SHORT PAPER

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Benzyltriphenylphosphonium peroxodisulfate: a mild and inexpensive reagent for selective oxidative deprotection of trimethylsilyl and tetrahydropyranyl ethers, ethylene acetals and ketals under non-aqueous and aprotic conditions[†]

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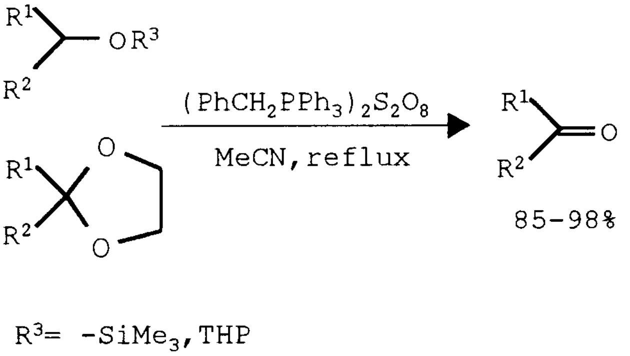
Benzyltriphenylphosphonium peroxodisulfate has been found to be an effective reagent for the oxidative deprotection of trimethylsilyl (TMS) and tetrahydropyranyl (THP) ethers, ethylene acetals and ketals to their corresponding carbonyl compounds in excellent yields. Selective oxidative deprotection of TMS ethers in the presence of THP ethers and ethylene acetals (ketals) makes this method a useful and practical procedure in organic synthesis.

Keywords: benzyltriphenylphosphonium peroxodisulfate

The protection of hydroxyl groups of alcohols by converting them to trimethylsilyl and tetrahydropyranyl ethers is one of the most fundamental and widely used transformations in modern synthetic chemistry.[1–8] Direct oxidation of these ethers to their corresponding carbonyl compounds under mild and aprotic conditions is also of synthetic value.[9–15]

The carbonyl group is one of the most versatile functional groups in organic chemistry. The protection of carbonyl compounds as their ethylene acetals and ketals is important particularly, in multi-step natural product synthesis. The most convenient and practical methods for the synthesis of these derivatives are the reaction of carbonyl compounds with ethylene glycol in the presence of an appropriate catalyst, with removal of water formed.[16–20] Deprotection of ethylene acetals and ketals to their parent carbonyl compounds under neutral, aprotic and non-aqueous conditions is of interest to synthetic organic chemists and several methods and catalysts have been proposed for this purpose.[21-23] However, some of the reported methods for the oxidative deprotection of trimethylsilyl and tetrahydropyranyl ethers, ethylene acetals and ketals encounter drawbacks such as strong protic and aqueous conditions, long reaction times, low yields of the products, tedious work-up and expensive reagents. Therefore, there is still a need to introduce a milder, more selective and inexpensive reagent for the conversion of the above mentioned derivatives to their carbonyl compounds.



Benzyltriphenylphosphonium peroxodisulfate $(PhCH_2PPh_3)_2S_2O_8$ is an inexpensive and stable oxidising agent. This reagent has been used for the oxidation of different organic compounds under non-aqueous and aprotic conditions.[24] Recently, we have introduced new methods for the oxidative deprotection of trimethylsilyl and tetrahydropyranyl ethers, ethylene acetals and ketals.[25–27] In continuation of our research in this area, we now report benzyltriphenylphosphonium peroxodisulfate as an efficient reagent for the conversion of TMS and THP ethers, ethylene acetals and ketals to their corresponding carbonyl compounds. For this purpose, first, we have studied the oxidative deprotection of 2-methoxybenzyltrimethylsilyl ether to 2-methoxybenzaldehyde with this reagent in common organic solvents such as MeCN, CH_2Cl_2, $CHCl_3$, THF and *n*-hexane. The experimental results show that MeCN and CH_2Cl_2 are suitable solvents for these oxidations (Table 1).

