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Rapid and efficient protection of alcohols and phenols, and deprotection of trimethylsilyl ethers catalyzed by a cerium-containing polyoxometalate

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Herein, we want to report a simple and convenient way for protection-deprotection of alcohols in the presence of ammonium decatungstocerate(IV) { $(NH_4)_8$ [CeW₁₀O₃₆]·20H₂O} as catalyst under ambient temperature in CH₃CN. Using 0.002 mmol of the catalyst, various alcohols and phenols were transformed easily to the corresponding TMS ethers in excellent yields. In the second part, various TMS ethers were successfully converted to the parent hydroxyl compounds in the presence of the ammonium decatungstocerate(IV) catalyst. Copyright © 2010 John Wiley & Sons, Ltd.

Keywords: catalysis; polyoxometalate; protection; deprotection; trimethylsilyl ethers

Introduction

The protection-deprotection of hydroxyl compounds is one of the most frequently employed transformations in multistep organic synthesis.^[1] In this connection, silvlation of alcohols is a commonly used method for their protection. Generally, formation of trimethylsilyl ethers is carried out by treating alcohols with trimethylsilyl chloride or trimethylsilyl triflate in the presence of an organic base,^[2] Li₂S^[3] and sometimes a nonionic super base catalyst.^[4] However, some of these methods have frequently suffered from drawbacks such as lack of reactivity or the difficulty in the removal of byproducts. 1,1,1,3,3,3-Hexamethyldisilazane (HMDS) is a stable, commercially available and cheap reagent for trimethylsilylation of hydrogen labile substrates^[5] that gives ammonia as the only byproduct, which is easily removed from the reaction medium. The main drawback of HMDS is its poor silvlating power which needs forceful conditions and long reaction times. Over the years, a variety of catalysts such as (CH₃)₃SiCl,^[6] silica chloride,^[7] ZnCl₂,^[8] nitrogen ligand complexes of metal chlorides,^[9] zirconium sulfophenyl phosphonate,^[10] I₂,^[11] LiClO₄,^[12] K-10 montmorilonite,^[13] tungstophosphoric acid,^[14] poly(*N*-bromobenzene-1,3-disulfonamide),^[15] CuSO₄·5H₂O,^[16] MgBr₂·OEt₂,^[17] LaCl₃,^[18] Fe(TFA)₃,^[19] Fe₃O₄,^[20] (*n*-Bu₄N)Br^[21] and ZrO(OTf)2^[22] have been reported for the silylation of hydroxyl groups using HMDS. However, in most of those reactions, long reaction times, drastic reaction conditions and the use of hazardous solvents or tedious work-up are needed.

Deprotection of TMS ethers to their corresponding alcohols under mild reaction conditions is of practical importance and several methods and catalysts such as bismuth(III) salts,^[23] NaBrO₃-NH₄Cl,^[24] PhCH₂PPh₃HSO₅,^[25] Zr(KPO₄)₂,^[26] potassium dodecatungstocobaltate(III) trihydrate,^[27] cobalt(II) tetrasulfophthalocyanine,^[28] trimethylsilyl bromide,^[29] CuBr₂,^[30] tetraethylammonium superoxide,^[31] DABCO-bromine,^[32] sulfated SnO₂^[33] and LiOAc^[34] have been reported for this transformation. However, in some of the reported methods one or more disadvantages, such as harsh reaction conditions, high reaction temperatures, long reaction times, high cost or toxicity of the reagents have been experienced. Consequently, the introduction of efficient and better methods for the preparation of TMS ethers and their deprotection using inexpensive, relatively non-toxic, easy handling and environmentally friendly catalysts is of practical importance and is still in demand.

