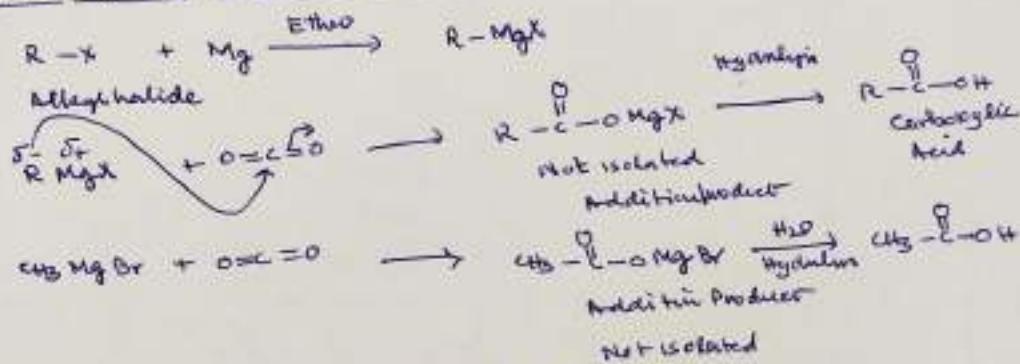
- Oxidation of primary alcohols or aldehydes

- Hydrolysis of nitriles or alkyl cyanides

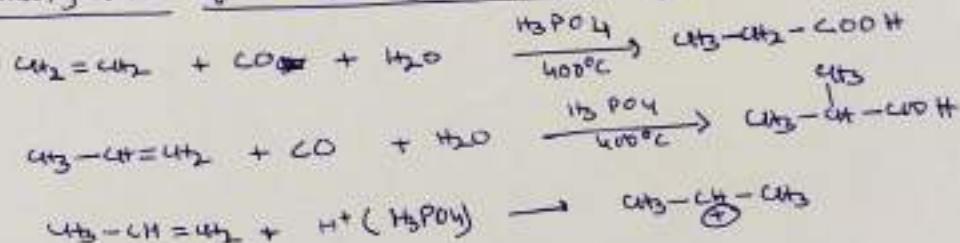


- Hydrolysis of Esters

- Reaction of Grignards with CO_2



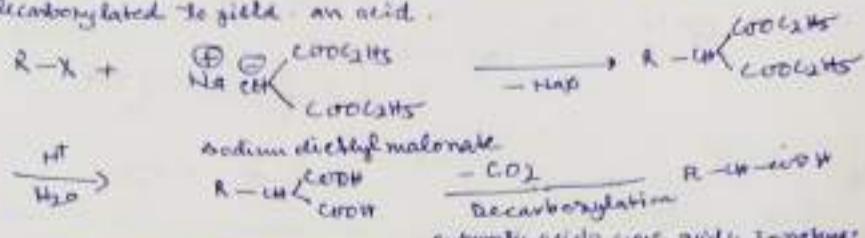
- Carboxylation of alkenes (Kolbe Reaction)



3.

Malonic ester synthesis

This involves the reaction of an alkyl halide with sodium derivative of diethyl malonate to give a substituted malonic ester. This can be hydrolysed and decarboxylated to yield an acid.



Acidity of carboxylic acid: Carboxylic acids are acidic in nature.

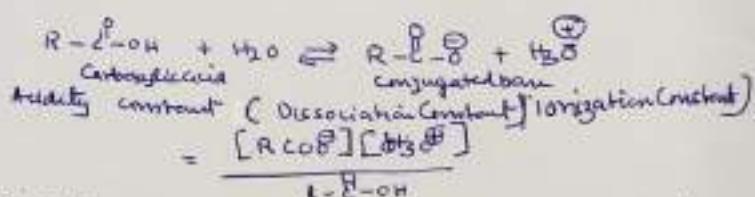
They can donate a proton and form salts with bases, $\text{R-COOH} + \text{NaOH} \rightarrow \text{R-COO}^- + \text{Na}^+$.

The carboxylic acids are ionized in water but ionization is very poor. Only one-tenth of acetic acid is ionized.

Only about 0.5% of acetic acid is ionized while a strong acid like HCl is almost completely ionized.

Acidity constant

Ionization in water is written as such

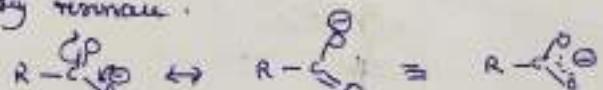


It is defined as concentration of products of ionization in moles per litres divided by the concentration of un-ionized acids.

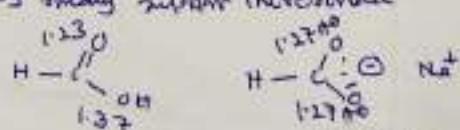
Reason for acidity

The acidic value or acidity constant depends upon the concentration of conjugated base, and concentration of conjugated base depends upon the stability of conjugated base.

The conjugated base, conjugate ion, $\text{C}_2\text{H}_4\text{OOCO}^-$ is stabilized by resonance.



X-ray study substantiates this view.



formate

MO picture

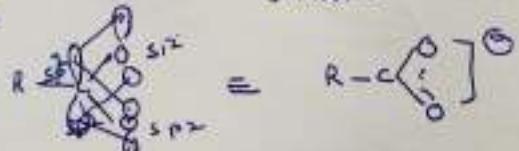
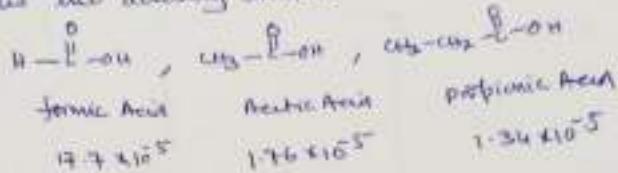
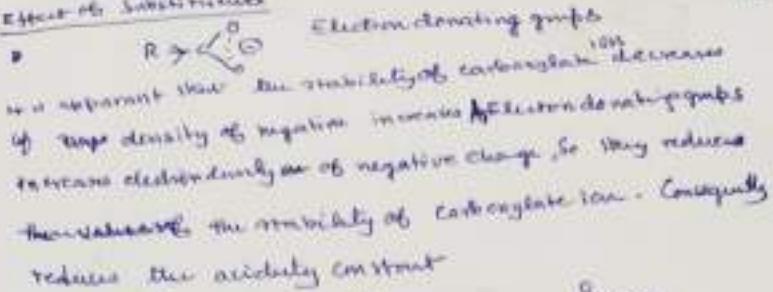


Table 2.2-10. Standardized variables

5

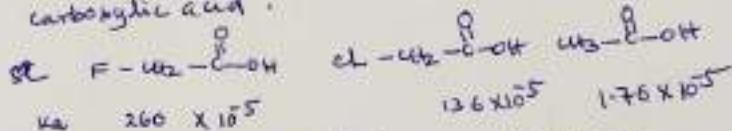


Electro desorption groups with strong graft

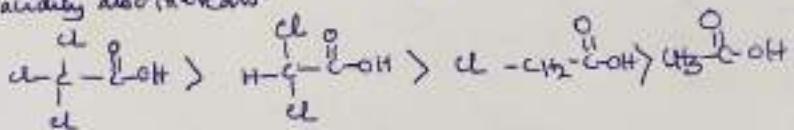
-Cl, Br, I, F, OH, CH₃, NO₂



As electron with strong groups decrease the density of negative charge of carboxylate ion, so increase the stability and increase the acidity constant of carboxylic acid.



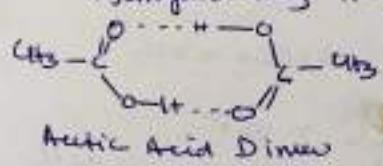
A decrease in electron - with strong group increases,
acidity also increases.



- Boiling points of carboxylic acids are higher than those of alcohols of same molecular weight. For example $\text{B.P. } ^\circ \text{C}$

Acetic Acid	$\text{CH}_3\text{-COOH}$	MW 60	118°
1-Propanol	$\text{CH}_3\text{-CH}_2\text{-CH}_2\text{-OH}$	MW 60	97°

Reason: Hydrogen bonding Acid molecules



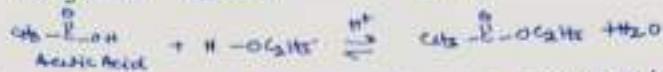
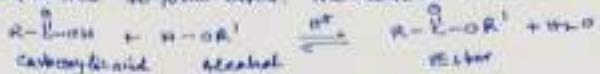
Schubertiana

Solubility
Lower carboxylic acid is completely
soluble in water due to hydrogen bonding.
As the hydrocarbon chain in acid lengthens,
the solubility of acid in water falls off
rapidly.

Reaction of carboxylic acids

Formation of esters

Carboxylic acids react with alcohols in the presence of strong acid catalyst like concentrated HCl to form esters. The reaction is reversible and is called interfacial esterification.

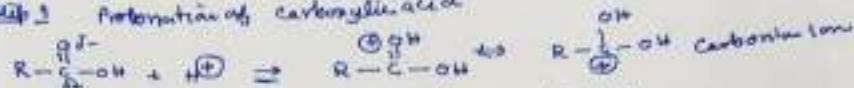


The equilibrium shifted to the right by using excess of alcohol or removal of water by distillation.

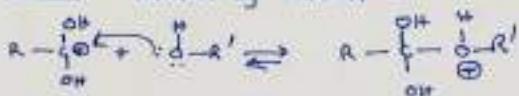
Mechanism

The mechanism of esterification involves the following steps:

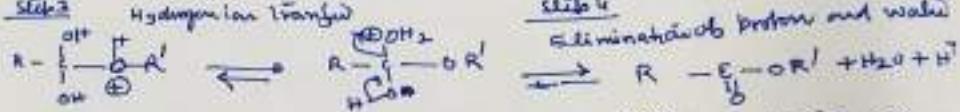
Step 1 Protonation of carboxylic acid



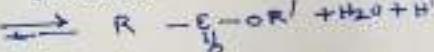
Step 2 Attack by nucleophile R'-OH (alcohol)



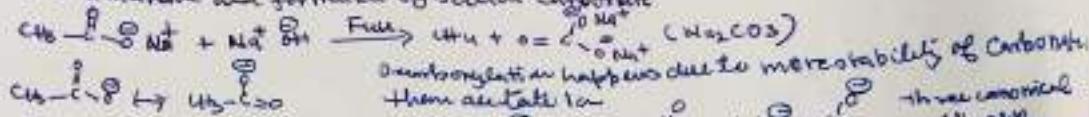
Step 3 Hydrogen ion transfer



Step 4 Elimination of proton and water



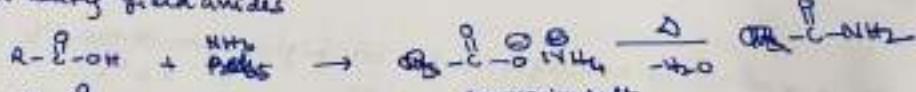
Decarboxylation: When cold sodium acetate is fused with calcium hydroxide or heated with the less fusible sodium carbonate ($\text{Na}_2\text{CO}_3 + \text{Ca}(\text{OH})_2$), salt decomposes with liberation of CO_2 and formation of sodium carbonate.



