UNIVERSITY OF ILORIN
ILORIN, NIGERIA
FACULTY OF PHARMACEUTICAL SCIENCES
DEPARTMENT OF PHARMACEUTICAL & MEDICINAL CHEMISTRY



PRACTICAL PHARMACEUTICAL QUANTITATIVE ANALYTICAL & SYNTHETIC ORGANIC CHEMISTRY

300 LEVEL MANUAL & WORKBOOK

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300 LEVEL

MANUAL & WORKBOOK

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PART 1

PCH301
PRACTICAL

PHARMACEUTICAL QUANTITATIVE ANALYTICAL CHEMISTRY

PHARMACEUTICAL QUANTITATIVE ANALYTICAL CHEMISTRY

1.0 Introduction

Classical method is quantitative chemical analysis which involves the measurement of the solution of accurately known concentration which is required to react quantitatively with a specific weight or the solution of the sample. A solution containing a known weight of the reagent (the titrant) is added in small lots to a known volume of solution (the analyte) containing the substance to be estimated. The completion of reaction is indicated by visible change brought about by the addition of view drops of a reagent which reacts only when the main reaction is at an end. The reagent which undergone this visible change is called an indicator. The point that indicated the completion of a reaction is called end point. The process of determining the volume of titrant for complete reaction is called titration.

SCHEDULE I

1.1 SELECTION OF SUITABLE INDICATOR FOR ACID-BASE TITRATION

In titration of an acid with a base, a proton is transferred from acid to a base, thus the reaction is often called neutralization and the products are salt and water at pH 7. The pH of a neutral solution is not always equal to 7. If the pH of a salt solution is not equal to 7 this indicate that one or more of the ions present has reacted with water to increase or decrease the $[H^+]$ i.e. the salt has been hydrolyzed.

An acid – base indicator is an organic compound usually added to an acid – base titration to indicate when the equivalence point has been reached. It is either a weak acid or weak base it can therefore take either of the equilibrium.

$$HIn \rightleftharpoons H^+ + In^-$$

The unionised form (HIn) has different colour from the ionised form (In^-). The colour of an otherwise colourless solution will therefore depend on the ratio of the two forms which in turn depend on the pH of the solution. Since the pH changes during titration, the colour of the solution containing the indicator will also change in the course of titration, so with appropriate choice of indicator, the colour change can be made to coincide with equivalence point and hence indicate the equivalence point.

When two differently coloured forms of an indicator are present in equal amount, it gives an intermediate colour which is often called a neutral colour of an indicator and does not always correspond to pH of 7. The particular pH at which an indicator displays its neutral colour is called pKa of that indicator, where Ka is the acid dissociation constant of the indicator. If indicator A shows its basic colour in water, it means that it most has pK_b less than 7 and as it has passed its natural colour at that pH, likewise if indicator B shows its acidic colour in water, its pKa must be greater than 7 as it has not reached its change point. The correct choice of an indicator for an acid – base titration depends on the pH of the salt solution at equivalence point. A suitable indicator for a particular titration should show a sharp colour change in the pH range at equivalence point.

1.1.1 Experiment 1

Record the approximate pH of the following salt solution using universal indicator

sodium nitrate

i. Potassium sulphate
ii. Ammonium chloride
iii. Ferric chloride
iv. Sodium acetate

Exercise

a) Comment on the suitability of using the term "neutralization" for all acid-base titrations.
b) Write ionic equations to represent the hydrolysis reaction for each of the following ions: carbonate, ammonium, acetate and ferric chloride.
c) Use the equation above to explain the observed decrease or increase in pH of the salt solution.
d) State with reasons whether the pH at equivalence point will be greater, equal to or less than 7 for the following pair of compounds:
   i. NaOH / CH_3COOH
   ii. Na_2CO_3 / HCl
   iii. H_2SO_4 / NH_4Cl
   iv. NaOH / HNO_3

1.1.2 Experiment 2

a) Determine the colour of the acidic and basic forms of each of the indicators provided, by the addition of few drops to 10 mL acid and alkaline solution provided. The indicators are methyl orange, Congo red, Phenolphthalein, Phenol red and Cresol red. Record your observation.
b) Add few drops of the above indicators to 10 mL of distilled water (pH = 7) and note whether the colour displayed is the acidic, neutral or basic colour of the indicator. From your result determine whether the pKa for each indicator is greater than, equal to or less than 7.

Exercise

Based on the result of pKa of various indicator observed above, proposed suitable indicators for each of the following acid-base titrations

i. NaOH / CH_3COOH
ii. $NaCO_3$ / HCl
iii. H_2SO_4 / NH_4OH
iv. NaOH / HNO_3

EXPERIMENTAL REPORT

Title:

Aim:

Methodology:

Results:

Discussion:

Conclusion:

1..1.3 Experiment 3

a) Titrate the sulphuric acid solution provided against ammonia solution. Carry out at least three separate titrations; using two indicators you consider suitable for the detection of equivalence point and one indicator you think will not be suitable. Comment on the relative volumes used in the titration and explain your results.

b) Titrate the sulphuric acid solution against sodium bicarbonate solution provided. Carry out two separate titrations. For the first titration, use methyl orange as indicator and for the second use phenolphthalene.

Exercise

Compare the volumes of the titrant required for each titration and explain your results.

EXPERIMENTAL REPORT

Title:

Aim:

Methodology:

Results:

Discussion:

Conclusion:

SCHEDULE II

1.2 ACID-BASE TITRATION IN AQUEOUS MEDIUM

The reaction between acid and alkaline in the formation of salt and water forms the bases of this analysis this process is known as neutralization reaction

1.2.1 Determination of Mixture of Borax and Boric Acid

Borax ($Na_2B_4O_7.10H_2O$) is determined by titration with a standard acid using methyl orange as an indicator (Va). The total Boric acid (H_3BO_3) is determined by titration with an alkaline using Phenolpthaleine as an indicator (Vb), from the difference Vb – Va, the boric acid content can be calculated.

Method

Dissolve 0.1g of sample of a mixture of Borax and Boric acid in 25 mL water with the aid of heat. Cool and titrate with 0.05M HCl using methyl orange as an indicator (Va). Add 25mL of neutralized glycerol and titrate with 0.05M Sodium hydroxide, using Phenolpthalene as indicator (Vb).

Calculate the percentage (w/v) of Boric acid and Borax respectively in the sample. Comment on your result.

Calculation:

$$Na_2B_4O_7.10H_2O + 2HCl \longrightarrow H_3BO_3 + 2NaCl + 5H_2O$$

The liberated Boric acid may then be titrated with standard alkali in the presence of mannitol or glycerol.

$$4H_3BO_3 + 4NaOH \xrightarrow{\text{mannitol}} 4NaBO_2 + 8H_2O$$

$Na_2B_4O_7.10H_2O \equiv 2HCl \equiv 4H_3BO_3 \equiv 4NaOH \equiv 4000$ mL of 1M NaOH.

In a mixture of Borax with Boric acid from equation 2

$H_3BO_3 \equiv NaOH \equiv H$

61.83g of $H_3BO_3 \equiv 1000$ mL 1M NaOH

0.006138g of $H_3BO_3 \equiv 1$ mL 0.lM NaOH

from equation one:

$Na_2B_4O_7.10H_2O \equiv 2HCl \equiv 2H$

381. 4g $\equiv 2000$ mL of 1M HCl

0.01907g of $Na_2B_4O_7.10H_2O \equiv 1$ mL 0.1M HCl

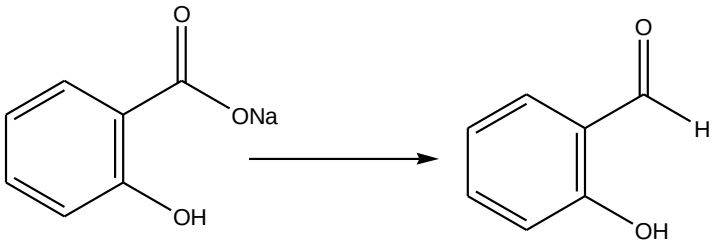
$$\%\, w/v\ of\ Borax\ = \frac{Va\ x\ 0.01907\ x\ F\ x\ 100}{Weight\ of\ sample}$$

$$\%\, w/v\ of\ Boric\ acid\ = \frac{Vb - 2Va\ x\ 0.006183\ x\ F\ x\ 100}{Weight\ of\ sample}$$

F = Factor of HCl

1.2.2 Assay of Sodium Salicylate

This assay is based on conversion of sodium salicylate by hydrochloric acid to salicylic acid



The salicylic acid produced is sufficiently acidic to affect any indicator that is used in the reaction. It is therefore necessary to remove the salicylic acid formed, so equal volume of water and ether are used in the titration

$C_6H_5(OH)COONa \equiv HCl \equiv 1000$ mL of 1M HCl solution

160.1g of C_6H_5 (OH) COONa $\equiv$ 1000 mL of 1M HCl solution

0.01601g of C_6H_5 (OH) COONa $\equiv$ 1 mL of 0.1M HCl solution

Method

Dissolve 0.5g of the sample provide in 20 mL of water. Transfer the solution into a separatory funnel. Add 20 mL of ether and 10 drops of Bromophenol blue indicator. Titrate with 0.1M HCl until a full green colour is obtained, shaking the separatory funnel occasionally while carrying out the titration.

Exercise

Calculate the percentage purity of salicylic acid in the sample.

EXPERIMENTAL REPORT

Title:

Aim:

Methodology:

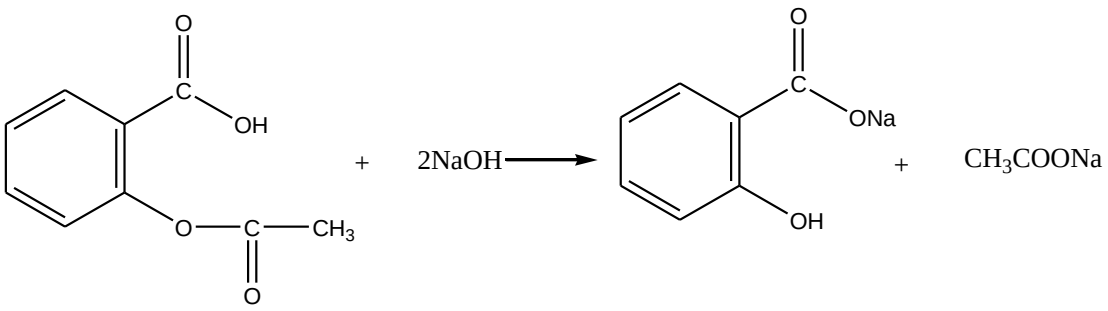
Results:

Discussion:

Conclusion:

1.2.3 Assay of Acetyl Salicylic Acid (Aspirin)

Assay of Aspirin is best carried out by back titration. The assay depends on the hydrolysis of Aspirin to acetic acid and salicylic acid and the immediate formation of their sodium salt by heating with excess alkali. The excess alkali is back titrated with standard acid using phenol red as indicator.



$CH_3COOC_6H_4COOH \equiv 2NaOH \equiv 2H$

180 g of $CH_3COOC_6H_4COOH \equiv 2000$ mL of 1M NaOH solution

0.045 g of $CH_3COOC_6H_4COOH \equiv 1$ mL of 0.5M NaOH solution

Method

Weight 1.0 g of the sample into a conical flask and add 50 mL of 0.05 M NaOH and immerse in boiling water bath for 10minutes, cool and titrate the excess alkali with 0.05M HCl using phenol red as indicator. Carry out the blank determination. The difference between the titrations represents the amount of alkali required by the Aspirin.

Exercise

Calculate the amount of Aspirin in the sample produced and comment on the purity of the sample.

EXPERIMENTAL REPORT

Title:

Aim:

Methodology:

Results:

Discussion:

Conclusion:

SCHEDULE III

1.3 NON-AQUEOUS ACID-BASE TITRATION

Non-aqueous titration involves the use of a solvent other than water as the medium for titration. The end point is determined by a color indicator, whose color depends on the hydrogen ion concentration of the medium. e.g., crystal violet in acetic acid is violet in alkaline blue-green in neutral and yellowish in acidic pH.

1.3.1 Standardisation of 0.1M Perchloric Acid and Assay of Adrenalin BP

Standardisation of 0.1M perchloric acid

Add 25 mL of anhydrous acetic acid into a dry stoppered 100 mL conical flask followed by 2 drops of crystal violet solution and titrate with 0.1M perchloric acid solution until the blue colour changes to blue-green (end point).

Weigh accurately 0.25g of pure potassium hydrogen phthalate, which has been dried at 120^{o}C for 2 hours and allow it to cool in a desiccator. Attach a reflux condenser fitted with silica gel drying tube immediately and warm until all the salt has dissolved, cool to room temperature, detach the condenser and titrate with perchloric acid solution as before. Deduce the volume of perchloric acid solution consumed by 25 mL of the acetic acid from your result. Calculate the factor of perchloric acid solution.

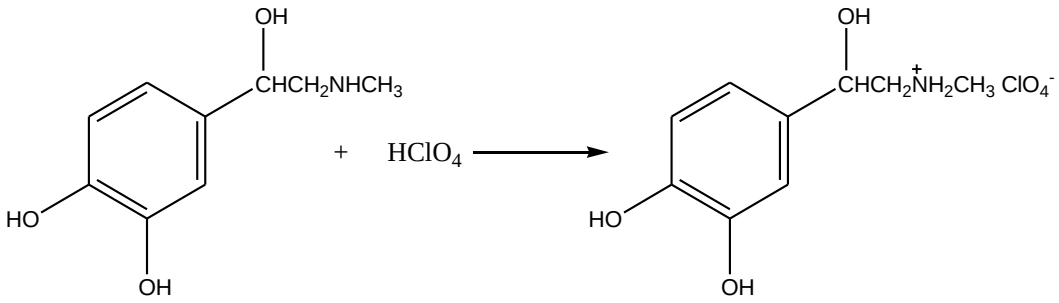
The standardisation is based on the following equation

$$C_6H_4\,(COOK)\,COOH + HClO_4 \longrightarrow C_6H_4\,(COOH)_2 + KClO_4$$

204.2 g $C_8H_5O_4K \equiv HClO_4 \equiv H \equiv 1000$ mL of 0.1M $HClO_4$

0.02042g of $C_8H_5O_4K \equiv 1$ mL of 0.1M $HClO_4$ solution

Assay of Adrenalin (BP)



Adrenaline Adrenaline perchlorate salt

183.2g of $C_aH_{13}O_3N \equiv HClO_4 \equiv H \equiv 1000$ mL 1M $HClO_4$ solution

0.01832g of $C_aH_{13}O_3N \equiv 1$ mL of 0.1M $HClO_4$ solution

Method

Weigh 0.25g of the sample of Adrenalin into a 250 mL conical flask. Dissolve it in 50 mL of glacial acetic acid solution with gentle warming. Add 2 drops of crystal violet solution as indicator and titrate with 0.1M perchloric acid solution. Carry out blank determination and make any necessary correction.

