The Anodic Deprotection of the Carbonyl Group Applied to Dethioacetalsation of Oses

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The anodic method of deprotection of carbonyl compounds (oxidative decomposition of gem-dithioacetals systems) is applied with success to sugars. Protected hydroxy groups like esters and cyclic acetals are not affected.

From a preliminary work devoted to the particular nature of thioacetals, further papers have described the capability of the electrochemical method to perform the deprotection of the carbonyl group according to the general equation:

\[
\begin{align*}
\text{R}^1\text{C}R^2 & \quad \text{SR}^3 & \quad \text{SR}^3 & \quad -2\text{e}^- + 2\text{Nu}^- \\
\text{H}_2\text{O} & \quad \text{R}^1\text{C}R^2 & \quad \text{Nu}^- & \quad 3\text{R}^3\text{SSR}^3
\end{align*}
\]

Reactions of this kind may be carried out either with aromatic aliphatic thioacetals. The oxidations were conducted under easy experimental conditions (e.g. wet acetonitrile at a platinum anode) with a good yield of the carbonyl product. It must be pointed out that indirect methods (using as a mediator electrogenerated cation radicals of triarylamines or polyaromatic hydrocarbons) have been also used with success.

However, it appears that the direct deblocking method, although tested mostly with aromatic ketones and aldehydes, has not been applied very extensively to polyfunctional systems implying two or three reactive groups in order to demonstrate the interest of the anodic oxidation in terms of selectivity due to the mildness of the reaction. Consequently, the deprotection of oses, owing to the fact that this class of compounds certainly present a high economic impact, may be proposed to be conducted anodically, while the chemical deblocking methods are far from satisfactory. We report here our results on the anodic reactivity of diethylidithioacetals and their transformation into the corresponding sugars. Adjacent hydroxyl groups may be acetylated (compounds 1, 2 and 3), possibly with the additional presence of a dioxolane in order to block two vicinal hydroxy groups (compounds 4, 5 and 6).

The direct anodic deprotection of oses as dithioacetals appears to be a selective method. Yields are high and the expected carbonyl compound is obtained pure after the work up procedure (Table). There is no isomerization, further oxidation or

<p>| Table. Anodic Deprotection of gem-Dithioacetals 1-6 Derived from Sugars |
|-----------------|-----------------|-----------------|-----------------|-----------------|
| R^1–C(SR^3)R^2   | R^1=C=O          | Yield (%)       | [α]_D(CHCl_3)   | Lit. [α]_D^5   |</p>
<table>
<thead>
<tr>
<th>R^1</th>
<th>R^2</th>
<th></th>
<th>(C_2H_5Cl_4)</th>
<th>(C_2H_5Cl_4)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>7</td>
<td>65</td>
<td>-23^\circ</td>
<td>-25^10</td>
</tr>
<tr>
<td>2</td>
<td>8</td>
<td>80</td>
<td>+8^\circ</td>
<td>+9.2^12,11</td>
</tr>
<tr>
<td>3</td>
<td>9</td>
<td>75</td>
<td>+4^\circ</td>
<td>+3^8</td>
</tr>
<tr>
<td>4</td>
<td>10^b</td>
<td>85</td>
<td>-75^\circ</td>
<td>-1^4</td>
</tr>
<tr>
<td>5</td>
<td>11^b</td>
<td>70</td>
<td>-74^\circ</td>
<td>-1^4</td>
</tr>
<tr>
<td>6</td>
<td>12^b</td>
<td>80</td>
<td>+8^\circ</td>
<td>-1^4</td>
</tr>
</tbody>
</table>

^a Semicarbazone in CHCl_3.
^b New compounds. \(^1^H\)- and \(^13^C\)-NMR spectral data reported in Ref. 12.
^c No data in the literature.
polymerization. The carbonyl moiety is selectively recovered and no additional oxidation process (e.g. formation of the corresponding carboxylic acid) was occurring.

In addition to the selectivity of the oxidation process (by use of the potentiostatic method), the buffering of the anolyte by an excess of solid sodium carbonate confers to the reaction mixture a moderate acidity which allows to keep the dioxolane ring intact.

Excess electricity consumption observed can be explained by the oxidation of organic sulfides as side-products formed by the anodic cleavage of the C–S bonds (for example, presence of diethyl disulfide). Their progressive appearance in the electrolysis mixture could be due to the slow decomposition of the immediate sulphonium salt (two-electron exchange with the attack of a nucleophile).

![Chemical Structure](image)

In all the cases, the sulfonium salt will be a precursor of the carbonyl compound either in solution or during the work up.

Consequently, the anodic method of deprotection seems extremely well adapted to the chemistry of the carbonyl groups of sugars and represents an attractive alternative to chemical methods for selective deblocking of dithiaoacetals under mild conditions.

Dithiaoacetals 1–6 all present an irreversible oxidation step well defined within the potential range +1.1 –+1.3 Volt vs Ag/Ag⁺ 0.1 M electrode. Electrolisis solvent was acetonitrile with lithium perchlorate (0.25 M) and 5% of water. To carry out macroelectrolyses, H-type cells were used: a glass frit separated anolyte (70 ml) and catholyte (30 ml). The working electrode was a platinum foil (A = 16 cm²) and the counter electrode was made of a graphite rod (A = 20 cm²). It is worthwhile to mention that any soluble electrolyte with non electroactive anion (BF₄⁻, PF₆⁻) may be also used.

**Anodic Deprotection of Sugar Dithiaoacetals 1–6; General Procedure:**

Anodic deprotection is performed on amounts of sugar (200 – 300 mg) corresponding to an anolyte concentration of about 10⁻³ M. The potentiostatic electrolysis (fixed oxidation potential, +1.1 V vs Ag/Ag⁺ 0.1 M) are stopped when the current has declined to at least 95%. The electricity consumptions are always much larger than 2 Faradays/mole⁻¹. For the electrolyses of 4, 5, 6, an insoluble base such as sodium carbonate is added to prevent a strong increase of the acidity in the course of the experiment. The opening of the acetal cycle moiety present additionally in the sugar does not occur.

After electrolysis, solutions are evaporated, saturated brine (25 ml) is added to water, the residue is extracted with a warm chloroform (60 ml), and the solvent evaporated. In all cases, crude yields of products are of the order of 80%. Deprotected sugars are shown to be selectively obtained by oxidation of 1–6 in mixture however with diethyl disulfide. In all cases, the produced carbonyl compound is carefully identified with an authentic sample (Table).

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