The Shirpur Education Society's
**H. R. Patel Institute of Pharmaceutical Education & Research, Shirpur**

# Practical Manual

## Pharmaceutical Organic Chemistry - I

## As per PCI Syllabus

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# Experiment No: 01

## Qualitative Analysis of Organic Compounds.

The analysis and identification of unknown organic compounds constitutes a very important aspect of experimental organic chemistry.

There is no definite set procedure that can be generally applied to organic qualitative analysis. Various books have different approaches, but a systematic approach based on the scheme given below will give good results.

**Students should, however, consult the laboratory manual and Textbook of Practical Organic Chemistry, A.I. Vogel (4th Edition).**

**Practical Notes**

Before outlining the general scheme, one or two points of practical importance should be noted.

(a) Quantities of substance for tests. For most tests about 0.1 g solid or 0.1 - 0.2 mL (2 - 3 drops) of liquid material (NOT MORE) should be used.

(b) Reagents likely to be met within organic analysis are on the reagent shelves. Students are advised to develop a general knowledge of the physical characteristics of common organic compounds. If in doubt about the expected result of a test between a certain compound and a reagent, carry out a trial test with a known compound and compare with the unknown.

(c) Quantities of substance derivatives. Students have wasted much time and material in the past by taking too large a quantity of substance for preparation of a derivative. In general, 0.5 - 1 g (or 0.5 - 1 mL) of substance gives the most satisfactory results.

If a practical book instructs one to use larger quantities (3 - 4 g or more), the quantities should be scaled down to 1 g or 1 mL of the unknown substance and corresponding quantities of reagents should be used.

**General Scheme of Analysis**

**A. Preliminary Tests**

(a) Note physical characteristics - solid, liquid, colour and odour.

(b) Perform an ignition test (heat small amount on metal spatula) to determine whether the compound is aliphatic or aromatic (i.e. luminous flame - aliphatic; sooty flame - aromatic).

**B. Physical Constants**

Determine the boiling point or melting point. Distillation is recommended in the case of liquids (see Appendix 3). It serves the dual purpose of determining the b.p., as well as purification of the liquid for subsequent tests.

**C. Analysis for elements present**

At C10 level, the elements present will be told to you, but read up the method.

**D. Solubility tests**

The solubility of the unknown in the following reagents provides very useful information. In general, about 3 mL of the solvent is used with 0.1 g or 0.2 mL (2 - 3 drops) of the substance. The class of compound may be indicated from the following table:

# SOLUBILITY TABLE

| REAGENT AND TEST | CLASS | GROUP OF COMPOUNDS |
|---|---|---|
| Soluble in cold or hot water. (If the unknown is soluble do NOT perform solubility tests below) | Neutral, acidic or basic. (Test with litmus or universal indicator paper) | Lower members of series. Neutral, e.g. alcohols; Acidic, e.g. acids, phenols; Basic, e.g. amines |
| Soluble in dil. HCl | Basic | Most amines (except III amines with only aromatic groups |
| Soluble in dil. NaOH | Acidic | Most acids, most phenols. |
| Soluble in $NaHCO_3$ | Strongly acidic | Most carboxylic acids. |
| Insoluble in water, acid and alkali | Neutral | Hydrocarbons, nitrohydro-carbons, alkyl or aryl halides, esters and ethers. Higher molecular weight alcohols, aldehydes and ketones |

**E. Group Classification Tests**

From the previous tests it is often possible to deduce the functional groups present in the unknown compound. Consult i.r. spectra when available.

Individual tests are then performed to identify and confirm the functional groups present.

# NOTE:

1. Students are strongly advised against carrying out unnecessary tests, since not only are they a waste of time but also increase the possibility of error. Thus it is pointless to first test for alcohol or ketone in a basic compound containing nitrogen! Instead tests for amines, etc. should be done on such a compound.

2. A systematic approach cannot be overemphasised in group classification tests to avoid confusion and error.

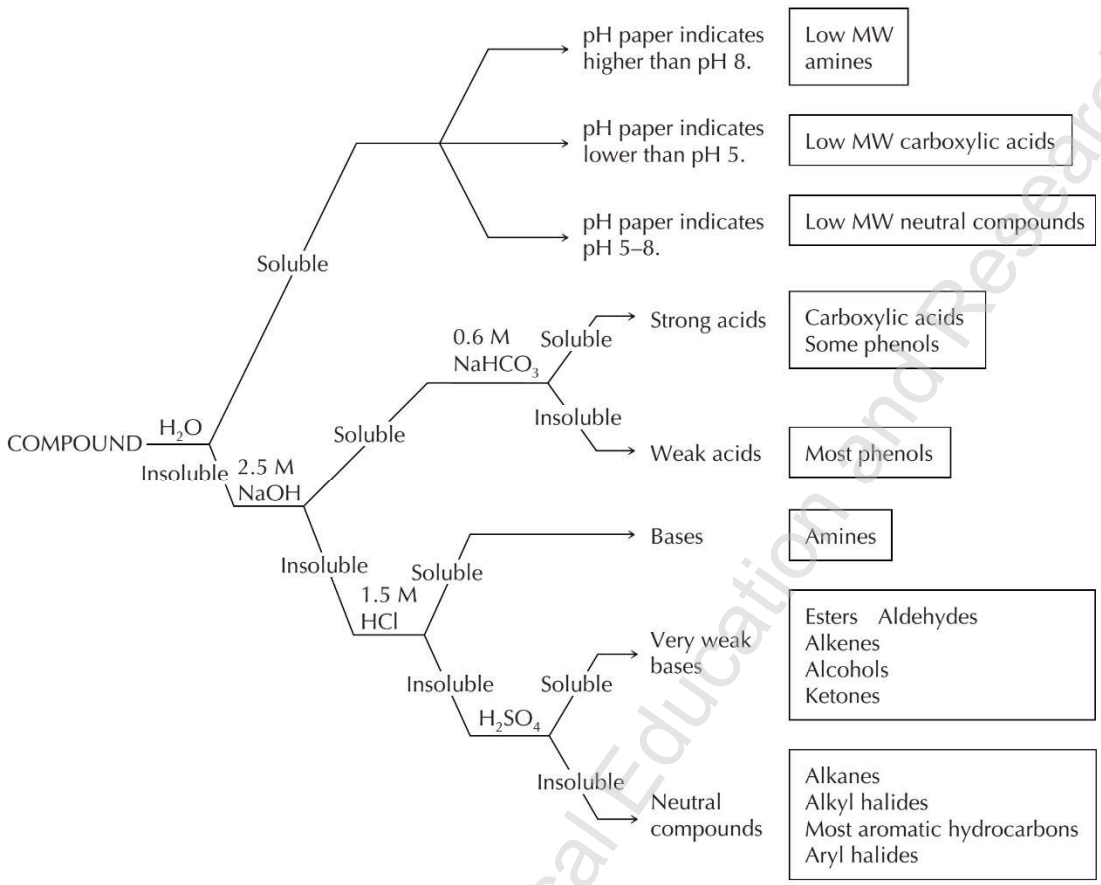



**Figure: Solubility flow chart**

## F. Consultation of Literature

Once the functional group has been identified, reference is made to tables in a book on organic analysis, for assessing possibilities and for the preparation of suitable solid derivatives.