In recent years, polyoxometalates (POMs) have been taken into consideration because of their properties and applications. This class of inorganic compounds is unmatched not only in terms of molecular structural diversity but also regarding reactivity and relevance to analytical chemistry, catalysis, medicine and materials science.^[35] The catalytic function of polyoxometalate compounds which are used in solution as well as in the solid state as acids and oxidation catalysts is receiving considerable attention.^[36] In the last two decades, the broad utility of polyoxometalates has been demonstrated in a wide variety of synthetically useful selective transformations of organic substrates.^[37] According to the author's previous studies regarding the use of POMs catalysts, especially those of cerium, in various organic reactions,^[38] and because of the necessity for new and effective synthetic methodologies, the authors intend for the first time to report a simple and convenient way for the protection-deprotection of alcohols in the presence of ammonium decatungstocerate(IV) {(NH₄)₈[CeW₁₀O₃₆]·20H₂O} as catalyst under ambient temperature in CH₃CN (Scheme 1).

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OH CH₃CN, HMDS, cat, rt

CH₃CN, cat, rt

OSiMe₃

Table 2. Catalytic conversion of TMS ethers into parent alcohols by

Scheme 1. Protection – deprotection of benzyl alcohol in the presence of $(NH_4)_8$ [CeW₁₀O₃₆]·20H₂O.

Table 1. Catalytic conversion of alcohols to TMS ethers in the presence of $(NH_4)_8$ [CeW₁₀O₃₆]·20H₂O in CH₃CN^a

Entry	Substrate	Time (s) Yield (%) ^b	
1	C ₆ H ₅ CH ₂ OH	<5	100
2	2-MeC ₆ H ₄ CH ₂ OH	<5	100
3	4-O ₂ NC ₆ H ₄ CH ₂ OH	120	98
4	2-FC ₆ H ₄ CH ₂ OH	<5	100
5	4-MeOC ₆ H ₄ CH ₂ OH	<5	100
6	2-BrC ₆ H ₄ CH ₂ OH	<5	100
7	3,4-(Methylenedioxy)benzyl alcohol	<5	100
8	4-(Me) ₃ CC ₆ H ₄ CH ₂ OH	<5	99
9	Thiophene-2-methanol	30	98
10	3-Pyridyl-1-methanol	30	100
11	PhCH ₂ CH ₂ CH ₂ OH	<5	100
12	PhCHMeCH ₂ OH	<5	100
13	PhCHCHCH ₂ OH	<5	99
14	1-C ₇ H ₁₅ OH	60	98
15	1-C ₈ H ₁₇ OH	30	99
16	Cyclohexanol	<5	100
17	2-Methylcyclohexanol	<5	100
18	(Ph) ₂ CHOH	<5	100
19	PhCH ₂ C(Me)OHCH ₃	60	90
20	1-Adamantanol	60	88
21	C ₆ H₅OH	30	99
22	4-CIC ₆ H ₄ OH	30	100
23	4-O ₂ NC ₆ H ₄ OH	60	95
24	1-Naphthol	30	100
25	1,3-butanediol	<5	99
26	2-HOC ₆ H ₄ CH ₂ OH	30	98 ^c
27	4-HO-3-MeOC ₆ H ₃ CH ₂ OH	30	100 ^c

^a All products were identified by comparison of their physical and spectral data with those of authentic samples.^[39] ^b GC yield.

^c Reaction was performed with 1.2 mmol of HMDS.

Experimental

General

All materials were purchased from Merck and Fluka chemical companies. All products were identified by comparison of their physical and spectral data with those of authentic samples,^[39] and yields refer to isolated products. GC analysis was performed on a Shimadzu GC-16A instrument with a flame-ionization detector using silicon DC-200 or carbowax 20-M columns. Infrared spectra were recorded on a Nicolet impact 400D spectrophotometer. ¹H-NMR spectra were recorded on a Bruker-AC 500 MHz spectrometer. Mass spectra were recorded on a Shimadzu GCMS-QP 1000 EX. The chemical purities of all silyl ethers were checked by gas chromatography and confirmed to be higher than 98%.