Exercise

Calculate the percentage purity of Adrenalin in the sample

Comment on whether the result obtained complies with British Pharmacopoeia requirement

EXPERIMENTAL REPORT

Title:

Aim:

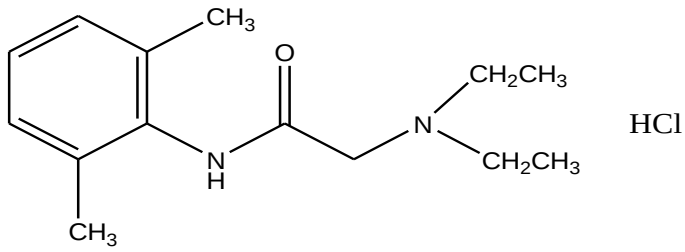
Methodology:

Results:

Discussion:

Conclusion:

1.3.2 Assay of Lidocaine (Lignocaine) Hydrochloride



Lidocaine (Lignocaine) Hydrochloride

This salt is completely ionized as follows:

$C_{14}H_{22}\ O\ N_{2.}HCl \longrightarrow C_{14}H_{22}ON_2^{+}\ H + Cl^{-}$

The chloride ion, (Cl^{-}) being too weak a base to be titrated even in glacial AcOH, Mercury (II) acetate must be added in this assay.

$2Cl^{-} + Hg\ (OAc)_2 \longrightarrow HgCl_2 + 2OAc^{-}$ (Ac = CH_3CO-)

$OAc^{-} + HClO_4 \longrightarrow HOAc + ClO_4^{-}$

$C_{14}H_{22}O\ N_2Cl \equiv Cl^{-} \equiv OAc \equiv HClO_4$

270.8g $C_{14}H_{22}ON_2.HCl \equiv$ 1000 mL $HClO_4$ solution.

0.0270g $C_{14}H_{22}ON_2.HCl \equiv$ 1 mL 0.1M $HClO_4$ solution.

Method

Weight accurately about 0.25 g of the sample of lidocaine hydrochloride into a 250 mL glass-stoppered conical flask. Add 30 mL of anhydrous glacial acetic acid solution and warm, if necessary, to effect solution. Cool the solution and add 6 mL of mercury II acetate solution and add 2 drops of crystal violet solution as indicator. Titrate with 0.1M perchloric acid. Repeat the determination until two concordant results are obtained. Perform a blank titration and make any necessary corrections.

Exercise

Calculate the percentage (w/w) of lidocaine hydrochloride in the sample provided

Why is mercury II acetate used in the titration?

EXPERIMENTAL REPORT

Title:

Aim:

Methodology:

Results:

Discussion:

Conclusion:

SCHEDULE IV

1.4 REDOX TITRATIONS

1.4.1 Preparation and Standardization of 0.02M Potassium Permanganate Solution

Preparations of $KMnO_4$

Dissolve 3.2g of $KMnO_4$ reagent grade in sufficient distilled water to produce 1000 mL solution. Boil the solution for 10 –15 min. and allow it to cool and store overnight. Filter through a cotton wool or sintered glass funnel to remove any precipitated manganese dioxide. Store the solution in clean dark brown stoppered glass bottle previously cleaned with chromic acid solution and rinsed well with water.

Standardization of $KMnO_4$

Weigh 0.63g of analar oxalic acid dihydrate accurately into a 100 mL volumetric flask, dissolve it in water and make up to volume. Pipette out 20 mL of the solution add concentrated H_2SO_4 (5 mL) and warm to about 70 ^oC (when the flask can just be held in the hand). Titrate with previously prepared $KMnO_4$ solution from the burette. The first few drops may impart pink colour to the solution for about twenty second wait until the colour disappears, then continue with the titration to a faint end point i.e., when a faint pink colour persists for about 30 second upon shaking the flask.

Calculation

$$2\,MnO_4 + 5(COOH)_2 + 6H^+ \longrightarrow 2Mn_2^+ + 10CO_2 + 8H_2O$$

$$(COOH)\,2 + O \longrightarrow 2CO_2 + H_2O$$

$$(COOH)_2 \longrightarrow 2CO_2 + 2H^+ + 2e^-$$

$H_2C_2O_4.2H_20 \equiv 2e^- \equiv 2H^+$

126.067g of $H_2C_2O_4.2H_20 \equiv$ 2000 mL 0.2M $KMnO_4$

0.006303g of $H_2C_2O_4.2H_2O \equiv$ 1 mL of 0.02M $KMnO_4$ solution

Calculate the actual molarity and volumetric factor of $KMnO_4$ solution provided.

EXPERIMENTAL REPORT

Title:

Aim:

Methodology:

Results:

Discussion:

Conclusion:

1.4.2 Assay of Hydrogen Peroxide

Hydrogen peroxide is marketed in four strengths, "10", "20", "40" and "100" volume concentrations. A 10-volume solution refer to the fact that the solution when fully decomposed by heat yield ten time its, volume of oxygen measured at 0 ^{o}C and should contain 3% w/w H_2O_2.

$2H_2O_2 \equiv 2H_2O + O_2$

Hydrogen peroxide and potassium permanganate, two oxidizing agents, mutually reduced each other, with evolution of oxygen.

Method

Pipette 10 mL of the diluted hydrogen peroxide solution into a 100 mL volumetric flask, adjust the volume with water and titrate 20 mL or 25 mL potion with previously prepared 0.02M $KMnO_4$ solution after adding 5 mL of 50% sulphuric acid

Equation

$$2KMnO_4 + 5H_2O_2 + 3H_2SO_4 \longrightarrow K_2SO_4 + 2Mn\,SO_4 + 8H_2O + 5O_2$$

$$2MnO_4^- + 6H^+ + 5H_2O_2 \longrightarrow 2Mn^{2+} + 8\,H_2O + 5O_2$$

$5H_2O_2 \equiv 5\,(O_2) \equiv 10\,H$

$5H_2O_2 \equiv 2\,MnO_4 \equiv 10e^-$

34.02g of $H_2O_2 \equiv$ 2000 mL of 0.2M $KMnO_4$ solution

0.001701g of $H_2O_2 \equiv$ 1 mL 0.02M $KMnO_4$ solution

$2\,H_2O_2 \equiv 2\,H_2O + O_2$

68.04 g ≡ 22.4 L of oxygen

32g ≡ 11.2 L/g

1g ≡ 329.2 mL of oxygen

1 mL of 0.02M $KMnO_4 \equiv$ 0.56 mL of oxygen

(i) Calculate the weight of H_2O_2 per mL of the sample

(ii) Calculate the % w/v of H_2O_2

1.4.3 Quantitative Determination of Calcium Gluconate by Redox Titration

The determination depends on precipitation of calcium as insoluble calcium oxalate by the addition of hot ammonium oxalate solution. The precipitate is transferred to a sintered glass filter and washed with dilute ammonium oxalate solution then with water. After that, the precipitate is dissolved with hot dilute sulphuric acid and the sulphate solution is titrated with 0.1N potassium permanganate. The reaction can be illustrated by the following equation

$$C_{12}H_{22}O_4Ca.H_2O + (NH_4)_2C_2O_4 \longrightarrow Ca(COO)_2 + H_2O + C_{12}H_{22}O_4(NH_4)_2$$

$$(COO)_2Ca.H_2O + H_2SO_4 \longrightarrow COOH + CaSO_4$$

$(COOH)_2 \longrightarrow 2CO_2 + 2H^+ + 2e$

Method

Weigh and powder two tablets of calcium gluconate and dissolve in 50 mL of hot water to form a clear solution. Filter and discard any residue. Add 5 mL of dilute hydrochloric acid to the filtrate, heat to boiling and add with stirring about 30 mL of ammonium oxalate and excess ammonium solution (alkaline to litmus). Continue heating for about an hour, allow mixture to cool, and then filter (suction or gravity). Wash the precipitate free of chloride with water (test filtrate at intervals with $AgNO_3$ solution). Dissolve precipitate by adding about 100 mL of hot dilute sulphuric acid in small aliquots. Warm to about 70°C and titrate with 0.1N potassium permanganate solution. (The temperature should be maintained). The Reagent:

i. HCI 32% w/v HCI
ii. $NH_4C_2(COONH_4)_2.H_2O$ solution 2.5 w/v in water
iii. Dilute NH_3 solution 10% w/v NH_3
iv. Dilute H_2SO_4 114g H_2SO_4 + 886 mL H_2O

Calculation:

224.2 $C_{12}H_{22}O_{14}C_{8.}H_2O \equiv$ 1000 mL 2M $KMnO_4$

224.2g of calcium gluconate monohydrate ≡ 1000 mL 0.2M $KMnO_4$

0.002242g of calcium gluconate ≡ 1 mL 0.2M $KMnO_4$

Content of calcium gluconate per tablet

a) $\frac{Average\ titre\ value\ x\ factor\ x\ 0.224}{Number\ of\ tablet} = Qg$

b) $Percentage\ content = \frac{Q}{Weight\ of\ calcium\ gluconate\ in\ each\ tablet} \times 100$

Compare the result with official specification. 98.5 - 102.0%

EXPERIMENTAL REPORT

Title:

Aim:

Methodology:

Results:

Discussion:

Conclusion:

1.4.4 Preparation of Standard $Na_2S_2O_3$. & Standardization of Iodine with $Na_2S_2O_3$Iodometry

Prepare 2.48 – 2.50g sodium thiosulphate pentahydrate using enough freshly boiled and cooled water to make 100 mL in a volumetric flask.

Standardisation of Iodine by Sodium Thiosulphate

Analar sodium thiosulphate ($Na_2S_2O_3.5H_2O$) can be used to standardise iodine solution, which oxidizes the former to sodium tetrathionate.

$$2S_2O_3^{2-} \longrightarrow S_4O_6^{2-} + 2e$$

$$I_2 + 2e \longrightarrow 2I^-$$

$2S_2O_3^{2-} \equiv I_2 \equiv 2e$

248.2g $Na_2S_2O_3.5H_2O \equiv$ 1 mL 0.05M iodine $\equiv$ 1000 mL 0.05M iodine

0.002482g $Na_2S_2O_3$: $5H_2O \equiv$ 1 mL 0.05M iodine

Pipette 25 mL of 0.05M iodine solution into a conical flask titrate with the previously prepared standard sodium thiosulphate solution using freshly prepared starch solution as indicator.

N.B. starch solution is added slowly when the titration solution becomes yellow.

Calculate the normality of the iodine solution.

1.4.5 Determination of the Percentage of Mercuric Chloride ($HgCl_2$)

This is reduced to metallic mercury by formaldehyde in alkaline solution. Oxidation of the mercury to mercuric iodide by excess iodine in the presence of acetic acid and potassium iodide is followed by back titration of the excess iodine.

$$HgCl_2 + HCHO + 3NaOH \longrightarrow Hg + 2NaCl + HCOONa + 2H_2O$$

$$Hg + I_2 \longrightarrow HgI_2$$

$$HgI_2 + 2KI \longrightarrow K_2HgI_4 \text{ (soluble)}$$

$HgCI_2 \equiv Hg + I_2 \equiv 2e$

271.5 g $HgCI_2 \equiv$ 2000 mL of IM iodine

0.01358 g $HgCI_2 \equiv$ 1 mL 0.1M iodine

Dissolve (0.15 g) of an accurately weighed sample in 45 mL water in a 250 mL stopper bottle and add the following reagents in sequence.

i. $CaCl_2$ (5 mL)
ii. KI (1 mL)
iii. Formaldehyde (1.5 mL)
iv. NaOH (7.5 mL)

On the addition of alkali, the calcium chloride reacts to form a fine precipitate of sodium hydroxide which keeps the mercury in a fine state of subdivision. This hastens the reaction with iodine. Shake continuously for 2 minutes; the mercuric chloride is reduced to mercury during this time. Add acetic acid (about10 mL), which should produce an acidic solution. Then add 0.05M iodine solution (25 mL) with pipette and shake vigorously until the mercury has dissolve (10 to 15 minutes vigorous shaking is required). Ensure that no fine globules of mercury remain undissolved. Back titrate the excess of iodine with 0.1M sodium thiosulphate solution using starch solution as indicator.

Calculation

Volume of 0.1M iodine solution equivalent $HgCl_2 \equiv$ (25x factor for iodine) – volume of 0.1M $Na_2S_2O_3 \equiv Z$ mL

Amount of $HgCl_2$ in the sample (g) $\equiv 0.01358Z$g.

Find the percentage of Hg Cl_2 in the sample.

EXPERIMENTAL REPORT

Title:

Aim:

Methodology:

Results:

Discussion:

Conclusion:

1.4.6 Quantitative Determination of Ascorbic Acid

Ascorbic acid is a reducing agent and can be oxidized to dihydroascrobic acid with iodine in acid solution.

$C_6H_8O_6 \rightarrow C_6H_6O_6 + 2H^+ + 2e$

$C_6H_8O_6 + I_2 \rightarrow C_6H_6O_6 + 2HI$

$C_6H_8O_6 \equiv 2e \equiv 2H$

176.12g $C_6H_8O_6 \equiv$ 2000 mL 1M 0.05M iodine solution.

0.008806g $C_6H_8O_6 \equiv$ 1 mL 0.05M iodine solution.

Method

Weigh and finely powder 2 tablets of ascorbic acid (vitamin C) and dissolve in about 100 mL of distilled water. Filter out the particulate matter to obtain a clear solution. Add 25 mL of 1M sulphuric acid and 3 mL of starch solution as indicator. Titrate the bulk solution at once with 0.05M iodine solution until a persistent violet-blue colour is obtained.

Note: to prepare dilute sulphuric acid, add sufficient sulphuric acid to water to make 25 mL of 14 mL of the concentrated sulphuric acid. The process must be cooled ice-cooled / salt-ice bath 88.6 + 11.4 mL.

Calculation

$$\text{Content of ascorbic acid in each tablet} = \frac{\text{Average titre x factor x 0.00881g}}{\text{Number of tablet}}$$

Calculate the percentage content of Ascorbic acid in the sample.

$$\text{Percentage content} = \frac{\text{Vg x 100}}{\text{Equivalent weight per tablet}}$$

Comment on the result and compared with the official specification

EXPERIMENTAL REPORT

Title:

Aim:

Methodology:

Results:

Discussion:

Conclusion:

1.4.7 Assay of Ferrous Sulphate

The assay depends on the oxidation of Ferrous ion (Fe^{2+}) to Ferric ion (Fe^{3+}) according to the following equation.

$Fe^{2+} \longrightarrow Fe^{3+} + e^-$

$FeSO_4 \equiv e \equiv H \equiv 1000$ mL of 1M cerric ammonium sulphate

151.19g of $FeSO_4 \equiv 1$ mL of 0.1M cerric ammonium sulphate

0.01519g of $FeSO_4 \equiv 1$ mL of 0.1M cerric ammonium sulphate

Method

Dissolve 0.5g of dried ferrous sulphate in a mixture of 30 mL water and 20 mL of 1M H_2SO_4 and titrate with 0.1M cerric ammonium sulphate, using ferrous sulphate as indicator.

