

Carboxylic acids

Presented by

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Professor & Head

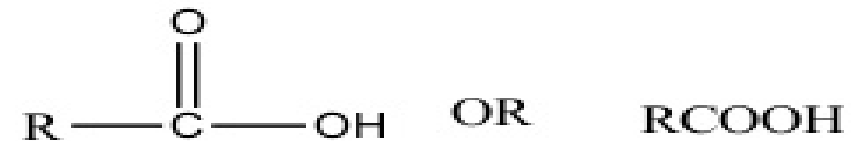
Department of Pharmaceutical Chemistry

QIS College of Pharmacy



Carboxylic acid

- Organic compounds which contain the carboxyl functional group are called as carboxylic acids.
- The name carboxyl is derived from carbonyl(C=O) and hydroxyl(OH) because in the carboxyl group these two groups are directly bonded to each other.



- Carboxyl group are further classified as monocarboxylic acid, dicarboxylic acid, tricarboxylic acid.
- The long chain monocarboxylic acids are commonly known as fatty acid.



Acidity of carboxylic acid

- Carboxylic acid are weak acids and ionize in water according to the following equation.



The equilibrium constant, K_{eq}

$$K_{eq} = \frac{[\text{RCOO}^-][\text{H}_3\text{O}^+]}{[\text{RCOOH}][\text{H}_2\text{O}]}$$

K_a value of carboxylic acid falls within the range of 10^{-4} - 10^{-5} , the K_a value for acetic acid= 1.74×10^{-5}

The ionization Constant: K_a

$$K_a = K_{eq} [\text{H}_2\text{O}] = \frac{[\text{RCOO}^-][\text{H}^+]}{[\text{RCOOH}]}$$

pK_a value of carboxylic acids falls within the range 4-5

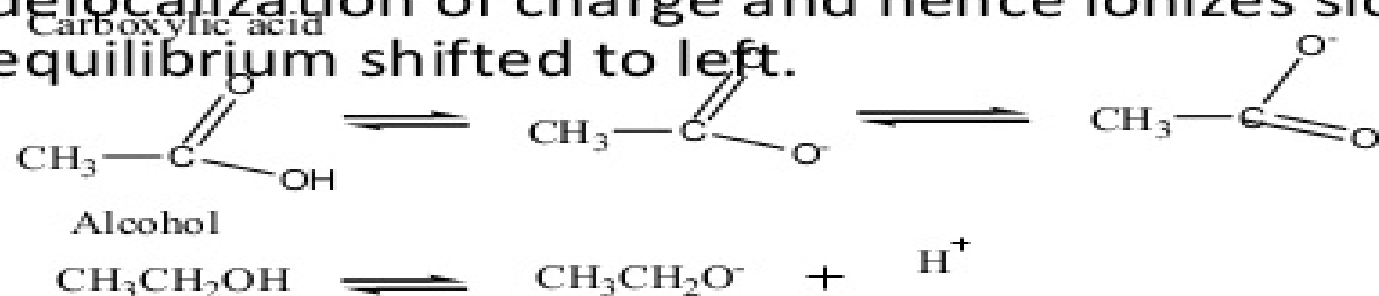
pK_a value of acetic acid =4.76

$$pK_a = -\log K_a$$



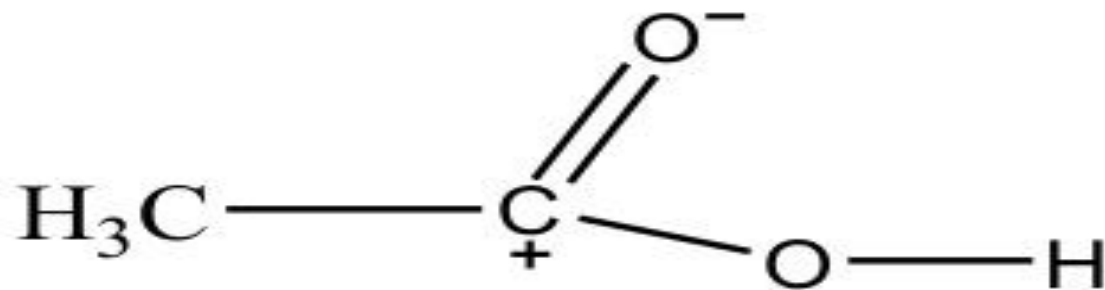
Why carboxylic acid is more acidic than alcohol

1. Lesser the pKa greater the acidity= pKa value for acid is 4-5 and alcohol is 14-16.
2. Ionization of carboxylic acid leads delocalization or shifting of negative charge from one oxygen to another hence separation and creation of unlike charge to produce force drive to ionize.
 - So equilibrium shifted to right side and carboxylic acid ionizes fastly than alcohol.
 - Ionization of alcohol to produce anion and there is no delocalization of charge and hence ionizes slowly and equilibrium shifted to left.



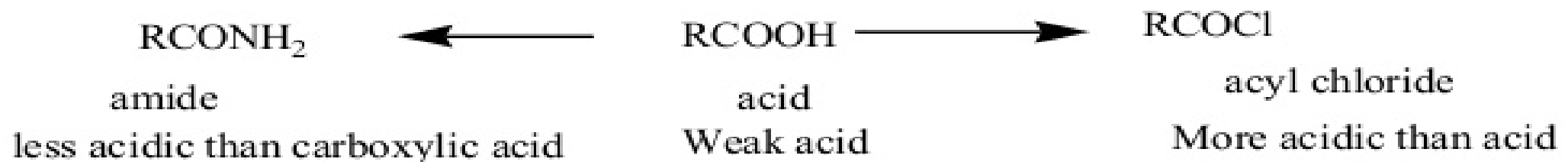
Why carboxylic acid is more acidic than alcohol

3. There is difference in electro negativity between carbon and oxygen, there is partial positive charge on carbonyl carbon which induces polarization of electron in O-H bond.
- Electron withdrawing effect of carbonyl carbon weakens OH bond and facilitates ionization of carboxylic acid compared to alcohol.

