

## COMPARATIVE STUDY OF MICROWAVE-INDUCED AND CONVENTIONAL SYNTHESIS OF SELECTED COMPOUNDS

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### ABSTRACT

Microwave-assisted organic synthesis (MAOS) has emerged as a promising and efficient approach in modern organic chemistry. This technique offers a clean, simple, rapid, and economical alternative for the synthesis of a wide range of organic molecules. Conventional synthesis methods generally require prolonged heating, complex setups, and large amounts of solvents and reagents, which increase costs and contribute to environmental pollution. In contrast, microwave-assisted synthesis supports the principles of green chemistry by minimizing reaction time, energy consumption, and waste generation. In the present study, microwave-induced and conventional synthesis methods were compared for selected organic compounds. The microwave reactions were carried out using a microwave synthesizer, and the resulting products were purified according to literature-reported work-up procedures and recrystallized using appropriate solvents. Reaction progress was monitored periodically—at short intervals for microwave-assisted reactions and at hourly intervals for conventional methods. The comparative results demonstrated the efficiency, simplicity, and environmental advantages of microwave-assisted organic synthesis over traditional techniques.

**KEYWORDS:** Conventional method, green chemistry, combinatorial chemistry, microwave reactions.

### INTRODUCTION

Microwave-assisted synthesis is a branch of green chemistry. Microwave-assisted synthesis has gained much attention in recent years. Microwave irradiation assisted chemical transformations are pollution free, eco-friendly and offer high yields together with simplicity in processing and handling.<sup>[1-5]</sup>

Heating reactions with traditional equipment, such as oil baths, sand baths and heating mantles, is not only slow but it creates a hot surface on the reaction vessel where products, substrates and reagents often decompose over time. Microwave energy, in contrast, is introduced into the chemical reactor remotely and passes through the walls of the reaction vessel, heating the reactants and solvents directly. Microwave dielectric heating drives chemical reactions by taking advantage of the ability of some liquids and solids to transform electromagnetic radiation into heat wherein chemical reactions are accelerated because of selective absorption of microwave energy by the polar molecules.<sup>[6]</sup> A properly designed vessel allows the temperature increase to be uniform throughout the sample, leading to fewer by-products and/or product decomposition. The use of microwave energy instead of conventional heating often results in good yields in a short time as compared with reaction by classical synthetic methods.<sup>[7-9]</sup>

Nowadays, microwave-assisted organic synthesis is gaining widespread acceptance in drug discovery laboratories. The rapid acceptance of this technology parallels the rising cost of R&D and decrease in the number of Food and Drug Administration (FDA) approvals, which have led to what is termed as a productivity crisis. Reducing the cost of failure, either by failing candidates sooner or by improving the overall probability of success, is the most powerful solution to improving R&D productivity. Microwave technology, by accelerating chemical reactions from hours or days to minutes, provides quick results. From time to time, microwave heating enables chemistries that were not previously possible by classical methods, expanding the realm of structures accessible to the chemist.<sup>[10]</sup>

Microwave induced organic reactions have emerged as a new 'Lead' in organic synthesis. The microwave enhanced chemical reactions are gaining importance due to the advantages and environmental friendly processes they offer, as compared to conventional reactions.<sup>[11,12]</sup>

Conventional methods of organic synthesis usually need longer heating time, elaborate and tedious procedures which result in higher cost of process and the excessive use of solvents, reagents leads to environmental pollution. Pharmaceutical chemistry laboratories use large quantities of toxic chemicals and solvents to perform reactions exposing laboratory persons including students and environment to related hazards.

In our laboratory, as part of our project, we have synthesized some selected heterocyclic molecules using microwave induced methods.<sup>[13,14,15]</sup> The Microwave technique was performed in domestic microwave oven (BAJAJ 1701 MT DLX) for synthesizing selective heterocyclic molecules. Similarly, the conventional synthesis of same were performed and compared with microwave induced synthesis method. It was found that the reaction time was comparatively less from hrs to mins and the % yield were found to be higher when compared to conventional method.

Each time the products were isolated, the % yield and quality of the products was compared with the one obtained by conventional method. Each reaction was repeated at least three times (different time intervals) and the products by studying their melting point and percentage yield the comparative results were tabulated in the Table No:1.

