MICROWAVE-ASSISTED SYNTHESIS: NEED OF THE HOUR

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ABSTRACT

Objective: Main purpose of our study was to explore and establish the utility and opportunities of microwave technology in carrying out common organic reactions like esterification, hydrolysis, benzoin condensation, benzilic acid rearrangement, Wolf-Kishner reduction and Cannizzaro reaction. Our aim was to use an environment-friendly green chemistry approach in carrying out the reactions, thus causing less exposure to hazardous chemicals. Methods: Conventional synthesis of the organic reactions was performed according to established synthetic procedures in literature. Microwave-assisted synthesis was carried out in CEM Discover Microwave Synthesizer and three parameters were closely monitored: temperature, reaction time and microwave irradiation power. Proper control of these three parameters yielded the desired products in a lesser time with higher yield and purity, as compared to that of conventional synthesis. Results: The synthesized compounds were characterized based on their physicochemical properties (state, colour, melting point, boiling point, thin layer chromatography (TLC) and spectroscopic data (UV, FTIR). The products obtained by microwave synthesis complied with that of conventional method, but with higher purity, better yield, lesser reaction time and less exposure to hazardous chemicals. Conclusion: Some common organic reactions were successfully exercised using microwave irradiation giving higher purity and better yield of the products as compared to that of conventional synthesis in a shorter span of time. Thus, we successfully carried out our synthetic work and believe that microwave-assisted synthesis will greatly help the scientific community, specially the students to perform complex organic reactions in a simple manner in the coming days.
KEYWORDS: Microwave-assisted synthesis, conventional, hazardous, purity, environment-friendly.

INTRODUCTION
Microwave-assisted organic synthesis is an invaluable technology for medicinal chemistry and drug discovery applications since it greatly reduces reaction time, typically from days or hours to minutes or even seconds.\(^1\) Many reaction parameters can be evaluated in a few hours to optimize the desired chemistry and it allows for the discovery of novel reaction pathways, which serve to expand ‘chemical space’ in general, and ‘biologically relevant, medicinal chemistry space’ in particular.\(^2\) We have carried out both traditional and microwave-assisted synthesis of common organic reactions like esterification,\(^3\) hydrolysis,\(^4\) benzoin condensation,\(^5\) benzilic acid rearrangement,\(^6\) Wolf-Kishner reduction\(^7\) and Cannizzaro reaction.\(^8\) Our aim was to use an environment-friendly green chemistry approach in carrying out the reactions, thus causing less exposure to hazardous chemicals.

MATERIALS AND METHODS
Conventional synthesis of the organic reactions was performed according to established synthetic procedures in literature. Microwave-assisted synthesis was carried out in a CEM Discover Microwave Synthesizer and three parameters were closely monitored: temperature, reaction time and microwave irradiation power. Proper combination of these three parameters which gave optimum yield of the desired compounds was taken as the reaction conditions for microwave-assisted synthesis. All reagents used for the work were of synthetic grade. The synthesized compounds were characterized based on their physicochemical properties (state, colour, solubility, melting point, boiling point, TLC and spectroscopic data (UV, FTIR). Melting and boiling points were recorded on a BUCHI M-560 melting point apparatus in open capillary tubes and are uncorrected. Purity of the compounds was checked by TLC using Silica Gel-G coated TLC plates and visualized in iodine chamber. UV (\(\lambda_{\text{max}}, \text{nm}\)) was recorded on LABINDIA UV-3200 spectrophotometer and IR spectra (\(\bar{\nu}_{\text{max}}, \text{cm}^{-1}\)) of the synthesized compounds were recorded on BRUKER ALPHA-T FTIR spectrometer.

