Partial Reductive Demethyliolation of α-Ketoketene S,S-Acetals with Sodium Borohydride/Nickel Chloride: A New, General Method for 2-Methylthio-1-alkenyl Ketones

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Alkylthiovinyl ketones, besides their use as a blocking group, have been shown to be versatile synthetic intermediates in organic synthesis. Many recent publications have been concerned with their synthetic utility rather than methods of preparation. The most commonly employed method involves the treatment of formyl derivatives (or their tosylates) of alkyl ketones with butyl mercaptan. The other methods involve either 1,4-addition of alkyl/aryl mercaptans to β-ketoacetylenes or the displacement reaction of β-chlorovinyl ketones with appropriate mercaptans. Although the latter two methods are useful, preparation of the starting materials involves inconvenient, multi-step synthetic operations. Our interest in the synthetic utility of α-ketoketene S,S-acetals, derived from a variety of active methylene compounds in a one-pot reaction, prompted us to investigate whether they could be reduced selectively to give the title compounds in useful yields.

Our literature survey revealed that there is only one report on the electrochemical reduction of 1a which gave the corresponding methylthiovinyl ketone 2a in 64% yield. We report here that partial reductive demethyliolation of α-ketoketene S,S-acetals 1 with sodium borohydride/nickel chloride gives the corresponding methylthio-2-alkenyl ketones 2 in good yields. Apparently, the reported methods require alkyl

![Diagram of reaction]


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Vgl. auch:

E. Pears, B. Abeysekara, J. R. Scheiffer, Tetrahedron Lett. 1979, 3279; hier weitere Literatur.


### Table 2: Methylthio-1-alkenyl Ketones 2a–n

<table>
<thead>
<tr>
<th>Product</th>
<th>Reflux time [h]</th>
<th>Yield [%]</th>
<th>m.p. [°C] or b.p. [°C]/torr</th>
<th>Molecular formula</th>
<th>I.R. (neat) v [cm⁻¹]</th>
<th>δ [ppm]</th>
<th>MS, m/e (M⁺)</th>
<th>Configuration</th>
</tr>
</thead>
<tbody>
<tr>
<td>2a</td>
<td>30</td>
<td>62</td>
<td>oil: 140–142°/1</td>
<td>140°/1</td>
<td>1643</td>
<td>2.32</td>
<td>(s, 3 H); 6.70 (d, 1 H, J=15 Hz); 7.4 (m, 3 H); 7.7–7.9 (m, 3 H)</td>
<td>178 E</td>
</tr>
<tr>
<td>2b</td>
<td>25</td>
<td>64</td>
<td>120–121°/1</td>
<td>C₅H₉OS (192.3)</td>
<td>1645</td>
<td>2.32</td>
<td>(s, 3 H); 2.38 (s, 3 H); 6.91 (d, 1 H, J=9 Hz); 7.0 (m, 3 H); 7.50–7.85 (d, 2 H)</td>
<td>192 Z</td>
</tr>
<tr>
<td>2c</td>
<td>10</td>
<td>50</td>
<td>69–70°</td>
<td>C₅H₉OS (212.7)</td>
<td>1632</td>
<td>2.42</td>
<td>(s, 3 H); 6.60 (d, 1 H, J=15 Hz); 7.32 (d, 2 H); 7.7–7.9 (m, 3 H)</td>
<td>212.5 E</td>
</tr>
<tr>
<td>2d</td>
<td>37</td>
<td>45</td>
<td>127–128.5°</td>
<td>C₅H₉OS (222.7)</td>
<td>1625</td>
<td>1.40</td>
<td>(t, 3 H); 2.37 (s, 3 H); 4.07 (q, 2 H); 6.85 (d, 2 H); 6.91 (d, 1 H, J=9 Hz); 7.15 (d, 1 H, J=9 Hz); 7.85 (d, 2 H)</td>
<td>222 Z</td>
</tr>
<tr>
<td>2e</td>
<td>12</td>
<td>42</td>
<td>thick, viscous oil</td>
<td>C₅H₉OS (222.7)</td>
<td>1640</td>
<td>1.28</td>
<td>(t, 3 H); 2.68 (q, 2 H); 3.75 (s, 3 H); 6.71 (d, 2 H); 6.82 (d, 1 H, J=9 Hz); 7.12 (d, 1 H, J=9 Hz); 7.80 (d, 2 H)</td>
<td>222 Z</td>
</tr>
<tr>
<td>2f</td>
<td>8</td>
<td>56 (51)</td>
<td>oil: 100–101°/1</td>
<td>C₅H₇OS (206.3)</td>
<td>1635</td>
<td>1.90</td>
<td>(s, 3 H); 2.30 (s, 3 H); 2.35 (s, 3 H); 6.81 (s, 1 H); 7.0–7.6 (A, B, m, 4 H)</td>
<td>206 Z</td>
</tr>
<tr>
<td>2g</td>
<td>25</td>
<td>57 (52)</td>
<td>oil: 129–130°/1</td>
<td>C₅H₇OS (206.3)</td>
<td>1635</td>
<td>1.05</td>
<td>(t, 3 H); 2.30 (s, 3 H); 2.45 (q, 2 H); 6.80 (s, 1 H); 7.2–7.7 (m, 5 H)</td>
<td>206 Z</td>
</tr>
<tr>
<td>2h</td>
<td>28</td>
<td>66 (55)</td>
<td>oil: 135°/1</td>
<td>C₅H₇OS (220.3)</td>
<td>1620</td>
<td>0.95</td>
<td>(t, 3 H); 1.4 (m, 2 H); 2.25 (s, 2 H); 2.35 (t, 2 H); 6.82 (s, 1 H); 7.3–7.6 (m, 5 H)</td>
<td>220 Z</td>
</tr>
<tr>
<td>2i</td>
<td>11</td>
<td>77 (65)</td>
<td>85 56°/1; 37–38°/1</td>
<td>C₅H(OS (116.2)</td>
<td>1690</td>
<td>2.15</td>
<td>(s, 3 H); 2.33 (s, 3 H); 5.90 (d, 1 H, J=15 Hz); 7.50 (d, 1 H, J=15 Hz)</td>
<td>116 E</td>
</tr>
<tr>
<td>2j</td>
<td>9</td>
<td>58</td>
<td>68°/1</td>
<td>C₅H(OS (204.3)</td>
<td>1660</td>
<td>2.48</td>
<td>(s, 3 H); 2.80 (A, B, q, 4 H); 7.0–7.4 (m, 3 H); 7.51 (s, 1 H); 7.9 (m, 1 H)</td>
<td>204 E</td>
</tr>
<tr>
<td>2k</td>
<td>10</td>
<td>60</td>
<td>thick, viscous oil</td>
<td>C₅H(OS (218.2)</td>
<td>1675</td>
<td>1.88</td>
<td>(A, B, q, 2 H); 2.25 (br t, 2 H); 2.40 (s, 3 H); 2.71 (t, 2 H); 6.2–7.8 (m, 5 H)</td>
<td>218 E</td>
</tr>
<tr>
<td>2l</td>
<td>12</td>
<td>57</td>
<td>thick, viscous oil</td>
<td>C₅H(OS (220.3)</td>
<td>1650</td>
<td>2.45</td>
<td>(s, 3 H); 2.60 (t, 2 H); 4.15 (t, 2 H); 6.7–7.1 (m, 2 H); 7.25 (s, 1 H); 7.1–7.4 (m, 1 H); 7.5–7.8 (m, 1 H)</td>
<td>220 E</td>
</tr>
<tr>
<td>2m</td>
<td>16.5</td>
<td>66</td>
<td>75 47–48°</td>
<td>C₅H(OS (142.2)</td>
<td>1705</td>
<td>1.6–2.5</td>
<td>(m, 6 H); 2.45 (s, 3 H); 7.10 (t, 1 H, J=1.5 Hz)</td>
<td>142 E</td>
</tr>
<tr>
<td>2n</td>
<td>10</td>
<td>62 (56)</td>
<td>oil: 95–97°/1</td>
<td>C₅H(OS (156.2)</td>
<td>1712</td>
<td>1.5–2.0</td>
<td>(m, 4 H); 2.0–2.6 (m, 4 H); 2.45 (s, 3 H); 7.25 (br t, 1 H)</td>
<td>156 E</td>
</tr>
</tbody>
</table>