Exercise

i. Calculate the percentage purity of *the* ferrous sulphate sample
ii. Comment on your result

1.4.8 Preparation and Standardization of 0.1M Sodium Thiosulphate Solution

Sodium thiosulphate pentahydrate is readily obtainable in a state of purity, but there is always uncertainty as to the exact water content because of the efflorescent nature of the salt, it is therefore unsuitable as a primary standard.

Preparation

Dissolve 25g of analar sodium thiosulphate crystal and 0.2g of Na_2CO_3 in freshly boiled and cooled water in a 1000 mL volumetric flask; make it up to volume using same solution.

Standardization

Weigh accurately 0.21g of potassium dichromate; dissolve in 100 mL of water in a 500 mL flask. Swirl it to dissolve the solid. Remove the stopper and quickly add 3g of KI, 2g of $NaHCO_3$ and 5 mL of 1M HCl. Insert the stopper gently and swirl to mix and allow to stand in the dark for 10min. Rinse the stopper and the inner wall of the flask with water and titrate the liberated iodine with sodium thiosulphate solution until the solution is yellowish green in colour then add 3 mL of starch mucilage and continue titration until the colour change to colourless. Repeat the determination to obtain 2 concordant results.

Calculate the factor of sodium thiosulphate solution

$K_2Cr_2O_7 + 6KI + 14HCl \rightarrow \quad 8KCl + 2CrCl_3 + 3I_2 + 7H_2O$

The liberated iodine reacts with $Na_2S_2O_3$ solution

$K_2Cr_2O_7 \equiv 6I \equiv 6000$ mL of 1M $Na_2S_2O_3$ solution

294.2g of $K_2Cr_2O_7 \equiv 6000$ mL of 1M $Na_2S_2O_3$ solution

49.3g of $K_2Cr_2O_7 \equiv 1000$ mL of 1M $Na_2S_2O_3$ solution

0.004903g of $K_2Cr_2O_7 \equiv 1$ mL of 0.1M $Na_2S_2O_3$ solution

1.4.9 Assay of Copper Sulphate ($CuSo_4$)

The determination of copper compounds depends on the instability of cupric iodide formed in the reaction between copper salt and potassium iodide. The cupric iodide breaks up into cuprous iodide and iodine; the iodine is then titrated with standard sodium thiosulphate solution

$2\ CuSO_4 + KI \quad \rightarrow \quad 2CuI_2 \ + \ 2K_2SO_4$

$2CuI_2 \ \leftrightarrow \quad Cu_2I_2 \ + \ I_2$

$2\ CuSO_4.5H_2O \equiv \ I_2 \equiv 2e^-$

2x249.7g of $CuSO_4.\ 5H_2O \equiv$ 2000 mL of 1M $Na_2S_2O_3$ solution

0.02497g of $CuSO_4{:}5H_2O \equiv$ 1 mL of 0.1M $Na_2S_2O_3$ solution

Method

Weight accurately 0.7g sample of copper sulphate into a 500 mL flask and dissolve it in about 50 mL of water, add Na_2CO_3 solution until the solution get slightly turbid (to remove any mineral acid). Add acetic acid to clear the solution and then 3 mL in excess. Add 2g of KI, then dilute to about 150 mL with water and titrate the liberated iodine with 0.1M sodium thiosulphate solution, when the brown colour of iodine solution has turned pale yellow, add 2 mL of starch mucilage (blue colour is evolved) and continue with titration drop by drop, near the end point, add 2g of solid ammonium thiocyanate and shake well. Complete the titration with shaking and allowing 10 seconds between each drop. The end point is when the colour changes from blue to white.

Exercise

Calculate the percentage of copper sulphate pentahydrate in the sample.

EXPERIMENTAL REPORT

Title:

Aim:

Methodology:

Results:

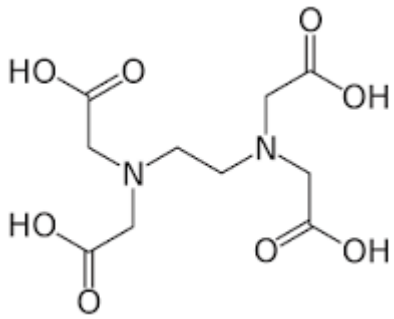
Discussion:

Conclusion:

SCHEDULE V

1.5 COMPLEXOMETRIC TITRATION

The formation of a simple complex rather than a series of complexes will clearly simplify complexometric titration and facilitate the detection of end points. Amino carboxylic acids are excellent complexing agent, the most important being ethylene diamine tetra acetic acid (EDTA), which chelates with many metals. Those compounds that result from combination of an electron donor with a metal ion to form a ring structure are known as chelates. The electron donor atoms in each chelating agent are almost always N, O or S. EDTA has the following structure and can be represented as H4Y.



In analytical work the most frequently used form of EDTA is disodium salt (disodium edetate), Na_2H_2Y EDTA forms complex with many 2, 3 and 4 valent cations e.g., magnesium disodium edetate and its metal complexes are colourless, hence sensitive indicators are necessary to detect the point in the titration of metallic salt solution with edetate. Such indicators are dyes, which form weak complex with metal ions, the complexes having the different colour from a free indicator. A metal indicator complex must be of lower stability than the corresponding metal-edetate complex, so that the metal edetate complex is formed only when free edetate is absent. At end point, the indicator-metal complex gives up its metal to the edetate and a sudden colour change occurs. Each indicator has a certain pH range over which it functions best; hence buffers are often used in complexometric titrations to maintain the pH at an optimum. Disodium Edetate is often used as 0.05M solution strength. EDTA can be used in (i) direct titration (ii) back-titration (iii) replacement substitutionn titration.

1.5.1 Standardisation of Sodium Edetate

Dissolve about 0.125g of zinc accurately weigh in hydrochloric acid (20% w/v HCI) and add a few drops of bromine water. Expel the excess bromine by boiling, add dilute sodium hydroxide solution until the solution is weakly acidic or neutral, dilute to about 125 mL. Add the necessary amount of ammonium chloride buffer solution pH to 10, dissolve the precipitate and add 2.5 mL in excess. Add about 25mg of mordant black II, mixed and titrate with sodium edetate solution until it turns bluish green.

$$Correction\ factor\ for\ sodium\ edetate\ = \frac{weight\ of\ zinc}{Volume\ of\ Sodium\ Edetate\ x\ 0.003268}$$

Applying the above method, find the factor for the supplied 0.05M Sodium Edetate

1.5.2 Analysis of Zinc Sulphate Eye Preparation

To 25 mL of dilute Zinc sulphate eye preparation in a flask, add about 5 mL of dilute hydrochloric acid and 70 mL of distilled water. Add 5 mL of ammoniumchloride buffer solution, titrate with 0.05M disodium edetate using mordant black II indicator.

Calculations

$Zn^{2+} + H_2Y^{2-} \longrightarrow ZnY + 2H^+$

$ZnSO_4 \equiv Zn^{2+} \equiv Na_2H_2Y.2H_2O$

287.5g of $ZnSO_4.7H_2O \equiv$ 1000 mL (IM) (Na_4H_2Y) Sodium Edetate

287.5g of $ZnSO_4.7H_2O \equiv$ 20000 mL 0.05M sodium edetate

0.0144g of $ZnSO_4.7H_2O \equiv$ 1 mL of 0.05M sodium edetate

From the volume of the titrant, calculate the amount of $ZnSO_4$ in the preparation.

$$Weight\ per\ \ mL\ of\ ZnSO4\ \ = \frac{Average\ titre\ x\ factor\ x\ 0.0144g}{25}$$

$$Percentage\ in\ eye\ preparation\ \ = \frac{A(g)x\ 100}{25}$$

EXPERIMENTAL REPORT

Title:

Aim:

Methodology:

Results:

Discussion:

Conclusion:

1.5.3 Determination of the percentage of $KAI(SO_4)_2.12H_2O$

This determination depends upon the reaction expressed by the following equation

$Al^{3+} + H_2Y^{2-} \longrightarrow AlY + 2H^+$

$KAl(SO_4)_{2:}\ 12H_2O \equiv Na_2H_2Y{:}3H_2O$

474.4g $KAl(SO_4)_2.12H_2O \equiv$ 1000 mL 1M Na EDTA

474.4g $KAl(SO_4)_2.12H_2O \equiv$ 20000 mL 0.05M Na EDTA

0.02372g $KAl(SO_4)_2.12H_2O \equiv$ 1 mL 0.05M Na EDTA

Dissolve about 1.7g of sample accurately weighed in sufficient water to produce 100 mL. To 20 mL of this solution, add 0.05M sodium edetate (30 mL) and water (100 mL), heat in a water bath for 10 mintes and cool. Add hexamine (lg) and titrate with 0.05M lead nitrate using four to five drops xylenol orange solution as indicator. The colour will change from that of the indicator (yellow at the pH of titration) to reddish purple, the colour of the lead complex indicator.

Note: The aluminum edetate complex is stable (Iog K = 15.5) but it is only formed slowly. Hence the sample is heated with excess sodium edetate to ensure complete complex formation. Hexamine acts as a buffer stabilizing the pH between 5 and 6, the optimum pH for the titration of sodium edetate with 0.05M lead nitrate using xylenol orange as indicator.

Calculation:

From the equivalence of sodium edetate, calculate the percentage of alum in the supplied sample.

Vol. Na EDTA equivalence to $KAl(SO_4)_2$ = Z mL

(Vol. Na EDTA X factor) – vol. $Pb(NO_3)_2$ x factor lead = Z mL

Amount of $KAl(SO_4)_2$ in the supplied Z x 0.02372g

$$\text{Percentage of } KAI(SO_4)_2 = \frac{0.02372\ Z \times 100}{\text{Amount taken}}$$

EXPERIMENTAL REPORT

Title:

Aim:

Methodology:

Results:

Discussion:

Conclusion:

SCHEDULE VI

1.6 GRAVIMETRIC ANALYSIS

The quantitative analysis which involves the separation of a given substance from the solution of the weighed sample, either as element or compound of highest purity and in a form that may be accurately weighted is termed as gravimetric analysis. The separation of the substance is carried out by precipitation in an insoluble form either through chemical or electrochemical method, by depositing a pure metal by electrolysis or by converting the substance to a gas, which is absorbed in suitable reagent.

The precipitation method is by far the most widely used. The analysis by precipitation involves a number of operations; like process of solution, precipitation, filtration, washing, igniting and weighing the residue are laborious and fraught with difficulties.

1.6.1 Estimation of Chlorides

Chloride ion is precipitated as silver chloride (AgCl) by adding excess of silver nitrate solution from a soluble chloride solution acidified with dilute nitric acid.

$NaCI + AgNO_3 \rightarrow AgCl + NaNO_3$

white precipitate.

The precipitate has low solubility, is easily obtained in a condition of nearly free of impurities and is readily filtered.

The filtered precipitate is washed and heated carefully to 100 – 110 ^oC to dry the precipitate; the precipitate is separated from filter paper, which is incinerated. The precipitate of silver chloride is weighted.

Calculation

Using the following relation: Ag ≡ CI ≡ NaCI ≡ KCI

$35.5gCl^- \equiv 143.5g\ AgCl$

$0.2474g\ Cl \equiv 1g\ AgCl$

Exercise

Calculate the percentage purity of the given sample of common salt, if 6.5g of the sample were dissolved per liter of the given solution.

A known sample of the given solution of common salt is treated with slight excess of silver nitrate solution. A white precipitate of silver chloride is produced.

$$NaCl + AgNO_3 \longrightarrow AgCl + NaNO_3$$

The precipitate is separated, washed, dried and weighed. From the weight of the precipitate, the percentage purity of common salt is calculated using the relation.

$$AgCl \longrightarrow NaCl$$

143.5 parts 58.5 parts by weight

Procedure

Pipette out 20 mL of the given solution of common salt into a 400 mL beaker. Dilute this solution to 150 mL with distilled water and add 1 mL of concentrated nitric acid into it. Wrap the outside surface of the beaker with a brown paper to protect the solution from light. Place a clean glass rod into it and cover the beaker with clock glass.

Take a test tube of M/10 Ag NO_3 solution and add into it the cold solution in small lots (1-2 mL at one time) with constant stirring until a slight excess is present. After addition the precipitate coagulate and a clear supernatant liquid is formed. Add a few mL of silver nitrate solution into the supernatant liquid from the side of the beaker place the beaker on the tripod stand slowly for complete precipitation. Remove the beaker from tripod stand and allow to stand for 30- 60 minutes undisturbed.

Filter the supernatant liquid using filter paper by decantation process, retaining as much of the precipitate in the beaker as possible. Wash the precipitate in the beaker with very little solution of nitric acid (2 drops of conc. HNO_3 add to distilled water). Transfer the supernatant after each washing. Finally transfer the precipitate in the filter cone by using the wash bottle spray.

Fill the filter cone half full of washing solution and allow it to drain completely. Repeat the washings two or three times and test the completeness of washing by adding a little hydrochloric acid into portion of the filtrate if no cloudiness is produced, the washing may be considered to be complete.

Finally, wash the precipitate two or three times with distilled water to remove nitric acid from the precipitate. Place the funnel with the filter cone containing the precipitate on a drying beaker. The beaker is then placed on a low Bunsen flame. The temperature is maintained at100-110^oC to expel all moisture. The heating is continued till the precipitate is dried and the nitric

paper loosens from the glass surface. Stop heating and remove the filter paper cone from the funnel, press the paper from outside between the fingers gently to loosen the precipitate flow paper. Transfer the precipitate to a clean watch glass place on a glazed paper and covers the watch glass funnel.

Burn the filter paper cone into a weighed crucible place on a glazed paper and incinerate the filter paper using a low flame. Add 2-3 drops of concentrated nitric acid followed by 1-2 drops of concentrated hydrochloric acid in order to convert silver to silver chloride. Heat gently on a low flame to remove excess of acids. Dry the residue in crucible and transfer the crucible into a dessicator to cool. Transfer the reserved precipitate of silver chloride into the crucible place on a glazed paper. Heat the crucible by a low Bunsen flame to prevent heating. This heating maintains a temperature of 120 – 150 ^{o}C, which expel all moisture from the precipitate. Heat the crucible for about one hour and cool it in dessicator and weigh. Repeat the heating until a constant weight of the crucible is obtained.

General Calculation

Strength of given solution of common salt = 6.5g per liter

Volume of common salt solution taken for precipitation = 20 mL

Weight of AgCl precipitate. per 20 mL of solution = Y g.

To calculate the weight of AgCI that would be produced from 100 mL.

20 mL of common salt solution produced Yg of AgCI

1000 mL of the solution would produce $= \frac{Y \times 1000}{20}$ = 50Y g of AgCl

To calculate the weight of pure NaCl which produced 50 g of AgCl using the following equation

AgCl ≡ NaCl

143.5 parts ≡ 58.5 parts by weight

143.5g of AgCl are obtained from 58.5g of NaCl

50 g AgCl would be obtained from

$$= \frac{58.5 \times 50a}{143.5} = \text{bg}$$

This is weight of pure NaCl present in 6.5g of common salt.

