JHARKHAND Rai University
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# PRACTICAL LAB MANUAL

## Medicinal Chemistry

## B. Pharm IV$^{th}$ Semester

| Sl. No | Name of the Experiment | Remark |
|---|---|---|
| **1** | Synthesis of Benzimidazole | |
| **2** | Synthesis of Benzotriazole | |
| **3** | Synthesis of Benzocaine | |
| **4** | Synthesis of 3-methyl-1-phenyl pyrazole-5-one. | |
| **5** | Synthesis of 4-benzylidene-2-phenyl oxazole-5-one | |
| **6** | Synthesis of Barbituric acid | |
| **7** | The assay of Chlorpromazine hydrochloride. | |
| **8** | The assay of Atropine. | |
| **9** | The assay of Ibuprofen | |
| **10** | The assay of Aspirin. | |
| **11** | The partition coefficient of succinic acid between ether and water. | |
| **12** | The partition coefficient of benzoic acid in benzene and water. | |
| **13** | Synthesis of Phenytoin | |
| **14** | Synthesis of Phenothiazine | |

**EXPERIMENT NO: 01** **Date:**

# Synthesis of Benzimidazole

**Aim:** To perform synthesis of Benzimidazole

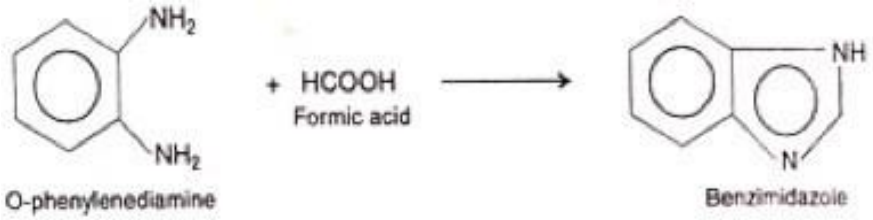
**Reference:**

B.S. Furniss, A.J. Hannaford, P.W.G. Smith, A.R. Tatchell, Vogel's Textbook of Practical Organic Chemistry, 5th Edition, Pg. 1162.

**Principle:**

Benzimidazole is prepared by the cyclization of o-phenylene diamine with formic acid. Benzimidazole is an example of intermediate used in bulk drug industry. It is the basic nucleus present in drugs like mebendazole and thiabendazole.

**Reaction:**




**Requirements:**

**Chemicals:** o-phenylene diamine, Formic acid, Sodium hydroxide

**Apparatus:** Round bottom flask, Beaker, Measuring cylinder, Buchner funnel

**Procedure:**

Placed 27 gm of o-phenylenediamine in a 250 ml round bottomed flask and added 17.5 gm of 90 percent formic acid. Heated the mixture on a water bath at 100°C for 2 hours. Cooled and added 10 percent sodium hydroxide solution slowly, with constant rotation of the flask, until the mixture was just alkaline to litmus. Filtered off the crude benzimidazole at the pump, washed with ice cold water, drained well and washed again with 25 ml of cold water. Dissolved the crude product in 400 ml of boiling water, added 2 gm of decolorizing carbon and digest for 15 minutes. Filtered rapidly at the pump through Buchner funnel and flask. Cooled the filtrate

to about 10°C, filtered off the benzimidazole, washed with 25 ml of cold water and dried at 100°C.

**Observation:**

Practical yield= ----------gm.

**Calculation:**

Molecular formula of o-phenylene diamine =

Molecular formula of Benzimidazole =

Molecular weight of o-phenylene diamine =

Molecular weight of Benzimidazole =

**Theoretical yield:**

……. gm of o-phenylenediamine forms …… gm Benzimidazole.

Therefore, ….. gm o-phenylene diamine will form ..... (X) gm Benzimidazole.

Theoretical yield = …….

$$\textbf{Percentage (\%) Yield} = \frac{\text{Practical Yield}}{\text{Theoretical yield}} \times 100$$

**Percentage yield =_____%**

**Result:**

**Conclusion:**

**Teachers Signature**

**EXPERIMENT NO: 02** **Date:**

# Synthesis of Benzotriazole

**Aim:** To perform synthesis of Benzotriazole

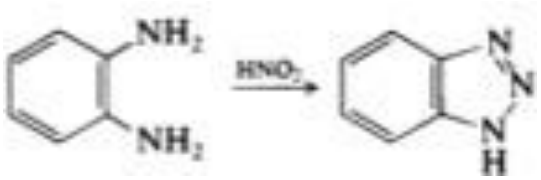
**Reference:**

B.S. Furniss, A.J. Hannaford, P.W.G. Smith, A.R. Tatchell, Vogel's Textbook of Practical Organic Chemistry, 5th Edition, Pg. 1163.

**Principle:**

Benzotriazole is formed when o-phenylenediamine reacts with nitrous acid (formed due to the reaction between sodium nitrite and acetic acid). Benzotriazole is an example of intermediate compound useful in bulk drug industry.