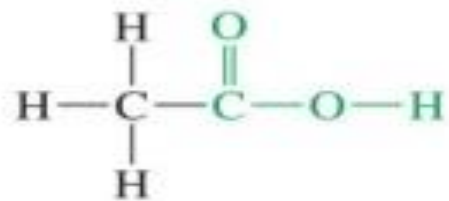


Effect of substituent's on acidity of carboxylic acid.

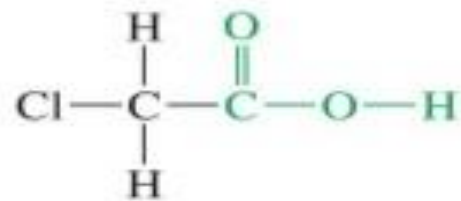
- Electron withdrawing group(Cl, Br, F) increases acidity-
Electron withdrawing group withdraws electron density from the carboxyl group and equilibrium shifted to right that increases acidity of carboxylic acid.
- Electron donating group(OH, NH₂) decreases the acidity-
Electron donating group adds electron density to carboxyl group and equilibrium shifted to left that decreases acidity of carboxylic acid.



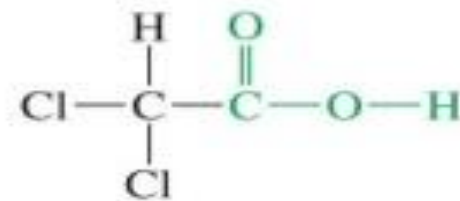
Substituent Effects on Acidity



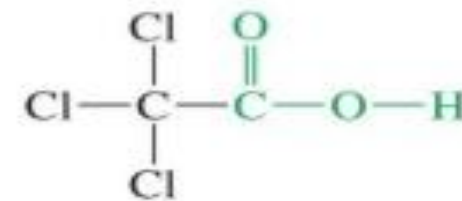
acetic acid
 $\text{p}K_a = 4.74$



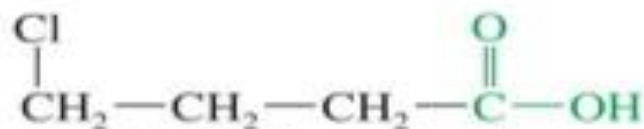
chloroacetic acid
 $\text{p}K_a = 2.86$



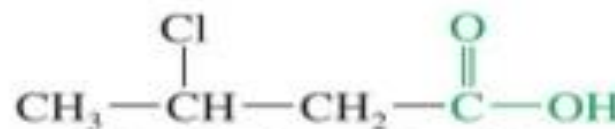
dichloroacetic acid
 $\text{p}K_a = 1.26$



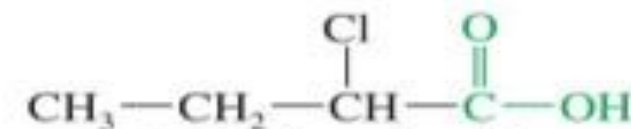
trichloroacetic acid
 $\text{p}K_a = 0.64$



4-chlorobutanoic acid
 $\text{p}K_a = 4.52$



3-chlorobutanoic acid
 $\text{p}K_a = 4.05$



2-chlorobutanoic acid
 $\text{p}K_a = 2.86$

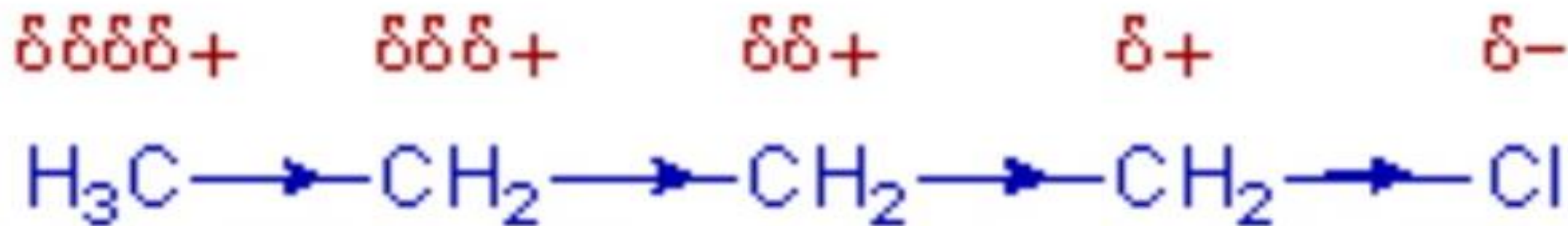
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- The magnitude of a substituent effect depends on its distance from the carboxyl group.



INDUCTIVE EFFECT

The polarization of a σ bond due to electron withdrawing or electron donating effect of adjacent groups or atoms is called inductive effect.



TYPES OF INDUCTIVE EFFECT

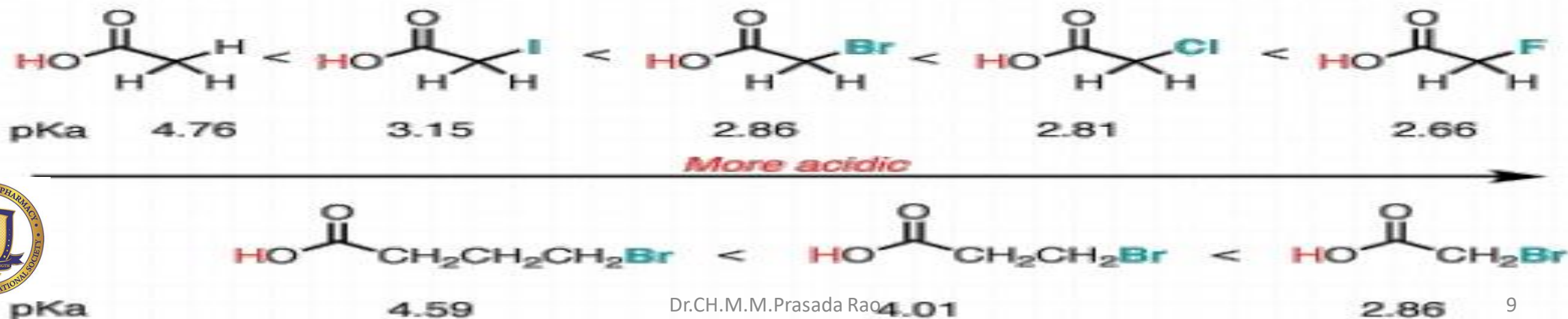
1. Negative Inductive effect (-I):

the electron withdrawing nature of groups or atoms is called negative inductive effect. It is indicated by -I, following are the examples of groups in the decreasing order of their -I effect:

