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A Convenient Method for the Hydrolysis of Diethylthioacetals Catalyzed by Trityl Perchlorate

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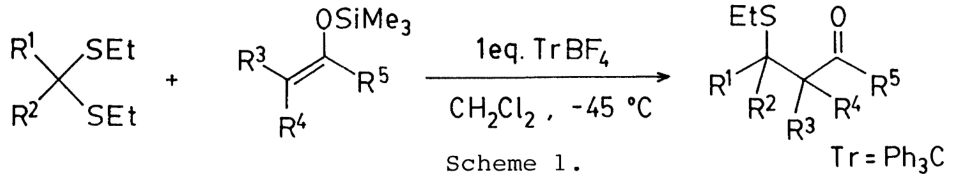
Treatment of diethylthioacetals with two equivalents of trityl methyl ether in the presence of a catalytic amount of trityl perchlorate, and successive quenching with aqueous sodium hydrogencarbonate gave parent carbonyl compounds, hydrolyzed products, in high yields under mild conditions. According to this method, it is also possible to hydrolyze diethylthioacetals selectively even when another thioacetal, such as 1,3-dithiane, coexisted in the same molecule.

Thioacetals are widely used in organic synthesis as the protected carbonyl compounds because of their stability under various conditions,1) and are also frequently employed in the synthesis of complex natural products as masked acyl anion equivalents, versatile synthetic intermediates.2) Hydrolysis of thioacetals to parent carbonyl compounds is generally carried out by the use of heavy metal salts, such as $HgCl_2$, $CuCl_2$, $AgNO_3$. In recent years, methods for hydrolysis of thioacetals without using such heavy metal salts have attracted much attention, and a number of methods, such as oxidative hydrolysis and alkylative hydrolysis, have been reported.1,2) However, some of these methods have several disadvantages; for example, it is impossible to apply oxidative hydrolysis to thioacetals having sulfide group in the same molecule, because sulfide group is also easily oxidized to sulfoxide. Therefore, it is still desired to develop a new method for hydrolysis of thioacetals under mild conditions.

Now, we wish to report a convenient method for the hydrolysis of diethylthioacetals by the use of two equivalents of trityl methyl ether in the presence of a catalytic amount of trityl perchlorate.

In the previous paper,3) it has been reported that the reaction of diethylthioacetals with silyl enol ethers is smoothly promoted by trityl tetrafluoroborate, and γ-ketosulfides are obtained in good yields (Scheme 1).

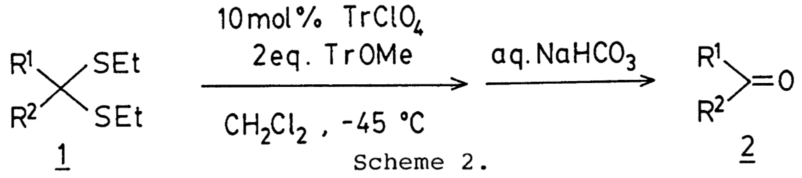


Scheme 1.

In this reaction, trityl cation plays an important role as an effective activator of thioacetals.[4] So we next tried the hydrolysis of thioacetals based on this characteristic property of "thiophilicity of trityl cation".

First, diethylthioacetal of 4-phenylcyclohexanone was treated with two equivalents of $TrBF_4$ and trimethylsilyl methyl ether in CH_2Cl_2 at -45 °C, and successive quenching with aqueous sodium hydrogencarbonate gave the parent ketone in 49% yield. After screening the reaction conditions taking diethylthioacetal of 4-phenylcyclohexanone as a model, it was found that the reaction was smoothly promoted by the use of two equivalents of TrOMe in the presence of a *catalytic* amount of $TrClO_4$ in CH_2Cl_2 at -45 °C, and quenching the resulting mixture with aqueous sodium hydrogencarbonate afforded the parent ketone in 95% yield. On the other hand, dimethylacetal of 4-phenylcyclohexanone was obtained in 86% yield when the reaction was quenched with pyridinemethanol.

