MICROWAVE-INDUCED CLAY-MEDIATED PREPARATION OF IMINES: ONE-POT SYNTHESIS OF β-LACTAMS

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Abstract: Microwave-induced montmorillonite-mediated preparation of imines has been achieved in the absence of solvent and these have been converted to β-Lactams in a one-pot operation.

Keywords: Microwave, Clay, Solventless, β-lactams

Introduction: Research on the synthesis of β-lactam has been the subject of intense interest for more than 60 years because of their medicinal properties. Our research has uncovered crucial anticancer activities of β-lactams derived from polyaromatic compounds. We have been working on clay-mediated reactions and microwave chemistry. During the course of this investigation, we became interested in the preparation of β-lactams in a one-pot operation. In this communication, we describe that synthesis of a few imines by reacting aromatic aldehydes and aromatic amines in the presence of clay using microwave-induced reaction. The resulting imines have also been converted to β-lactams in excellent yields.

Experimental: Reaction of aromatic aldehydes and aromatic amines was performed in a domestic microwave oven in the presence of montmorillonite clay K10. The on-off cycle present in the microwave oven was used to irradiate the mixture each one minute interval and the mixture was irradiated for approximately 4 minutes. TLC of the reaction mixture was performed and compared with known authentic imines and it was found that the reaction was completed. The mixture was then brought at room temperature. Acid chlorides were then added to the reaction mixture followed by N-methylmorpholine. The reaction was then again irradiated for 4 minutes. Dichloromethane was then added to the reaction mixture after cooling and clay was filtered off. The organic component was then washed with dilute hydrochloric acid solution, water and sodium bicarbonate. The organic layer was then dried. TLC and NMR of the crude reaction mixture indicated the formation of β-lactams. The crude NMR was analyzed to determine the ratio of the isomeric β-lactams.
Table 1: Synthesis of Imines in the presence of clay using microwave-induced reactions

<table>
<thead>
<tr>
<th>Aldehydes</th>
<th>Amines</th>
<th>Imines</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CHO</td>
<td>NH₂</td>
<td><img src="CHO_NH2.png" alt="image" /></td>
<td>90</td>
</tr>
<tr>
<td>CHO</td>
<td>NH₂</td>
<td><img src="CHO_NH2_OCH3.png" alt="image" /></td>
<td>90</td>
</tr>
<tr>
<td>CHO</td>
<td>NH₂</td>
<td><img src="CHO_NH2_OCH3.png" alt="image" /></td>
<td>88</td>
</tr>
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</tr>
</tbody>
</table>
Results: Despite enormous successes in the preparation of β-lactam, solventless one-pot synthesis of these types of important compounds remains a challenge. Our experience in β-lactam chemistry, microwave-induced reaction and clay-mediated reactions has been combined in a effort to prepare β-lactams in a one-pot reaction. The results are very encouraging since this method produces β-lactam in comparable yields like the conventional step-wise methods. The stereochemistry of the β-lactams were also found to be identical (mostly trans) with the compounds reported earlier. Clearly, this present method has several advantages over known methods. The advantages are: no solvents are necessary, one-pot preparation, economical, controlled stereochemistry, rapid procedure, simple extraction and isolation method. The results described herein deserve special attention since it appears that clay has served as the dehydrating agent in the formation of imines. This method can be performed in milligram scale to multi-gram scale. It is not necessary to isolate the intermediate imines.

Scheme-1: Preparation of β-lactams following one-pot method using microwave-induced reaction.

\[
\begin{align*}
\text{Ar}_1 & \quad \text{ZOOH}_2\text{COCl} \\
\text{Ar}_2 & \quad \text{clay} \\
1 & \quad 2 & \quad 3 & \quad 4 \\
\text{a: } z = \text{OAC} & \quad 3:4 = 95:5 \\
\text{b: } z = \text{OPh} & \quad 3:4 = 90:10
\end{align*}
\]

Conclusion: In conclusion, a one-pot preparation of trans β-lactams using microwave-induced clay-mediated reaction has been developed. It is believed that clay can serve as a dehydrating agent and therefore, it allows the formation of the intermediate imines.

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References


