Experiment – 1

Synthesis And Characterization Of Sulphanilamide

Aim:-To perform the synthesis and characterization of Sulphanilamide.

Reference: Vogel's Textbook of Practical Organic Chemistry (5th ed.), Furniss, B. S.; Hannaford, A. J.; Smith, P. W. G.; Tatchell, A. R. (1989), Page no. 883.

Chemical and reagents:
Acetanilide 25g
Chlorosulphonic acid 63ml
Ammonia solution 120ml

Glassware and apparatus:- weighing balance, round bottom flask, glass rod, pipette, measuring cylinder, funnel, beaker, melting point apparatus, TLC plates etc.

Principle:- acetanilide when treated with an excess of chlorosulphonic acid gives P-acemidobenzensulphonyl chloride, which readily reacts with ammonia to give p-acetamidobenzene sulphonamide. This compound on hydrolysis gives sulphanilamide. The following are the reaction involved:

Procedure:-
step - 1
Add 25 g of powdered aceanilide to 63ml of chlorosulphonic acid taken in 250ml conical flask.
Heat the content of the flask to 60-70^{0}C for 2hours.
Cool the mixture and then pour it carefully on to crushed ice (around 500g) whereby the P- acetamidobenzene sulphonyl chloride separates out as white solid.
Filter of the product at the pump, wash it thoroughly with water and drain.
This can be used as the raw material for the next step.
Step-2

Place the above obtained chloride salt in a 500ml conical flask and add 120ml of conc. Ammonia (a vigorous reaction with evolution of heat will follow).
Stir the mixture at 70^0C for 30 minutes with occasional stirring.
Cool the mixture and make the mixture just acidic with dilute sulphuric acid.
Filter off the precipitate P-acetamidobenzne sulphonamide at the pump, wash it well with cold water and thoroughly drain it.

Step-3

Take the product from the above step and mix with hydrochloric acid (10ml of conc. HCl and 20ml water) and boil this mixture under reflux for 1 hour.
Filter the boiling solution and add sodium carbonate until the effervescence stops and the sulphonamide is precipitated as a white powder. Cool the mixture and filter off the sulphonamide obtained, wash with water and dry. The yield is 10g and the melting point of the sulphanilamide obtained is 163^0C

Observation and calculations:

Theoretical yield of the Product	
Practical yield of the Product	
Melting point	

% age yield = Theoretical yield/Practical Yield X 100

Result :- The percentage yield of synthesized Sulphanilamide was found to be ….

Experiment 2

Synthesis of 7-Hydroxy-4-Methyl Coumarin

Aim:-To perform the synthesis of 7-hydroxy-4-methyl coumarin.

Reference: Vogel's Textbook of Practical Organic Chemistry (5th ed.), Furniss, B. S.; Hannaford, A. J.; Smith, P. W. G.; Tatchell, A. R. (1989), Page no. 1193.

Chemical and reagents:
Resorcinol- 3.7g
Ethyl acetoacetate- 4.5g
Conc. Sulphuric acid-15 ml

Glassware and apparatus:- weighing balance, round bottom flask, glass rod, pipette, measuring cylinder, funnel, beaker, melting point apparatus, TLC plates etc.

Procedure: The nitration of 7-hydroxy-4-methyl Coumarin using concentrated nitric acid and sulfuric acid at 5°C gave two nitro isomers i.e. 7-hydroxy-4-methyl-8-nitro Coumarin & 7-hydroxy4-methyl-6-nitro Coumarin. In a conical flask, 7-hydroxy-4-methyl Coumarin (1.2 g) was dissolved in conc. H_2SO_4 acid (10 ml.) and then keep the flask in an ice bath. When the temperature inside the flask is below 1°C, 2 ml of nitrating mixture (0.5ml of concentrated nitric acid and 1.5 ml of concentrated sulfuric acid) taking care that the temperature does not rise above 10°C, after the addition was completed, removed the flask from the ice bath and keep it at room temperature for an hour. The flask shook occasionally during this period and then poured with stirring in a beaker containing crushed ice. The crude product filtered, which is a mixture of 6 and 8 nitro derivatives, and washed with cold water. The crude mixture was transferred in a conical flask containing ethanol and boiled. The residue is 6-nitro-4-methyl-7-hydroxy coumarin. Concentrated the filtrate, and cooled in an ice bath, 8-nitro derivative soon crystallized out. Recrystallized from ethanol and collect 8-nitro-4-methyl-7-hydroxy coumarin

Observation and calculations:

Theoretical yield of the Product	
Practical yield of the Product	
Melting point	

% age yield = Theoretical yield/Practical Yield X 100

Result:- The percentage yield of synthesized 7-hydroxy-4-methyl coumarin was found to be ….

