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A Novel Method for the Synthesis of Para-hydroxybenzoic Acid

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Abstract — Para-hydroxybenzoic acid is widely used in large amounts in polymerization and co-polymerization reactions in the commercial manufacture of plastics, and in the commercial manufacture of dyes and fungicides. Further certain of its esters, i.e. ethyl and propyl para-hydroxybenzoate, possess anesthetic and antiseptic properties, and are also widely used as preservatives. Till now, para-hydroxybenzoic acid has been prepared by a relatively complicated synthesis. Synthesis was done by using Kolbe-process which involves carboxylation reactions of phenols or sodium phenoxides. As a result, the compound is in limited supply and available only at a relatively high price. The principle object of this invention is to provide a process which may be simply performed, which employs inexpensive materials, and which will provide large amount of para-hydroxybenzoic acid at a reasonable price. The present invention relates to a process for the preparation of para-hydroxybenzoic acid by using acylation of phenols by using phenol, methyl carbamate, sodium hydroxide, different solvents and AlCl3 as catalyst, and the mixture is heated under reflux for 21 hours at a temperature of about 80-100oC. The reaction mixture is cooled. After cooling the reaction mixture is hydrolysed, and then filtered. The filtrate obtained is solid and it is dried. This dried solid is para-hydroxybenzoic acid. The analysis of para-hydroxybenzoic was done on gas-chromatography. About 80% of para-hydroxybenzoic acid was synthesized

Keywords : Acylation, para-hydroxybenzoic acid, alkyl-para-hydroxybezoate, hydrolysis, catalyst

Introduction

Para-Hydroxybenzoic acid, also known as p-hydroxybenzoic acid or 4-hydroxybenzoic acid (PHBA), is a mono-hydroxybenzoic acid, a phenolic derivative of benzoic acid. It is a white crystalline solid that is slightly soluble in water and chloroform but more soluble in polar organic solvents such as alcohols and acetone. 4-Hydroxybenzoic acid is primarily known as the basis for the preparation of its esters, known as parabens, which are used as preservatives in cosmetics and some ophthalmic solutions. PHBA is isomeric with 2-hydroxybenzoic acid, known as salicylic acid, a precursor to aspirin. Para-hydroxybenzoic acid and their derivatives have found a wide applications as food presevatives and stabilizers (antioxidants), as well as for synthesis of liquid crystalline polyethers [1-3].Para-hydroxybenzoic acid can be synthesized by both chemical and biological method. Parabens have been attracting great interest because of their importance in synthetic organic chemistry.Parabens have been widely used as antimicrobial preservative agents in foods, beverages, drugs and cosmetics for more than fifty years due to their broad antimicrobial spectrum, [4]. Paraben are very versatile in terms of food preservatives, differing from the other preservatives such as benzoates, propionates and sorbates because they are not weak acid compounds but have a wide ph range. The antimicrobial activity of parabens is directly dependent on the chain length [5, 6]. In the plant world, 4-hydroxybenzoic acid and its derivatives are commonly found in various vegetable foods, such as barley, strawberries, black currants, peaches, carrots, onions, cocoabeans, vanilla; further in foods prepared from fruit plants such as grapes and fruit juices, yeast extract, wine vinegar and also in cheeses [7]. Methyl paraben found application in the synthesis of dimethyl 4, 4 - (tetraphaioyldioxy) dibenzoates as a reactant for monomer preparation [8]. Methyl and propyl p-hydroxybenzoate are used in Rhamnolipid based formulation for fire suppression and chemical and biological hazards [9] Methyl and propyl p-hydroxy benzoates are used in collagen

or gelatin based crumble as a preservatives [10]. Polyester is a manufactured fiber in which the fiber-forming substance is any long-chain, synthetic polymer composed of at least 85% of an ester of a substituted aromatic carboxylic acid [11]

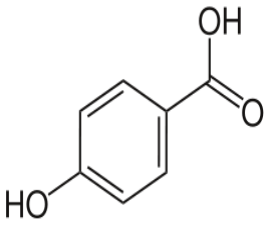

Fig. 1: Structure of Para-hydroxybenzoic acid

Properties of Para-hydroxybenzoic acid: The properties of para- hydroxybenzoic acid is listed in the table below:

Table.1: Properties of para-hydroxybenzoic acid

Chemical Formula	C7H6O3
Molar mass	138.121 g/mol
Appearance	White Crystalline
Odor	Odorless
Density	1.46 g/cm3
Melting point	214.5 °C
Boiling point	n/a decomposes
Solubility in water	0.5 g/100 ml
Solubility	Soluble in alcohol,eter,acetone, slightly soluble in chloroform
log P	1.58

MATERIALS AND METHODOLOGY

Materials

Phenol (CAS No: 108-95-2, white crystalline, molecular formula: C6H5OH, molecular weight: 94.11g/mol, IUPAC name : Phenol or Carbolic acid) , was procured from Thomas Baker (Chemicals) Pvt. Ltd., Mumbai, India. The second chemical used was Methyl Carbamate (CAS No: 598-55-0, white solid, molecular formula : C2H5NO2, molecular weight: 75g/mol,IUPACname :Methyl Carbamate or Methylurethane), was procured from Thomas Baker (Chemicals) Pvt. Ltd., Mumbai, India. AlCl3 catalyst, TS-1 catalyst, Titanium dioxide, and Zinc Oxide (all of AR grade) were obtained from Merck Specialties Pvt. Ltd., Mumbai, India. All chemicals were analytical grades (AR) and were used as received from the suppliers.

Experimental Setup:

The experimental setup based on the synthesis of para-hydroxybenzoic acid consists of three-necked round bottom flask, along with a stirrer, a condenser which is attached to one of its neck, condenser is used for the reflux condition i.e. to reflux the solvent present in the reaction. It also consists the thermostat. Thermostat is used for measuring the temperature of the reaction. This all the apparatus is assembled and the whole setup is kept in the oil-bath for the reaction. The experimental setup is as shown in the figure.

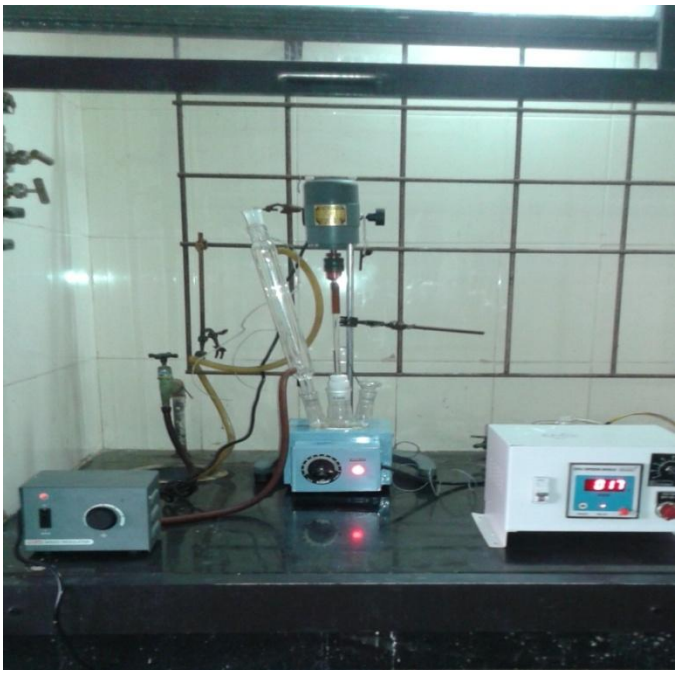

Fig. 2: Schematic representation of the experimental setup

Reaction Mechanism of PHBA

The mechanism for the synthesis of 4-hydroxybenzoic acid consists of three steps. The reaction mechanism is as shown in figure 3. The three steps are as follows:

1. Formation of sodium phenoxide
2. Formation of methyl-4-hydroxybenzoate
3. Formation of 4-hydroxybenzoic acid or Hydrolysis of methyl-4-hydroxybenzoate

Step1: Formation of sodium phenoxide:

In this step phenol is reacted with sodium hydroxide in the presence of toluene and methanol. In this step 23.5 g of phenol is dissolved in 875ml of toluene and 10 g of sodium hydroxide is dissolved in 150 ml of methanol. These two reactants are added together in the three necked round bottom flask. The round bottom flask consists of an overhead stirrer attached to one neck, the second neck is attached to the thermocouple where we get the temperature of the reaction mixture, third neck consists of the distillate condenser attached to it. The

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reaction mixture is stirred continuously till the temperature reaches 110 deg C. All the solvent i.e. methanol and toluene is evaporated and white powder is obtained which is sodium phenoxide

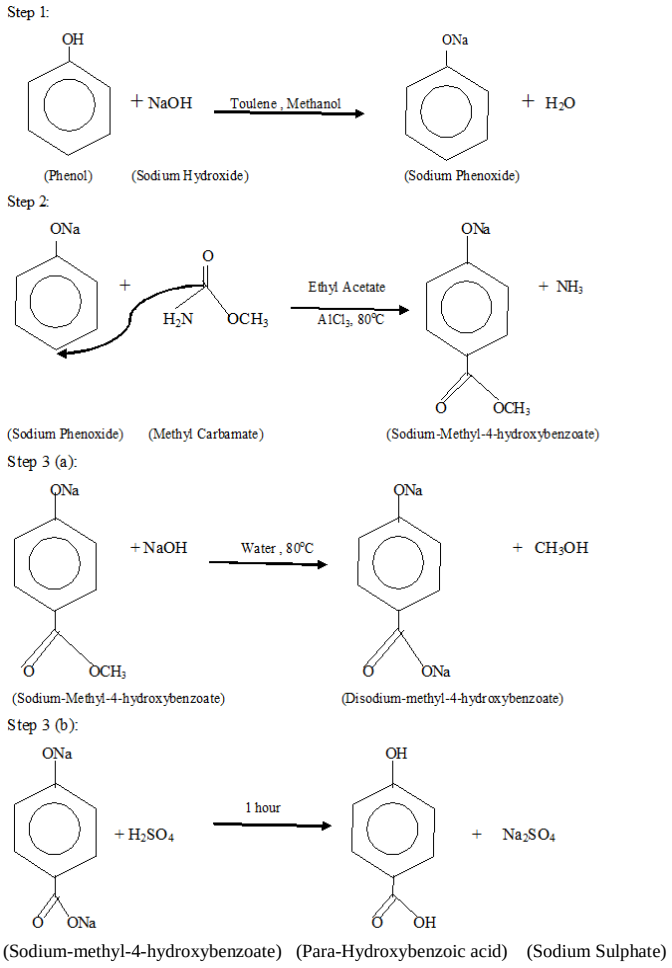

Fig.3: Reaction Mechanism of PHBA

Step 2: Formation of methyl-4-hydroxybenzoate:

In this step the sodium phenoxide obtained in the step 1 is reacted with methyl carbamate in the presence of ethyl acetate as a solvent and catalyst used here is AlCl3 under reflux condition. The molar ratio of the reactants taken is in 1:1 ratio. Catalyst loading is taken 5% of the main reactant. The reaction is stirred continuously under reflux at a temperature of about 80oC to 85oC for about 21 hours. After 21 hours a white precipitate is formed. The powder obtained is known as methyl-4-hydroxybenzoate

Step 3: Formation of para-hydroxybenzoic acid or Hydrolysis of methyl-4-hydroxybenzoate:

In this step the sample obtained in the step 2 ie 1 g of methyl-4-hydroxybenzoate is taken. To this sample 20 ml of 2N NaOH is added. Boil this solution until the solution concentrates to about 10 ml. Cool the solution. Check the pH of the sample it is pure basic. Then acidify it with dilute sulfuric acid. A white precipitate is formed. Filter it and wash it thoroughly with water. Dry the filtrate. Analyze the filtrate that is obtained on gas chromatography and after analysis wegetpara-hydroxybenzoic acid is formed

RESULTS

a) Calibration

A calibration curve is a general method for determining the concentration of a substance in an unknown sample by comparing the unknown to a set of standard samples of known concentration. The concentrations of the analyte and instrument response for each standard can be fit to a straight line, using linear regression analysis .This can be described by the equation y = mx, where y is the instrument response, m represent the sensitivity. Here we have done the calibration for phenol and methyl-para-hydroxybenzoate.

1) Calibration curve for phenol

Table 2: Concentration plot data for phenol

Concentration	Area
0.01	960157
0.03	1026412
0.05	1791519
0.07	3235615
0.09	3611743
0.11	3500879
0.13	4871879
0.15	4795076

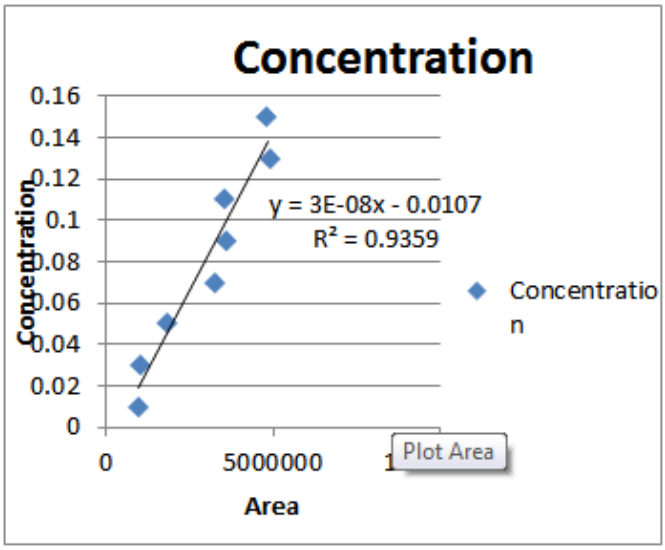

Fig. 4: Area Vs Concentration

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2) Calibration curve for Methyl-Para-hydroxybenzoate

Table 3: Concentration plot data for methyl-para-hydroxybenzoate

Concentration	Area
0.05	232424
0.07	449646
0.09	926937
0.11	1237824
0.13	1534264
0.15	2220952

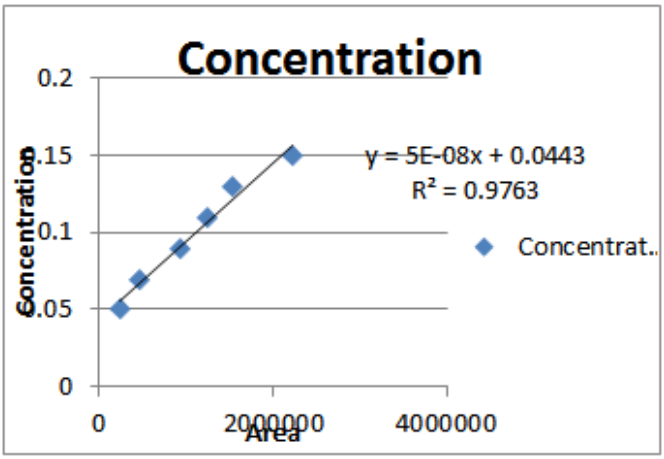

Fig. 5: Area Vs Concentration

b) GC results

➢ Standard Methyl-Para hydroxybenzoate (MPHB)

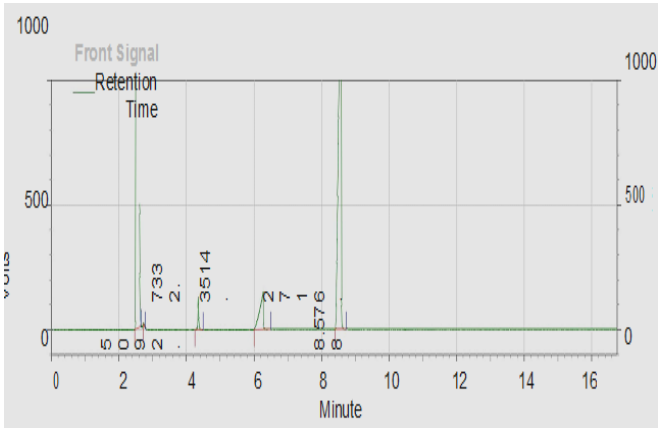

Fig. 6: GC plot for standard MPHB

A standard sample of 1mg/ml of methyl-para-hydroxybenzoate was prepared. This standard sample was run on GC. The peak of the standard was obtained at a retention time of 8.576, the samples obtained in the second step of the reaction was analysed in the same manner and compared with the standard methyl-para-hydroxybenzoate. The graphs obtained for the samples are shown below

i. Sample R20_MPHB

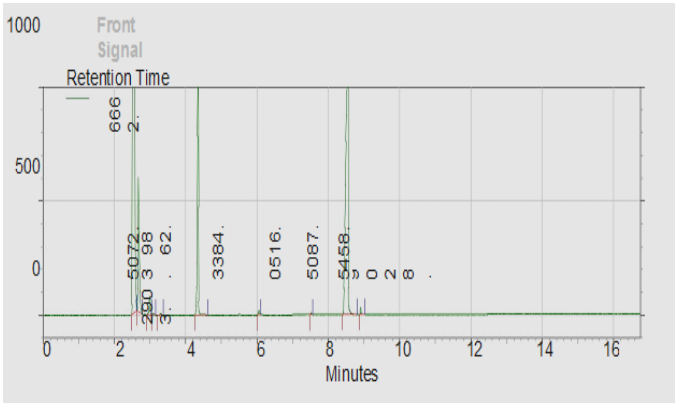

Fig. 7: GC plot for sample R20 for reaction step 2

Calculations: We will find the percentage conversion of MPHB

% Conversion =1 - (Area of std MPHB - Area of the Sample) (Area of std MPHB)

= 1 – (69608425 45079362)

69608425

= 1 - 0.2523

= 0.7477 or 74.77 % MPHB is converted in the synthesized sample

Similarly, other samples were also run and their % in conversion was calculated.

➢ Standard para-hydroxybenzoic acid(PHBA)

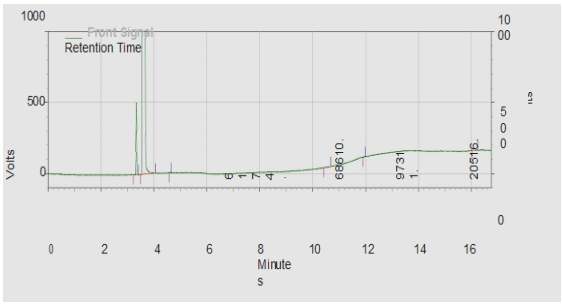

Fig. 8: GC plot for standard PHBA

A standard 0.01 mol of p-hydroxybenzoic acid sample was run on GC. The run is shown in the above graph. The retention time of the standard sample was found to be 11.973, the run taken for different samples are as follows:

i. Sample R20

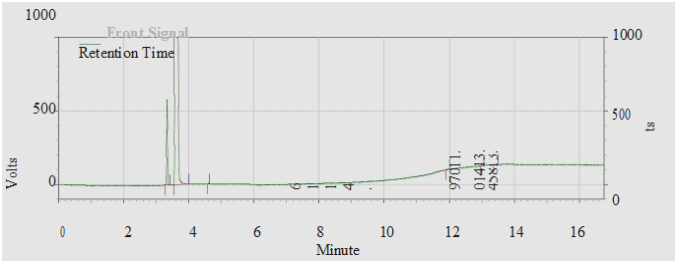

Fig. 9: GC plot for sample R20 for reaction step 3

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ii. Sample R21

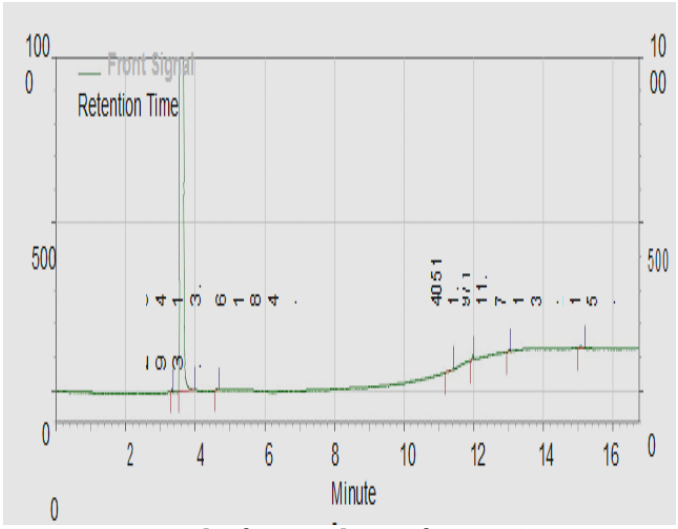

Fig. 10: GC plot for sample R21 for reaction step 3

iii. Sample R22

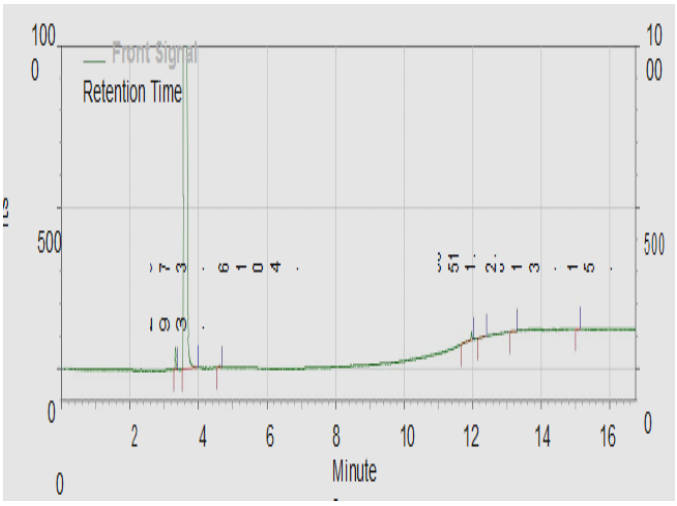

Fig. 11: GC plot for sample R22 for reaction step 3

iv. Sample R23

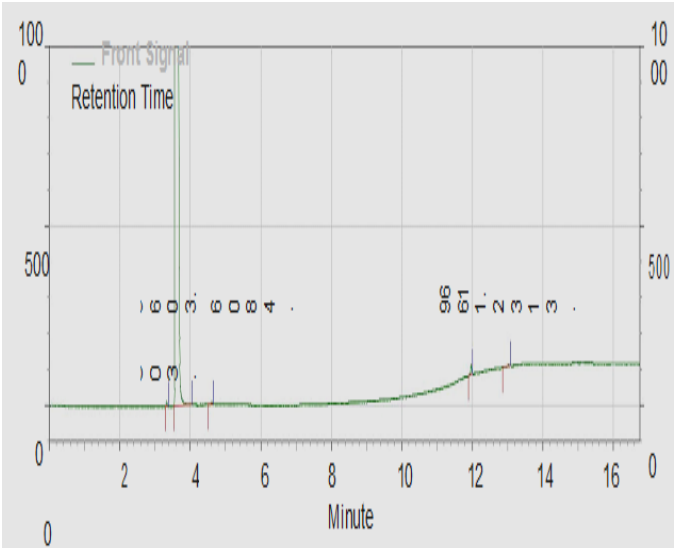

Fig. 12: GC plot for sample R23 for reaction step 3

v. Sample R24

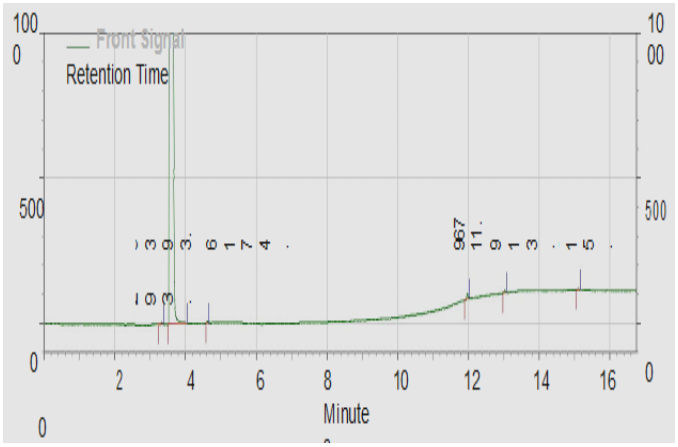

Fig. 13: GC plot for sample R24 for reaction step 3

vi. Sample R25

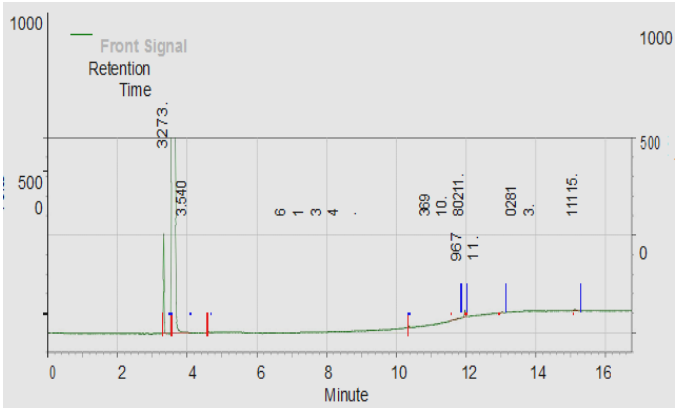

Fig. 14: GC plot for sample R25 for reaction step 3

The conversion of the reactants i.e. phenol and methyl carbamate to para-hydroxybenzoic acid is calculated by the formula

% Conversion = 1— (Area of std PHBA Area of the Sample)(Area of std PHBA)

The calculation for the sample R20 is shown

% Conversion = 1— (Area of std PHBA Area of the Sample)

(Area of std PHBA)

= 1 – (566666 –95715)566666

= 1 –0.831

= 0.169 or 16.9% PHBA is converted in the synthesized sample

Similarly, calculating for the remaining samples, we get the results as shown in following table

sTable 4: % Conversion of PHBA

Sample no.	Area	% Conversion
Standard 0.01 mol PHBA	566666	-------
R20	95715	0.168
R21	223739	0.394
R22	491401	0.867
R23	495121	0.873
R24	501238	0.884
R25	517644	0.913

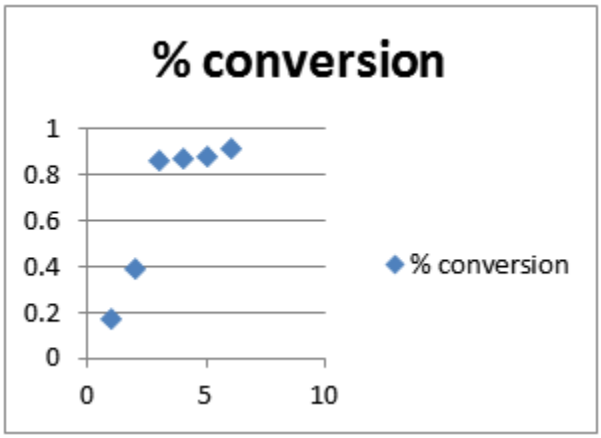

Fig .15: % conversion of PHBA

CONCLUSION

Para-hydroxybenzoic acid is synthesized by using acylation. Carboxylation of phenols was the method which was used uptil now for the synthesis of para-hydroxybenzoic acid. But, acylation is the new and novel method for the synthesis of para-hydroxybenzoic acid. In acylation the reaction between phenol, methyl carbamate, and the acylating catalyst AlCl3 was used. In this reaction a new reactant methyl carbamate was used. By doing the literature survey we understood that uptil now no work is done on methyl carbamate. So we selected this as the reactant, and this was a proposed reaction, and the reaction was successful. First methyl-parahydroxybenzoate was synthesized with a maximum percentage of 75%. After the hydrolysis of methyl-parahydroxybenzoate under specific condition para-hydroxybenzoic acid was synthesized. The maximum percentage of p-hydroxybenzoic acid obtained was 91.4%. Para-hydroxybenzoic is used in large amounts in polymerization reactions in the manufacture of plastics, and in the manufacture of dyes.

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