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OXIDATIVE DEPROTECTION OF TRIMETHYLSILYL ETHERS, TETRAHYDROPYRANYL ETHERS, AND ETHYLENE ACETALS WITH BENZYLTRIPHENYLPHOSPHONIUM PEROXYMONOSULFATE UNDER MICROWAVE IRRADIATION

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OXIDATIVE DEPROTECTION OF TRIMETHYLSILYL ETHERS, TETRAHYDROPYRANYL ETHERS, AND ETHYLENE ACETALS WITH BENZYLTRIPHENYLPHOSPHONIUM PEROXYMONOSULFATE UNDER MICROWAVE IRRADIATION

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ABSTRACT

This paper describes the oxidation deprotection of trimethylsilyl ethers, tetrahydrophyranyl ethers and deprotection of ethylene acetals to afford carbonyl compounds using benzyltriphenylphosphonium peroxymonosulfate (1) (PhCH₂PPh₃HSO₅) in the presence of a catalytic amount of bismuth chloride under microwave irradiation. This reagent is a stable white powder, which has been prepared by the dropwise addition of an aqueous solution of benzyltriphenylphosphonium chloride to an aqueous solution of oxone[®] at room temperature.

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The protection and deprotection of the hydroxy functional groups can play an essential role in synthetic strategy.¹ The transformation of alcohols to the corresponding trimethylsilyl ethers is a very common way to protect hydroxy groups.¹⁻³ In recent years a wide variety of methods have been reported for oxidative cleavage of trimethylsilyl ethers to the corresponding carbonyl compounds,⁴⁻⁷ but some of the mentioned methods encounter drawbacks such as the requirement for aqueous reaction conditions, use of expensive reagents, long reaction times, low yields of the products and tedious work-up. Therefore, introduction of new methods and inexpensive reagents for such functional group transformations is still in demand. The tetrahydropyranyl (THP) group is one of the most frequently used groups to protect alcohols and phenols.^{1,8} Owing to the outstanding stability of tetrahydropyranyl ether under a variety of reaction conditions, 3,4-dihydro-2H-pyran is still a reagent of choice for protection of the alcohol group in peptide, nucleotide and carbohydrate chemistry.9 Since direct transformation of tetrahydropyranyl ethers to their carbonyl compounds is rare in the literature, 5,7,10-13 introduction of new methods is desirable. Acetal formation is the most widely used protecting method for aldehydes and ketones,¹ however, deprotection of acetals and ketals to the corresponding carbonyl compound is a useful transformation in organic synthesis.^{13–18}

Organic reactions that are assisted by microwave irradiation have recently attracted attention.¹⁹ The most advantage of these methods over conventional classical method is that they show cleaner reactions, decreased reaction time and easier work-up. In continuation of our ongoing program to develop environmentally benign methods using solid supports,²⁰ we wish to report a novel and efficient method for the oxidative deprotection of trimethylsilyl and tetrahydropyranyl ethers to the corresponding carbonyl compounds by using benzyltriphenylphosphonium peroxymonosulfate (1) in the presence of a catalytic amount of bismuth chloride under microwave irradiation. This compound can also react as an efficient reagent to transform ethylene acetals to the corresponding carbonyl compounds in the presence of a catalytic amount of bismuth chloride under microwave irradiation.

Benzyltriphenylphosphonium peroxymonosulfate (1) is a mild, efficient, stable and cheap reagent, which has been used for our studies under microwave irradiation. This reagent is a white powder, which is prepared by the dropwise addition of an aqueous solution of oxone,[®] to an aqueous solution of benzyltriphenylphosphonium chloride at room temperature.^{20b} Filtration and drying of the precipitates resulted in a white powder, which could be stored for months without losing its oxidation ability. The amounts of HSO₅⁻ in this reagent have been determined by an iodometric titration method.²¹ The measurements are consistent with almost 99% by weight of active oxidizing agent.