4. Electronegativity and inductive effects:

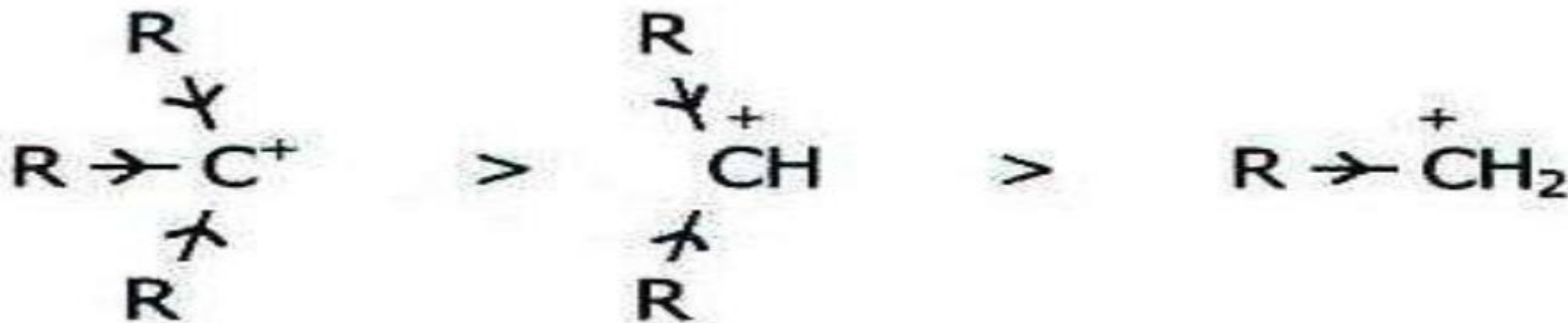
Two principles - electron-withdrawing substituents can increase acidity of a nearby atom, which **increases with electronegativity** and **decreases with increasing distance to the atom**.

Electronegativity increases in the order $F > Cl > Br > I$:



2. Positive Inductive effect (+I):

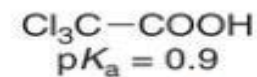
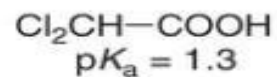
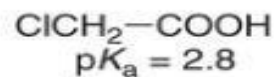
It refers to the electron increasing nature of the groups of atoms and is denoted by +I. the following are the examples of groups in the decreasing order of their +I effect.



Inductive Effects in Carboxylic Acids

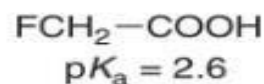
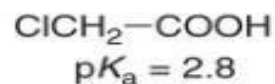
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- The larger the number of electronegative substituents, the stronger the acid.



Increasing acidity
Increasing number of electronegative Cl atoms

- The more electronegative the substituent, the stronger the acid.



F is more electronegative than Cl.

stronger acid

- The closer the electron-withdrawing group to the COOH, the stronger the acid.



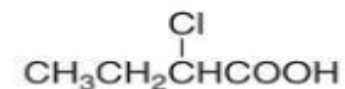
4-chlorobutanoic acid

$pK_a = 4.5$



3-chlorobutanoic acid

$pK_a = 4.1$



2-chlorobutanoic acid

$pK_a = 2.9$



Increasing acidity
Increasing proximity of Cl to COOH



TABLE 20-4

 Values of K_a and pK_a for Substituted Carboxylic Acids

Acid	K_a	pK_a
F_3CCOOH	5.9×10^{-1}	0.23
Cl_3CCOOH	2.3×10^{-1}	0.64
$Cl_2CHCOOH$	5.5×10^{-2}	1.26
O_2N-CH_2COOH	2.1×10^{-2}	1.68
$NCCH_2COOH$	3.4×10^{-3}	2.46
FCH_2COOH	2.6×10^{-3}	2.59
$ClCH_2COOH$	1.4×10^{-3}	2.86
$CH_3CH_2CHClCOOH$	1.4×10^{-3}	2.86
$BrCH_2COOH$	1.3×10^{-3}	2.90
ICH_2COOH	6.7×10^{-4}	3.18
CH_3OCH_2COOH	2.9×10^{-4}	3.54
$HOCH_2COOH$	1.5×10^{-4}	3.83
$CH_3CHClCH_2COOH$	8.9×10^{-5}	4.05
$PhCOOH$	6.46×10^{-5}	4.19
$PhCH_2COOH$	4.9×10^{-5}	4.31
$ClCH_2CH_2CH_2COOH$	3.0×10^{-5}	4.52
CH_3COOH	1.8×10^{-5}	4.74
$CH_3CH_2CH_2COOH$	1.5×10^{-5}	4.82

stronger acids



Physical properties of Carboxylic acid

- Lower carboxylic acids are liquid with disagreeable odors.
- Boiling points and melting point of carboxylic acids increases with increasing molecular weight. Carboxylic acid is associated with dimeric structures and intermolecular interaction with each other, so it has higher boiling point.
- Carboxylic acids also interact with water molecules by hydrogen bonding through carbonyl group and hydroxyl group and because of hydrogen bonding interaction carboxylic acids are more water soluble than alcohol, ethers, aldehydes and ketones.
- IR spectroscopy: IR stretch of carbonyl group is observed at 1700cm^{-1} - 1725cm^{-1} .
- NMR spectroscopy: the chemical shift of carbonyl compounds are observed at δ -2.-2.5



