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Benzyltriphenylphosphonium chlorate (BTPPC) as a new and mild reagent for oxidative deprotection of trimethylsilyl and tetrahydropyranyl ethers of benzylic alcohols under non-aqueous conditions

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Abstract—Oxidative deprotection of trimethylsilyl and tetrahydropyranyl ethers of benzylic alcohols to the corresponding carbonyl compounds with benzyltriphenylphosphonium chlorate in the presence of aluminum chloride in acetonitrile under reflux conditions or at room temperature is reported. © 2002 Elsevier Science Ltd. All rights reserved.

1. Introduction

The protection and deprotection of the hydroxy functional group 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 ethers under a variety of reaction conditions, 3,4-dihydro-2*H*-pyran is still a reagent of choice for protection of the alcohol group in peptide, nucleotide and carbohydrate chemistry.[9] The direct transformations of tetrahydropyranyl ethers are rare in the literature.[5,7,10–13]

Sodium chlorate is an inexpensive, water-soluble and stable oxidizing reagent that is commercially available. This reagent is insoluble in non-aqueous solvents. Very recently, we have introduced new reagents, which are able to oxidize different substrates under non-aqueous conditions.[13] Here we wish to report a novel and efficient method for the oxidative deprotection of trimethylsilyl and tetrahydropyranyl ethers to the corresponding carbonyl compounds with benzyltriphenylphosphonium chlorate **BTPPC** in acetonitrile under reflux conditions or at room temperature.

Benzyltriphenylphosphonium chlorate ($Ph_3P^+CH_2PhClO_3^-$) **BTPPC** is a mild, efficient, stable and cheap reagent, which has been used for our studies under non-aqueous conditions. This reagent is a white powder, which is prepared by the dropwise addition of an aqueous solution of $NaClO_3$ to an aqueous solution of benzyltriphenylphosphonium chloride at room temperature. Filtration and drying of the precipitate produced a white powder, which could be stored for months without losing its oxidation ability. This reagent is quite soluble in methylene chloride, chloroform, acetone, and acetonitrile and insoluble in non-polar solvents such as carbon tetrachloride, *n*-hexane and diethylether.

2. Results and discussion

At first, we decided to investigate the oxidative deprotection of benzyltrimethylsilyl ether in acetonitrile at room temperature or under reflux conditions without catalyst with this reagent, and observed that in the absence of catalyst the reaction at room temperature or under reflux conditions does not proceed at all. For this aim, the catalytic effects of several Lewis acids such as $ZnCl_2$, $FeCl_3{\cdot}6H_2O$, $AlCl_3$ and $BiCl_3$ were thoroughly investigated. Surprisingly,

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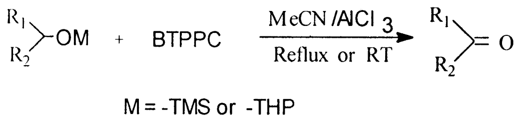
Table 1. Oxidative deprotection of trimethylsilyl ethers with **BTPPC/AlCl$_3$** in refluxing acetonitrile

Entry	Substrate	Product	Time (h)	Yield (%)[a]
1	$PhCH_2OTMS$	PhCHO	0.25	100
2	$2\text{-}MeOC_6H_4CH_2OTMS$	$2\text{-}MeOC_6H_4CHO$	5	85
3	$3\text{-}MeOC_6H_4CH_2OTMS$	$3\text{-}MeOC_6H_4CHO$	5	90
4	$3\text{-}NO_2C_6H_4CH_2OTMS$	$3\text{-}NO_2C_6H_4CHO$	7	90
5	$2,5\text{-}(MeO)_2C_6H_3CH_2OTMS$	$2,5\text{-}(Me)_2C_6H_3CHO$	8	75
6	PhCH(Me)OTMS	PhCOMe	0.7	100
7	$4\text{-}ClC_6H_4CH(Me)OTMS$	$4\text{-}ClC_6H_4COMe$	4	99
8	$Ph_2CHOTMS$	Ph_2CO	0.3	95
9	$4\text{-}PhC_6H_4CH(Me)OTMS$	$4\text{-}PhC_6H_4COMe$	0.5	90
10	α-TetralolTMS	α-Tetralone	0.45	95
11	$4\text{-}NO_2C_6H_4OTMS$	$4\text{-}NO_2C_6H_4CHO$	7	90
12	$PhCH_2CH_2CH_2OTMS$	$PhCH_2CH_2CH_2OH$	10	85
13	$PhCH_2CH_2OTMS$	$PhCH_2CH_2OH$	10	90
14	$PhCH{=}CH\text{–}CH_2OTMs$	$PhCH{=}CHCH_2OH$	10	20

Substrate/oxidant/AlCl$_3$ (1:1:0.2).