**Reaction:**




**Requirements:**

**Chemicals:** o-phenylenediamine, Glacial acetic acid, Sodium nitrite

**Apparatus:** Round bottom flask, Reflux condenser, Beaker, Measuring cylinder, Buchner funnel

**Procedure:**

Dissolved 10.8 gm of o-phenylenediamine in a mixture of 12 gm of glacial acetic acid and 30 ml of water contained in a 250 ml beaker. Cooled the solution to 15°C, stirred magnetically and then added a solution of sodium nitrite in 15 ml water in one portion. Continued stirring and then chilled in an ice bath. Collect the pale brown solid and wash with 30 ml portions of ice cold water. Dissolved the solid in about 130 ml of boiling water, added decolourising charcoal, filtered and allowed the filtrate to cool to about 50°C before adding a few crystals of the crude benzotriazole which have been retained for seeding.

**Observation:**

Practical yield= ----------gm.

**Calculation:**

Molecular formula of o-phenylene diamine =

Molecular formula of Benztriazole =

Molecular weight of o-phenylene diamine =

Molecular weight of Benztriazole =

**Theoretical yield:**

……. gm of o-phenylene diamine forms …… gm Benztriazole.

Therefore, ….. gm o-phenylene diamine will form ..... (X) gm Benztriazole.

Theoretical yield = …….

$$\textbf{Percentage (\%) Yield} = \frac{\text{Practical Yield}}{\text{Theoretical yield}} \times 100$$

**Percentage yield =_____%**

**Result:**

**Conclusion:**

**Teachers Signature**

**EXPERIMENT NO: 03** **Date:**

# Synthesis of Benzocaine

Aim: To perform synthesis of Benzocaine

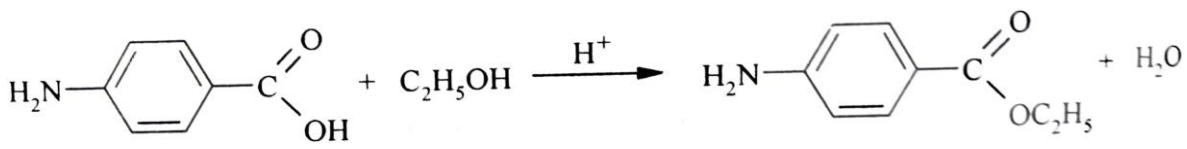
**Reference:**

Siddiqui AA, Siddiqui S., Experimental Pharmaceutical Chemistry, 3rd Edition, CBS Publishers & Distributors Pvt. Ltd., New Delhi, 2019, 230-231.

**Principle:**

Benzocaine is prepared from p-aminobenzoic acid by Fisher esterification. It is obtained as rhombohedra crystals from ether, mp 88-90°C, and fairly stable in air. 1 gm dissolves in about 2.5 L water, 5 ml ethanol, 2 ml $CHCl_3$, 4 ml ether, and in 30 to 50 ml of expressed almond oil or olive oil. Benzocaine is usually employed as an ointment to relieve pain associated with ulcers, wounds, burns, and mucous surfaces. It is also used as a lubricant and anaesthetic on intra-tracheal catheters, pharyngeal and nasal airways, nasogastric and endoscopic tubes etc. It is included in proprietary creams, lozenges, ointments, powders, sprays, and suppositories to relieve pain from damaged skin surfaces and inflamed mucous membranes.

**Reaction:**




p-Amino benzoic acid Benzocaine

**Requirements:**

**Chemicals:** p-amino benzoic acid, Absolute ethanol, concentrated sulfuric acid, Sodium bicarbonate.

**Apparatus:** Round bottom flask, Beaker, Conical flask, Measuring cylinder, Funnel

**Procedure:**

Dissolved 5 gm of p-amino benzoic acid and 40 ml of absolute ethanol in a round-bottom flask with a magnetic stirbar. Then cooled the mixture in an ice bath and added slowly 1 mlof concentrated sulfuric acid. It was then boiled gently under reflux for about 7 minutes. After completion of reaction, the mixture was allowed to cool and the contents were transferred to a beaker containing 30 ml of water. Then sodium bicarbonate solution was added. Filtered the benzocaine precipitates and rinsed the precipitates. The solid was allowed to dry. Recrystallization was done from aqueous alcohol.

**Observation:**

Practical yield= ----------gm.

**Calculation:**

Molecular formula of Benzocaine =

Molecular formula of p-amino benzoic acid =

Molecular weight of Benzocaine =

Molecular weight of p-amino benzoic acid =

**Theoretical yield:**

-----gm of p-amino benzoic acid gives ----- gm of Benzocaine.

Therefore, …… gm p-amino benzoic acid will form .....(X) gm Benzocaine.