It should be noted that whilst two substances with the same functional group may sometimes have very similar b.p. or m.p., solid derivatives can usually be chosen from the literature, with m.p. differences of about 10 (or more), which distinguish between the two possibilities.

**Example:**

| COMPOUND | B.P. | DERIVATIVES (M.P.) | |
|---|---|---|---|
| | | 2,4-DNPH | SEMICARBAZONE |
| Diethyl ketone | 102 | 156 | 139 |
| Methyl n-propyl ketone | 102 | 144 | 112 |

**G. Preparation of derivatives**

The final characterisation of the unknown is made by the preparation of suitable solid derivatives. The derivative should be carefully selected and its m.p. should preferably be between 90 - 150 for ease of crystallisation and m.p. determination.

Preparation of one derivative should be attempted. The derivative should be purified by recrystallisation, dried and the m.p. determined. Derivatives should be submitted correctly labelled for assessment together with the record.

Recording of Results

The results should be recorded in a systematic manner. Results should be recorded in the practical book at the time (not written up afterwards).

A record should be made of every test carried out, no matter whether a **NEGATIVE RESULT HAS BEEN OBTAINED**.

Test, observation and inference should be given.

At the conclusion of the analysis a brief summary of results should be included, giving the name, b.p. or m.p., and formula of the analysed compound.

Qualitative Analysis for Elements (for reference only)

In organic compounds the elements commonly occurring along with carbon and hydrogen, are oxygen, nitrogen, sulphur, chlorine, bromine and iodine. The detection of these elements depends upon converting them to water-soluble ionic compounds and the application of specific tests.

Lassaigne's Sodium Fusion Test

C, H, O, N, S, X → NaX

NaCN

$Na_2S$

NaCNS

**PROCEDURE**

Place a piece of clean sodium metal, about the size of a pea into a fusion tube. Add a little of the compound (50 mg or 2 - 3 drops).* Heat the tube gently at first, allowing any distillate formed to drop back onto the molten sodium. When charring begins, heat the bottom of the tube to dull redness for about three minutes

and finally plunge the tube, while still hot, into a clean dish containing cold distilled water (6 mL) and cover immediately with a clean wire gauze.**

*For liquids it is better to first melt the sodium add the liquid drop by drop.

**CAUTION: The tube shatters, and any residual sodium metal reacts with water. Stir the mixture, boil for 1 - 2 minutes, on a tripod and filter hot through a fluted paper.

The 'fusion' filtrate which should be clear and colourless, is used for the SPECIFIC

**TESTS DESCRIBED BELOW:**

1. To a portion (2 mL) of the 'fusion' filtrate add 0.2 g of powdered ferrous sulphate crystals. Boil the mixture for a half a minute, cool and acidify by adding dilute sulphuric acid dropwise. Formation of a bluish-green precipitate (Prussian blue) or a blue solution indicates that the original substance contains nitrogen. If no precipitate appears, allow to stand for 15 minutes, filter and inspect filter paper.

**2.SULPHUR(SULPHIDE)**

To the cold 'fusion' filtrate (1 mL) add a few drops of cold, freshly prepared, dilute solution of sodium nitroprusside. The latter may be prepared by adding a small crystal of the solid to 2 mL of water. Production of a rich purple colour indicates that the original substance contains sulphur. This test is very sensitive. Only strong positive results are significant.

**3.HALOGENS(HALIDES)**

Acidify a portion (1 mL) of the 'fusion' filtrate with 2N nitric acid, and if nitrogen and/or sulphur are present, boil for 1 - 2 minutes.* Cool and add aqueous silver nitrate (1 mL), compare with a blank. Formation of a heavy, white or yellow precipitate of silver halide indicates halogen. If a positive result is obtained: acidify the remaining portion of the 'fusion' filtrate with dilute sulphuric acid, boil and cool. Add carbon tetrachloride (1 mL) and a few drops of freshly prepared chlorine water.

Shake the mixture.

(a) If the carbon tetrachloride layer remains colourless - indicates chlorine.

(b) If the carbon tetrachloride layer is brown - indicates bromine.

(c) If the carbon tetrachloride layer is violet - indicates iodine.

*If nitrogen and/or sulphur are also present, the addition of silver nitrate to the acidified 'fusion' solution will precipitate silver cyanide and/or silver sulphide in addition to the silver halides. The removal of hydrogen cyanide and/or hydrogen sulphide is effected by boiling the 'fusion' solution. GROUP CLASSIFICATION **TESTS**

Some functional group tests are listed below. Students should refer to a practical text book for details, and further information, e.g. Vogel.

**Tests for unsaturation**

1. Cold dilute potassium permanganate solution.

2. Solution of bromine in carbon tetrachloride.

**Tests for compounds containing nitrogen**

**1. Amines**

(a) Nitrous acid.

(b) Confirmatory tests.

**2. Compounds which give amines or ammonia on acid or alkaline hydrolysis:**

Amides, substituted amides, anilides, nitriles.

**3. Compounds which give amines on reduction:**

Nitro, nitroso, azo, hydrazo, nitriles.

Tests for compounds containing C, H and possibly oxygen

1. **Carboxylic acids**

Na2CO3 or NaHCO3 solution liberate carbon dioxide.

2. **Phenols**

(a) Sodium hydroxide solution (soluble). Insoluble in and no CO2 from NaHCO3 (except when electron attracting groups present, e.g. 2,4-dinitrophenol).

(b) Ferric chloride solution.

(c) Bromine water.

**3. Aldehydes and Ketones**

(a) 2,4-dinitrophenylhydrazine (as Brady's reagent) for C=O.

(b) Iodoform test for CH3CO-.

**4. Aldehydes only (reducing properties)**

(a) Fehling's solution.

(b) Tollen's reagent (ammoniacal AgNO3 solution).

(c) Jones reagent.

**5. Alcohols**

(a) Lucas' reagent to distinguish I, II and III alcohols.

(b) Jones reagent.

(c) Metallic sodium (use dry liquid and dry tube).

**6. Sugars**

(a) Molisch's test.

