Microwave-Assisted Synthesis of 3-Styrylchromones in Alkaline Ionic Liquid

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A simple, highly efficient and environmentally benign method for the synthesis of 3-styrylchromones from 3-formylchromones and 4-nitrophenylacetic acid/4-nitrotoluene in the presence of catalytic amount of basic ionic liquid 1-butyl-3-methylimidazolium hydroxide [(bmim)OH] carried out under the influence of microwave irradiation. This method gives remarkable advantages such as, short reaction times, simple work-up procedure and moderate to good yields. The ionic liquid was successfully reused for four cycles without significant loss of activity.

Key Words: 3-Styrylchromone, 3-Formylchromone, [Bmim]OH, Microwave irradiation

Introduction

Styrylchromones constitute a small but significant group of oxygenated heterocyclic compounds which have shown marked biological activities. Synthetic 2-styrylchromone derivatives exhibit potent cytotoxic, anti-allergic, anti-viral, and anti-cancer activity. Horzamethionine is exceptionally cytotoxic to P388 lymphocytic leukemia and HL-60 promyelocytic leukemia cell lines in vitro and appears to be a selective inhibitor of RNA synthesis and 6-Desmethoxyhorzamethionone showed cytotoxicity to 9 KB cell lines. Despite the relationship of 3-styrylchromones with the well-studied 2-styrylchromones very little is known about their biological activities; only anti-fungal and anti-bacterial activities have been reported. Due to great importance, many synthetic strategies have been employed for the synthesis of 3-styrylchromone. In 2002, Shingare and coworkers reported the condensation of 3-formylchromones with 2,4-dinitrotoluene in the presence of pyridine. A modification of this method which consists of the condensation of 3-formylchromones with 4-nitrophenylacetic acid followed by decarboxylation reaction, allowed the synthesis of new 3-styrylchromone derivatives. The synthetic method for 3-styrylchromones involves the Wittig reaction of 3-formylchromones with benzylidene yields and gives an isomeric mixture of (E) and (Z) 3-styrylchromones. The obtained isomers have been separated by thin layer chromatography. Also, Samat et al. reported the synthesis of novel 3-styrylchromones which can also be regarded as 3-styrylflavones. These compounds have been obtained from the reaction of 1-(2-hydroxyphenyl)-3-phenylpropan-1,3-diones and phenyl acetaldehydes under a mild acid-catalyzed condition. These methods have not been entirely satisfactory, owing to such drawbacks as low yields, long reaction time, expensive and toxic catalysts. Chromones and their derivatives of different oxidation level are well known naturally occurring oxygen-containing heterocyclic compounds which perform important biological functions in nature. It is known that certain natural and synthetic derivatives possess important biological activities such as anti-tumor, anti-hepatotoxic, anti-oxidant, anti-inflammatory, anti-spasmolytic, oestrogenic and anti-bacterial.

In recent years, application of ionic liquids in organic synthesis have attracted considerable attention due to their special properties such as good solvating capability, wide liquid range, negligible vapor pressure, easy recycling, high thermal stability and rate enhancers. Nowadays, much attention has been focused on organic reactions catalyzed by ionic liquids. Particularly, imidazolium ionic liquids have been successfully used in many organic transformations includes Diels-Alder, Wittig, Hantzsch condensation. The science of green chemistry is developed to meet the increasing demand of environmentally benign chemical processes. The application of microwaves (MWs), as an efficient heating source for organic reactions and it has been reported in the literature. The main advantage of microwave assisted organic synthesis is the shorter reaction time using only small amount of energy. Many microwave-assisted transformations offer additional convenience in the field of organic synthesis because of simple experimental procedure and high yields.

