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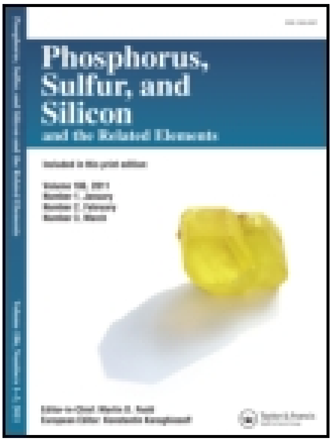

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$Cu(NO_3)_2 \cdot 3\ H_2O$ as an Efficient Reagent for the Chemoselective Trimethylsilylation of Primary Alcohols and Oxidation of Trimethylsilyl Ethers

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$Cu(NO_3)_2 \cdot 3\ H_2O$ AS AN EFFICIENT REAGENT FOR THE CHEMOSELECTIVE TRIMETHYLSILYLATION OF PRIMARY ALCOHOLS AND OXIDATION OF TRIMETHYLSILYL ETHERS

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GRAPHICAL ABSTRACT

$$PhCH_2OH \xrightarrow[\text{Solvent-free, r.t., 20 min, 91\%}]{Cu(NO_3)_2 \cdot 3\ H_2O \text{ (0.75 mmol), HMDS (1.3 mmol)}} PhCH_2OTMS$$

Abstract *$Cu(NO_3)_2 \cdot 3\ H_2O$ can be used as an efficient reagent for the chemoselective trimethylsilylation of primary benzylic and aliphatic alcohols with hexamethyldisilazane (HMDS). This reagent is also able to oxidize the obtained trimethylsilyl ethers to the corresponding carbonyl compounds in the presence of wet SiO_2 and KBr. In this study, all reactions are performed in the absence of a solvent and good-to-high yields are obtained.*

Keywords $Cu(NO_3)_2 \cdot 3\ H_2O$; alcohols; trimethylsilylation; oxidation; solvent-free conditions

INTRODUCTION

Hexamethyldisilazane (HMDS) is one of the most important reagents widely used for the protection of alcoholic hydroxy groups during a multistep synthesis. A number of reagents have been reported for the promotion of silylation of alcohols with HMDS, including sulfonic acid,[1] K-10 montmorillonite,[2] zirconium sulfophenyl phosphonate,[3] Me_3SiCl,[4] silica chloride,[5] $Al(HSO_4)_3$,[6] $Fe(HSO_4)_3$,[7] $ZrCl_4$,[8] tungstophosphoric acid,[9] saccharin sulfonic acid,[10] sulfonic acid-functionalized ordered nanoporous silica,[11] trichloroisocyanuric acid,[12] cupric sulfate penthydrate,[13] copper triflate,[14] mono- and dibromo-5,5-diethylbarbutiric acids,[15] 1,3-dibromo-5,5-diethylbarbutiric acid,[16] lanthanum trichloride,[17] tribromomelamine,[18] $PhMe_3N^+Br_3^-$,[19] niobium (V) chloride,[20] N,N′-di-iodo-N,N′-1,2-ethanediyl bis(*p*-toluenesulfonamide),[21] *p*-toluenesulfonyl chloride,[22] and silica-supported zinc chloride.[23] However, some of the reported methods suffer from one or more of the following disadvantages: long reaction times, low selectivity, forceful conditions, tedious work-up procedure, and use of toxic, expensive, or moisture-sensitive reagents. Hence, the introduction of new procedures to circumvent these problems is still in demand.

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In 2007, Heravi et al. reported that $Cu(NO_3)_2 \cdot 3\ H_2O$ is able to efficiently catalyze the protection of aldehydes as the corresponding 1,1-diacetates.[24] Motivated by this study and in continuation of our ongoing research program on the development of new methods for the protection of hydroxy groups,[4–8,10] we have investigated the applicability of $Cu(NO_3)_2 \cdot 3\ H_2O$ in the promotion of trimethylsilylation of alcohols with HMDS.

RESULTS AND DISCUSSION

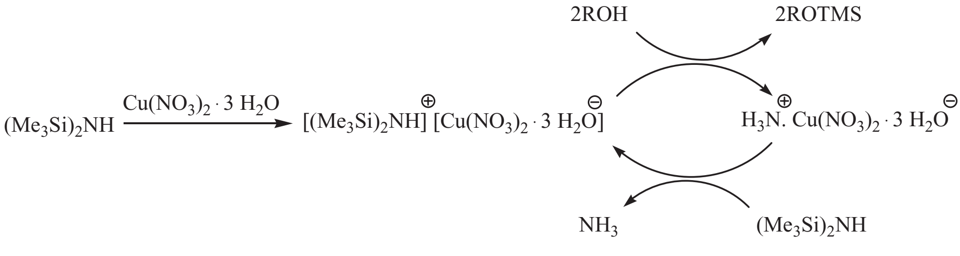
Initially, benzyl alcohol was chosen as a model substrate for the silylation reaction. Optimization of the reaction conditions showed that the best results were obtained when benzyl alcohol was treated with 1.3 equivalents of HMDS in the presence of 0.75 equivalent of $Cu(NO_3)_2 \cdot 3\ H_2O$ in the absence of a solvent at room temperature (20 min, 91% isolated yield) (Scheme 1).