**7. Esters**

(a) Hydroxamic acid test.

(b) Hydrolysis.

Write up of the identification of an unknown organic compound

Date.....

Compound containing C, H (N, Hal, S)

Physical characteristics ..... (solid, liquid, gas, colour, odour, etc.)

Ignition test..... (aromatic or aliphatic)

Physical constant ..... (boiling point or melting point)

Solubility tests (in tabular form)

Group classification tests (in tabular form)

| Test | Observation | Inference |
|---|---|---|

From the above tests and observations the given compound is probably a .....(acid, phenol, aldehyde, etc.)

Consultation of literature (Possibilities) M.P. of derivative

(a)

(b)

(c)

Preparation of derivative (method of preparation)

Observed m.p. of derivative

Lit. m.p. of derivative

Result

Compound No. ..... is ..... (give formula)

# TESTS FOR FUNCTIONAL GROUPS

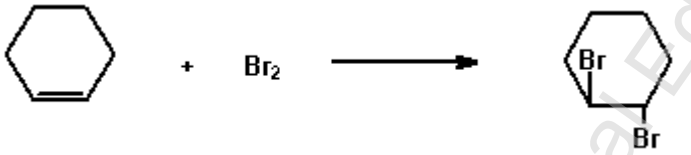
## I. UNSATURATED COMPOUNDS

Two common types of unsaturated compounds are alkenes and alkynes characterised by the carbon-carbon double and triple bond, respectively, as the functional group. The two common qualitative tests for unsaturation are the reactions of the compounds with (a) bromine in carbon tetrachloride and (b) potassium permanganate.

**(a) 2% Bromine in carbon tetrachloride**

Dissolve 0.2 g (or 0.2 mL) of the compound in 2 mL of carbon tetrachloride or another suitable solvent and add the solution dropwise to 2 ml of 2% bromine solution in carbon tetrachloride and shake.

e.g.

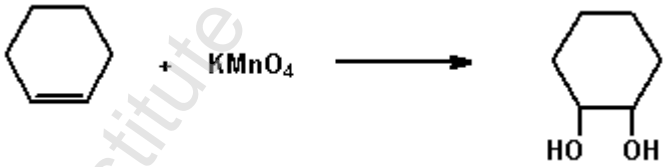



Rapid disappearance of the bromine colour to give a colourless solution is a positive test for unsaturation.

**NOTE: The reagent is potentially dangerous. Keep it off your skin and clothes; protect your eyes and nose.** (b) 2% Aqueous potassium permanganate

Dissolve 0.2 g (or 0.2 mL) of the substance in 2 mL of water (acetone may also be used as solvent). Add the potassium permanganate solution dropwise and observe the result.

e.g.




For a blank determination, count the number of drops added to 2 mL of acetone before the colour persists. A significant difference in the number of drops required in the two cases is a positive test for unsaturation.

## II. COMPOUNDS CONTAINING NITROGEN

1. Amines

(a) Reaction with nitrous acid Dissolve the amine (0.5 mL) in concentrated acid (2.0 mL) and water (3 mL) and cool the solution to 0 - 5 in an ice-bath for 5 minutes. Add a cold solution (ice-bath) of sodium nitrite (0.5 g) in water (2.0 mL) from a dropper, with swirling of the test tube, still keeping the mixture in the ice-bath.

**AMINE REACTION**

**I aliphatic N2 evolved.**

**RNH2 + HNO2 -> ROH + N2 + H2O**

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**I aromatic Diazonium salt is formed.**

**ArNH2 + HNO2 -> ArN=N+**

**Add the cold diazonium solution and with swirling to a cold solution of 2-naphthol (0.2 g) in 5% NaOH solution (2 mL). An orange-red azo dye is formed.**

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**II aliphatic and Yellow oily nitrosamines are generally formed.**

**II aromatic R2NH + HNO2 -> R2N-NO**

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**III aliphatic No visible reaction.**

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**III aromatic Dialkylanilines yield green solid p-nitroso compounds (if p-position unsubstituted).**

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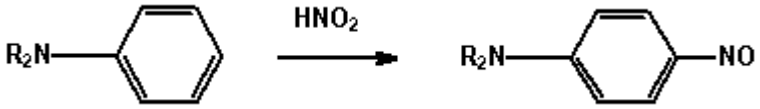


(b) Reaction with benzenesulphonyl chloride

Benzenesulphonyl chloride reacts with primary and secondary but not with tertiary amines to yield substituted sulphonamides.

```
e.g.  (a)  C6H5SO2Cl + H-NHR + NaOH   ->  C6H5SO2NHR + NaCl + H2O
      (b)  C6H5SO2Cl + H-NR2  + NaOH  ->  C6H5SO2NR2  + NaCl + H2O
```

The substituted sulphonamide formed from a primary amine dissolves in the alkali medium whilst that produced from a secondary amine is insoluble in alkali.

Place 0.5 mL (or 0.5 g) of the compound, 15 - 10 mL of 5% NaOH and 1 mL of benzenesulphonyl chloride in a test tube, stopper the tube and shake until the odour of the sulphonyl chloride has disappeared. The solution must be kept alkaline (if no reaction has occurred, the substance is probably a tertiary amine).

If a precipitate appears in the alkaline solution, dilute with about 10 mL of water and shake; if the precipitate does not dissolve, a secondary amine is indicated.

If there is no precipitate, acidify it cautiously to congo red with concentrated hydrochloric acid (added dropwise): a precipitate is indicative of a primary amine.

2. Amides R-CO-NH2

Simple primary amides can be decomposed by boiling with alkali and thereby evolving ammonia.

```
e.g.  CH3-CO-NH2  + NaOH -> CH3-CO2- Na+ + NH3
```

Boil 0.5 g of the compound with 5 mL of 10% sodium hydroxide solution and observe whether ammonia is evolved.

