



Recrystallization

Lecturer

Ahmed Ghalib Abdulsalam

Aim of

Experiment:

To purify samples of organic compounds that are solids at room temperature by using minimum amount of an appropriate hot solvent. (Ex. Benzimidazole).

Recrystallization

- It is primary method for purifying solid organic compounds. Compounds obtained from natural sources or from reaction mixtures almost always contain impurities. The impurities may be insoluble, soluble, and colored impurities. To obtain a pure compound these impurities must be removed.

Chooses a solvent for Recrystallization

The proper choice of a solvent is an important part of the crystallization.

The ideal solvent should be

1. Chemically inert toward the solute.
2. Dissolve the solute readily at its boiling point but sparingly at low temperature (0 – 25°C).
3. Dissolve impurities very easily.
4. Not be flammable of low cost and of low toxicity.

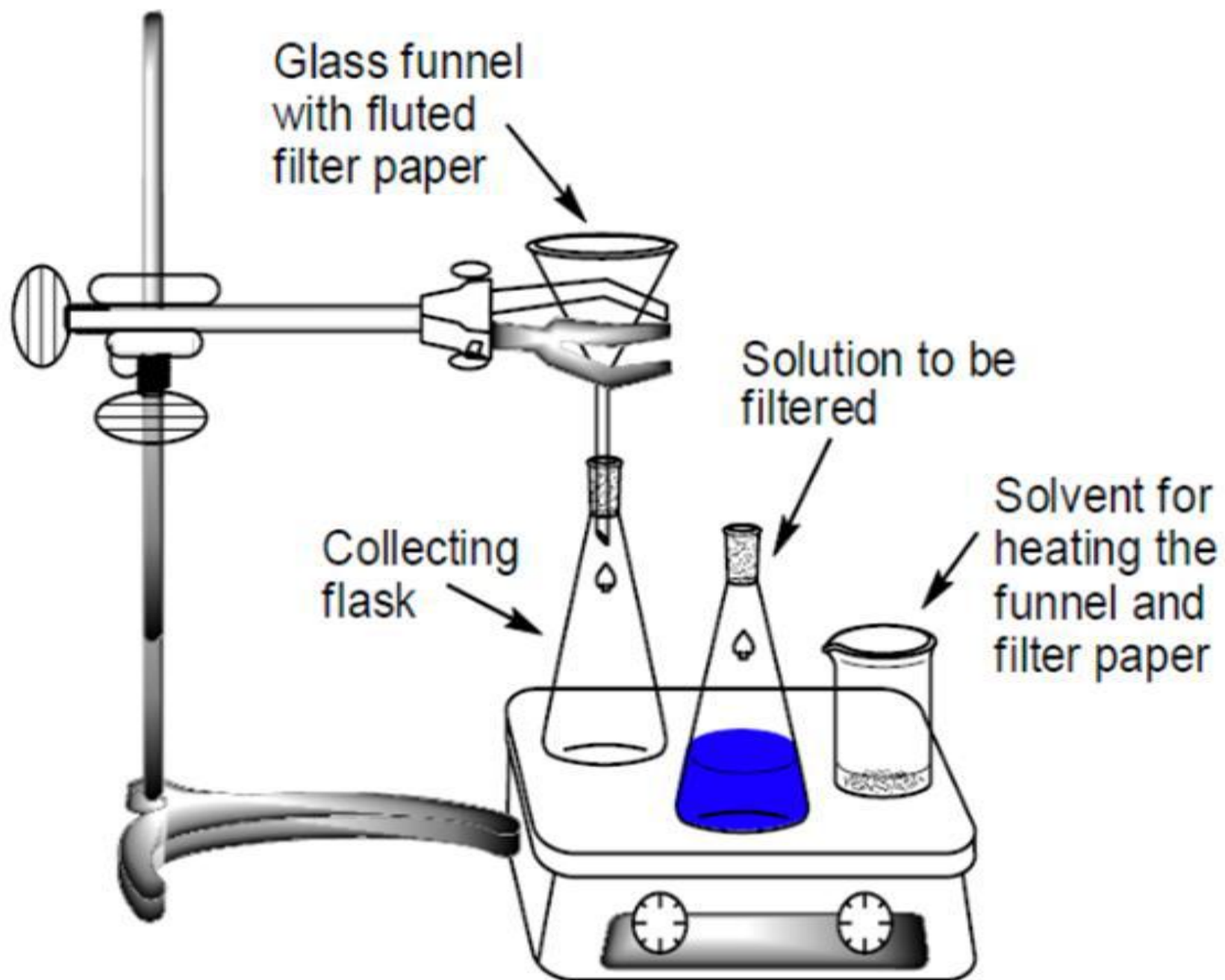
Note: Solvents extensively used for recrystallization include water, ethanol, chloroform, ether, acetone, and benzene.

Procedure (Crystallization of Benzimidazole):

1. Take your prepared organic compound (**Impure Benzimidazole**) and put it in a conical flask.
2. Add minimum amount of hot solvent (**water**) to conical flask until dissolving the compound.
3. Add a small amount of hot solvent to another conical flask and put it on the heater and put a funnel on it with a fluted filter paper wetted with the hot solvent.
4. Hot filtration of the compound.
5. After the filtration is complete, wash the filter paper with hot solvent to ensure that the entire compound is collected inside the conical flask.

6. Cool the conical flask with cold water to obtain crystals of the pure compound.
7. Filter and collect the compound on a pre-weighted filter paper.
8. Drying and weighing to obtain the practical weight of the prepared compound (use oven for drying).
9. Calculation

$$\text{Yield \%} = \frac{\text{Practical wt.}}{\text{Theoretical wt.}} * 100$$





Preparation of 6-Methyl-4-oxo-1,2,3,4-tetrahydro-2-mercaptopyridine

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Introductio:

The tetrahydropyridine systems are found in numerous natural and synthetic compounds, many of which have interesting pharmacological properties. Treatment of symptoms like those for Parkinson's disease.

Parkinson's disease:

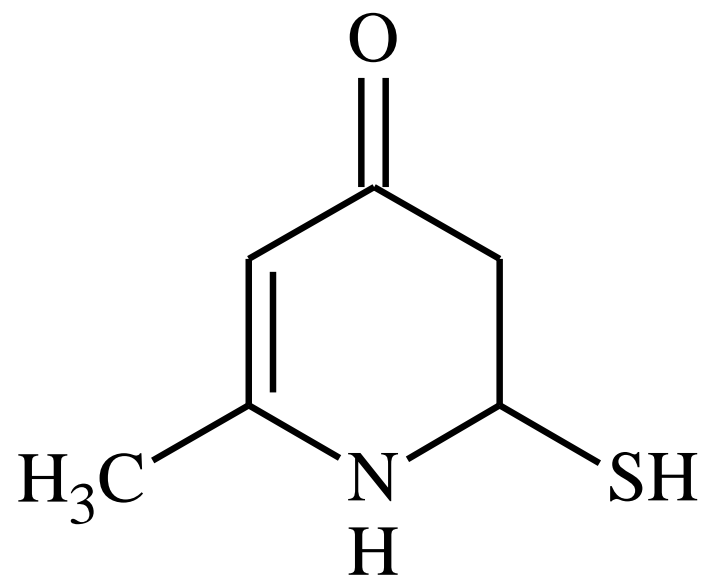
A long-term degenerative disorder of the central nervous system (CNS) that mainly affects the motor system.

They have been synthesized and studied because of their interesting biological properties and widely clinically used.

e.g. 1-Methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP) is a well-known neurotoxin.

