Communications

SYNTHESIS

used in biochemistry for the reduction of a variety of coenzymes and enzymes\(^1\) and in organic chemistry to reduce several types of functional groups, especially those containing nitrogen\(^3,4\).

One is struck, however, at the sparseness of reports of the reduction of carbonyl compounds by this commonly available reagent. The reductions of acetone and benzaldehyde were claimed (without experimental detail) over a century ago\(^5\) and more recently the reductions of benzil to benzoin\(^6,7\) and of cyclohexanone to cyclohexanol\(^8\) (in 10\% yield) have been reported. We are unaware of other pertinent literature.

We have now developed experimental conditions under which a variety of aldehydes and relatively unhindered ketones\(^1\) can be reduced to the corresponding alcohols\(^2\) by sodium dithionite. The experimental procedures are simple, the yields are good, and the dangers, inconvenience, and expense of metal hydride reagents are avoided.

A number of examples are given in the Table. Roughly the same procedure was used for all reductions. If sufficiently soluble the substrate is dissolved in water, otherwise a 50:50 mixture of water and dioxan is used. Excess sodium hydrogen carbonate is used to keep the reaction mixture basic (otherwise no reaction occurs). The reaction mixture is held at reflux for 4 h and the sodium dithionite is added in portions (a batch of the reagent loses most of its reducing properties after one hour under the conditions used).

Most ketones are only sluggishly reduced in water or water/dioxan. However, the yields improve dramatically on using dimethylformamide/water in a 50:50 mixture (for comparison see Table). A satisfactory explanation for the beneficial effect of dimethylformamide is lacking.

Carboxylic acids and amides are not reduced under these circumstances and esters and nitriles are hydrolyzed. The reduction of levulinic acid gives an example of a selective transformation with sodium dithionite.

In summary we believe that this procedure offers a simple and useful alternative to metal hydride reductions of unhindered ketones. Sodium dithionite is inexpensive and easy to use; this recommends its use. A fuller description of the chemistry of this reagent will be published in due course.

Sodium Dithionite as a Reductant for Aldehydes and Ketones

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Sodium dithionite, Na\(_2\)S\(_2\)O\(_4\), is a reducing agent widely applied both in the laboratory and industry\(^1\). It is commonly used in biochemistry for the reduction of a variety of coenzymes and enzymes\(^1\) and in organic chemistry to reduce several types of functional groups, especially those containing nitrogen\(^3,4\).

We have now developed experimental conditions under which a variety of aldehydes and relatively unhindered ketones\(^1\) can be reduced to the corresponding alcohols\(^2\) by sodium dithionite. The experimental procedures are simple, the yields are good, and the dangers, inconvenience, and expense of metal hydride reagents are avoided.

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In summary we believe that this procedure offers a simple and useful alternative to metal hydride reductions of unhindered carbonyl compounds. Sodium dithionite is inexpensive and easy to use; this recommends its use. A fuller description of the chemistry of this reagent will be published in due course.

General Procedure for the Reduction of Aldehydes and Ketones:

A solution of substrate (50 mmol) in dioxan (175 ml) or dimethylformamide for more difficultly reducible substrates (see Table), is added to water (175 ml) containing sodium hydrogen carbonate (27.5 g). When no cosolvent is used, the substrate is added neat. Sodium dithionite (12.5 g) is added and the reaction mixture refluxed for 4 h during which time three additional 12.5 g portions of sodium dithionite are added. The reaction is carried out under an atmosphere of nitrogen. After cooling to room temperature, water is added until the solution becomes clear and thereafter the solution is extracted with ether (fururyl alcohol and \(\gamma\)-valerolactone were isolated by continuous extraction with ether for 7 and 72 hours respectively). When dimethylformamide is used as cosolvent the ether extracts are back-washed twice with water to remove traces of dimethylformamide. After drying (MgSO\(_4\) and removal of the ether, the products are isolated by either distillation or recrystallization. Identification is based on the following:

\[
\begin{align*}
\text{O} & \quad \text{Na}_2\text{S}_2\text{O}_4 / \text{solvent} \\
\text{R} & \quad \text{c} - \text{R} \\
\text{OH} & \quad \text{R} - \text{C} - \text{R} \\
1 & \quad \text{2}
\end{align*}
\]
Table. Reduction of Aldehydes and Ketones (1) to Alcohols (2) with Sodium Dithionite (Na$_2$S$_2$O$_4$)