[a] Yield based on the isolated products after column chromatography.



Scheme 1.

only AlCl$_3$ was an effective catalyst for these reactions. The optimum molar ratio of aluminum chloride for this purpose was 0.2 molar ratio. Primary and secondary trimethylsilyl ethers were converted to their corresponding carbonyl compounds with benzyltriphenylphosphonium chlorate in the presence of 0.2 molar ratio of aluminum chloride in refluxing acetonitrile in high yields (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 **BTPPC** in the presence of 0.2 molar ratio of aluminum chloride. The reaction of primary and secondary tetrahydropyranyl ethers was completed in acetonitrile at room temperature and the corresponding products were obtained in good to excellent yields (Table 2 and Scheme 1).

As shown in Tables 1 and 2, in comparison to benzylic OTMS and OTHP ethers when we tried for oxidative deprotection of the aliphatic and allylic OTMS and OTHP ethers with this reagent, alcohols were the final products and corresponding carbonyl compounds were not obtained at all. Therefore this reagent is not suitable for oxidative deprotection of aliphatic and allylic OTMS and OTHP ethers. It is clear from Tables 1 and 2 that the functional groups such as NO$_2$ and MeO, decrease the rate of reaction. This could be the effect of producing complexes of these functional groups with AlCl$_3$.

In order to evaluate the synergy between **BTPPC** and aluminum chloride in these reactions, several experiments have been performed. The reaction of $C_6H_4CHMeOTMS$ (1 mmol) with **BTPPC** (1 mmol) without aluminum chloride was unsuccessful and $C_6H_4CHMeOTMS$ was unchanged after 2 h refluxing in acetonitrile. When aluminum chloride and $C_6H_4CHMeOTMS$ in acetonitrile without **BTPPC** was used (1 mmol) after 2 h refluxing, the corresponding alcohol was obtained in 10% yield. Only in the case of using **BTPPC** in the presence of catalytic amounts of aluminum chloride (0.2 mmol) the corresponding ketone was obtained in excellent yield (Table 1).

Table 2. Oxidative deprotection of tetrahydropyranyl ethers with **BTPPC/AlCl$_3$** in acetonitrile at room temperature

Entry	Substrate	Product	Time (h)	Yield (%)[a]
1	$PhCH_2OTHP$	PhCHO	3	100
2	$2\text{-}MeOC_6H_4CH_2OTHP$	$2\text{-}MeOC_6H_4CHO$	8	50
3	$3\text{-}MeOC_6H_4CH_2OTHP$	$3\text{-}MeOC_6H_4CHO$	4	30
4	$4\text{-}MeOC_6H_4CH_2OTHP$	$4\text{-}MeOC_6H_4CHO$	4	55
5	$3,4\text{-}(MeO)_2C_6H_3CH_2OTHP$	$3,4\text{-}(MeO)_2C_6H_3CHO$	8	30
6	$2,5\text{-}(MeO)_2C_6H_3CH_2OTHP$	$2,5\text{-}(MeO)_2C_6H_3CHO$	9	48
7	PhCH(Me)OTHP	PhCOMe	2	94
8	$4\text{-}ClC_6H_4CH(Me)OTHP$	$4\text{-}ClC_6H_4COMe$	2	95
9	$Ph_2CHOTHP$	Ph_2CO	2	95
10	α-TetralolTHP	α-Tetralone	5	91
11	$4\text{-}ClC_6H_4CH_2OTHP$	$4\text{-}ClC_6H_4CHO$	1	100
12	$4\text{-}NO_2C_6H_4OTHP$	$4\text{-}NO_2C_6H_4CHO$	8	63
13	$2\text{-}NO_2C_6H_4OTHP$	$2\text{-}NO_2C_6H_4CHO$	10	50
14	$PhCH_2CH_2OTHP$	$PhCH_2CH_2OH$	10	85
15	$PhCH{=}CHCH_2OTHP$	$PhCH{=}CHCH_2OH$	10	30

Substrate/oxidant/AlCl$_3$ (1:1:0.2).

[a] Yields based on the isolated products after purification with column chromatography.

3. Conclusion

In conclusion, in this study we have introduced a new reagent for the oxidative cleavage of different types of protected functional groups under non-aqueous and homogeneous conditions. The stability, easy preparation, high selectivity of the reagent, easy work-up, mild reaction conditions, and high yields of the products, make this method a novel and useful one for oxidative deprotection of trimethylsilyl and tetrahydropyranyl ethers to afford the corresponding carbonyl compounds in acetonitrile in the presence of aluminum chloride.