Synthesis of Phenyl Acetate (Esterification Reaction)

Conventional: 30 ml ethanol, 2 ml conc. HCl and 6 g benzoic acid were mixed together in a RBF and refluxed for 2 h 15 min at 40-45\(^0\)C. Excess alcohol was removed by heating on
water bath. The mixture was then cooled in an ice bath and 10% Na2CO3 added to neutralise excess acid. Then the mixture was transferred into a separating funnel, lower layer discarded and dried with anhydrous MgSO4. A thick oily colourless solution with a fruity smell was obtained. [9]

**Microwave:** The same reaction was carried out in microwave synthesizer at 85 °C temperature, 150 Watt power for 3 min 30 s using equimolar quantity of the reactants.

![Scheme 1: Esterification Reaction](image)

**Synthesis of Ethyl Benzene (Wolf-Kishner Reduction)**

**Conventional:** 10 ml acetophenone, 30 ml diethylene glycol, 9 ml hydrazine hydrate and KOH pellets were taken in a RBF and refluxed for 1.5 h at 70-75 °C. The reaction mixture was cooled to room temperature, transferred to a separating funnel and lower aqueous layer was discarded. The aqueous layer was again transferred to a separating funnel and extracted with 10 ml ether. The reaction mixture was heated on water bath to remove excess ether. The resultant mixture was dried with anhydrous MgSO4 and a yellowish solution with gasoline-like smell was obtained. [10]

**Microwave:** Ethyl benzene was synthesized under microwave irradiation in 5 min at 110 °C temperature and 160 Watt power using same quantity of the reactants as that in conventional synthesis.
Synthesis of Benzyl Alcohol (Hydrolysis Reaction)

**Conventional:** 15 g benzyl chloride in NaOH solution (4 g in 10 ml) was taken in a RBF and refluxed for 1 h at 40-48 °C. 10 ml conc. H2SO4 was added through the condenser during the reaction. A colourless solution was obtained which was later dried with anhydrous MgSO4 to yield the pure compound.

**Microwave:** The same reaction was carried out in microwave synthesizer in equimolar quantity at 65 °C temperature and 160 Watt power for 6 min.

Synthesis of Phenyl Methanol (Cannizzaro Reaction)

**Conventional:** 5 g KOH dissolved in 15 ml of water was cooled in an ice bath. 16 ml benzaldehyde was then added it. The reaction mixture was shaken until it converted to a thick emulsion. It was then poured into a RBF and refluxed at 40-48 °C for 3 h 30 min. The reaction mixture was poured in a separating funnel and extracted with ether twice. The lower layer was discarded and heated on a water bath to remove excess ether. The reaction mixture
was then cooled and shaken with 5 ml sodium bisulfide solution to remove excess benzaldehyde. The powder was dried with anhydrous MgSO4 to yield the final product. 

**Microwave:** Cannizzaro reaction was successfully carried out in microwave synthesizer in 8 min at 90 °C temperature and 150 Watt power.

![Scheme 4: Cannizzaro Reaction.](image)

**Synthesis of Benzil (Benzoin Condensation)**

**Conventional:** 4 g crude benzoin mixed with 20 ml conc. HNO3 was taken in a RBF and refluxed at 50-55 °C for 1.5 h with occasional stirring for complete evolution of nitrogen oxide gas. The reaction mixture was poured into 50 ml cold water for complete crystallisation. A yellowish solid obtained was later recrystallized from ethanol to obtain the pure compound. 

**Microwave:** Benzil was synthesized in microwave using same proportion of the reactants at 80 °C temperature and 155 Watt power in 2 min 30 s.

![Scheme 5: Benzoin Condensation](image)
Synthesis of Benzilic Acid (Benzilic Acid Rearrangement)

Conventional: A solution of 10 g KOH in 70 ml of water, 30 ml rectified spirit and 5 g recrystallized benzil was taken in a RBF. A deep bluish black colour was produced. The reaction mixture was then heated at 55 °C for 1 h and kept into a porcelain dish overnight. Potassium salt of benzilic acid crystallised out. It was then dissolved in 10 ml water containing 2 ml conc. HCl. A red brown precipitate was obtained which was recrystallized from methanol to get the desired pure product.