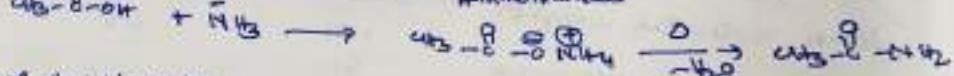
acetate ion loss canonical $\text{O}=\overset{\text{O}}{\underset{\text{Na}^+}{\text{C}}}-\text{O}^{\oplus}\text{Na}^+ \rightleftharpoons \text{O}=\overset{\text{O}}{\underset{\text{Na}^+}{\text{C}}}-\text{O}^{\oplus}\text{Na}^+$ three canonical structures

Formation of Amides: Carboxylic acids react with ammonia to give salts

which on heating yield amides

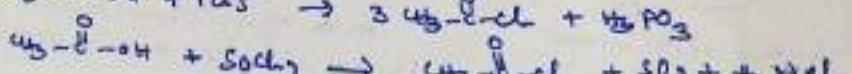
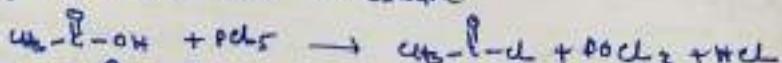


ammonium salt



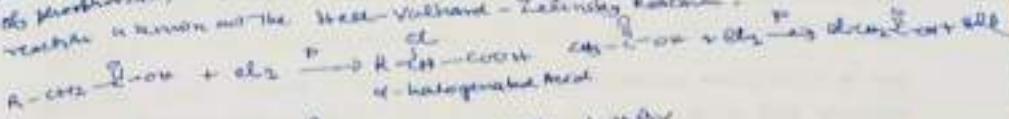
Formation of Acid halides

Carboxylic acid reacts with phosphorus halides or thionyl chloride (SOCl_2) to form acid halides. For example,

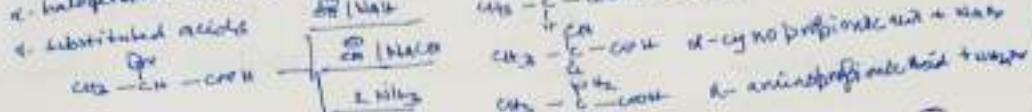


Hell-Volhard-Zelinsky Reaction

When carboxylic acids that contain an α -hydrogen is treated with N_2H_4 , carbon monoxide is evolved, α -hydrogen atoms are replaced by nitrogen or hydrazine, thus reaction is known as the Hell-Volhard-Zelinsky Reaction.



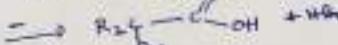
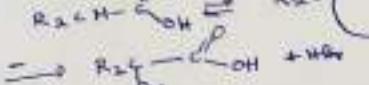
α -halogenated acids are convenient starting materials for preparing other α -substituted acids



only activated α -hydrogen atoms are

replaceable by halogen. The facts suggest that α -halogenation involves cyclic form

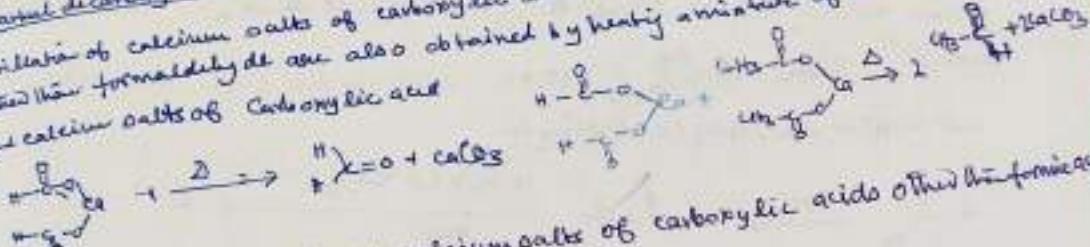
in equilibrium with the α -carbon atom



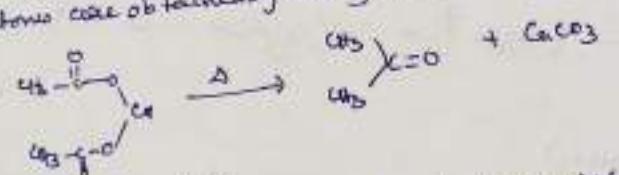
Secondary lactone

By partial decarbonylation of calcium salts of carboxylic acid:

Distillation of calcium salts of carboxylic acids to give carbonyl carbonyls. Aldehydes and their formalddehyde are also obtained by heating mixture of calcium formate and calcium salts of carboxylic acid

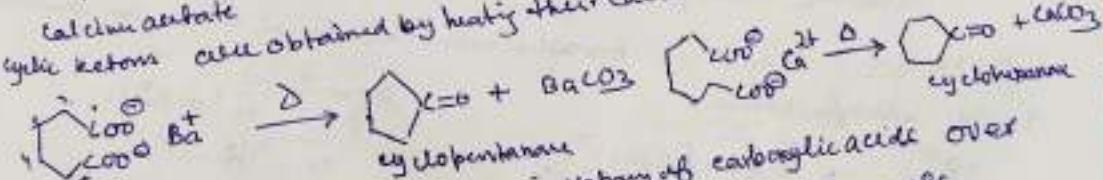


Ketones are obtained by heating calcium salts of carboxylic acids other than formic acid

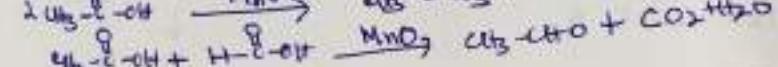
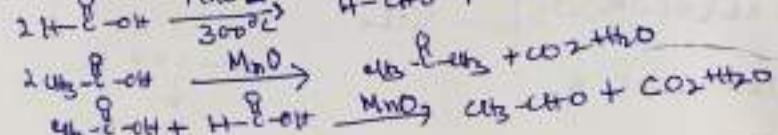
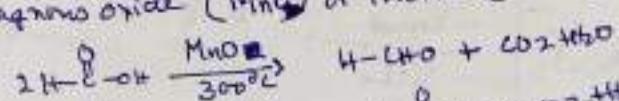


Calcium acetate

Cyclic ketones are obtained by heating their calcium or barium salts



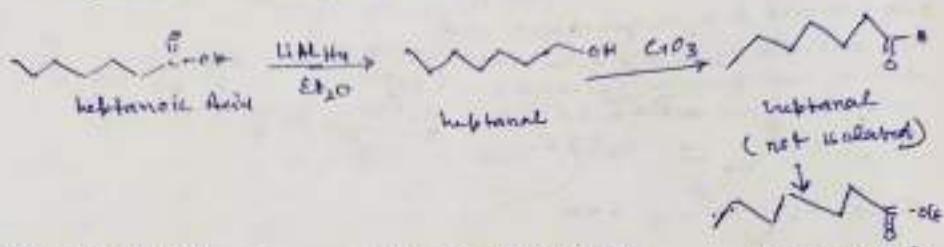
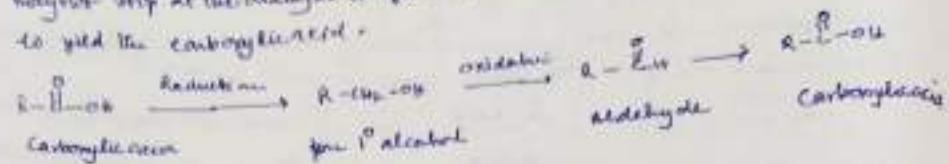
Carbonyl compounds are also obtained by heating vapors of carboxylic acids over magnesia oxide (MnO_2) or Thoria (ThO_2) heated to 300° to 400°C



By reduction of carbonylic acids and its derivatives

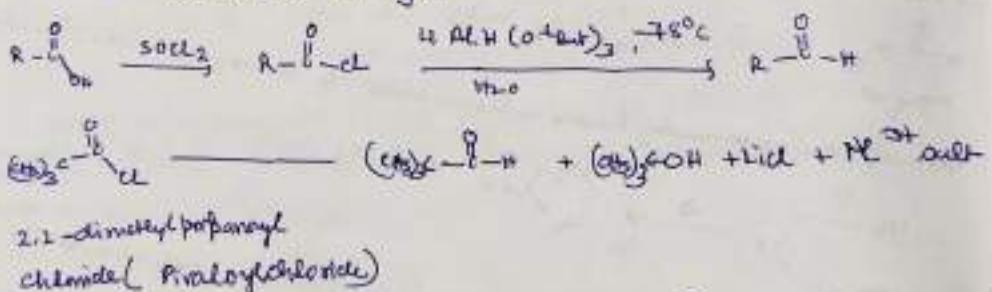
(ii) Sugars and aldehydes

This is most widely used indirect method for the synthesis of carbonyl compounds. The reaction involves first the reduction of carbonylic acid to primary alcohol and its subsequent oxidation to aldehydes. It is possible that the reaction may stop at the aldehyde stage and the oxidation may proceed further to yield the carboxylic acid.

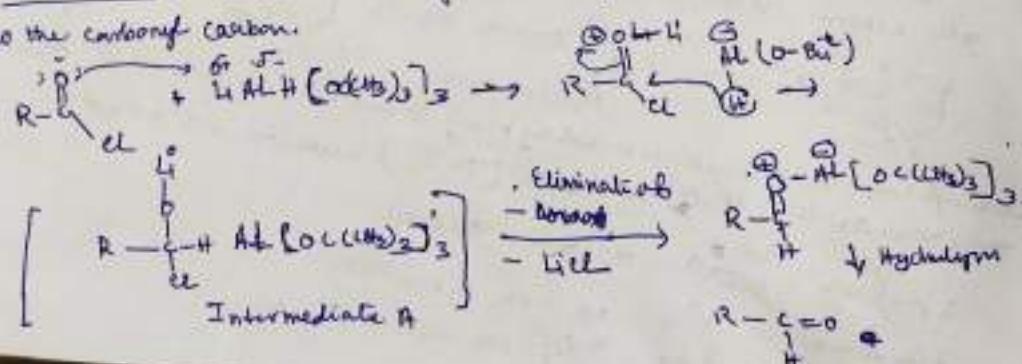


However, acid chlorides, esters and nitriles, which are easily prepared from carboxylic acid, can be reduced directly to aldehyde.