Percentage purity of common salt $= \frac{\text{b x 100}}{6.5}$

Note: Reagents provided: -

a) A solution of sodium chloride by dissolving 7.0g per liter.

b) Solution of silver nitrate and concentrated nitric acid.

i. Avoid the use of tap water for precipitation and washing liquids since it contains CI^- ions.

ii. Nitric acid is added to the solution as an aid in coagulating the precipitate and to prevent the precipitate of the silver salt like carbonate, phosphate, etc.

iii. The solution is briskly stirred with the glass rod on adding silver nitrate solution as this coagulates the precipitate more quickly

iv. Light decomposes silver chloride and if the precipitate from light the effect is negligible, even though the colour of the precipitate may change from white to gray or purplish violet owing to the time dispersion of colloidal silver or the surface of the silver chloride particles.

1.6.2 Determination of Aluminium as Oxinate in Sample of Ammonium Alum

"Oxine" or 8 hydroxyquinoline is used in the gravimetric determination of numerous metals with which it gives precipitates of corresponding oxinate complexes.

Method

Dry two sintered glass crucibles (number 3) at 110 – 120^{o}C to constant weight. Weigh accurately 0.4g of ammonium aluminum sulphate and dissolve it in 100 mL water, warm the solution to about 60-80^{o}C. Add excess reagent (2%w/v of water and acetic acid). If precipitate has not already formed add slowly 2M ammonium acetate solution until a precipitate just appears. Heat to boiling and then add 25 mL of 2M ammonium acetate solution drop wise and with constant stirring to ensure complete precipitation. Allow to cool, filter and wash the precipitate with cold water. Dry to constant weight at 130 -140^{o}C.

Exercise

Calculate the percentage of Aluminum in the sample

EXPERIMENTAL REPORT

Title:

Aim:

Methodology:

Results:

Discussion:

Conclusion:

1.6.3 Determination of Percentage Na_2SO_4 in Sample of Sodium Sulphate

The determination is based on the precipitation of barium sulphate when excess of Barium chloride solution is added to an aqueous solution of sodium sulphate. The precipitate is filtered off dried and weighed.

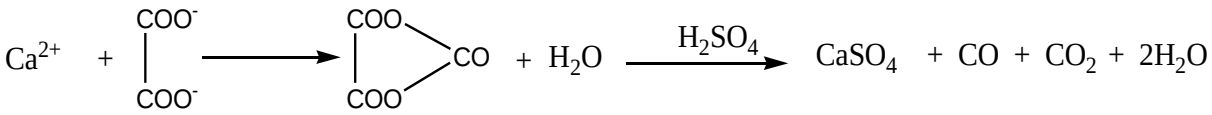
$Na_2SO_4 + BaCl_2 \rightarrow BaSO_4 + 2NaCl$

Method

Weigh accurately about 0.4g of the sample into a 600 mL beaker and add 300 mL of water acidified with 1 mL of conc. HCl. Cover the beaker with a watch glass heat the solution gently to boiling while stirring. Pour excess of 5% w/v $BaCl_2$ solution. Allow the precipitate formed to settle then add a few more drops of $BaCl_2$ for complete precipitation. Heat the beaker on water bath for 30 minutes. Filter the clear solution using mininum sunction. Wash the precipitate three times with hot water, then transfer the suspension to filter paper. Then watch the precipitate three times with methylated spirit and dry on the oven to constant weight

1.6.4 Determination of Calcium in Calcium Sulphate

This determination is based on preparation of calcium as insoluble oxalate by the addition of ammonium oxalate. The calcium oxalate formed is then converted to calcium sulphate by addition of concentrated sulphuric acid



$Ca^{2+} \equiv Ca(COO)_2H_2O \equiv CaSO_4$

$40.08g \equiv 136.1g$ of $CaSO_4$

$0.2945g \equiv 1g\ CaSO_4$

Method

Weight 0.4g of calcium carbonate into a clean 400 mL beaker equipped with stirring rod and a watch glass. Add 10 mL of water followed by 20 mL HCl and cover with the watch glass. Heat gently to dissolve the solid, then boil for several minutes to expel carbon dioxide. Rinse down the sides of the beaker and the bottom surface of the watch glass with distill water, dilute to 200 mL add two drops of methyl red indicator. Add 50 mL of 6% w/v solution of ammonium oxalate and heat the solution to about 80^0C. Add 2M ammonium solution drop wise from a teat pipette with continuous stirring until the indicator changes from red to yellow. Allow the solution to stand for 1 hour without any further heating and test the supernatant liquid for complete precipitation by adding a few drops of ammonium oxalate solution.

Decant the clear solution through a Whatman No. 30 filter paper. Wash the precipitate thoroughly with 200 mL of cold solution of ammonium oxalate (0.2% w/v). Cover the funnel with filter paper and place in the oven (100^oC) to remove moisture.

Transfer the paper and content to previously ignited or weighed porcelain crucible. Heat carefully with small flame until the paper is charred, heat more strongly until all carbon has been burned form the residue, then allow the residue and content to cool.

Moisten the cool residue with about 5 drops of H_2SO_4, heat gently until all the H_2SO_4 has evaporated, allow it to cool, remoistened with H_2SO_4, heat gently again to remove the acid, and finally heat the crucible and the contents over a moderate flame for 1 hour. Allow it to cool in a desicator and weigh.

Repeat the addition of H_2SO_4 and heat until the weight of the crucible and content is constant.

Exercise

Calculate the percentage of calcium in the sample of calcium carbonate

EXPERIMENTAL REPORT

Title:

Aim:

Methodology:

Results:

Discussion:

Conclusion:

1.6.5 Molecular Weight Determination

A known volume of an alkali solution treated with barium chloride solution to produce a white precipitate of barium sulphate as represented by the equation

$M_2SO_4 + BaCl_2 \rightarrow BaSO_4 + 2MCl$

The white precipitate of $BaSO_4$ is separated by filtration. It is washed, ignited and weighed to get the weight of the precipitate.

$BaSO_4 \equiv M_2SO_4$

233 part ≡ (2M + 96) by weight

The molecular weight M is calculated by:

Weight of M_2SO_4 in 20 mL ≡ Mol. weight of M_2SO_4

Weight of $BaSO_4$ from 20 mL ≡ Mol. weight of M_2SO_4

Experimental

17.4g of the sulphate of an alkali metal is dissolve per liter of the solution. Calculate the molecular weight of the alkali metal by gravimetric method.

Procedure: pipette 20 mL of a given Sulphate solution into a 200 mL beaker and add 1 mL of conc. HCI, dilute the solution to 50 mL with distilled water, and boil the solution.

Add about 20 mL of 5% solution of Barium chloride drop-wise to the hot solution and constantly stir it vigorously with a glass rod. Allow the precipitate to settle for further precipitate adding a few drops of barium chloride until the excess of it is present. Wash the glass rod into the beaker on a water bath for 1 hour to digest the suspension of the precipitate. (Do not allow the solution to boil). The crystalline precipitate becomes larger and settles down leaving a clear supernatant liquid.

Add a few drops of barium chloride to check that not further precipitation occurs. Filter the supernatant liquid by decantation using Whatman No 42. Make sure you retain the precipitate in the beaker. Wash the precipitate in the beaker with hot water and repeat the washing through the filter paper. Repeat the washing 2 to 3 times and finally transfer the precipitate into the filter paper using spray of water from wash bottle. Loosen any precipitate that adheres to the beaker with a glass rod. Wash the precipitate 5 to 6 times with hot water making sure that the wash bottle jet is directed to the top of the paper and let each water run through before adding another portion of water. Test the last washing collected for turbidity by testing for chloride ion with nitric acid and silver nitrate solution. The washing is complete when turbidity is noticed.

1.6.6 Gravimetric Determination of Atomic Weight of an Alkali Metal Sulphate

Given: Alkali metal sulphate (M_2SO_4) solution (17.4g per liter of distilled water)

5% Aqueous barium chloride solution

Equation: $M_2SO_2 + BaCl_2 \rightarrow BaSO_4 + 2MCl$

Procedure: Pipette 20 mL aliquot of the given alkali metal sulphate solution into a 200 mL beaker and acidify with 1 mL conc. Hydrochloric acid. Dilute to 50 mL with distilled water. Bring to near boiling on a water bath or a hot plate, and add barium chloride solution dropwise with constant stirring until no visible precipitate of barium sulphate is obtained then add 5 mL excess of the precipitant. Record the total volume of barium chloride added. Continue heating on the water bath or hot plate until the precipitated barium sulphate has become crystalline and the supernatant liquid is clear.

Filter the barium suphate through a previously weighed Whatman No. 42 paper and wash with 5 mL portions of distilled hot water, first by decantation and subsequently on the filter until free from chloride (when test of filtrate with a drop of silver nitrate solution gives no precipitate of silver chloride.

Transfer the filter and precipitate to a weighed porcelain crucible and dry in the oven at 120^oC for 20 minutes each to constant weight. Obtain the weight and the mole quantity of barium sulphate formed. Using the information obtained calculate the molecular weight of the alkali metal sulphate and thereby the gram atomic mass of the alkali metal cation.

Note: 1 Mole of M_2SO_4 will give 1 Mole of $BaSO_4$ (233) $\equiv$ (2M + 96) parts by weight

Hence 1M $M_2SO_4 \equiv BaSO_4$

X grams of M_2SO_4 gave Y grams of $BaSO_4$

$$\frac{\text{X grams of } M_2SO_4}{\text{MW of } Ba_2SO_4} \equiv \text{Z Moles } M_2 \equiv \frac{\text{Y grams } BaSO_4}{M_2SO_4} \equiv \frac{\text{Z Moles } BaSO_4}{233}$$

Knowing that the mole quantity of $BaSO_4$ obtained is equal to the mole quantity of M_2SO_4, then the molecular weight of the alkali metal sulphate may now be calculated.

Z moles of M_2SO_4 = X grams of M_2SO_4

$$\therefore \text{Mol. Wt } M_2SO_4 = \frac{\text{X grams of } M_2SO_4}{\text{Z moles of } M_2SO_4}$$

*Normally the filter paper should be flared if ashless.

From the derived molecular weight of M_2SO_4 subtract the weight of $SO_4 \equiv (96)$ and divide by 2 in this case to obtain the gram atomic mass of M.

$$\frac{\text{Mol. Weight } M_2SO_4}{2} - 96 = \text{gram atomic mass of M.}$$

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PART 2

PCH302
PRACTICAL
CHARACTERIZATION
&
SYNTHETIC
ORGANIC
CHEMISTRY

CHARACTERIZATION & SYNTHETIC ORGANIC CHEMISTRY

2.0 Introduction

The practical Pharmaceutical organic chemistry covers the characterization, identification of organic compounds particularly organic pharmaceuticals. The practical also involves investigation of the solubility profiles of organic pharmaceuticals and other chemicals that are of relevance to pharmacy and chemistry programmes. Simple techniques for the separation of mixtures and characterization of unknown compounds were being introduced.

The synthesis of simple organic pharmaceutical compounds will expose the students to synthetic techniques. The synthesis involved typical reaction mechanisms that are also taught in the theory classes.

Objective

The aim of the practical is to equip the students with skill that will enable them to be able to identify and analyze organic pharmaceuticals.

Purification

In order to identify an unknown compound correctly a systematic and logical approach must be followed carefully.

Firstly, one must ensure the purity of the unknown. If the unknown is a solid its melting point is determined. Unless for high molecular weight compounds the melting point of a pure substance is either sharp or melts within a narrow range of about 3^{o}C, when this is not the case then purification of the compound by either crystallization or sublimation is necessary for correct identification.

Liquids are purified by distillation at atmospheric pressure for stable compounds. High boiling and unstable liquid compounds may be purified by distillation at reduced pressure using a vacuum pump. A micro boiling point determination apparatus is used for small samples as well as for larger samples.

A simple distillation apparatus may however be used for larger samples. Boiling range of 5^{o}C is acceptable for liquid samples.

SCHEDULE I

2.1 SYSTEMATIC CHARACTERIZATION AND IDENTIFICATION OF ORGANIC COMPOUNDS

2.1.1 Appearance and Smell

Most organic solids and liquids are colourless in their pure states except for certain compounds with functional groups such as nitro (NO_2), nitroso (NO), diazo (N≡N), long conjugation as in polyalkanes, akynes and polycyclic aromatic compounds, colour in organic compounds with such chromophoric groups are usually enhanced when acid forming groups such as amino, phenolic hydroxyl, sulphonic acid are present. In the absence of these chromophores a coloured organic sample is considered impure.

Smell is subjective property and the perception of this may differ between individuals, just as some are colour blind. However, there exists general characteristics smell or odour for certain class of compounds:

Volatile amines	- fishy
Esters	- fruit-like
Acids, acids chlorides, anhydrides	- choking and lachrymatory
Sulphides	-lachrymatory and rotten egg.
Isocyanides	- obnoxious

2.1.2 Determination of Elements in Organic Compounds

Aside from carbon, hydrogen and oxygen, the elements usually encountered in qualitative organic analysis are limited in most cases to:

Nitrogen: Amines, amino acids, ammonium salts, amides ureas, imides, nitro compounds and cyanides.

Sulphur: Sulphides, sulphones, sulphoxides, sulphonic acids, and derivatives, thiols, thioethers and thio-compounds (as in heterocyclics) and sulphuric acid esters.

Halogens: Acyl, alkyl and aryl and sulphonyl halides and ammonium salts.

Phosphorus: Phosphate esters, salts and phosphorus containing compounds.

Cations: Metallic salts of organic acids e.g., sodium, potassium, iron, calcium, lithium, silver and lead.

The presence of nitrogen, sulphur and the halogens and phosphorus may be detected by sodium fusion test in accordance with the Lassaigne's method. While the other elements, may be detected by the conventional methods in qualitative inorganic analysis.

The absence of the above elements in a given organic sample helps narrow the possibilities of choice to simple hydrocarbons, aldehydes, ketones, carboxylic acids and their esters, alcohols and carbohydrates respectively.

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2.1.3 Lassaigne's Test for Organic Compounds

SOLIDS

Add a piece of metallic sodium (2-3mm cube) into an ignition tube carefully and heat gently to a molten state, then add about 200 mg of the solid sample and heat the mixture gently until it solidifies, then briskly and maintain at the red heat. While still hot drop the ignition tube with its contents into a 50 mL beaker containing 15 mL distilled water. Boil for 3-4 min and filter the solution using a Hirsch funnel and filter paper. Use the filtrate for the following identification tests.

LIQUIDS

For liquids, follow the procedure above, but heat the ignition tube and its sodium content until the tube is about a third full of sodium vapour. Then carefully introduce the liquid (0.2 mL) drop wise and continue the operation as described above.

Fusion of an organic compound as per above converts any possible elements such as sulphur and halogens to their sodium salts and nitrogen to sodium cyanide.