## III. COMPOUNDS CONTAINING C, H AND POSSIBLY OXYGEN

1. Carboxylic acids - test with 5% aq. NaHCO3

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R-CO2H + NaHCO3   ->  R-CO2- Na+ + CO2   + H2O
```

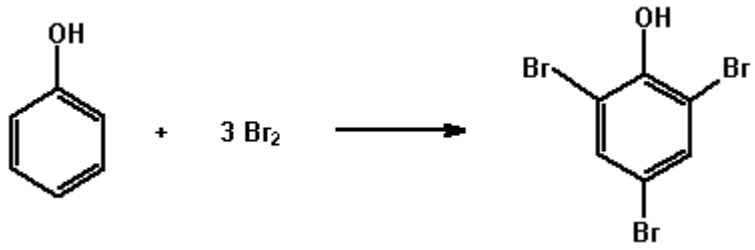
Sodium hydrogen carbonate reacts with carboxylic acids to give the sodium salt of the acid and liberates carbon dioxide. If the acid is insoluble in water and the reaction is sluggish dissolve the acid in methanol and add carefully to a saturated

sodium hydrogen carbonate solution, when a vigorous effervescence will be observed.

2. Phenols [Soluble in NaOH and produce no CO2 from NaHCO3]

(a) Bromine water

Phenols are generally highly reactive towards electrophilic reagents and are readily brominated by bromine water. e.g.




Dissolve or suspend about 0.05 g of the compound in 2 mL of dilute hydrochloric acid and add bromine water dropwise until the bromine colour remains. A white precipitate of the bromophenol may form. Solid bromophenol derivatives can be used for the confirmation of the structure of a phenol (of the preparation of derivatives).

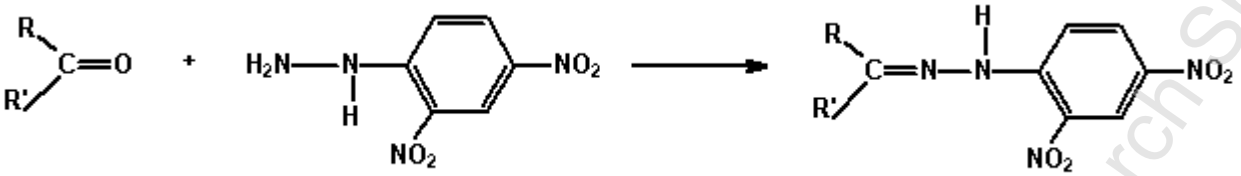
(b) Ferric chloride test

Most phenols react with iron (III) chloride to form coloured complexes. The colours vary - red, purple, blue or green - depending on various factors, e.g. the phenolic compound used, the solvent, concentration. Since some phenols do not give colours, a negative test must not be taken as significant without supporting information.

Dissolve 0.05 g of the compound in 2 mL water (or a mixture of water and ethanol if the compound is not water-soluble) and add an aqueous solution of ferric chloride dropwise. Observe any colour changes which may occur.

3. Aldehydes and ketones

(a) 2,4-Dinitrophenylhydrazine (as Brady's reagent) A test for the carbonyl group (C=O) in aldehydes and ketones. 2,4-Dinitrophenylhydrazine gives sparingly soluble yellow or red 2,4-dinitrophenylhydrazones with aldehydes and ketones.



R, R' = hydrogen or alkyl

Add 3 mL of the reagent to 2 drops of the compound in a test tube and shake. If no precipitate forms immediately, warm and allow to stand for 5 - 10 minutes. A crystalline precipitate indicates the presence of a carbonyl compound.

The bench reagent is very dilute and is intended for qualitative tests only and should not be used in the preparation of a derivative for identification purposes. (b) Iodoform test for CH3CO-

Dissolve 0.1 g (or 5 drops) of the compound in 2 mL of water; if it is insoluble in water add sufficient dioxan to produce a homogeneous solution. Add 2 mL of 5% NaOH solution and then introduce the potassium iodide - iodine reagent dropwise with shaking until a definite dark colour of iodine persists. Allow to stand for 2 - 3 minutes; if no iodoform separates at room temperature, warm the test tube in a beaker of water at 60 . Add a few more drops of the iodine reagent if the faint iodine colour disappears. Continue the addition of the reagent until a dark colour is not discharged after 2 minutes heating at 60. Remove the excess of iodine by the addition of a few drops of dilute sodium hydroxide solution with shaking, dilute with an equal volume of water, and allow to stand for 10 minutes. The test is positive if a yellow precipitate of iodoform is deposited. Filter off the yellow precipitate, dry upon pads of filter paper and determine the m.p. Iodoform melts at 120 (it can be recrystallised from methanol- water).

The reaction is given by acetaldehyde and simple methyl ketones. Alcohols containing the CH3CHROH group will be oxidised under the reaction conditions and also give a positive test.

4. Aldehydes only (reducing properties).

(a) Fehling's solution

Aldehydes reduce Fehling's solution to yellow or red copper (I) oxide.

Preparation of the reagent: Mix equal volumes of Fehling's solution solution I (aqueous alkaline potassium tartrate) and Fehling's solution II (copper sulphate solution).

Add 2 drops (or 0.05 g) of the compound and 2 - 3 drops of the reagent and heat on a boiling water bath for 3 - 4 minutes.

The test is positive for aliphatic aldehydes, but is often indecisive for aromatic aldehydes where Jones' Reagent is often useful (see 5).

(b) Tollen's reagent (Ammonical silver nitrate solution)

Aldehydes are readily oxidised to carboxylic acids and will reduce Tollen's reagent to produce a silver mirror on the inside of a clean test tube.

FIRST clean up a test tube with a little hot nitric acid (fume cupboard) and rinse with distilled water.

Preparation of the reagent: To 1 mL of silver nitrate solution add a few drops of sodium hydroxide. Then add dilute ammonium hydroxide dropwise until the precipitate just dissolves.

Add 2 - 3 drops of the compound in methanol to 2 - 3 mL of Tollen's solution contained in a very clean test tube. If no reaction takes place in the cold, warm gently in a water bath.

**CAUTION:** After the test, pour the contents of the test tube into the sink and wash the test tube with dilute nitric acid. Any silver fulminate present, which is highly explosive when dry, will be destroyed.

(c) Jones Reagent (See section under alcohols).

5. Alcohols

The tests for the hydroxyl group not only detect the presence of the group, but may also indicate whether it is primary, secondary or tertiary.

(a) Jones Reagent ($CrO_3$-$H_2SO_4$ in $H_2O$)

This reagent distinguishes primary and secondary alcohols from tertiary alcohols; the test is based on the much greater resistance to oxidation of tertiary alcohols compared to the other two types. Aldehydes also give a positive test.

Place 1 mL of acetone in a test tube and dissolve one drop of a liquid or ca 10 mg of a solid alcohol or aldehyde in it. Add one drop of the reagent to the acetone solution and shake the tube to mix the contents. Primary and secondary alcohols react within two seconds as indicated by the disappearance of the orange colour of the reagent and the formation of a green or blue-green precipitate or emulsion. Tertiary alcohols do not react even after 3 minutes.

```
(I)   RCH2OH  ->  RCHO  ->  RCO2H

(II)    R2CHOH  ->  R2C=O

(III)   R3COH  ->  no visible reaction.
```

(b) Lucas' Reagent [$ZnCl_2$ - conc. HCl]

This reagent converts alcohols into the corresponding alkyl chlorides. Zinc chloride (a Lewis acid) increases the reactivity of alcohols towards acid. The test depends on the rate of reaction of primary, secondary, and tertiary alcohols with the reagent at room temperature.