Theoretical yield =

$$\textbf{Percentage (\%) Yield} = \frac{\text{Practical yield}}{\text{Theoretical yield}} \times 100$$

**Percentage yield =_____%**

**Result:**

**Conclusion:**

**Teachers Signature**

**EXPERIMENT NO: 04** **Date:**

# Synthesis of 3-methyl-1-phenyl pyrazole-5-one

**Aim:** To perform synthesis of 3-methyl-1-phenyl pyrazole-5-one

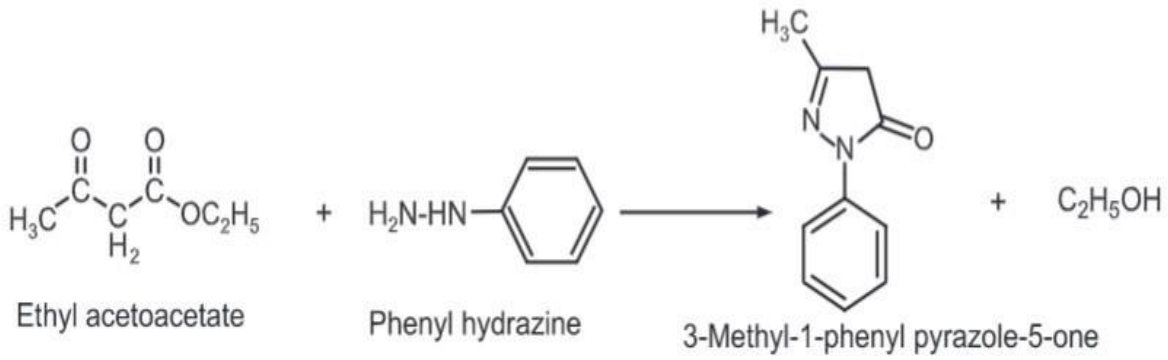
**Reference:**

A. Tiwari, R. Kumar, A practical book of Medicinal Chemistry, Nirali Prakashan, Pune, 2019, 1.

**Principle:**

3-methyl-1-phenyl pyrazole-5-one is synthesized by condensation of phenyl hydrazine and ethyl acetoacetate. It is an example of intermediate used in bulk drug industry. In thissynthesis ethylacetoacetate is used along with hydrazine. Ethylacetoacetate is heated with an equal quantity of phenyl hydrazine. On further heating ring formation occurs with loss of ethanol. Resultant compound is methyl phenyl pyrazolone.

**Reaction:**




**Requirements:**

**Chemicals:** Phenyl hydrazine, Ethyl acetoacetate, Ether, Ethanol

**Apparatus:** Round bottom flask, Reflux condenser, Beaker, Glass rod, Funnel, Measuring cylinder

**Procedure:**

A mixture of phenyl hydrazine (3.65 ml) and ethyl acetoacetate (4.9 ml) were heated in a round bottom flask on a boiling water bath for 2 hours. The reaction mixture was stirred with the help of a glass rod. Then, the reaction mixture was cooled and to it was added 20 ml etherwith

stirring. The separated product was filtered, washed with ether and recrystallized with dilute ethanol.

**Observation:**

Practical yield= ----------gm.

**Calculation:**

Molecular formula of 3-methyl-1-phenyl pyrazole-5-one =

Molecular formula of Ethyl acetoacetate =

Molecular weight of 3-methyl-1-phenyl pyrazole-5-one =

Molecular weight of Ethyl acetoacetate =

**Theoretical yield:**

……. gm of Ethyl acetoacetate forms …… gm 3-methyl-1-phenyl pyrazole-5-one.

Therefore, ….. gm Ethyl acetoacetate will form.....(X) gm 3-methyl-1-phenyl pyrazole-5-one.

Theoretical yield = …….

$$\textbf{Percentage (\%) Yield} = \frac{\text{Practical Yield}}{\text{Theoretical yield}} \times 100$$

**Percentage yield =_____%**

**Result:**

**Conclusion:**

**Teachers Signature**

**EXPERIMENT NO: 05** **Date:**

# Synthesis of 4-benzylidene-2-phenyl oxazole-5-one

**Aim:** To perform synthesis of 4-benzylidene-2-phenyl oxazole-5-one

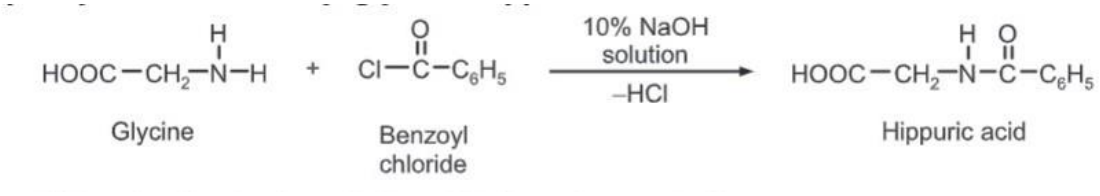
**Reference:**

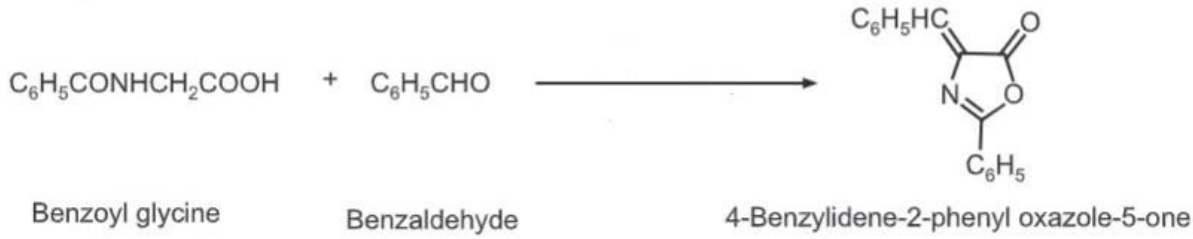
A. Tiwari, R. Kumar, A practical book of Medicinal Chemistry, Nirali Prakashan, Pune, 2019, 5-6.