CHEMISTRY

THE CHEMICAL STRUCTURE

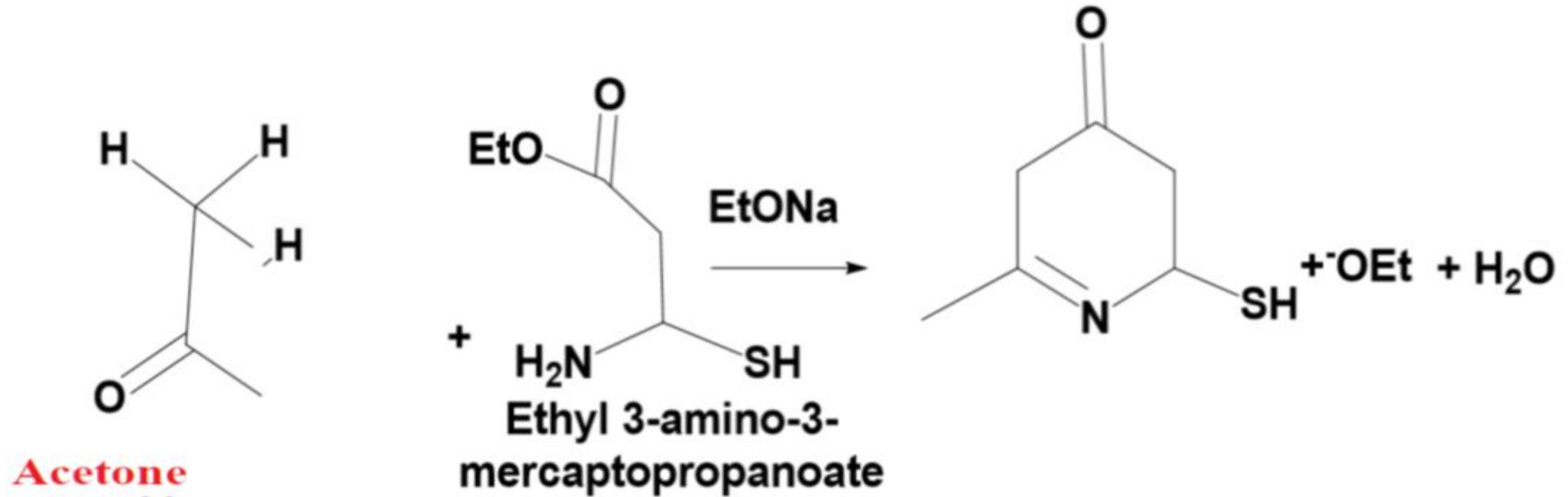


6-Methyl-4-oxo-1,2,3,4-tetrahydro-2-mercaptopyridine

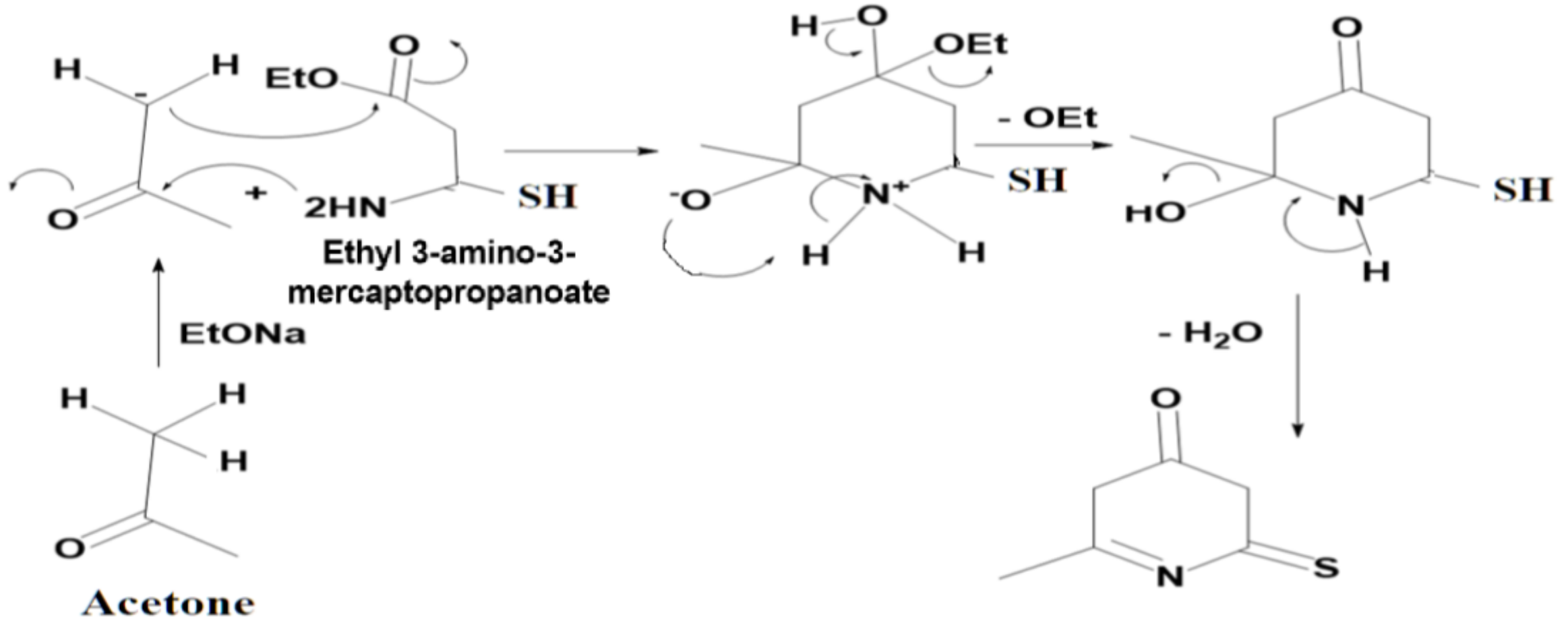
Molecular Formula: C₆H₉NOS

Molecular Weight: 143 g/mole

Preparation Equation:



Reaction Mechanism:



Procedure:

1. In 250ml round bottom flask add 2ml of acetone and 0.185g of sodium ethoxide (EtONa) then add 4.05g of (EAMP) Ethyl-3-amino-3-mercapto propanoate
2. Reflux the resulting mixture in water or sand bath at 100°C for 2hours.
3. After completion cool and filter the solution to collect the solid product.
4. The pure product obtained by recrystallization in hot ethanol

Calculations

Chemicals	Amount	M.wt.	Moles	Equivalents
EAMP	4.053g	149g/mol	0.0272	1
Acetone	2ml	58g/mol d=0.79g/ml	0.0272	1
EtONa	0.185g	68g/ml	0.0272	10%

Theoretical Yield:

- ❖ **149g of EAMP yields 143g of MOTMP**
- ❖ **4.053g EAMP will form Xg of MOTMP**

Calculations:

Theoretical Yield=

Initial M.wt. = Final M.wt.

$$149 = 143$$

$$4.053\text{g} = X$$

$$X = 143 \times 4.053/149$$

$$X = 3.89\text{g}$$

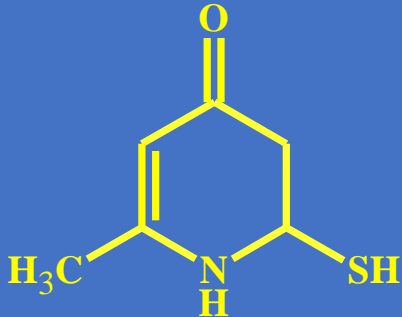
Practical Yield=

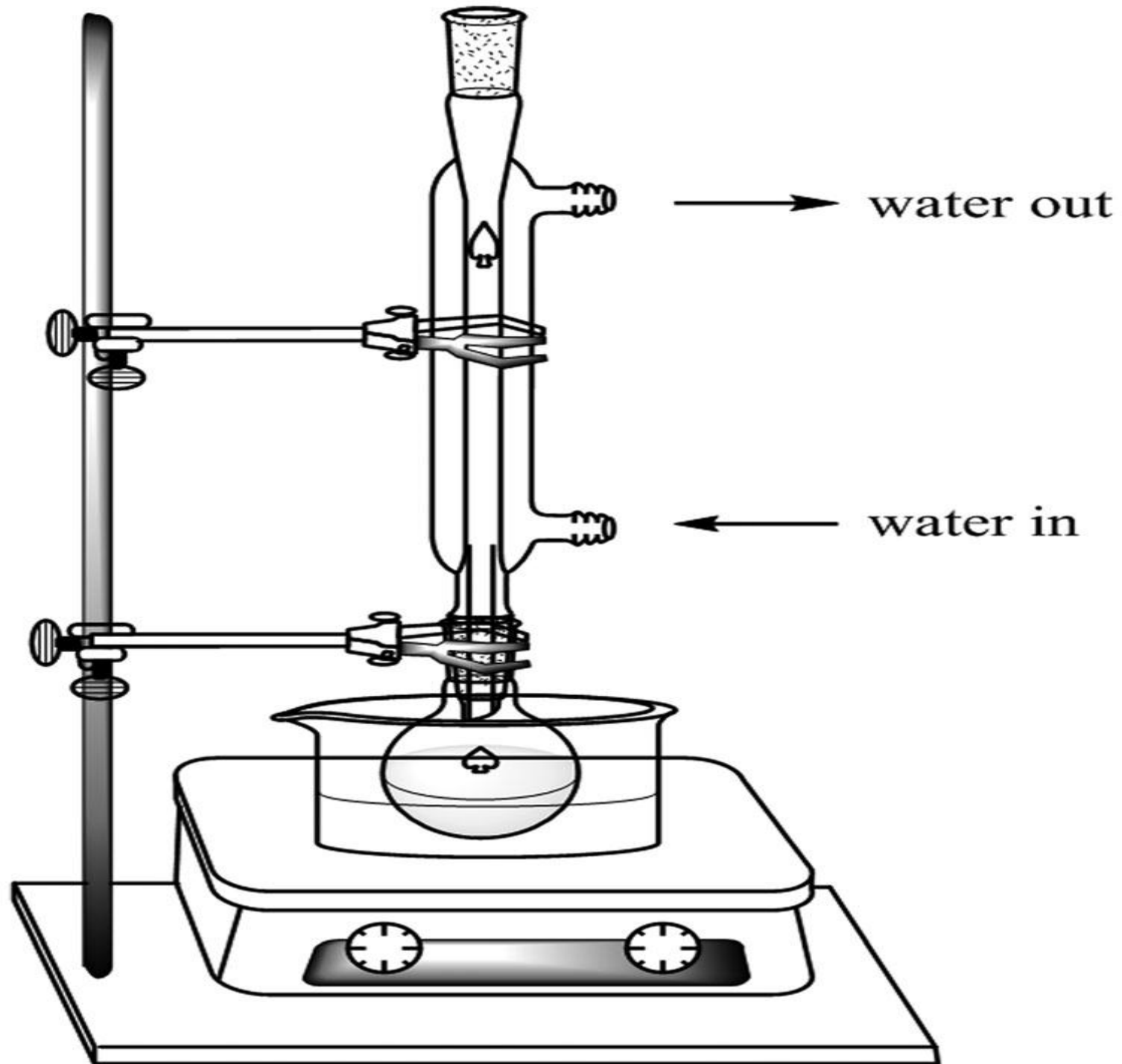
Percentage Yield=

$$\% = \text{Practical Yield} \times 100 / \text{Theoretical Yield}$$

$$\% = \text{-----}\%$$

Report

<i>Chemical Structure</i>	 <chem>Cc1cc(=O)nc(S)c1</chem>
<i>Molecular Formula</i>	
<i>Molecular Weight</i>	
<i>Theoretical Weight</i>	
<i>Practical Weight</i>	
<i>Percentage Yield</i>	
<i>Melting Point</i>	





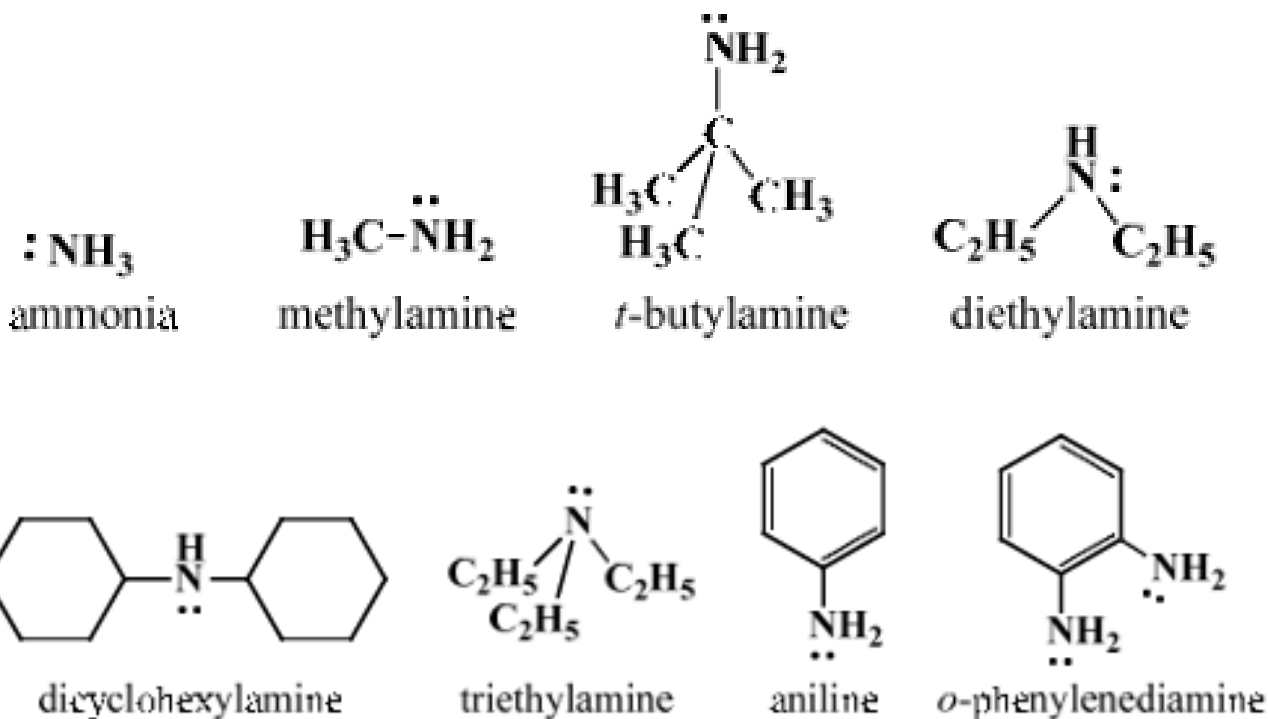
Practical of Organic Chemistry-III

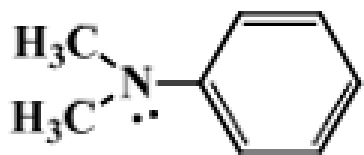
Classification of Reactions of Amines (Amines Tests)

Lecturer

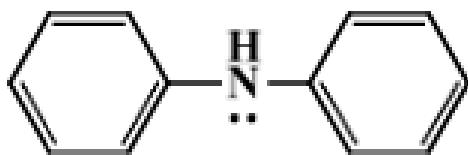
Ahmed Ghalib Abdulsalam

Amines are basic organic compounds that are considered as derivatives of ammonia. They are classified as primary, secondary, or tertiary according to the number of groups attached to the nitrogen atom: RNH_2 , R_2NH , or R_3N respectively where (R-) is any alkyl or (Ar-) any aryl group.