```
(I)   RCH2OH  ->  no reaction at room temperature.

(II)    R2CHOH  ->  R2CHCl  +  H2O  (1 hour or maybe longer)

(III)   R3COH   ->  R3CCl + H2O (immediately)
```

To 1 mL of the alcohol in a small test tube add 6 mL of Lucas' reagent at room temperature. Close the tube with a cork, shake and allow to stand.

(i) Primary alcohols - the aqueous phase remains clear (except allyl alcohol - droplets after 7 minutes).

(ii) Secondary alcohols - very slow reaction (~ 1 hour or maybe longer) when droplets of alkyl chloride may be seen.

(iii) Tertiary alcohols - very fast reaction and droplets of the alkyl chloride formed almost immediately.

6. Sugars, Carbohydrates

Molisch's Test

This is a general test for carbohydrates. Dissolve 20 - 30 mg of the compound in 2

mL water and add 0.5 mL of the reagent (a 20% solution of 2-naphthol in ethanol). Pour 2 mL of concentrated sulphuric acid from a dropper carefully down the side of the tube so that the acid forms a layer beneath the aqueous solution without mixing with it. A red colouration, changing to dark purple forms at the interface. Carry out a second test on a blank solution.

7. Esters

Hydroxamic acid test

```
R-CO-OR'  + H2N-OH  ->  R-CO-NH-OH + R'-OH
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Esters react with hydroxylamine in the presence of sodium hydroxide to form the sodium salt of the corresponding hydroxamic acid. On acidification and addition of ferric chloride the magenta-coloured iron (III) complex of the hydroxamic acid is formed.

It is always advisable to ensure that an unknown compound does not give a colour with iron (III) chloride before carrying out the hydroxamic acid test.

Procedure for hydroxamic acid test

(a) Ferric chloride test

Dissolve a drop or a few small crystals of the compound in 1 mL of 95% ethanol (rectified spirit) and add 1 mL of M hydrochloric acid. Note the colour produced when 1 drop of 5% iron (III) chloride is added to the solution. If a pronounced violet, blue, red or orange colour is produced, the hydroxamic acid test described below is NOT APPLICABLE.

(b) Hydroxamic acid test

Mix 1 drop or several small crystals (ca 0.05 g) of the compound with 1 mL of 0.5 M hydroxylamine hydrochloride in 95% ethanol and add 0.2 mL of 6 M aqueous sodium hydroxide. Heat the mixture to boiling and after the solution has cooled slightly add 2 mL of M hydrochloric acid. If the solution is cloudy, add 2 mL of 95% ethanol. Observe the colour produced when 1 drop of 5% iron (III) chloride solution is added. If the resulting colour does not persist, continue to add the reagent dropwise until the observed colour pervades the entire solution. Usually

only 1 drop of the iron (III) chloride solution is necessary. Compare the colour with that produced in test (a). A positive test will be a distinct burgundy or magenta colour as compared with the yellow colour observed when the original compound is tested with iron (III) chloride solution in the presence of acid. It is often advisable to conduct in parallel the test with, say, ethyl acetate, to ensure that the conditions for this test are correct.

# THE PREPARATION OF DERIVATIVES OF ORGANIC COMPOUNDS

The preliminary examination and group classification tests indicate the particular class (functional group) to which an unknown organic compound may belong. Further characterisation and identification depends on the selection and preparation of a suitable solid derivative and accurate determination of its melting point (best, between 90 - 150 ).

The following table lists some of the classes of organic compounds and a selection of derivatives that may be prepared to characterise them. Check with the tables of melting points in Vogel which derivatives are most suitable for the characterisation of your particular compound.

| CLASS OF COMPOUND | DERIVATIVES |
|---|---|
| 1. ALCOHOLS | 3,5-dinitrobenzoate |
| 2. PHENOLS | benzoate, acetate, bromo-derivative |
| 3. ALDEHYDES AND KETONES | semicarbazone, 2,4-dinitrophenyl-hydrazone, oxime |
| 4. ACIDS | Anilide, amide, p-toluidide. |
| 5. AMINES | benzoyl, acetyl and sulphonamide derivatives |

## METHODS FOR THE PREPARATION OF DERIVATIVES

### ALCOHOLS

(i) 3,5-Dinitrobenzoates

3,5-Dinitrobenzoyl chloride is usually partially hydrolysed and should be prepared in the pure state by heating gently a mixture of 3,5-dinitrobenzoic acid (1 g) and phosphorus pentachloride (1.5 g) in a dry test tube, until it liquifies (5 min).* The liquid is poured on a dry watch glass and allowed to solidify. The phosphoryl chlorides are removed by pressing the solid with a spatula on a wad of filter paper.

The residual acid chloride is suitable for immediate use in the preparation of the derivatives.

*Work under fume hood. Fumes are irritating to the eyes and nose.

The 3,5-dinitrobenzoyl chloride is mixed with the alcohol (0.5 - 1 mL) in a loosely corked dry test tube and heated on a steam bath for about 10 min. Secondary and tertiary alcohols require up to 30 min. On cooling add 10 mL sodium hydrogen carbonate solution, stir until the ester crystallises out, and filter at the pump. Wash with a little carbonate solution, water and suck dry. Recrystallise from the minimum hot ethanol or light petroleum. Cool slowly to avoid the formation of oily droplets of your ester.

**PHENOLS**

(i) Benzoates (Schötten-Baumann method).

To the phenol (0.5 g) is added 5% sodium hydroxide (10 mL) in a well-corked boiling tube or a small conical flask. Benzoyl chloride (2 mL) is added in small quantities at a time, and the mixture shaken vigorously with occasional cooling under the tap or in ice-water. After 15 min the solid benzoate separates out: the solution should be alkaline at the end of the reaction; if not alkaline, or if the product is oily, add a solid pellet of sodium hydroxide and shake again. Collect the benzoate, wash thoroughly with cold water, and recrystallise from alcohol or light petroleum.

(ii) Acetates

Acetates of many simple phenols are liquids; however, this is a suitable derivative for polyhydric and substituted phenols. The phenol (0.5 g) is dissolved in 10% sodium hydroxide solution and an equal quantity of crushed ice is added, followed by acetic anhydride (2 mL). The mixture is vigorously shaken in a stoppered test tube until the acetate separates. The product is filtered and recrystallised from alcohol.

(iii) Bromo derivatives

The phenol (0.3 g) is suspended in dilute hydrochloric (10 mL) and bromine water

added dropwise until no more decolourisation occurs. The bromo derivative which precipitates out is filtered off and recrystallised from alcohol.