Experiment 3

Synthesis of Chlorobutanol

Aim:-To perform the synthesis of Chlorobutanol.

Reference: The Merck Index. 9th ed. Rahway, New Jersey: Merck & Co., Inc., 1976., p. 270

Chemical and reagents:
Dry acetone, Chloroform, potassium hydroxide

Glassware and apparatus:- weighing balance, round bottom flask, glass rod, pipette, measuring cylinder, funnel, beaker, melting point apparatus, TLC plates etc.

Principle:- It is formed by the simple nucleophillic additionof chloroform and acetone. Chlorobutanol is a preservative, sedative, hypnotic and weak local anesthetic similar in nature to chloral hydrate. It has antibacterial and antifungal properties. Chlorobutanol is typically used at a concentration of 0.5% where it lends long term stability to multi-ingredient formulations. However, it retains antimicrobial activity at 0.05% in water. Chlorobutanol has been used in anesthesia and euthanasia of invertebrates and fishes. It is a white, volatile solid with a menthol-like odor.

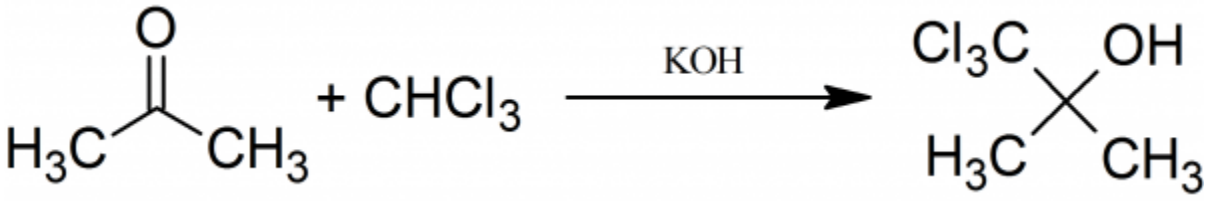
Procedure:- Combine 90 mL of acetone, 10 mL of chloroform and 2 g of potassium hydroxide, stir the mixture vigorously at -5°C for 2h. After which the suspension was filtered, the filter needs to be washed with acetone, then distill at 60°C until the weight of the solution remains constant. Then pour the chlorobutanol into a bigger beaker and add 100 mL of ice-cold water. Filter and

store the filtered sludge. Recrystallize in ethanol to get pure solid chlorobutanol hemihydrate crystals.

Or

To a mixture of 500 g of dry acetone and 1000 g of chloroform, cooled to below 0° C and continuously stirred, are added gradually, over a period of 60 hours, 325 g of finely powdered potassium hydroxide. After being allowed to stand at room temperature for a further 36 hours with intermittent stirring the mass is filtered and the residue washed with acetone. The combined filtrates are distilled, unchanged chloroform and acetone are recovered, and the fraction passing over between 165° C and 172° C is collected separately. The distillate is poured in water, crystallisation sets in, and when this is complete the solid is filtered off and recrystallized from a mixture of alcohol and water. Chlorobutanol is extremely volatile even at ordinary temperatures, and requires to be dried with great care to avoid loss. Chlorobutanol forms white glistening crystals having a camphoraceous odor and taste. Chlorobutanol melts, when anhydrous, 96-97° C. Soluble in water and in 90% ethyl alcohol.

Preparation of chlorobutanol:-



Observation and calculations:

Theoretical yield of the Product	
Practical yield of the Product	
Melting point	

% age yield = Theoretical yield/Practical Yield X 100

Result:- The percentage yield of synthesized Chlorobutanol was found to be ….

Experiment-4

Synthesis of Triphenyl Imidazole.

Aim-: To perform the synthesis of Triphenyl Imidazole.

Reference: Vogel, H. G. (Ed.), Drug discovery and evaluation: Pharmacological assays, 2nd edition, Springer- Verlag Berlin Heidelberg Publication, New York, 2002; 716-725.

Chemical and Reagents- Benzil (10mmol), Benzaldehyde (10mmol) and Ammonium Hydrogen Phosphate (0.513g)**,** Ammonium acetate (1.2g)**.**

Glassware and apparatus:- weighing balance, round bottom flask, glass rod, pipette, measuring cylinder, funnel, beaker, melting point apparatus, TLC plates etc.

Principle- The Debus-Radziszewsi imidazole synthesis is an organic reaction used for the synthesis of imidazole from a dicarbonyl, an aldehyde, and ammonia. The dicarbonyl component is commonly glyoxal, but also include various 1,2-diketones and ketos aldehyes. The method is used to produce several imidazoles. The process is an example of a multicomponent reaction.