**Principle:**

The principle involved in the preparation of 4-benzylidene-2-phenyl oxazole-5-one is dehydration followed by cyclization method. The active methylene group react with aromatic aldehydes. Benzoyl glycine reacts with benzaldehyde followed by dehydration gives 4-benzylidene-2-phenyl oxazole-5-one. The hippuric acid is formed by reacting glycine with benzoyl chloride.

**Reaction:**




**Requirements:**

**Chemicals:** Glycine, Sodium hydroxide, Benzoyl chloride, Concentrated hydrochloric acid, Benzaldehyde, Acetic anhydride, Anhydrous sodium acetate, Ethanol

**Apparatus:** Round bottom flask, Reflux condenser, Beaker, Glass rod, Funnel, Measuring cylinder

**Procedure**

About 1 gm of glycine was dissolved in aqueous sodium hydroxide solution (10 ml) in a flask

and to it 1.5 ml of benzoyl chloride was added. The mouth of the flask was plugged with cotton and was shaken vigorously. Then 1-2 drops of conc. HCl was added. The product was filtered, washed with water and recrystallized.

A mixture of benzaldehyde, benzoyl glycine, acetic anhydride and anhydrous sodium acetate was taken in a conical flask and the contents were heated on sand/oil bath till the mixture had liquified completely. Now, the contents were heated on a water bath for two hours. Then it was cooled, and to it 25 ml ethanol was added slowly. The product was filtered, washed with hot water, dried, and recrystallized.

**Observation:**

Practical yield= ----------gm.

**Calculation:**

Molecular formula of 4-benzylidene-2-phenyl oxazole-5-one =

Molecular formula of Benzoyl glycine =

Molecular weight of 4-benzylidene-2-phenyl oxazole-5-one =

Molecular weight of Benzoyl glycine =

**Theoretical yield:**

……. gm of Benzoyl glycine forms …… gm 4-benzylidene-2-phenyl oxazole-5-one. Therefore, ….. gm Benzoyl glycine will form.....(X) gm 4-benzylidene-2-phenyl oxazole-5-one.

Theoretical yield = …….

$$\textbf{Percentage (\%) Yield} = \frac{\text{Practical Yield}}{\text{Theoretical yield}} \times 100$$

**Percentage yield =_____%**

**Result:**

**Conclusion:**

**Teachers Signature**

**EXPERIMENT NO: 06** **Date:**

# Synthesis of Barbituric acid

**Aim:** To perform synthesis of Barbituric acid

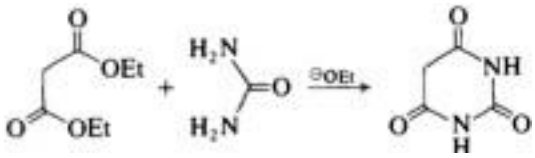
**Reference:**

A. Kar, Advanced Practical Medicinal Chemistry, New Age International Publishers, New Delhi, 3rd edition, Pg. 337-339.

**Principle:**

Barbituric acid are usually synthesized by carrying out the condensation of either diethyl malonate or its respective alkylated derivatives with urea in the critical presence of a base. Therefore, the interaction of diethyl malonate with urea in the presence of sodium ethoxide perceptively results in the formation of hydro-2,4,6-Trioxo pyrimidine. Barbituric acid may be gainfully utilized in the preparation of its various structural analogues.

**Reaction:**




**Requirements:**

**Chemicals:** Sodium metal pieces, Absolute ethanol, Diethyl malonate, Calcium chloride, concentrated hydrochloric acid, Urea

**Apparatus:** Round bottom flask, Beaker, Conical flask, Measuring cylinder, Funnel, Reflux condenser

**Procedure:**

In a 2-litre round bottomed flask, fitted with a double surface reflux condenser, 11.5 gm of clean sodium was placed. Then, 250 ml of absolute ethanol was added in one portion. Then, 80 gm of diethyl malonate was added, followed by a solution of 30 gm of dry urea in 250 ml of hot absolute ethanol. The mixture was shaken well, fitted with a calcium chloride guard- tube to the top of the condenser and the mixture was refluxed for 7 hours in an oil bath heatedto 110°C. A white solid separated out. The reaction mixture was treated with 450 ml of hot water and then with concentrated hydrochloric acid, with stirring, until the solution was acid. The

xresulting solution was filtered and left in the refrigerator overnight. The solid was filteredat the pump, washed with 25 ml of cold water, drained well and then dried at 100°C for 4 hours.

**Observation:**

Practical yield = ---------- gm.

**Calculation:**

Molecular formula of Diethyl malonate =

Molecular formula of Barbituric acid =

Molecular weight of Diethyl malonate =

Molecular weight of Barbituric acid =

**Theoretical yield:**

……. gm of Diethyl malonate gives ..... gm of Barbituric acid.