Table 1 Percent conversion of $2\text{-MeOC}_6H_4CH_2OTMS$ to 2-MeOC_6H_4CHO with $(PhCH_2PPh_3)_2S_2O_8$ in different solvents under reflux condition

Solvent	t/min	Yield/%
MeCN	5	94
CH_2Cl_2	60	92
$CHCl_3$	60	55
THF	60	20
n-Hexane	60	5

When a variety of trimethylsilyl and tetrahydropyranyl ethers were treated with benzyltriphenylphosphonium peroxodisulfate, the corresponding carbonyl compounds were obtained in excellent yields (Table 2). Under the same reaction conditions, ethylene acetals and ketals were also transformed to their corresponding aldehydes and ketones efficiently (Table 3). It is important to note that the reaction medium was almost neutral, so that some of the sensitive functionalities such as the carbon-carbon double bond remained intact (Table 2, entries 7, 20 and Table 3, entry 5).

In order to show the selectivity of the described method, we have also performed several competitive oxidative deprotection reactions. We found that trimethylsilyl ethers are oxidised selectively in the presence of tetrahydropyranyl ethers, ethylene acetals and ketals (Table 4). These selectivities are of value in organic synthesis.

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[†] This is a Short Paper, there is therefore no corresponding material in *J Chem. Research (M).*

Table 2 Oxidative deprotection of TMS and THP ethers with $(PhCH_2PPh_3)_2S_2O_8$ in refluxing MeCN

Run	Substrate	Product	t/min	Yield/%[a]
1	$PhCH_2OTMS$	PhCHO	10	96
2	$2\text{-}MeOC_6H_4CH_2OTMS$	$2\text{-}MeOC_6H_4CHO$	5	94
3	$3\text{-}MeOC_6H_4CH_2OTMS$	$3\text{-}MeOC_6H_4CHO$	10	92
4	$4\text{-}MeOC_6H_4CH_2OTMS$	$4\text{-}MeOC_6H_4CHO$	5	93
5	$3\text{-}O_2NC_6H_4CH_2OTMS$	$3\text{-}O_2NC_6H_4CHO$	10	91
6	$4\text{-}O_2NC_6H_4CH_2OTMS$	$4\text{-}O_2NC_6H_4CHO$	10	93
7	$PhCH{=}CHCH_2OTMS$	PhCH=CHCHO	10	94
8	PhCH(Me)OTMS	PhCOMe	10	98
9	PhCH(OTMS)COPh	PhCOCOPh	10	96
10	$4\text{-}ClC_6H_4CH(Me)OTMS$	$4\text{-}ClC_6H_4COMe$	10	95
11	$4\text{-}BrC_6H_4CH(Me)OTMS$	$4\text{-}BrC_6H_4COMe$	10	96
12	α-TetralolTMS	α-Tetralone	5	95
13	$CH_3(CH_2)_7OTMS$	$CH_3(CH_2)_6CHO$	60	85
14	$PhCH_2OTHP$	PhCHO	15	95
15	$3\text{-}MeOC_6H_4CH_2OTHP$	$3\text{-}MeOC_6H_4CHO$	15	94
16	$4\text{-}MeOC_6H_4CH_2OTHP$	$4\text{-}MeOC_6H_4CHO$	15	94
17	$2\text{-}O_2NC_6H_4CH_2OTHP$	$2\text{-}O_2NC_6H_4CHO$	20	91
18	$4\text{-}O_2NC_6H_4CH_2OTHP$	$4\text{-}O_2NC_6H_4CHO$	20	93
19	$4\text{-}ClC_6H_4CH_2OTHP$	$4\text{-}ClC_6H_4CHO$	20	92
20	$PhCH{=}CHCH_2OTHP$	PhCH=CHCHO	20	93
21	$Ph_2CHOTHP$	Ph_2CO	20	98
22	$4\text{-}ClC_6H_4CH(Me)OTHP$	$4\text{-}ClC_6H_4COMe$	20	96
23	$CH_3(CH_2)_6OTHP$	$CH_3(CH_2)_5CHO$	90	87
24	$CH_3(CH_2)_7OTHP$	$CH_3(CH_2)_6CHO$	90	85

[a]Isolated yields.