**ALDEHYDES AND KETONES**

(i) Semicarbazones

Dissolve semicarbazide hydrochloride (1 g) and sodium acetate (1.5 g) in water (8 - 10 mL), add the aldehyde or ketone (0.3 mL) and shake. Shake the mixture for a few minutes and then cool in ice-water. Filter off the crystals, wash with a little cold water and recrystallise from methanol or ethanol.

(ii) 2,4-Dinitrophenylhydrazones

Suspend 0.25 g of 2,4-dinitrophenylhydrazine in 5 mL of methanol and add 0.5 mL of concentrated sulphuric acid cautiously. Filter the warm solution and add a solution of 0.2 g of the carbonyl compound in 1 mL of methanol. Recrystallise the derivative from methanol, ethanol or ethyl acetate.

(iii) Oximes

Hydroxylamine hydrochloride (0.5 g) is dissolved in water (2 mL). 10% sodium hydroxide (2 mL) and the carbonyl compound (0.2 - 0.3 g) dissolved in alcohol (1 - 2 mL) are added, the mixture warmed on a steam bath for 10 min and then cooled in ice. Crystallisation is induced by scratching the sides of the test tube with a glass rod. The oximes may be crystallised from alcohol.

**ACIDS**

(i) Amides, anilides and p-toluidides

The acid (0.5 g) is refluxed with thionyl chloride (2 - 3 mL) in a fume cupboard for about 30 mins.* It is advisable to place a plug of cotton wool in the top of the reflux condenser to exclude moisture. The condenser is removed and the excess of thionyl chloride is distilled off (b.p. 78). The acid chloride thus produced is treated with concentrated ammonia solution (5 mL) or aniline (0.5 - 1 mL) or p-toluidine (0.5 - 1 g), when the solid derivative separates out. It is collected and recrystallised from alcohol adding decolourising charcoal if found necessary.

*Alternately use $PCl_5$ to form the acid chloride.

**AMINES**

(i) Acetyl derivatives (acetamides)

Reflux gently in a small dry flask under a dry condenser the amine (1 g) with acetic anhydride (3 mL) for 15 min. Cool the reaction mixture and pour into 20 mL cold water. Boil to decompose the excess acetic anhydride. Cool and filter by suction the insoluble derivative. Recrystallise from ethanol.

(ii) Benzoyl derivatives (benzamides)

Suspend 1 g of the amine in 20 mL of 5% aqueous sodium hydroxide in a well-corked flask, and add 2 mL benzoyl chloride (fume hood!), about 0.5 mL at a time, with constant shaking. Shake vigorously for 5 - 10 min until the odour of the benzoyl chloride has disappeared. Ensure that the mixture remains alkaline. Filter off the solid derivative, wash with a little cold water and recrystallise from ethanol.

(iii) Benzenesulphonamides

To 1 g of the amine in 20 mL of 5% sodium hydroxide solution in a well-corked flask add 1 mL benzenesulphonyl chloride (fume hood!). Shake the mixture until the odour of the sulphonyl chloride disappears. Check that the solution is alkaline. Acidify if necessary to obtain the precipitated derivative. Concentrated hydrochloric acid added dropwise should be used. Filter the product, wash with a little cold water and suck dry. Recrystallise from ethanol.

# Experiment No: 02

**Aim:** To synthesize p-nitroaniline from p-nitroacetanilide.

**Reference:** Comprehensive practical organic chemistry, Preparation and Qualitative Analysis, V. K. Ahluwalia, RenuAggarwal, First edition, published in India, University press,2000, pg. no. 221-222

**Principle:** The process cannot obtain direct by nitration of aniline. It is necessary to protect the amine group by acetylation. Nitrogen of acetanilide leads to p-nitroacetanilide (major product) which on hydrolysis gives p-nitroaniline.

**Procedure:**A mixture of 5gm of p-nitroacetanilide (0.028 mole) and sulphuric acid (70 %, 30 mlconc. $H_2SO_4$) (obtained by cautiously addingto 20 ml of conc. $H_2SO_4$to 30 ml of distilled water) is refluxed for 25 – 30 minutes or till a test solution remains clear on dilution with water. The solution is poured into cold water (200 ml) and the solution rendered alkaline by adding excess sodium hydroxide solution (10 %).

The separated p-nitroaniline is filtered, washed with water and crystallised from dilute alcohol (1:1). The yeild is 3.5 gm (92 %); melting point is 147 – 148°C.

**Result:**

Theoretical yield =

Practical yield =

% yield =

Melting point =

# Experiment No: 03

**Aim:** To synthesize phenol benzoate from phenol.

**Reference:** Systematic lab experiment in organic chemistry, Arunsethi, NEW AGE International Pvt. Ltd., 2003, pg. no. 619.

**Requirement:**

**Apparatus:** Reflux condenser, round bottom flask, funnel, beaker

**Chemical:** Phenol

**Procedure:** In 100 ml conical flask, dissolve 2.5 gmof phenol in 35 ml of 10 % sodium hydroxide and then add 5 ml of benzoyl chloride to it. Cork the flask properly and shake mixture vigorously for 20 minutes by which time the pungent smell of benzoyl chloride get abated and solid product is obtained.

Filter off phenyl benzoate at pump, wash with water and then recrystallize from rectified spirit. Phenyl benzoate as colourless needles, melting point 68-69 °C (3 – 3.5 gm).

# Experiment No: 04

**Aim:** To perform synthesis of benzanilide (acetanilide) from aniline.

**Reference:** Systematic lab experiments in organic chemistry, ArunSethi, New Age International Pvt. Ltd., 2003, pg. no. 611.

**Procedure:** In 100 ml round bottom flask fitted with reflux condenser place 5 ml of aniline and 10 ml of 1:1 acetic acid and acetic anhydride mixture (5 ml acetic acid and 5 ml acetic anhydride). Heat mixture gently under reflux for 15-20 min on oil bath and then pour the contents while still hot with stirring into a 200 ml beaker containing 100 ml ice cold water. Stir the mixture vigorously to hydrolyse the excess of acetic anhydride. After all the acetanilide has been precipitated,collect it on the buchner funnel and wash with cold water. Recrystallize the crude product from boiling water. If the product is excessively coloured add a pinch of animal charcoal to hot water and filter hot through the glass wool/cotton plug. Pure colourlesscrystal of acetanilide melt at 110° C (5 – 5.5 gm).

# Experiment No: 05

To perform synthesis of 9,10anthroquinone from anthracene.

Reference: Systematic lab experiments in organic chemistry, ArunSethi, New Age International Pvt. Ltd., pg. no. 642.