<table>
<thead>
<tr>
<th>Substrate</th>
<th>Product</th>
<th>Solvent</th>
<th>Yield [%]</th>
<th>m.p. or b.p./torr</th>
<th>Lit. m.p. or b.p./torr</th>
<th>1H-N.M.R. δ [ppm]</th>
</tr>
</thead>
<tbody>
<tr>
<td>$n$-C$_6$H$_5$-C H$_2$-H</td>
<td>$n$-C$_6$H$_5$-CH$_2$-OH</td>
<td>H$_2$O</td>
<td>63</td>
<td>157°/760 158°/760$^a$</td>
<td>0.16 - 1.76 (m, 11H), 1.89 (s, 1H), 3.63 (s, 2H)</td>
<td>4.37 (s, 2H), 4.38 (s, 1H), 7.17 (s, 5H)</td>
</tr>
<tr>
<td>C$_6$H$_5$-C H$_2$-H</td>
<td>C$_6$H$_5$-CH$_2$-OH (1:1)</td>
<td>H$_2$O/dioxan</td>
<td>84</td>
<td>89°/8 93°/10$^a$</td>
<td>3.49 (s, 1H), 4.51 (s, 2H), 6.29 (m, 2H), 7.40 (m, 1H)</td>
<td></td>
</tr>
<tr>
<td>$n$-C$_6$H$_5$-C H$_2$</td>
<td>$n$-C$_6$H$_5$-CH$_2$</td>
<td>H$_2$O</td>
<td>90</td>
<td>65.5°/9 68 69°/20$^a$</td>
<td>0.67 - 2.60 (m, 10H), 3.38 (s, 1H), 3.58 (m, 1H)</td>
<td></td>
</tr>
<tr>
<td>H$_2$O/dioxan (1:1)</td>
<td>H$_2$O</td>
<td>80</td>
<td>160°/760 161°/760$^a$</td>
<td>1.30 - 2.36 (m, 15H) 3.91 (s, 1H)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>$n$-C$_6$H$_5$-C H$_2$-OH</td>
<td>$n$-C$_6$H$_5$-CH$_2$-H</td>
<td>H$_2$O</td>
<td>97</td>
<td>296 300° 296.2 - 297.7$^a$</td>
<td>3.91 (s, 1H)</td>
<td></td>
</tr>
<tr>
<td>C$_6$H$_5$-C H$_2$-OH</td>
<td>C$_6$H$_5$-CH$_2$</td>
<td>H$_2$O/dioxan (1:1)</td>
<td>30</td>
<td>—</td>
<td>—</td>
<td></td>
</tr>
<tr>
<td>H$_2$O/DMF (1:1)</td>
<td>H$_2$O/DMF</td>
<td>94</td>
<td>85.5°/9 100°/18$^a$</td>
<td>1.39 (d, 3H), 3.47 (s, 1H), 4.76 (q, 1H), 7.26 (s, 5H)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>H$_2$O</td>
<td>H$_2$O</td>
<td>50</td>
<td>—</td>
<td>—</td>
<td></td>
<td></td>
</tr>
<tr>
<td>H$_2$O/dioxan (1:1)</td>
<td>H$_2$O/dioxan (1:1)</td>
<td>94</td>
<td>65.5-67° 69°</td>
<td>3.14 (s, 1H), 5.56 (s, 1H), 7.22 (s, 10H)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>C$_6$H$_5$-C H$_2$</td>
<td>C$_6$H$_5$</td>
<td>H$_2$O/DMF (1:1)</td>
<td>84</td>
<td>70-71°/9 86-87°/20$^a$</td>
<td>0.64 - 1.60 (m, 13H), 1.84 (s, 1H), 3.75 (m, 1H)</td>
<td></td>
</tr>
<tr>
<td>H$_2$O/dioxan (1:1)</td>
<td>H$_2$O/dioxan (1:1)</td>
<td>54</td>
<td>79°/9 86-90°/14$^a$</td>
<td>1.42 (d, 3H), 1.63 - 2.80 (m, 4H), 4.70 (m, 1H)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>H$_2$O</td>
<td>H$_2$O</td>
<td>54</td>
<td>79°/9 100°/22</td>
<td>1.39 (d, 3H), 3.47 (s, 1H), 4.76 (q, 1H), 7.26 (s, 5H)</td>
<td></td>
<td></td>
</tr>
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<td>H$_2$O/dioxan</td>
<td>H$_2$O/dioxan</td>
<td>54</td>
<td>79°/9 86-90°/14$^a$</td>
<td>1.42 (d, 3H), 1.63 - 2.80 (m, 4H), 4.70 (m, 1H)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

$^a$ Determined by G.L.C. (conditions: 6 ft x $\frac{1}{8}$ in column, SS 10% Carbowax 20M on Chromosorb WAW 80-100 mesh; column temperature: 150° (acetoephene reaction); 230° (benzophenone reduction).

on melting or boiling points, infrared, and 1H-N.M.R. spectra, and comparison with authentic materials.

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1 See, for example: U. Baumgarte, Textilveredlung 2, 896 (1967).
3 E. Grandmougin, J. Prakt. Chem. 76, 124 (1907).
9 Handbook of Chemistry and Physics, 52nd Edt., Cleveland, Ohio, 1972.

Synthese von Keten-O-trimethylsilyl-S-alkyl-monothioacetaten

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Die extreme Reaktionsfähigkeit von Trifluoromethansulfon säure-trimethylsilyester (Trimethylsilyl-triflat, 1) erlaubte erstmals die direkte Silylierung von Carbonyl-estern$^2$. Wir fanden nun, daß Thiocarbonsäure-S-ester (2) bereits bei 0°-20° in Gegenwart molarer Mengen Triäthyamin in exothermer Reaktion durch 1 regioselektiv am Carbonyl-Sauerstoff zu Keten-O-trimethylsilyl-S-alkyl-monothioacetaten (3) silyliert werden.

Zur Erzielung hoher Ausbeuten empfiehlt es sich (insbesondere in Fällen von zu Kondensationen neigenden S-Estern), die Ester 2 zusammen mit 1 zuverlässig und Triäthyamin zutropfen zu lassen. Mit S-Athyl-thiocarboxylaten (2, R$^1$ = C$_2$H$_5$) führt die Reaktion im allgemeinen zu $Z$-/E-Gemischen von 3, mit $t$-Alkylestern (2, R$^1$ = t-C$_4$H$_9$) dagegen nur zu einem der beiden Stereoisomeren, wie die 1H-N.M.R.-Spektren zeigen.

Ausgehend von S,S'-Dialkyli-1,4-dithioseccuchinan (4) erhält man analog die Bis-O,S-seccetal 5.