The ammonium decatungstocerate(IV) icosahydrate was prepared according to the literature.^[40] The structure of the catalyst

(NH ₄) ₈ [0	$I_{4}_{8}[CeW_{10}O_{36}] \cdot 20H_{2}O$ in CH ₃ CN				
Entry	Substrate	Time (min)	Yield (%) ^a		
1	C ₆ H ₅ CH ₂ OSiMe ₃	30	100		
2	4-CIC ₆ H ₄ CH ₂ OSiMe ₃	15	90		
3	2-FC ₆ H ₄ CH ₂ OSiMe ₃	30	95		
4	2-MeC ₆ H ₄ CH ₂ OSiMe ₃	120	80		
5	2-O ₂ NC ₆ H ₄ CH ₂ OSiMe ₃	60	70		
6	2-HOC ₆ H ₄ CH ₂ OSiMe ₃	120	85		
7	4-MeOC ₆ H ₄ CH ₂ OSiMe ₃	30	90		
8	2,4-Cl ₂ C ₆ H ₃ CH ₂ OSiMe ₃	5	95		
9	4-HO-3-H ₃ COC ₆ H ₃ CH ₂ OSiMe ₃	60	100		
10	3-Pyridyl-1-methyl-OSiMe₃	30	65		
11	Anthracene-9-CH ₂ OSiMe ₃	5	90		
12	PhCHCHCH ₂ OSiMe ₃	30	100		
13	PhCHMeCH ₂ OSiMe ₃	15	99		
14	PhCH ₂ CH ₂ CH ₂ OSiMe ₃	60	90		
15	n-C ₈ H ₁₇ OSiMe ₃	120	60		
16	n-C ₇ H ₁₅ OSiMe ₃	60	85		
17	Cyclohexyl-OSiMe ₃	30	95		
18	1,3-(Me ₃ SiO) ₂ C ₄ H ₇	5	100		
19	Adamantyl-OSiMe ₃	90	100		
20	Me ₃ COSiMe ₃	30	80		
21	$C_6H_5OSiMe_3$	30	90		
22	4-CIC ₆ H ₄ OSiMe ₃	30	55		
23	4-O2NC6H4OSiMe3	30	60		

was confirmed by IR, NMR, thermal gravimetric analysis (TGA) and elemental analysis. Thermal gravimetric analysis was performed on the catalyst (between 40 and 600 °C), and the results indicated that the hydration numbers are between 18 and 21.

90

60

General Procedure for Protection of Alcohols into Trimethylsilyl Ethers at Room Temperature

To a solution of alcohol (1 mmol), and HMDS (hexamethyldisilazane, 0.6 mmol) in CH₃CN (3 ml), the catalyst (0.002 mmol) was added. The mixture was stirred at room temperature for a few seconds and the progress of the reaction was monitored by GC. After completion of the reaction, filtration was carried out and the catalyst, because of its insolubility, was easily removed from the mixture. After that, evaporation of the solvent under reduced pressure, gave the pure product (Table 1).

General Procedure for Deprotection of Trimethylsilyl Ethers

To a solution of trimethylsilyl ether (1 mmol) in acetonitrile (3 ml), ammonium decatungstocerate(IV) was added (0.1 mmol). The mixture was stirred for an appropriate time at room

24

^a GC yield.

1-Naphthyl-OSiMe₃

Table 3. Comparison of results between $(NH_4)_8$ [CeW ₁₀ O ₃₆]·20H ₂ O and some of the recently reported catalysts for the protection of benzyl alcohol by HMDS							
Entry	Catalyst	Catalyst (mol%)	Time (min)	Yield (%)	Reference		
1	1,3-dibromo-5,5-diethylbarbituric acid	10	30	95	[41]		
2	HClO ₄ -SiO ₂	30	2	100	[42]		
3	TBBDA	4	30	90	[15]		
4	Nanoporous solid silica sulfonic acid	2	80	100	[43]		
5	$Fe(F_3CCO_2)_3$	2.5	5	92	[19]		
6	H ₃ PW ₁₂ O ₄₀	1	23	90	[44]		
7	TiCl ₂ (OTf)-SiO ₂	1	5	92	[45]		
8	(NH ₄) ₈ [CeW ₁₀ O ₃₆]·20H ₂ O	0.2	0.05	100	-		