Procedure: In a 1000 ml round bottom flask fitted with reflux condenser place 2.5 gm of anthracene and 13 ml of glacial acetic acid. Heat the flask on wire gauze so that most of the anthracene dissolves. In the meantime prepare chromium trioxide solution by dissolving 5 gm of chromium trioxide in 5 ml water and 13 ml glacial acetic acid. Remove the flask from the heat source and then add this freshly prepared chromium trioxide solution in portions such that the mixture continues to reflux. As the oxidation proceeds the anthracene will completely dissolve in the boiling acetic acid during the addition of chromium trioxide solution. After the addition is complete reflux the reaction mixture for another 15 minutes. Cool and pour the contents with stirring in a 200 ml beaker containing 100 ml of ice cold water. Collect the precipitated anthraquinone on buchnerfunnel, wash it first with hot water then with dilute sodium hydroxide and finally with cold water. Recrystallize the crude product with hot glacial acetic acid and obtain yellow crystals of anthraquinone, m.p. 273° C (yield 2 – 2.5 gm).

Note:

i) Anthraquinone can also be purified by the process of sublimation.
ii) Similarly 1,4napthoquinone can be prepared by using 6.4 gm of naphthalene, 12 gm chromium trioxide and 15 ml glacial acetic acid.

# Experiment No: 06

Aim: To perform synthesis of p-bromo acetanilide from acetanilide.

Reference: Systematic lab experiments in organic chemistry, ArunSethi, New Age International Pvt., Ltd., 2003, pg. no. 686-687.

Procedure: In a 100 ml conical flask dissolve 5 gm of acetanilide in 17 ml glacial acetic acid and then cool the flask by keeping it in an ice bath. Add slowly and with stirring 12.1 ml of bromine solution (2.1 ml bromine in 10 ml glacial acetic acid). After the addition is complete remove the flask from the ice bath and keep it at room temperature for 30 minutes. Shake the flask occasionally during this period. Pour the reddish orange coloured solution with stirring in a 200 ml beaker containing 50 gm of crushed ice. Filter off the precipitated solid with suction on buchner funnel and wash with cold water. Recrystallize from ethanol and collect crystals of p-bromo acetanilide, m.p. 166 – 167 °C (Yield 4.5 – 5.0 gm).

# Experiment No: 07

Aim: To perform synthesis of 2,4,6 – tribromo phenol from phenol.

Reference: Systematic lab experiments in organic chemistry, ArunSethi, New Age International Pvt., Ltd., 2003, pg. no. 687.

Procedure: In 250 ml conical flask dissolve 4 gm of phenol in 30 ml of glacial acetic acid. Add dropwise with stirring a solution of 12 ml of bromine in 30 ml glacial acetic acid. After the addition is complete continue the stirring process for another 10 minutes and then keep the mixture at room temperature for 20 minutes. Cool the flask in ice bath and add 100 ml of ice water to it. Collect the precipitate by suction on buchnerfunnel and wash with cold water. Recrystallize the tribromo derivative from ethanol, mp 93 – 95 °C.

# Experiment No: 08

Aim: To study geometrical isomerism using sterisomers.

Reference: Bhupinder Mehta, Manju Mehta, Organic Chemistry, Prentice Hall of India Private Ltd., 2006, pg. no. 86 – 87.

Theory:

The compounds having similar molecular formulae but different arrangement of atoms or groups in space around the double bond are called geometrical isomers and the phenomenon is known as geometrical isomerism.

The geometrical isomerism arises due to restricted rotation about a carbon-carbon double bond. A complete rotation around carbon-carbon double bond causes breaking of π bond.

**Necessary and sufficient condition for geometrical isomerism**

An alkene of type abC = Cxy exhibits geometrical isomerism if a≠b and x ≠y. In an alkene, if either of the double bonded carbons is attached to two identical groups or atoms, no geometrical isomerism will exist.

There are three different ways in which groups a, b, x, and y can be arranged around carbon-carbon double bond. The configuration of the geometrical isomers is designated by

- *Cis – trans* system
- *E – Z* system

- *Cis – trans* system
  This system is used for designating the alkenes in which the two olefinic carbons have at least one similar group or atom present on them. For example, the alkenes of the type abC = Cab and abC =Cax exhibit *cis-trans*isomerism. It is noted that
    i) the term *cis*is used when two similar atoms or groups are present on same sides across the double bond and
    ii) the term *trans*- is used when two similar atoms or groups are present on opposite sides across the double bond.

The *cis*- and *trans*- isomers differ in their physical properties. In general, *trans*- isomers are more stable compared to *cis*- isomers. In *cis*- isomers, the groups present on the same side experience van der Waals repulsive forces due to steric factors.

Dipole moment values can be used effectively for distinguishing *cis*- and *trans*- isomers. The *trans*- isomers have zero dipole moment as the bond dipole on opposite sides cancel each other.

# Experiment No: 09

Aim: To study steriomer of lactic acid (optical isomerism of lactic acid).

Reference: Text book of organic chemistry, ArunBahal, B. S. Bahal, New Delhi, 18th edition, 2006, pg. no. 26.

Theory:

Lactic acid (2-hydroxy proponoic acid) is an example of a compound which shows optical isomerism. It contains one as asymmetric carbon atom.

Two three dimensional as possible for lactic acid.

1) dextro (+) lactic acid: It rotate a plane of polarized light in right direction.
2) Leaveo (-) lactic acid: It rotates plane of polarized light in left direction.

Both are optically active.

(±) lactic acid : Combination of equal amount of leavo and dextro isomers. It is optically inactive. i.e. racemic mixture with melting point 18°C.

# Experiment No: 10

Aim: To study stereo model of meso-tartaric acid (optical isomerism of tartaric acid).

Reference: Text book of organic chemistry, ArunBahal, B. S. Bahal, New Delhi, 18th edition, 2006, pg. no. 128.

Theory:

Tartaric acid (2,3dihydroxybutanidioc acid) contains two asymmetric carbon atom.

Four forms of tartaric acid.

1) (+) tartaric acid: It rotate plane of polarized light in right direction.
2) (-) tartaric acid: It rotate plane of polarized light in left direction.
   Both are optically active.
3) Meso- tartaric acid: It is optically inactive because of plane of symmetry.
4) (±) tartaric acid: It does not rotate plane of polarized light. It is optically inactive.

