Synthesis of triazones in aqueous media under microwave irradiation

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Three component condensation of \(N,N'\)-dimethylurea, aqueous formaldehyde and primary amines under microwave irradiation leads to triazones in high yields.

Water as a medium accelerates many organic reactions such as Claisen rearrangement, Aldol and Michael condensations, addition of nucleophiles to carbonyl compounds. Recently, microwave dielectric heating is rapidly becoming an established procedure in organic synthesis in organic solvents or dry media. \(1,3,5\)-Tri-\(N\)-substituted-hexahydro-2-oxo-1,3,5-triazines (triazones) group have been known for many years in literatures. Triazones are used for protection of amino groups, as well as for the synthesis of polyamines, polyfunctional amino acids and amino alcohols. Many water soluble triazones are used as fertilizers.

Three methods have been reported for the synthesis of triazones: (a) The reaction of phenyl isocyanates with azomethines in the presence of zinc chloride. (b) The reaction of hydrochloric salt of a primary amine with 4-oxo-oxadiazinanone. (c) The reaction of three component condensation of primary amines with \(N,N'\)-disubstituted urea and aqueous formaldehyde with a co-solvent such as toluene, ethanol or ethyl acetate. All these methods have some disadvantages like long reaction period, low yields, acidic conditions and use of an organic solvent at the reflux conditions.

In continuation of our work on the synthesis of triazones using microwave irradiation, herein we wish to report the synthesis of triazones through three component condensation of primary amines, \(N,N'\)-dimethylurea and aqueous formaldehyde (37%) in water using microwave irradiation (Scheme I).

Water has high dielectric constant with a permanent dipole moment which allows the coupling between the oscillating electric field and the molecular tumbling to occur with high efficiency heating. Also, water is a suitable solvent for these compounds. To begin the reaction, the formaldehyde might combine with primary amines to give imine-fomaldehyde copolymer or oligomeric set of formaldehyde adducts which could be converted to triazones. In the \(^1\)H NMR spectra of triazones, the ring protons appear at \(\delta \) 4.05-4.20 ppm, and in the IR spectra these compounds show strong amide bonds in the region 1620-1640 cm\(^{-1}\). The reaction time and the yields of triazones are summarized in Table I.

In conclusion, the three component condensation of formaldehyde, \(N,N'\)-dimethylurea and primary amines in aqueous media using microwave irradiation provides triazones. The high yields, the low reaction period, easy set-up and work-up are advantages of this method.

Experimental Section

IR spectra were recorded on a Perkin-Elmer spectrometer. \(^1\)H NMR were measured on a Bruker AC-100 (100 MHz) spectrometer in CDCl\(_3\) and
Table I—$^1$H NMR spectra and yields of triazones

<table>
<thead>
<tr>
<th>Compd</th>
<th>Ring Protons</th>
<th>Methyl Protons at 1&amp;3 Positions</th>
<th>Protons in the Substituent</th>
<th>Yield (%)</th>
<th>Reaction Period (min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>4a</td>
<td>4.05</td>
<td>2.80</td>
<td>2.60 (s, 3H, CH₃)</td>
<td>71</td>
<td>2</td>
</tr>
<tr>
<td>4b</td>
<td>4.10</td>
<td>2.85</td>
<td>2.75 (q, 2H, CH₂), 1.05 (t, 3H, CH₃)</td>
<td>76</td>
<td>2</td>
</tr>
<tr>
<td>4c</td>
<td>4.20</td>
<td>2.80</td>
<td>2.70 (t, 2H, CH₂), 1.50 (m, 2H, CH₃), 1.00 (t, 3H, CH₃)</td>
<td>86</td>
<td>2</td>
</tr>
<tr>
<td>4d</td>
<td>4.10</td>
<td>2.90</td>
<td>2.70 (m, 1H, CH), 1.00 (d, 6H, 2CH₃)</td>
<td>83</td>
<td>3</td>
</tr>
<tr>
<td>4e</td>
<td>4.10</td>
<td>2.90</td>
<td>2.80 (t, 2H, CH₂), 2.20 (m, 2H, CH₃), 1.30 (m, 2H, CH₂), 1.90 (t, 3H, CH₃)</td>
<td>84</td>
<td>3</td>
</tr>
<tr>
<td>4f</td>
<td>4.20</td>
<td>2.90</td>
<td>2.80 (m, 1H, CH), 1.50 (m, 2H, CH₂), 1.15 (d, 3H, CH₃), 0.95 (t, 3H, CH₃)</td>
<td>80</td>
<td>3</td>
</tr>
<tr>
<td>4g</td>
<td>4.10</td>
<td>2.86</td>
<td>2.52 (d, 2H, CH₂), 1.70 (m, 1H, CH), 0.94 (d, 6H, 2CH₃)</td>
<td>80</td>
<td>3.5</td>
</tr>
<tr>
<td>4h</td>
<td>4.26</td>
<td>2.85</td>
<td>1.18 (s, 9H, 3CH₃)</td>
<td>70</td>
<td>4.5</td>
</tr>
</tbody>
</table>

Chemical shifts are reported on the δ scale in ppm down field from TMS as internal reference. A domestic microwave oven (Moulinex FM 2735) at 2450 MHz (850 Watts) was used in all experiments.

General procedure for preparation of triazones.

A mixture of N,N' -dimethylurea (3 mmol), aqueous formaldehyde (8 mmol) and primary amine (5 mmol), in a beaker was irradiated in microwave oven at 850 watt for the period indicated in Table I. The reaction mixture was washed with water and extracted with dichloromethane. The organic phase was separated, dried (Na₂SO₄) and concentrated by rotary evaporator. Purification of the crude product by distillation in vacuo afforded the triazones 4.

Acknowledgement

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References

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