Thus, it became apparent that hydrolysis of diethylthioacetals was effectively achieved by the use of two equivalents of TrOMe in the presence of a catalytic amount of $TrClO_4$. Then, hydrolysis of diethylthioacetals having various functional groups was examined according to the procedure depicted in Scheme 2. And the results are summarized in Table 1.



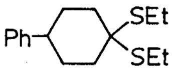
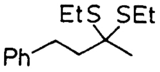
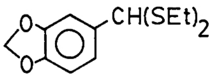
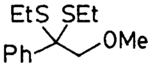
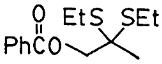
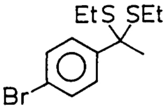
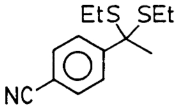
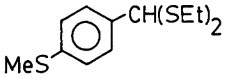
Scheme 2.

As shown in Table 1, various functional groups were tolerated during hydrolysis (entries 4-9). It is also noted that under the reaction conditions sulfide group was left intact (entry 9), which was oxidized to sulfoxide by oxidative hydrolysis of thioacetals.

Although there have been a wide variety of methods for hydrolysis of thioacetals, the method for the selective hydrolysis between two different thioacetals was little known.[5] In the present study, it was found that diphenylthioacetal and 1,3-dithiane were hardly hydrolyzed under the reaction conditions mentioned above. Consequently, the selective hydrolysis between diethylthioacetal and diphenylthioacetal was successfully carried out as shown in Scheme 3. The selective hydrolysis of diethylthioacetal was also carried out when 1,3-dithiane coexisted in the same molecule (Scheme 4). This method for the selective hydrolysis between two different thioacetals would enhance synthetic usefulness of the present reaction.

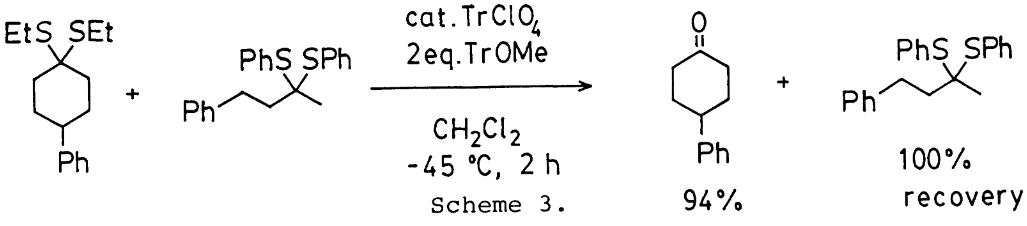
Typical procedure is described for hydrolysis of 1,1-diethylthio-4-phenylcyclohexane: Under argon atmosphere to a CH_2Cl_2 solution (2 ml) of $TrClO_4$ (0.04 mmol) and TrOMe (0.8 mmol) was added 1,1-diethylthio-4-phenylcyclohexane (0.4 mmol) in CH_2Cl_2 (3 ml) at -45 °C, and the reaction mixture was stirred for 2.5 h at this temperature. The reaction was quenched with aqueous solution of $NaHCO_3$, and stirring was continued for a few minutes. The organic layer was separated, and then aqueous layer was extracted with CH_2Cl_2. After the evaporation of the solvent the residue was purified with preparative TLC to afford 4-

Table 1. Hydrolysis of diethylthioacetals

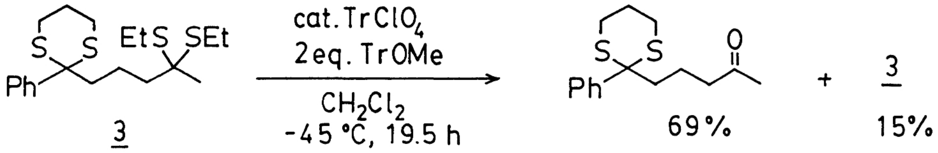
Entry	Thioacetal $\underline{1}$	Reaction time/h	Yield/%[a)]
1		2.5	95
2		2.5	96
3	$PhCH(SEt)_2$	2	85
4		7	86
5		6.5	96
6		1.5[b)]	94
7		6	89
8		19	84
9		26.5	86

a) Isolated yields. All the products gave satisfactory NMR and IR spectra.

b) The reaction was carried out at 0 °C.