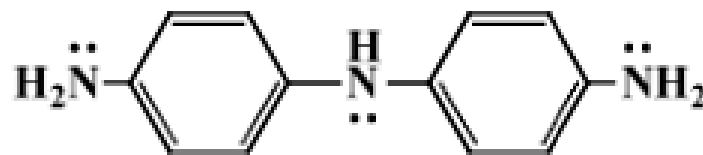




N,N-dimethylaniline



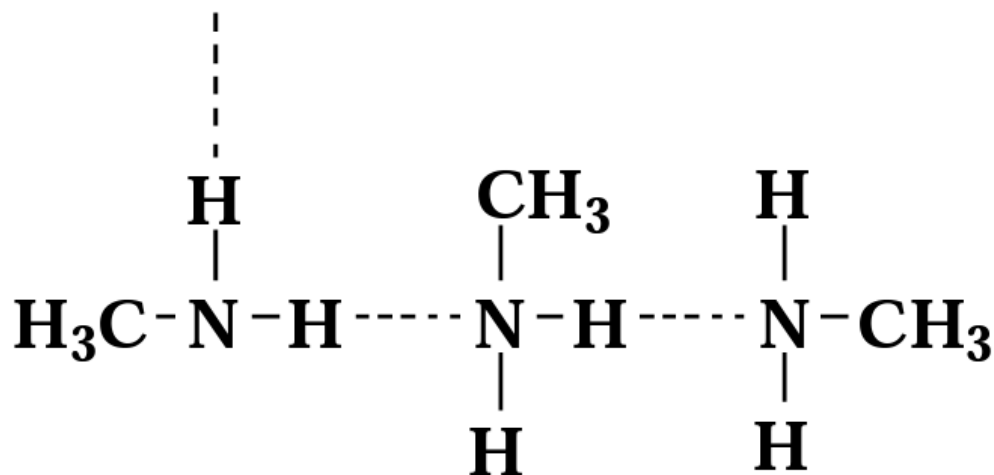
diphenylamine



p,p-diaminodiphenylamine

Physical properties

Like ammonia, amines are polar compounds and all of them can form intermolecular hydrogen bonds except tertiary amines.



They have lower boiling points than alcohols or carboxylic acids of the same molecular weight but higher boiling points than nonpolar compounds. Methylamine is gas while *o*-phenylenediamine and *p,p*-diamino diphenyl methane are solids. The others are liquids.

All amines are capable of forming hydrogen bonds with water, thus those with six carbon atoms or less are quite soluble in water.

The others are soluble in organic solvents as ether, alcohol and benzene.

All of them have fish like odour except the methylamines and ethylamines which smell just like ammonia.

Aromatic amines are colourless when pure, but they are easily oxidized by air becoming coloured. They are generally very toxic and can be absorbed through the skin.

Chemical Reactions (Chemical Test)

- 1) Solubility test
- 2) Litmus test
- 3) Azo-dye test
- 4) Nitrous acid test
- 5) Hinsbrg test

Solubility Test

Materials Required

1. Unknown
2. dil. HCl

Procedure

1. Add some drops of dil. HCl to the unknown in the test tube.
2. Shake the tube and note the solubility.

pH-Paper Test

Materials Required

1. Unknown
2. pH-paper

Procedure

Add some drops of the unknown to the pH-paper and note the change of colour

Azo-dye Test

Materials Required

1. Unknown dissolved in diluted HCl.
2. Sodium nitrite (NaNO_2) D.W.
3. β -Naphthol dissolved in diluted NaOH.
6. Test tubes and Droppers
7. Ice water

Procedure

Frist) Take three test tubes

In Test Tube A

Add 5 drops of (unk.+HCl) solution to the test tube.

In Test Tube B

Add 5 drops of sodium nitrite solution (NaNO_2 +D.W.).

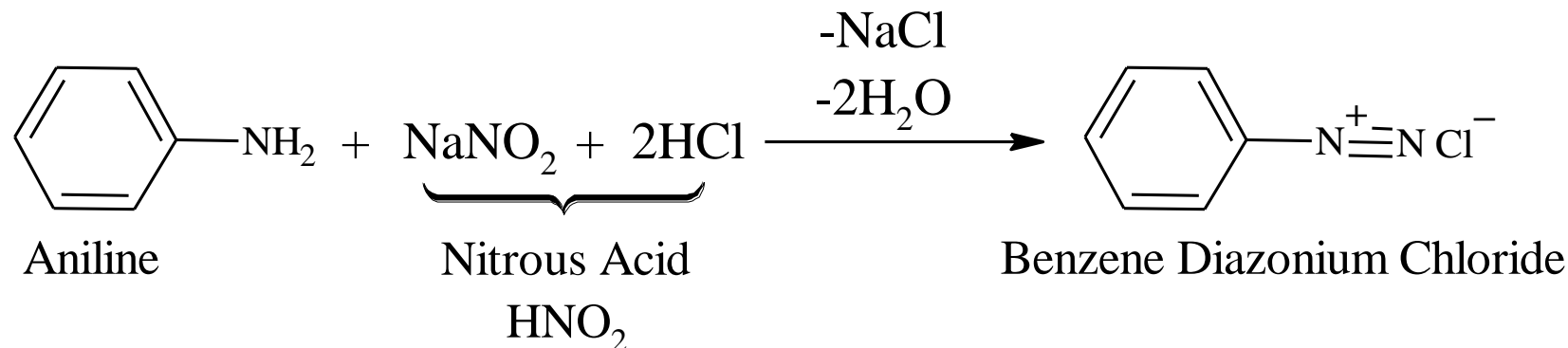
In Test Tube C

Add 10 drops of (β -Naphthol+NaOH) solution.

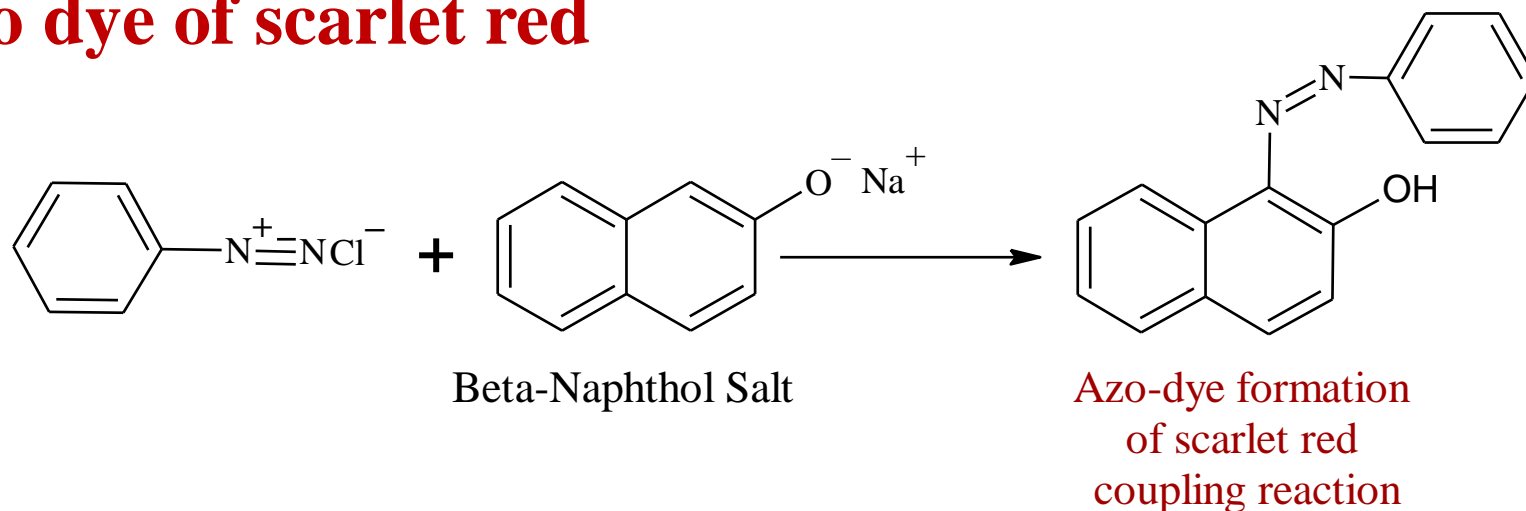
Second) Cool the three test tubes in the ice bath and then add solution in (test tube B) to the solution in (test tube A).

Third) 1°amines react with nitrous acid that form in situ to form diazonium salt (here benzene diazonium chloride)

The Reaction Equation of Primary Amine (Aniline) with Nitrous Acid which Made In situ



Fourth) The resulting solution (**diazonium salt**) is added to the β -naphthol solution in (**test tube C**) to produce an **Azo dye of scarlet red**



Nitrous Acid Test

Materials Required

1. Unknown of three types of Amines dissolved in diluted HCl.
2. Sodium nitrite dissolved in D.W.

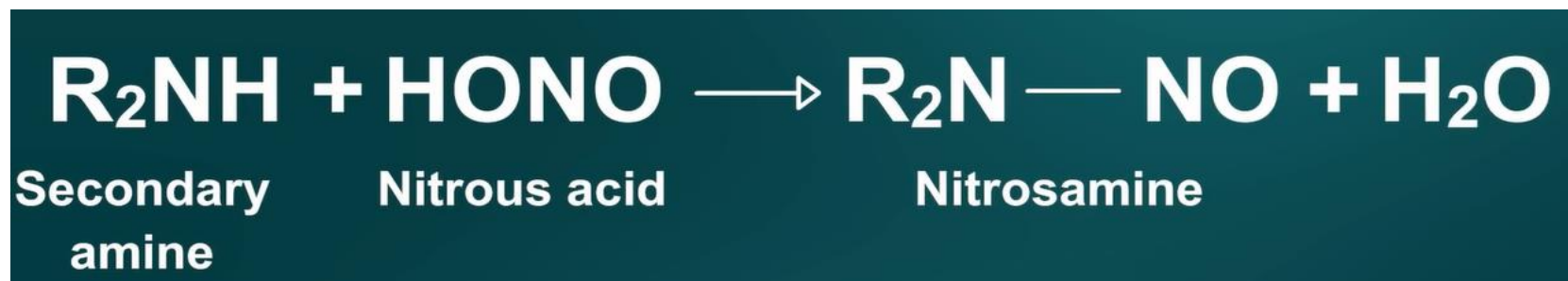
Procedure

1. Take three types of amines 1°, 2° and 3° dissolved in diluted HCl and put them in three labeled test tubes **A**, **B** and **C** respectively.
2. Put small quantity of sodium nitrite solution in test tube, then cool all test tubes in ice bath.
3. Then add some drops of sodium nitrite solution to each test tube and observe the result.

