One-Pot α-Bromoacetalization of Carbonyl Compounds

Sandhya Visweswariah, G. Prakash, Vidyu Bhushan, S. Chandrasekaran*

Department of Chemistry, Indian Institute of Technology, Kanpur 208016, India

α-Bromoacetals of carbonyl compounds are useful synthetic intermediates in that they serve as precursors to α,β-unsaturated ketones\(^1,2\), particularly in cyclic systems where the dehydrobromination of α-bromoketones is complicated by side reactions\(^3\). In general, α-bromoacetals of carbonyl compounds are prepared by a two-step sequence involving bromination of the ketone followed by acetalization\(^4,5\) or acetalization of the carbonyl compound followed by bromination\(^1,2,6\), and the yields are only moderate. Sathoh et al.\(^7\) have shown that in the case of steroidal ketones, α-bromoacetals can be obtained using a very large excess of copper(I) bromide as the brominating agent in ethylene glycol. This procedure is not particularly useful for medium to large scale preparations.

We report herein a useful procedure for the one-pot α-bromoacetalization of carbonyl compounds under mild conditions.

\[
\begin{align*}
\text{R}_1^1\text{C} = \text{O} & \quad + \quad \text{R}_2^2\text{C} = \text{Ohesive glycol (1 : 1) at room temperature (28°C) for 20-30 h leads to the formation of the corresponding α-bromoacetals 3 in good to excellent yield. Reaction at higher temperatures gives lower yields and leads to the formation of some dibromo compounds. Results are summarized in the Table.}
\end{align*}
\]

This one-pot bromoacetalization probably involves bromination of acetics and ketones which are in equilibrium. In some cases (ketones 1j and 1k), work up of the reaction mixture after a few hours afforded the corresponding unbrominated acetal as the major product. Phenyltrimethylammonium tribromide, the utility of which was first recognized by Marquet and Jacques\(^8\), has the advantage of high stability and ease of preparation. It is much less electrophilic than molecular bromine and is more selective. Anhydrous tetrahydrofuran which is used as a solvent in this reaction acts as a buffer by reacting with the liberated hydrobromic acid and hence the α-bromoacetals are isolated in high yield.

We consider that this one-pot bromoacetalization reaction will be a highly useful method because of its ease, simplicity, and mildness of conditions.

α-Bromoacetalization of Carbonyl Compounds; General Procedure:

To a stirred solution of the ketone 1 (10 mmol) in tetrahydrofuran (12 ml) and ethylene glycol (2; 12 ml) is added phenyltrimethylammonium tribromide (11-20 mmol). The homogeneous reaction mixture is stirred at room temperature (28°C) for 20-30 h and then poured into a cold solution of 10% sodium hydrogen carbonate (250 ml) and 5% sodium thiosulphate (25 ml) and extracted with ether (2 x 100 ml). The combined organic extract is washed with water (3 x 100 ml) and brine (100 ml) and dried with anhydrous sodium sulfate. The solvent is re-

0039-7881/82/0432-0309 $ 03.00 © 1982 Georg Thieme Verlag · Stuttgart · New York
<table>
<thead>
<tr>
<th>Ketone (1)</th>
<th>α-Bromoacetal (3)</th>
<th>Reaction time [h]</th>
<th>Yield [%]</th>
<th>m.p. [°C] or b.p. [°C]/torr</th>
<th>Molecular formula</th>
<th>M.S. m/e (M⁺)</th>
</tr>
</thead>
<tbody>
<tr>
<td>a</td>
<td>H₂C=C=CH₂</td>
<td>20</td>
<td>90</td>
<td>69-70°/14</td>
<td>73-74°/18³</td>
<td>182, 180</td>
</tr>
<tr>
<td>b</td>
<td>C₂H₅-C=C₂H₅</td>
<td>24</td>
<td>89</td>
<td>64-68°/2.5</td>
<td>60-68°/3¹⁰</td>
<td>210, 208</td>
</tr>
<tr>
<td>c</td>
<td>H₂C=C=CH₂ - Br</td>
<td></td>
<td></td>
<td></td>
<td>(65%)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>(35%)</td>
<td></td>
</tr>
<tr>
<td>d</td>
<td>t-C₆H₅-C=CH₂</td>
<td>22</td>
<td>82</td>
<td>85-90°/15</td>
<td>C₆H₅BrO₂</td>
<td>224, 222</td>
</tr>
<tr>
<td>e</td>
<td></td>
<td>24</td>
<td>90</td>
<td>95-100°/15</td>
<td>C₆H₅BrO₂</td>
<td>208, 206</td>
</tr>
<tr>
<td>f</td>
<td></td>
<td>27</td>
<td>89</td>
<td>90-92°/5</td>
<td>C₆H₅BrO₂</td>
<td>222, 220</td>
</tr>
<tr>
<td>g</td>
<td></td>
<td>30</td>
<td>81</td>
<td>77-80°/0,5</td>
<td>C₆H₅BrO₂</td>
<td>236, 230</td>
</tr>
<tr>
<td>h</td>
<td></td>
<td>28</td>
<td>79</td>
<td>—</td>
<td>C₆H₅BrO₂</td>
<td>236, 234</td>
</tr>
<tr>
<td>i</td>
<td>C₆H₅-C=CH₂</td>
<td>22</td>
<td>86</td>
<td>61¹</td>
<td>C₆H₅BrO₂</td>
<td>244, 242</td>
</tr>
<tr>
<td>j</td>
<td></td>
<td>6</td>
<td>65</td>
<td>—</td>
<td>C₆H₅O₂</td>
<td>156</td>
</tr>
<tr>
<td>k</td>
<td></td>
<td>5</td>
<td>68</td>
<td>—</td>
<td>C₆H₅O₂</td>
<td>128</td>
</tr>
</tbody>
</table>

¹ Yields of isolated products of ≥ 90% purity as determined by ¹H-N.M.R. spectrometry and T.L.C.
² Satisfactory microanalyses obtained: C ± 0.34, H ± 0.25.
³ Product isolated by column chromatography on alumina (eluents: petroleum ether, 5% ether/petroleum ether).

moved under reduced pressure to yield the α-bromoacetal which is further purified by distillation or chromatography and characterized by ¹H-N.M.R., I.R., mass spectra, and microanalysis.

Financial Assistance by SERC of the Department of Science and Technology. New Delhi is gratefully acknowledged.

Received: September 3, 1981
(Revised form: October 23, 1981)