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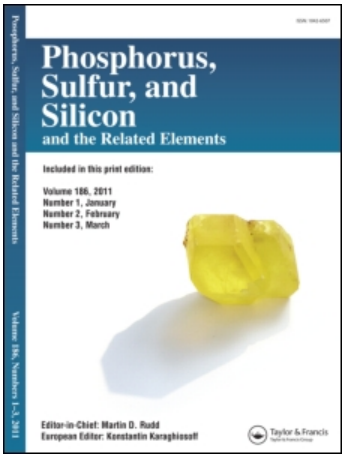


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# A Convenient Method for Dethioacetalization of 1,3-Dithiolanes and 1,3-Dithianes Using Benzyltriphenylphosphonium Peroxymonosulfate in Aprotic Solvent

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Online publication date: 27 October 2010

**To cite this Article** Hajipour, A. R. , Mallakpour, S. E. , Mohammadpoor-Baltork, I. and Adibi, H.(2002) 'A Convenient Method for Dethioacetalization of 1,3-Dithiolanes and 1,3-Dithianes Using Benzyltriphenylphosphonium Peroxymonosulfate in Aprotic Solvent', Phosphorus, Sulfur, and Silicon and the Related Elements, 177: 12, 2805 — 2811
**To link to this Article: DOI:** 10.1080/10426500214884
**URL:** http://dx.doi.org/10.1080/10426500214884

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*Phosphorus, Sulfur and Silicon*, 2002, Vol. 177:2805–2811
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1042-6507/02 $12.00 + .00
DOI: 10.1080/10426500290146839

# A CONVENIENT METHOD FOR DETHIOACETALIZATION OF 1,3-DITHIOLANES AND 1,3-DITHIANES USING BENZYLTRIPHENYLPHOSPHONIUM PEROXYMONOSULFATE IN APROTIC SOLVENT

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(Received March 11, 2002; accepted May 10, 2002)

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*Benzyltriphenylphosphonium peroxymonosulfate in the presence of bismuth chloride was found to be an efficient and mild reagent for the dethioacetalization of 1,3-dithiolanes and 1,3-dithianes to the corresponding carbonyl compounds under aprotic conditions.*

*Keywords:* 1,3-Dithianes; 1,3-dithiolanes; benzyltriphenylphosphonium peroxymonosulfate; carbonyl compounds; dethioacetalization

## INTRODUCTION

The protection of certain functional groups and the deprotection of the protected derivatives constitute important processes in the synthetic chemistry of polyfunctional molecules including the total synthesis of natural products. Cyclic thioacetals such as 1,3-dithiolanes and 1,3-dithianes find wide applications in organic synthesis, particularly as carbonyl protecting groups[1] or intermediates in the reductive transformation of carbonyl compounds to the corresponding hydrocarbons[2] or olefins.[3] Many procedures are available in the literature for the preparing of thioacetals.[4] However, the dethioacetalization to the corresponding carbonyl compounds is not an easy process because of the stability

We are thankful to the Isfahan University of Technology (IUT) Research Council for the partial support of this work.

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of these derivatives in both acidic and basic conditions and is usually carried out through hydrolytic[5] or oxidative methods.[6] Recently, for selective deprotection of thioacetals in aprotic solvent manganese-based oxidants ($KMnO_4$, $BaMnO_4$, and $MnO_2$) also has been reported.[7] However, some of these methods invariably require longer reaction times and involve toxic metal ions and expensive reagents which are detrimental to the environment. Therefore, there is a need for a simple, less expensive and safer method for deprotection of thioacetals.