temperature, and the progress of the reaction was monitored by GC. After completion of the reaction, the mixture was filtered and evaporation of the solvent followed by chromatography on a short column of silica gel, gave the pure product (Table 2).

Results and Discussion

At first, the focus was on the catalytic role of (NH₄)₈ [CeW₁₀O₃₆]·20H₂O. In the initial studies to find the optimized reaction condition, the reaction of benzyl alcohol (1 mmol) in the presence of various catalytic amounts of ammonium decatungstocerate(IV) in acetonitrile was carried out. It was found that excellent yields can be obtained with 0.002 mmol of the catalyst. For the protecting reagent (HMDS), it was observed that 0.6 mmol is the optimal amount. The protection was efficiently achieved under the above-mentioned conditions, and the experimental results showed that the presence of the catalyst is crucial to obtain full conversion of the alcohols. CH₃CN was chosen as the best solvent because we obtained lower yields with other solvents such as CH₂Cl₂, CHCl₃, THF and *n*-C₆H₆. To show the vastness of the reaction, the study was extended to a wide variety of benzylic and aliphatic alcohols as well as phenols to afford the corresponding TMS ethers (Table 1). In all these cases, very clean reactions and excellent yields were observed. Using the above reaction condition, various phenols (Table 1, entries 21-23) were transformed easily to the corresponding TMS ethers in excellent yields. Interestingly, protection of a phenolic OH group is possible in the presence of an alcoholic hydroxyl group (Table 1, entries 26 and 27). This method was also used for protection of secondary and tertiary alcohols (Table 1, entries 16–20) and excellent yields were observed.

In other investigations, suitable reaction conditions for the deprotection of TMS ethers to the parent hydroxyl compounds were studied. At first, various solvents for this reaction were tested and CH₃CN showed the best performance among the other solvents: i.e. (CH₃CH₂)₂O, CH₂Cl₂, CHCl₃, THF and *n*-C₆H₆.

Optimization of the amount of catalyst was the next step and the best amount was found to be 0.1 mmol of ammonium decatungstocerate(IV). In the above deprotection reaction, the presence of the catalyst was necessary to attain the full conversion of TMS ethers, and in the absence of the catalyst only 3% conversion was observed. To demonstrate the efficiency of this method, various TMS ethers were successfully converted to the parent hydroxyl compounds under ambient reaction conditions (Table 2). By this procedure, aliphatic TMS ethers were easily converted to the corresponding alcohols in good yields (Table 2, entries 15 and 16). Similarly, phenolic and cyclic TMS ethers were converted to the corresponding hydroxyl compounds under this reaction condition (Table 2, entries 17, 21-23).

In order to show the applicability and efficiency of (NH₄)₈ [CeW₁₀O₃₆]·20H₂O, some of the recently reported methods about the protection of benzyl alcohol were compared with the present results. The present method proved to be superior to most of the previously reported methods, as shown in Table 3.

Conclusion

In this study, a convenient and efficient protocol for the protection of alcohols with HMDS and deprotection of trimethylsilyl ethers in acetonitrile at room temperature has been successfully developed. High to excellent yields, short reaction times, operational simplicity, low cost, easy availability and non-toxicity of the catalyst are noteworthy advantages of the present method, which make this procedure a useful and attractive addition to the currently available methods.