$$PhCH_2OH \xrightarrow[\text{Solvent-free, r.t., 20 min, 91\%}]{Cu(NO_3)_2 \cdot 3\ H_2O\ (0.75\ \text{mmol}),\ \text{HMDS}\ (1.3\ \text{mmol})} PhCH_2OTMS$$

Scheme 1

After optimization of the reaction conditions, different types of primary benzylic and aliphatic alcohols were subjected to trimethylsilylation under the determined conditions. As shown in Table 1, the corresponding trimethylsilyl ethers were obtained in excellent yields. No elimination and rearrangement byproducts were observed at all. Secondary and tertiary alcohols and phenols silylate slower than primary alcohols using this method and the reaction is in most cases incomplete (Table 1, entries 14–20). In addition, amines and thiols are resistant to this reagent and remained unchanged in the reaction mixture (Table 1, entries 21–23). Therefore, this methodology shows selectivity and is suitable for the selective trimethylsilylation of primary benzylic and aliphatic alcohols in the presence of the abovementioned substrates (Table 1, entries 24–27).

Although the actual role of $Cu(NO_3)_2 \cdot 3\ H_2O$ is not clear, the mechanism shown in Scheme 2 seems to be the most probable one.

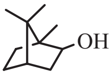
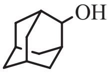
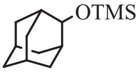
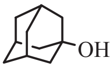
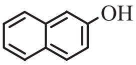
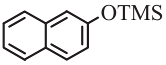
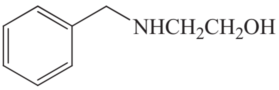
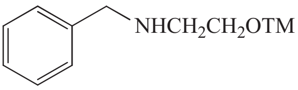


Scheme 2

In order to show the efficiency of the proposed method, Table 2 compares some of the results obtained by our method with some of those reported in the literature.

Recently, KBr was used as an efficient reagent for the promotion of oxidation of alcohols with periodic acid and iodic acid in the presence of wet SiO_2.[27] Our studies revealed that the oxidation of the trimethylsilyl ethers obtained occurs efficiently using $Cu(NO_3)_2 \cdot 3\ H_2O$ in the presence of KBr/wet SiO_2 under the conditions presented in

Table 1 Trimethylsilylation of alcohols catalyzed by $Cu(NO_3)_2 \cdot 3\,H_2O$[a,b]