Microwave: The same reaction was performed in 7 min at 77 °C temperature and 155 Watt power under microwave irradiation.

\[ \text{Benzil} + \text{KOH} \rightarrow \text{Benzilic Acid} \]

Scheme 6: Benzilic Acid Rearrangement

RESULTS AND DISCUSSION

The products obtained by microwave-assisted synthesis complied with that of conventional method, but with higher purity, better yield, lesser reaction time and less exposure to hazardous chemicals. Microwave reactions were exercised at higher temperatures as compared to conventional synthesis to obtain the desired products. Physicochemical properties of the synthesized compounds is presented in Table 1.
Table 1: Physicochemical and spectral analysis of the synthesized compounds

<table>
<thead>
<tr>
<th>Compound</th>
<th>State and Colour</th>
<th>Solubility</th>
<th>M.P / B.P (^{(0)\text{C}})</th>
<th>Rf</th>
<th>% Yield</th>
<th>UV (\lambda_{\text{max}}) (nm)</th>
<th>FTIR (cm(^{-1}))</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phenyl Acetate</td>
<td>Colourless liquid</td>
<td>Chloroform</td>
<td>196-198</td>
<td>194-196</td>
<td>0.73</td>
<td>0.77</td>
<td>69 76</td>
</tr>
<tr>
<td>Ethyl Benzene</td>
<td>Yellow liquid</td>
<td>Acetone, Ethanol</td>
<td>133-137</td>
<td>135-139</td>
<td>0.83</td>
<td>0.76</td>
<td>58 74</td>
</tr>
<tr>
<td>Benzyl Alcohol</td>
<td>Colourless liquid</td>
<td>Acetone, Methanol</td>
<td>196-200</td>
<td>191-193</td>
<td>0.67</td>
<td>0.73</td>
<td>68 76</td>
</tr>
<tr>
<td>Phenyl Methanol</td>
<td>Colourless liquid</td>
<td>DMSO</td>
<td>201-206</td>
<td>196-198</td>
<td>0.75</td>
<td>0.70</td>
<td>65 68</td>
</tr>
<tr>
<td>Benzil</td>
<td>Yellow solid</td>
<td>Ethanol</td>
<td>95-99</td>
<td>97-99</td>
<td>0.80</td>
<td>0.83</td>
<td>70 79</td>
</tr>
<tr>
<td>Benzilic Acid</td>
<td>Brown solid</td>
<td>Water</td>
<td>143-148</td>
<td>144-146</td>
<td>0.68</td>
<td>0.69</td>
<td>67 78</td>
</tr>
</tbody>
</table>

A: Conventional Synthesis, B: Microwave-assisted synthesis
Table 2: Comparison between the reaction temperature and reaction time of conventional and microwave-assisted synthesis.

<table>
<thead>
<tr>
<th>Compound</th>
<th>Reaction Temperature (°C)</th>
<th>Reaction Time</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>a</td>
<td>b</td>
</tr>
<tr>
<td>Phenyl Acetate</td>
<td>40-45</td>
<td>85</td>
</tr>
<tr>
<td>Ethyl Benzene</td>
<td>70-75</td>
<td>110</td>
</tr>
<tr>
<td>Benzyl Alcohol</td>
<td>40-48</td>
<td>65</td>
</tr>
<tr>
<td>Phenyl Methanol</td>
<td>40-48</td>
<td>90</td>
</tr>
<tr>
<td>Benzil</td>
<td>50-55</td>
<td>80</td>
</tr>
<tr>
<td>Benzilic Acid</td>
<td>55</td>
<td>77</td>
</tr>
</tbody>
</table>

a: Conventional synthesis, b: Microwave-assisted synthesis

Fig.1: Advantages of microwave over conventional synthesis in our present study

CONCLUSION

Some common organic reactions were successfully exercised using microwave irradiation giving higher purity and better yield of products as compared to that of conventional synthesis in a shorter span of time. Thus, we successfully carried out our synthetic work and believe that microwave-assisted synthesis will greatly help the scientific community, specially the students to perform complex organic reactions in a simple manner in the coming days.
ACKNOWLEDGEMENT
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REFERENCES