Experimental

Melting points were obtained on a melting point apparatus with capillary tubes and are uncorrected. IR spectra were recorded on Perkin-Elmer FTIR Spectrophotometer in KBr disc. H NMR spectra were recorded on Varian 300 MHz spectrophotometer in CDCl3 as a solvent and TMS as an internal standard. Microwave irradiation was carried out in a microwave oven (BPL, 800T, 2450 MHz) with power output of 800 W. Synthesis of substituted 3-styrylchromone 3 (a-j). A mixture of substituted 3-formylchromone (1 mmol), 4-nitrophenyl-
acetic acid/4-nitrotoluene (1 mmol), [bmim]OH (5 mol%) were taken in a beaker (50 mL). The reaction mixture was mixed properly with the help of glass rod and irradiated (180 Watt) for a period of 5 sec at a time. The progress of reaction was monitored by TLC. After completion of reaction, the reaction content cooled to room temperature. The product was extracted with diethyl ether (2 × 20 mL) and the insoluble ionic liquid [bmim]OH directly recycled in subsequent runs. The organic layer was washed by brine (2 × 10 mL), dried over anhydrous NaSO4 and solvent removed on rotary evaporator under reduced pressure. The crude solid compounds were crystallized by acetic acid to afford the desired products 3 (a-j). All the products were characterized by IR, 1H NMR and mass spectra and by comparison of their physical characteristics with those of the authentic compounds.

**Spectral data of principal compounds.** Compound (3a): 1H NMR (CDCl3, 300 MHz, δ ppm): 2.25 (s, 3H), 6.70 (s, 1H), 7.60 (s, 1H), 7.23 (s, 1H), 7.10 (d, 1H, J = 12 Hz), 6.80 (d, 1H, J = 12 Hz), 7.50 (d, 2H, J = 8.1 Hz), 8.20 (d, 2H, J = 8.1 Hz). Compound (3b): 1H NMR (CDCl3, 300 MHz, δ ppm): 2.70 (s, 6H), 6.90 (s, 1H), 7.26 (s, 1H), 7.21 (s, 1H), 7.10 (d, 1H, J = 12 Hz), 6.80 (d, 1H, J = 12 Hz), 7.50 (d, 2H, J = 8.1 Hz), 8.20 (d, 2H, J = 8.1 Hz). Compound (3c): 1H NMR (CDCl3, 300 MHz, δ ppm): 6.79 (d, 1H, J = 8 Hz), 7.40 (d, 1H, J = 8 Hz), 7.70 (s, 1H), 7.21 (s, 1H), 7.10 (d, 1H, J = 12 Hz), 6.80 (d, 1H, J = 12 Hz), 7.50 (d, 2H, J = 8.1 Hz), 8.20 (d, 2H, J = 8.1 Hz).

**Results and Discussion**

In continuation of our research interest in microwave-assisted...
Table 2. Recycling of [bmin]OH for the synthesis of 3-(4-nitrostyryl)-6-chloro-4H-chromone-4-one 3c.a

<table>
<thead>
<tr>
<th>Entry</th>
<th>Cycleb</th>
<th>Yield (%)c</th>
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<tr>
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</tr>
<tr>
<td>2</td>
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<td>3rd</td>
<td>59</td>
</tr>
<tr>
<td>5</td>
<td>4th</td>
<td>59</td>
</tr>
</tbody>
</table>

aReaction condition: 1a (1 mmol), 2 (1 mmol) and [bmin]OH (5 mol%) under microwave irradiation; bReaction time-5 min; cIsolated yield.

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Table 2 shows no loss of efficiency with regard to reaction time and yield after four successive runs.

Conclusion

In conclusion, we have emphasized a new and effective methodology for the synthesis of 3-styrylchromone derivatives. The notable merits of the present methods are short reaction times, simple work-up procedure and moderate to good yield of products. Moreover, the [bmin]OH was successfully reused for four cycles without significant loss of activity. Thus a rapid, convenient and environmentally benign method for the synthesis of compounds of type 3 (a-j) have been achieved. To the best of our knowledge this is the first report on synthesis of 3-styrylchromones derivatives in basic ionic liquid.

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References

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