NITROGEN

To about 1 mL of filtrate add 1 mL of 10% solution of iron (II) sulphate and drop wise, add some 2 mL sodium hydroxide solution until a heavy precipitate of iron hydroxide is obtained. Boil for 2 min., and acidify with hot 2M sulphuric acid solution (test with litmus).

A deep blue precipitate or colouration (Prussian blue) confirms presence of nitrogen. Unsatisfactory fusion reaction will yield mainly a heavy green precipitate. If sulphur is present, a black precipitate is obtained on addition of ferrous sulphate, but hydrogen sulphide is evolved when acidified.

SULPHUR

To filtrate add about 1 mL freshly prepared sodium nitroprusside solution. Presence of sulphur is indicated by a pink to purple colouration.

HALOGENS

To 1 mL of the cold filtrate add excess 2M nitric acid and then silver nitrate solution. If nitrogen or sulphur was detected earlier boil this to expel hydrogen sulphide and hydrogen cyanide (***caution*** – poisonous gas, carry out this operation in a fume cupboard).

Presence of one or more of chlorine, bromine or iodine is indicated by a white or yellow precipitate. Confirm the identity of the respective halogens as follows:

a) Only chlorine, bromine or iodine is present. To 1 mL original filtrate acidify with dilute sulphuric acid; add 1 mL chloroform and two drops chlorine water of 1% solution of sodium hypochlorite. Shake well, allow separation of the two phases. Note colour of chloroform layer:

Brown	- bromine
Purple	- iodine
Colourless	- chlorine.

b) Presence of more than one halogen.

i) To 2 mL filtrate add excess 2M nitric acid, then 1 mL 5% mercury (II) chloride solution. Presence of iodine is indicated by the appearance of a yellow precipitate which changes to orange or red upon standing, or immediately.

ii) To another 2 mL filtrate, add 2 mL dichromate oxidizing mixture, and then boil gently for 2 min. Presence of bromine is indicated when the vapour turns filter paper dipped in Schiff's reagent purple.

iii) To a third portion of same fusion filtrate add excess 2M nitric acid, then silver nitrate solution. Treat the filtered precipitate with (saturated ammonium carbonate solution and conc. Ammonia 4:1 volume) in excess. If residue remains, filter and treat with dilute nitric acid. A white precipitate indicates presence of chlorine.

FLUORINE

Two mL of the test solution is acidified with acetic acid, boiled and cooled. Dip a piece of filter paper in a zirconium-alizarin solution (1% alizarin in ethanol + 0.4% zirconium nitrate), apply two drops to acidic fusion solution on the paper, dry. Fluorine is indicated by a red to yellow colour change.

PHOSPHORUS

Treat a further 2 mL portion of the fusion solution with 0.5 mL conc. Nitric acid followed by 5% solution of ammonium molybdate. Heat on a boiling water baths for 2 min. Phosphorus is indicated by the appearance of a yellow precipitate.

OXYGEN

Add the unknown neat, if liquid, or as a saturated chloroform or benzene solution if solid to a 100mg powdered mixture of equal weights of potassium thiocyanate and ferric chloride or sulphate in a test tube. Oxygen is indicated by a purple colouration in the organic layer.

2.1.4 Action of Heat

Heat a little of the substance on a metal spatula or crucible lid, note whether it burns, if so state colour and texture of flame.

Alkenes, alkynes & Aromatic compounds: smoky flame

Aliphatic compounds: blue or clear yellow flame.

Residue: Metallic salt of acid, phenol, bisulphate salt of aldehyde, ketone, imide, enol, oxime or hydroxamic acid.

2.1.5 Action of Soda Lime

Mix about 200 mg of the unknown with twice amount of soda lime in a fusion tube and heat strongly over a small Bunsen flame. Check the nature of the gas evolved other than that of starting material.

Ammonia (test with litmus): ammonium salts, amides, imides and urea.

Carbon dioxide (acid to wet litmus): carboxylic acids and their salts.

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SCHEDULE II

2.2 CLASSIFICATION AND CHEMICAL CHARACTERIZATION OF ORGANIC COMPOUNDS

A convenient and easy method for the classification of organic compounds is by their solubility property in a selected number of solvents, namely water, diethyl ether, 5% aqueous sodium hydroxide, 5% aqueous sodium bicarbonate, 5% aqueous hydrochloric acid and concentrated sulphuric acid.

A substance is considered soluble in a medium if it dissolved to the extent of 3% at room temperatures in a given medium. This classification may be carried out before or after knowledge of the elements present in the compound is established.

Low molecular weight compounds with about 5-carbon atoms, either polar or non-polar, acidic, basic or neutral are usually soluble in water. Since most organic compounds within medium range of molecular weight do dissolve in diethyl ether any water-soluble compound which fails to dissolve in this medium must be considerably polar in nature due to substituent effects. So, the two types may be classified by their solubility or non-solubility in these two solvents. Sub-classification of each type under acidic, basic or neutral compounds is then made with litmus paper.

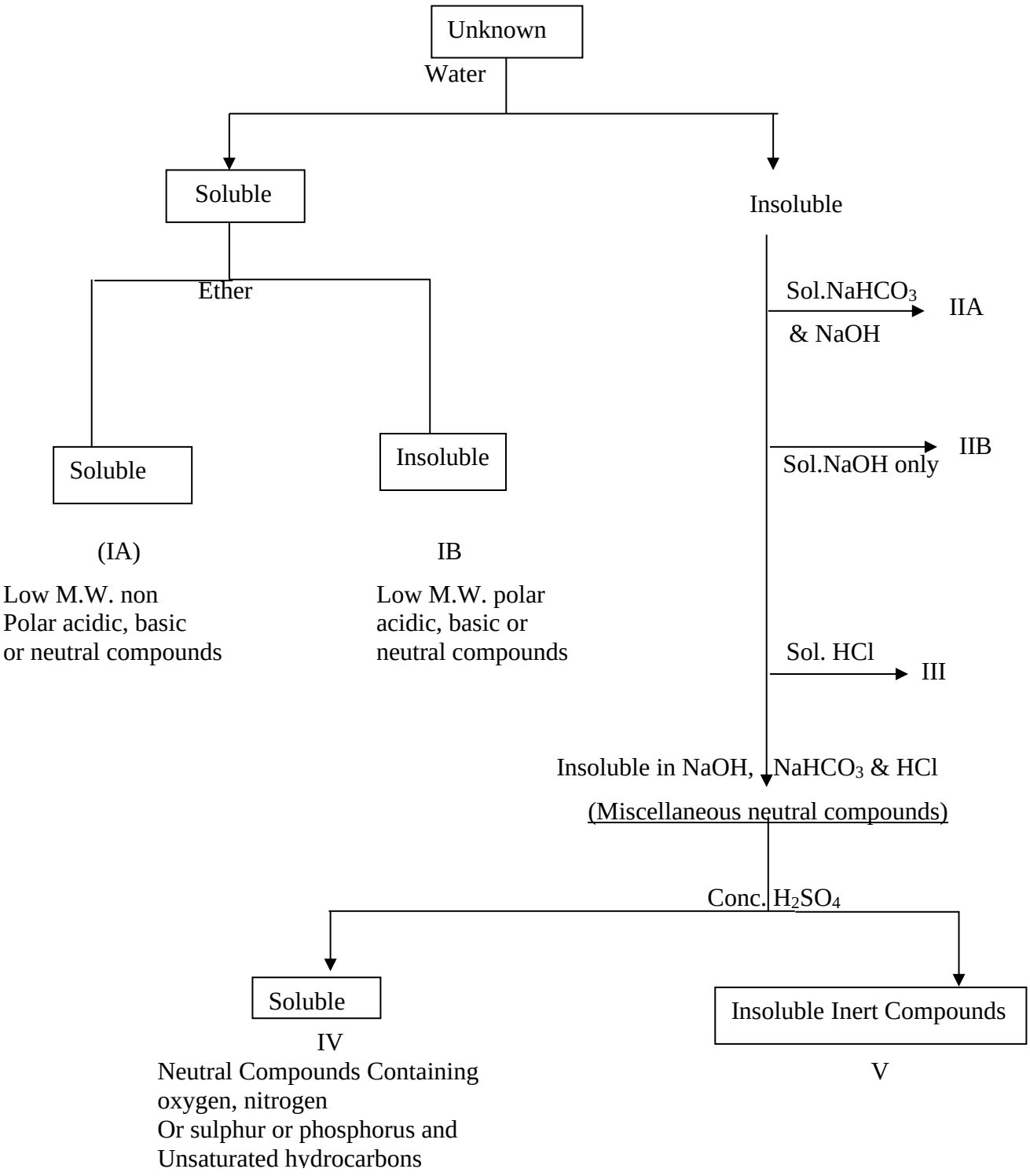
Water soluble substance will invariably dissolve in the aqueous base or aqueous hydrochloric acid usually employed in the diagnostic tests. Hence any water-soluble substance need only be tested with litmus paper to establish its behaviour with this test.

Water insoluble compounds are not tested for solubility in ether for the reasons given above; but they are tested for their solubility in sodium hydroxide, sodium bicarbonate and hydrochloric acid. Strong and weak acids dissolve in 5% sodium hydroxide but weak acids do not. Hence these diagnostic reagents can be used to differentiate between strong acids such as carboxylic and sulphuric acids and negatively substituted phenols as against the weak acids such as phenols, enols, imides and oximes.

Compounds which contain sulphur, nitrogen or oxygen do invariably dissolve in concentrated sulphuric acid. Unsaturated aliphatic polynuclear and alkyl substituted

aromatic compounds dissolve readily in concentrated sulphuric acid and could be differentiated in this way. Hydrocarbons are inert to sulphuric acid.

A solubility classification of organic compounds is given in the scheme below:



2.2.1 Classification of Compounds According to Solubility

Group	Type of Compounds
IA (water and ether)	Low molecular weight amines, alcohol, aldehydes, ketones, acids, acid halides, esters, nitrites, di-and trihydric phenols, anhydrides and acetals.
IB (sol water only)	Metal salts, amine salts, phenoxides, carbohydrates, polyols, amino acids, diamines, polybasic acids, hydroxy aldehydes, polyhydroxy ketones and acids.
IIA (sol. 5% NaOH 5%$NaHCO_3$)	High molecular weight acids, negatively substituted phenols.
IIB (sol. 5% NaOH only)	Phenols, sulphonamides of primary amines, primary and secondary nitro compounds, imides, thiophenols, enols, quinones.
III (sol. 5% HCl)	Aliphatic amines and aromatic amines containing not more than one N- phenyl groups, hydrazines.
IV (sol. Conc. H_2SO_4 only)	Alcohols, aldehydes, ketones, esters, unsaturated compounds in addition to those containing nitrogen and sulphur, some polyalkyl aromatic compounds
V (insol. in all media above)	Aromatic and aliphatic hydrocarbons and their halogen derivatives, diaryl ethers.

With knowledge of elements present in the given unknown (s) and establishment of the functional groups present by infrared and partly from solubility classification, the next step is to confirm these by the characteristic's chemical reactions of individual functions.

Exercise

Students are to follow carefully the chemical tests detailed below, and hence identify and confirm the nature of the functional group (s) present in the given sample (s).

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SCHEDULE III

2.3 DETERMINATION OF FUNCTIONAL GROUPS IN ORGANIC COMPOUND

Knowledge of the functional group present in an unknown organic compound is of immense importance in elucidating the structure of such a compound.

It is easy to establish whether an unknown compound is an acid or base, neutral, polar or non-polar by solubility tests in water, ether and the use of indicator paper for acidic and basic compounds, but relatively more difficult to do so for other types of functional groups except by chemical and spectroscopic methods including colour reactions which also underline chemical reactions.

2.3.1 Determination of Functional Group Using Spectroscopic Method

The most modern approach for establishing the functional group or groups present in an organic compound is by spectroscopic methods, especially by the use of Infra-Red (IR) spectroscopy.

It is therefore important that the IR spectrum of an unknown be carefully examined for the functions present, such as an amino, carboxylic, ketonic, aldehydic, aromatic, unsaturation, hydroxyl ester and amide functions etc. The infrared and some nuclear magnetic resonance spectra of some representative compounds are provided in appendix.

Study the relevant spectra carefully and deduce the possible functional group or groups. Based on results of elemental analysis, spectra and diagnostic chemical tests, and melting or boiling point determination, a search for the identity of the unknown is made with reference to a standard table of class of organic compounds their physical constants and suitable derivatives for each class.

2.3.2 Groups Containing C, H & O: Acidic, Aldehydes and Ketonic Compounds

I Acidic Compounds

Chemical Test	Observation	Inference
To 0.2g substance in 5 mL H_2O or aqueous ethanol, add 1 drop 2M NaOH. Test solution with 2-3 drops 3DH 1014 indicator.	Green colouration (In the absence of acidic material, added base causes color to change from green to pink).	RCOOH ArOH enol.
To equal volume of sat. solution of substance in 50% aq. EtOH add 5% aq. $NaHCO_3$.	CO_2 evolved.	RCOOH
To an aqueous solution of substance add 1 – 2 drops of neutral ferric chloride solution.	Wide range of colouration.	Phenol/enol
To a methanolic solution of substance add 5% methanolic ferric chloride solution (use anhydrous $FeCl_3$).	Wide range of colouration.	Phenol/enol
If tests 3 and 4 are positive. Dissolve 50 mL mercuric nitrate in 2M nitric acid and add substance.	Grey precipitate of mercury is observed immediately.	Enol.

II Aldehydic and Ketonic Compounds

Chemical Test	Observation	Inference
Dissolve 0.2g substance in 5M HCl (if water soluble) or in ethanolic phosphoric acid if otherwise, add 2, 4-dinitrophenylhydrazine (Brady's reagent).	Yellow-red precipitate.	RCHO/R_2C=O
To substance add 2M ammoniacal silver nitrate solution, warm on a water bath. (If substance is not soluble in water add some ethanol).	Silver mirror.	Aliphatic aldehyde
If (2) negative, treat 5% silver nitrate with 2 drops 2M NaOH, dissolve precipitate in 2M ammonium hydroxide and proceed as in above.	Silver mirror	Aromatic aldehyde
To unknown add 3 drops of 5% chromium trioxide in 2M sulphuric acid. Warm on water bath at 40 – 50^{o}C for 1 min.	Red - green colour	Alcohol
Dissolve unknown in water, dioxane or acetone, add 3 or 4 drops 40% Cerium (iv) nitrate in 2M nitric acid.	Yellow – red colour	Alcohol

If tests (4) and (5) are positive and substance is a solid, dissolve it in water; add 10% ethanolic 1-naphthol, followed by slow addition (*down side of test tube*) of conc. Sulphuric acid.	Violet colour at liquid interphase.	Carbohydrates
If (6) above is positive add to substance a few drops of Fehling's solution A and B warm on a boiling water bath for up to 5 mins.	Brick-red precipitate.	Reducing carbohydrate
Dissolve substance in water, add a few drops of cupric acetate in 1% aqueous acetic acid. Boil gently for 2 mins.	Brick-red precipitate.	Monosaccharide
If (8) is positive, dissolve 0.1g each of substance and 1,3,5-trihydroxybenzene (phloroglucinol) in 2 mL 2M hydrochloric acid. Heat to boiling for 2 mins.	Pale yellow Intense red-brown colour.	Hexose Pentose
Iodoform test for methyl ketones, If ketone is present take small amount of substance, add 5% aq. iodine in potassium iodide solution and add 5N NaOH drop wise until the iodine colour is discharged.	A yellow precipitate of iodoform	Methyl ketone

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III Esters, Anhydrides and Lactones

Chemical Test	Observation	Inference
Add substance to a mixture of equal volumes of saturated methanolic hydroxylamine hydrochloride and methanolic potassium hydroxide. Heat on a boiling water bath, cool, acidify with 0.2M HCl; and add 3 drops of 5% aqueous ferric chloride solution.	Red to violet colour. Do not run this test if presence of phenol or enol is confirmed in test 1, 3 & 4.	Ester or lactones or anhydride.
Dissolve substance in ethanol add 1 drop each of sat. solution of methanolic potassium hydroxide and phenolthalein. Heat on a boiling water bath. Repeat procedure without the substance.	Pink colour fades in test solution.	Ester or lactone or anhydride.
If test (1) and (2) are positive, dissolve substance in benzene or chloroform and add 2 drops aniline. Warm for 1 – 2min.	Precipitate formed.	Anhydride.