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References

- [1] T. W. Green, P. G. M. Wuts, Protective Groups in Organic Synthesis, 3rd edn, John Wiley & Sons: New York, 1999.
- [2] E. J. Corey, A. Venkateswarlu, J. Am. Chem. Soc. 1972, 94, 6190.
- G. A. Olah, B. G. B. Gupta, S. C. Narang, R. Malhotra, J. Org. Chem. [3] 1979, 44, 4272.
- [4] a) B. A. D. Sa, D. McLeod, J. G. Verkade, J. Org. Chem. 1997, 62, 5057; b) B. A. D. Sa, J. G. Verkade, J. Am. Chem. Soc. 1996, 118, 12832.
- [5] M. Lalonde, T. H. Chan, Synthesis 1985, 817.
- [6] a) S. H. Langer, S. Connell, J. Wender, J. Org. Chem. 1958, 23, 50; b) P. Gauttret, S. El-Ghamarti, A. Legrand, D. Coutrier, B. Rigo, Synth. Commun. 1996, 26, 707.
- [7] F. Shirini, M. A. Zolfigol, K. Mohammadi, Phosphorus, Sulfur, Silicon Relat. Elem. 2003, 178, 1567.
- H. Firouzabadi, B. Karimi, Synth. Commun. 1993, 23, 1633.
- [9] H. Firouzabadi, A. R. Sardarian, Z. Khayat, B. Karimi, S. Tangestaninejad, Synth. Commun. 1997, 27, 2709.
- [10] M. Curini, F. Epifano, M. C. Marcotullio, O. Rosati, U. Constantino, Synth. Commun. 1999, 29, 541.
- [11] B. Karimi, B. Golshani, J. Org. Chem. 2000, 65, 7228.
- [12] N. Azizi, M. R. Saidi, Organometallics 2004, 23, 1457.
- [13] Z. H. Zhang, T. S. Li, F. Yang, C. G. Fu, Synth. Commun. 1998, 28, 3105.
- [14] H. Firouzabadi, N. Iranpoor, K. Amani, F. Nowrouzi, J. Chem. Soc., Perkin Trans. 1 2002, 2601.

- [15] R. Ghorbani-Vaghei, M. A. Zolfigol, M. Chegeny, H. Veisi, *Tetrahe*dron Lett. **2006**, 47, 4505.
- [16] B. Akhlaghinia, S. Tavakoli, Synthesis 2005, 1775.
- [17] M. M. Mojtahedi, H. Abbasi, M. S. Abaee, J. Mol. Catal. A: Chem. 2006, 250, 6.
- [18] A. V. Narsaiah, J. Organomet. Chem. 2007, 692, 3614.
- [19] H. Firouzabadi, N. İranpoor, A. A. Jafari, M. R. Jafari, *J. Organomet. Chem.* **2008**, 693, 2711.
- [20] M. M. Mojtahedi, M. S. Abaee, M. Eghtedari, *Appl. Organomet. Chem.* 2008, 22, 529.
- [21] F. Shirini, M. Abedini, J. Iran. Chem. Soc. 2008, 5, S87.
- [22] M. Moghadam, S. Tangestaninejad, V. Mirkhani, I. Mohammadpoor-Baltork, S. Chahardahcheric, Z. Tavakoli, J. Organomet. Chem. 2008, 693, 2041.
- [23] H. Firouzabadi, I. Mohammadpoor-Baltork, S. Kolagar, Synth. Commun. 2001, 31, 905.
- [24] A. Shaabani, A. Karimi, Synth. Commun. 2001, 31, 759.
- [25] A. R. Hajipour, S. E. Mallakpour, I. Mohammadpoor-Baltork, H. Adibi, Synth. Commun. 2001, 31, 1625.
- [26] M. Curini, F. Epifano, M. C. Marcotullio, O. Rosati, M. Rossi, A. Tsadjout, Synth. Commun. 2000, 30, 3181.
- [27] M. H. Habibi, S. Tangestaninejad, V. Mirkhani, I. Mohammadpoor-Baltork, B. Yadollahi, *Tetrahedron Lett.* **2001**, *42*, 6771.
- [28] A. Shaabani, A. H. Rezayan, M. Heidary, A. Sarvari, Catal. Commun. 2008, 10, 129.
- [29] S. Tasadaque, A. Shah, P. J. Guiry, Org. Biomol. Chem. 2008, 6, 2168.
- [30] S. Bhatt, S. K. Nayak, *Tetrahedron Lett.* **2006**, *47*, 8395.
- [31] R. S. Raghuvanshi, K. N. Singh, Synth. Commun. 2007, 37, 1371.
- [32] M. Tajbakhsh, M. M. Heravi, S. Habibzadeh, Synth. Commun. 2007, 37, 2967.
- [33] M. H. Bhure, I. Kumar, A. D. Natu, C. V. Rode, *Synth. Commun.* **2008**, *38*, 346.
- [34] B. Wang, H. Sun, Z. Sun, J. Org. Chem. 2009, 74, 1781.