1° Amine, Test tube A produces bubbles of nitrogen gas



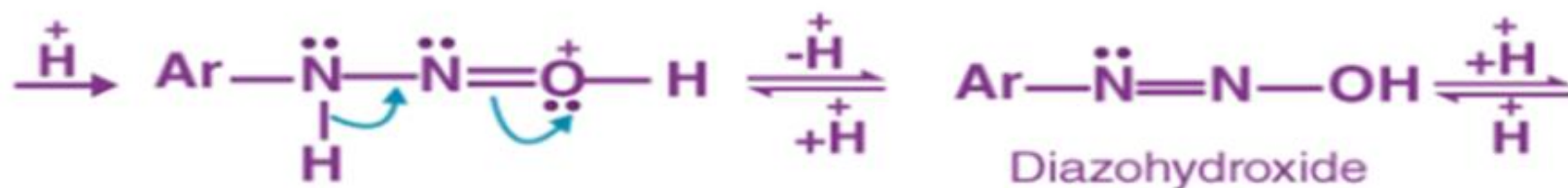
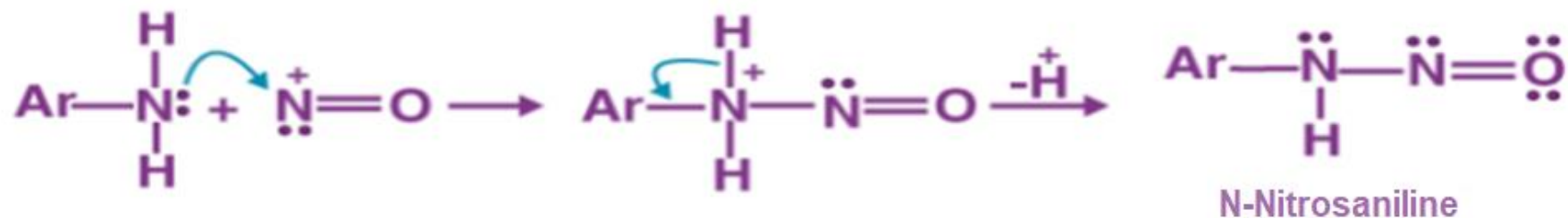
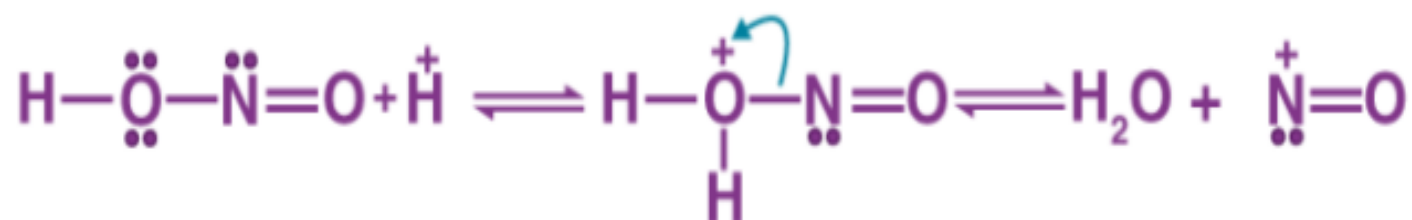
2° Amine, Test tube B, produces yellow nitrosamine



3° Amine, Test tube C produces a soluble nitrite salt



Reaction Mechanism



Hinsberg Test

Materials Required

1. Unknown of three types of Amines.
2. Benzene sulfonyl chloride.
3. 10% NaOH solution.
4. 5% HCl

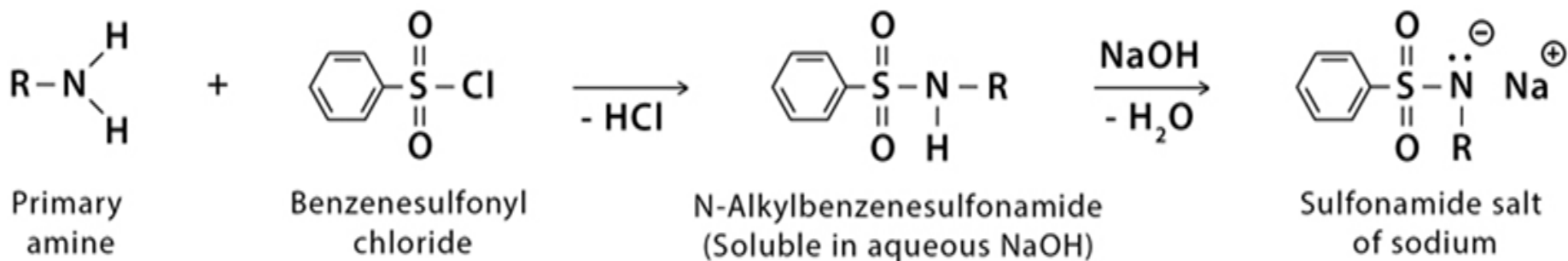
Procedure

1. Add 8-10 drops of amine to a three test tubes.
2. Add 10 drops of benzene sulfonyl chloride to three test tubes.
3. Add 10 mL 10% NaOH to three test tubes.
4. Shake vigorously to mix.
5. Check for the presence of a single layer (**primary amine**) or a double layer (**secondary or tertiary amine**) in the solution.

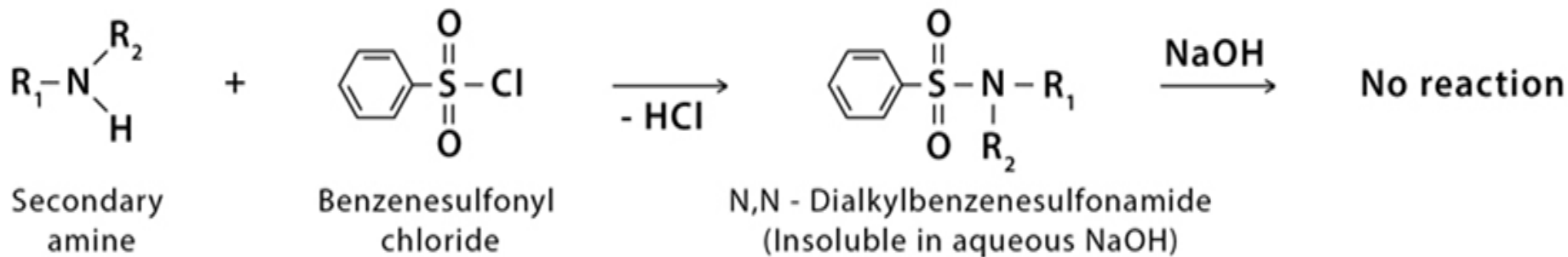
5. In there is a double layer, draw off the lower aqueous layer with a separatory funnel and check if the organic layer is soluble in 5% HCl (If it is not soluble, then secondary amine is present)

Reaction Equations

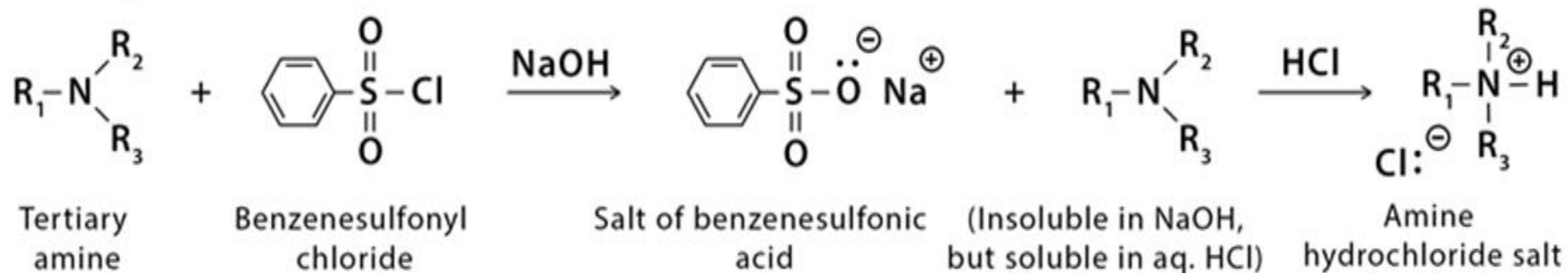
Primary amine



Secondary amine



Tertiary amine





Practical of Organic Chemistry-III

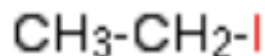
Identification of Alkyl and Aryl Halides {Comparison between Chloro, Bromo and Iodo butane}

Lecturer

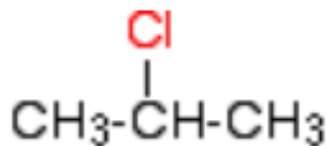
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Alkyl halides or Haloalkanes: are organic compounds formed by the replacement of hydrogen atoms in an aliphatic hydrocarbon by halogen atoms (Fluorine **F**, chlorine **Cl**, bromine **Br** or iodine **I**).

