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A novel approach towards dethioacetalization reactions with H_2O_2–$SOCl_2$ system

Kiumars Bahrami [a,b,*], Mohammad Mehdi Khodaei [a,b,*], Maryam Tajik [a], Vida Shakibaian [a]

[a] Department of Organic Chemistry, Faculty of Chemistry, Razi University, Kermanshah 67149-67346, Iran
[b] Nanoscience and Nanotechnology Research Center (NNRC), Razi University, Kermanshah 67149-67346, Iran

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Abstract

A simple and efficient protocol for the deprotection of dithioacetal, 1,3-dithianes and 1,3-dithiolanes has been developed using H_2O_2–$SOCl_2$ reagent system. In addition to the absence of overoxidation products for oxidation-prone substrates, high chemoselectivity, the low cost and availability of the reagents, simplicity of the method, short reaction times, and excellent yields can also be considered as strong points for this method.

Keywords: Deprotection; Carbonyl protecting group; Dethioacetalization; Dithioacetals; Hydrogen peroxide

Protection of carbonyls and their deprotection at some appropriate stage are important transformations often encountered in synthesis of multifunctional natural and unnatural organic compounds because of their ubiquity and remarkable synthetic flexibility. As a carbonyl protecting group, the S,S-acetal function has found wide use in organic synthesis due to its easy access [1] and high stability towards both acidic and basic conditions. In addition, S,S-acetals are often used as acyl anion equivalents in C–C bond forming reactions [2]. A variety of methods for deprotection of dithioacetals to carbonyl compounds have been developed to date [3–11].

Nevertheless, these methods have some disadvantages such as long reaction times, toxic reagents, expensive catalysts or not readily available reactives, and unwanted side reactions. Hence, improved methods for dethioacetalization using cheap and less toxic reagents coupled with simple reaction conditions are required. In this respect, we are interested in introducing an efficient reagent system to overcome these limitations.

As part of our continuing studies on the use of hydrogen peroxide in organic synthesis [12], we now wish to report a reasonably simple and efficient method for the chemoselective dethioacetalization of dithioacetals using H_2O_2 in the presence of $SOCl_2$ in excellent yields (Scheme 1).

We have selected 2-phenyl-1,3-dithiolane (Table 1, entry 1) as a model compound to examine the effects of different amount of H_2O_2 and $SOCl_2$ in acetonitrile at room temperature. The best result (94% yield) was obtained by carrying out the reaction with 1:2:1 mol ratios of thioacetal, H_2O_2 and $SOCl_2$ for 1 min. In the absence of $SOCl_2$ no

* Corresponding authors at: Department of Organic Chemistry, Faculty of Chemistry, Razi University, Kermanshah 67149-67346, Iran.
E-mail address: kbahrami2@hotmail.com (K. Bahrami).

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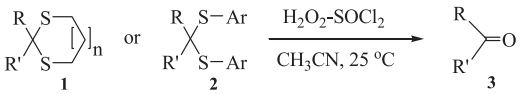


n = 0, 1
R, R' = Alkyl, aryl, H

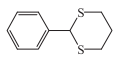
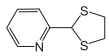
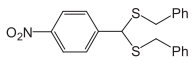
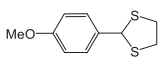
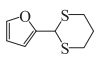
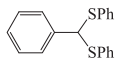
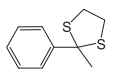
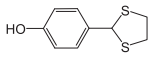
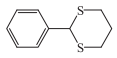
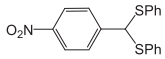
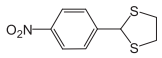
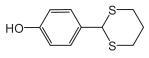
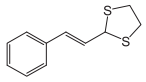
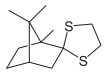
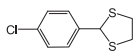
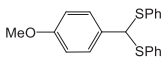
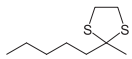
Scheme 1. Deprotection of thioacetals.

dethioacetalization of the model compound was observed, even after prolonged reaction times. In a blank reaction, $SOCl_2$ alone without H_2O_2 was found to give low yield of product. These results mean that both a H_2O_2 and $SOCl_2$ are essential for the dedithioacetalization to occur. We also studied the use of HCl instead of $SOCl_2$ for this purpose. Our observations show that this reaction remained incomplete and only 53% of the desired product was obtained after 1 h.

Acetonitrile is the solvent of choice as the best results were obtained. Other solvents such as chloroform, dichloromethane, toluene, and ethyl acetate are not as effective as acetonitrile.

To determine functional group compatibility and to investigate chemoselectivity in this reaction, a variety of dithioacetals, 1,3-dithianes and 1,3-dithiolanes of aromatic and aliphatic aldehydes and ketones were subject to the optimized deprotection conditions. As illustrated in Table 1, thioacetals carrying either electron-donating or electron withdrawing substituents reacted very well to give the corresponding aldehydes in excellent yields with high purity. These substrates selectively underwent deprotection reaction without undergoing further structural changes in their functional groups. For example, acid sensitive thioacetal such as 2-(1,3-dithiolan-2-yl)furan worked well without the formation of any side products, which are normally observed either in the presence of protic or Lewis acids (Table 1, entry 13).

Table 1
Deprotection of dithioacetals, 1,3-dithiolanes and 1,3-dithianes with H_2O_2–$SOCl_2$ in CH_3CN.[a]

Entry	Substrate	Yield %[b] (t/min)	Entry	Substrate	Yield %[b] (t/min)
1		94 (1)	11		92 (1)
2		92 (5)	12		90 (3)
3		92 (1)	13		93 (1)
4		95 (1)	14		92 (2)
5		92 (1.5)	15		94 (1)
6		91 (5)	16		92 (3)
7		91 (3)	17		93 (2)
8		93 (1)	18		90 (6)
9		92 (1)	19		95 (1)
10		92 (2)	20		92 (2)

[a] All of the products are known compounds, which were identified from their physical constants [15], their spectral data (IR, ^{1}H NMR) and comparison with authentic samples (superimposable IR and co-TLC).
[b] Yields refer to pure isolated products.