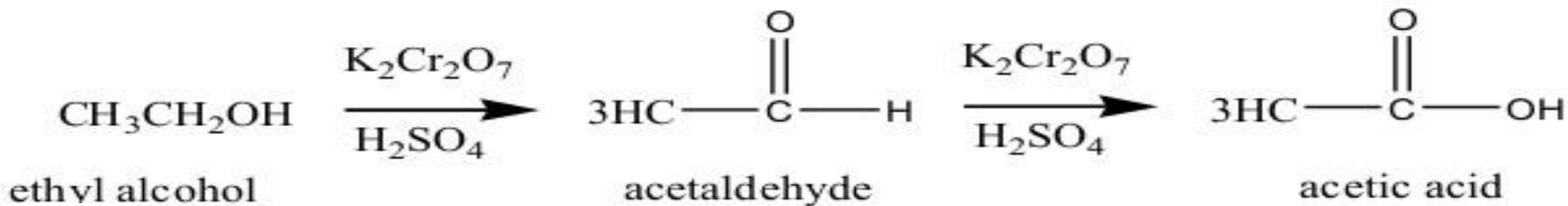
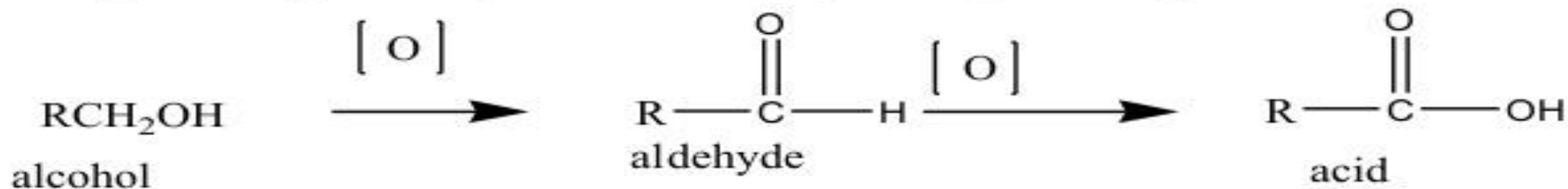
Methods of preparation of carboxylic acid

1. Oxidation of primary alcohols and aldehydes
2. Oxidation of alkenes
3. Hydrolysis of Nitriles
4. Hydrolysis of esters
5. Carboxylation of Grignard method
6. Carboxylation of alkenes
7. From malonic ester



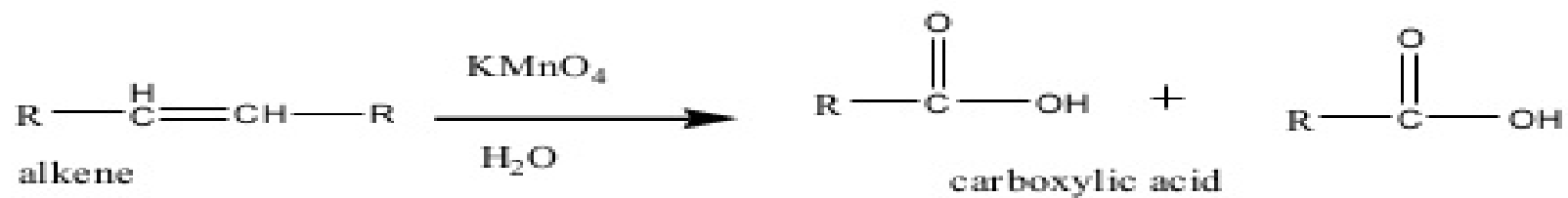
METHODS OF PREPARATION OF CARBOXYLIC ACID

1. Oxidation of primary alcohols and aldehydes: Primary alcohols and aldehydes on oxidation with sodium or potassium dichromate and sulphuric acid, or potassium permanganate, give the corresponding carboxylic acids.

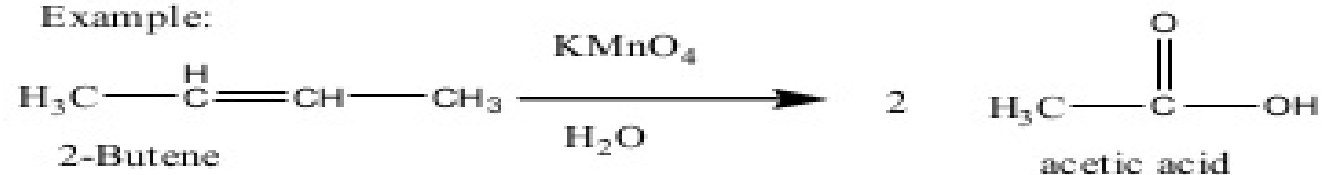


METHODS OF PREPARATION OF CARBOXYLIC ACID

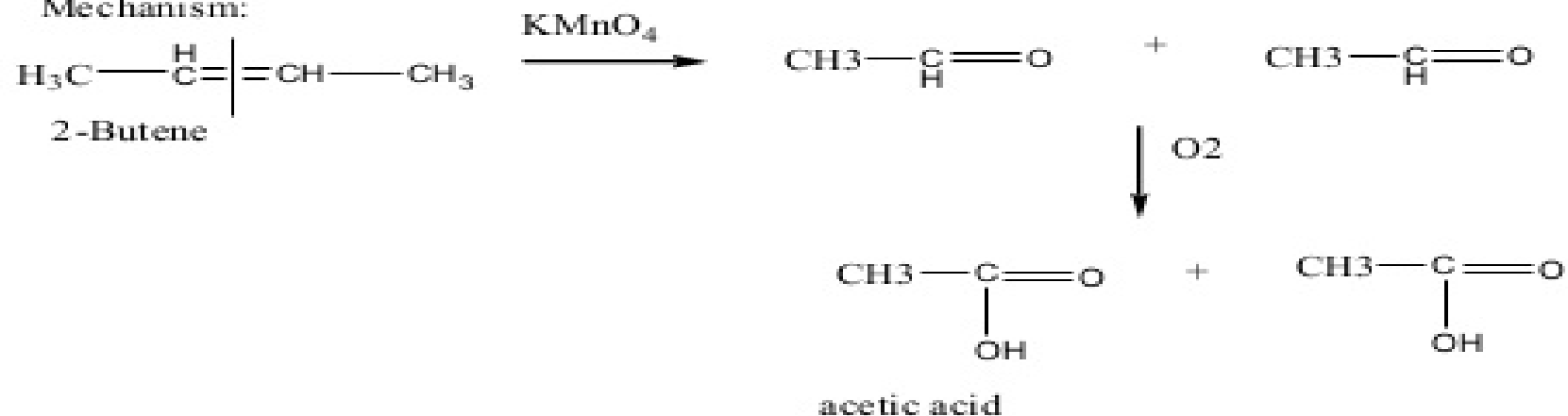
2. Oxidation of alkenes: Alkenes react with basic potassium permanganate under vigorous conditions to produce carboxylic acid.