Oxone ($2KHSO_5.KHSO_4.K_2SO_4$) is an inexpensive, water-soluble and stable oxidizing reagent that is commercially available, but this reagent is insoluble in organic solvents and buffering is needed due to its acidity.[8] Recently, we have reported benzyltriphenylphosphonium peroxymonosulfate **1** ($PhCH_2Ph_3PHSO_5$) as a mild, inexpensive, and efficient oxidising reagent for oxidation of alcohols to aldehydes and ketones under aprotic[9a] or solvent-free conditions,[9b] oxidative deprotection of trimethylsilyl and tetrahydropyranyl ethers and ethylene acetals under nonaqueous conditions[9c] or microwave irradiation,[9d] conversion of oximes, phenylhydrazones, 2,4-dinitrophenylhydrazones and semicarbazones to carbonyl compounds in aprotic solvent,[9e] oxidation of urazoles to triazolinediones in a solventless system[9f] and selective oxidation of sulfides and thiols to the corresponding sulfoxides and disulfides under solvent-free conditions.[9g] We now report benzyltriphenylphosphonium peroxymonosulfate **1** as an efficient and selective reagent for the deprotection of 1,3-dithiolanes **2a–d** and 1,3-dithianes **2e–w** to the corresponding carbonyl compounds **3a–w** under aprotic and nonaqueous conditions.

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Benzyltriphenylphosphonium peroxymonosulfate **1**, a mild, efficient, stable, and cheap reagent, is a white powder, quite soluble in dichloromethane, chloroform, acetone, and acetonitrile and insoluble in nonpolar solvents such as carbon tetrachloride, *n*-hexane and diethyl ether. This reagent is readily prepared by the dropwise addition of an aqueous solution of Oxone to an aqueous solution of benzyltriphenylphosphonium chloride in quantitative yield at room temperature and could be stored for months without losing its potency.[9] The amounts of $HSO_5^-$ in this reagent have been determined by an iodometric titration method[10] and the measurements are consistent with almost 99% by weight of active oxidising agent.

## RESULTS AND DISCUSSION

Deprotection of thioacetals with reagent **1** proceeds under nonaqueous conditions. Initially, the effect of various solvents such as $Et_2O$, $CH_2Cl_2$,

THF, $CHCl_3$, and $CH_3CN$ on the deprotection of 2-(3-nitrophenyl)-1,3-dithiane **2f** as a model compound with reagent **1** in the presence of bismuth chloride at reflux was examined. Only acetonitrile was a suitable solvent for this oxidation system. Then, we explored the role of the reagent **1** in the presence of hydrated and anhydrous metal salts such as $ZnCl_2$, $FeCl_3.6H_2O$, $AlCl_3$, and $BiCl_3$ in dry aprotic solvent for the deprotection of **2f**. It was found that $BiCl_3$ was effective metal salt for the promotion of the reaction in dry acetonitrile. Addition of $BiCl_3$ in dry acetonitrile under reflux in the absence of reagent **1** did not effect any changes on dethioacetalization of **2f** after prolonged reaction times. The reagent **1** also was an ineffective compound for deprotection of **2f** in the absence of $BiCl_3$ in dry acetonitrile. The optimum molar ratio of thioacetal, to $BiCl_3$ to oxidant **1** (1:1:2) is found to be ideal for complete deprotection of thioacetals **2a–w** to carbonyl compounds **3a–w** while the reaction remains incomplete with lesser amounts for example 1:1:1 and 1:1:1.5.

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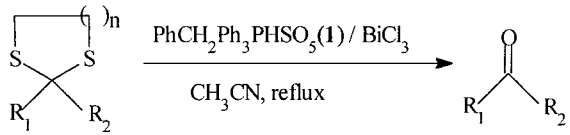
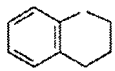
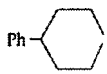
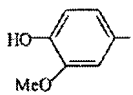
By using this method, deprotection of a thioacetal is achieved by stirring a homogeneous mixture of a thioacetal **2**, BiCl3, and a twofold excess of reagent **1** in refluxing acetonitrile. The reaction time is usually between 1–6 h. The carbonyl compounds **3** are isolated by filtering the reaction mixture followed by washing the solid residue with solvent. Evaporation of filtrate under vacuum followed by flash chromatography on $SiO_2$ often produces pure carbonyl compound **3** in high yield (Table I and Scheme 1).