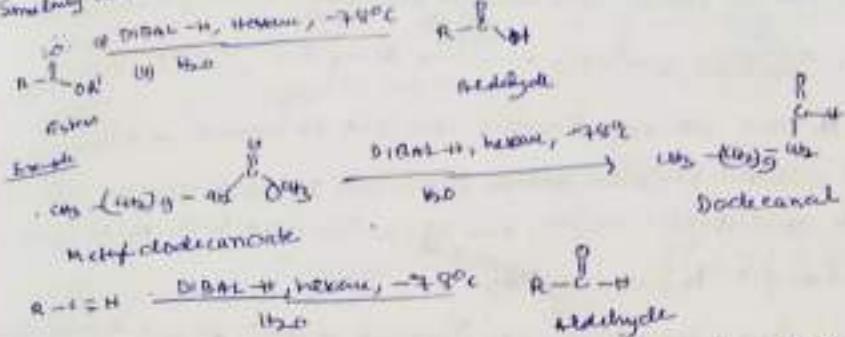
Weaker reducing reagent ($\text{LiAlH}(\text{C}_2\text{H}_5)_3$, $\text{LiAlH}(\text{C}_2\text{H}_5)_2\text{Cl}$), and dissociated aluminium hydride $\text{AlH}(\text{C}_2\text{H}_5)_2\text{Li}^+$, DIBAL oxidises the acid, acid halide, $\text{C}_2\text{H}_5\text{COCl}$ and nitrile directly to aldehyde.



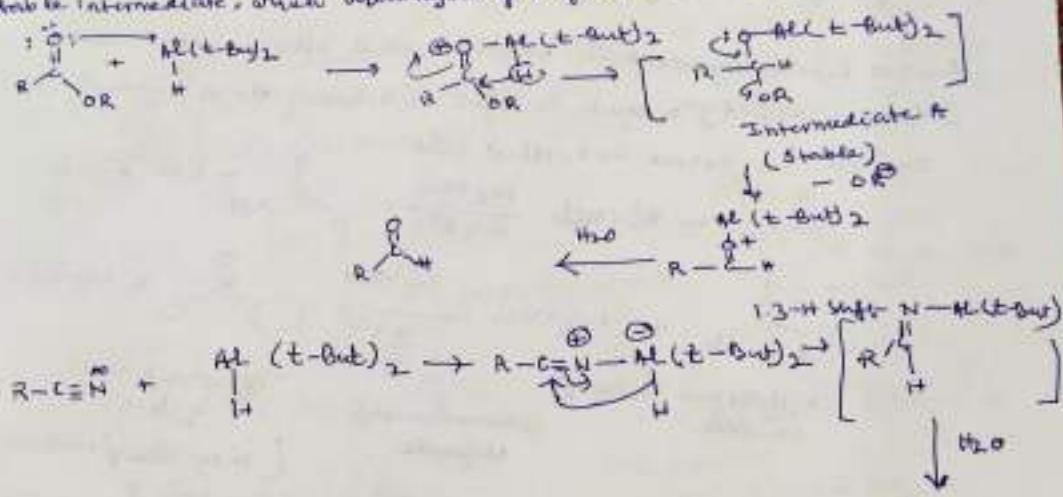
Mechanism: Reduction is brought about by transfer H^+ ion from aluminium atom to the carbonyl carbon.



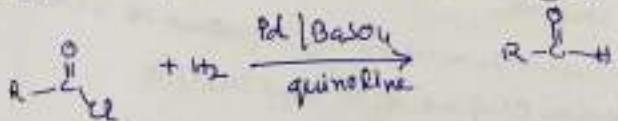
Similarly other substituted carboxylic acids can also be reduced to aldehydes by use of $\text{LiBH}_3 \text{Li}-\text{H}$



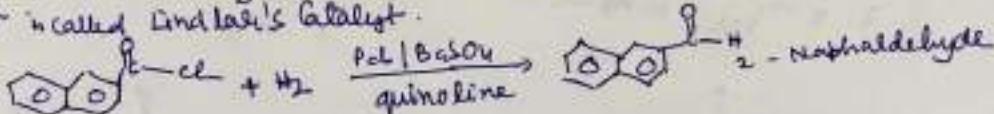
Low temperature and calculated amount of reagent is needed to avoid over-reduction.
In both the reactions, transfer of hydride to carbonyl carbon leads to the generally stable intermediate, which upon hydrolysis yields the aldehyde.



Acid chlorides can also be reduced by hydrogenating them over a catalyst (Supported over BaSO_4) that harbors poisoned palladium activated with quinoline (to prevent further reduction of aldehyde)



This reaction is commonly known as Rosenmund Reduction and the deactivated catalyst is called Lindlar's Catalyst.



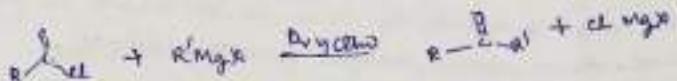
(b) Enzymes form acyl-enzyme and carboxy-enzyme
 Carboxy-enzyme on reaction with alkali or CO_2 liberate acid to regeneration of enzyme

$$\text{R}-\ddot{\text{O}}-\text{H} \xrightarrow[\text{alkali}]{\text{catalyse}} \text{R}-\ddot{\text{O}}-\text{H}^+ \xrightarrow{\text{CO}_2} \text{R}-\ddot{\text{O}}-\text{H} + \text{H}_2\text{O} \xrightarrow{\text{catalyse}} \text{R}-\ddot{\text{O}}-\text{H}$$

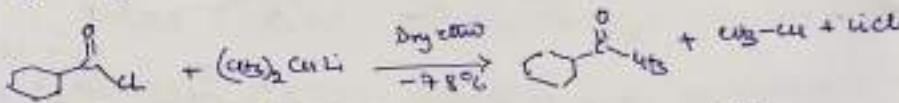
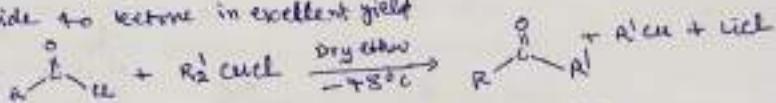
regen. of enzymes which

Reaction of ester with Grignard reagent also lead to significant side reactions which are not isolated because ketone themselves are more reactive than ester towards nucleophilic reagent and they further react with second equivalent of Grignard reagent to form alcohol

Benzal chloride reacts with Grignard reagent to give ketone due to further reaction with ketone.



Another typical organometallic reagent called lithium diethylcuprate (Gilman reagent) is quite helpful in achieving clean conversion of acid chloride to ketone in excellent yield

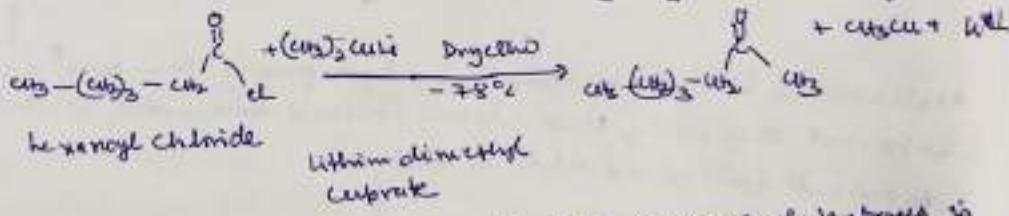


cyclohexene carbonyl
chloride

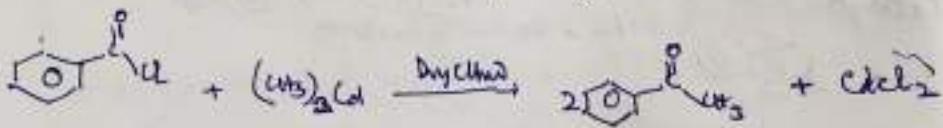
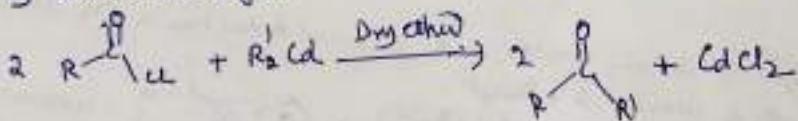
Lithuanian High
Court

cyclohexyl methyl
ketone.

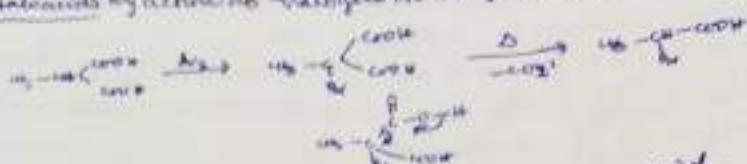
(γ -cyclohexyl ethanone)



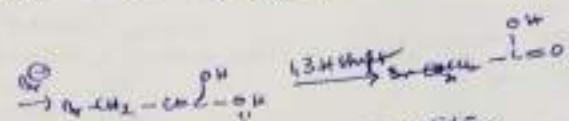
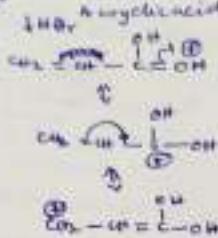
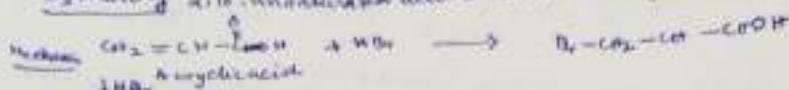
However, one of the most versatile method of synthesis of ketones is by reaction of organocadmium compound with acid chloride.