Procedure

Method-1

1) In a round bottom flask benzil (10mmol), benzaldehyde(10mmol) and ammonium hydrogen phosphate(0.513g) in an oil bath at room temperature as in.
2) Then the reaction mixture is heated to 100^0C for 20 minutes.
3) After completion of reaction which is monitored by TLC.
4) The mixture is washed with water the solid product is purified by recrytallization from ethanol.

Method-2

1) Benzil (1m mol), suitable benzaldehyde (1mmol), and ammonium acetate (1.2g) were dissolved in boiling glacial acetic acid (16ml).
2) The reaction mixture is refluxed for 5-24 hour.
3) The reaction progress was monitored by TLC.
4) After the reaction completion, the reaction mixture was poured into ice water,
5) Then washed several times with ethyl acetate. The combined extracts were dried over $MgSO_4$.
6) The purification was done by flash column chromatography.
7) The compound was obtained in 46% yield.

Observation and calculations:

Theoretical yield of the Product	
Practical yield of the Product	
Melting point	

% age yield = Theoretical yield/Practical Yield X 100

Result:- The percentage yield of synthesized Triphenyl Imidazole was found to be ….

Experiment-5

Synthesis of Tolbutamide

Aim-: To perform the synthesis of Tolbutamide.

Reference: The Merck Index. 9th ed. Rahway, New Jersey: Merck & Co., Inc., 1976., p. 1223

Glassware and apparatus:- weighing balance, round bottom flask, glass rod, pipette, measuring cylinder, funnel, beaker, melting point apparatus, TLC plates etc.

Principle:- Tolbutamide is an oral antihyperglycemic agent used for the treatment of non-insulin-dependent diabetes mellitus (NIDDM). It is structurally similar to acetohexamide, chlorpropamide and tolazamide and belongs to the sulfonylurea class of insulin secretagogues, which act by stimulating β cells of the pancreas to release insulin. Sulfonylureas increase both basal insulin secretion and meal-stimulated insulin release. Medications in this class differ in their dose, rate of absorption, duration of action, route of elimination and binding site on their target pancreatic β cell receptor. Sulfonylureas also increase peripheral glucose utilization, decrease hepatic gluconeogenesis and may increase the number and sensitivity of insulin receptors. Sulfonylureas are associated with weight gain, though less so than insulin.

Procedure:-

Method -1

1) P-toluene is treated with sulfenyl chloride.
2) P-toluene sulfenyl chloride obtained is condensed with n-butyl urea.
3) The product treated with alkaline KMnO4 to give tolbutamide.

Method – 2

1) P-toluene sulphonamide and urea are heated together.
2) The product is treated with methanol in the presence of sulphuric acid and then with butlyamine.

Observation and calculations:

Theoretical yield of the Product	
Practical yield of the Product	
Melting point	

% age yield = Theoretical yield/Practical Yield X 100

Result:- The percentage yield of synthesized Tolbutamide was found to be ….

Experiment-6

Synthesis of Hexamine

Aim-: To perform the synthesis of Hexamine.

References: G. Pass and H. Sutcliffe, Practical inorganic chemistry, preparations, reactions and instrumental methods . Chapman and Hall Ltd., London, 1968, pp. 80-81.

Glassware and apparatus:- weighing balance, round bottom flask, glass rod, pipette, measuring cylinder, funnel, beaker, melting point apparatus, TLC plates etc.

Principle:- **Hexamethylenetetramine** or **methenamine**, also known as **hexamine** or **urotropin**, is a heterocyclic organic compound with the formula $(CH_2)_6N_4$. This white crystalline compound is highly soluble in water and polar organic solvents. It has a cage-like structure similar to adamantane. It is useful in the synthesis of other chemical compounds, e.g., plastics, pharmaceuticals, rubber additives. It sublimes in vacuum at 280 °C. The molecule has a symmetric tetrahedral cage-like structure, similar to adamantane, whose four "corners" are nitrogen atoms and "edges" are methylene bridges. Although the molecular shape defines a cage, no void space is available at the interior for binding other atoms or molecules, unlike crown ethers or larger cryptand structures.

