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Aerobic deprotection of monothioacetals catalyzed by trichlorooxyvanadium

Masayuki Kirihara,* Yuta Ochiai, Nobuka Arai, Shinobu Takizawa, Takefumi Momose and Hideo Nemoto *

Faculty of Pharmaceutical Sciences, Toyama Medical and Pharmaceutical University, Sugitani 2630, Toyama 930-0194, Japan

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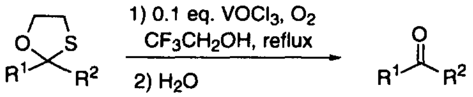
Abstract

Monothioacetals are easily deprotected into carbonyls using a catalytic amount of trichlorooxyvanadium under an oxygen atmosphere.

Keywords: thioacetals; vanadium; vanadium compounds.

The monothioacetals (*S,O*-acetals) are widely used as a carbonyl protecting group in organic synthesis due to their stability under both acidic and basic conditions.[1] Moreover, a cyclic *S,O*-acetal such as 1,3-oxathiane is a versatile synthetic reagent as an acyl anion equivalent.[2] In spite of the synthetic importance of the monothioacetals, only a few methods for the deprotection of monothioacetals have been developed, and most of the known deprotection methods require the use of a stoichiometric or an excess amount of reagents.[3]

Here we describe a novel aerobic deprotection of *S,O*-acetals catalyzed by trichlorooxyvanadium ($VOCl_3$) (Scheme 1).[4,5]



Scheme 1.

The *S,O*-acetals were efficiently deprotected in the presence of $VOCl_3$ in 2,2,2-trifluoroethanol under an oxygen atmosphere. The results are summarized in Table 1. The dithioacetal (*S,S*-acetal) was also deprotected under the same conditions, however, it took much longer to complete the reaction (entry 8).[6]

We observed that the color of the reaction mixture was initially a dark yellow, and then changed to green. The 'green' of the reaction mixture strongly suggests the presence of the V(IV) species. At present

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* Corresponding authors. Tel: +81 76 434 7533; fax: +81 76 434 4656; e-mail: kirihara@ms.toyama-mpu.ac.jp

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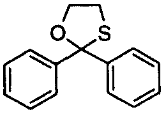
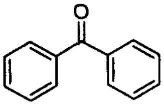
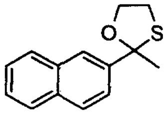
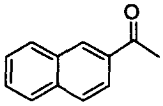
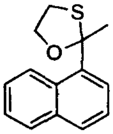
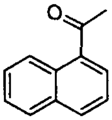
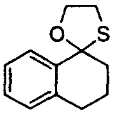
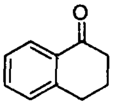
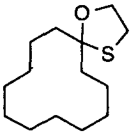
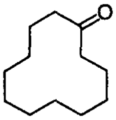
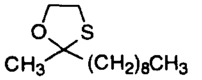
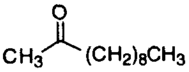
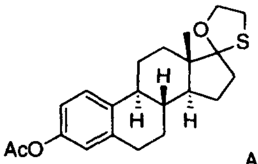
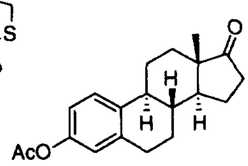
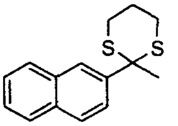
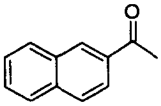
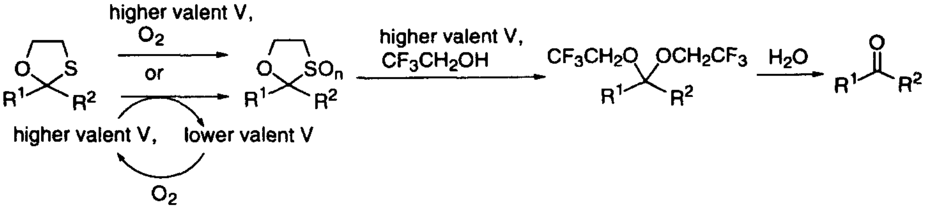
Table 1

Entry	Starting Material	Product	Reaction Time (hr)	Yield (%)
1			5.0	100
2			3.0	94
3			3.0	91
4			17.5	73
5			3.5	94
6			3.0	97
7			5.0	94
8			182 (7 days, 14 hr)	85

it is not clear what is the 'real' active species. A possible mechanism for this reaction is illustrated in Scheme 2.



Scheme 2.

The sulfur atom of an *S,O*-acetal was oxidized to the sulfoxide (*n*=1) or sulfone (*n*=2).[7] The transacetalization[8] then proceeded to afford a trifluoroethylacetal that can easily be hydrolyzed into a carbonyl.

The general experimental procedure for the deprotection is as follows: To a solution of the monothioacetal (1.0 mmol) in 2,2,2-trifluoroethanol (20 ml) was added vanadium oxytrichloride (0.1 mmol) under an oxygen atmosphere. The mixture was heated under reflux for 3–17.5 h. After cooling, saturated sodium bicarbonate (0.1 ml) was added and the resulting mixture was dried over magnesium sulfate, filtered through Celite and evaporated to afford the crude product. Purification by silica gel column chromatography (*n*-hexane/ethyl acetate) afforded the pure sample.

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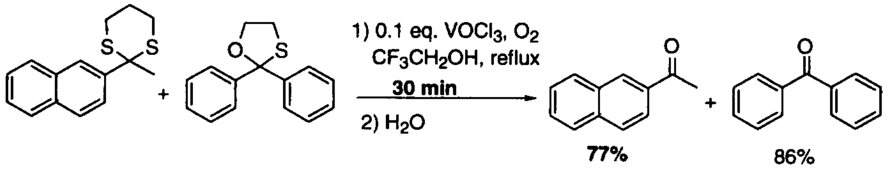
4. Nishide et al. reported the demonothioacetalization catalyzed by Ag(I)-I_2: Nishide, K.; Nakamura, D.; Yokota, K.; Sumiya, T.; Node, M.; Ueda, M.; Fuji, K. *Heterocycles* **1997**, *44*, 393–404.
5. Ravindranathan et al. reported that *S,O*-acetals were converted into carbonyls in the presence of a catalytic amount of trimethylsilyl trifluoromethanesulfonate (TMSOTf). However, this method is restricted to the *S,O*-acetals bearing an aryl ring: Ravindranathan, T.; Chavan, S. P.; Dantale, S. W. *Tetrahedron Lett.* **1995**, *36*, 2285–2288.

6. Interestingly, the dedithioacetalization was promoted in the presence of a monothioacetal. In the case of the equimolar mixture of the dethioacetal of 2-acetonaphtone and the monothioacetal of benzophenone, a 77% yield of 2-acetonaphtone was obtained in 30 min. In the absence of the monothioacetal, 2-acetonaphtone was obtained in only 7% yield under the same conditions. Further details of this result are currently under investigation.



7. There are two possibilities concerning the oxidation of the sulfur atom: (1) higher valent vanadiums catalyzed the oxidation with oxygen; and (2) higher valent vanadiums directly oxidized the sulfur atom. The resulting lower valent vanadium was reoxidized into the higher valent vanadiums by oxygen.
8. Higher valent vanadiums [V(V) and V(IV)] are known to act as Lewis acids, and we observed that acetals (*O,O*-acetals) were converted into carbonyls under the same conditions.