Entry	Substrate	Product	Time (min)	Yield (%) ^b
1	PhCH ₂ OTMS	РСНО	3	90
2	2-MeOC ₆ H ₄ CH ₂ OTMS	2-MeOC ₆ H ₄ CHO	3	85
3	3-MeOC ₆ H ₄ CH ₂ OTMS	3-MeOC ₆ H ₄ CHO	3	91
4	3-O ₂ NC ₆ H ₄ CH ₂ OTMS	3-O ₂ NC ₆ H ₄ CHO	5	90
5	2,5-(MeO) ₂ C ₆ H ₃ CH ₂ OTMS	2,5-(Me) ₂ C ₆ H ₃ CHO	3.5	80
6	PhCH(Me)OTMS	PhCOMe	3	99
7	4-ClC ₆ H ₄ CH(Me)OTMS	4-ClC ₆ H ₄ COMe	4	93
8	Ph ₂ CHOTMS	Ph ₂ CO	5	94
9	4-PhC ₆ H ₄ CH(Me)OTMS	4-PhC ₆ H ₄ COMe	5	92
10	α-Tetralol TMS	α-Tetralone	3	95
11	PhCH ₂ OTHP	PhCHO	3.5	90
12	2-MeOC ₆ H ₄ CH ₂ OTHP	2-MeOC ₆ H ₄ CHO	4	88
13	3-MeOC ₆ H ₄ CH ₂ OTHP	3-MeOC ₆ H ₄ CHO	3.5	83
14	4-MeOC ₆ H ₄ CH ₂ OTHP	4-MeOC ₆ H ₄ CHO	3.5	96
15	3,4-(MeO) ₂ C ₆ H ₃ CH ₂ OTHP	3,4-(MeO) ₂ C ₆ H ₃ CHO	3	80
16	2,5-(MeO) ₂ C ₆ H ₃ CH ₂ OTHP	2,5-(MeO) ₂ C ₆ H ₃ CHO	4	85
17	PhCH(Me)OTHP	PhCOMe	3.5	80
18	4-ClC ₆ H ₄ CH(Me)OTHP	4-ClC ₆ H ₄ COMe	5	90
19	Ph ₂ CHOTHP	Ph ₂ CO	5	84
20	α-Tetralol THP	α-Tetralone	4	88

Table 1. Oxidative Deprotection of Trimethylsilyl and Tetrahydropyranyl Ethers with Reagent (1) Under Microwave Irradiation^a

^aSubstrate/Oxidant/BiCl₃, (1:1:0.4). ^bYields based on the isolated products after column chromatography.

At first, the oxidative deprotection was performed by mixing one equivalent of the reagent (1) and bismuth chloride with benzyltrimethylsilyl ether in a mortar and ground the mixture with a pestle until the formation of a homogeneous mixture (1 min). Then, the reaction mixture was transferred to an Erlenmeyer flask and irradiated in a microwave oven, until TLC showed complete disappearance of the starting material. However, the starting material remained intact during the solid phase irradiation. So, we tested several solvents such as carbon tetrachloride, hexane, toluene, acetonitrile and dichloromethane. Finally, dichloromethane was found to be a microwave active solvent for this aim. In order to evaluate the effect of bismuth chloride in this reaction, we tried the oxidative deprotection of the desired silyl ether with the reagent (1) without using any catalyst. The reaction does not complete under the reaction condition, for this aim, the catalytic effects of several Lewis acids such as ZnCl₂, FeCl₃ 6H₂O, AlCl₃ and BiCl₃ were thoroughly investigated. Surprisingly, only BiCl₃ was found to be an effective catalyst during this investigation. The optimum molar ratio of bismuth chloride for this purpose was 0.4 molar ratio. Primary and secondary trimethylsilyl ethers were converted to their corresponding carbonyl compounds with benzyltriphenylphosphonium peroxymonosulfate (1) in the presence of 0.4 molar ratio of bismuth chloride in dichloromethane under microwave irradiation in high yields and short reaction times (Table 1 and Scheme 1). Interestingly, overoxidation of the products was not observed by this method. In order to evaluate the ability of this reagent, we also decided to convert tetrahydropyranyl ethers to their carbonyl compounds with the reagent (1). The reaction of primary and secondary tetrahydropyranyl ethers was completed in the presence of bismuth chloride in dichloromethane under microwave irradiation and the corresponding products were obtained in good to excellent yields (Table 1 and Scheme 1).

$$\begin{array}{c} R_{1} \\ R_{2} \\ \hline OX \\ R_{1} \\ \hline OX \\ R_{1} \\ \hline OX \\ R_{2} \\ \hline OX \\ R_{1} \\ \hline OX \\ R_{1} \\ \hline OX \\ R_{2} \\ \hline OX \\ R_{1} \\ \hline OX \\ R_{1} \\ \hline OX \\ R_{2} \\ \hline OX \\ R_{1} \\ \hline OX \\ \hline OX \\ R_{1} \\ \hline OX \\ C$$

Benzyltriphenylphosphonium peroxymonosulfate (1) was also used to transform ethylene acetals to the corresponding carbonyl compounds in dichloromethane under microwave irradiation in the presence of 0.4 molar ratio of bismuth chloride in good to high yields (Table 2 and Scheme 1).