The molecule behaves like an amine base, undergoing protonation and *N*-alkylation

Procedure:-

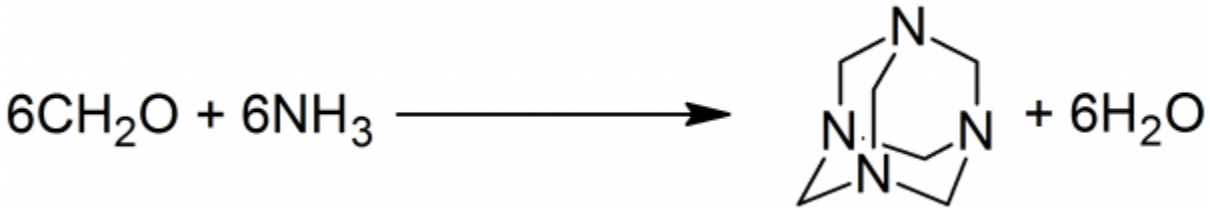
Method:- 473 g of a 38 % formaldehyde solution, is treated with 700 g of 20% ammonium hydroxide solution, until the solution is slightly alkaline. The mixture is allowed to stand, for several hours and if necessary more ammonia being added. The solution is filtered and then evaporated in vacuum to a thick paste. The hexamine crystals are filtered off washed with ethyl alcohol, and dried. To obtain pure hexamine it is recrystallized from water or

alcohol. Hexamine forms colorless, odorless crystals, which are soluble in water, and 90 % alcohol. It does not melt on heating, but sublimes at a temperature of about 260° C.

Method:- II

1) Place 10 mL of 37% formaldehyde and 9 mL of ammonia into a round bottomed flask(100 mL).
2) Evaporate the solution on a Rota vapor.
3) During evaporation a white residue (urotropine) is formed.
4) Add another portion of ammonia (14 mL) to dissolve the solid.
5) Once more place the flask onto a Rota vapor and evaporate the solvent.
6) Repeat that step once more with an additional portion of ammonia (14 mL).
7) After evaporating, add 15 mL of anhydrous ethanol and dissolve the solid by heating under reflux.
8) Filter the hot mixture on the Büchner funnel. ·Add 10 mL diethyl ether to the filtrate and cool down.
9) Filter the precipitated urotropine, wash it with anhydrous ethanol, drain well and then dry on air. Weigh the product, calculate the yield and measure the melting point. (lit. 214-215

Reaction :-



Observation and calculations:

Theoretical yield of the Product	
Practical yield of the Product	
Melting point	

% age yield = Theoretical yield/Practical Yield X 100

Result:- The percentage yield of synthesized Hexamine was found to be ….

Experiment-7

Assay of Isoniazid

Aim-: To perform the assay of Isoniazid.

References: Journal of Analytical Chemistry, 70 (6). pp. 696-699. ISSN 1608-3199

Chemicals :-

Isoniazid- 0.4gm

Potassium bromate- 2.783gm

Potassium bromide- 0.2gm

Methyl red-few drops

Glassware and apparatus:- weighing balance, round bottom flask, glass rod, pipette, measuring cylinder, funnel, beaker, etc.

Principle –isoniazid is isonicotinic acid hydrazide. The principle involved in assay of isoniazid tablet is redo titration. It is oxidized to isonicotinic acid by bromine in the presence of HCl to give hydrogen bromide with the evolution of nitrogen. Bromine is released as titration proceeds and reacts with isoniazid but the solution of bromine is not stable. Therefore to the solution potassium bromide is added which is slowly reacted with potassium bromated. The reaction between potassium bromide, HCl and potassium bromated releases bromine which oxidized isoniazid. At the end the point the HCl is depleted, where the methyl red solution changes from red to yellow.

Preparation of 0.0167 M Potassium Bromated

1. Weigh accurately Potassium bromated (2.783g, 0.0167M) and dissolved in minimum quantity of distilled water.

2. Mae the volume upto 100 ml using distilled water.

Procedure for assay:-

1. Weigh accurately 20 tablets of isoniazid and reduce them to a fine powder.
2. Weigh out a quantity of powder equivalent to 0.4 g of isoniazid into dry conical flask and dissolve in 50ml of water as completely as possible.
3. Filter the solution and wash the residue several times and mix with the original solution. Mae up the filtered solution to 250 ml with water.
4. To 50ml of the above solution, add 50ml of water and 0.2g of potassium bromide and 10ml of dilute HCl.
5. Titrate the resulting solution slowly with 0.0167 M Potassium bromated with continuous stirring using methyl red as indicator until the colour changes from red to yellow.
6. Equivalent factor: each ml of 0.0167 M Potassium bromated is equivalent to 0.00342 g of isoniazid.

Observation table

Sr. No.	**Volume in conical flask**	**Burette reading(ml)**		**Final Reading**
		Initial Reading	**Final Reading**	

Calculation

$$\%\text{age Purity} = \frac{\text{Volume of Potassium bromated X IP factor X 100}}{\text{Weigh of isoniazid}}$$

Result:- %age purity of isoniazid was found to be ----------

Experiment-8

Assay of Chloroquine Phospahate

Aim-: To perform the assay of Chloroquine Phospahate.

Reference: Moffat, A.C.; Osselton, M.D.; Widdop, B., Eds.; Clarke's Analysis of Drugs and Poisons, 4th ed; Pharmaceutical Press: London, 2011 pp 201-202.