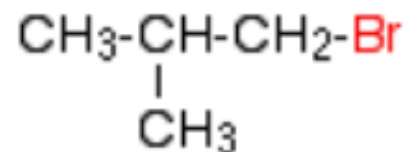
They contain halogen atoms attached to the ***sp*³** hybridized carbon atom of alkyl groups. some examples of Alkyl halide include;



iodoethane



2-chloropropane

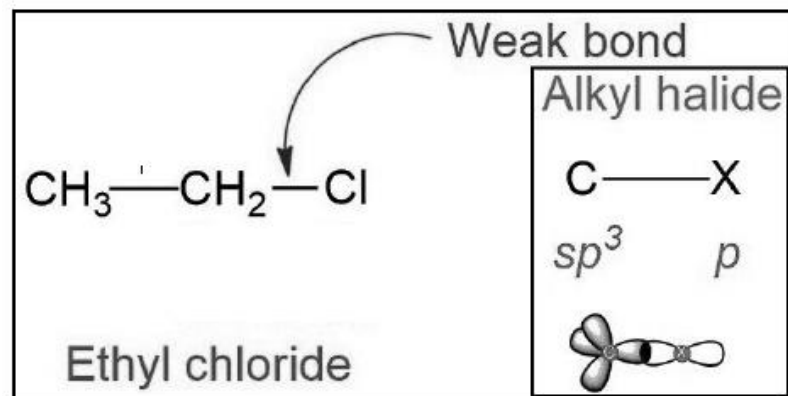


1-bromo-2-methylpropane

One of the simple alkyl halides is **Chloroethane**

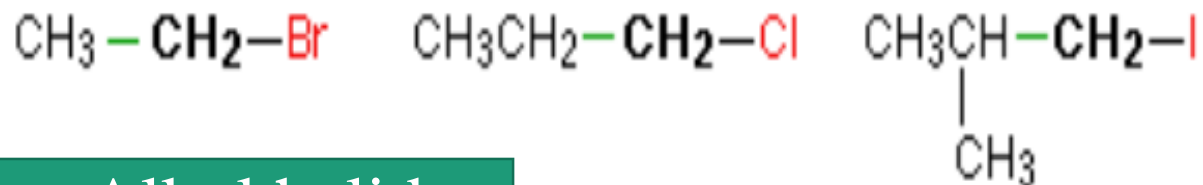
It has been used as:

1. Refrigerant الثلاجات
2. Aerosol spray propellant دافع لرش البخاخات
3. Anesthetic مخدر
4. Blowing agent for foam packaging عامل نفخ للفوم
5. In dentistry it is used as one of the means of diagnosing a 'dead tooth'



Alkyl Halide can be classified on the basis of Position of Halogen atom Along the Chain of Carbon Atom:

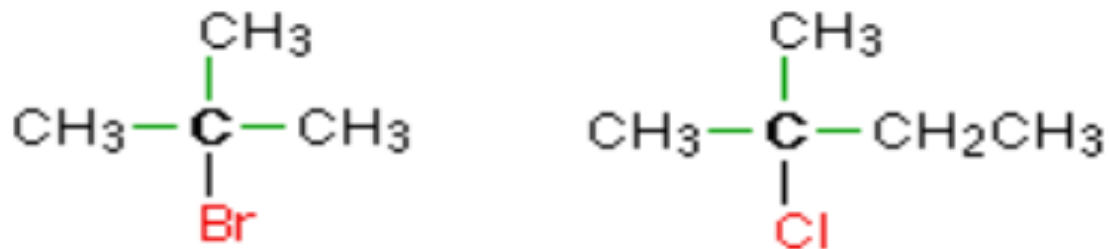
Primary Alkyl halides



Secondary Alkyl halides



Tertiary Alkyl halides



Physical properties of alkyl halide or Haloalkanes

1. Boiling point orders.



2. Bond strength of haloalkanes decreases as the size of the halogen atom increases. Thus, the order of bond strength is $CH_3F > CH_3Cl > CH_3Br > CH_3I$

3. Dipole moment decreases as the electronegativity of the halogen atom decreases.

4. Haloalkanes polar but are insoluble in water as they do not form hydrogen bond with water.

5. Density order is



Test of alkyl halides

Simple alkyl halides respond to the common characterization tests, they are readily distinguished from alkanes by qualitative analysis, which shows the presence of halogen.

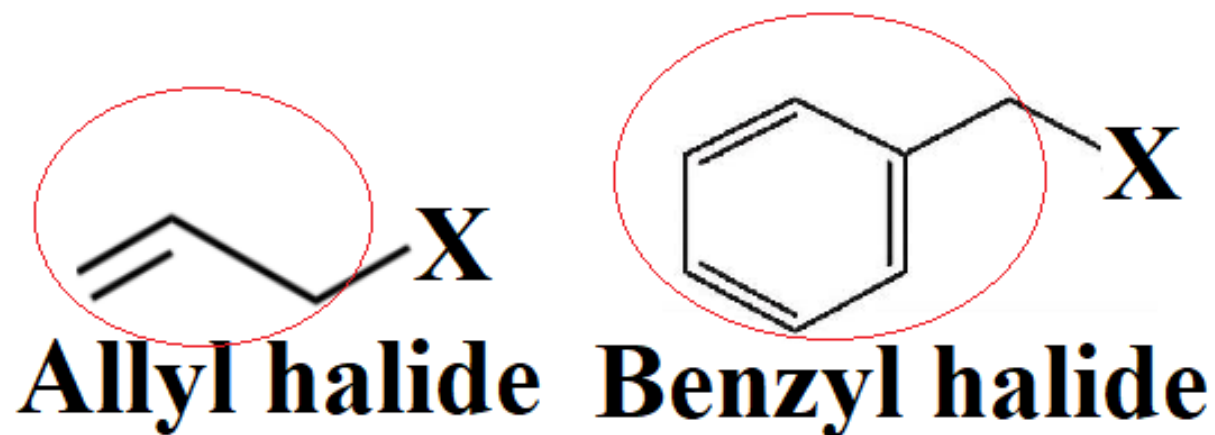
In many cases, the presence of halogen can be detected by warm the unknown for a few minutes with alcoholic silver nitrate (AgNO_3)

Halogen is indicated by formation of a precipitate that is insoluble in diluted nitric acid.

As in almost all reactions of organic halides, reactivity toward alcoholic silver nitrate follows the sequence:

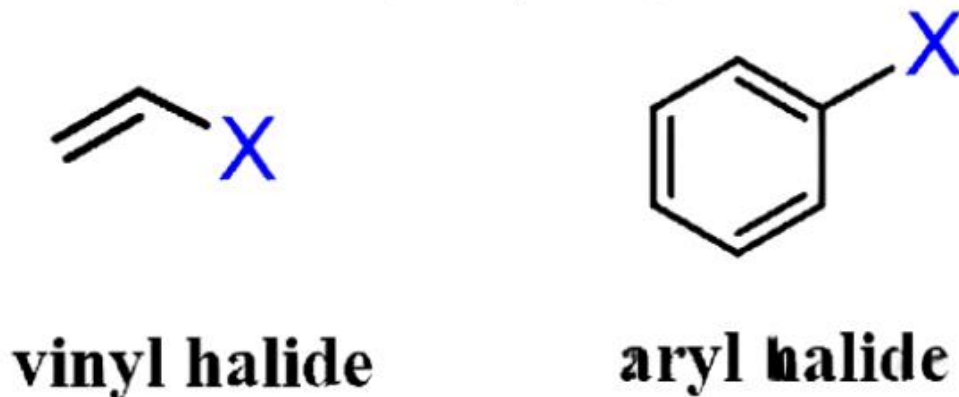


Allyl and benzyl halides are highly reactive



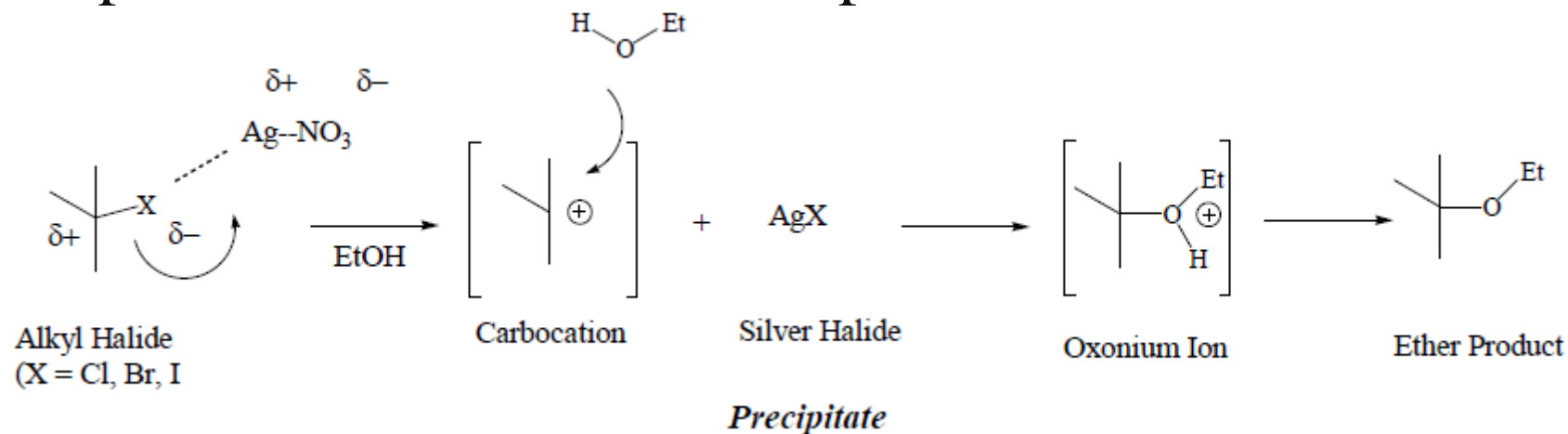
Vinyl and aryl halides **do not** react.

$X = \text{F, Cl, Br, I}$



The test reaction is of the S_N^I type.

The S_N^I reaction is a **S**ubstitution **N**ucleophilic **U**nimolecular reaction where the rate determining step is dependent on the electrophile but not on the nucleophile.



Silver ion is believed to shift reaction toward this mechanism by pulling halide away from the alkyl group.

The halogenoalkane is warmed with alcoholic silver nitrate solution (AgNO_3) so that the halogen atom is displaced as a halide ion via S_N^I reaction.

Various precipitates may be formed from the reaction between the silver and halide ions:



Table 1

ion present	observation
Cl⁻	white precipitate
Br⁻	very pale cream precipitate
I⁻	very pale yellow precipitate

It is actually difficult to distinguish between these colors, especially if there isn't much precipitate. You can sort out which precipitate you have by adding ammonia solution.

Table 2

original precipitate	observation
AgCl	precipitate dissolves to give a colorless solution
AgBr	precipitate is almost unchanged using dilute ammonia solution, but dissolves in concentrated ammonia solution to give a colorless solution
AgI	precipitate is insoluble in ammonia solution of any concentration

PROCEDURE

{Comparison between Chloro, Bromo and Iodobutane}

1. Add **2ml** of ethanol to three labeled test tubes **A, B, C**
2. Add **3-4 drops** of the **1-Chlorobutane**, **1-Bromobutane** and **1-Iodobutane** to the three test tubes **A, B, C** respectively.
3. Add about **1mL** of silver nitrate solution to each test tube.
4. Stop the test tubes on rack and immerse them in water bath of **50°C**, and leave it for few minutes.

Observation the Results

1. 1-iodobutane reacts immediately and form a pale-yellow precipitate.
2. After few minutes 1-bromobutane reacts to form a pale-cream precipitate
3. After at least 30 minutes the 1-chlorobutane reacts to form very thin white precipitate.



