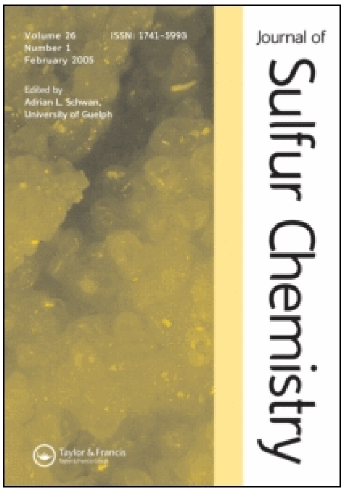

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Benzyltriphenylphosphonium tribromide: a mild, regenerable and efficient reagent for the deprotection of dithioacetals

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RESEARCH ARTICLE

Benzyltriphenylphosphonium tribromide: a mild, regenerable and efficient reagent for the deprotection of dithioacetals

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Benzyltriphenylphosphonium tribromide (**1**) is used as a regenerable and efficient reagent for deprotection of dithioacetals in dichloromethane/methanol as solvent in room temperature. The reaction can be carried out in excellent yield and short reaction time and the purification of products is straightforward.

Keywords: Benzyltriphenylphosphonium tribromide; Thioacetals; Deprotection.

1. Introduction

Dithioacetals are useful protecting groups, routinely used in organic synthesis [1]. However, the generation of carbonyl compounds from the corresponding dithioacetals is a demanding task [2] because of the stability of these dithio-acetals and -ketals under acidic and basic conditions. There are several dethioacetalization methods [3], which involve the use of heavy metal salts such as mercury(II) chloride [4], mercury(II) oxide, boron trifluoride–diethyl ether [5], cerium(IV) ammonium nitrate [6], and selenium dioxide [7], which are very toxic to the environment. Consequently, there is a demand for the development of new methods which proceed under mild and environmentally benign conditions, such as that recently reported using visible light [8].

2. Results and discussion

In continuing our research on ammonium and phosphonium salts [9], we have recently reported the synthesis of benzyltriphenylphosphonium tribromide (BTPTB, **1**) and its application for useful bromination of aromatic compounds [10]. Herein we report a new method for the synthesis of (**1**) by oxidation of bromide ion by Oxone® ($2KHSO_5$, $KHSO_4$, K_2SO_4). Various

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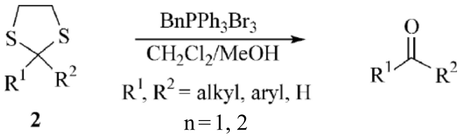
methods have been reported in the literature for the preparation of tribromides by oxidation of bromide ion [11], but most of the oxidants are expensive. In this method Oxone® was used as an inexpensive oxidant for preparation of tribromide ion by oxidation of bromide ion in aqueous solution (scheme 1).

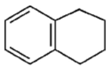
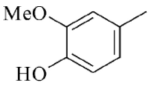
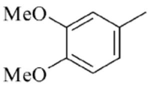
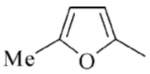
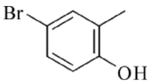
$$\mathrm{BzPPh_3Br} \xrightarrow[\mathrm{H_2O}]{\mathrm{Oxone\ /NaBr}} \underset{\mathbf{1}}{\mathrm{BnPPh_3Br_3}}$$

SCHEME 1



SCHEME 2

Table 1. Deprotection of dithioacetals (**2**) to the corresponding carbonyl compounds using benzyltriphenylphosphonium tribromide (**1**)[a,b].

Substrate	R^1	R^2	*n*	Time (*t*/min)	Yield (%)[b]
2a	Ph	Ph	2	12	80
2b	4-ClC_6H_4	Ph	2	10	60
2c	4-BrC_6H_4	CH_2Br	2	10	95
2d	4-ClC_6H_4	CH_3	2	2	90
2e	4-BrC_6H_4	CH_3	2	10	85
2f			2	10	85
2g	-$(CH_2)_2CHPh(CH_2)_2$-		2	10	70
2h	2-$O_2NC_6H_4$	H	2	8	95
2i	3-$O_2NC_6H_4$	H	2	12	96
2j	4-$O_2NC_6H_4$	H	2	5	98
2k	4-ClC_6H_4	H	2	8	98
2l	2-$MeOC_6H_4$	H	2	5	95
2m		H	2	7	85
2n	2-$O_2NC_6H_4$	H	1	10	85
2o	3-$O_2NC_6H_4$	H	1	10	80
2p	3-ClC_6H_4	H	1	10	90
2q	2-HOC_6H_4	H	1	10	90
2r		H	1	5	92
2s		H	1	5	95
2t		H	1	10	90

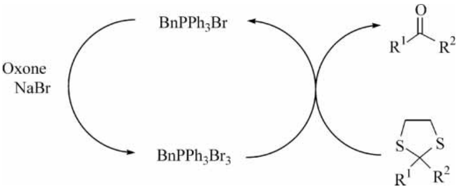
[a] Confirmed by comparison with authentic samples (IR, TLC and ^{1}H-NMR) [7], [13].