10
Unconscious by action of transverse aortic valve which followed my decubitus.



By treating α,β-unsaturated acids with halogen acid

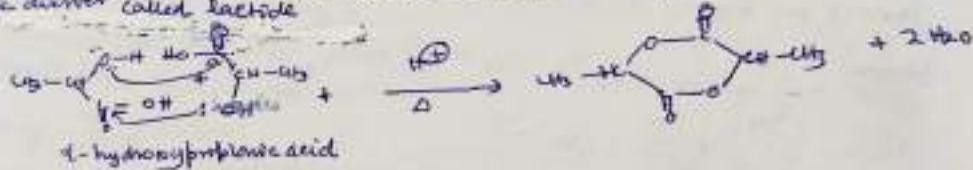


1,4-addition dominates over 1,2-addition

Here is anti-Markovnikov addition

Activity of fluorinating hydrox acids with little mineral acid (H_2SO_4)
Traces halogen acid salts

- hydroxy acid when heated with a halogen acid salt, it makes up one diester called lactide

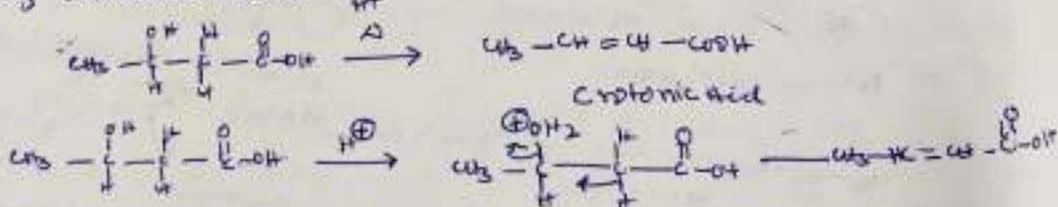


Lactuca sativa - 2 modes

For best alignment of structures for formaldehyde makes lactate

P-hydroxy Acid

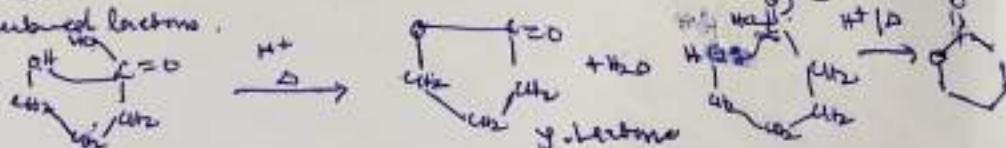
β -hydroxy dehydrate by splitting out OH and H from adjacent carbon atoms forming unsaturated acids.



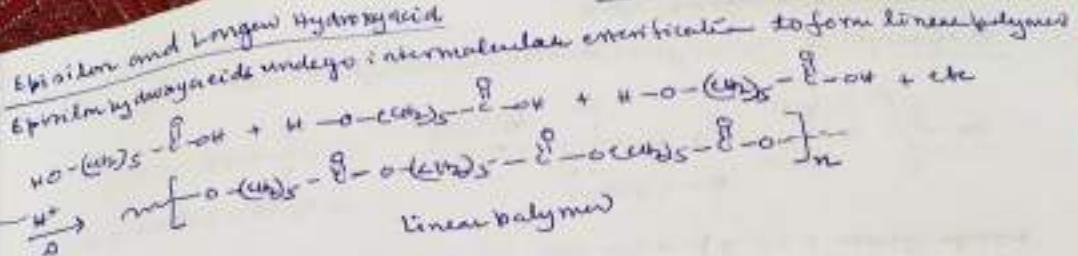
Gamma and Delta Hydroxy Acids

γ and δ -hydroxy acids form internal esters known as Lactones.

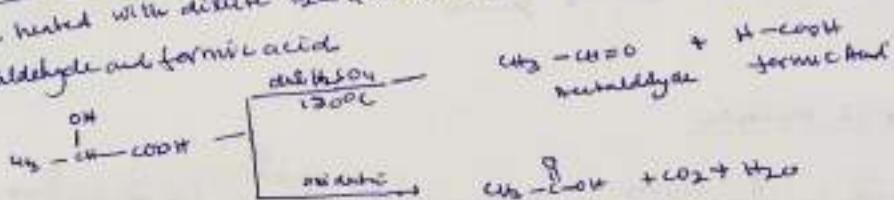
γ -Hydroxy acids makes 5-membered lactones whereas δ -hydroxy acids makes 6-membered lactones.



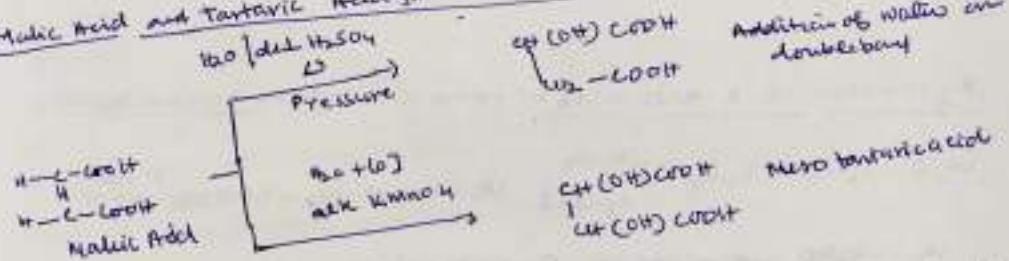
Epsilon and Long Hydroxyacid



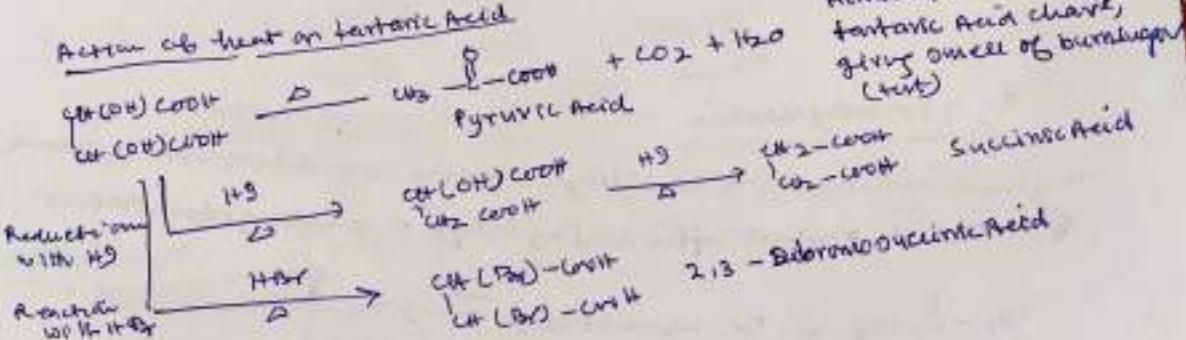
Reaction of α -hydroxy carboxylic acid with HgSO_4
When heated with dilute HgSO_4 at 130°C , lactic acid decomposes to yield acetaldehyde and formic acid



Malic Acid and Tartaric Acid from Maleic Acid

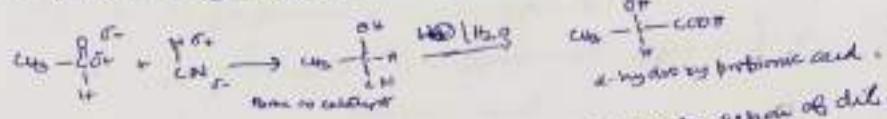


Action of heat on tartaric acid



Preparation of α -hydroxy acids

By hydrolysis of cyanohydrins derived from aldehyde or ketone



Hydrogen cyanide is a very poisonous gas. It is produced in α -OHA by action of dil. H₂S_O₄ on potassium cyanide.

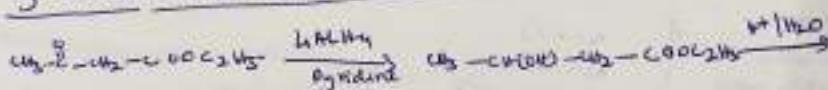


By H₂O₂ reaction



Mechanism

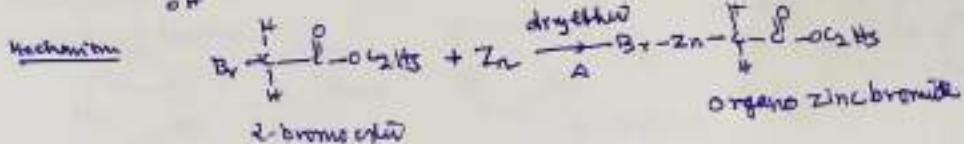
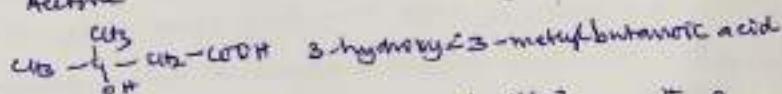
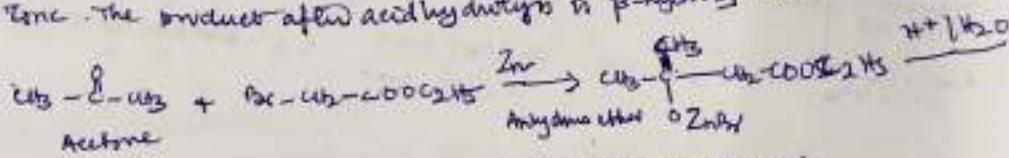
By reduction of β -keto acids or esters with LiAlH₄ impure by pyridine

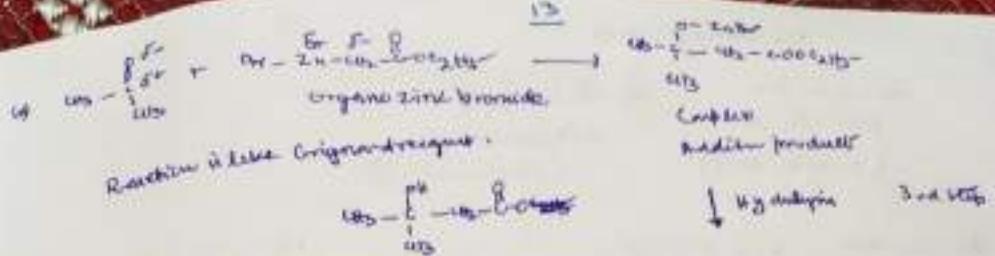


By reformatory reaction

Solvent - Anhydrous ethyl

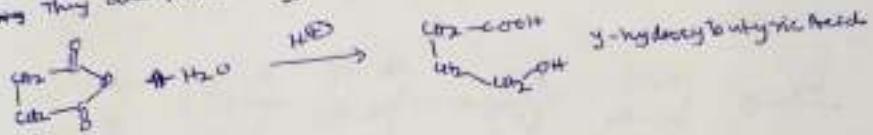
This involves treatment of an aldehyde or ketone with a bromo ester in presence of ZnCl₂. The product after acidic hydrolysis is β -hydroxy ester. For example,