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α-alkyl groups also gave the respective 2f–h in 56–60% overall yields. The ketene S,S-acetals 1i derived from acetone yielded the corresponding 2i in 77% yield. When the cyclic ketene S,S-acetals 1j–n were reduced under similar conditions, the respective 2j–n were obtained in 57–66% overall yields. When the reduction of 1a was carried out in the presence of excess of nickel chloride (5 equiv), a complex mixture of propiophenone, 2a and the saturated β-thioacetal was obtained. Similarly the reduction of 1a in the presence of sodium boro-
hydride and cobalt chloride yielded a mixture of partially and completely reduced products.

The configurations of the compounds 2a–2n were assigned on the basis of their N.M.R. spectra. Compounds 2a, 2c, 2i and 2b, 2e were assigned trans-(E) and cis-(Z) configurations, respectively, on the basis of coupling constants of the vinyl protons (Table). The vinyl proton cis to acryl/acetyl group in 2a, 2e, and 2i appears at $\delta = 7.5$ ppm or higher. Similarly, the lower chemical shifts of $\delta = 6.8$ ppm in the compounds 2f–2h were assigned to the vinyl protons trans to the benzoyl group. The compounds 2j–2n, which exhibited chemical shifts for vinyl protons of $\delta = 7.10$–7.50 ppm were also assigned the (E)-configuration. It may be noted that in all these reductions, the formation of only one predominant isomer is observed. The mechanism of the reduction in favour of one predominant isomer is interesting and will be discussed in a subsequent paper.

1-Alkylthio-2-alkenyl Ketones (2a–n); General Procedure:
To a stirred suspension of nickel chloride hexahydrate (38 g, 0.16 mol) in ethanol (150 ml), sodium borohydride (7.6 g, 0.2 mol) is slowly added (15 min) and the mixture is further stirred for 10 min. A solution of ketene 3,5-acetal 1 (0.06 mol) in ethanol (50 ml) is added to the black suspension and the mixture is further stirred at room temperature for 10 min. It is then heated under reflux on an oil bath with stirring for the stated time (Table), until the starting material has disappeared completely (T.L.C.). The mixture is filtered hot through a sintered funnel and the black residue is washed with boiling chloroform (3 x 200 ml). The combined filtrate is washed with water (2 x 300 ml), the organic layer is dried with sodium sulfate, and evaporated to give a dark viscous liquid, which is passed through a silica gel column (Method A). Elution with hexane/benzene (9:1) (2a–g, 2m–2a) or ethyl acetate/hexane (1:99) (2h–l) gives the methylthioketenyl ketones 2a–n as yellow viscous liquids/crystalline solids (T.L.C. single spot) (Table).

In a few cases (1b, 1i, 1m, and 1n), ethanol from the reaction mixture obtained after refluxing, is removed under reduced pressure and the slurry is directly passed through a silica gel column (Method B). Elution with hexane/ethyl acetate (95:5) gives the corresponding 2b, 2i, 2m, and 2n in higher yields (Table) (T.L.C. single spot, N.M.R. shows 99% purity) though the products are darker in colour.

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