THE FACILE REMOVAL OF THE ETHYLENE HEMITHIOACETAL AND -KETAL PROTECTING GROUP.

THE REACTION OF CHLORAMINE-T WITH 1,3-OXATHIOLANES.

David W. Emerson,
The University of Michigan, Dearborn Campus,
Dearborn, Michigan 48128, U.S.A.

and

Hans Wynberg,
Department of Organic Chemistry, The University,
Zernike laan, Groningen, The Netherlands.

(Received in UK 10 May 1971; accepted in UK for publication 19 May 1971)

The importance of the ethylene hemithioacetal or -ketal protecting group in steroid chemistry is well documented. The oxathiolanes derived from steroids and other aldehydes and ketones are generally stable. Regeneration of the carbonyl compounds previously required acid catalyzed hydrolysis or Raney nickel desulphurization.1a,2

We now wish to report that when 1,3-oxathiolanes are treated with a solution of sodium N-chloro-p-toluenesulphonamide (Chloramine-T) in water, ethanol or methanol under mild conditions, good to excellent yields of the corresponding aldehydes or ketones are obtained (Table). For example, 1,4-oxathiaspiro[4,4]nonane, Ia, affords cyclopentanone in 91% yield when treated for two minutes with Chloramine-T in 85% methanol-water at 25°C (equation 1). Cyclopentanone was identified by its semicarbazone derivative and determined quantitatively by GLC. It is clear from the present results that a wide variety of 1,3-oxathiolanes will undergo the reaction and that other functional groups can be tolerated using Chloramine-T under the reaction conditions. For example, ethyl acetoacetate is obtained in 96% yield from ethyl 2-methyl-1,3-oxathiolane-2-acetate, i.e.
The other products vary with the amount of Chloramine-T used. In all cases there can be isolated p-toluenesulphonamide and a compound mp 159° (dec.) identified as 2-hydroxyethyl p-toluenesulphonimidosulphine-p-toluenesulphonylimine, II, by elemental analysis (C<sub>16</sub>H<sub>16</sub>N<sub>2</sub>O<sub>3</sub>S<sub>3</sub>), IR spectrum (OH at 3465 cm<sup>-1</sup>, NH at 2660 cm<sup>-1</sup>, Nujol), and NMR spectrum (two methylene triplets, 3.48 s (SCH<sub>2</sub>) and 4.18 s (OCH<sub>2</sub>) J<sub>AB</sub> = 4.9 cps, pyridine-d<sub>5</sub>). Compounds closely related to II are formed in the reactions of Chloramine-T or -B with a variety of organosulphur compounds. A third product, bis [2-hydroxyethyl]disulphide, III, is formed when less than two moles of Chloramine-T per mole of oxathiolane is used. III can be eliminated from the reaction mixture by reaction with more Chloramine-T to form II as might be expected by analogy with the behaviour of other disulphides.

On the basis of these results and the observation that 1,3-dithiolanes and 1,3-dithianes behave similarly, the reaction may be viewed as proceeding via the formation of an unstable sulphilimine, IV, and a zwitterion, V (reaction 2). We defer a full discussion of mechanism until later.

\[
\begin{align*}
\text{III} & \rightarrow \text{II} \\
\text{III} & \rightarrow \text{IV} \\
\text{IV} & \rightarrow \text{V} \\
\text{V} & \rightarrow \text{I}
\end{align*}
\]

The present results indicate that a new method is now available for the removal, under mild conditions, of the ethylene hemithioacetal or -ketal protecting group. The existence of this method in addition to older methods of greater severity adds a new dimension to the practice of carbonyl group protection during synthesis.

We acknowledge helpful discussions with Prof. B.E. Hoogenboom and Dr. J.M. Pal. One of us (D.W. E.) thanks the Regents of the University of Michigan for granting a sabbatical leave for 1970-71 and the Department of Organic Chemistry, The Rijksuniversiteit, Groningen for hospitality for the period of this leave.
REFERENCES

   (b) L.F. Fieser, ibid., 76, 1945 (1954).

   (b) C. Djerassi, M. Gorman, and J.A. Henry, ibid., 77, 4647 (1955).
   (c) C. Djerassi, M. Shamma, and T.Y. Kan, ibid., 80, 4723 (1958).
   (d) F. Kipnis and J. Ornfelt, ibid., 71, 3555 (1949).
   (e) N.C. De and L.R. Feodor, ibid., 90, 7266 (1968).

   (b) J.R. Alexander and H. McCombie, ibid., 1932, 2087.
   (c) G. Bullmer and F.G. Mann, ibid., 1945, 666.


### Preparation of Oxathiolanes and their Reaction with Chloramine-T

<table>
<thead>
<tr>
<th>Compound</th>
<th>R'</th>
<th>Synthetic Method, Ref.</th>
<th>bp (Torr) or [mp]OC</th>
<th>Yield, %</th>
<th>Ref.</th>
<th>Mole Chloramine-T</th>
<th>Reaction Yield of BR,CO</th>
</tr>
</thead>
<tbody>
<tr>
<td>la</td>
<td></td>
<td></td>
<td>73 (10)</td>
<td>66</td>
<td>(10)</td>
<td>85% MeOH·H₂O</td>
<td>85% MeOH·H₂O</td>
</tr>
<tr>
<td>lb</td>
<td></td>
<td></td>
<td>90 (10)</td>
<td>66</td>
<td>(10)</td>
<td>96% EtOH·H₂O</td>
<td>96% EtOH·H₂O</td>
</tr>
<tr>
<td>lc</td>
<td></td>
<td></td>
<td>85-88 (1)</td>
<td>66</td>
<td>(1)</td>
<td>96% EtOH·H₂O</td>
<td>96% EtOH·H₂O</td>
</tr>
<tr>
<td>ld</td>
<td></td>
<td></td>
<td>39-41.1-40</td>
<td>66</td>
<td>(2)</td>
<td>85% MeOH·H₂O</td>
<td>85% MeOH·H₂O</td>
</tr>
<tr>
<td>le</td>
<td></td>
<td></td>
<td>79-81 (1)</td>
<td>66</td>
<td>(1)</td>
<td>96% EtOH·H₂O</td>
<td>96% EtOH·H₂O</td>
</tr>
<tr>
<td>lf</td>
<td></td>
<td></td>
<td>85-88 (1)</td>
<td>44</td>
<td>(1)</td>
<td>96% EtOH·H₂O</td>
<td>96% EtOH·H₂O</td>
</tr>
<tr>
<td>lg</td>
<td></td>
<td></td>
<td>102.5-103.5</td>
<td>66</td>
<td>(24)</td>
<td>95% MeOH·H₂O</td>
<td>95% MeOH·H₂O</td>
</tr>
<tr>
<td>lh</td>
<td></td>
<td></td>
<td>66 (24)</td>
<td>61</td>
<td>(1a )</td>
<td>85% MeOH·H₂O</td>
<td>85% MeOH·H₂O</td>
</tr>
<tr>
<td>li</td>
<td></td>
<td></td>
<td>66 (24)</td>
<td>67</td>
<td>(2a)</td>
<td>96% EtOH·H₂O</td>
<td>96% EtOH·H₂O</td>
</tr>
<tr>
<td>lj</td>
<td></td>
<td></td>
<td>66 (24)</td>
<td>67</td>
<td>(2a)</td>
<td>96% EtOH·H₂O</td>
<td>96% EtOH·H₂O</td>
</tr>
</tbody>
</table>

*Yield and identification by GLC analysis basis oxathiolane. Estimated error ± 4%. b) Isolated as a solid.*