IV Quinones

Visual examination Add 1 – 2 drops of 2M sodium hydroxide solution.	Red to yellow colour when pure. Pronounced intensification of original colour.	Quinone. Quinone.

Ethers

Warm at 40 – 50^{o}C with conc. sulphuric acid.	Compound dissolves completely without charring.	Ether. (This test is not confirmatory).

2.3.3 Chemical Characterization of Functional Groups Containing C & H

I Alkenes/Alkynes/other Hydrocarbons

Treat sample with 1% $KMnO_4$ solution and shake well.	Purple colour is discharged rapidly in cold.	Alkenes/alkynes.
Dissolve sample in carbon tetrachloride add 2 drops 5% bromine in carbon tetrachloride.	Red-brown colour discharged without evolution of hydrogen bromide.	Alkenes/alkynes
Tests (1) and (2)	All are negative.	Other hydrocarbons.

(Readily oxidized compounds also test positive to 1 & 2).

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2.3.4 Chemical Characterization of Functional Groups Containing Amines, Amides, Amino Acids

Dissolve substance in 2M hydrochloric acid and cool to 5^{o} C on ice. Add 3 or 4 drops of 5% aqueous sodium nitrate solution.	Effervescence; nitrogen evolved and clear solution obtained.	1^{o} aliphatic amines amino acids or amide.
	No effervescence, clear solution.	1^{o} aromatic amine or 3^{o} amine.
	Dark brown solution.	3^{o} aromatic amine unsubstituted in 4-position.
If clear solution in (1) add a few drops of it to a 5% solution of 2-naphthol dissolved in 2M sodium hydroxide.	No effervescence cloudy solution or emulsion.	Amine or aryl hydrazine.
	Bright red to dark brown precipitate.	1^{o} aromatic amine.
Dissolve substance in 2M hydrochloric acid cold, add excess of Fehling's solution and heat on a boiling water bath for 5 minutes.	No colouration (ignore White to yellow precipitates).	1^{o} aliphatic amine,
	Brick-red precipitate.	3^{o} amine, amino acid or amide. Substituted hydrazine.
Dissolve substance in water and add 1% methanolic ninhydrin. Warm gently.	Violet colour.	α or-β-amino acid.

2.3.5 Chemical Characterization of Functional Groups Containing Ammonium salts, amides, imides or Nitrites

Add conc. sodium hydroxide solution to sample, heat strongly for about 2 mins.	Ammonia evolved.	Ammonium salt, amide, imide or nitrite.
If (1) is positive, add 2M sodium hydroxide solution and cool.	Compound dissolves and ammonia is evolved.	Ammonium salt.
Mix substance with sulphur in a dry test tube. Test the vapours produced with an absorbent strip treated with 1% aqueous ferric nitrate solution.	Red stain on paper.	Nitrile.
If test (1) is positive but (2) and (3) are not, prepare a saturated methanolic solution of substance and mix with saturated methanolic potassium hydroxide solution.	White precipitate.	Imide
Add 70% sulphuric acid to the substance and reflux for 10 min. Cool to 5^{o}C in ice and add 5% solution of sodium nitrite.	Bright red to brown precipitate.	N-aryl substituted amide
Pour into 5% solution of 2-naphtho in 2M sodium hydroxides.	No coloured precipitate (ignore white-yellow precipitate).	Possibly N-alkyl substituted amide.

2.3.6 Chemical Characterization of Functional Groups Containing Nitro Compounds

Add few drops of 2M sodium hydroxide to a 1 mL aqueous solution of ferrous sulphate, and then finally add the sample. Heat on a boiling water bath for not more than 2 minutes. Repeat experiment above but omit the addition of sample.	Grey to green precipitate in test solution changing to brown.	Nitro compound.
Dissolve compound in acetone and add 3-5 drops of 5% titanium (III) chloride or sulphate solution, warm gently.	Mauve colour is discharged within 2 min.	Nitro compound.
If tests (1) and (2) are positive, reduce nitro compound with tin in 7M HCl warming for 15 min. Filter, cool to $5^{o}C$ (ice).	Red to dark brown.	Aromatic nitro compound.
Add 5% aqueous $NaNO_2$. Add this to 5% solution of 2-naphthol in 2M NaOH.	No colour precipitate.	Aliphatic nitro compound.
Add 2M sodium hydroxide solution to sample.	Intense yellow or orange coloured solution or precipitate.	Nitro phenol.

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2.3.7 Chemical Characterization of Functional Groups Containing C, H, O & Halogen

To a saturation of sample in 2M nitric acid, add aqueous silver nitrate.	White precipitate.	Acyl halides.
If (1) above is negative, treat substance with methanolic KOH. Boil for 2 min. Cool acidify with 2M nitric acid and add 2% ethanolic $AgNO_3$.	White to yellow precipitate to be formed cold or on slight warming.	Alkyl halide.
Tests (1) and (2) are negative.		Aryl halide / vinyl halide

2.3.8 Chemical Characterization of Functional Groups Containing C, H, O & S

Test aqueous solution with blue litmus paper.	Acidic reaction.	Sulphonic acid RSO_2OH.
Odour	Unpleasant and penetrating.	Thiol or thiophenol (RSH) or impure thioether R-S-R, 1^o or 2^o thiols.
If test (2) positive, dissolve sample in ethanol, add solid $NaNO_2$, then 2M sulphuric acid.	Red colour, Green colour changing to red on standing. No colour.	1^o or 2^o thiols thiophenol thioether, R-S-R.

2.3.9 Chemical Characterization of Functional Groups Containing O & P (Phosphate Esters)

Reflux sample with 30% aqueous NaOH for 20 min and then distill off all the volatile materials. Acidify residue with 2M sulphuric acid, extract with ether and add a solution of ammonium molybdate in conc. nitric acid to the aqueous phase. Warm but do not boil.	Yellow precipitate	Phosphate ester

2.3.10 Chemical Characterization of Functional Groups Containing H, Halogen, N (Amine and Quaternary Ammonium Salts)

To an aqueous solution of sample add excess nitric acid followed by aqueous $AgNO_3$.	White to yellow precipitate.	Hydrohalide salt of a base or ammonium salt.
If test is positive add excess of alkali and extract mixture with ether. Dry extract over anhydrous Na_2SO_4 and remove ether on water bath.	Examine residue obtained for type of amine.	Hydrohalide salt or amine.
	No residue obtained.	Quaternary ammonium salt.

2.3.11 Chemical Characterization of Functional Groups Containing Halogens, O & S (Sulphonyl Halides)

Heat substance in water for 10 min. Cool, acidify with 2M nitric acid then add aqueous $AgNO_3$.	White to yellow precipitate.	Sulphonyl halide

2.3.12 Chemical Characterization of Functional Groups Containing C, H, N, O & S (Sulphonamides, Thioamides, Amine Sulphates)

Heat with solid KOH	Ammonia evolved. Amine evolved.	Sulphonamide RSO_2NH_2 N-substituted sulphonamide RSO_2 NRR. Examine nature of amine accordingly.
Heat substance with 2M H_2SO_4	H_2S evolved.	Thioamide $RCSNH_2$
Dissolve substance in water and acidify with 2M aqueous HCl; add $BaCl_2$ solution.	White precipitate.	Sulphate salt to base.

2.3.13 Chemical Characterization of Functional Groups Containing H, N, O & P

Dissolve sample in water and treat with conc. HNO_3 and aqueous ammonium molybdate. Warm, but do not boil.	Yellow precipitate	Phosphate of a base.

EXPERIMENTAL REPORT

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Results:

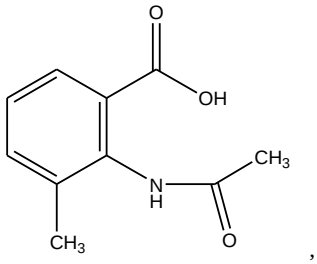
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SCHEDULE IV

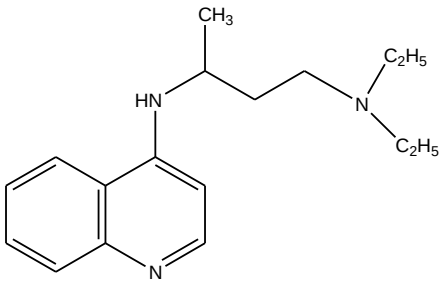
2.4 SEPARATION OF MIXTURES OF ORGANIC COMPOUNDS

Organic compounds have different chemical structure and hence different pharmaceutical properties. The difference in solubility can be employed to separate mixture of organic compounds. Organic acids and bases can be modified with their respective salts – so as to alter their solubility profile. Mixture of either organic acid or base can be separated by modifying the solubility of one of the two or more components followed by extraction with organic solvents. For example, separation of chloroquine and aspirin mixture.



Aspirin

,



Chloroquine

2.4.1 Water soluble + insoluble compounds

Add enough water to mixture and warm on water bath (care to be taken not to lose volatile compounds if any). Filter hot using filter paper and Hirsch funnel or a sintered glass funnel. Wash thrice with hot water. Collect and dry the water insoluble component. Concentrate the filtrate, cool and allow crystals to form. Filter, dry and weigh. Completely boil off water and collect residue, dry and weigh.

Exercise

Calculate the percent weight of respective compounds (water insoluble and water-soluble component)

The above procedure may be used in the case of soluble and insoluble mixture of compounds in organic solvents, (e.g., ethanol, benzene, chloroform etc) except that the soluble component is extracted with the solvent instead of water.

2.4.2 Organic Acid and Organic Base

Convert the organic acid to its sodium salt using 10% sodium hydroxide solution. Extract the organic base with ether, chloroform, ethyl acetate or any other suitable organic solvent. Dry extract with anhydrous sodium carbonate, filter and recover the base by boiling of solvent, record weight.

Acidify the aqueous solution containing the acid sodium salt, with dilute hydrochloric acid, cool and recover by filtration any separated solids, wash with deionized or distilled water, dry and record weight.

For acidic liquid sample, extract with a suitable organic solvent and record weight upon removal of solvent.

Exercise

Calculate % weight of the respective components.

2.4.3 Organic Acid + Organic Base + Neutral Organic Compound

It is most likely that the organic acid and base present in the mixture combine to form a water-soluble ammonium carboxylate salt.

Disperse mixture in water and recover the neutral compound by extraction with an organic solvent such as chloroform, ether, ethyl acetate or dichloromethane. Dry solvent over anhydrous magnesium sulphate or sodium sulphate. Filter and recover compounds by removal of solvent. Record the weight.

To the aqueous solution add dilute sodium hydroxide solution, extract with chloroform or dichloromethane, dry over anhydrous sodium carbonate, filter and remove solvent. Record weight of amine recovered.

To the aqueous solution add dilute hydrochloric acid, cool in ice water, filter off any crystals that separate. Dry and record weight and melting point if solid. If the organic acid is a liquid carry out the procedure as in section 2 above.

Exercise

Calculate % weight of each compound.

An alternative procedure to the above is to convert the acidic compound to its salt, extraction of the basic and neutral compounds with an appropriate organic solvent. The extract is then acidified with dilute hydrochloric acid and the neutral component extracted with a suitable solvent. The basic and acidic aqueous solutions are treated with hydrochloric acid and dilute sodium hydroxide respectively to recover the acidic and the basic components.

EXPERIMENTAL REPORT

Title:

Aim:

Methodology:

Results:

Discussion:

Conclusion:

SCHEDULE V

2.5 PREPARATION OF DERIVATIVES FOR CHARACTERIZATION OF UNKNOWN

Unknown compound such as organic alcohol and acid can be identified by converting them into their derivative that possess sharp melting point, boiling point and other physical parameters. It is a known fact that some high molecular weight esters of carboxylic acid poss sharp and high melting point. This property makes them suitable derivatives. This therefore introduces the students to the techniques of derivatization which is often encountered in drug modification (SAR) or Drug Design.

2.5.1 Carboxylic Acids

a) Esters

Some high molecular weight esters of carboxylic acids possess sharp and high melting points (M.P.) suitable as derivatives e.g.:

P-Nitrobenzyl esters: $RCOONa + P\text{-}NO_2 – PhCH_2Br \rightarrow P\text{-}NO_2\text{-}PhCH_2\text{-}OCOR$

Dissolve 0.1g of the acid in about 0.5 mL water. Add dropwise a solution of 2M sodium hydroxide until it is just alkaline to phenolphthaline. Adjust the pH carefully to neutral with dil. HCl. Add the salt solution to 0.1g of P-nitrobenzyl bromide dissolved in 1 mL ethanol. The solution should be homogenous otherwise more ethanol should be added. Reflux for 1 hour and cool with crystallization of the ester. Filter and recrystallize from aqueous ethanol.

Exercise

Determine the melting point.

b) Amides, anilides, P-toluides

These are suitable derivatives for carboxylic and sulphonic acids. The acids are converted to their acylhalides or sulphonyl halides which readily react with amines. Reactions are at times violent and may require cooling with ice.

(Carry out this reaction in a fume cupboard)

Place 0.1g of acid in a small round bottomed flask, add about 3 mL of thionyl chloride and attach a reflux condenser. Reflux for 30mins. on the steam bath. Distil off unreacted thionyl chloride

Add the acid chloride to a cold solution of conc. ammonia (2 mL). Allow the reaction to subside and add 5 mL cold water. Filter, wash with cold water and crystallize from ethanol or aqueous ethanol if crystallization is not possible with water.

In the case of anilides and P-toluides add 0.2g of the amine to the crude acid chloride, allow to react fully with stirring (glass rod), then add dilute HCl to dissolve unreacted amine and follow procedure as above.