Example:



Mechanism:



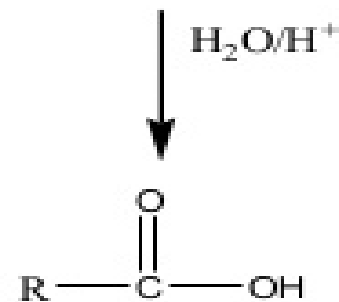
METHODS OF PREPARATION OF CARBOXYLIC ACID

3. Hydrolysis of Nitriles: Nitriles give the carboxylic acid on hydrolysis in acidic or basic solution.

Acidic hydrolysis



Basic Hydrolysis

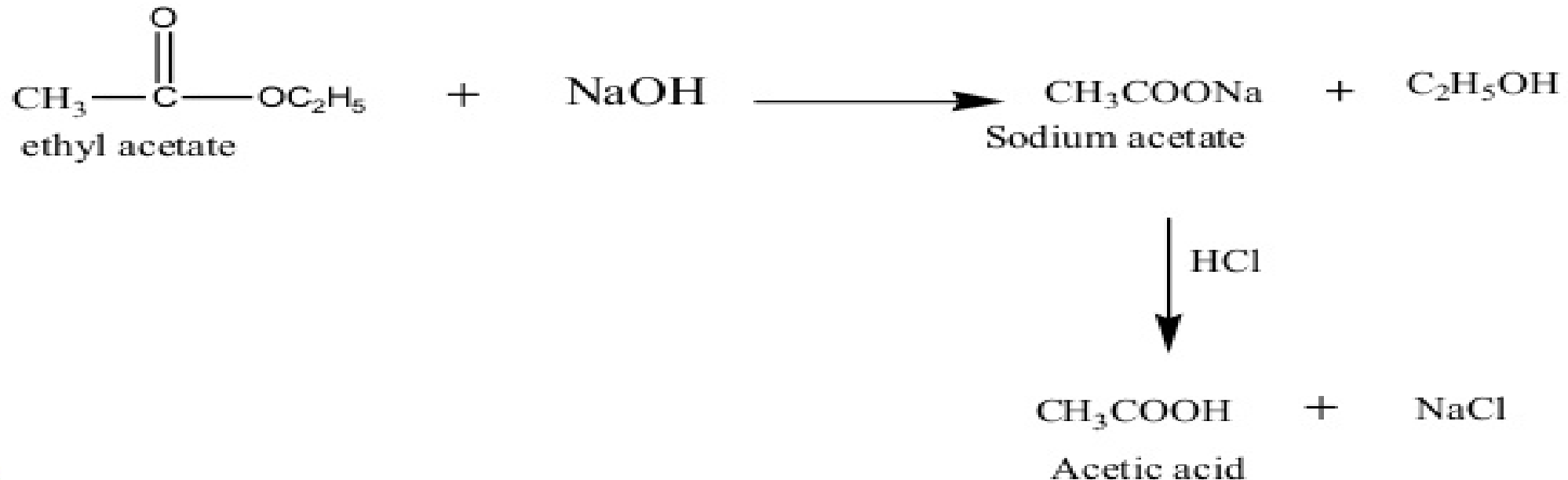


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METHODS OF PREPARATION OF CARBOXYLIC ACID

4. Hydrolysis of esters: When ester is boiled with concentrated aqueous NaOH, and treatment with acid to give carboxylic acid.

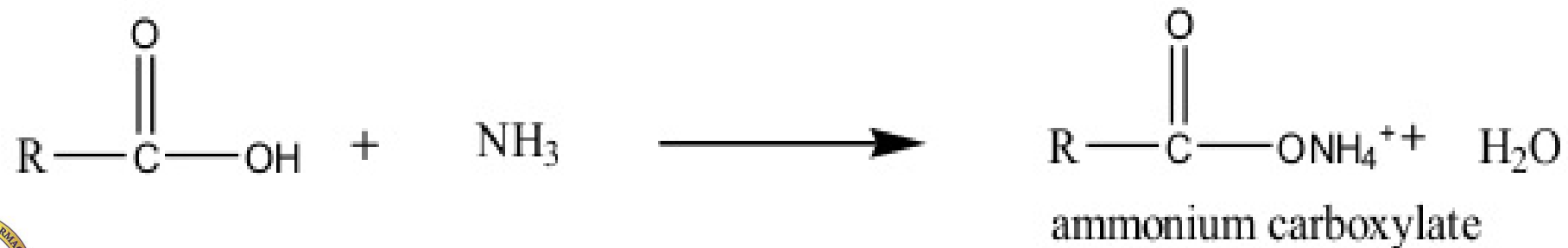
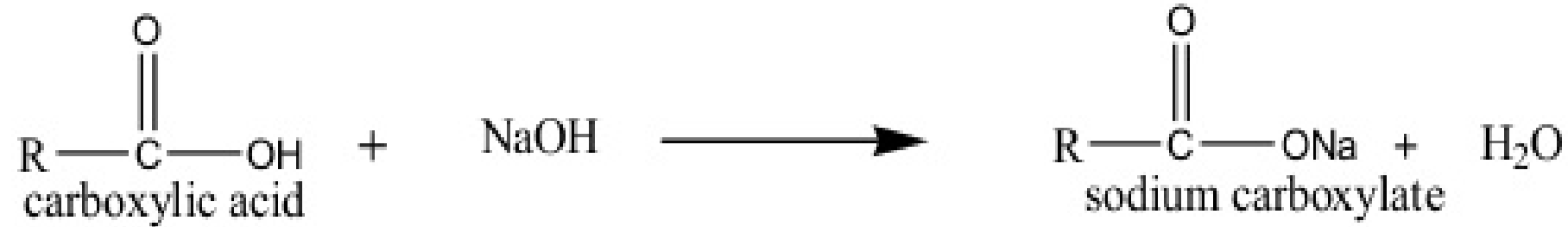