Practical of Organic Chemistry-III

Salts of Carboxylic Acids

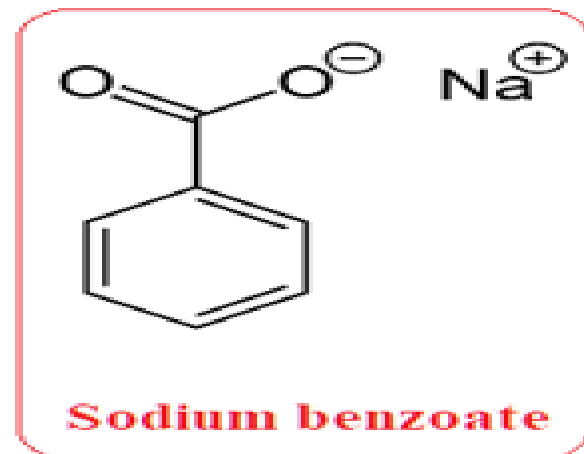
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Sodium benzoate: has the chemical formula $\text{C}_7\text{H}_5\text{O}_2\text{Na}$ with M.wt. 144.1 g/mole, It is the sodium salt of benzoic acid and exists in this form when dissolved in water.

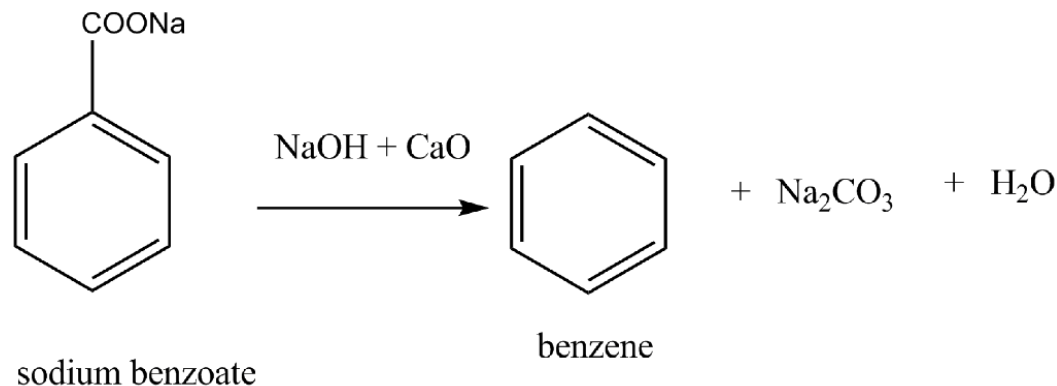
Physical properties:

1. It is a white crystalline powder.
2. Density (1.44 g/mL).
3. Melting point $>300^\circ\text{C}$.
4. Odorless compound that has a sweet.
5. Soluble in water (1gm/ 2mL water).

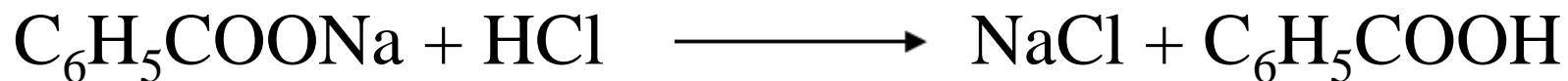


Chemical properties:

1. In combination with ascorbic acid (vitamin C) sodium benzoate and potassium benzoate form benzene, (H.W.) most beverages that contained both ascorbic acid and benzoate have benzene levels that were below those considered dangerous for consumption by the World Health Organization (5ppb), Heat and light can increase the rate at which benzene is formed.
2. Sodium benzoate is heated with soda-lime and when it gets decarboxylated benzene is obtained.



3. Sodium benzoate reacts with hydrochloric acid to produce benzoic acid.

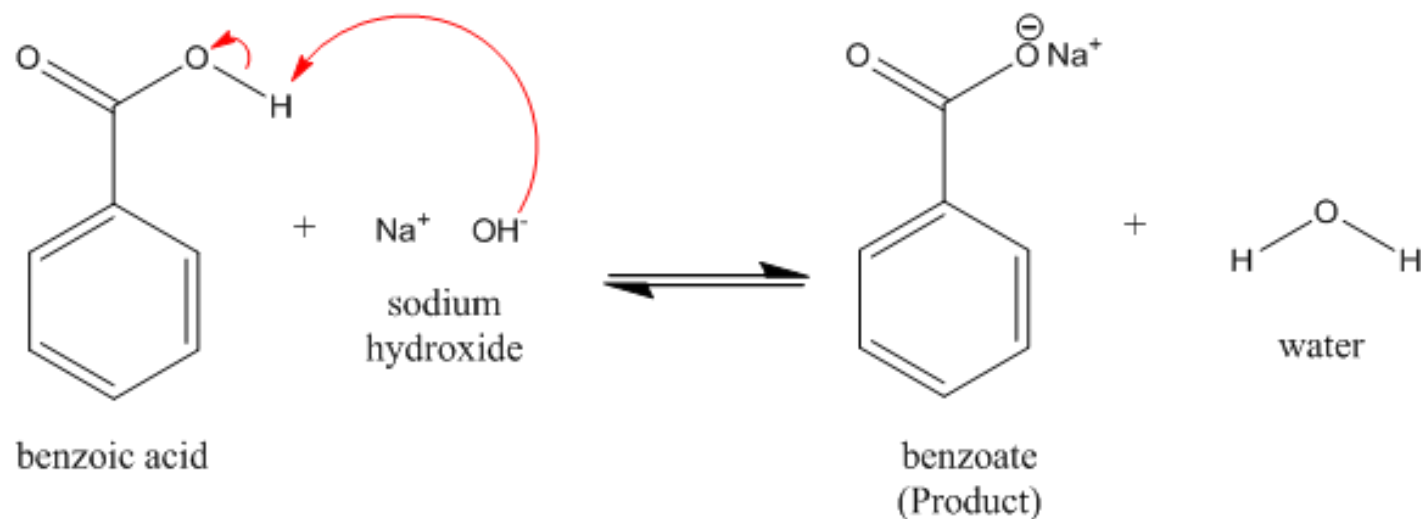


Pharmaceutical application:

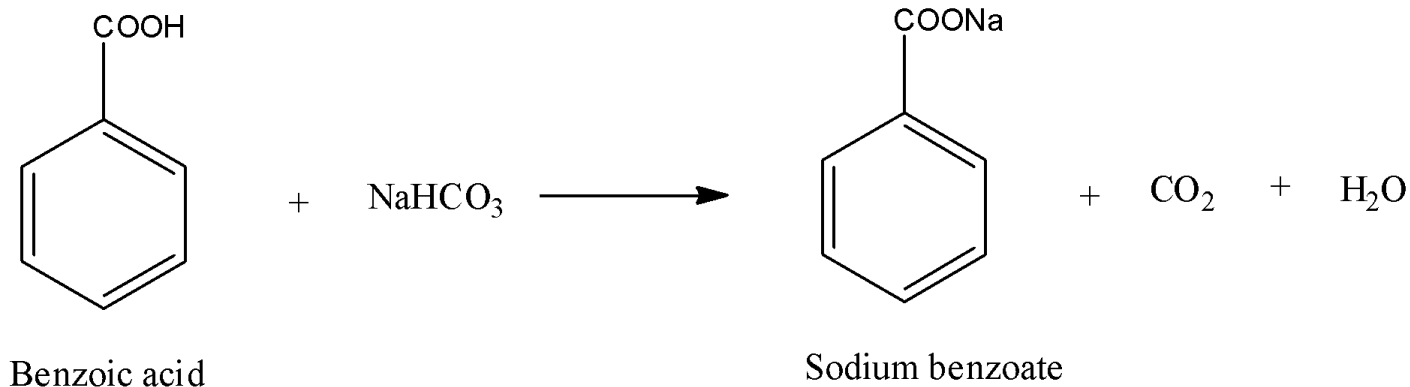
1. Sodium benzoate has antibacterial and antifungal properties and uses as preservative in pharmaceutical formulation including oral preparation in concentrations up to 0.5 %. It is also a common ingredient of cough preparations.
2. Sodium benzoate is used as a treatment for urea cycle disorders due to its ability to bind amino acids. This leads to excretion of these amino acids and a decrease in ammonia levels.
3. Sodium benzoate is use in cosmetic products like mouthwash, toothpaste, deodorant, lotion, and shampoo.

Sodium Benzoate Preparation:

It can be produced by the neutralization of benzoic acid with sodium hydroxide.



Sodium benzoate can also be prepared by adding benzoic acid to a hot, concentrated solution of sodium bicarbonate until the effervescence ceases.



General procedure:

1. Prepare (25mL) of (1M) NaOH solution by dissolving (1gm) of NaOH in (15mL) of water and adjust the final volume to (25mL).
2. Dissolve (3.05gm) of benzoic acid in (25mL) of (1M) NaOH solution.
3. Evaporate the water to get the final product salt.

Calculations:

Chemicals	Amount	M.wt.	Moles	Equivalents
B.A.	3.05g	122g/mol	0.025	1
NaOH	25ml	40g/mol	0.025	1

Theoretical Yield=

Practical Yield=

Initial M.wt. = Final M.wt.

122g/mole = 144.1g/mole

3.05g = X

X = $144.1 \times 3.05 / 122$

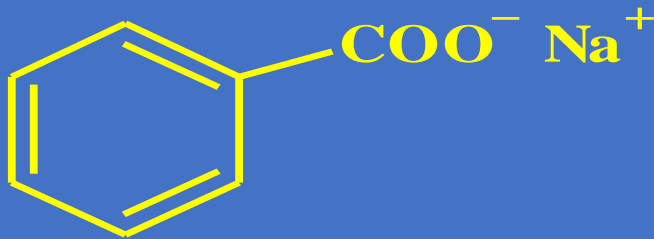
X = 3.6g

Percentage Yield=

% = $\text{Practical Yield} \times 100 / \text{Theoretical Yield}$

% = ----- %

Report:

<i>Chemical Structure with Name</i>	 Sodium Benzoate
<i>Molecular Formula</i>	
<i>Molecular Weight</i>	
<i>Theoretical Weight</i>	
<i>Practical Weight</i>	
<i>Percentage Yield</i>	
<i>Melting Point</i>	