Therefore, ….. gm Diethyl malonate will form ..... (X) gm Barbituric acid

Theoretical yield = …….

$$\textbf{Percentage (\%) Yield} = \frac{\text{Practical Yield}}{\text{Theoretical yield}} \times 100$$

**Percentage yield =_____%**

**Result:**

**Conclusion:**

**Teachers Signature**

**EXPERIMENT NO: 7** **Date:**

# The assay of Chlorpromazine hydrochloride

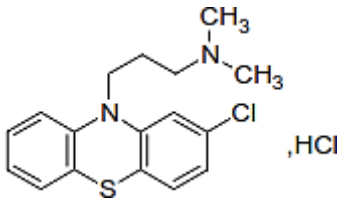
**Aim:** To perform the assay of Chlorpromazine hydrochloride.

**Reference:**

Indian Pharmacopoeia, 2007, The Indian Pharmacopoeia Commission, Ghaziabad, Volume 2, page 303-304.

**Principle:**

Chlorpromazine Hydrochloride is 2-chloro-10-(3-dimethylaminopropyl) phenothiazine hydrochloride. Chlorpromazine is estimated by non-aqueous titration which is suitable for titration of weak acid and weak base. In this non aqueous solvents like perchloric acid and methyl orange is used as an indicator. The mercuric acetate replaces the halide ion in chlorpromazine with acetate ion which is a strong base. At the end point blue colour is obtained.




**Chlorpromazine Hydrochloride**

**Requirements:**

**Chemicals:** Perchloric acid, Glacial acetic acid, Acetone, Mercuric acetate, Chlorpromazine hydrochloride, Crystal violet, Methyl orange, Potassium hydrogen phthalate

**Apparatus:** Measuring cylinder, Conical flask, Volumetric flask, Burette, Beaker

**Procedure:**

**Standardization of 0.1 M perchloric acid solution**

0.5 gm of potassium hydrogen phthalate was dissolved in 25 ml of glacial acetic acid and few drops of crystal violet indicator was added. The solution was titrated with 0.1 M $HClO_4$ till blue green colour appears.

**Assay of Chlorpromazine hydrochloride**

Accurately about 0.6 gm was weighed out, dissolved in 200 ml of acetone and 15 ml of

mercuric acetate solution was added to it. Titration was carried out with 0.1 M perchloric acid, using a saturated solution of methyl orange in acetone as indicator. A blank titration was also carried out.

1 ml of 0.1 M perchloric acid is equivalent to 0.03553 g of $C_{17}H_{19}ClN_2S$, HCl.

**Calculation:**

**Standardization of 0.1 M $HClO_4$ solution:**

**Molarity =**

**Assay of Chlorpromazine:**

**% purity of Chlorpromazine hydrochloride =** $\frac{0.03\$\$3 \& V \& \text{❍}^{*}+\text{rit}/}{\text{❍}^{*}+\text{rit}/ \& \mathbf{O}} \text{ X } 100$

**Where,**

**V = Volume of Perchloric acid used**

**W= Weight of sample**

**Result:**

**Conclusion:**

**Teachers Signature**

**EXPERIMENT NO: 8** **Date:**

# The assay of Atropine Sulphate

**Aim:** To perform the assay of Atropine Sulphate.

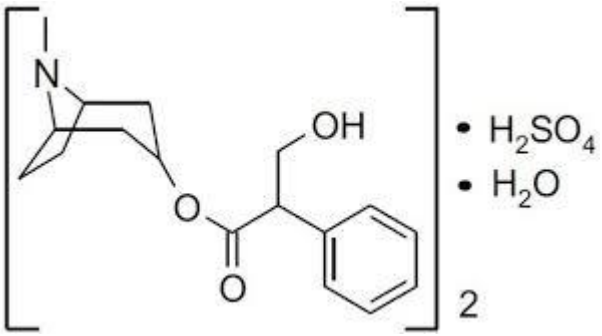
**Reference:**

Indian Pharmacopoeia, 2007, The Indian Pharmacopoeia Commission, Ghaziabad, Volume 2, page 135-136.

**Principle:**

Atropine is assayed by non-aqueous titration which is generally used for the titration of weak acid with weak base. In this titration non-aqueous solvent (perchloric acid) and crystal violet solution is used as an indicator. At the end point blue colour is obtained.

## Atropine Sulphate




**Requirements:**

**Chemicals:** Atropine sulphate, Potassium hydrogen phthalate, Perchloric acid, Glacial acetic acid, Crystal violet

**Apparatus:** Measuring cylinder, Conical flask, Volumetric flask, Burette, Beaker

**Procedure:**

**Standardization of 0.1 M perchloric acid solution**

0.5 gm of potassium hydrogen phthalate was dissolved in 25 ml of glacial acetic acid and few drops of crystal violet indicator was added. The solution was titrated with 0.1 M $HClO_4$ till blue green colour appears.

**Assay of Atropine Sulphate**

Accurately about 0.5g was weighed out and dissolved in 30 ml of anhydrous glacial acetic acid. Titration was carried out with 0.1 M perchloric acid and the end point was determined potentiometrically. A blank titration was also carried out.

1 ml of 0.1M perchloric acid is equivalent to 0.06768 g of ($C_{17}H_{23}NO_3$), $H_2SO_4$.