Reactions of Carboxylic acid

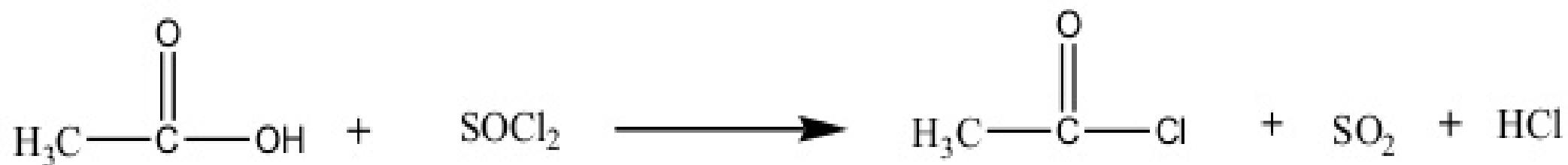
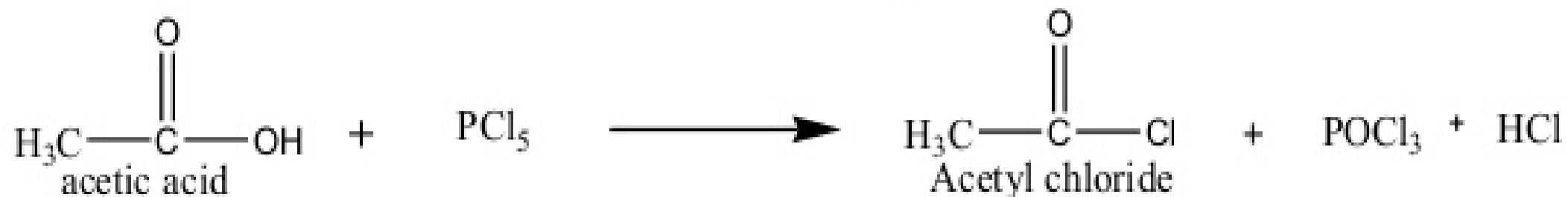
1. Salt formation
2. Formation of acyl halides
3. Formation of amides.
4. Formation of anhydrides
5. Formation of esters
6. Esterification using diazomethane
7. Reduction with aluminium hydride
8. Reduction with dibrono.
9. α -halogenation



1. Salt formation

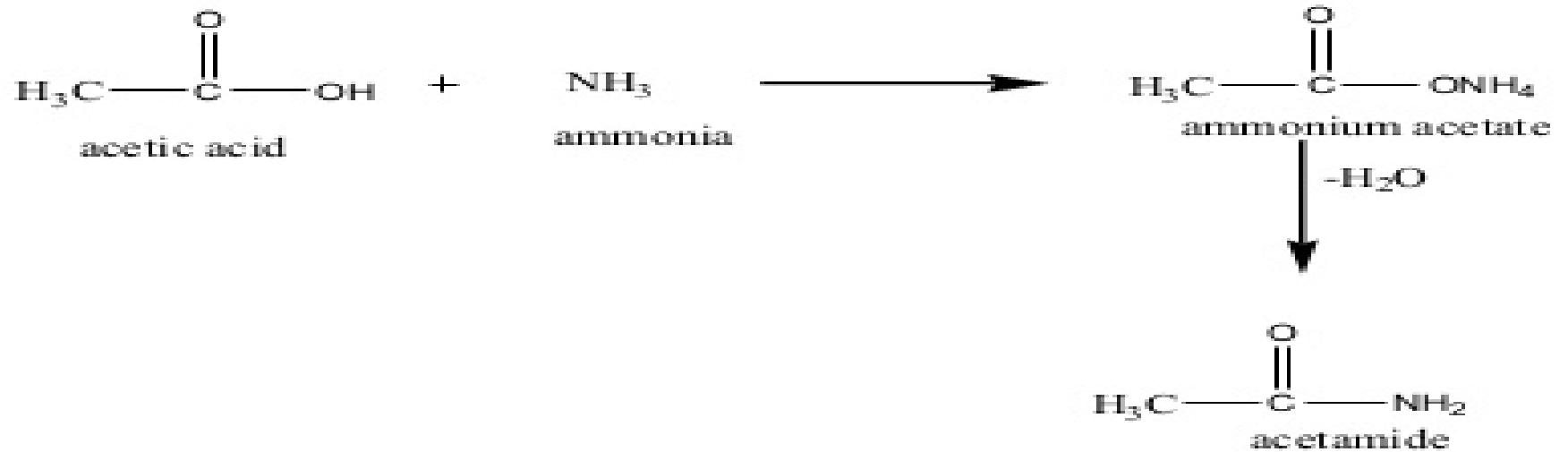
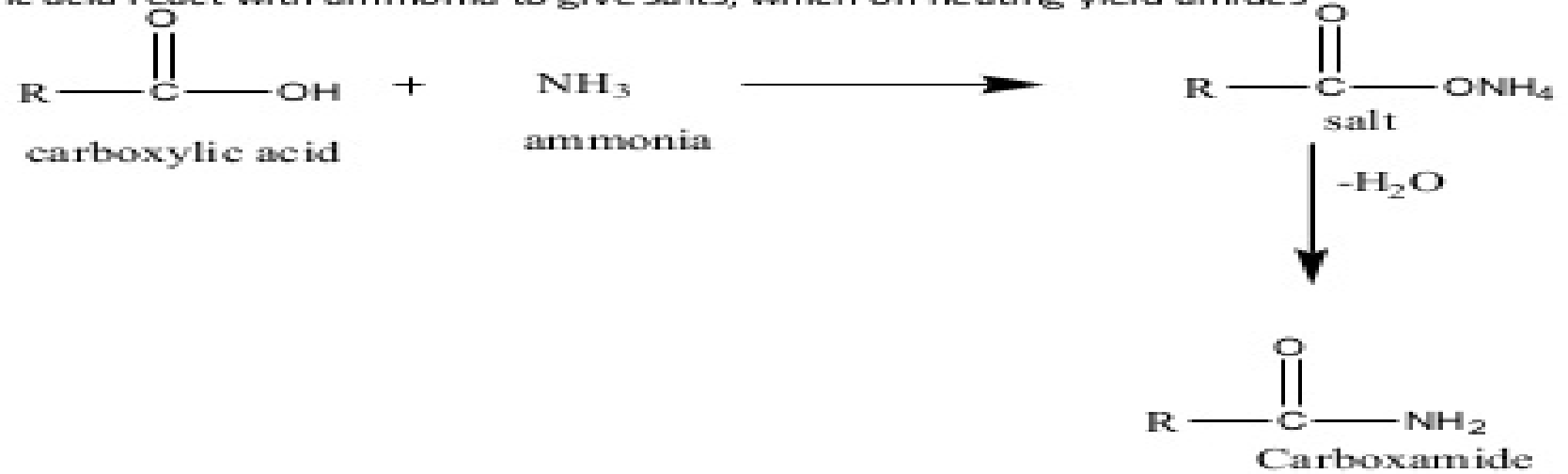