For sulphonic acid those are converted to their chlorides by heating with about 0.2g phosphorus pentachloride (P_2O_5) for 30mins., at 100^{o}C. Wash off inorganic materials with water, and react the sulphonyl chloride residue with conc. ammonia, and heat on the steam bath for 15 min. Filter amide and crystallize from ethanol or water.

In the event the unknown is an acid anhydride carry out amidation as described for acyl halides.

c) N, N-Dibenzylammonium carboxylate salts

The salts of carboxylic acids with N, N-dibenzylamine serve as useful derivatives for the characterization of this class of compounds and they are quite easy to prepare.

Dissolve 0.6g of the acid in methanol and add 1.0g of N, N-dibenzylamine. Allow mixture to stand for 30mins. when crystals separate. Filter, wash with cold methanol, dry at 100^{o}C for 15 min and determine melting point. Salt may be recrystallized from ethyl acetate.

2.5.2 Amines (Primary and Secondary)

a) Benzamides

The Schotten-Baumann Reaction:

$$R_2NH + PhCOCl \rightarrow R_2NCOPh$$

Dissolve 0.15 mL of benzoyl chloride in 3 mL chloroform or ether or ethyl acetate, cool in ice. Add portion-wise with stirring or shaking 0.3 mL or 0.1g of the amine dissolved in the same solvent. Allow reaction to come to completion. Boil off solvent on the steam bath and pour residue in ice cold water. Filter and crystallize from aqueous ethanol or water.

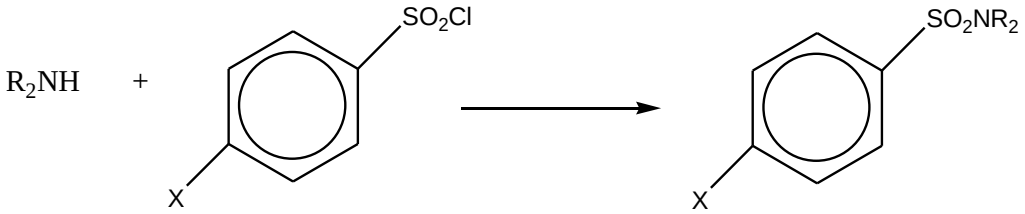
The above reaction may be run in pyridine by first adding the acid chloride to pyridine followed by the amine neat. In this instance the quantity of amine is reduced in half. The reaction is then allowed to go to completion and poured in water, solids are filtered and washed, then the amide crystallized, dried and melting point determined.

b) Acetamide:

$$R_2NH + CH_3(CO)_2O \longrightarrow R_2N\text{-}COCH_3$$

Dissolve 0.1g of the amine in 0.2 mL glacial acetic acid, add about 0.2 mL of acetic anhydride and warm on a water bath for 5 min at 60°C cool and then add 2 mL of water with stirring. Allow to stand for crystals to separate; or otherwise add conc. ammonia, filter, wash well with water and crystallize from aqueous alcohol, water or alcohol.

c) Benzene or Toluene sulphonamides



Prepare the derivatives as in (a) above if pyridine is used and no crystals or solids separate upon addition of water, then acidify with dilute hydrochloric acid and continue as usual.

d) 2,4-dinitrophenyl Derivative

R_2NH + 2,4-dinitrochlorobenzene → 2,4-dinitroarylamine

Heat a mixture of equal amounts (0.1g) of the amine and chloro-2,4-dinitrobenzene for 5 – 10 minutes. Cool and crystallize from ethanol.

2.5.3 Tertiary Amines

a) Methiodides of Tertiary Amines

$R_3N + CH_3I \longrightarrow R_3N^+CH_3I^-$

A mixture of 0.1g of the amine and 0.2 mL of methyl iodide is thoroughly agitated and kept for 5 min at room temperature then heated at 60°C for another 5 min, cooled in ice to crystallize. Recrystallize from acetone.

b) Amine Picrates

Dissolve the amine (0.1g) in 5 mL of benzene, warm on the water bath then add 0.1g picric acid. Cool, filter off salt and crystallize from benzene.

EXPERIMENTAL REPORT

Title:

Aim:

Methodology:

Results:

Discussion:

Conclusion:

2.5.4 Alcohols

Phenol (Esters Derivatives of Phenols)

a) Aryl Benzoates

Convert the phenol to its sodium salt by dissolving 0.1g in 1.5 mL 2M sodium hydroxide solution. Add 0.15 mL benzoyl chloride portion wise with shaking and cooling in water continue shaking for about 15 min until no perceptible odour of benzoyl chloride remains, otherwise add more sodium hydroxide until slightly alkaline and shake for another 10 min. filter off solids and wash well with water. Crystallize from ethanol or aqueous acetone. Alternatively, the reaction may be carried out in pyridine. In this case the phenol in 1 mL pyridine is heated with benzoyl chloride on a water bath for 15 min, cooled and 5 mL ice cold water added. The solids are filtered off, washed well with water and crystallized accordingly.

b) Benzene- and Toluene sulphonates of Phenols

Reaction is carried out in pyridine according to the procedure described above for aryl benzoates.

c) Aryl 3, 5-Dinitrobenzoates

Reflux mixture of phenol (0.1g); pyridine (1.0 mL) and 3, 5-dinitrobenzoyl chloride (0.2g) for 15-30 min in 2 mL anhydrous benzene. Boil off benzene on water bath. Pour residue in water, filter and wash cake well with water and crystallize from aqueous alcohol. Other suitable solvents such as petroleum ether, chloroform or tetrachloromethane may be used.

d) 2, 4-Dinitrophenyl Ether of Phenols

A 0.1g quantity of the phenol is converted to the potassium salt with 1 mL of 10M of the base then mixed with 0.1g chloro-2,4-dinitrobenzene and heated for 1 hour at 100^{o}C. The mixture is treated with water and precipitate filtered, washed well with water and crystallized from ethanol.

Ester Derivatives of Alcohols

a) Benzoates, P-nitro and 3, 5-Dinitrobenzoates of Alcohols: A mixture of 0.1g alcohol and 0.2g acyl chloride is heated over a low flame for about 5 min. Cooling yields crystalline ester which may be recrystallized from petroleum ether (40 – 60^{o}C) or carbon tetrachloride.

b) **Acetic Ester Derivatives of Alcohols:** (only for those alcohols yielding solid derivatives). The alcohol (0.1g) and 1 mL of acetic anhydride are refluxed for 30min. Excess anhydride is removed with water aspirator; water added and product crystallized from a suitable solvent. Alternatively, acetyl chloride could be substituted for acetic anhydride. Water is then added to decompose the acid chloride and the separated solids washed well with water and crystallized. (Tertiary alcohols only form alkyl chlorides only by this method).

EXPERIMENTAL REPORT

Title:

Aim:

Methodology:

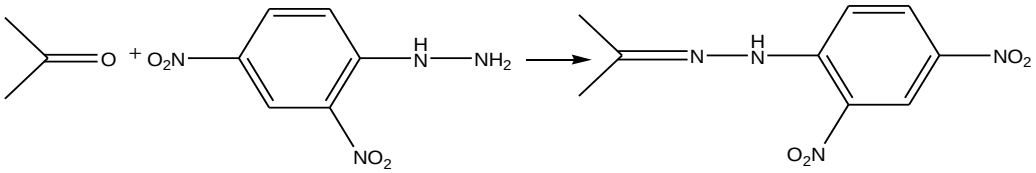
Results:

Discussion:

Conclusion:

2.5.5 Aldehydes and Ketones

a) 2,4-Dinitrophenylhydrazone



A solution of 0.1g of the carbonyl compound is mixed with about 4 mL of the Brady's reagent (acidic solution of 2,4-dinitrophenylhydrazine) and shaken, then heated for 5 min on a water bath. Cooling yields a precipitate, otherwise a few drops of sulphuric acid are added and the mixture kept until crystals separate. Recrystallization from water or ethanol may be necessary.

b) Semicarbazones

To 0.1g semicarbazide hydrochloride and 0.15g of sodium acetate in a few drops of water is added about 0.1g of the carbonyl compound. A small volume of ethanol may be added to effect complete dissolution of the carbonyl compound. Mixture is allowed to stand for a few minutes for crystals to separate; otherwise, it is heated on a water bath for about 10 minutes, diluted with water and solids filtered, then crystallized from alcohol, acetic acid or benzene.

c) Oximes

$>C=O + NH_2\text{-}OH \quad \rightarrow \quad >C= N\text{-}OH$

To 0.1g of carbonyl compound dissolved in 0.5 mL ethanol is added 0.1g hydroxylamine hydrochloride and 0.1g sodium acetate dissolved in 0.5 mL water; the mixture is refluxed for 15 min. Cool and made neutral to litmus with dilute hydrochloric acid. The solids are filtered and crystallized from alcohol.

2.5.6 Amides, Esters and Nitriles

These are characterized by hydrolysis in conc. aqueous or ethanolic potassium hydroxide under reflux. The component parts are then identified by their physical properties and appropriate derivatives subsequently.

Amides --- amine + carboxylic or sulphonic acid.

Esters --- acid + alcohol

Nitriles --- acid + NH_3

EXPERIMENTAL REPORT

Title:

Aim:

Methodology:

Results:

Discussion:

Conclusion:

2.5.7 Nitro Compounds

Nitro compounds are reduced to amines and characterized accordingly

A suspension of the nitro compound 0.1g in conc. hydrochloric acid is mixed with a pinch of zinc dust or granules and heated for about 30 min. Unreacted zinc is separated and solution made basic with conc. sodium hydroxide solution and extracted with chloroform, ether or ethyl acetate or filtered off and washed if solid. The amine obtained is then derivatized as described for this class of compounds.

2.5.8 Picrates of Aromatic Hydrocarbons

Crystalline molecular complexes formed by aromatic hydrocarbons with picric acid are conveniently used for the characterization of this class of compounds.

Preparation:

A concentrated alcoholic solution of the hydrocarbon is mixed with equal amount of picric acid; the complex formed on cooling is filtered and crystallized from ethanol.

2.5.9 Nitration of Aromatic Compounds

To a suspension of the aromatic compound in conc. sulphuric acid is cooled to 5^{o}C in ice-water mixture and 4 mL of conc. nitric acid is added dropwise with stirring. (***Note***, some nitration mixtures may react violently). The mixture is subsequently heated at 45^{o}C on a water bath for about 10 min., and poured onto ice flakes; the solids are filtered off and crystallized from aqueous ethanol.

For negatively substituted aromatic compounds, fuming nitric acid is substituted for conc. nitric acid (with fuming sulphuric acid if need be) and heated on a steam bath for about 10 min.

EXPERIMENTAL REPORT

Title:

Aim:

Methodology:

Results:

Discussion:

Conclusion:

SCHEDULE VI

2.6 ORGANIC SYNTHESIS

Majority of organic pharmaceuticals are synthetic products. The synthetic routes mostly employed include the mechanism such as addition, rearrangement, reduction, acylation etc. However, for a successful synthesis, the reaction conditions must be met and reactants must be accurately measured or weighed.

At the end of the synthesis, the product is usually dried, weighed and identified. The method for identification involves the measurement of melting point (M.P). and Boiling Point (B.P) for a liquid, U.V. spectrophotometric determination, Infrared (IR) in some instances Nuclear magnetic resonance or the combination of all of the above so as to arrive at the final structure of the synthesized compound.

The synthesized compound should be labeled properly and the percentage yield calculated accurately.

Example of Calculation:

Acylation of salicylic acid $\longrightarrow$ Acetyl salicylic acid

$$\text{Salicylic acid } (C_7H_6O_3) \xrightarrow{\text{acylation}} \text{Acetyl salicylic acid } (C_9H_8O_4)$$

M.W. ≡ 138 M.W. ≡ 180

138g of salicylic acid is expected to yield 180g of acetyl salicylic acid.

This implies:

2g of salicylic acid will give $\frac{180 \times 2g}{138}$ of Acetylsalicylic acid

= 2.61 g of acetylsalicylic acid (Theoretical yield).

If on completion of the experiment, the actual yield is 1.5g,

$$\% \text{ yield} = \frac{\text{actual yield} \times 100}{\text{Theoretical yield}} = \frac{1.5 \times 100}{2.61}$$

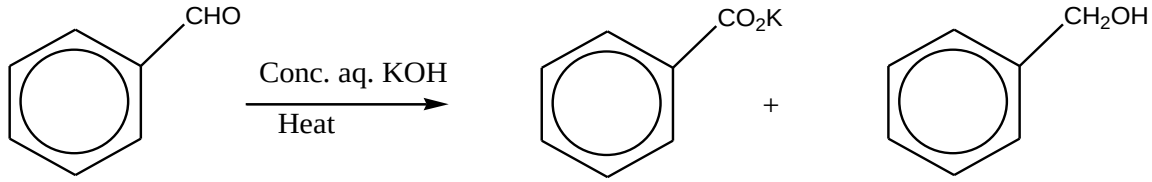
$$= 57.5\%$$

2.6.1 Preparation of Benzyl Alcohol Using Cannizaro's Reaction

Preparation of a known organic compound is considered as reconfirmation of the organic compound. Knowing how to prepare these compounds and recrystallizing them prepares the

students for the field of organic synthesis. This part will expose students to certain synthetic methods for the preparation of Benzyl alcohol using cannizaro's reaction, Benzoin using Benzoin condensation. P-nitro acetanilide by Nitration of acetamilide and many others.

Cannizzaro Reaction



To 2 mL of benzaldehyde in a large test tube add a cold solution of 2 g potassium hydroxide dissolved in 2 mL water, cork the tube tightly and shake the mixture the mixture until the next practical period or for 24h. Add about 1 mL water shake well. Add more water if all the crystals do not dissolve. Extract the solution with 3 x 10 mL diethyl ether using a 50 mL separatory funnel preserve the aqueous phase. Wash the ether extract with 3 x 10 mL aqueous sodium bisulphite to remove unreacted benzaldehyde. Wash again with 3 x 10 mL water, reject the aqueous. Dry the organic solution over anhydrous sodium carbonate. Filter, boil off ether and collect residual benzyl alcohol as viscous oil. Record the weight.

Prepare the 3, 5-dinitrobenzoate ester accordingly. Determine weight and melting point.

Acidify the aqueous extract with 5 mL conc. hydrochloric acid, 4 mL of water and 5g of crushed ice, and stir vigorously. Cool in ice-water bath for crystallization. Filter off crystals, wash with cold water. Dry; record the weight and melting point.

Calculate % yield of benzyl alcohol and benzoic acid based on the amount of benzaldehyde used.

Condensation of Benzaldehyde with aniline

$PhCHO + PhNH_2 \rightarrow PhCH=N\text{-}Ph + H_2O$

0.22M → 0.22M

Place the contents in a 50 mL round bottomed flask, heat the benzaldehyde-aniline mixture for 30 min., with reflux, cool and dissolve in methanol, place the solution in an ice-water bath and allow to crystallize. Filter, dry in air or in a dessicator, obtain weight and melting point.

Exercise: Suggest the mechanism for the above reaction.

Calculate percent yield based on theory.