**Calculation:**

**Standardization of 0.1 M $HClO_4$ solution:**

**Molarity =**

**Assay of Atropine Sulphate:**

**% purity of Atropine Sulphate =**

**Result:**

**Conclusion:**

**Teachers Signature**

**EXPERIMENT NO: 9** **Date:**

# The assay of Ibuprofen

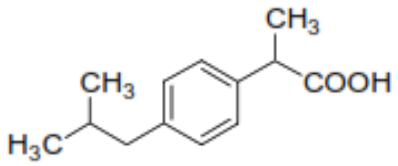
**Aim:** To perform the assay of Ibuprofen.

**Reference:**

Indian Pharmacopoeia, 2007, The Indian Pharmacopoeia Commission, Ghaziabad, Volume 2, page 599-600.

**Principle:**

Ibuprofen is 2-(4-isobutylphenyl)propionic acid. Ibuprofen is an example of non-steroidal anti-inflammatory drug (NSAID). It is also having analgesic and anti-pyretic activity. It is widely used in the management of pain and fever. Ibuprofen is aryl acetic acid derivative and is weakly acidic in nature. It is estimated by alkalimetry. In this method, the alcoholicsolution of Ibuprofen is titrated against a standard solution of sodium hydroxide using solution of phenolphthalein as indicator.




**Ibuprofen**

**Requirements:**

**Chemicals:** Ibuprofen, Sodium hydroxide, Phenolphthalein, Ethanol, Oxalic acid

**Apparatus:** Burette, Conical flask, Volumetric flask, Bulb pipette, Beaker, Funnel

**Procedure:**

**Standardization of sodium hydroxide solution**

The sodium hydroxide solution was standardized using a standard solution of oxalic acid and phenolphthalein indicator.

**Assay of Ibuprofen**

Accurately about 0.4 gm was weighed out and dissolved in 100 ml of ethanol (95 percent). It was titrated with 0.1 M sodium hydroxide using 0.2 ml of phenolphthalein solution asindicator. A blank titration was also carried out.

1 ml of 0.1 M sodium hydroxide is equivalent to 0.02063 g of $C_{13}H_{18}O_2$.

**Calculation:**

**Standardization of sodium hydroxide solution**

**Assay of Ibuprofen:**

**% purity of Ibuprofen =**

**Result:**

**Conclusion:**

**Teachers Signature**

**EXPERIMENT NO: 10** **Date:**

# The assay of Aspirin

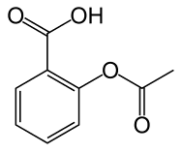
**Aim:** To perform the assay of Aspirin.

**Reference:**

Indian Pharmacopoeia, 2007, The Indian Pharmacopoeia Commission, Ghaziabad, Volume 2, page 127-128.

**Principle:**

Aspirin or Acetyl salicylic acid is an example of analgesic and antipyretic, which is widely used in the management of pain. It is estimated by acidimetry and alkalimetry. Its determination depends upon the alkaline hydrolysis of aspirin to acetic acid and salicylicacid, followed by back titration of the excess alkali using phenol red as indicator. A blank determination is needed in this assay.




**Aspirin**

**Requirements:**

**Chemicals:** Sodium hydroxide, Oxalic acid, Hydrochloric acid, Phenolphthalein, Aspirin, Phenol red, Ethanol

**Apparatus:** Measuring cylinder, Conical flask, Volumetric flask, Burette

**Procedure:**

**Standardization of sodium hydroxide solution**

The sodium hydroxide solution was standardized using standard solution of oxalic acid and phenolphthalein indicator. Later, the hydrochloric acid was standardized using the standardized sodium hydroxide solution.

**Assay of Aspirin**

Accurately about 1.5 gm was weighed out and dissolved in 15 ml of ethanol. To it, was added 50.0 ml of 0.5 M sodium hydroxide, boiled gently for 10 minutes, cooled and titrated the excess

of alkali with 0.5 M hydrochloric acid using phenol red solution as indicator. The operation was repeated without the substance under examination. The difference between the titrations represented the amount of sodium hydroxide required.

1 ml of 0.5 M sodium hydroxide is equivalent to 0.04504 g of $C_9H_8O_4$.

**Calculation:**

**Standardization of sodium hydroxide solution:**

**Assay of Aspirin:**

**% purity of Aspirin =**

**Result:**

**Conclusion:**

**Teachers Signature**

**EXPERIMENT NO: 11** **Date:**

# The partition coefficient of succinic acid between ether and water

**Aim:** To determine the partition coefficient of succinic acid between ether and water.

**Reference:**

R.S. Gaud, G.D. Gupta, Practical Physical Pharmacy, CBS Publishers & Distributors, New Delhi, page 145-146.

**Principle**:

When an excess amount of solid or liquid is added to a mixture of two immiscible liquids while this substance is slightly soluble in both immiscible liquids. It will distribute itself between the two phases until saturation if mixed by shaking vigorously. If the insufficient amount of substance is added in two immiscible liquids to the saturation, it gets distributed intwo layer at a definite ratio, this phenomenon is called as distribution law or partition law.The ratio constant is called as partition coefficient or distribution coefficient. It is independent of the total amount of the substance dissolved.

$$K = \frac{C1}{C2}$$

Where, K is a constant known as distribution or partition coefficient. $C_1$ and $C_2$ are the concentration of a solute in the two immiscible liquids.