2. Formation of Acyl halides



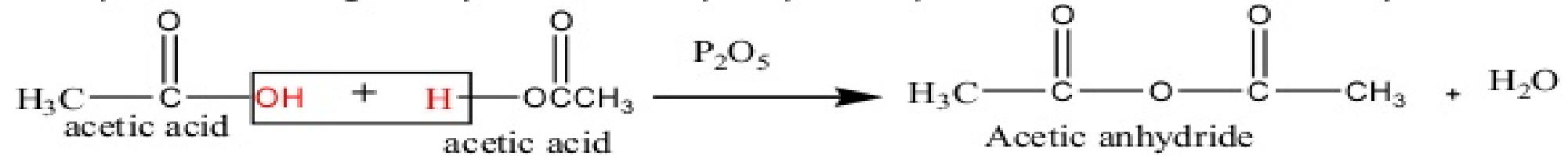
3. Formation of amide

- Carboxylic acid react with ammonia to give salts, which on heating yield amides

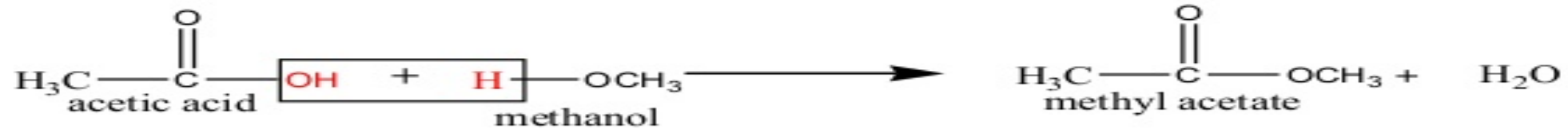


4. Formation of anhydride

Carboxylic acid undergo dehydration with phosphorus pentoxide to form acid anhydride



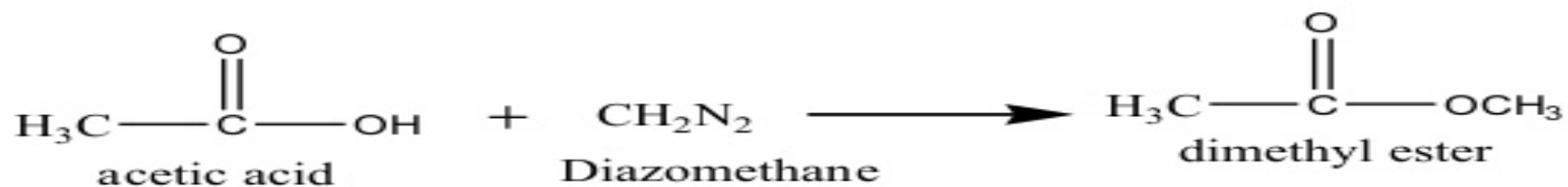
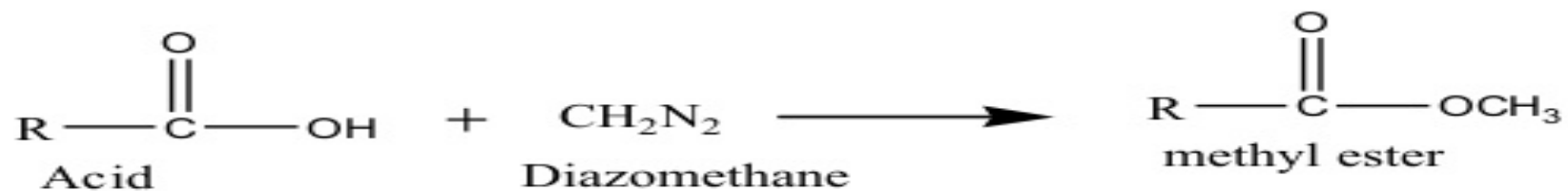
5. Formation of ester



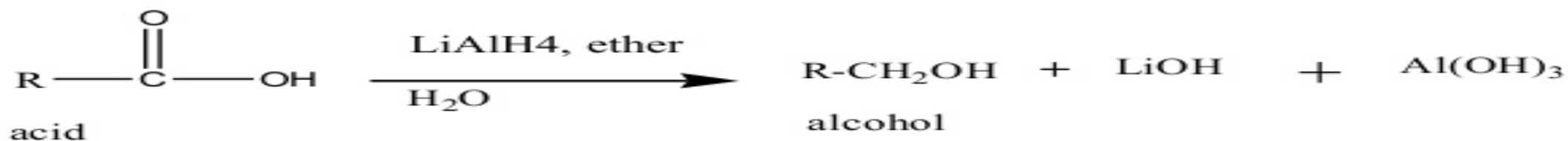
Carboxylic acid react with alcohols in the presence of strong acid to form esters