## MATERIAL AND METHODS

All reagents used were of synthetic grade. Melting point were recorded by open capillary method and are uncorrected. Experimental were performed using microwave synthesizer (catalyst). Comparatively the reactions were performed using conventional methods of synthesis using reflux condenser. The reactions were monitored with silica gel G at specific hours of synthesis. The time for the conventional and microwave assisted synthesis were noted.

**General procedure****1. 3,4-DIHYDRO-1-HYDROXY-4-OXOPHTHALAZINE<sup>[16]</sup>****Conventional Method****PROCEDURE**

A mixture of hydrazine hydrate (5.5 g) and phthalic anhydride (3 g) in ethanol (25 mL) was taken in a 100 ml round bottomed flask. The mixture was heated on water bath at 100 °C for half hour. Then, the mixture was cooled and filtered and then washed by petroleum ether (3 x 40 mL). The volume of solvent was reduced, and the mixture was kept at room temperature, a solid separated out was filtered and recrystallized.

**Microwave Method**

**The beaker was then placed in a domestic microwave oven (BAJAJ 1701 MT DLX) at 190 watts for 6 minutes**

A mixture of hydrazine hydrate (5.5 g) and phthalic anhydride (3 g) in ethanol (25 mL) was taken in a beaker and was then placed in a domestic microwave oven (BAJAJ 1701 MT DLX) at 190 watts for 6 minutes. Then, the mixture was cooled and filtered and then washed by petroleum ether (3 x 40 mL). The volume of solvent was reduced and the mixture was kept at room temperature, a solid separated out was filtered and recrystallized.

**2. 3-METHYL-1-PHENYL-5-PYRAZOLONE<sup>[17]</sup>****Conventional Method**

PROCEDURE: - A mixture of phenyl hydrazine (5.4 g; 6.35 mL) and Ethyl acetoacetate (6.4 g; 4.9 mL) was taken in a 100 ml round bottomed flask. The mixture was heated under reflux at 120 °C for 1 hour. Then, the mixture was cooled, the red oily solution was obtained, then the ether (50 mL) was added with constant stirring so that the product gets solidified. The precipitate obtained was filtered and recrystallized from aqueous ethanol (50%)

**Microwave Method**

PROCEDURE: - A mixture of phenyl hydrazine (5.4 g; 6.35 mL) and Ethyl acetoacetate (6.4 g; 4.9 mL) was taken in a 100 ml beaker. The mixture was then placed in a domestic microwave oven (BAJAJ 1701 MT DLX) at 190 watts for 6 minutes. Then, the mixture was cooled, the red oily solution was obtained, then the ether (50 mL) was added with constant stirring so that the product gets solidified. The precipitate obtained filtered and recrystallized from aqueous ethanol (50%).

**3. 7-HYDROXY-4-METHYL COUMARIN<sup>[18]</sup>****Conventional Method**

PROCEDURE: - A mixture of resorcinol (5.5 g) and Ethyl acetoacetate (6.5 g) with sulphuric acid (50 mL, 75%) was taken in a 100 ml round bottomed flask. the mixture was heated on water bath at 100 °C for half hour. the dark green solution obtained was cooled and added in crushed ice with constant stirring. the precipitate obtained was filtered and washed with cold water. (100 mL). The precipitate obtained was filtered and recrystallized from methanol.

**Microwave Method**

PROCEDURE: - A mixture of resorcinol (5.5 g) and Ethyl acetoacetate (6.5 g) with sulphuric acid (50 mL, 75%) was taken in a 100 ml beaker. The mixture was then placed in a domestic microwave oven (BAJAJ 1701 MT DLX) at 190 watts for 6 minutes. The dark green solution obtained was cooled and added in crushed ice with constant stirring. the precipitate obtained was filtered and washed with cold water. (100 mL). The precipitate obtained was filtered and recrystallized from methanol.

#### 4. HYDANTOIN, OR GLYCOLYLUREA<sup>[19]</sup>

##### Conventional Method

**PROCEDURE:** - Step I- A mixture of hydantoic acid and Aq. NaOH solution was added to a mixture of glycine and urea in a R.B.F. The mixture was shaken well and heated at 110-115°C for 1 hr. Then it was cooled to 60°C and then acidified with conc. HCl to congo red after that the product obtained was filtered out, washed & recrystallized with methanol.

Step-2: Preparation of hydantoin A mixture of hydantoin acid (1 gm), conc. HCl and water was heated at 110-115°C for 15 min. A solid product was formed which was separated, filtered, and recrystallized from water.