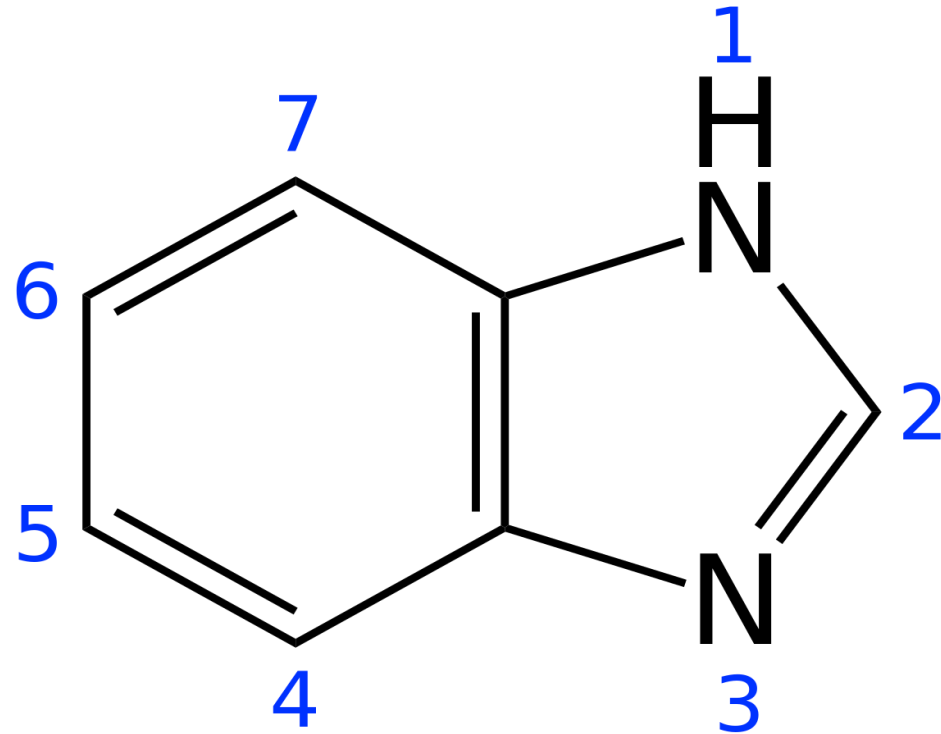


Synthesis of Benzimidazole

Lecturer

Ahmed Ghalib Abdulsalam

***Aim of Experiment: Synthesis of Benzimidazole from
o-Phenylenediamine***



118.139 g/mol

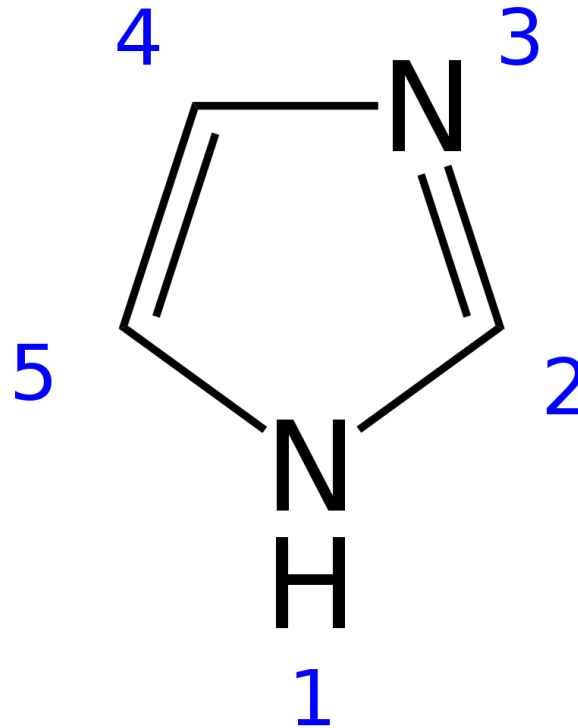
Theory:

Benzimidazole, is Heterocyclic Compound

Heterocyclic compounds are cyclic compounds that has at least one atom other than carbon as a member of the ring, the study of this branch of organic chemistry which dealing with the synthesis, properties, and applications of these heterocycles that is called ***Heterocyclic Organic Chemistry***.

Chemical structure:

It composed of benzene ring fused with imidazole ring, it is an aromatic heterocycle, classified as a diazole, and has non-adjacent nitrogen atoms (five membered heterocyclic ring with two nitrogen atoms separated by carbon atom and double bond), because of imidazole ring fused with benzene ring it called Benzimidazole.



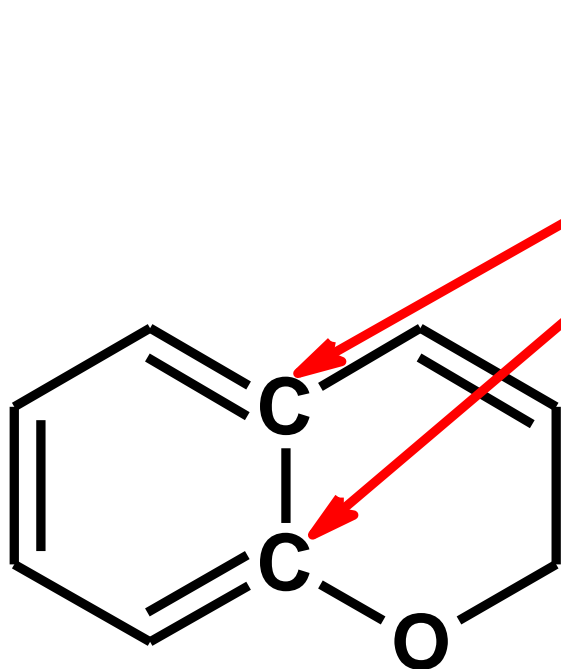
What is fused rings?

Fused rings, are two rings share two adjacent atoms.

In other words, the rings share one covalent bond, *i.e.* the so-called bridgehead atoms are directly connected.

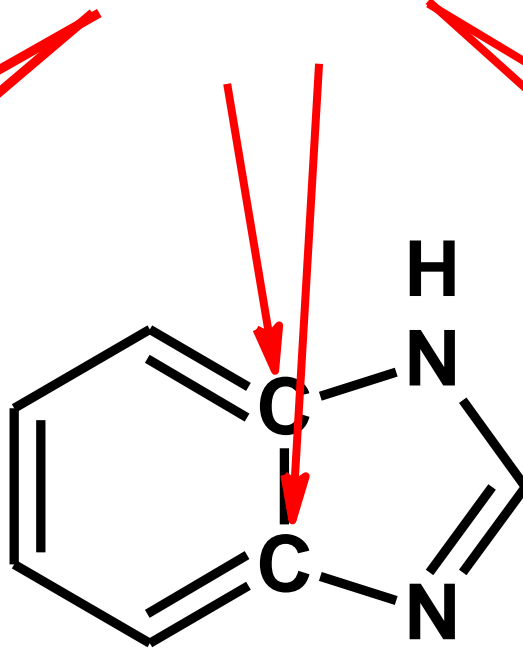
Most bicyclic systems consist of benzene ring are named systematically, by use of the prefix benz- or benzo- to indicate the presence of the benzene ring.