4. Experimental

4.1. General

Trimethylsilyl ethers and tetrahydropyranyl ethers were prepared according to described procedures.[3a,14–16] All yields refer to isolated products. The products were characterized by comparison with authentic samples (IR and ^{1}H NMR spectra, melting and boiling points and TLC). All ^{1}H NMR spectra were recorded at 90 or 500 MHz in $CDCl_3$ and CCl_4 relative to TMS (0.00 ppm), ^{13}C NMR spectra were recorded at 125 MHz in DMSO-d_6 and IR spectra were recorded on Shimadzu 435 IR spectrophotometer. All reactions were carried out in acetonitrile under reflux conditions or at room temperature The Tarbiat Modarres University, Tehran, IR, Iran performed elemental analysis.

4.1.1. Preparation of benzyltriphenylphosphonium chlorate (1) BTPPC. A solution of benzyltriphenylphosphonium chloride (19.0 g, 49 mmol) in water (100 mL) was prepared, then $NaClO_3$ (5.22 g, 49 mmol) in water (100 mL) was added dropwise to the above solution and stirred for 1 h at room temperature. The resulting precipitate was filtered and washed with cooled distilled water (50 mL), and dried in a desiccator under vacuum over calcium chloride to afford a white powder (19.25 g, 90% yield), which decomposed at 181–182°C to a dark-brown material. ^{1}H NMR: δ 7.93–6.87 (m, 20 H), 4.7 (d, 2H, J=25.6 Hz, CH_2–P). ^{13}C NMR: δ 135.28, 135.25, 134.32, 134.24, 131.07, 131.03, 130.19, 130.09, 128.99, 128.97, 128.69, 128.66, 127.45, 127.43, 118.01, 117.36, 29.68 (d, J=193 Hz, C–P). IR (KBr): 1298, 1269, 1098, 1060, 700, 658, 590 cm^{-1}. Anal. Calcd for $C_{25}H_{22}ClO_3P$: C, 68.73; H, 5.04%. Found: C, 68.90; H, 5.20%.

4.1.2. Oxidative deprotection of trimethylsilyl ethers with BTPPC/$AlCl_3$—a general procedure. In a round-bottomed flask (25 mL) equipped with a reflux condenser and a magnetic stirrer, a solution of trimethylsilyl ether (1 mmol) and $AlCl_3$ (0.03 g, 0.2 mmol) in acetonitrile (10 mL) was prepared. **BTPPC** (0.44 g, 1 mmol) was added to the solution and refluxed for 0.25–10 h. The reaction progress was followed by TLC (eluent: cyclohexane/ethylacetate: 8:2). The reaction mixture was then cooled to room temperature and the solid was then separated through a short pad of silica gel and washed with acetonitrile (15 mL). The filtrate was evaporated and the resulting crude material was purified by column chromatography on silica gel using a mixture of ethyl acetate and hexane as eluent (10:90). Pure carbonyl compounds were obtained in 75–100% yields (Table 1).

4.1.3. Oxidative deprotection of tetrahydropyranyl ethers with BTPPC/$AlCl_3$—a general procedure. In a round-bottomed flask (25 mL) and a magnetic stirrer, a solution of tetrahydropyranyl ether (1 mmol) and $AlCl_3$ (0.03 g, 0.2 mmol) in acetonitrile (10 mL) was prepared. **BTPPC** (0.44 g, 1 mmol) was added to the solution and stirred at room temperature for 1–10 h. The reaction progress was followed by TLC (eluent: cyclohexane/ethylacetate: 8:2). The reaction mixture was then cooled to room temperature and the solid was then separated through a short pad of silica gel and washed with acetonitrile (15 mL). The filtrate was evaporated and the resulting crude material was purified by column chromatography on silica gel using a mixture of ethyl acetate and hexane as eluent (10:90). Pure carbonyl compounds were obtained in 30–100% yields (Table 2).

4.1.4. Oxidative deprotection of 1-(4-chlorophenyl) ethanol trimethylsilyl ether with BTPPC/$AlCl_3$—a typical procedure. In a round-bottomed flask (25 mL) equipped with a reflux condenser and a magnetic stirrer, a solution of 1-(4-chlorophenyl) ethanol trimethylsilyl ether (0.22 g, 1 mmol) and $AlCl_3$ (0.03 g, 0.2 mmol) in acetonitrile (10 mL) was prepared. **BTPPC** (0.44 g, 1 mmol) was added to the solution and was refluxed for 4 h. The reaction progress was followed by TLC (eluent: cyclohexane/ethylacetate: 8:2). The reaction mixture was then cooled to room temperature and the resulting solid was then separated through a short pad of silica gel and washed with acetonitrile (15 mL). Evaporation of the solvent gave 4-chloroacetophenone. The yield was 0.15 g (99%).^{1}H NMR: δ 2.6 (s, 3H), 7.4–7.7 (d, 2H, J=6 Hz), 7.9–8.2 (d, 2H J=6 Hz) (Table 1).