Chemicals:-

Chloroquine Phospahate – 0.05gm

Glacial acetic acid – 50ml

Potassium hydrogen phthalate – 0.3g

Crystal violet – few drops

Perchloric acid – q.s.

Glassware and apparatus:- weighing balance, glass rod, pipette, measuring cylinder, funnel, beaker, etc.

Principle:- The assay of chloroquine phosphate is carried out by non- aqueous titrimetry. Chloroquine Phospahate is chemically RS-4-(7-chloro-quinolinylamine)-pentyldiethylamine diphosphate. It exists in 2 isomeric forms. It is weak base having a pH of 4.8-6.0. They do not give sharp end point when titrated in aqueous medium. So it is analyzed by non aqueous method.

In non aqueous titration non aqueous solvents such as acetic acid, acetone and weak organic bases like tetrabutylammonium hydroxide in methanol, potassium, sodium or lithium methoxide in toluene-methanol, are used for titration of weekly basic and weekly acidic substances respectively.

Reaction:-

Preparation of 0.1M Perchloric acid

1. Mix an accurately measured volume of perchloric acid (8.5ml) with anhydrous Glacial acetic acid (500ml).
2. Then add 25 ml of acetic anhydride.
3. Cool the mixture to room temperature and make up the volume to 1000ml using anhydrous.
4. Glacial acetic acid.
5. Allow the solution to stand for overnight.

Standardization of 0.1M Perchloric acid

1. Accurately weigh about 0.1g of potassium hydrogen phthalate and dissolve it in 10 ml of Glacial acetic acid.
2. Add few drops of crystal violet solution and titrate with .1M perchloric acid until the color changes from violet to emerald green.
3. Perform the blank determination and make the necessary corrections.

Procedure:-

1. Weigh accurately about 0.05gm of chloroquine phosphate in to a conical flask and dissolve in 10 ml of anhydrous Glacial acetic acid with the aid of heat if necessary.
2. Add few drops of crystal violet solution and titrate the resulting solution with 0.1 M perchloric acid until the colour changes from violet to emerald green.
3. Perform the blank determination and make the necessary corrections.
4. Equivalent factor: each ml of 0.1 M Perchloric acid is equivalent to 0.02579 g of chloroquine phosphate.

Observation table (for standardization)

Sr. No.	**Volume in conical flask**	**Burette reading(ml)**		**Final Reading**
		Initial Reading	**Final Reading**	

Observation table (For Assay)

Sr. No.	Volume in conical flask	Burette reading(ml)		Final Reading
		Initial Reading	Final Reading	

Calculation

(A) For Standardization of perchloric acid

$$\text{Normality} = \frac{\text{weigh} \times 1000}{\text{Equivalent weigh of potassium hydrogen phthalate} \times \text{volume}}$$

$$\text{Normality} = \frac{0.1 \times 1000}{204.2 \times \text{----------}}$$

(B) For assay of Chloroquine phosphate

$$\%\text{age Purity} = \frac{\text{Volume of perchloric acid} \times \text{IP factor} \times 100 \times \text{Normality of P.A}}{\text{Weigh of chloroquine phosphate} \times \text{normality of P.A}}$$

Result:-%age purity of chloroquine phosphate was found to be ----------

Experiment-9

Assay of Dapsone Tablets

Aim-: To perform the assay of Dapsone Tablets.

Reference: G. Pass and H. Sutcliffe, Practical inorganic chemistry, preparations, reactions and instrumental methods . Chapman and Hall Ltd., London, 1968, pp. 89-90.

Principle:- The principle involved in the assay of Dapsone tablets is diazotization. Aromatic primary amines like Dapsone react with nitrous acid to form diazonium salt. Nitrous acid is prepared in situ by reacting sodium nitrite with concentrated HCl 0^0C to 5^0C. The observation of the end point is depends on small excess of nitrous acid present at that point which can be visually determined by using starch iodide suspension as an external indicator. The iodine liberated react with starch to produce blue colour.

Preparation of 0.1 M Sodium Nitrite Solution

1. Weigh accurately about 6.9 g of sodium nitrite and dissolve in few ml of water.
2. Dilute the resulting solution up to 1000ml with distilled water.

Procedure for the standardization of Sodium Nitrite

1. Accurately weigh about 0.1 g of sulphanilic acid in to conical flask, add 1.5 g of potassium bromide followed by 15 ml of 2.0 M HCl and cool to below 10^0C.
2. Titrate the mixture with 0.1 M Sodium Nitrite solution at a temperature not exceeding 10 0C untiul a drop of solution immediately gives blue color when drawn quickly by means of a fine glass rod across the surface of starch paper.
3. Titration is complete when the end point is reproducible after the titrated solution is allowed to stand for one minute.
4. Each ml of 0.1 M NaNO2 is equivalent to 0.01732 g of sulphanilic acid.