**Microwave Method: Step I-** A mixture of hydantoic acid and Aq. NaOH solution was added to a mixture of glycine and urea in a R.B.F. The mixture was then placed in a domestic microwave oven (BAJAJ 1701 MT DLX) at 190 watts for 6 minutes. Then it was cooled to 60°C and then acidified with conc. HCl to congo red after that the product obtained was filtered out, washed & recrystallized with methanol.

**Step-2: Preparation of hydantoin:-**A mixture of hydantoin acid (1 gm), conc. HCl and water was placed in beaker and kept in microwave for 3 mins. A solid product was formed which was separated, filtered and recrystallized from water.

#### 5. METHYL SALICYLATE [OIL OF WINTERGREEN]<sup>[20]</sup>

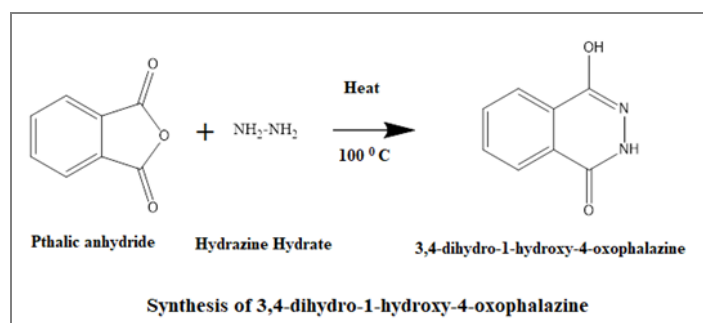
##### Conventional Method

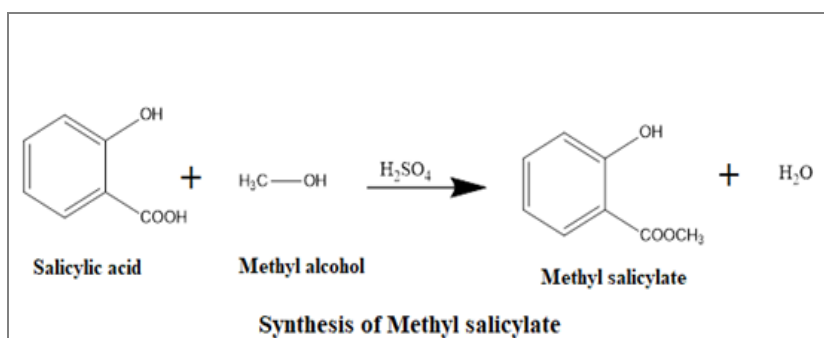
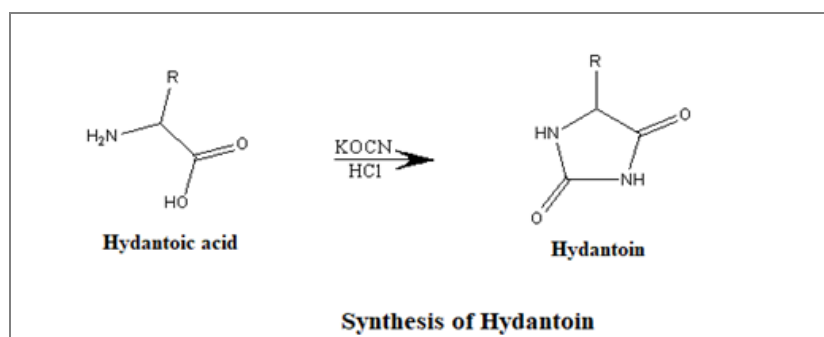
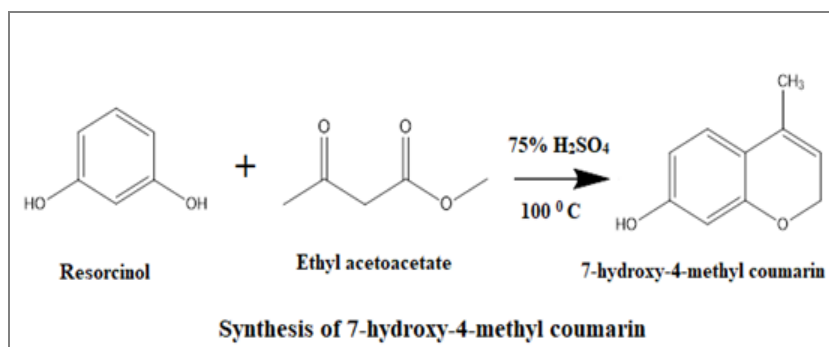
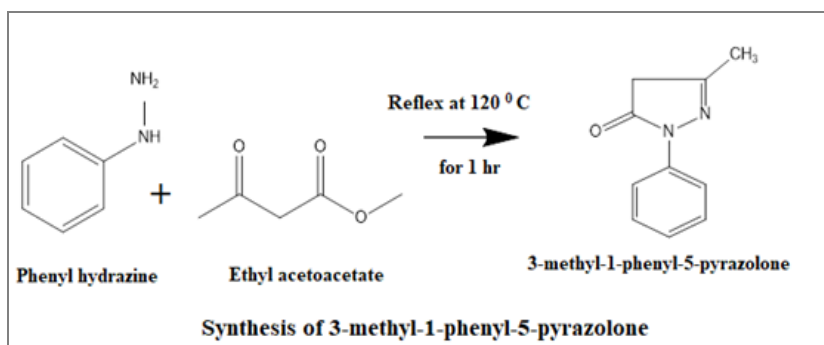
**PROCEDURE:** - A solution of salicylic acid (17 gm) absolute methyl alcohol (30 mL) and conc. H<sub>2</sub>SO<sub>4</sub> (5 mL) was refluxed for 3 hr under anhydrous condition. Excess ethanol was removed by distillation (steam bath) and then the residual product was poured into water. The obtained Methyl salicylate was extracted with ether. The ether extract was washed with Na<sub>2</sub>CO<sub>3</sub> solution (till free of acid) and finally with water. It was dried and distilled. Characteristic smell of methyl salicylate (oil of Wintergreen) was obtained from the product.