In conclusion, we report here the preparation of benzyltriphenylphosphonium peroxymonosulfate (1) as a mild, inexpensive and stable oxidizing agent. The oxidizing reagent is very easily prepared from commercially available starting materials and can be stored for months without losing its activity. This reagent is an efficient, mild and inexpensive reagent for oxidative deprotection of trimethylsilyl and tetrahydropyranyl ethers and deprotection of ethylene acetals to the corresponding carbonyl compounds in high yields under microwave irradiation.

EXPERIMENTAL

Trimethylsilyl ethers, tetrahydropyranyl ethers, ethylene acetals were prepared according to described procedures.^{3a,14,23,24} The reagent (1) was

Entry	Substrate	Product	Time (min)	Yield (%) ^b
1	Actophenoneethylene acetal	Acetophenone	4	91
2	2-Methoxybenzaldehydeethylene acetal	2-Methoxybenzaldehyde	4	90
3	2-Nitrobenzaldehydeethylene acetal	2-Nitrobenzaldehyde	6	80
4	2-Chloroactophenoneethylene acetal	2-Chloroactophenone	5	85
5	α -Tetraloneethylene acetal	α-Tetralone	4	95
6	4-Phenylacetophenoneethylene acetal	4-Phenylacetophenone	5	88

Table 2. Deprotection of Ethylene Acetals with Reagent (1) Under Microwave Irradiation^a

^a Substrate/Oxidant/BiCl₃ (1:1:0.4). ^b Yields based on the isolated products after purification with column chromatography.

prepared according to described procedures.^{20b} All of the yields refer to isolated products. All of the products were characterized by comparison of their spectral (IR, ¹H-NMR and TLC) and physical data (melting and boiling point) with those of authentic samples.^{5,13,22} All ¹H-NMR spectra were recorded at 90 MHz in CDCl₃ and CCl₄ relative to TMS (0.00 ppm). The Research Institute of Petroleum Industry, Tehran, I.R. Iran performed elemental analysis. The apparatus used for the oxidative deprotection was a Samsung domestic microwave oven (2450 MHz, 900 W) without any modification, but all of the reactions were carried out in a hood with strong ventilation.

Oxidative Deprotection of Trimethylsilyl and Tetrahydropyranyl Ethers with Reagent (1) Under Microwave Irradiation

General Procedure

Trimethylsilyl ether or tetrahydropyranyl ether (1 mmol) and BiCl₃ (0.13 g, 0.4 mmol) was added to benzyltriphenylphosphonium peroxomonosulfate (0.466 g, 1 mmol) and the mixture was ground with a pestle in a mortar to form a homogeneous mixture (1 min). After transferring the mixture to an Erlenmeyer flask and adding $3 \text{ mL CH}_2\text{Cl}_2$, it was irradiated with microwave oven (900 W), until TLC showed complete disapprearance of starting material (Table 1). Then CCl₄ was added to the reaction mixture and after vigorous stirring, the mixture was filtered off. Evaporation of the solvent gave pure carbonyl compound.

Deprotection of Ethylene Acetals with Reagent (1) Under Microwave Irradiation

General Procedure

Ethylene acetal (1 mmol) and BiCl₃ (0.13 g, 0.4 mmol) was added to benzyltriphenylphosphonium peroxomonosulfate (0.466 g, 1 mmol) and the mixture was ground with a pestle in a mortar to form a homogeneous mixture. After transferring the mixture to an Erlenmeyer flask and adding $3 \text{ ml CH}_2\text{Cl}_2$, it was irradiated with microwave oven (900 W), until TLC showed complete disappearance of starting material (Table 2). Then CCl₄ (20 ml) was added to the reaction mixture and after vigorous stirring, the mixture was filtered off. The filtrate was evaporated on a rotary evaporator to afford pure carbonyl compound.

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