Procedure for assay:-

1. Weigh 20 tablets of dapsone accurately and reduce to fine powder with the help of a mortar and pestle.
2. Weigh a quantity of powder equivalent ti 0.1 g of dapsone into a conical flask and dissolve in mixture of 6.0 ml of water and 6.0 ml of 2.0 m. HCl
3. Cool the mixture to below 10^0C and titrate against 0.1 M Sodium Nitrite at a temperature not exceeding 10^0C until a drop of solution gives dark blue color when drawn quickly across the surface of starch iodide paper with a glass rod.
4. Titration is complete when the end point is reproducible after the titrated solution is allowed to stand for one minute.
5. Each ml of 0.1 M $NaNO_2$ is equivalent to 0.01242g of dapsone.

Observation table (for standardization)

Sr. No.	**Volume in conical flask**	**Burette reading(ml)**		**Final Reading**
		Initial Reading	**Final Reading**	

Observation table (For Assay)

Sr. No.	**Volume in conical flask**	**Burette reading(ml)**		**Final Reading**
		Initial Reading	**Final Reading**	

Calculation

For Standardization of Sodium Nitrite

(A)

$$\text{Normality} = \frac{\text{weigh X 1000}}{\text{Equivalent weight of potassium hydrogen phthalate X volume}}$$

$$\text{Normality} = \frac{0.1 \quad X \quad 1000}{204.2 \quad X \quad \text{----------}}$$

(B) For assay of dapsone

$$\%\text{age Purity} = \frac{\text{Volume of perchloric acid X IP factor X 100 X Normality of P.A}}{\text{Weigh of dapsone X normality of P.A}}$$

Result:- %age purity of dapsone was found to be ----------

Experiment-9

Assay Of Chlorpheniramine Maleate

Aim-: To perform the assay of Chlorpheniramine Maleate.

Reference: British Pharmacopoeia,. Her Majesty's Stationary Office, London (1). 1993; pp.126.

Chemicals:-

Perchloric acid – 8.5 ml

Acetic anhydride – 25 ml

Glacial Acetic Acid – 1000ml

Chlorpheniramine Maleate – 500mg

Crystal Violet – Few Drops

Glassware and apparatus:- weighing balance, glass rod, pipette, measuring cylinder, funnel, beaker, burette etc.

Principle :- Chlorpheniramine Maleate is first generation antihistamine used in the prevention of the symptoms of allergic conditions such as rhinitis and urticaria. Its side effects are relatively weak compared to other first – generation antihistamines. Chlorpheniramine Maleate is one of the most commonly used antihistamines in small- animal veterinary practice. Although not generally approved as an antidepressant or anti – anxiety medication, chlorpheniramine appears to have hese properties as well.

The assay of chlorpheniramine maleate is carried out by non aqueous titrimetry. Chlorpheniramine Maleate is chemically but-2-enedioic acid;3-(4-chlorophenyl)-N,N-dimethyl-3-pyridin-2-ylpropan-1-amine. They do not give sharp end point when titrated in aqueous medium. So it is analysed by non aqueous method.

Reaction

Preparation of 0.1M perchloric acid

1. Mix an accurately measured volume of perchloric acid (8.5 ml) with anhydrous glacial acetic acid (500ml)
2. Then add 25 ml of acetic anhydride.
3. Cool the mixture to room temperature and make up the volume to 1000ml using anhydrous glacial acetic acid.
4. Aloe the solution to stand for overnight.

Standardization of 0.1M perchloric acid

1. Accurately weigh about 0.1 g potassium hydrogen phthalate and dissolve it in 10 ml of glacial acetic acid.
2. Add few drops of crystal violet solution and titarate with 0.1 M perchloric acid until the color changes from violet to emerald green.
3. Perform the blank determination and make the necessary corrections.

Procedure for assay

1. Dissolve about 500mg of chlorpheniramine maleate accurately weighed in 20ml of glacial acetic acid.
2. Add 2 drops of crystal violet indicator.
3. Titrate the contents of the flask with 0.1 N perchloric acid.
4. Perform the blank determination and make any necessary corrections.

IP factor: each ml of 0.1 M perchloric acid is equivalent to 19.54mg of chlorpheniramine maleate.