# Experiment No: 11

**Aim:** -To understand the construction, working and calibration of Refractometer.

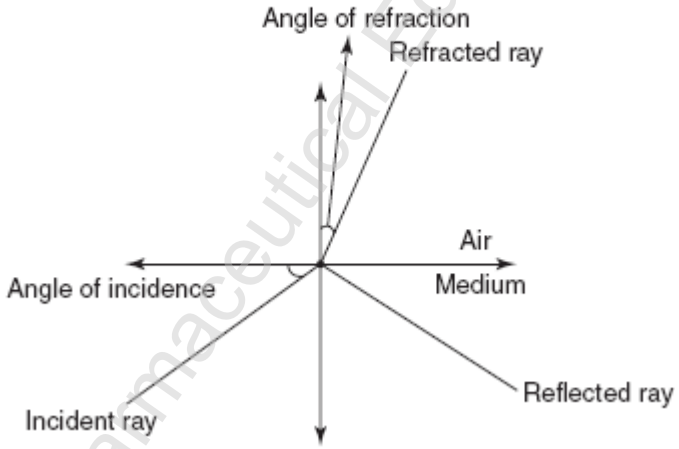
**Reference:** - A practical approach to pharmaceutical analysis instrumental and manual by Rajesh Kumar Neha S.N. Meyyanathan, Chandra shekhar Sharma, Mahesh Verma and C.S.Bhan, CBS publishers, 1st edition 2008, page no 127- 128 .

**Requirements**:-Abbe Refractometer

**Principle:-**

Refractometry is the method of measuring the refractive index of substances. Refractive index is defined as the ratio of the speed of light in a vacuum to the speed of light in another substance is defined as the index of refraction or refractive index (n) for the substance.

$$\text{Refractive index } (n) = \frac{\text{speed of light in a vacuum}}{\text{speed of light in a substance}}$$




Light refraction through liquids to determine the amount of dissolved solids in liquids by passing light through a sample and showing the refraction angle on scale.

Refraction index of prism should be greater than that of sample.

**Construction:-**

i) It essentially consists of a two glass prism A & B.
ii) The surface of B prism is polished, while that of A is finely ground.
iii) The two prisms can be rotated about a horizontal axis immediately beneath a telescope T & they can be held in contact with the help of a clamp C.

iv) An arm R which is attached with the metal case carrying the prism move along a graduated scale, the reading of which gives directly the refractive index if the liquid under examination .

**Working:-**

The beam if light passes from a suitable source is reflected by the mirror M. passes' through the lower prism A & illuminates the upper surface PR.

i) A drop of liquid under examination id placed upon the surface of A.
ii) On clamping the prism A & B, film of the liquid spreads between them.
iii) The light is refracted by mirror M is scattered into the liquid film at different angle of incidence.
iv) A particular ray going along the grazing incidence will pass through the prism B at an angle I which is equal to the critical angle

**Applications:**

- To check the purity of the sample.
- Used for qualitative and quantitative analysis.

Calibration:-Refractive index of water was found to be 1.678

Result:-The construction, working and calibration of Refractometer were studied.

# Experiment No: 12

**Aim: -** To Determine refractive index of given liquid sample by using Abbe Refractometer.

**Reference:-**

A practical approach to pharmaceutical analysis instrumental and manual by Rajesh Kumar Name S.N. Meyyanathan, Chandra shekhar Sharma, Mahesh Verma and C.S.Bhan, CBS publishers, 1st edition 2008 , page no 127-128

Equipments:-

1. Glassware's –
2. Abbe Refractometer.
3. Soft brush or cotton.
4. Plastic pipe attachment.

**Principle of Abbe Refractometer:-**

Light refraction through liquid to determine the amount of dissolved solids in liquids by passing light through a sample and showing the refracted angle of scale.

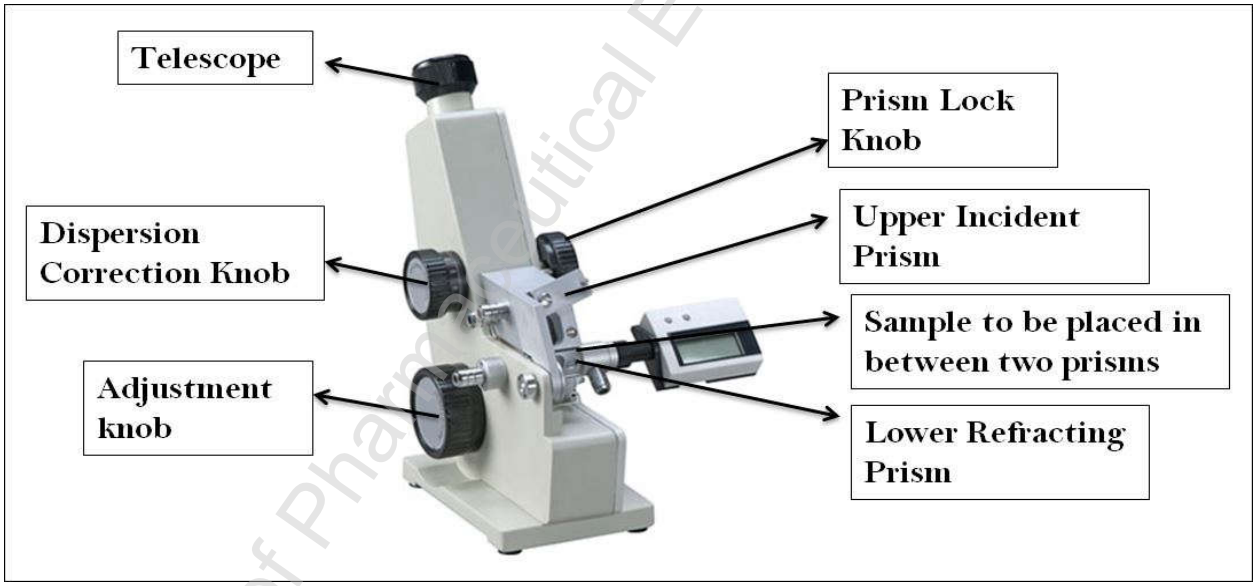



**Figure 1: Abbes Refractometer (CYBERLAB)**

**Procedure:-**

i) Plan the apparatus to front of proper light source.
ii) Clean the apparatus using soft cloth and wipe the prism by soft brush.
iii) Place a drop of distilled water and adjust the instrument.
iv) Focus the telescope eye piece on the cross section of the instrument and rotate the index arm until a

Colored band or fringe is seemed through the telescope.

v) Adjust the eye piece on the movable arm to give sharp focus on the scale and record the refractive index to the third place.

vi) Take a least three reading of each sample and its means used for the calculation.

vii) Take a least three reading of each sample and its mean used for calculation.

viii) Open the prism by turning the lock nut and closed its property.

ix) Take three reading of each sample of liquid.

**Result:-**

The refractive index of given liquid at temp **- was** found to be.

| Sample | R. I |
|---|---|
| D.W | |
| A | |
| B | |
| C | |
| D | |