Table 3 Oxidative deprotection of ethylene acetals and ketals with $(PhCH_2PPh_3)_2S_2O_8$ in refluxing MeCN

Run	Substrate	Product	t/min	Yield/%[a]
1	Benzaldehydeethylene acetal	Benzaldehyde	15	93
2	3-Methoxybenzaldehydeethylene acetal	3-Methoxybenzaldehyde	15	94
3	2-Nitrobenzaldehydeethylene acetal	2-Nitrobenzaldehyde	15	95
4	4-Chlorobenzaldehydeethylene acetal	4-Chlorobenzaldehyde	15	95
5	Cinnamaldehydeethylene acetal	Cinnamaldehyde	15	92
6	4-Chlorobenzophenoneethylene ketal	4-Chlorobenzophenone	15	93
7	4-Bromoacetophenoneethylene ketal	4-Bromoacetophenone	10	95
8	4-Phenylcyclohexanoneethylene ketal	4-Phenylcyclohexanone	10	92
9	α-Tetraloneethylene ketal	α-Tetralone	15	96

[a]Isolated yields.

Table 4 Competitive oxidative deprotection of TMS and THP ethers, ethylene acetals and ketals with $(PhCH_2PPh_3)_2S_2O_8$ in refluxing CH_2Cl_2

Run	Substrate[a]	Product	t/h	Yield/%[b]
1	$2\text{-}MeOC_6H_4CH_2OTMS$ $4\text{-}ClC_6H_4CH(Me)OTHP$	$2\text{-}MeOC_6H_4CHO$ $4\text{-}ClC_6H_4COMe$	1	85 5
2	$2\text{-}MeOC_6H_4CH_2OTMS$ $PhCH_2OTHP$	$2\text{-}MeOC_6H_4CHO$ PhCHO	1	87 4
3	$4\text{-}ClC_6H_4CH(Me)OTMS$ $4\text{-}ClC_6H_4CH_2OTHP$	$4\text{-}ClC_6H_4COMe$ $4\text{-}ClC_6H_4CHO$	1	86 6
4	$4\text{-}ClC_6H_4CH(Me)OTMS$ $PhCH_2OTHP$	$4\text{-}ClC_6H_4COMe$ PhCHO	1	87 5
5	$4\text{-}ClC_6H_4CH(Me)OTMS$ 4-Chlorobenzaldehydeethylene acetal	$4\text{-}ClC_6H_4COMe$ 4-Chlorobenzaldehyde	1	87 5
6	$4\text{-}ClC_6H_4CH(Me)OTMS$ 4-Bromoacetophenoneethylene ketal	$4\text{-}ClC_6H_4COMe$ 4-Bromoacetophenone	1	88 3
7	$2\text{-}MeOC_6H_4CH_2OTMS$ 4-Chlorobenzaldehydeethylene acetal	$2\text{-}MeOC_6H_4CHO$ 4-Chlorobenzaldehyde	1	85 6
8	$2\text{-}MeOC_6H_4CH_2OTMS$ 4-Bromoacetophenoneethylene ketal	$2\text{-}MeOC_6H_4CHO$ 4-Bromoacetophenone	1	89 4

[a]Substrates/oxidant (1:1:1). [b]GLC yields.

In conclusion, benzyltriphenylphosphonium peroxodisulfate is a stable, inexpensive and efficient reagent for the selective oxidative deprotection of TMS and THP ethers, ethylene acetals and ketals.

Experimental

All of the products were characterised by comparison of their physical and spectral data with those of authentic samples. TMS and THP ethers, ethylene acetals and ketals were prepared according to the described procedures.[3,4,16] Benzyltriphenylphosphonium peroxodisulfate was prepared as described previously.[24]

General procedure for the oxidative deprotection of TMS and THP ethers, ethylene acetals and ketals with $(PhCH_2PPh_3)_2S_2O_8$: To a solution of substrate (1 mmol) in MeCN (15 ml), was added benzyltriphenylphosphonium peroxodisulfate (0.898 g, 1 mmol) and the mixture was stirred magnetically under reflux conditions for 5–90 min. The progress of the reaction was monitored by TLC (eluent: *n*-hexane–EtOAc, 10:1). The reaction mixture was cooled to room temperature and filtered. The solid material was washed with MeCN (20 ml). The filtrates were combined and evaporated. The resulting crude material was purified on a silica-gel plate with appropriate eluent. Pure carbonyl compounds were obtained in 85–98% yields (Tables 2 and 3).

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