Observation table (for standardization)

Sr. No.	**Volume in conical flask**	**Burette reading(ml)**		**Final Reading**
		Initial Reading	**Final Reading**	

Observation table (For Assay)

Sr. No.	Volume in conical flask	Burette reading(ml)		Final Reading
		Initial Reading	Final Reading	

Calculation

(B) For Standardization of perchloric acid

$$\text{Normality} = \frac{\text{weigh} \times 1000}{\text{Equivalent weigh of potassium hydrogen phthalate} \times \text{volume}}$$

$$\text{Normality} = \frac{0.1 \times 1000}{204.2 \times \text{----------}}$$

(B) For assay of chlorpheniramine maleate

$$\%\text{age Purity} = \frac{\text{Volume of perchloric acid} \times \text{IP factor} \times 100 \times \text{Normality of P.A}}{\text{Weigh of chlorpheniramine maleate} \times \text{normality of P.A}}$$

Result:- %age purity of chlorpheniramine maleate was found to be ----------

Experiment-10

Aim-: To perform the assay of metronidazole

Reference: M. E. Wol, John Wiley and Sons, "Text book of Burgers Medicinal Chemistry," fourth ed., New York, 1979. Page no. 222-22

Chemicals:-

2- phenylacetamide - 5mg

Penicillin G potassium RS - 5mg

Glassware and apparatus:- weighing balance, glass rod, pipette, measuring cylinder, funnel, beaker, burette etc.

Principle :- Metronidazole [2-methyl-5-nitroimidazole-1-ethanol] is white or creamy–white crystalline powder with a slight odor and a bitter slightly saline taste and it darkens on exposure to light. It is practically soluble as 1 g in 100 ml of water; 1 g in 200 ml of alcohol; 1 g in 250 ml of chloroform and slightly soluble in ether. Metronidazole is one of the azole group antimicrobial agents as shown in figure, which is effective against anaerobic (but not aerobic) microorganism. The infections are often polymicrobial that is the anaerobic bacteria are found in mixed infection with other anaerobes. The anaerobic bacteria include gram-positive, gram-negative, cocci and bacilli.

Nonaqueous titration of metronidazole tablets:

It includes following steps :
(i) Titrant used.
(ii) Preparation of 0.1 N Perchloric acid.
(iii) Standardization of 0.1 N Perchloric Acid.
(iv) Solvent/indicator used.
(v) assay of metronidazole.

(i) Titrant used :
Solution of $HClO_4$ in either glacial acetic acid or dioxane solution is used for

titration of weak bases. Generally $HClO_4$ with a normality of 0.1N to 0.05N is used.

(ii) Preparation of 0.1 N Perchloric acid ($HClO_4$):

Materials Required :
8.5 ml of perchloric acid (70.0 to 72.0%) ; 1 Litre of glacial acetic acid ; 30ml of acetic anhydride.

Procedure :
Gradually mixed 8.5 ml of perchloric acid to 900 ml of glacial acetic acid with vigorous and continuous stirring. After that added 30 ml acetic anhydride and make up the volume to 1 litre with glacial acetic acid and allow to stand for 24 hours before use.

The acetic anhydride reacts with the water (approx. 30%) in perchloric acid and some traces in glacial acetic acid thereby making the resulting mixture practically anhydrous.

H_2O	+	$(CH_3CO)_2O$	→	$2CH_3COOH$
Water		Acetic anhydride		Acetic acid

(iii) Standardization of 0.1 N Perchloric Acid :
Weighed accurately about 0.5 g of potassium hydrogen phthalate in a 100 ml conical flask. And added 25 ml of glacial acetic acid and attached a reflux condenser fitted with a silica-gel drying tube. Warmed until the salt gets dissolved completely. Cooled and titrated with 0.1 N perchloric acid where crystal violet (2 drops) is used as an indicator. (end point Blue to Blue-Green (0.5% w/v)

$2CH_3COOH$	+	$RCOO^-$	→	RCOOH	+	CH_3COOH
Acetic acid		Acetate ion		Formic acid		Acetic acid

$KHC_8H_4O_4$ +	$HClO_4$ →	$C_8H_6O_4$ +	$KClO_4$
Potassium biphthalate	Perchloric acid	Phthalic acid	Pot. chlorate

204.14 g $C_8H_5O_4K \equiv HClO_4 \equiv 1000$ ml
or, 0.02041 g $C_8H_5O_4K \equiv 1$ ml of 0.1 N $HClO_4$
Strength of 0.1N Perchloric acid
= (wt. of potassium hydrogen phthalate taken)/Vol. of Perchloric acid x 0.02042

(iv) Solvent/Indicator Used :

Solvent used :
Glacial acetic acid alone or sometimes in combination with some aprotic solvents is often used. The other solvents are $CHCl_3$, benzene, chloro benzene, acetic anhydride and various combinations of these sometime glycohydrocarbon mixtures are also used.