2.6.2 Preparation of Benzoin (Benzoin Condensation)

$2PhCHO + NaCN \longrightarrow PhCHOH\text{-}COPh$

In a 50 mL round, bottomed flask equipped with a reflux condenser place 6.5 mL of ethanol 5.0 g (4.75 mL) benzaldehyde and 0.5g sodium cyanide in 5 mL water. Reflux for 30min. on a water bath. Cool to induce crystallization of benzoin. Filter; wash with ice cold water, dry and record weight.

Recrystallize from 4 mL of ethanol.

Exercise: Suggest the mechanism for the above reaction.

2.6.3 Nitration of Acetanilide

$$PhNHCOCH_3 + HNO_3 \xrightarrow{H_2SO_4} P\text{-}NO_2\text{-}PhNHCOCH_3$$

Add drop wise a cold 2.2 mL of conc. nitric acid (in 1.4 mL conc. H_2SO_4) to a mixture of 5 g acetanilide, 5 mL acetic acid and 10 mL concentrated sulphuric acid in 100 mL conical flask cool to 5 – 10^oC with ice. Allow to stand for 1 hour on completion of addition. Pour mixture onto crushed ice, filter and collect the P-nitroacetanilide. Wash well with water and crystallize from ethanol.

Record weight and calculate % yield based on theory.

Exercise: Suggest the mechanism for the above reaction.

2.6.4 Hydroxylation of Oleic Acid

$$CH_3(CH_2)_7\,CH{=}CH(CH_2)_7COOH + KMnO_4 \longrightarrow \underset{\text{9,10-dihydroxystearic acid}}{CH_3(CH_2)_7CH(OH)\text{-}CH(OH)\text{-}(CH_2)_7COOH}$$

Prepare the potassium salt of oleic acid by mixing a 2g solution of potassium hydroxide in 40 mL water and 2.0g of oleic acid in a 250 mL conical flask. Ensure complete dissolution of the acid in the caustic solution. Add 60g crushed ice to the solution and keep temperature between 3 – 5^oC. Add 2.0g potassium permanganate and stir vigorously to ensure complete dissolution of the oxidants keep for 10 – 20 min. Bubble sulphur dioxide through the solution to destroy any residual permanganate. Acidify with conc. hydrochloric acid, filter and wash well the hydroxy acid with water. Crystallize from ethanol and dry at 80 ^oC in an oven. Record weight and calculate percent yield based on theory.

Exercise: Suggest the mechanism for the above reaction.

EXPERIMENTAL REPORT

Title:

Aim:

Methodology:

Results:

Discussion:

Conclusion:

2.6.5 Bromination of Cinnamic Acid

$$PhCH{=}CH\text{-}COOH + Br_2 \longrightarrow PhCHBr\text{-}CHBr\text{-}COOH$$

Place a solution of 1g of cinnamic acid in 5 mL chloroform, in a 50 mL conical flask. Cool, and to this add in one portion, 1.08g of bromine in 1 mL chloroform. Allow to stand for 10 min., filter off the dibromide and wash with 1 mL cold chloroform. Allow to dry in air, record weight and melting point. Determine % yield based on theory.

Exercise: Suggest the mechanism for the above reaction.

2.6.6 Preparation of Acetyl Salicylic Acid (Aspirin)

$$OH\text{-}PhCOOH \xrightarrow{\text{Acetic anhydride / conc.}H_2SO_4} \text{Aspirin}$$

To 1.0g of salicylic acid in a large test tube add 2 mL acetic anhydride. Add two drops of conc. sulphuric acid, place in a 100 mL beaker of hot water for 5 minutes, pour mixture to 50 mL water in a 125 mL conical flask. Stir and chill in ice. Scratch and collect the separated crystalline solids. Weigh, determine m.p. and calculate yield based on theory.

Exercise: Suggest the mechanism for the above reaction.

2.6.7 Preparation of Methyl Salicylate (Oil of Winter Green)

$$OH\text{-}PhCOOK + CH_3I \longrightarrow o\text{-}OH\text{-}PhCO_2CH_3$$

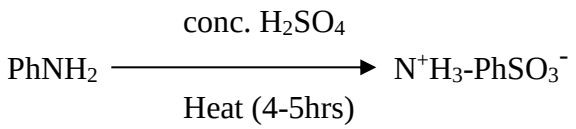
Carefully weigh 5.6g potassium hydroxide into a 250 mL conical flask and add 50 mL methanol. Stir until dissolved, cool and to this add 13.8 g of salicylic acid and stir again until a clear solution is obtained. Add to the cold mixture 0.12 mol (7.6 mL) methyl iodides. Stopper tightly with a cork stopper and allow to stand until the next practical period.

Distill off methanol and unreacted methyl iodide and add ice cold water to residue. Extract the oil of winter green with chloroform. Dry over anhydrous magnesium sulfate, filter and distil off chloroform. Weigh and calculate crude yield based on theory.

Determine the purity of your product by spotting on a 5 x 20 cm silica gel plate. Develop with chloroform. Place the plate in an iodine chamber until colour is developed. Determine R_f of your product.

Exercise: Suggest the mechanism for the above reaction.

2.6.8 Synthesis of Sulphanilic Acid



Place 26.4 g of aniline in 250 mL conical flask on a round bottomed flask. Cool in ice and to this add carefully 40 mL conc. sulphuric acid. Support the flask in an oil bath or sand bath and heat the mixture at 180 – 190^{o}C in a fume cupboard for 4 – 5 h.

Cool mixture to 50^{o}C in an ice bath. Pour into 400 mL cold water or crushed ice. Filter after 10 minutes of standing, wash thrice with 10 mL portion of cold water. Dissolve the acid in 500 mL boiling water, cool to crystallize, filter off the dihydrated product and wash with 10 mL cold water. Dry between filter papers. Determine yield based on theory.

Exercise: Suggest the mechanism for the above reaction.

EXPERIMENTAL REPORT

Title:

Aim:

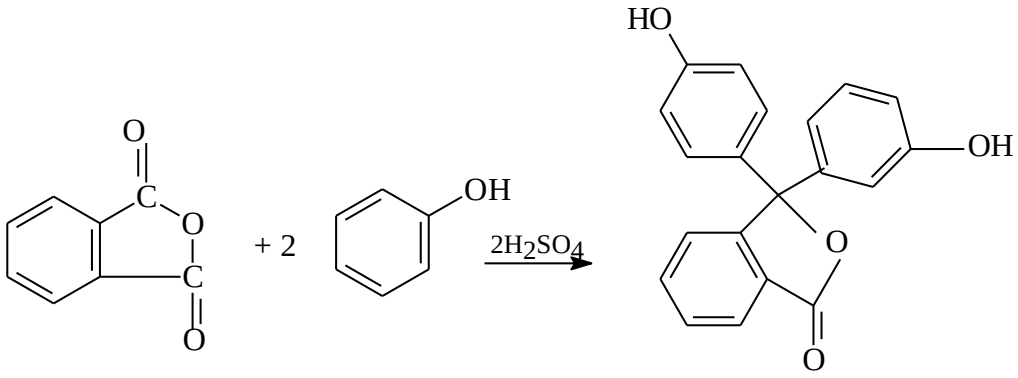
Methodology:

Results:

Discussion:

Conclusion:

2.6.9 Synthesis of Phenophthalein



Heat a mixture of 25g phthalic anhydride, 20.4g phenol and 20g (11 mL) of conc. sulphuric acid in an oil or sand bath at 115 – 120^{o}C for 9 hours. Pour while hot into 1L hot water in a 2L beaker, boil until phenol odour disappears. Make up solution back to 1L. Cool, filter and wash with water. Dissolve residue in dilute sodium hydroxide and filter. Acidify with acetic acid and a few drops of dilute hydrochloric acid. Allow to stand overnight. Filter off the separated phenolphthalein and dry. Crystallize from ethanol–water. Determine weight and % yield based on theory.

Exercise: Suggest the mechanism for the above reaction.

2.6.10 Synthesis of Sulphacetamide

Place 1.7g of sulphanilamide in a 10 mL test-tube; add 5 mL water to this. Shake well and then place in cold water, add 1 mL of 40% NaOH solution, shake well to effect complete dissolution of the amide. When all the substance has gone into solution, add 1 mL acetyl chloride drop wise. Ensure that the test-tube remains in the cold-water bath throughout. Allow separated solids to settle and then filter to collect product. Wash well with 5 mL water. Discard filtrate; dry your product in air. Record weight and determine the melting point, calculate theoretical yield and actual yield.

Expel the moisture, dry the precipitate and gently remove the filter paper. Press the paper gently between the fingers to loosen the precipitate from the paper. Transfer the precipitate powder to a clean wash place on a glazed paper and cover with a funnel. Incinerate the filter paper separately in a weighed crucible using a Bunsen flame trill the filter paper is completely changed and is converted into white ash.

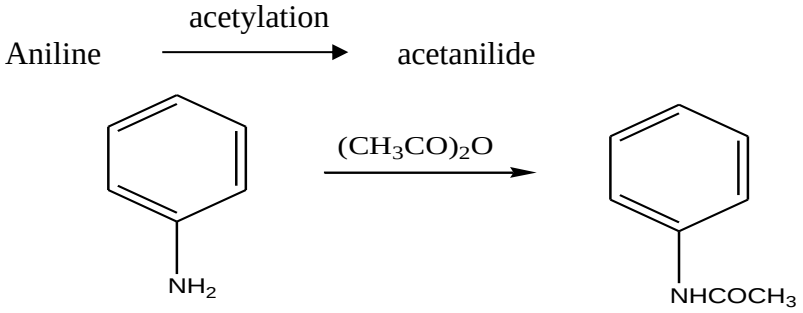
Transfer the reverse precipitate of $BaSO_4$ into the crucible and heat it on a flame to a dull red heat (60 –80^{o}C) for about 20 minutes. Weigh the crucible and ignite again for 10 minutes in

the flame, cool and weigh. Repeat this until a constant weight of the crucible is obtained. Cool and place in a desiccator to cool it to room temperature and weigh.

Exercise: Suggest the mechanism for the above reaction.

2.6.11 Preparation of Acetanilide from Aniline

Acetanilide is a precursor in the synthesis of sulfanilamide which is considered to be the parent compound of all sulfonamides, Sulfonamides are antibacterial agents that are commonly used in medicine. The synthesis of acetanilide involves the acetylating of aniline using acetic anhydride. At the end of the synthesis the theoretical yield and the percentage yield are going to be calculated as demonstrated below:



M.W. = X M.W. = Y

X g of aniline will yield Y g of acetanilide

:. For 1g of aniline (assuming lg was used)

$\frac{Y \times l}{X}$ = theoretical yield = Z

If on completion of the experiment, the yield of the product in 0.85g,

$$\% \text{ yield} = \frac{\text{Actual of the product}}{\text{Theoretical yield}} \times 100$$

$$= \frac{0.85 \times 100}{Z}$$

Method:

2g of aniline (toxic) is taken into clean dry boiling tube or round bottom flask. To this, 3g of acetic anhydride is added (convert these to volume) and attach to a reflex condenser. Reflux gently for 30 minutes, using a wire gauge. Pour the still hot contents of the tube or flask into a beaker containing 100 mL ice-cold water. The acetanilide precipitates as a crude solid. Filter the precipitates using Buchner funnel and wash with 10 mL water. Dry the crystal by sucking air through the pad of crystal, in the Buchner funnel. Weight the crude crop and recrystallize from water containing 1% v/v ethanol. Using melting point apparatus determine the melting

point of the synthesized acetanilide. Record the yield of crude and recrystallized product, and its melting point. Finally calculate the theoretical yield and the percentage yield of the product.

Exercise:

Suggest the mechanism of the reaction in the above synthesis

2.6.12 Synthesis of Sulphanilamide from Acetanilide

Sulphanilamide belongs to the sulphonamide group of antibacterial. It is considered to be the parent compound of sulphonamides. Sulphonamides are bacteriostatic agents that are active against Streptococcal and Pneumococcal infections and are commonly used in medicine. The synthesis of acetanilide involves the acetylating of aniline using acetic anhydride. At the end of the synthesis the theoretical yield and the percentage yield are going to be calculated as demonstrated below:

$$\text{Aniline} \xrightarrow{\text{acetylation}} \text{acetanilide}$$

M.W = X M.W. = Y

X g of aniline will yield Y g of acetanilide

:. For 1g of aniline (assuming lg was used)

$\frac{Y \times 1}{X} \equiv$ theoretical yield $\equiv Z$

If on completion of the experiment, the yield of the product in 0.85g,

$$\% \text{ Yield} \equiv \frac{\text{Actual of the product}}{\text{Theoretical yield}} \times 100$$

$$\equiv \frac{0.85}{Z} \times 100$$

The synthesis of sulphanilamide involves the introduction and removal of an acetyl blocking group to control the course of the synthesis.

Method:

Take 2 g of acetanilide into an element flask; reduce the surface area of the acetanilide by melting it in the flask over a soft flame and then rotating the flask to spread the material with a thin film over the bottom of the flask. Stopper the flask and store.

Prepare a gas trap for HCl fumes with tubing from the above flask to a funnel and insert the funnel over water. Take exactly 5 mL of chlorosulphuric acid with a dry measuring cylinder. (**Caution:** *this reagent is extremely hazardous; it will cause burn therefore do not pour into*

the sink). Cool the acetanilide in an ice bath, add the chlorosulphuric acid into the flask and connect the flask with the trap. Remove the flask from the ice- bath (although you can return it if the reaction becomes too vigorous). After about 15 minutes when most of the solid has dissolved, warm the flask on a steam bath, continue heating for about 10 minutes unit the solid has disappeared. Cool the liquid (trap still connected) and then pour it onto 100 mL of ice. Add water to the flask and transfer the residue to the main solution. Stir and heat the solid sulphonyl chloride with a spatula until the lumps are broken up collect in a Buchner funnel and wash with a little water. This sulphonyl chloride is called P-acetamidobenzene sulphonyl chloride.

Transfer the moist P- acetamidobenzene sulphonyl chloride to the original 125 mL Erlenmeyer flask. Add 40 mL of conc. aqueous ammonia stir and shake. As the reaction proceed the granular sulfonyl chloride give way to a thin paste of the amide. Warm on water bath, cool and collect the solids. Wash the solid with water press and drain thoroughly. The solids formed are p-acetamidobenzene sulphonamide.

Transfer the cake of acetamidobenzenesulphonamide to the same Erlenmeyer flask and add 100 mL of 6M HCl. Heat to boiling over a low flame until all the solid has dissolved and continue gentle boiling for about 10 minutes. Cool the solution, and add water to replace that lost in evaporation; add activated charcoal as filter. The filtrate is then treated with solid $NaHCO_3$ with stirring until the pH is neutral. Collect the solid sulfanilamide, wash with water and air dry. Record the yield and then determine the melting point of the product. Calculate the theoretical yield and the percentage yield.

Exercise:

Suggest the mechanism of reaction in steps B- C in the above equation

EXPERIMENTAL REPORT

Title:

Aim:

Methodology:

Results:

Discussion:

Conclusion:

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