One-Pot Microwave Assisted Solid Phase Synthesis of Cyclic Imides from Cyclic Anhydrides

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In this study, a simple one-pot microwave assisted solid phase synthesis of cyclic imides from cyclic anhydrides by the use of KBr as solid phase, urea and thiourea as reagents in good yield are reported.

Key Words: Microwave irradiation, One-pot synthesis, Solid phase, Cyclic imides, Anhydrides.

INTRODUCTION

The microwave synthesis is utilized as a powerful and effective technique to promote a group of chemical reactions. Among the microwave class reactions, the microwave-assisted solid phase synthesis has emerged as a powerful variety form1-6. Imides having interesting functionality, due to their various presences in the natural products and in the pharmacologically active compounds. There are a few important and effective synthesis of imide derivatives from anhydride compounds7-10. Some of this methods were used for synthesis of important compounds such as phthalimide, maleimide and thalidomide by the use of urea and thiourea under microwave irradiation8,9. The synthesis of 2,3-dimethylmaleimide in solid phase by the use of urea was reported10. Compound 3 was used as a reagent in synthesis of maleimides and as an amino group protecting agent for superoxide dismutase. Some of the maleimides have been prepared by reaction of the appropriate maleic anhydrides with either ammonium acetate or methyl ammonium acetate in boiling acetic acid11.

Second order amides and lactams, which need not be N-substituted, can be converted to imides by oxidation with a hydrogen peroxide or peracid and a transition metal salt12,13. The metal ion catalyzed decomposition organic peroxyacids has been long known. The oxidation of amides to imides with air and transition metal ions have been reported, although the yields are quite low and the time of oxidation reactions is long14-22.

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The conversion of lactams, without any N-substitution, to cyclic imides by oxidation with an oxidative agent such as peracetic acid or t-butyl hydrogen peroxide and a transition metal salt such as manganic II or III salts under irradiation of microwave was reported\textsuperscript{23-26}.

In this study, we wish to report one-pot microwave assisted solid phase synthesis of cyclic imides 2, 4 and 6 from cyclic anhydrides 1, 3 and 5 using urea (H\textsubscript{2}N–CO–NH\textsubscript{2}) and thiourea (H\textsubscript{2}N–CS–NH\textsubscript{2}) in good yield. It is found that the various metallic halides such as AlCl\textsubscript{3}\textsuperscript{27}, CuBr\textsubscript{2}\textsuperscript{28}, FeCl\textsubscript{3}\textsuperscript{29}, BiCl\textsubscript{3}\textsuperscript{30}, ZnCl\textsubscript{2}\textsuperscript{31}, InCl\textsubscript{3}\textsuperscript{32} and TaCl\textsubscript{3}\textsuperscript{33} have been apparently safely employed in microwave-assisted synthetic reactions\textsuperscript{34}. For this study, KBr was used as solid phase for the reactions. There is no by-products and only final products have been considered. Good purification allows excellent products recovery.

**EXPERIMENTAL**

The simple imides synthesized (2, 4 and 6) in present studies, are known compounds and those physical data, infrared and \textsuperscript{1}H NMR spectra were essentially identical with those of authentic samples\textsuperscript{35,36}. The FT-IR spectra was recorded as KBr pellets on a Shimadzu FT-IR 8000 spectrometer. \textsuperscript{1}H NMR spectra was determined on a 300 MHz Bruker spectrometer.

**Typical procedure:** As a typical reaction procedure, a mixture of phthalic anhydride 5 (0.05 g, 33.78 mmol), urea (0.025 g, 41.17 mmol, 1 equiv.) and KBr (1.0 g) are ground by pestle and mortar to give a uniform mixture. The mixture was transferred to a dried heavy wall Pyrex tube. The tube was sealed and then exposed to microwave oven. The condition of microwave-irradiation was shown in Table-1. Boiling water (5-8 mL) is then added. Then was added CHCl\textsubscript{3} to the cooled mixture (10-15 mL). The
combined organic layers are washed (NaCl sat. aq., 10 cm³). After separation
the organic layer was dried with MgSO₄. The solvent was evaporated under
vacuum. The product as a white powder was remained. Purification by dry
column vacuum chromatography¹³ (eluting with 0-100 % EtOAc in 40-60
petroleum ether with increments of 10 %) gives phetalimide as a colourless
crystalline solid 6 (0.038 g, 75 %) (Table-1).

### Conclusion

The simple one-pot microwave assisted solid phase synthesis of cyclic
imides from cyclic anhydrides described here to synthesize imides 2, 4 and
6 from anhydrides 1, 3 and 5, respectively. Comparison this procedure
with the other methods confirm the facility and rapidity of this method for
synthesis of the imides from the appropriate anhydrides.

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### TABLE-1

<table>
<thead>
<tr>
<th>Compd. / m.f. / m.p. (°C)</th>
<th>IR (cm⁻¹)*</th>
<th>¹H NMR (δ ppm)*</th>
<th>Mass (m/z)*</th>
<th>CH₃-CO-NH₂ MW Time (min) Power (W) Yield (%)</th>
<th>CH₃-CS-NH₂ MW Time (min) Power (W) Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2 C₄H₃NO₂, 91-93</td>
<td>3260, 3060, 1768, 1100-1350</td>
<td>10.5 (NH br.), 6.7 (s, 2H, C=C)</td>
<td>97 (100), 69 (86), 54 (59)</td>
<td>3 600 70 2 600 79</td>
<td></td>
</tr>
<tr>
<td>4 C₆H₇NO₂, 111-114</td>
<td>3253, 2950, 2880, 1774, 1700, 1677, 1100-1350</td>
<td>10.2 (NH br.), 1.9 (s, 2CH₃)</td>
<td>125 (100), 126 (4), 104, 82, 54</td>
<td>4 600 50 3 600 53</td>
<td></td>
</tr>
<tr>
<td>6 C₈H₅NO₂, 180-183</td>
<td>3266, 3190, 3080, 2860, 1770, 1710, 1690, 1488, 1100-1350</td>
<td>10.5 (NH br.), 7.9 (d, 2H, 7-9(H)), 7.4 (d, 2H, 2-1H)</td>
<td>147 (100), 148 (4), 104, 76, 66, 50</td>
<td>3 600 75 2 600 73</td>
<td></td>
</tr>
</tbody>
</table>

*See references.
REFERENCES


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