An efficient microwave assisted solvent-free general route to cyclic enaminones

Kaushik Chanda, Milan Chandra Dutta & J N Vishwakarma*
Organic Research Lab, Department of Chemistry,
St. Anthony's College, Shillong 793 001, India
E-mail: jnvishwakarma@rediffmail.com

Received 9 December 2003; accepted (revised) 23 April 2004

1,3-Cyclohexanedione and dimedone have been reacted with primary amines in domestic microwave oven to give cyclic enaminones 2a-h in very good to excellent yields.

IPC: Int.Cl. 7 C 07 C 49/543

In course of our ongoing program on the development of newer synthetic strategies for heterocyclic compounds, we required enaminones derived from 1,3-cyclohexanedione and dimedone. Our literature survey at this stage revealed that there are a few methods known in the literature. Some of the recent strategies for the synthesis of enaminones include the reaction of diketones or β-hydroxyketones with primary amine in the presence of boron trifluoride or by azeotropic removal of water.

However, these methods involve thermal and dry conditions, azeotropic removal of water and use of toxic solvent like benzene.

Microwave-induced Organic Reaction Enhancement (MORE) chemistry reactions are extremely fast, cleaner than conventional reactions and lead to higher atom economy (less chemical waste). Because of short time requirement, ease of workability and eco-friendliness, microwaves provide an alternative green approach to environmentally unacceptable procedures using toxic and expensive reagents.

The growing interest in microwave-assisted reactions prompted us to take up the synthesis of enaminones 2 by the condensation of 1,3-diketones 1 with appropriate primary amines (Scheme I) under microwave irradiation and results of our investigation are reported herein.

Thus, when a mixture of 1,3-cyclohexanedione and aniline (1:1) was irradiated in a domestic microwave oven for 2 min, work-up of the reaction mixture yielded the desired condensation product 2a in 93% yield, which was characterized as 3-anilinocyclohex-2-en-1-one on the basis of analytical and spectral data. Condensation of 4-chloroaniline and benzylamine with cyclohexanedione proceeded in a similar manner and the corresponding enaminones 2b and 2d were obtained in 88 and 98% yields, respectively. Synthesis of 2e involved treatment of the ketone with two equivalents of methylvamine (40% aqueous solution).

Condensation of dimedone with primary amines could be achieved under similar conditions giving 2e-h in 93-98% overall yields. The reaction of dimedone with methylamine went to completion when a mixture (1:3) of the two was subjected to microwave irradiation.

In conclusion, we have demonstrated a practical application of microwave assisted, solvent-free condensation of cyclic ketones with primary amines in domestic microwave oven in very good to excellent yields.

Experimental Section

Mps were recorded by open capillary method and are uncorrected. The IR spectra were recorded on a Perkin-Elmer 983 spectrometer; 1H NMR (90 MHz) spectra on a Varian EM-390 spectrometer; and high-resolution 1H NMR (300 MHz) spectra on a Bruker ACF-300 spectrometer (chemical shifts in δ, ppm) with reference to TMS as internal reference. Microwave irradiation was carried out in a Samsung domestic oven (model CE2733G) operating at 2450 MHz.

General procedure. A mixture of 1,3-diketone (1 mmole) and primary amine (1 mmole) in a 10 mL conical flask placed in a beaker, was irradiated in a...
Table I—Synthesis of cyclic enaminones

<table>
<thead>
<tr>
<th>Compd</th>
<th>R</th>
<th>R_1</th>
<th>Yield (%)</th>
<th>Time (sec)/ Power (watt)</th>
<th>M.p. °C (lit. m.p.) (solvent of cryst.)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2a</td>
<td>H</td>
<td>C_6H_5</td>
<td>93</td>
<td>60/300</td>
<td>173-74 (176-78[^1]) (MeOH)</td>
</tr>
<tr>
<td>2b</td>
<td>H</td>
<td>4-ClC_6H_4</td>
<td>88</td>
<td>270/180</td>
<td>190-91 (190-91.5[^6]) (Hexane-EtOAc)</td>
</tr>
<tr>
<td>2c</td>
<td>H</td>
<td>Me</td>
<td>83</td>
<td>15/100</td>
<td>68-69 (67-67.5[^5]) (Hexane-Benzene)</td>
</tr>
<tr>
<td>2d</td>
<td>H</td>
<td>C_6H_5CH_2</td>
<td>98</td>
<td>60/300</td>
<td>125-26 (125-27[^10]) (EtOAc)</td>
</tr>
<tr>
<td>2e</td>
<td>Me</td>
<td>C_6H_5</td>
<td>94</td>
<td>90/300</td>
<td>183-84 (181-83[^8]) (Hexane-Benzene)</td>
</tr>
<tr>
<td>2f</td>
<td>Me</td>
<td>4-ClC_6H_4</td>
<td>93</td>
<td>780/300</td>
<td>206-08 (208-10[^10]) (EtOAc)</td>
</tr>
<tr>
<td>2g</td>
<td>Me</td>
<td>Me</td>
<td>98</td>
<td>270/180</td>
<td>152-53 (153-54[^2]) (Hexane-EtOAc)</td>
</tr>
<tr>
<td>2h</td>
<td>Me</td>
<td>C_6H_5CH_2</td>
<td>98</td>
<td>120/300</td>
<td>131-32 (130-31[^12]) (Hexane-EtOAc)</td>
</tr>
</tbody>
</table>

domestic microwave oven. After the completion of the reaction (monitored by TLC), water formed during the reaction was distilled under reduced pressure to give a solid mass, which was triturated with hexane, filtered and then recrystallized from appropriate solvent to give the enaminones 2a-h (Table I). For 2c, 2 mmole of methylamine and for 2g, 3 mmole of methylamine (40% aqueous solution) were used. The products were identified by IR and NMR spectroscopy and also by comparing their mps with those of the authentic products.

The IR and NMR spectral data of enaminones 2a and 2e are given below.

3-Anilinocyclohex-2-en-l-one 2a: IR (KBr): 1533, 1593, 3257, 3445 cm⁻¹; ¹H NMR (CDCl₃): δ 1.97-2.03 (m, 2H), 2.33 (t, 2H), 2.50 (t, 2H), 5.56 (s, 1H), 6.95 (s, 1H, exchangeable with D₂O), 7.12-7.17 (m, 3H), 7.27-7.33 (m, 2H).

3-Anilino-5,5-dimethylcyclohex-2-en-l-one 2e: IR (KBr): 1533, 1566, 3237, 3443 cm⁻¹; ¹H NMR (CDCl₃): δ 1.06 (s, 6H, 2×CH₃), 2.17 (s, 1H), 2.35 (s, 1H), 5.55 (s, 1H), 7.10-7.15 (m, 3H), 7.26-7.31 (m, 2H), 7.50 (s, 1H, exchangeable with D₂O).

Acknowledgements

The authors thank the Principal, Rev. Fr. Ioannis Warpakma, SDB for the facilities and Rev. Fr. Stephen Mavely, SDB and Rev. Fr. Joseph Nellanatt, SDB for their encouragement during the course of this investigation. The financial support from ICAR-NATP-PIU is gratefully acknowledged. Authors (KC and MCD) thank ICAR for Senior Research Fellowships. Thanks are also due to the Heads of RSIC-CDRI (Lucknow) and RSIC-NEHU (Shillong) for recording spectra.

References