Indicators used:
Crystal violet 0.05% w/v in glacial acetic acid, methyl red 0.1% w/v in anhydrous methanol, oracet blue 0.5% w/v in glacial acetic acid.

(v) assay of metronidazole :
In general, the reaction-taking place between metronidazole and perchloric acid may be expressed as follows :

Hence,
17.12 mg or 0.01712 g of $C_6H_9N_3O_3 \equiv 1$ ml of 0.1 N $HClO_4$

Procedure:
Weighed accurately about 0.3 g of metronidazole sample into a 250 ml conical flask; added Glacial acetic acid (50 ml), warmed gently. Cooled and titrated with 0.1 N perchloric acid using α -Naphtol benzein as indicator.

Calculations:

The percentage of metronidazole present in the sample is given by:

Sr. No.	Volume in conical flask	Burette reading(ml)		Final Reading
		Initial Reading	Final Reading	

Application of metronizadole:

As it is an antibiotic it is used to treat bacterial infections of the vagina, stomach, skin, joints, and respiratory tract.

Experiment-11

Draw the chemical structure with program ChemDraw

Aim-: To draw the chemical structure with drawing program ChemDraw.

Reference: ChemDraw16.0 User Guide.

Procedure: Use ChemDraw to draw the structure of each of these molecules and ions, all on the same page. Label each structure. Print one copy of the entire page, after you have finished drawing everything. Make sure nothing appears on the page except these drawings. Be sure to type your name at the top right hand corner of the page.

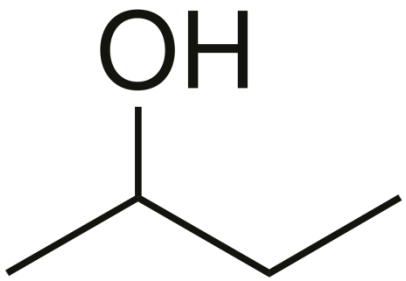
Structures to Draw:

- 2-butanol
- trans-3-bromocyclopentanol
- 1-(2,4,5-trimethylphenyl)ethanone
- Benzoic acid
  The benzoate ion (conjugate base of benzoic acid), showing all lone pairs of electrons on the oxygen atoms and the position of the formal negative charge cis-1-t-butyl-4-methylcyclohexane, showing it in its most stable conformation (you must show a chair conformation for the cyclohexane ring, with appropriate placement of the axial and equatorial positions for the attached groups)
- caffeine

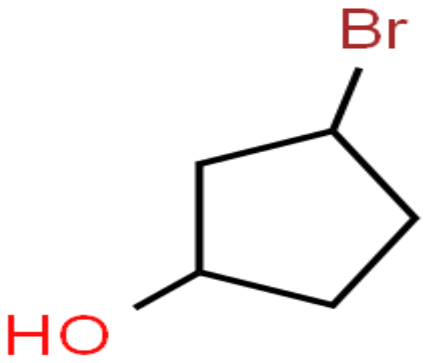
Notes for ChemDraw:

When start a compound, one must start with a bond, not a single atom. For example, you cannot start a structure by putting a text element, such as "C" (which represents carbon). If one want to have a molecule, such as bromochlorofluoromethane, you must first draw the bonds being attached to a single center atom (in this case it would be a carbon atom), and then label all the atoms afterward.

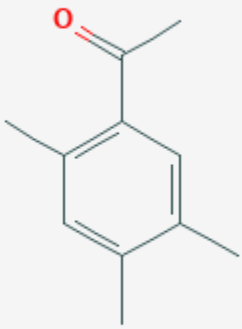
You must also be certain to connect all atoms using the connection tool (a little black square box will appear). If this connection tool does not appear, bonds or text will not be attached.



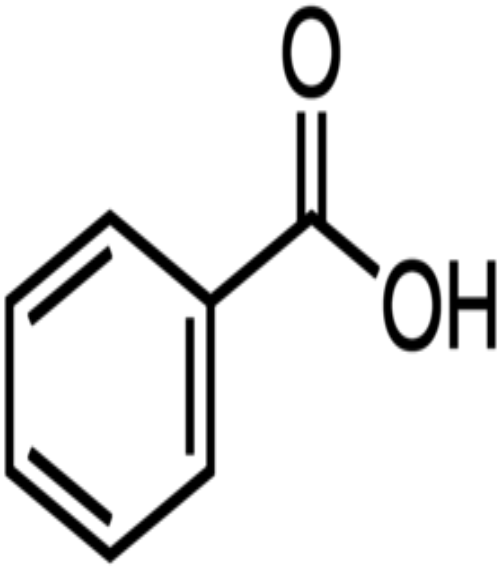
2-butanol



trans-3-bromocyclopentanol



1-(2,4,5-trimethylphenyl)ethanone



Benzoic acid