Aldehydes and Ketones from Thioacetals

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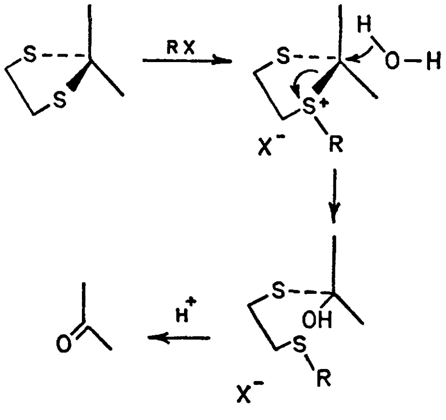
Summary Thioacetals are converted into the parent aldehyde or ketone in good yield either by methyl iodide in moist acetone or by methyl fluorosulphonate and water in liquid sulphur dioxide.

Thioacetals have long been used as a protecting group in synthesis.[1] However, because of their relative stability, they are often difficult to hydrolyse to the parent carbonyl compound. Various methods have been designed to overcome this drawback, *e.g.*, use of mercury(II)[2,3] or cadmium[4] salts, acidic conditions,[5] and oxidation to a more labile disulphone.[6]

Since sulphides usually react with alkylating agents, leading to sulphonium intermediates, which are susceptible to attack even by mild nucleophiles like water, thioacetals would be expected to yield carbonyl compounds, according to the mechanism shown in the Scheme.



Scheme

We have found that this prediction is correct: thioacetals, such as ethylene or propylene thioacetals, as well as those derived from mercaptoethanol or αα'-dimercaptodurene[7] can be smoothly converted into ketones or aldehydes, using either of the following methods.

Method A. A solution of the thioacetal in acetone containing a small amount of water is heated under reflux for several hours with an excess of methyl iodide, until no starting material can be detected by t.l.c. With acid-sensitive compounds it may be advisable to operate in the presence of powdered carbonate to neutralize the HI formed. Sodium, calcium, or barium carbonate may be used.

Method B. A solution of the thioacetal in liquid sulphur dioxide, is treated with an excess of methyl fluorosulphonate.[8] After a few minutes, water is added, and the SO_2 is allowed to evaporate. The excess of methyl fluorosulphonate and water is distilled off, the residue is extracted by an organic solvent, and worked-up as usual.

Various thioacetals have been submitted to these methods of hydrolysis: some of the data are reported in the Table.

Table

Starting carbonyl compound	Thioacetal	Yield (%) Thioacetal → carbonyl compound)	
Androstan-3-one	Ethanedithiol	85	A
		77	B[a]
Dihydrotestosterone	Ethanedithiol	85	A
	Propane-1,3-dithiol	71	A
	Mercaptoethanol	75	A
17α-Ethynyltestosterone	Ethanedithiol	85	A[b]
5β-Cholan-24-al	Ethanedithiol	60	A[b]
Acetophenone	αα'-Dimercaptodurene	90	A

[a] Use of water enriched (6%) in $H_2{}^{18}O$ leads to a ketone containing *ca.* 5% of ^{18}O. [b] Carbonate added.

Since a small amount of water is required to carry out this reaction, it can be used for the preparation of ^{18}O labelled aldehydes or ketones. Labelled androstan-3-one can readily be prepared by method B.

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