Properties and Reactions of 1,3-Oxathianes

I. Preparation of 1,3-Oxathiane and Its 2- and 6-Alkyl Derivatives

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As their symmetrical analogs, the 1,3-dioxanes\(^1\)\(^-\)\(^4\) and 1,3-dithianes\(^5\)\(^-\)\(^6\) had recently been extensively studied, 1,3-oxathianes were considered very interesting objects for conformational and kinetic investigations. As a continuation of our series of papers dealing with aliphatic heterocycles,\(^7\)\(^-\)\(^9\) this paper reports the preparation of 1,3-oxathiane and several of its 2- and 6-alkyl derivatives:

\[
\begin{array}{c}
R_1 \quad \text{HOCHR}_3 \\
\text{C} = O \\
R_2 \\
\text{HSCH}_2
\end{array}
\]

\[
\begin{array}{c}
R_1 \\
\text{O} \\
\text{CH}_2 \\
R_3 \\
\text{H}_2\text{O}
\end{array}
\]

\(R_1 = \text{H or Me}; \quad R_2 = \text{Me, Et, \text{Pr}^1, \text{or t-Bu}; \quad R_3 = \text{H or Me}}\)

3-Mercapto propanol was prepared from 3-chloropropanol (Fluka AG) and thiourea (Fluka AG) by the method of Clinton et al.\(^*\) (Table 1). 1-Methyl-3-mercapto propanol was prepared from thiourea and 3-chloro-1-methylpropanol and 3-chloro-3-methylpropanol by the same method. The isomeric chloroalkanols were not separated since thiourea was found to react predominantly with the primary halide. The yield of 1-methyl-3-mercapto propanol was only about 25%, but as the mixture of chloroalkanols contained only 63% of the primary halide, the actual yield was about 40% (Table 1).

The mixture of the above chlorobutanol was prepared by methanalysis of a 63:37 mixture of the primary and secondary esters formed when 1,3-butanediol (Fluka AG) reacted with acetyl chloride.\(^10\)\(^\:\)\(^11\)

1,3-Oxathiane and its derivatives were prepared from 3-mercapto propanol or 1-methyl-3-mercapto propanol and the appropriate aldehyde or ketone by the following general method:

A mixture consisting of 0.1 mole of mercaptoalkanol, 0.11 mole of the aldehyde or ketone, 0.1 g of p-toluene sulfonic acid, and 50 ml of dichloromethane was boiled in a water entrainment unit until the formation of water ceased. The solution was neutralized with diethylamine and filtered. The dichloromethane was removed by distillation and the residue was fractionated at reduced pressure.

Physical constants of the prepared 1,3-oxathianes are shown in Table 2.

Aldehydes were found to react with the mercaptoalkanols rapidly (1–2 h) and the yields were very satisfactory (60–70%) except that formaldehyde gave 1,3-oxathiane in only 20% yield. Acetone was the most reactive ketone, whereas t-butyl methyl ketone reacted very slowly (after 5 days, the yield of acetal was 30–35%).

The purities of the prepared compounds were checked with a Perkin-Elmer F 11 gas chromatograph equipped with a column containing 5% Carbopack B on Chromosorb W (60/80 mesh). Most of the synthesized compounds were run through a Perkin-Elmer F 21 preparative gas chromatograph equipped with a 4.5 m x 3/8 in column containing 5%...
Table 2. Physical constants of the prepared 1,3-oxathianes.