**SCHEME 1**

This method offers a simple, mild, and efficient route for converting thioacetals to the corresponding carbonyl compounds. As evident from the results presented in Table I, functional groups such as $NO_2$ and MeO increase the duration of reaction. This could be the effect of producing complexes between these functional groups with $BiCl_3$. Notably, aldehydes did not undergo further oxidation to their carboxylic acids under the reaction conditions. To demonstrate the utility of the procedure described here, a macroscale reaction (10 g) was carried out at

**TABLE I** Deprotection of 1,3-Dithianes and 1,3-Dithiolanes with Reagent **1** in the Presence of Bismuth Chloride in Refluxing Acetonitrile[a,b]

| Product | $R_1$ | $R_2$ | n | Time (h) | Yield (%)[c] |
|---|---|---|---|---|---|
| **3a** | Ph | Me | 1 | 2 | 95 |
| **3b** | 4-Cl—$C_6H_4$ | Me | 1 | 3 | 88 |
| **3c** | 2-$MeOC_6H_4$ | H | 1 | 4 | 87 |
| **3d** | 3-Pyridyl | Me | 1 | 2 | 96 |
| **3e** | 2-$O_2N$—$C_6H_4$ | H | 2 | 6 | 85 |
| **3f** | 3-$O_2N$—$C_6H_4$ | H | 2 | 6 | 87 |
| **3g** | 4-$O_2N$—$C_6H_4$ | H | 2 | 6 | 90 |
| **3h** | 4-Cl—$C_6H_4$ | H | 2 | 3 | 91 |
| **3i** | 4-Br—$C_6H_4$ | $CH_2Br$ | 2 | 4 | 85 |
| **3j** |  | — | 2 | 2 | 95 |
| **3k** | Ph | H | 2 | 1 | 99 |
| **3l** | $Me_2CHCH_2$ | Me | 2 | 5 | 85 |
| **3m** | 4-Cl—$C_6H_4$ | Me | 2 | 2 | 98 |
| **3n** | Ph | Ph | 2 | 3 | 95 |
| **3o** | 2-Pyridyl | Ph | 2 | 3 | 94 |
| **3p** | 4-Cl—$C_6H_4$ | Ph | 2 | 2.5 | 92 |
| **3q** | 2-$MeOC_6H_4$ | H | 2 | 4 | 88 |
| **3r** | 4-$MeOC_6H_4$ | H | 2 | 3 | 89 |
| **3s** | Ph | Me | 2 | 1 | 95 |
| **3t** | $CH_3(CH_2)_5$ | H | 2 | 5 | 86 |
| **3u** |  | — | 2 | 4 | 90 |
| **3v** |  | — | 2 | 4 | 87 |
| **3w** |  | H | 2 | 1 | 91 |

[a] Substrate/$BiCl_3$/Oxidant (1:1:2).
[b] Confirmed by comparison with known samples.[11]
[c] Yield of isolated carbonyl compound after purification.

reflux condition for the deprotection of 2-methyl-2-(4-chlorophenyl)-1,3-dithiolane **2b** to afford 4-chloroacetophenone **3b** in 91% yield.

A comparison of the results of deprotection of thioacetals by our method (**I**) with those reported for $MnO_2/AlCl_3$ (**II**),[7] Oxone/wet $Al_2O_3$ (**III**)[6e] and $SeO_2$ (**IV**)[6h] is shown in Table II. This reagent is superior to reported reagents in terms of high yield and the amount of oxidant required.

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**TABLE II** Comparison of Deprotection of Thioacetals by Our Method with Those Reported in the Literature

| | | | Yield (%)/Time (min) | | | |
|---|---|---|---|---|---|---|
| $R_1$ | $R_2$ | n | **I**[a] | **II**[b] | **III**[c] | **IV**[d] |
| Ph | H | 2 | 99/60 | 96/90 | 70/50 | — |
| 4-Cl—$C_6H_4$ | H | 2 | 91/180 | 92/120 | — | — |
| Ph | Me | 1 | 95/120 | — | 91/120 | 98/25 |

[a]Substrate/$PhCH_2Ph_3PHSO_5$/$BiCl_3$ (1:2:1).
[b]Substrate/$MnO_2$/$AlCl_3$ (1:7:1.5).
[c]Substrate/Oxone/wet $Al_2O_3$ (1:5).
[d]Substrate/$SeO_2$ (1:5).