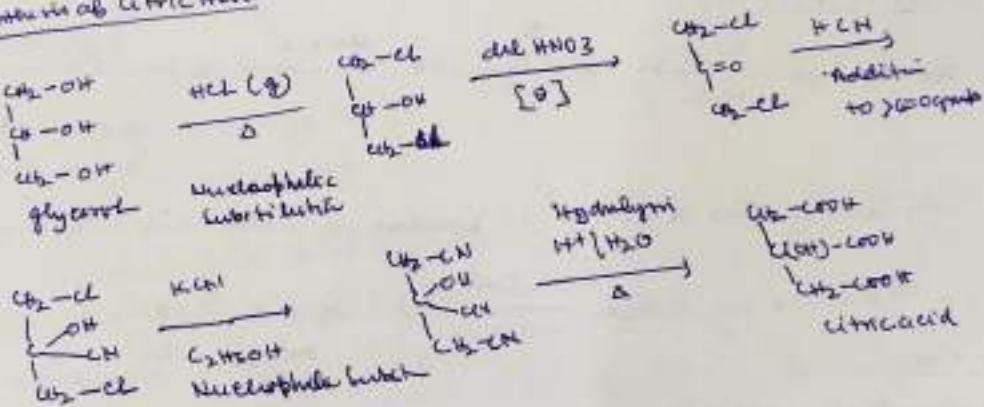


LiH_2SO_4

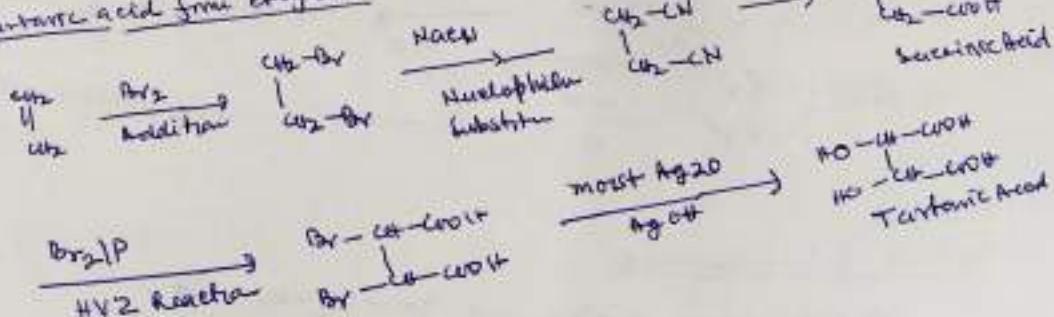
for yield & longer hydrolysis time
they are prepared by hydrolysis of corresponding lactone

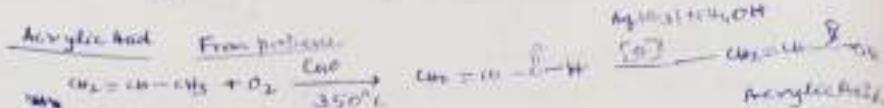
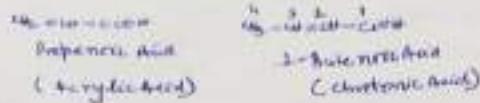
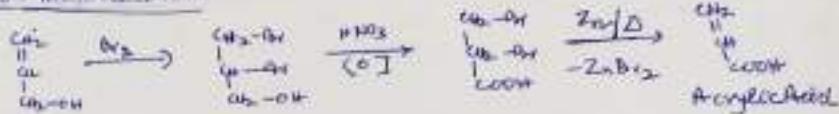
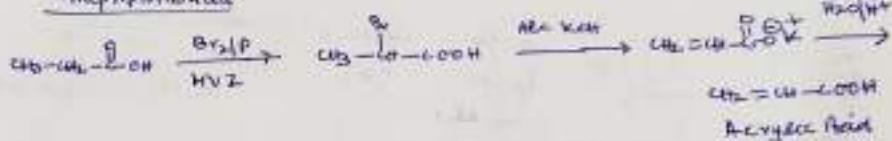


Synthesis of Citric Acid

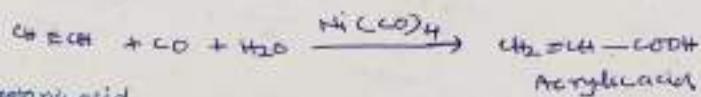
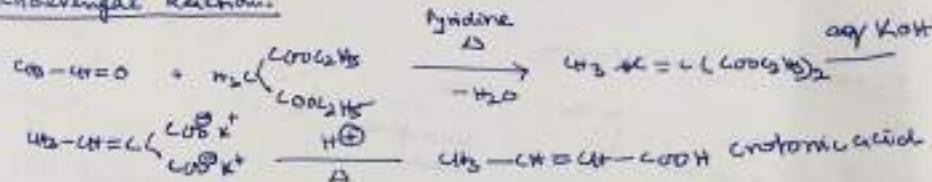


Tartaric acid from ethylene

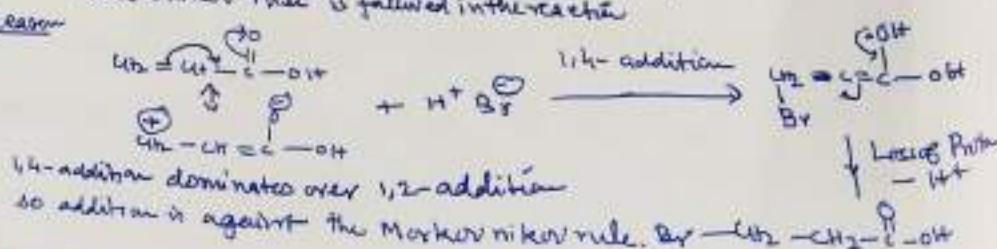


Unsaturated AcidFrom Acrylic acidFrom propiophenone

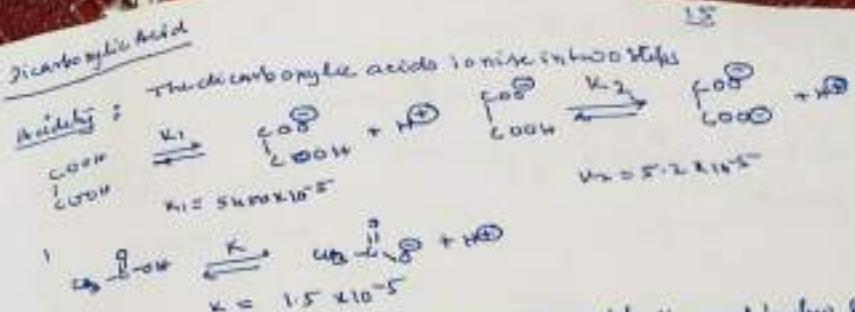
By carbonylation of acetene in presence of water and nickel carbonyl catalyst

CarboxylationKraut-Kolthoff ReactionsReactionAddition of halogen acids

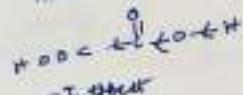
MARKOVNIKOV rule is followed in the reaction



Dicarboxylic acid



Acidity constant of first ionization of oxalic acid is much higher than the 2nd ionization and even from acetic acid. The reason is electron-withdrawing nature of -COOH group and more stabilization of HOOC^2+ by conjugation.

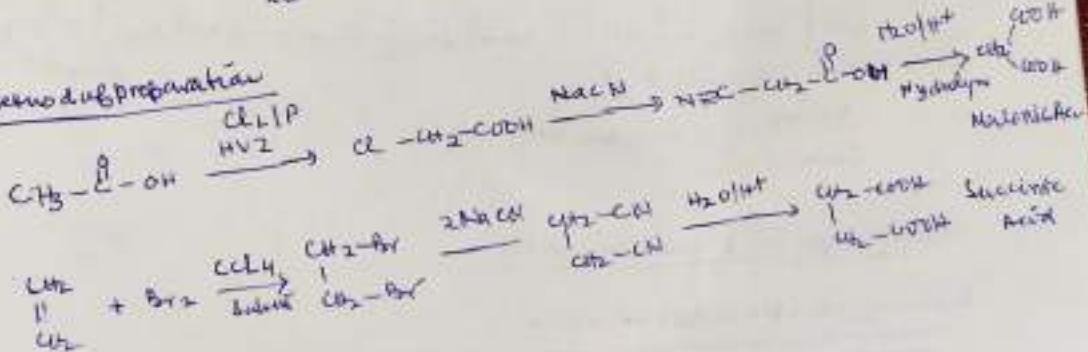


Whereas in case of second ionization of oxalic acid, the -carboxyl group -COOH is attached to carbonyl carbon. Negative charged carbonyl ion increases the energy needed to remove H^+ ion and thus weaker the acid strength than K_1 .

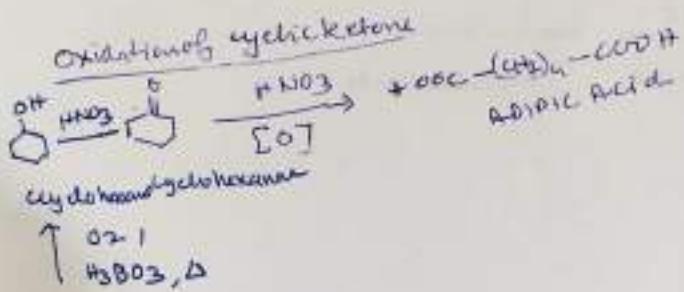
The inductive effect becomes weaker as the $\text{HOOC}-\text{COOH}$ groups are further separated by CH_2 group and K_1 decreases as we ascend the series.

	K_1	K_2	Succinic Acid K_1	K_2
Malonic acid	1.7×10^{-5}	0.23×10^{-5}	6.8×10^{-5}	0.24×10^{-5}

Method of Preparation



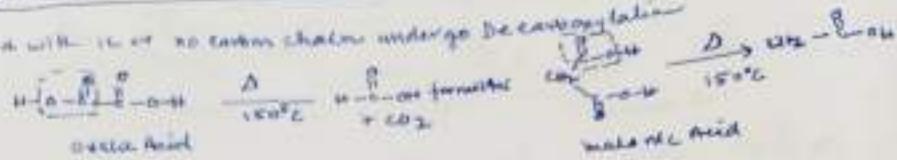
Oxidation of cyclic ketone



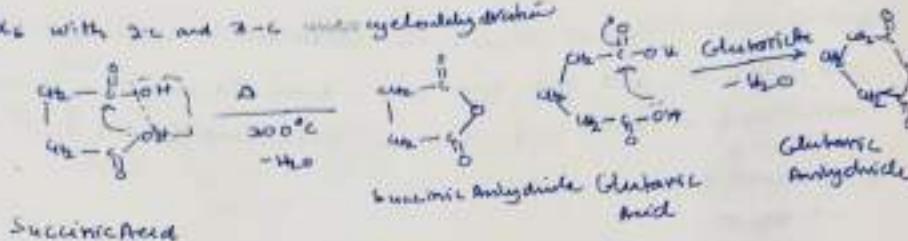
16

Acidic degrad - Dicarboxylic acid

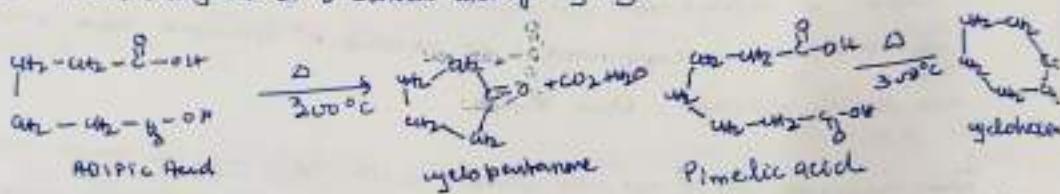
(i) Acids with 1 or 2 carbon chains undergo decarboxylation