##### Microwave Method

**PROCEDURE:** - A solution of salicylic acid (17 gm) absolute methyl alcohol (30 ml) and conc. H<sub>2</sub>SO<sub>4</sub> (5 mL) was kept in microwave oven for 3 mins. Excess ethanol was removed by distillation (steam bath) and then the residual product was poured into water. The obtained Methyl salicylate was extracted with ether. The ether extract was washed with Na<sub>2</sub>CO<sub>3</sub> solution (till free of acid) and finally with water. It was dried and distilled. Characteristic smell of methyl salicylate (oil of Wintergreen) was obtained from the product.

##### Reaction





**Table 1: Yields, Melting points and total reaction time for synthesised pharmaceutical compounds.**

| Name of the compound                    | % yield from MWI | Time taken by conventional synthesis in min/hours | Time taken by MWI in minutes |
|-----------------------------------------|------------------|---------------------------------------------------|------------------------------|
| 3,4-dihydro-1-hydroxy-4-oxophthalazine  | 92               | 30 (half hr)                                      | 6                            |
| 3-methyl-1-phenyl-5-pyrazolone          | 80               | 1 hr                                              | 6                            |
| 7-hydroxy-4-methyl coumarin             | 86               | 30 (half hr)                                      | 6                            |
| Hydantoin                               | 94               | Step I: 1 hr<br>Step II: 15min                    | Step I: 6<br>Step II: 3      |
| Methyl salicylate (oil of wintergreen). | 78               | 45                                                | 10                           |

## CONCLUSION

From the above results, the microwave aid technique may be inferred that the synthesis of a large number of organic medicinal molecules is an efficient, quick, easy, and environmental friendly approach. Furthermore, the yield is enhanced. Thus the synthesis of medicinal products, intermediates and chemicals is a realistic and feasible approach.

For the synthesis of a variety of organic compounds, the approach offers a clean, simple, efficient, quick and environmentally friendly process, with new tools in organic synthesis. The time taken to synthesize the microwave synthesis is substantially decreased. This technique has an important benefit, which includes a fast speed of reaction time with improved yield and product quality. The approach to green chemistry is viewed as essential since that technology is more environmentally friendly and usable in the laboratory and might have a major influence on combinatory chemistry, screening, medicinal chemistry and drug discovery.

From comparing this, we can notice, in comparison to the usual technique, that produced synthetic chemicals by microwave is a greener way. So we may conclude that green synthesis aided by Microwave is an excellent approach in green chemistry, governing a multi-nominated organic reaction flexible platform.

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