- [35] a) M.T. Pope, A. Muller (Eds.), Polyoxometalate Chemistry From Topology via Self-Assembly to Applications, Kluwer Academic Publishers: Dordrecht, 2001; b) T. Yamase, M.T. Pope (Eds.), Polyoxometalate Chemistry for Nano-Composite Design, Kluwer Academic: New York, 2002.
- [36] a) I. V. Kozhevnikov, J. Mol. Catal. A: Chem. 2007, 262, 86; b) C. L. Hill, J. Mol. Catal. A: Chem. 2007, 262, 2; c) M. V. Vasylyev, R. Neumann, J. Am. Chem. Soc. 2004, 126, 884; d) R. Neumann, A. M. Khenkin, Chem. Commun. 2006, 2529.
- [37] a) N. Mizuno, M. Misono, Chem. Rev. 1998, 98, 199; b) Y. Izumi, K. Urabe, M. Onaka, Zeolite, Clay and Heteropoly Acid in Organic Reactions, Kodansha/VCH: Tokyo, 1992.
- [38] a) V. Mirkhani, S. Tangestaninejad, L. Alipanah, Synth. Commun. 2002, 32, 621; b) V. Mirkhani, S. Tangestaninejad, B. Yadollahi, L. Alipanah, Tetrahedron 2003, 59, 8213; c) V. Mirkhani, S. Tangestaninejad, B. Yadollahi, L. Alipanah, Catal. Lett. 2003, 91, 120; (d) V. Mirkhani, S. Tangestaninejad, M. Moghadam, B. Yadollahi, L. Alipanah, Monatsh. Chem. 2004, 135, 1257; e) V. Mirkhani, S. Tangestaninejad, B. Yadollahi, L. Alipanah, Catal. Lett. 2005, 101, 93.
- [39] M. Moghadam, S. Tangestaninejad, V. Mirkhani, I. Mohammadpoor-Baltork, S. Gharaati, Appl. Organometal. Chem. 2009, 23, 446.
- [40] a) R. D. Peacock, T. J. R. Weakley, J. Chem. Soc. A **1971**, 1836;
 b) R. Shiozaki, H. Goto, Y. Kera, Bull. Chem. Soc. Jpn. **1993**, 66, 2790.
- [41] A. Khazaei, M. A. Zolfigol, Z. Tanbakouchian, M. Shiri, K. Niknam, J. Saien, *Catal. Commun.* 2007, 8, 917.
- [42] H. A. Shaterian, F. Shahrekipoor, M. Ghashang, J. Mol. Catal. A, 2007, 272, 142.
- [43] D. Zareyee, B. Karimi, *Tetrahedron Lett.* 2007, 48, 1277.
- [44] H. Firouzabadi, A. A. Jafari, J. Iran. Chem. Soc. 2005, 2, 85.
- [45] H. Firouzabadi, N. Iranpoor, S. Farahi, J. Organomet. Chem. 2009, 694, 3923.