[b] Yield of isolated pure product after purification.

The reaction proceeds easily and the solution becomes yellow with concurrent precipitation of yellow or orange-yellow **1**. The precipitate shows an intense electronic absorption at 279 nm typical of tribromide ion (Br_3^-) [12].

Reagent **1** was examined with several dithioacetals (**2a–2t**) to produce the corresponding carbonyl compounds in excellent yields. The deprotection step is achieved by treating the dithioacetals with BTPTB in dichloromethane/methanol solution at room temperature (scheme 2). The reaction is complete within a short period. The results are summarized in table 1.

The reactions are relatively clean with no over-oxidation to the corresponding carboxylic acid being observed. It is significant that no bromination takes place either at the activated aromatic ring such as **2q** and **2t** or on the α-carbon in ketones **2c–2f**. In addition, in this method purification of products is straightforward. We found that in the absence of BTPTB the reaction does not proceed at room temperature. Another advantage of this method is that reagent **1** can be regenerated. After extraction of the deprotected compounds, the aqueous layer was treated with a fresh bath of the aqueous Oxone/NaBr mixture to regenerate the reagent **1** in quantitative yield. (scheme 3)



SCHEME 3

In conclusion a simple and efficient method has been developed for deprotection of dithioacetals to the corresponding carbonyl compounds at room temperature. This work represents a rapid and very convenient method for dedithioacetalization of 1,3-dithiolanes and 1,3-dithianes in excellent yields with high purity. This methodology is superior to reported methods from the point of view of yield, short reaction time, inexpensive and regenerable reagent, and the straightforward work-up of ketone products.

3. Experimental

3.1 *General*

Products were characterized by comparison with authentic samples (IR, ^{1}H-NMR spectrum, melting point, and TLC analysis) obtained by literature methods [7], [13]. The starting dithioacetals were prepared by reported methods [14]. All mps were taken on a Gallenkamp melting apparatus and are uncorrected. ^{1}H NMR spectra were recorded on a 300 MHz NMR spectrometer operating at 300 MHz. The spectra were measured in CCl_4 and $CDCl_3$ relative to TMS (0.00 ppm). IR spectra were recorded on a Shimadzu 435 IR spectrophotometer. Spectra of solids were obtained using KBr pellets. UV spectra were recorded on SASCO V-570 UV spectrophotometer.

3.2 *General procedure*

3.2.1 ***Preparation of benzyltriphenylphosphonium tribromide (BTPTB, 1).*** To a stirred solution of benzyltriphenylphosphonium bromide (0.01 mol, 3.88 g) and sodium bromide (0.023 mol, 2.37 g) in water (100 mL) was added dropwise a solution of Oxone® ($2KHSO_5 \cdot KHSO_4 \cdot K_2SO_4$) (0.022 mol, 13.65 g) in water (20 mL) at rt until a yellow precipitate was formed. After being stirred for 30 min the mixture was filtered, and washed with water (3 × 30 mL). The filter cake was dried, and recrystallized from $CHCl_3$ to afford (BTPTB, **1**) as yellow crystals (4.15 gr, 70%), mp 136–137 °C; IR υ 3050 (m), 2950 (s), 1580 (s), 1415 (s), 1115 (s), 900 (m) cm^{-1}; ^1H NMR δ 7.53–7.88 (m, 20H) 2.82 (d, J 12.5 Hz, 2H); ^{13}C NMR δ 134.5, 134.4, 132.5, 132.3, 129.7, 129.3, 116.4; UV (CH_2Cl_2) λ_{max} 279 nm (Calc. for $C_{25}H_{22}Br_3P$: C, 50.84; H, 3.72%. Found: C, 50.74%; H, 3.60%).

3.2.2 ***Deprotection of dithioacetals by reagent 1.*** A solution of an appropriate dithioacetal (2 mmol) and BTPTB (2 mmol) in a mixture of CH_2Cl_2 (5 mL) and methanol (2 mL) was stirred at room temperature for the time noted in table 1, with monitoring of the reaction by TLC (silica gel; ethyl acetate–cyclohexane 15:85). After disappearance of starting material the solvent was evaporated off. The mixture was washed with Et_2O and filtered, and the filter cake was washed with Et_2O. The combined filtrate and washings were evaporated under reduced pressure. The crude product was purified by flash chromatography on SiO_2 (eluent Et_2O) to afford the desired carbonyl compound.

3.2.3 ***General procedure for regeneration of 1.*** The filter cake recovered in the general deprotection procedure was dissolved in water (20 mL) and to this stirred solution was added sodium bromide (4.6 mmol) and (dropwise) a solution of Oxone® (4.4 mmol) in water (10 mL) at room temperature until a yellow precipitate was formed. After being stirred 30 min the mixture was filtered, and washed with water (3 × 10 mL). The filter cake was dried and recrystallized from $CHCl_3$ to afford BTPTB **1** as yellow crystals (0.77 g, 65% recovery).

Acknowledgments

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