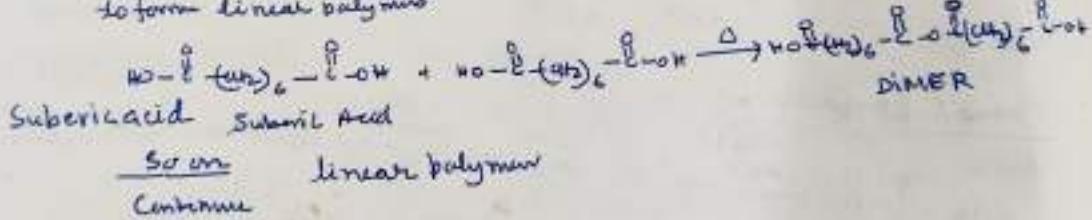
(ii) Acids with 3 & 4 C undergo cyclization



3. Acid with four or 5 carbon undergo cyclization to ketone

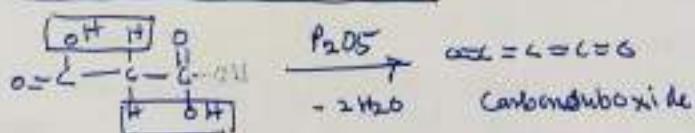


4. Acids with 6-carbon or higher chain undergo intermolecular dehydration to form linear polymer



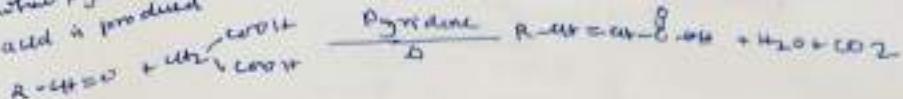
Degradation of Dicarboxylic acids

Decomposition of phosphorus pentoxide

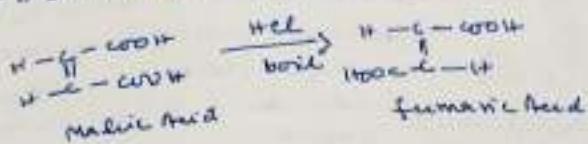


Kraus-Kolbe Reaction

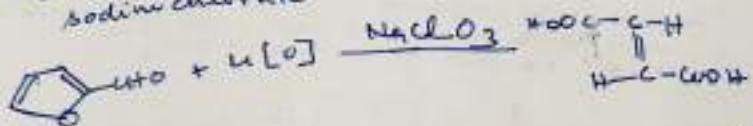
When pyridine solution of malonic acid and aldehyde is heated, it is converted into a product.



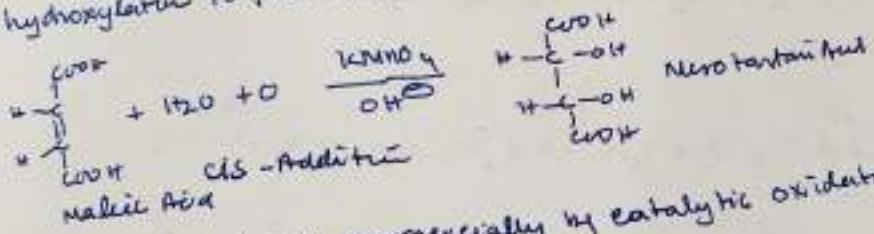
- When malic acid is boiled with concentrated hydrochloric acid or sodium hydroxide, it is converted into fumaric acid.



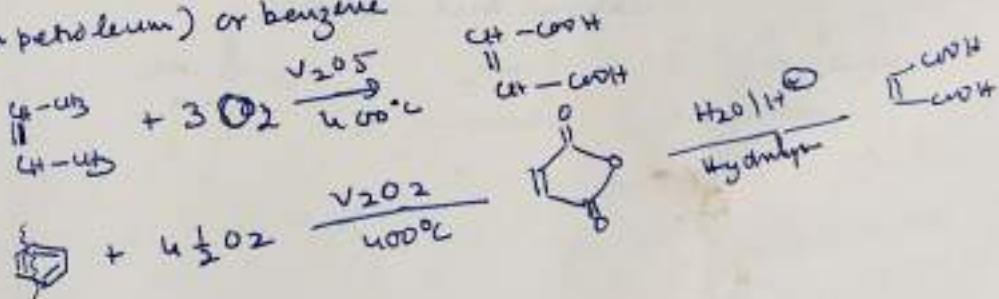
- Again, fumaric Acid is also obtained by oxidation furfural with sodium chlorate.

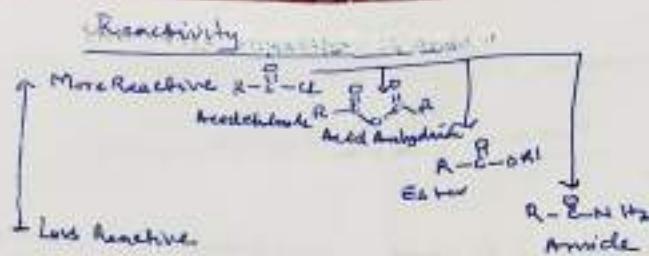


- Fumaric Acid is treated with alkaline KMnO_4 salt, it undergoes hydroxylation to form mesotartaric acid.



Malic Acid is prepared commercially by catalytic oxidation of 2-butene (from petroleum) or benzene.





IB

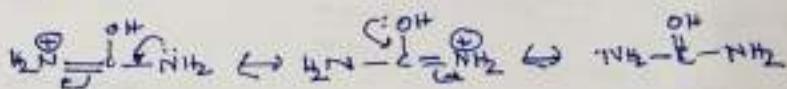
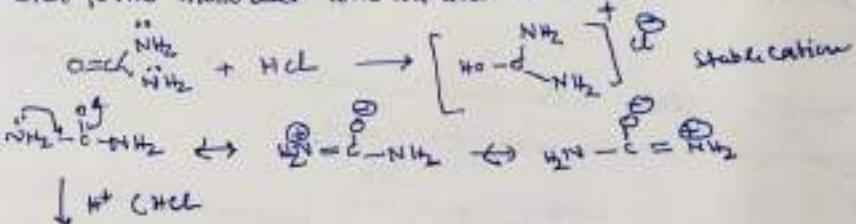
Substitution
Mechanism
in acids

Amides are least reactive of the acid derivatives. The reason is the resonance in amides.

$\text{R}-\overset{\text{O}}{\underset{\text{H}_2\text{O}}{\text{C}}} \leftrightarrow \text{R}-\overset{\text{O}^+}{\underset{\text{H}_2\text{O}}{\text{C}}}^+$ since electron pair of nitrogen is not readily available to an acid amide.
Amides are more stable than carboxylic acids because they have more stable resonance forms.

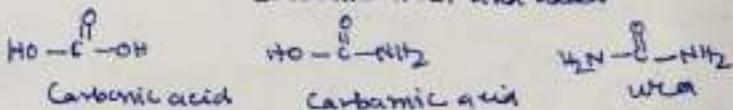
Amides are neutral compounds and do not form salts with acids.

Whereas urea reacts like an acid in most of cases, but it is less acidic than water due to its strong hydrogen bonding.



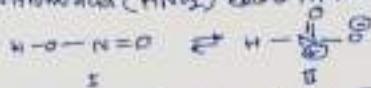
- Carbonic acid is a labile acid. It forms two amides,

carbamyl acid and urea

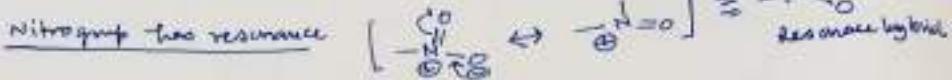
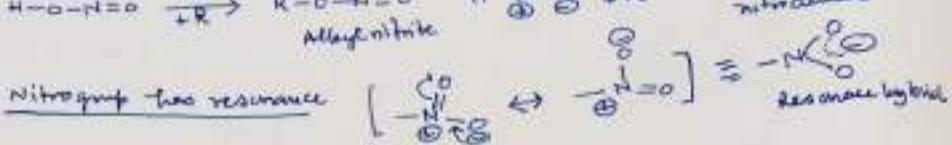
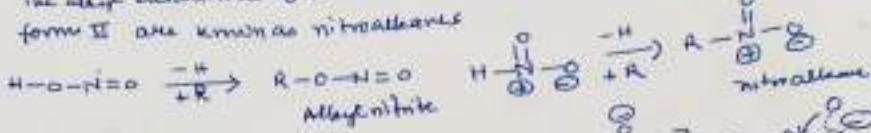


Nitroalkanes

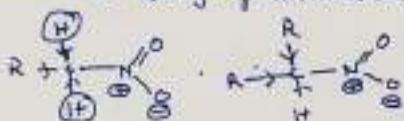
Nitromethane (HNO_2) exists in the following tautomeric forms



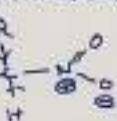
The alkyl derivatives of form I are known as alkynitrites and those of form II are known as nitroalkanes.



- NO_2 group is a powerful electron-withdrawing group and exerts β -effect.
It is due to positive charge of nitrogroup and oxygen atoms of nitrogroup.
Therefore, α -hydrogen of nitroalkane is highly activated and most of reactions of primary nitroalkane are initiated by α -hydrogen.