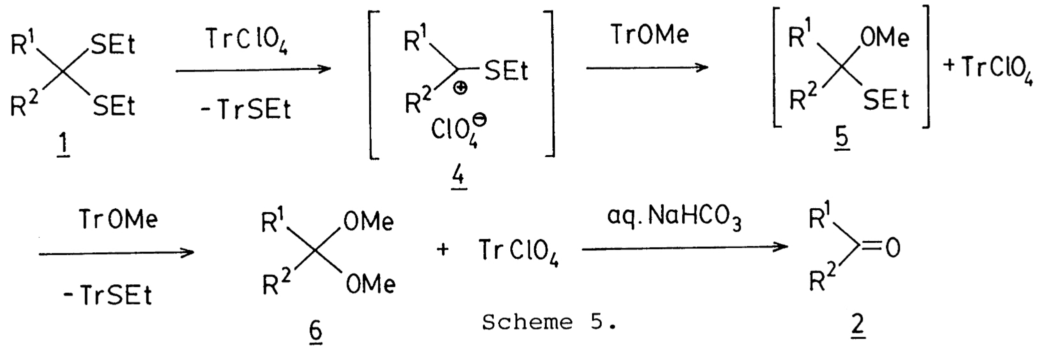
Scheme 3.



Scheme 4.

phenylcyclohexanone (0.38 mmol, 95%).

In the present examples, yellow color of trityl cation was maintained throughout the reaction, and trityl ethyl sulfide was isolated as co-product. In addition, when the reaction was quenched with base, pyridinemethanol, the corresponding dimethylacetal was obtained. These results indicate that the reaction pathway shown in the following Scheme 5 is most reasonable. That is, thioacetal (1) was activated by $TrClO_4$, and carbenium ion (4) was generated accompanied with the elimination of TrSEt. Then the nucleophilic attack of TrOMe to the carbenium ion (4) produced hemithioacetal (5) along with the regeneration of $TrClO_4$. Finally, dimethylacetal (6) was formed by repetition of the similar reaction mentioned above. When the reaction was quenched with aqueous sodium hydrogencarbonate, dimethylacetal (6) was converted to the parent carbonyl compound (2),$^{6)}$ and treatment of the reaction mixture with pyridinemethanol gave dimethylacetal (6), respectively. As a result, it is noted that trityl methyl ether act as both a nucleophile and a source of trityl cation.



Scheme 5.

Thus, according to the present method, the hydrolysis of diethylthioacetals is carried out under mild conditions without using heavy metal salts. And it is also noted that diethylthioacetal was selectively hydrolyzed when another thioacetal, such as 1,3-dithiane, coexisted in the same molecule.

References

1) T. W. Greene, "Protective Groups in Organic Synthesis," John Wiley & Sons, New York (1981), pp. 129-138.

2) B. -T. Gröbel and D. Seebach, Synthesis, 1977, 357.

3) M. Ohshima, M. Murakami, and T. Mukaiyama, Chem. Lett., 1985, 1871.

4) Backinowsky et al. reported that the reaction of sugar 1,2-thioorthoesters with trityl ethers in the presence of $TrClO_4$ afforded 1,2-*trans*-glycosides: L. V. Backinowsky, T. E. Tsvetkov, N. F. Balan, N. E. Byramova, and N. K. Kochetkov, Carbohydr. Res., 85, 209 (1980).

5) It has been reported that, by the use of isoamyl nitrite, diethylthioacetal of aldehyde was selectively hydrolyzed when diethylthioacetal of ketone coexisted: K. Fuji, K. Ichikawa, and E. Fujita, Tetrahedron Lett., 1978, 3561.

6) Treatment of benzaldehyde dimethylacetal with a catalytic amount of $TrClO_4$, and successive addition of aqueous sodium hydrogencarbonate gave benzaldehyde, hydrolyzed product, in good yield.

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