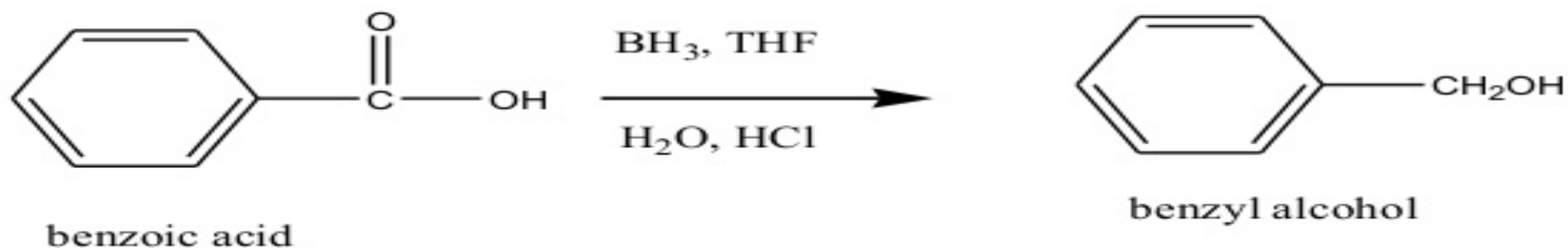
6. Esterification using diazomethane



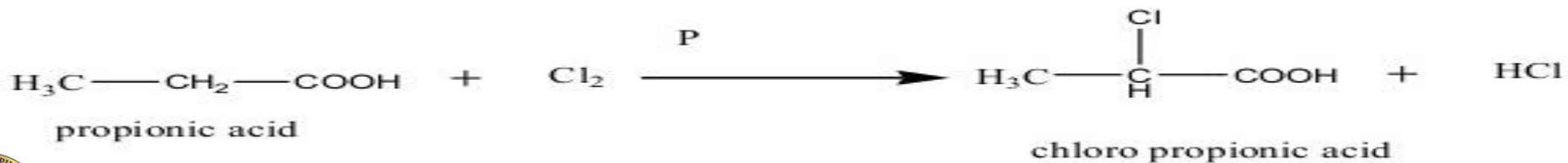
7. Reduction with lithium aluminium hydride



8. Reduction with diborane



9. α -halogenation



Qualitative test for carboxylic acid.

Sr. No	Test	Observation	Inference
1.	Sodium bicarbonate test: 0.2-0.3 gm of compound+ 2ml saturated solution of NaHCO_3	Strong evolution of CO_2 .	Carboxylic acid
2.	Esterification test: 0.2 gm sample in test tube +10 drops of ethyl alcohol+ 2 drops of Conc. H_2SO_4	Fragrant smell	Carboxylic acid
3.	Fluorescein test: 0.1 gm of sample+ 0.1 gm resorcinol + 0.5 ml of conc. H_2SO_4 . Heat the mixture and pour into beaker containing Dil NaOH	Green fluorescence	Carboxylic acid



Qualitative test for amide.

Sr. No	Test	Observation	Inference
1.	Sodium hydroxide test: 0.1 gm sample + 10 drops of NaOH solution and boil	Evaluation of ammonia which turns turmeric paper red	Amide is present
2.	Hydroxamic acid test: 0.2 gm of sample + 2 ml hydroxylamine hydrochloride+ boil on water bath for 5 min. Cool and few drops of alc. FeCl_3	Bluish red color	Aliphatic amide
3.	Nitrous acid test: 0.2 gm of sample + 2ml of dil HCl + 2 ml of NaNO_2 solution	Brisk effervescence due to evolution of N_2	Amide is confirmed
4.	Hydrogen peroxide test: 0.2 gm of sample+ 1 ml of water and add 7-8 drops of H_2O_2 , heat to boiling . Cool and add drops of FeCl_3	Blue color	Aromatic amide



Qualitative test for ester.

Sr. No	Test	Observation	Inference
1.	Phenolphthalein test: 0.1 gm of sample + water+ 2 drops of phenolphthalein + dil NaOH solution drop by drop till pink color persist	Disappearance of pink color	Ester group present
2.	Hydroxamic acid test: Mix 0.4 gm of compound with hydroxyl amine in ethanol and ethanolic sodium hydroxide , heat and cool, add HCl and then add FeCl ₃	Deep red color	Ester group present



Sr. No	Name of acid	Structure	Uses
1.	Acetic acid		Synthesis of acetone, ester, cellulose acetate and polyvinyl acetate, Perfumes, plastic dyes, pharmaceuticals
2.	Lactic acid		Food preservative, curing agent, flavoring agent, decontaminant for meat processing
3.	Tartaric acid		Carbonated beverages and efferevescent tablets, backing powder, as mordant, silvering of mirror, tanning, for preparation of rochelle salt, emetic tartar
4.	Citric acid		Laxative, acidulant in carbonated soft drinks, jams, jellies, candies, ferric ammonium citrate as blue print paper, esters(tributyl citrate as good plastisizers
5.	Succinic acid		Manufacturing of lacquers, dyes, volumetric analysis for acid base titration
6.	Oxalic acid		Redox titration, Ink stain remover, Mordant in dyeing and calico printing, manufacture of inks and metal polishes, allyl alcohol, formic acid.
7.	Salicylic acid		Keratolytic(peeling agent), treatment of acne, antidandruff, psoriasis,
9.	Benzoic acid		Germicide- urinary tract infection, and disinfection, food preservative- sodium benzoate
10.	Benzyl benzoate		Treatment of Scabis, spasmolytic, excipients in testosterone replacement medication
11.	Dimethyl phthalate		Insect repellent for mosquitoes and flies, ectoparasitocide, solid rocket repellent, plastic
12.	Methyl salicylate		Muscle relaxant for pain, arthritis, brushing, backaches
13.	Acetyl salicylate		Pain killer, anti-inflammatory and anticoagulant