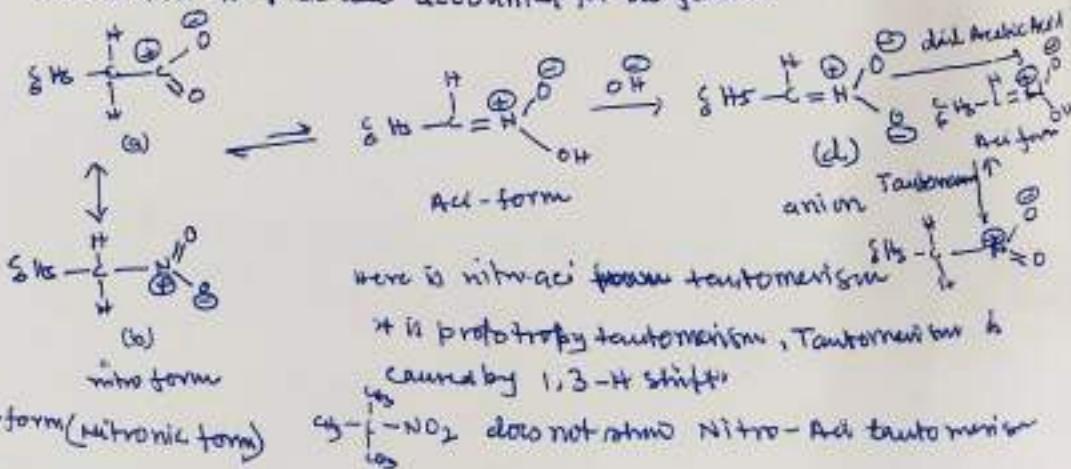
1° nitroalkane

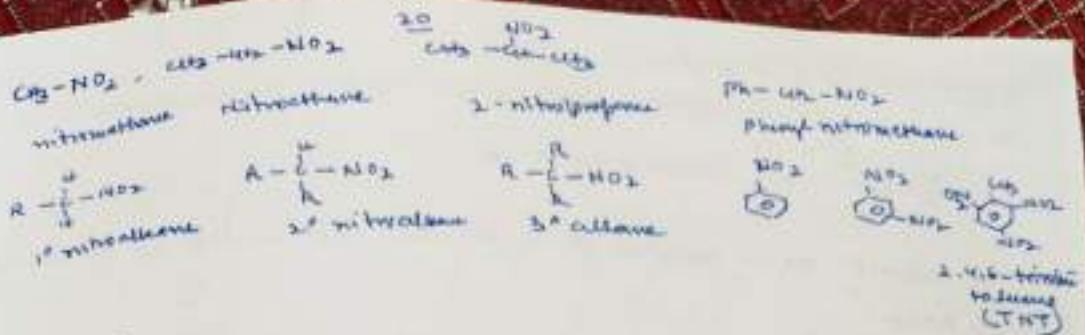


2° nitroalkane

Acidity

Let us a particular example. $\text{Ph}-\overset{\oplus}{\underset{\ominus}{\text{N}}}(\text{O})$ Phenyl nitromethane, light yellow oil gives a neutral test with indicator paper but when shaken with aq alkali it dissolves. Careful acidification of aq salt at 0°C with dil acetic acid gives a colorless oil mp 36°C . It behaves like a true acid (immediately soluble in cold bicarbonate salt) is called aci-form; on standing it slowly reverts to more stable nitro-form, a pseudoid. The facts are accounted for as follows:



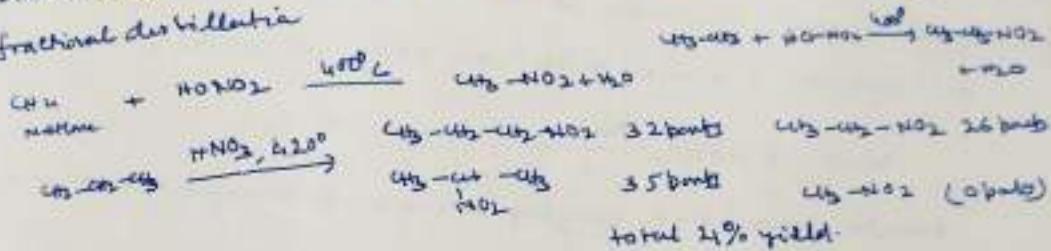


Performance

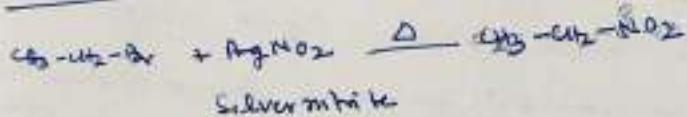
By vapour phase Nitration of Alkanes

By vapour phase nitration
commercial nitro - passing a gaseous mixture of an alkane and nitric acid through a metal tube at 400°C . With almost other than methane, a mixture of nitroalkanes is obtained which can be separated by

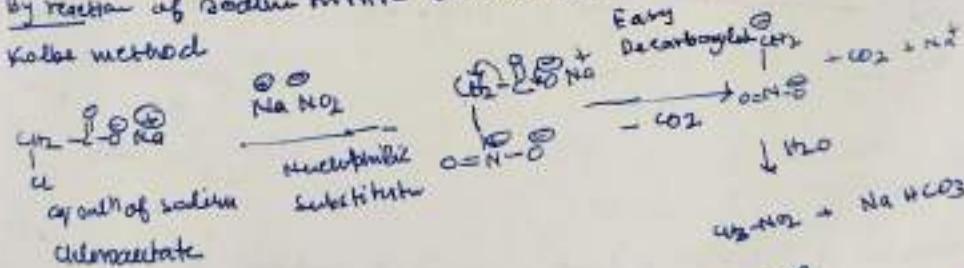
fractional des billets



Reaction with silver nitrate with alkyl halide

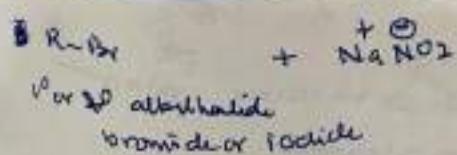


By reaction of Sodium nitrite with d-Halo carboxylic acid
Kolbe method Early Decarbonylation

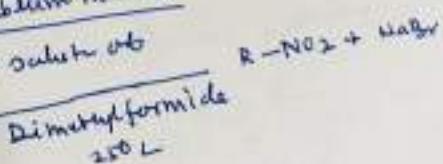


An Empirical Laboratory Method

N-Kombium method



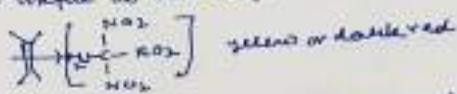
in Zukunft sehr



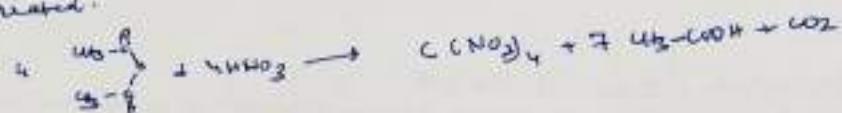
$\approx 12^{\circ}\text{C}$
yield is low and no impurities
for preparation

Tetrinitromethane (mp 13.8°)

It is useful as test reagent because it forms yellow complex with alkene



The aromatic requires caution, it is volatile, toxic and liquid & flammable if heated.



Aromatic nitro compounds

Direct nitration: nitration of an aromatic compound is usually carried out by heating it a mixture of conc HNO_3 and conc H_2SO_4 acid.

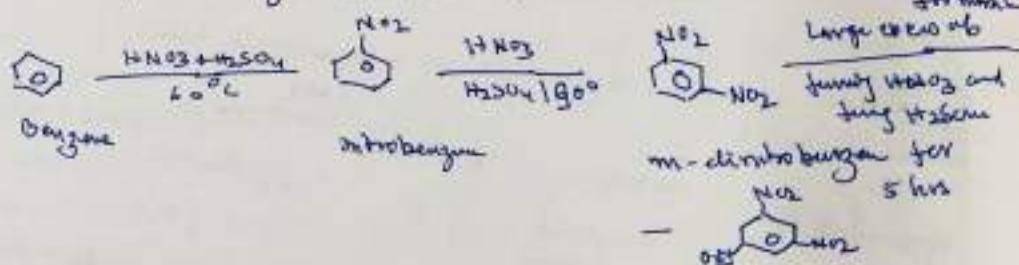


Reaction is controlled by varying strength of nitrating mixture and temperature of the reaction.

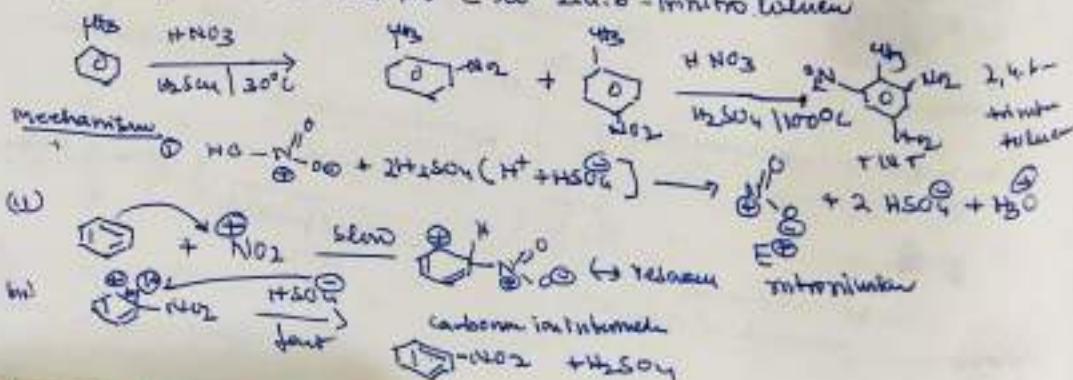
For unreactive Aromatic need elevated temp like $\text{C}_6\text{H}_5\text{NO}_2 \xrightarrow[\Delta]{\text{H}_2\text{SO}_4}$

For reactive compound need lower temp $\text{C}_6\text{H}_5\text{NO}_2$

For example: Benzene needs 60°C for nitration whereas nitrobenzene needs 5°C for nitration.

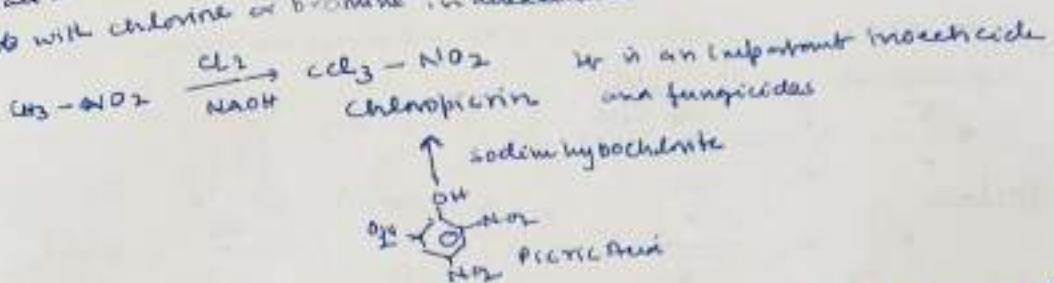


Nitration of toluene is done at a lower temp due to o and p-nitrobenzene are further nitrated at 100°C to 2,4,6-trinitrotoluene



