Note

Single step synthesis of $4H$-1,4-benzothiazines

Vibha Srivastav, Rajni Gupta & R R Gupta*
Department of Chemistry, University of Rajasthan, Jaipur 302 004, India

Received 13 April 1999; accepted (revised) 10 May 1999

Single step synthesis of 4$H$-1,4-benzothiazines involving condensation and oxidative cyclization of 2-amino-5-bromo-3-methylbenzenethiol 1 with $\beta$-diketones/$\beta$-ketoesters 2 in dimethyl sulfoxide is reported.

$4H$-1,4-Benzothiazines resemble structurally to phenothiazines in having a fold along nitrogen-sulfur axis which is one of the structural specificity to impart biological activities to phenothiazines. $4H$-1,4-Benzothiazines are anticipated to possess a wide spectrum of biological activities similar to that of phenothiazines.

Results and Discussion

Substituted $4H$-1,4-benzothiazines have been synthesized by one-pot reaction involving condensation and oxidative cyclization of 2-amino-5-bromo-3-methylbenzenethiol 1 with $\beta$-diketones/$\beta$-ketoesters 2 in dimethyl sulfoxide. The reaction is believed to proceed through the formation of an intermediate enaminoketone 3. Under experimental conditions 2-amino-5-bromo-3-methylbenzenethiol 1 is readily oxidized to bis(2-aminophenyl) disulfide 1a, which cyclises to $4H$-1,4-benzothiazines 4 by scission of sulfur-sulfur bond due to high reactivity of $\alpha$-position of enaminoketone system 3 towards nucleophilic attack (Scheme I). The characterization data of synthesized benzothiazines 4a-e are given in Table I. IR data of synthesized benzothiazines are in accordance with their assigned molecular structures.

Experimental Section

All the melting points are uncorrected. The purity has been checked by thin layer chromatography and the structures have been assigned by elemental analysis and spectral data. Infrared spectra of all the compounds have been scanned in KBr on a Nicolet-Magna IR spectrophotometer model 550, and NMR.

Scheme I

$R' / R^2 = \text{CH}_3 / \text{C}_6\text{H}_4(\text{OCH}_3)_p, \text{CH}_3/\text{C}_6\text{H}_5(\text{Cl})_p, \text{CH}_3/\text{C}_6\text{H}_5(\text{OCH}_3)_p, \text{CH}_3/\text{C}_6\text{H}_5/\text{C}_6\text{H}_3$
The characterization data of 4H-1,4-benzothiazines 4a-e.

<table>
<thead>
<tr>
<th>Compd</th>
<th>Mol. formula</th>
<th>mp (°C)</th>
<th>Yield (%)</th>
<th>Found (Calcd) %</th>
<th>IH NMR data</th>
</tr>
</thead>
<tbody>
<tr>
<td>4a</td>
<td>C₁₀H₁₆NS₄O₂Br</td>
<td>85</td>
<td>47</td>
<td>53.25</td>
<td>(85.38 54.10 3.59) (s, 1H, 8(H), 7.73-6.94 (m, 6H, Ar(H)), 4.12 (s, 3H, OCH₃), 2.51 (s, 3H, CH₃ at C₁)</td>
</tr>
<tr>
<td>4b</td>
<td>C₁₀H₁₆NS₄O₂Br</td>
<td>103</td>
<td>42</td>
<td>54.20</td>
<td>(54.28 5.28 11.32) (s, 1H, 8(H), 7.70 &amp; 4.12 (2s, 6H, ArH), 2.31 (s, 3H, CH₃ at C₃); 1.26 (s, 3H, CH₃)</td>
</tr>
<tr>
<td>4c</td>
<td>C₁₀H₁₆NS₄O₂BrCl₂</td>
<td>79</td>
<td>40</td>
<td>47.70</td>
<td>(67.55 2.79 3.26) (s, 1H, NH), 7.29-5.80 (m, 5H, ArH), 2.00 (s, 3H, CH₃ at C₁), 1.21 (s, 3H, CH₃ at C₃)</td>
</tr>
<tr>
<td>4d</td>
<td>C₁₀H₁₆NS₄O₂BrBr</td>
<td>90</td>
<td>40</td>
<td>40.78</td>
<td>(40.90 2.55 3.97) ArH), 2.78 (s, 3H, CH₃ at C₃)</td>
</tr>
<tr>
<td>4e</td>
<td>C₁₀H₁₆NS₄O₂Br</td>
<td>90</td>
<td>33</td>
<td>62.35</td>
<td>(62.55 3.79 3.32) (s, 1H, NH), 7.80-6.20 (m, 12H, ArH), 2.10 (s, 3H, CH₃ at C₃)</td>
</tr>
</tbody>
</table>

spectra in DMSO-d₆ on a Jeol FX90 Q FT NMR at 90 MHz using TMS as an internal standard.

Preparation of 4H-1,4-benzothiazines 4a-e. To the stirred suspension of β-diketones/β-ketoesters (2; 0.01 mole) in dimethyl sulfoxide (5 mL) was added 2-amino-5-bromo-3-methylbenzenethiol (1; 0.01 mole) and the resulting mixture was refluxed for 20-30 min. The reaction mixture was concentrated and washed with pet. ether and crystallized from methanol to get 4a-e.

References
1 R R Gupta (Ed.), Phenothiazines and 1,4-Benzothiazines - Chemical and Biomedical Aspects, (Elsevier, Amsterdam), 1988.