<table>
<thead>
<tr>
<th>1,3-Oxathiane</th>
<th>B.p., °C/torr</th>
<th>nD 20</th>
<th>d4 20</th>
<th>Obs. (R_D)</th>
<th>Calc.</th>
<th>Yield %</th>
</tr>
</thead>
<tbody>
<tr>
<td>--- a</td>
<td>48/11</td>
<td>1.5026</td>
<td>1.0867</td>
<td>28.31</td>
<td>28.12</td>
<td>29</td>
</tr>
<tr>
<td>6-Me</td>
<td>52–54/13</td>
<td>1.4920</td>
<td>1.0504</td>
<td>32.65</td>
<td>32.74</td>
<td>30</td>
</tr>
<tr>
<td>2-Me</td>
<td>66–70/24</td>
<td>1.4922</td>
<td>1.0520</td>
<td>32.61</td>
<td>32.74</td>
<td>77</td>
</tr>
<tr>
<td>2-Et</td>
<td>73–75/19</td>
<td>1.4856</td>
<td>1.0090</td>
<td>37.59</td>
<td>37.39</td>
<td>69</td>
</tr>
<tr>
<td>2-Pr(^1)</td>
<td>75–78/16</td>
<td>1.4853</td>
<td>0.9954</td>
<td>42.13</td>
<td>42.07</td>
<td>60</td>
</tr>
<tr>
<td>2,2-diMe(^b)</td>
<td>65–68/17</td>
<td>1.4890</td>
<td>1.0187</td>
<td>37.46</td>
<td>37.37</td>
<td>65</td>
</tr>
<tr>
<td>cis-2,6-diMe</td>
<td>54–56/12</td>
<td>1.4827</td>
<td>1.0109</td>
<td>37.34</td>
<td>37.37</td>
<td>69</td>
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<td>cis-2-Et-6-Me</td>
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<td>1.4771</td>
<td>0.9803</td>
<td>42.16</td>
<td>42.00</td>
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<tr>
<td>cis-2-Pr(^1)-6-Me</td>
<td>69–72/13</td>
<td>1.4747</td>
<td>0.9682</td>
<td>46.58</td>
<td>46.66</td>
<td>60</td>
</tr>
<tr>
<td>2-Et-2-Me</td>
<td>61–65/10</td>
<td>1.4936</td>
<td>1.0139</td>
<td>41.96</td>
<td>42.00</td>
<td>57</td>
</tr>
<tr>
<td>2-Pr(^1)-2-Me</td>
<td>64–67/10</td>
<td>1.4923</td>
<td>0.9987</td>
<td>46.49</td>
<td>46.66</td>
<td>40</td>
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<tr>
<td>2-t-Bu-2-Me</td>
<td>94–97/27</td>
<td>1.4942</td>
<td>0.9846</td>
<td>51.56</td>
<td>51.56</td>
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<tr>
<td>2,2,6-triMe</td>
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<td>1.4789</td>
<td>0.9879</td>
<td>41.97</td>
<td>41.99</td>
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<tr>
<td>2,6-diMe-2-Et(^c)</td>
<td>62–64/12</td>
<td>1.4812</td>
<td>0.9791</td>
<td>46.54</td>
<td>46.64</td>
<td>65</td>
</tr>
<tr>
<td>trans</td>
<td>1.4804</td>
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<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>cis</td>
<td>1.4827</td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2,6-diMe-2-Pr(^{trans})</td>
<td>68–70/12</td>
<td>1.4819</td>
<td>0.9682</td>
<td>51.32</td>
<td>51.31</td>
<td>58</td>
</tr>
<tr>
<td>2,6-diMe-2-t-Bu(^{trans})</td>
<td>68–70/11</td>
<td>1.4827</td>
<td>0.9609</td>
<td>55.95</td>
<td>56.19</td>
<td>35</td>
</tr>
</tbody>
</table>

\(^a\) B.p. 67°C/10 torr, nD 20 1.5029 in Ref. 12. \(^b\) B.p. 55–56°C/13 torr, nD 20 1.4888 in Ref. 12. \(^c\) A mixture of stereoisomers.

Carbowax 20 M on Chromosorb G (60/80 mesh). In the case of 2-ethyl-2,4-dimethyl-1,3-oxathiane, the isomeric forms were also separated, but in the case of the other compounds only the cis or trans form was isolated owing to the great differences in the stabilities.

Also the NMR and mass spectra of the studied 1,3-oxathianes were recorded and found to be consistent with the structures and molecular weights of the compounds, but these will be discussed in a later paper.

8. References to other 1,3-dioxane or 1,3-dithiane works may be obtained from the above references.

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