Bridgehead Atoms
Two Rings share two Adjacent Atoms



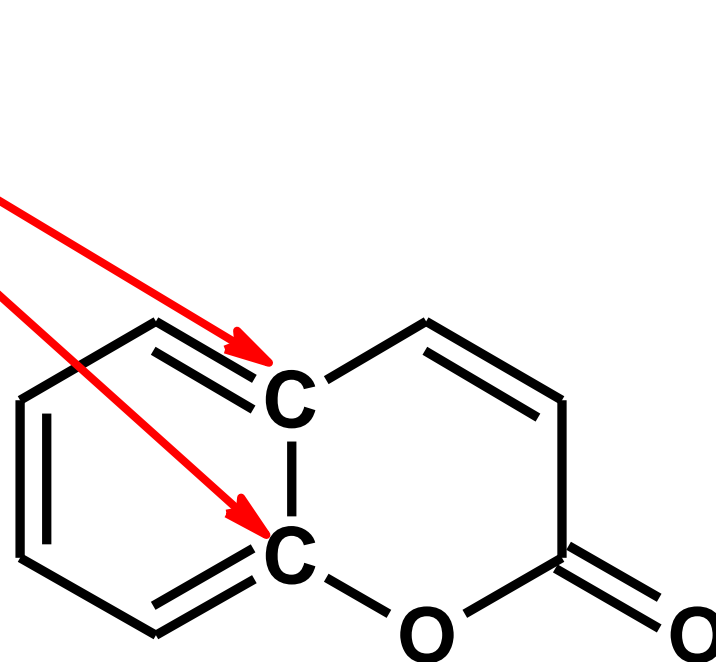
2H-benzopyran

2H-chromene



1,3-benzodiazole

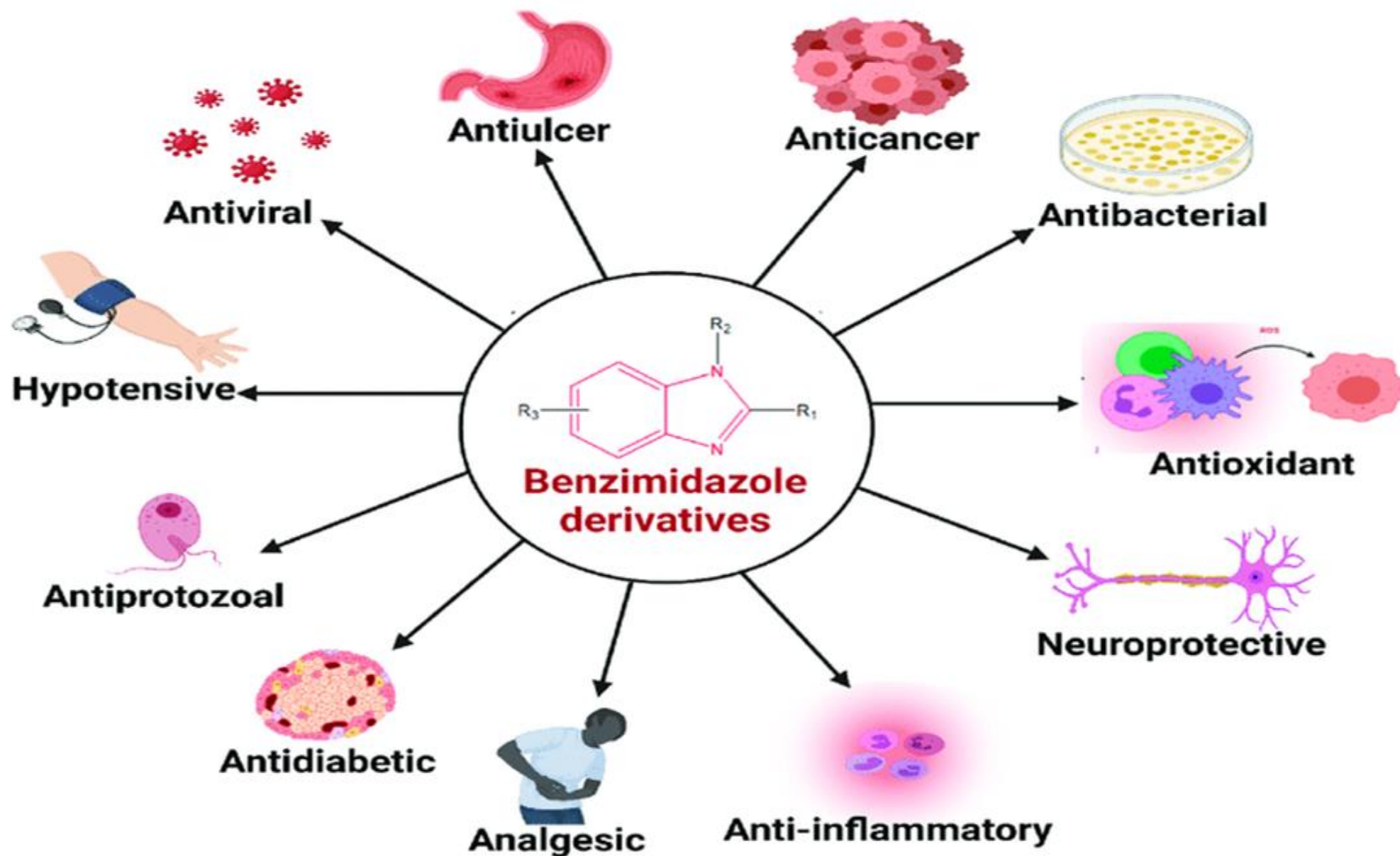
Benzimidazole



2H-benzopyran-2-one

Coumarin

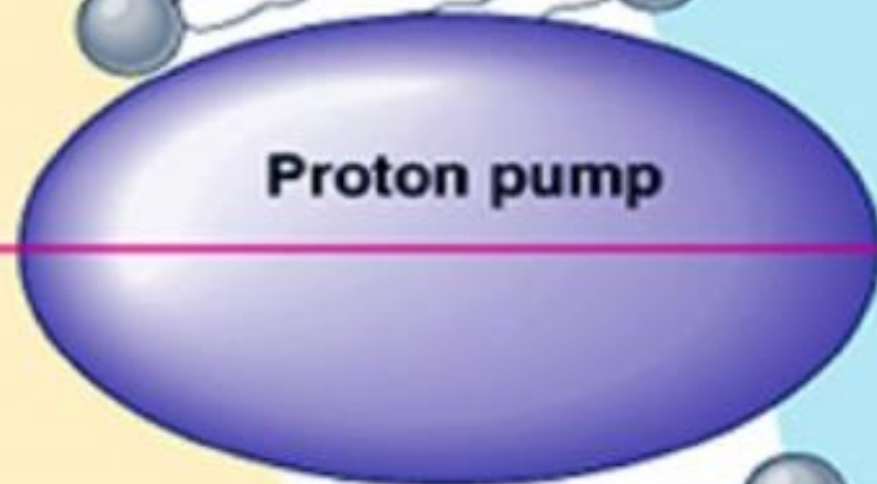
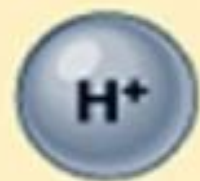
Biological Activities of Benzimidazole Derivatives



DRUGS CONTAIN THIS IMPORTANT RING

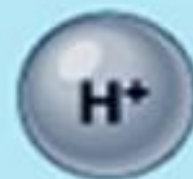
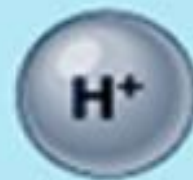
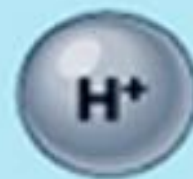
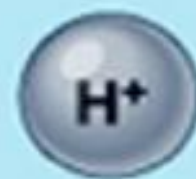
1. The proton-pump inhibitors (antacids) such as Omeprazole.



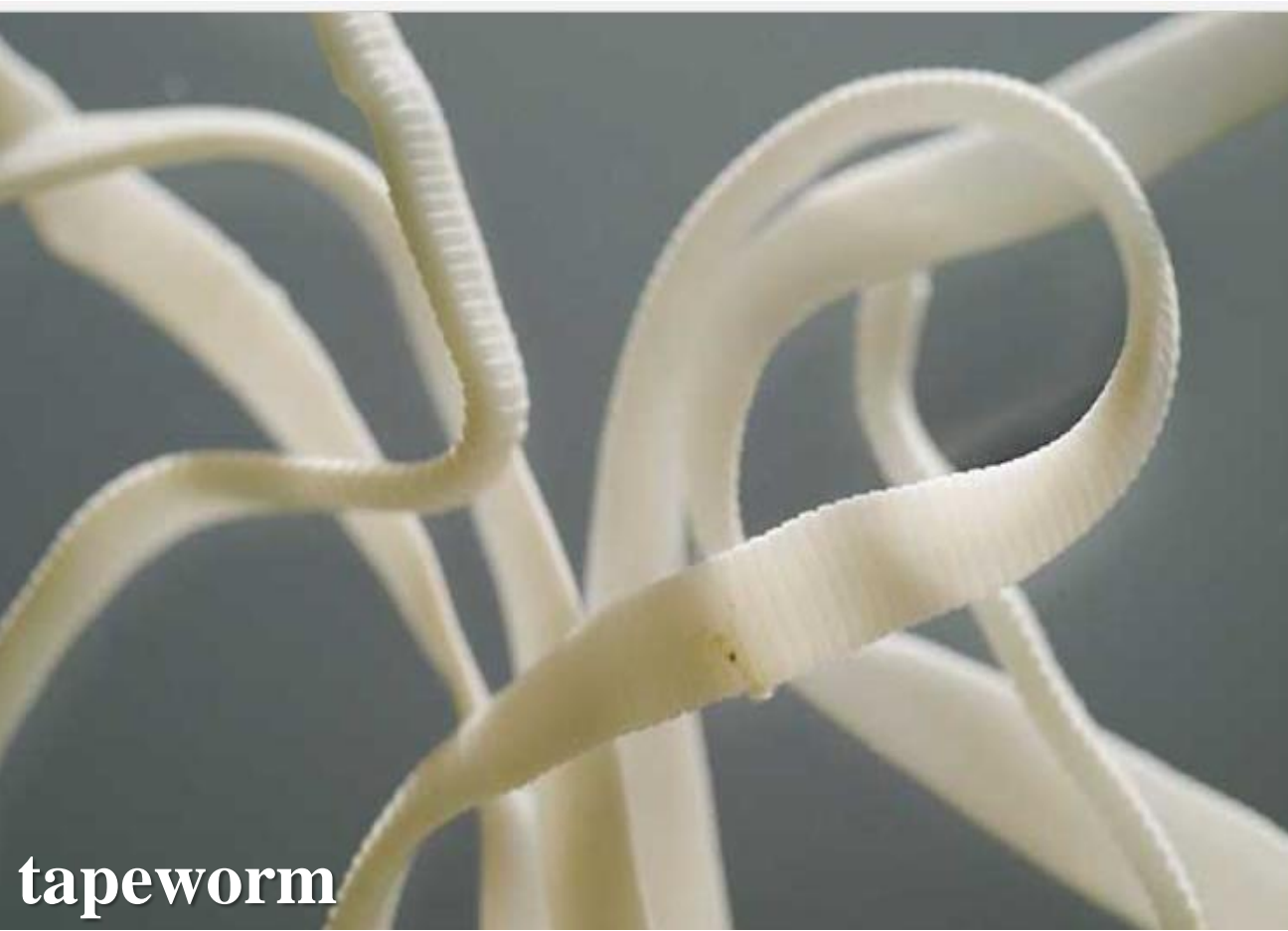


Proton pump

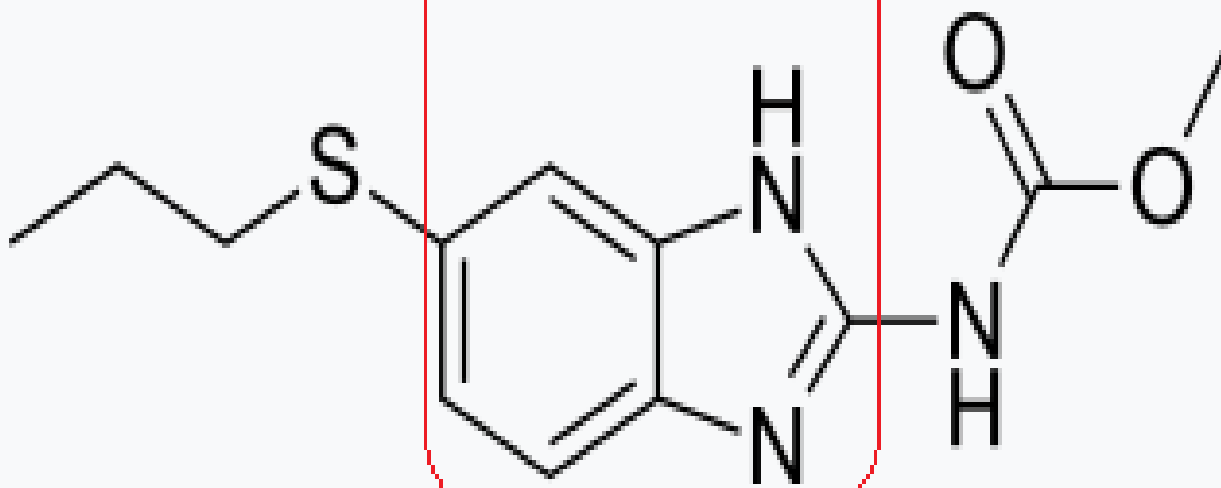
EXTRACELLULAR
FLUID



2. Albendazole Important drug contains this ring, it is used to treatment of a variety of parasitic worm such as tapeworm and pinworm.



**Benzimidazole
moiety**



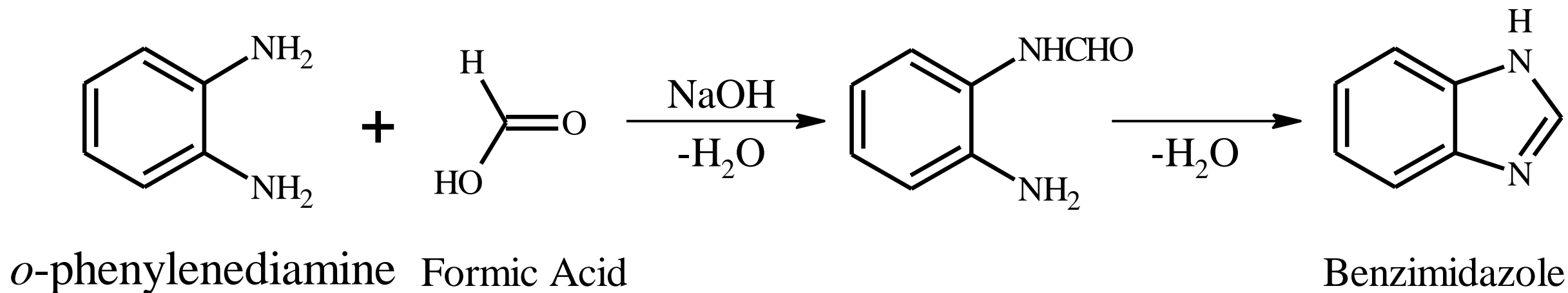
Albendazole

Synthesis Theory:

A simple and efficient procedure for the synthesis of benzimidazole through a one-pot condensation of *o*-phenylenediamines with formic acid in presence of sodium hydroxide at 100°C for two hours. The product is crystallized from water.

Reaction Properties:

- i) Short time
- ii) Easy and quick isolation of prepared compound
- iii) Excellent yields



Synthesis Mechanism:

