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International Journal of Pharmacy and Herbal Technology (Online)

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MICROWAVE ASSISTED SYNTHESIS OF BENZOCAINE

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ABSTRACT

The goal of the project is to use microwave technology to synthesise benzocain and evaluate its antibacterial qualities. Benzodiazepines are the best example of anaesthetic agents. According to the protocol, it is made by condensation of amino benzoic acid and HCl with ethanol, a CNS depressant, serving as a solvent. Additional UV spectrum verification of benzocain production. Additional proof for synthesised benzocain was supplied by FTIR. The fluorescence behaviour of the synthesised benzocain was examined. Benzocaine's antibacterial activity against Escherichia coli and Staphylococcus aureus has been verified. In general, green chemistry principles are used in the synthesis of benzocaine, and the use of ethanol assures its safety. The utilization of microwave synthesis for the synthesis of benzocaine and a possible antibacterial drug results in a reduction of both time and cost.

Here, we report a microwave-assisted benzocaine synthesis that makes use of easily accessible precursors and microwave irradiation as the heating medium. The efficacy and adaptability of the microwave-assisted method were demonstrated when the reaction was tuned to provide high yields under moderate circumstances. Using spectroscopic methods, the synthesised benzocaine was characterised, confirming its authenticity and purity.

Keywords HCl, amino benzoic acid, benzocain, ethanol, purity, Reaction, microwave, spectroscopy.

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Received on 06 July, 2024, Accepted 15 July, 2024

Please cite this article as: Anuse Gauri et.al Microwave Assisted Synthesis of Benzocaine International Journal of Pharmacy And Herbal Technology 2024.

INTRODUCTION

A microwave is a type of electromagnetic radiation that operates between 300 to 300,000 MHz, at the lower end of the electromagnetic spectrum. Only molecular rotation, not molecular structure, is impacted in this electromagnetic energy area. However, 2.45 GHz is the appropriate penetration depth for those circumstances [1]. Due to molecules' specific absorption of microwave energy, microwave irradiation has become more and more popular over the past ten years as a potent technique for the quick and effective synthesis of a wide range of compounds. This phenomenon depends on a material's capacity to take in microwave radiation and transform it into heat. Heat is produced when a microwave oscillates molecules across a substance. The entire material is heated by microwave heating at the same rate, simultaneously, quickly, and at a high rate of reaction [2]. Since different materials react differently to microwave radiation, not all materials can be heated by microwaves. Materials that absorb microwaves, such as water, are crucial for microwave chemistry.

"The design, manufacture, and use of chemical products and processes to reduce or eliminate the production and use of hazardous substances" is the definition of "green chemistry." The chemical procedure needs to be reliable, effective, and affordable in order to be approved [3]. "The invention, design, and application of chemical products and processes to reduce or to eliminate generation of hazardous substances" is what constitutes "green chemistry. The acceptability of process chemistry is dependent upon a robust, efficient, and cost-effective chemical process [4]. Green chemistry designs its synthesis schemes with the least possible negative impact on the environment. Conventional methods are extensively documented and employed for a range of chemical synthesises. Microwave-assisted organic synthesis is a new "lead" in the field [5].

Principle Of Microwave Heating

The radio is located within the microwave oven. A microwave oven's radio frequency (RF) operating frequency is roughly 2500 MHz. Radio waves at this frequency have no fascinating characteristics; they quickly transform into atomic sound and subsequently heat[6]

The fundamental mechanism of heating in a microwave oven is the interaction of electromagnetic wavelengths at specific frequencies with reactive material components. Heat is generated by friction or friction and sometimes both when there is electricity.

there based on three mechanisms

Dipolar polarization

The alignment of polar molecules in reaction to an external electric field is known as dipolar polarisation. An electric dipole moment can be produced when the positive and negative charge

in polar molecules, like those found in water or other organic compounds, are separated.[7] These dipoles align with the external electric field when it is applied, causing the material to become net polarise.Dipolar polarisation is important when it comes to microwave heating. When polar molecules, such those found in food, are exposed to microwave radiation, their oscillating electric field allows the molecules to quickly realign themselves to match the shifting field. The constant reorientation causes friction between the molecules, which adds to the process of heating overall by producing heat. One important process by which microwave radiation is transformed into thermal energy inside the substance being heated is dipolar polarisation[8]

Conduction mechanism

Heat is transferred by conduction, which is the direct interaction of molecules within a material. This mechanism involves the transfer of heat energy from hotter to colder locations.

Conduction in solids, such metals, is mainly the movement and vibration of atoms or electrons ton transfer thermal energy. For example, when a metal rod is heated at one end, the atoms or electrons there acquire kinetic energy and start to vibrate more quickly. After colliding with nearby atoms, these vibrating atoms or electrons impart some of their energy to them. This process keeps happening, which causes the heat energy to spread throughout the substance [9].

Interfacial polarization

When exposed to an electric field, polar molecules in a material align and reorient, which is the mechanism of interfacial polarisation. This happens in the context of microwave heating because polar molecules continually spin and realign to fit the direction of the alternating electric field created by the microwave radiation. Because of the constant movement, the material gets heated by molecular friction. Stronger interfacial polarisation is exhibited by materials with greater dipole moments, which leads to more effective heating under microwave radiation[10]

Methodology

Microwave-assisted synthesis is a technique used to accelerate chemical reactions by utilizing microwave irradiation. It's particularly beneficial for reactions that typically require high temperatures and long reaction times. Benzocaine synthesis, as an example, can be conducted using this method.

Setup

Set up a microwave reactor that can handle the specific conditions required for the reaction. Ensure all safety precautions are in place.

Reaction Vessel

Use a suitable reaction vessel that can withstand microwave irradiation. Typically, a microwave-transparent vessel like glass or a specialized microwave reaction vessel is used[11]

Ingredients

Prepare the necessary reagents for benzocaine synthesis. This usually involves p-aminobenzoic acid and ethanolamine or ethylene glycol as starting materials.

Catalyst

If necessary, add a catalyst to the reaction mixture to enhance the reaction rate. Common catalysts for benzocaine synthesis include acids like sulfuric acid or strong bases like sodium hydroxide

Microwave Conditions

Determine the optimal microwave conditions for the reaction. This includes the power level and duration of microwave irradiation. Typically, higher power levels and shorter irradiation times are preferred to minimize side reactions and maximize yield.

Reaction Procedure

Combine the starting materials, catalyst (if used), and any solvent required in the reaction vessel. Mix thoroughly to ensure homogeneity

Microwave Irradiation

Place the reaction vessel in the microwave reactor and irradiate the reaction mixture according to the predetermined conditions.[12]

Monitoring

Periodically monitor the progress of the reaction using analytical techniques such as TLC (thin-layer chromatography) or HPLC (high-performance liquid chromatography). Adjust the reaction time if necessary.

Workup

Once the reaction is complete, allow the reaction mixture to cool to room temperature. Then, carry out the necessary workup procedures to isolate the benzocaine product. This typically involves filtration, solvent evaporation, and purification techniques such as recrystallization [13]

Experimental work

Typically, p-amino benzoic acid and ethanolamine undergo a condensation reaction to produce benzocaine. This is a condensed version of the process [14].

A 100 ml conical flask containing 3 grammes of para amino benzoic acid, 20 ml of ethanol, and 3 grammes of condensation hydrochloric acid (HCl) are used in the procedure.

MWI was applied, and the combination was exposed to 60 seconds of 60% (540W) microwave radiation.[15]

After cooling to room temperature, the reaction product was added to cold water and neutralised with sodium carbonate.

After being removed from the ethanol, the product was filtered, cleaned with water, dried, recrystallized.

IR Spectrum uses synthesised benzocaine further

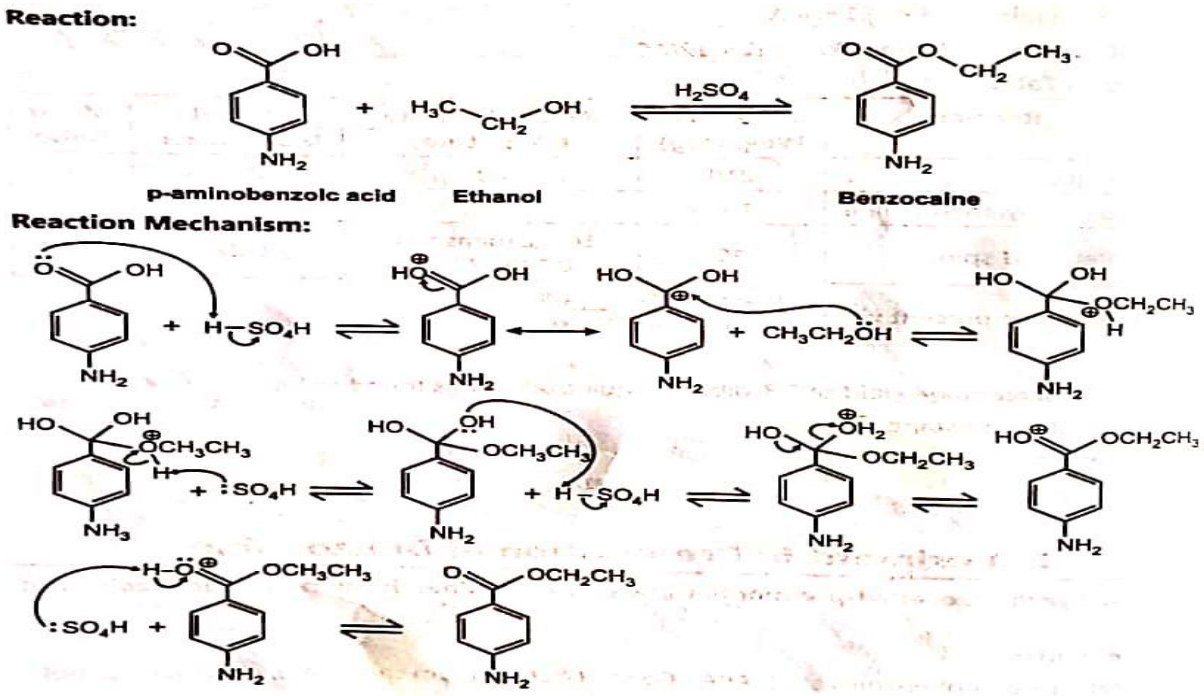

Figure No.1.: Reaction mechanism

Principle

By using an acid-catalyzed nucleophilic acyl substitution process, the Fisher Esterification procedure produces benzocaine by directly converting carboxylic acid and alcohol to ester.

The reaction between an alcohol and a carboxylic acid is reversible but happens very slowly. It takes several days for reflux to reach equilibrium.[16]

It takes a few hours to achieve the same point of equilibrium when 3% of dry hydrogen chloride or concentrated sulfuric acid is introduced to a combination.

Although using too much acid is often convenient, if the acid is pricey, a significant amount of surplus alcohol is typically used instead. Benzocaine is found as sulphate salk because esterification uses sulfuric acid. [17]

Observation Table:

Sr. No	Reactant	Molecular wt.	Quality Taken	Quality Given	Molar Ratio
1	P-amino benzoic acid	137	4g	0.03	1
2	Absolute Alcohol	46	27ML	0.46	15.86
3	Conc.H2SO4	96	5ML	0.09	3.22

Table No.1: Observation table

Calculation

Theoretical yield = 4.81 g

Practical yield = 8

Percentage yield = Practical yield / theoretical yield ×100

= 4.2/4.81×100

Percentage yield = 87.31 %

RESULT

Identification Test of Benzocaine

Sr. No	Test	Observation	Inference
1	Dissolve 0.10 g in 5 mL of water, add 3 drops of hydrochloric acid and 5 drops of iodide	Brown PPT	Test is positive
2	Heat 0.05 g with 2 drops of acetic acid and 4 drops of sulfuric acid .	Odour produced	Test is positive
3	About 0.35 g yields the reaction described for the identification of primary aromatic amines.	Orange-red colour	Test is positive

Table No.2: Identification Test

Observation Assay of Benzocaine

Sr. No	Titration	Burette Reading		Mean
		Initial	Final	
1	Sample: 0.3 gm of benzocaine dissolve in 50 ml of HCL titrate with sodium nitrate.	0.0ml	17ml	**17 ml**
2	Blank: 50ml HCL titrate with sodium nitrate	0.0ml	33ml	**33ml**

Table No. 3: Assay

Colour	White
Apperance	White,crystalline powder
Odour	Odourless
State	Solid
Solubility	Soluble in organic solvent like ethanol, chloroform
Melting Point	88-90^{0}C
PKA Determination	2.5
Density	1.17g/cm^{3}at20^{0}C
Molecular Weight	165.19g/mol
PH	7.0-7.5
Rf value	0.34

Table No.4: Preliminary test of benzocaine

DISCUSSION

Microwave-assisted synthesis of benzocaine has been a topic of research aimed at improving efficiency and sustainability in pharmaceutical manufacturing

Microwave irradiation accelerates the reaction kinetics by rapidly and uniformly heating the reaction mixture. This can lead to significantly shorter reaction times compared to conventional heating methods. Research has demonstrated that microwave-assisted reactions can be completed in minutes to hours, which is much faster than traditional methods that may take several hours to days.

Studies have shown that microwave irradiation can enhance the yield of benzocaine synthesis. Higher yields are often attributed to the efficient heating that minimizes side reactions and promotes the formation of desired products. Microwave-assisted synthesis can lead to products with high purity levels. The controlled heating conditions help to maintain the integrity of the molecular structure and reduce impurities in the final product.

Researchers have investigated the mechanistic aspects of microwave-assisted reactions. Understanding the specific effects of microwave irradiation on the reaction pathway and intermediate species can provide insights into optimizing reaction conditions for benzocaine synthesis. Comparative studies have been conducted to evaluate the efficiency and cost-effectiveness of microwave-assisted synthesis versus traditional methods

CONCLUSION

Organic synthesis has been revolutionised by microwave assisted methods. Consequently, this methodology has swiftly acquired recognition as an advantageous instrument for expediting the procedures involved in drug discovery and development. The best example of an anaesthetic agent is benzocaine. The process described in the study calls for the condensation of amino benzoic acid and HCl with ethanol serving as a solvent and acting as a CNS depressant.Amino benzoic acid and HCl condense to produce benzocain. UV spectra confirm the further synthesised benzocain. FTIR provides more proof of the synthesised benzocain. The synthetic benzocain huorescence behaviour was studied. It has been confirmed that benzocain has antibacterial activity against Staphylococcus aureus and Escherichia coli. Overall, the synthesis of benzocain involves the use of green chemistry principles, and the usage of ethanol ensures its safety.

The produced substances underwent antibacterial activity testing. 10µg, 15µg, and 30µg of the substance per millilitre were tested for antibacterial activity. A quarter of the synthesised compounds (30 µg/ml) exhibited gand antimicrobial activity against gramme positive (Bacillus cereus, Staphylococcus aureus), gramme negative (Ecoli, Pseudomonus aeruginosa), and fungal strains (Aspergillus fumigates, Aspergillus niger), and were more potent than standard.

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