**Requirements:**

**Chemicals:** Succinic acid, Ether, Phenolphthalein, Sodium hydroxide
**Apparatus:** Beaker, Measuring cylinder, Volumetric flask, Separating funnel

**Procedure:**

A solution of succinic acid in water was prepared. Then, 30 ml, 40 ml, and 50 ml of this solution was transferred in three stoppered flask. To it, 20 ml and 10 ml of water was addedto make total 50 ml. Then, 50 ml of ether was added, shaken vigorously and each flask was allowed to stay at constant thermostatic temperature. The two layers were then separated out. 10 ml of ether layer was pipetted out and to it 25 ml of water, phenolphthalein indicator was added and titrated with 0.05 N sodium hydroxide solution. The procedure was then repeated with the

aqueous layer.

**Observation:**

| **Volume of 0.05 N NaOH consumed** | | |
|---|---|---|
| | **Ether layer** | **Aqueous layer** |
| **Flask 1** | | |
| **Flask 2** | | |
| **Flask 3** | | |

**Determination of K values**

| **Sl. No** | **$C_{ether}$** | **$C_{aqueous}$** | **$K = C_{ether}/C_{aqueous}$** |
|---|---|---|---|
| **Flask 1** | | | |
| **Flask 2** | | | |
| **Flask 3** | | | |

**Result:**

**Conclusion:**

**Teachers Signature**

**EXPERIMENT NO: 12** **Date:**

# The partition coefficient of benzoic acid in benzene and water

**Aim:** To determine the partition coefficient of benzoic acid in benzene and water.

**Reference:**

R.S. Gaud, G.D. Gupta, Practical Physical Pharmacy, CBS Publishers & Distributors, NewDelhi, page 148-150.

**Principle**:

When an excess amount of solid or liquid is added to a mixture of two immiscible liquids while this substance is slightly soluble in both immiscible liquids. It will distribute itself between the two phases until saturation if mixed by shaking vigorously. If the insufficient amount of substance is added in two immiscible liquids to the saturation, it gets distributed intwo layer at a definite ratio, this phenomenon is called as distribution law or partition law.The ratio constant is called as partition coefficient or distribution coefficient. It is independent of the total amount of the substance dissolved.

$$K = \frac{C1}{C2}$$

Where, K is a constant known as distribution or partition coefficient. $C_1$ and $C_2$ are the concentration of a solute in the two immiscible liquids.

**Requirements:**

**Chemicals:** Benzoic acid, Benzene, Phenolphthalein, Sodium hydroxide

**Apparatus:** Beaker, Measuring cylinder, Volumetric flask, Separating funnel

**Procedure:**

A solution of benzoic acid in benzene was prepared. Then, 30 ml, 40 ml, and 50 ml of this solution was transferred in stoppered flasks. To it, 20 ml and 10 ml of benzene was added to make total 50 ml. Then, 50 ml of water was added with vigorous shaking. The two layers were then separated out. 10 ml of benzene layer was pipetted out and to it 20 ml of water wasadded, and titrated

with 0.05 N sodium hydroxide solution using phenolphthalein as indicator. The procedure was then repeated with the aqueous layer. The normality andconcentration of benzoic acid was calculated.

**Observation:**

| **Volume of 0.05 N NaOH consumed** | | |
|---|---|---|
| | **……. layer** | **…… layer** |
| **Flask 1** | | |
| **Flask 2** | | |
| **Flask 3** | | |

**Determination of K values**

| **Sl. No** | **$C_{benzene}$** | **$C_{aqueous}$** | **K = ……..** |
|---|---|---|---|
| **Flask 1** | | | |
| **Flask 2** | | | |
| **Flask 3** | | | |

**Result:**

**Conclusion:**

**Teachers Signature**

**EXPERIMENT NO: 13** **Date:**

# Synthesis of Phenytoin

**Aim:** To perform synthesis of Phenytoin

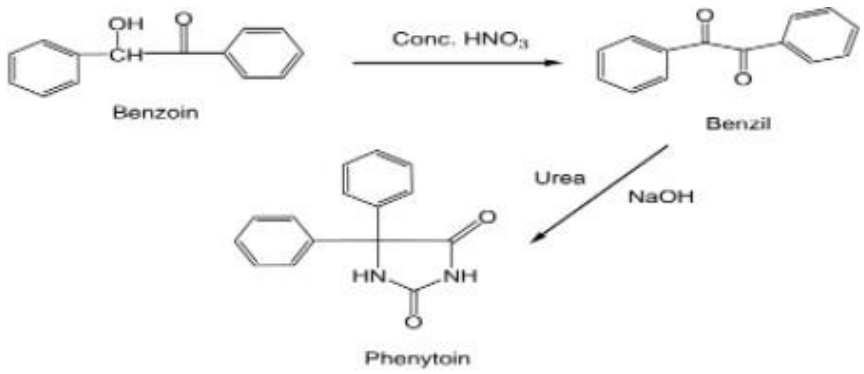
**Reference:**

G. Devala Rao, Practical Medicinal Chemistry, 1st edition, Birla Publications Pvt. Ltd., Delhi, 2007-2008, 12-13.

**Principle:**

Phenytoin is obtained as a powder having mp 295– 298°C. It is almost insoluble in water; 1 gm dissolves in about 60 ml ethanol; 30 ml acetone; and soluble in alkali hydroxides. Diphenyl hydantoin or phenytoin is prepared by condensing benzil with urea to give an intermediate product. This on acidification yields the required compound. Phenytoin is an example of anti-epileptic drug and widely used in the management of epilepsy. It is one of the drugs of choice for the management of generalized tonic-clonic seizures, complex partial seizures; and simple partial seizures. Parenterally, it is used for the control of status epilepticus of the generalized grand-mal type; and also in the control and management of seizures taking place during neurosurgery. IV phenytoin may be useful in the treatment of paroxysmal atrial tachycardia, ventricular tachycardia and digitalis-induced cardiac arrythmias.