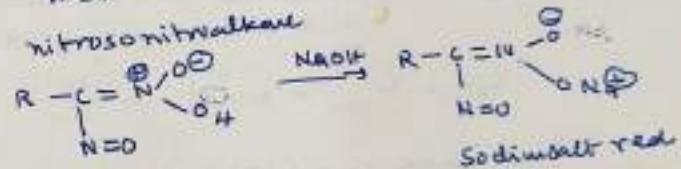
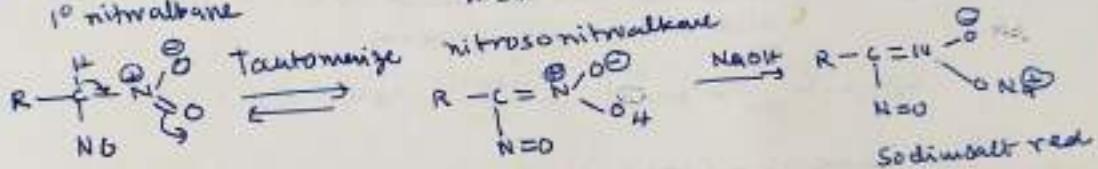
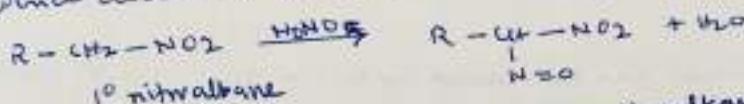
Reaction with Halogen

1° and 2° nitroalkanes are readily halogenated in α -position by treatment with chlorine or bromine in alkaline soln²²



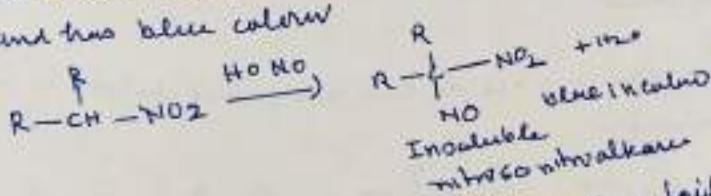
Reaction with Nitrous Acid: $1^\circ, 2^\circ, 3^\circ$ nitroalkanes being too, one or no α -hydrogen atoms react differently with nitrous acid

1° nitroalkane reacts with nitrous acid to form nitroso-nitroalkane which dissolves in NaOH salt to form Sodium salt of nitrosoacid (red)



2° nitroalkane

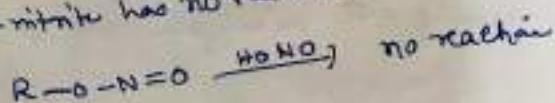
A secondary nitroalkane gives nitroso-nitroalkane which has no α -hydrogen and hence incapable of forming nitroic acid. It is insoluble in alkali and has blue colour



3° nitroalkane having no α -hydrogen atom fails to react with nitrous acid

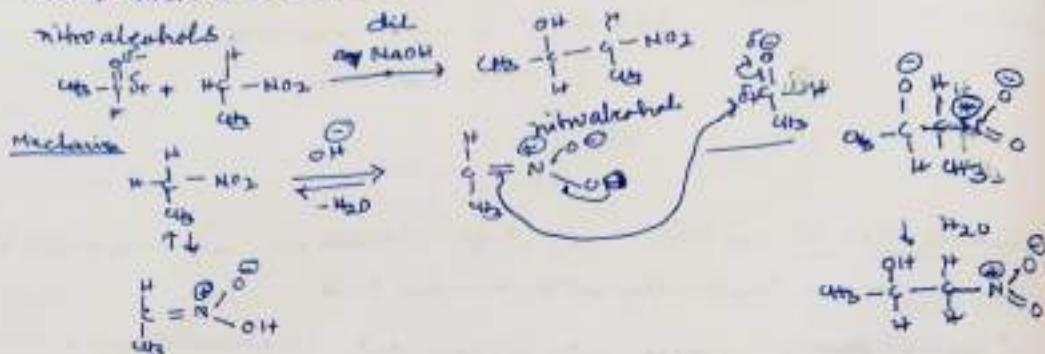
The different behaviour of nitrous acid with $1^\circ, 2^\circ, 3^\circ$ nitroalkanes forms the basis of the Victor-Meyer test for distinction between $1^\circ, 2^\circ, 3^\circ$ nitroalkanes.

Alkyl nitrite has no reaction with nitrous acid

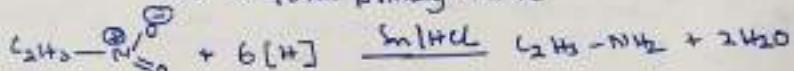


Condensation with aldehydes and ketones

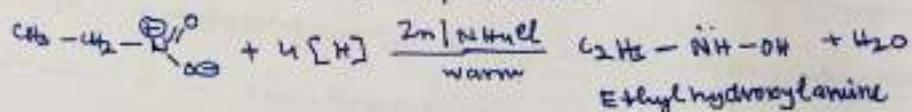
1° and 2° nitroalkane in presence of dil. sodium hydroxide salt undergo aldol addition or condensation with aldehydes and ketones to give nitroalcohols.



Reduction : Nitroalkane can be reduced with tin or iron and hydrochloric acid to form primary amines

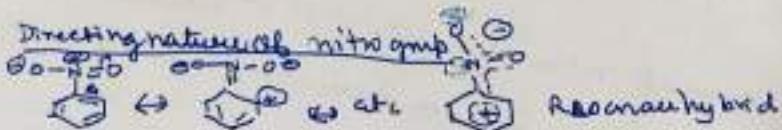
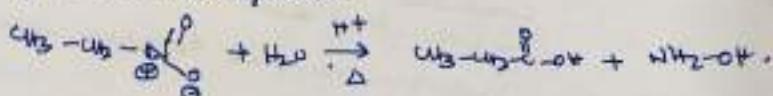


When reduced in neutral salt with Zn dust and aq/NH_4^+ ammonium chloride, nitroalkanes yield allylic hydroxyl amines.



Hydrolysis of Hydroxyamine

Nitroalkanes when boiled with conc HCl or conc H_2SO_4 , are hydrolysed to form carbonylamine and hydroxyamine



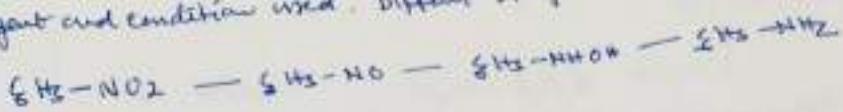
NO_2 group directs -I effect, strong electron-withdrawing group. So partial positive charge develops on α and β -position. In such way, deactivates the ring for E^{\oplus} . So incoming E^{\ominus} on benzene ring goes at α -position

24

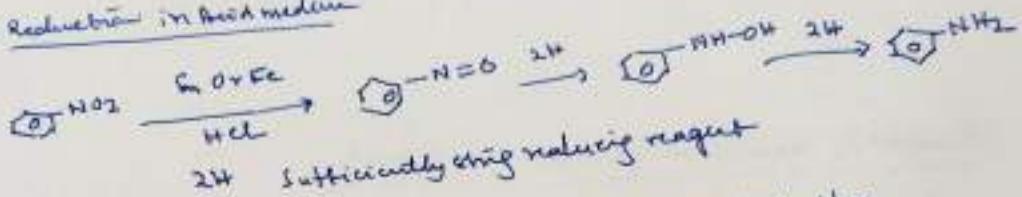
Nitro groups show two type of chemical reactions through - NO_2 group
and reactions through benzene ring

Reactions involving - NO_2 group

Aromatic nitro compounds give a variety of interesting products depending upon reagent and condition used. Different stages are as follows

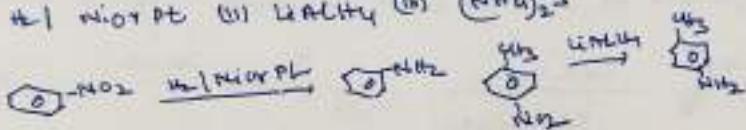


(a) Reduction in Acid medium



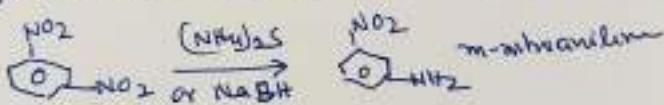
The reduction of $\text{C}_6\text{H}_5-\text{NO}_2$ to NH_2 can also be accomplished by

(i) H_2 over Pt (ii) LiAlH_4 (iii) $(\text{NH}_4)_2\text{S}$

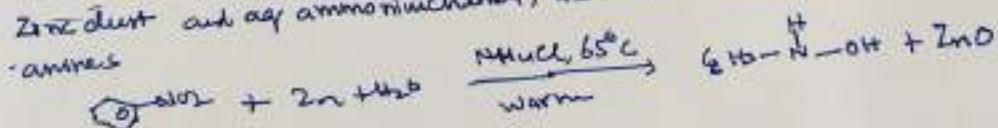


Selective reduction

The reduction of m -dinitrobenzene with ammonium sulphide or sodium hydroxide (NaOH) reduces only one NO_2 group on dinitro compounds

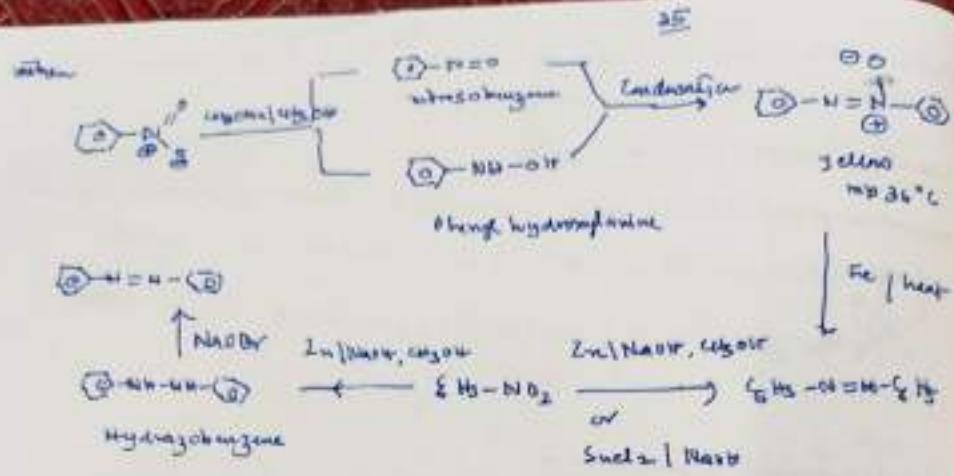


Reduction in neutral medium, when reduced with neutral reducing reagent like zinc dust and NH_4Cl , aromatic nitro compounds form aryl hydrazines



Reduction in alkaline medium gives Aminobenzene , Hydroxybenzene and A3benzene

When nitrobenzene is reduced with mild reagent in an alkaline medium, then happens condensation between first two products of reduction, nitrobenzene and phenyl hydroxylamine



Electrolytic Reduction gives $\text{p}-\text{aminophenol}$

When nitrobenzene is reduced by electrolysis in conc H_2SO_4 soln,
through hydroquinone as it is produced, rearranges to give β -aminophenol.