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References

1. Greene, T. W.; Wuts, P. G. M. *Protective Groups in Organic Synthesis*; 2nd ed; Wiley: New York, 1991.
2. (a) Colvin, E. W. *Chem. Soc. Rev.* **1978**, *7*, 15. (b) Lalonde, M.; Chan, T. H. *Synthesis* **1985**, 817. (c) Schaumann, E. In *Houben-Weyl*, Kropf, H., Ed.; 4th ed, Thieme: Stuttgart, 1984.
3. (a) Firouzabadi, H.; Karimi, B. *Synth. Commun.* **1993**, *12*, 1663. (b) Firouzabadi, H.; Khayat, Z.; Sardarian, A. R.; Tangestaninejad, S. *Iranian J. Chem., Chem. Engng* **1996**, *15*, 54 *Chem. Abstr.* **1997**, *127*, 220704.
4. Muzart, J. *Synthesis* **1993**, 11.
5. Baltork, I. M.; Pouranshirvani, Sh. *Synthesis* **1997**, 756.
6. Firouzabadi, H.; Badparva, H.; Sardarian, A. R. *Iranian J. Chem., Chem. Engng* **1998**, *17*, 33.
7. Heravi, M. M.; Ajami, D.; Ghassemzadeh, M. *Synthesis* **1999**, 393.
8. Sarkar, A.; Yemul, O. S.; Bandgar, B. P.; Gaikwad, N. B.; Wadgaonkar, P. P. *Org. Prep. Proced. Int.* **1996**, *28*, 613.

9. Hoyer, S.; Laszlo, P. *Synthesis* **1985**, 655.
10. Sonnet, P. E. *Org. Prep. Proced. Int.* **1978**, *10*, 91.
11. Parish, E. J.; Kizito, S. A.; Heidepriem, R. *Synth. Commun.* **1993**, *22*, 223.
12. Baltork, I. M.; Hajipour, A. R.; Mohammadi, H. *Bull. Chem. Soc. Jpn* **1998**, *71*, 1699.
13. (a) Hajipour, A. R.; Mahboobkhah, N. *Synth. Commun.* **1998**, *28*, 3143. (b) Hajipour, A. R.; Mahboobkhah, N. *Indian J. Chem.* **1998**, *37B*, 285. (c) Hajipour, A. R.; Mahboobkhah, N. *J. Chem. Res. (S)* **1998**, 122. (d) Hajipour, A. R.; Mahboobkhah, N. *Indian J. Chem.* **1998**, *37B*, 1041. (e) Hajipour, A. R.; Baltork, I. M.; Kianfar, G. *Bull. Chem. Soc. Jpn* **1998**, *71*, 2055. (f) Hajipour, A. R.; Baltork, I. M.; Kianfar, G. *Indian J. Chem.* **1998**, *37B*, 607. (g) Hajipour, A. R.; Mahboobkhah, N. *Org. Prep. Proced. Int.* **1999**, *31*, 112. (h) Hajipour, A. R.; Baltork, I. M.; Niknam, K. *Org. Prep. Proced. Int.* **1999**, *31*, 335. (i) Baltork, I. M.; Hajipour, A. R.; Haddadi, A. R. *J. Chem. Res. (S)* **1999**, 102. (j) Hajipour, A. R.; Mallakpour, S. E.; Adibi, H. *Chem. Lett.* **2000**, 460. (k) Hajipour, A. R.; Mallakpour, S. E.; Imanzadeh, Gh. *Chem. Lett.* **1999**, 99. (l) Hajipour, A. R.; Mallakpour, S. E.; Baltork, I. M.; Khoee, S. *Chem. Lett.* **2000**, 120. (m) Hajipour, A. R.; Mallakpour, S. E. *J. Chem. Res. (S)* **2000**, 32. (m) Hajipour, A. R.; Mallakpour, S. E. *J. Chem. Res. (S)* **2000**, 32. (n) Hajipour, A. R.; Mallakpour, S. E.; Khoee, S. *Synlett* **2000**, 740.
14. Maksens, F. A. *J. Synth.* **1981**, 501.
15. Maity, G.; Roy, S. C. *Synth. Commun.* **1993**, *23*, 1667.
16. Tanemura, K.; Horaguchi, T.; Suzuki, T. *Bull. Chem. Soc. Jpn* **1992**, *65*, 304.