Selenium(IV) Oxide Mediated Cleavage of 1,3-Dithiolanes: A Convenient Method of Dedithioacetalization

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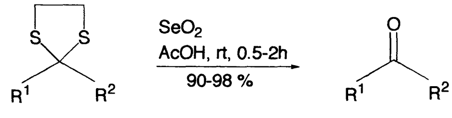
Received 20 June 1994; revised 30 August 1994

A simple and efficient method for the selenium(IV) oxide mediated cleavage of a variety of 1,3-dithiolanes is reported.

1,3-Dithiolanes are commonly used as intermediates for the reductive conversion of carbonyl compounds to their parent hydrocarbons[1] or in the synthesis of olefins.[2] Their primary use, however, involves the protection of the carbonyl function, bringing out numerous useful applications in organic synthesis[3,4] and total syntheses of natural products.[5] Thus, there is a considerable interest in efficient, general methods for their formation or cleavage. 1,3-Dithiolanes are usually obtained by acid-catalyzed condensation of carbonyl compounds with ethane-1,2-dithiol. Lewis acid catalysts used for this purpose include boron trifluoride etherate,[6] zinc(II) chloride,[7] aluminum(III) chloride,[8] titanium(IV) chloride,[9] lanthanum(III) chloride,[10] tellurium(IV) chloride,[11] tetrachlorosilane[12] and organotin triflates.[13] The cleavage of 1,3-dithiolanes is usually performed using mercury(II) or copper(II) salts, although a plethora of alternative methods is available.[4,14] Each of these methods has specific applications and limitations which depend upon the functionality and steric hindrance present in the substrate. In addition, problems often arise from the lability of the structure towards the deprotection reagents.

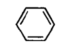
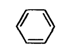
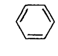
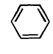
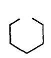
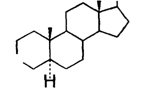
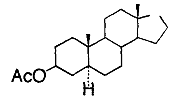
In this report is presented a simple and efficient procedure for the cleavage of 1,3-dithiolanes with selenium(IV) oxide (selenium dioxide). The salient features of the method are the high yields of recovered carbonyl compounds and the generality, which is demonstrated by derivatives bearing a variety of substituents (Table). The method proved to be particularly effective with C-3 and C-17 dithiolane derivatives of steroid ketones, which are usually removed under more vigorous conditions.[15] Furthermore, the reaction conditions are relatively mild so that other common groups, such as esters and ethers, remain intact and other functionality is unaffected by the selenium dioxide action.[16]

The reaction conditions given in the experimental section have been optimized. We point out, however, that the use of acetic acid as solvent is essential, since reaction in aprotic solvents such as tetrahydrofuran, dichloromethane or toluene furnished only a trace of the deprotected product. Reactions in aqueous mixtures of acetonitrile or acetone required prolonged reaction times (20–30 h) and resulted in lower yields. Although heating the reaction mixture shortened the reaction times (e.g. reaction of **1a** at 50 °C was complete within 15 min), the yield evidently decreased because the oxidative action of the reagent was facilitated, leading to a variety of byproducts. A 5:1 excess of selenium dioxide is the most suitable ratio, since smaller amounts of the reagent required much longer reaction time and furnished various byproducts, while larger excesses (as much as 10:1) slightly shortened the reaction time without significantly increasing the yield.



1 a-h **2 a-h**

Table: Cleavage of 1,3-dithiolanes with selenium dioxide

1,2	R^1	R^2	Time (min)	Yield^a (%)
a		CH_3	25	98
b		H	50	96
c			120	91
d	$CH_3CH_2CH_2CH_2$	H	100	90
e	$CH_3CH_2CH_2$	CH_3	70	94
f			120	92
g			90	96
h			120	94

^{a}Yield of isolated products **2** based on **1**

In conclusion, the present method provides a fast and practical procedure for the high yield cleavage of 1,3-dithiolanes, suitable for a variety of compounds.

All starting materials were purchased from either Aldrich or Steraloids. 17β-Benzyloxy-5α-androstan-3-one (**1g**) was prepared from 5α-dihydrotestosterone by benzylation. 1,3-Dithiolanes (**1a–h**) were prepared from the corresponding ketone or aldehyde (**2a–h**) by treatment with ethane-1,2-dithiol and boron trifluoride–diethyl ether complex in dichloromethane, according to a general procedure.[6] The reaction products were analyzed by capillary GLPC using a Hewlett-Packard Ultra 1 column. Products were identified by simultaneous injection of authentic compounds and by GC–MS or spectroscopic data (^{1}H NMR and IR spectra). Product yields were determined with the aid of a calibration curve which relates the response factors of the product to the response factors of dodecane (used as internal standard).

Cleavage of 1,3-Dithiolanes by Reaction with Selenium Dioxide; General Procedure:

SeO_2 (1.25 mmol) was added to a solution of dithiolane (0.25 mmol) in AcOH (4 mL) and the reaction mixture was stirred at r.t. for 0.5–2 h (Table). The mixture was filtered and the filtrate was evaporated under reduced pressure. The resulting oil was dissolved in Et_2O (10 mL), washed with aq $NaHCO_3$ (5 mL) and dried ($MgSO_4$). Removal of the solvent under reduced pressure gave the deprotected product (Table).

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