**Reaction:**




**Requirements:**

**Chemicals:** Benzil, Sodium hydroxide, Alcohol, Concentrated hydrochloric acid, Urea

**Apparatus:** Round bottom flask, Beaker, Measuring cylinder, Buchner funnel, Reflux condenser, Petri dish

**Procedure:**

9 gm of benzil, 3 gm of urea, 20 ml of 30% sodium hydroxide solution and 75 ml of alcohol was taken in a round bottom flask. A reflux condenser was set up with the flask and the flask was boiled for $^1/_2$ hour. Then the mixture was poured in a beaker of cold water. The contents of the flask were acidified with hydrochloric acid, when phenytoin had precipitated out as a crystalline mass. The product was filtered at the pump and was washed thoroughly with water. The product was recrystallized from ethanol.

**Observation:**

Practical yield= ----------gm.

**Calculation:**

Molecular formula of Phenytoin =

Molecular formula of Benzil =

Molecular weight of Phenytoin =

Molecular weight of Benzil =

**Theoretical yield:**

……. gm of Benzil gives .....gm of Phenytoin.

Therefore, ….. gm Benzil will form .....(X) gm Phenytoin

Theoretical yield = …….

$$\textbf{Percentage (\%) Yield} = \frac{\text{Practical Yield}}{\text{Theoretical yield}} \times 100$$

**Percentage yield =_____%**

**Result:**

**Conclusion:**

**Teachers Signature**

**EXPERIMENT NO: 14** **Date:**

# Synthesis of Phenothiazine

**Aim:** To perform synthesis of Phenothiazine

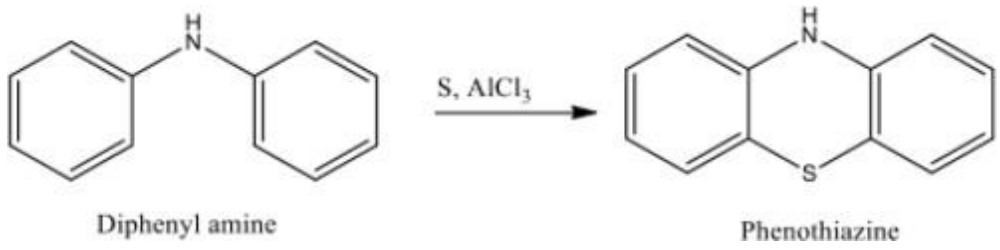
**Reference:**

P. Mondal, S. Mondal, Handbook of Practical, Pharmaceutical Organic, Inorganic and Medicinal Chemistry, Educreation Publishing, New Delhi, 2019, 189-190.

**Principle:**

Diphenylamine undergoes cyclization reaction with sulphur and anhydrous aluminium chloride at 140-150°C and forms a melted mass with the evolution of hydrogen sulphide gas. Further the melted mass is extracted with distilled water and followed by dilute alcohol pure phenothiazine separates out a residue.

**Reaction:**




Diphenyl amine Phenothiazine

**Requirements:**

**Chemicals:** Diphenylamine, Sulphur, Anhydrous Aluminium chloride, Alcohol

**Apparatus:** Round bottom flask, Beaker, Glass rod, Funnel, Measuring cylinder, Thermometer.

**Procedure:**

22 gm of diphenylamine, 8.2 gm of sulphur, and 3.2 gm of anhydrous aluminium chloride was melted together. The reaction temperature sets 140-150°C with the rapid evolution of hydrogen sulphide, by lowering the temperature, a few degrees the reaction rate was decreased. When the reaction had moderated, the temperature was raised to 160°C for a time. The melted mass, when cool, was ground up and extracted, first with water and then with dilute alcohol. The residue consisted of almost pure yellowish leaflets crystals of phenothiazine. It was recrystallized from alcohol.

**Observation:**

Practical yield= ----------gm.

**Calculation:**

Molecular formula of Diphenylamine =

Molecular formula of Phenothiazine =

Molecular weight of Diphenylamine =

Molecular weight of Phenothiazine =

**Theoretical yield:**

……. gm of diphenylamine gives..... gm of Phenothiazine.

Therefore, ….. gm diphenylamine will form..... (X) gm Phenothiazine

Theoretical yield = …….

$$\textbf{Percentage (\%) Yield} = \frac{\text{Practical Yield}}{\text{Theoretical yield}} \times 100$$

**Percentage yield =** _____%

**Result:**

**Conclusion:**

**Teacher's Signature**