In conclusion, we report a new and efficient methodology for the regeneration of aldehydes and ketones from thioacetals under aprotic conditions. The stability, routine preparation of the reagent and easy work-up make this method a novel and useful one relative to the present methodologies for regeneration of carbonyl compounds from thioacetals.

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## EXPERIMENTAL

### General

All of the yields refer to isolated products after purification. All of the products were characterized by comparison of their spectral (IR, $^1$H-NMR, and TLC) and physical data (melting and boiling points) with those of authentic samples.[11] All $^1$H-NMR spectra were recorded at 90 MHz in $CDCl_3$ relative to TMS as an internal standard and IR spectra were recorded on Shimadzu 435 IR spectrometer. The reagent **1** was prepared according to our previously reported procedures.[9] The carbonyl derivatives were prepared from the corresponding carbonyl compounds and 1,2-ethanedithiol and 1,3-propanedithiol according to the reported procedures.[4]

### Deprotection of 1,3-Dithiolanes with Reagent 1 in Refluxing Acetonitrile

#### *General Procedure*

In a round-bottom flask (25 mL) equipped with a condenser and a magnetic stirrer, to a solution of 1,3-dithiolane **2a–d** (1 mmol) and bismuth chloride (0.315 g, 1 mmol) in dry acetonitrile (5 mL) was added

benzyltriphenylphosphonium peroxymonosulfate **1** (0.7 g, 2 mmol). The reaction mixture was stirred under reflux conditions for the time specified in Table I. After disappearance of starting material monitored by TLC, the mixture was cooled to room temperature, filtered and the filter cake washed with acetonitrile (10 mL). The filtrate was evaporated under reduced pressure. The crude product was purified by flash chromatography on $SiO_2$ (eluent: cyclohexane) affording the desired carbonyl compound **3a–d**.

## Deprotection of 1,3-Dithianes with Reagent 1 in Refluxing Acetonitrile

### *General Procedure*

In a round-bottom flask (25 mL) equipped with a condenser and a magnetic stirrer, to a solution of 1,3-dithiane **2e–w** (1 mmol) and bismuth chloride (0.315 g, 1 mmol) in dry acetonitrile (5 mL) was added benzyltriphenylphosphonium peroxymonosulfate **1** (0.7 g, 2 mmol). The reaction mixture was stirred under reflux conditions for the time specified in Table I. After disappearance of starting material monitored by TLC, the mixture was cooled to room temperature and filtered off. The filter cake was washed with acetonitrile (10 mL) and the filtrate was evaporated under reduced pressure to afford the crude carbonyl compound. The crude product was purified by flash chromatography on $SiO_2$ (eluent: cyclohexane) affording the carbonyl compound **3e–w**.

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## Macroscale Deprotection of 1,3-Dithiolanes

### *Typical Procedure*

In a round-bottom flask (1 L) equipped with a condenser and a magnetic stirrer, to a solution of 2-methyl-2-(4-chlorophenyl)-1,3-dithiolane **2b** (10 g, 43.3 mmol) and bismuth chloride (13.6 g, 43.3 mmol) in dry acetonitrile (200 mL) was added benzyltriphenylphosphonium peroxymonosulfate **1** (30.31 g, 86.6 mmol). The reaction mixture was stirred under reflux conditions for 3 h. After disappearance of starting material monitored by TLC, the reaction mixture was cooled to room temperature and filtered through a sintered glass funnel and the filter cake was washed with acetonitrile (150 mL). The filtrate was evaporated under reduced pressure and the resulting crude material was purified by flash chromatography on $SiO_2$ (eluent: cyclohexane) to afford 4-chloroacetophenone **3b** (6.06 g, 91%), bp 231–232°C/760 Torr (Lit.[11] bp 232°C/760 Torr). IR (KBr): $\nu = 3050$ (m), 2890 (m), 1680 (s), 1590 (s), 1400 (m), 1250 (s), 830 (m), 760 (m) $cm^{-1}$. $^1$H-NMR ($CDCl_3$, 90 MHz): $\delta = 2.6$ (s, 3H), 7.4–7.7 (d, 2H, $J = 6$ Hz), 7.9–8.2 (d, 2H, $J = 6$ Hz) ppm.

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