Entry	Substrate	Product	Time (h)	Yield (%)	References
1	$PhCH_2OH$	$PhCH_2OTMS$	0.3	91	Ghorbani-Choghamarani et al. (2008)[18]
2	$2\text{-}ClC_6H_4CH_2OH$	$2\text{-}ClC_6H_4CH_2OTMS$	2.25	88	Zareyee and Karimi (2007)[11]
3	$4\text{-}ClC_6H_4CH_2OH$	$4\text{-}ClC_6H_4CH_2OTMS$	0.5	90	Ghorbani-Choghamarani et al. (2008)[18]
4	$3,4\text{-}ClC_6H_3CH_2OH$	$3,4\text{-}ClC_6H_3CH_2OTMS$	0.6	87	Zareyee and Karimi (2007)[11]
5	$4\text{-}BrC_6H_4CH_2OH$	$4\text{-}BrC_6H_4CH_2OTMS$	0.75	92	Ghorbani-Choghamarani et al. (2008)[18]
6	$2\text{-}MeC_6H_4CH_2OH$	$2\text{-}MeC_6H_4CH_2OTMS$	0.8	90	Zareyee and Karimi (2007)[11]
7	$4\text{-}Me_3CC_6H_4CH_2OH$	$4\text{-}Me_3CC_6H_4CH_2OTMS$	1.3	91	Rajagopal et al. (2009)[25]
8	$2\text{-}NO_2C_6H_4CH_2OH$	$2\text{-}NO_2C_6H_4CH_2OTMS$	3	85	Zareyee and Karimi (2007)[11]
9	$4\text{-}NO_2C_6H_4CH_2OH$	$4\text{-}NO_2C_6H_4CH_2OTMS$	2	87	Ghorbani-Choghamarani et al. (2008)[18]
10	$4\text{-}MeOC_6H_4CH_2OH$	$4\text{-}MeOC_6H_4CH_2OTMS$	0.6	90	Firuozabadi et al. (2002)[9]
11	$PhCH_2CH_2OH$	$PhCH_2CH_2OTMS$	0.3	91	Ghorbani-Choghamarani et al. (2008)[18]
12	$PhCH_2CH_2CH_2OH$	$PhCH_2CH_2CH_2OTMS$	0.5	90	Firuozabadi et al. (2002)[9]
13	Ph_2CHOH	$Ph_2CHOTMS$	6	50	Ghorbani-Choghamarani et al. (2008)[18]
14			5	50	Firuozabadi et al. (2002)[9]
15			6	60	Ghorbani-Choghamarani et al. (2008)[18]
16			6	50	Zareyee and Karimi (2007)[11]
17	Ph_3COH	Ph_3COTMS	4	0[c]	—
18	PhOH	PhOTMS	7	80	Ghorbani-Choghamarani et al. (2008)[18]
19	$4\text{-}Me_2CHC_6H_4OH$	$4\text{-}Me_2CHC_6H_4OTMS$	3	90	Kadam and Kim (2009)[26]
20			7	80	Firuozabadi et al. (2002)[9]
21	$4\text{-}BrC_6H_4SH$	$4\text{-}BrC_6H_4STMS$	3	0[c]	—
22	C_6H_5SH	C_6H_5STMS	3	0[c]	—
23	$C_6H_5NH_2$	C_6H_5NHTMS	3	0[c]	—
24	$2\text{-}ClC_6H_4CH_2OH + Ph_3COH$	$2\text{-}ClC_6H_4CH_2OTMS + Ph_3COTMS$	3	100[d] + 0[d]	—
25	$PhCH_2OH + PhOH$	$PhCH_2OTMS + PhOTMS$	0.3	90[d] + 10[d]	—
26	$2\text{-}ClC_6H_4CH_2OH + C_6H_5SH$	$2\text{-}ClC_6H_4CH_2OTMS + C_6H_5STMS$	2	100[d] + 0[d]	—
27	$2\text{-}ClC_6H_4CH_2OH + C_6H_5NH_2$	$2\text{-}ClC_6H_4CH_2OTMS + C_6H_5NHTMS$	3	90[d] + 10[d]	—
28			0.4	100[d]	—

[a] Products were identified spectroscopically and also by the conversion of the silyl ethers to the corresponding alcohols.

[b] Isolated yields.

[c] Starting material was recovered unchanged.

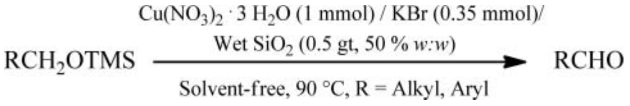
[d] Conversion (GC).

Table 2 $Cu(NO_3)_2 \cdot 3\ H_2O$-catalyzed trimethylsilylation of benzyl alcohol in comparison with other methods reported in the literature

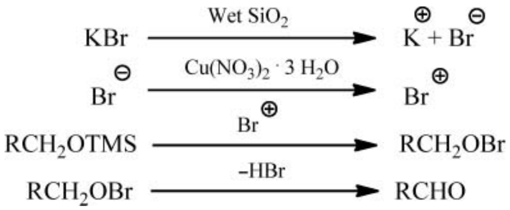
Entry	Catalyst/Condition	Solvent	Time (min)	Yield (%)	References
1	$Fe(HSO_4)_3$; reflux	CH_3CN	100	70	Shirini et al. (2008)[7]
2	$H_3PW_{12}O_{40}$; 55–60 °C	Neat	23	90	Firuozabadi et al. (2002)[9]
3	Sulfonic acid-functionalized ordered nanoporous silica; r.t.	CH_2Cl_2	80	99	Zareyee and Karimi (2007)[11]
4	TCCA; r.t.	CH_2Cl_2	240	90	Khazaei et al. (2007)[12]
5	1,3-Dibromo-5,5-diethylbarbituric acid; r.t.	Neat	30	95	Khazaei et al. (2007)[16]
6	$LaCl_3$; r.t.	CH_2Cl_2	180	91	Narsaiah (2007)[17]
7	$Cu(NO_3)_2 \cdot 3\ H_2O$; r.t.	Neat	20	91	This work

Scheme 3. All reactions are performed in the absence of a solvent at 90 °C and excellent yields are obtained (Table 3).

On the basis of the results obtained and literature reports[27,28] a mechanism for the reaction can be suggested, which is shown in Scheme 4.



Scheme 3



Scheme 4

In conclusion, we have developed a mild, efficient, and chemoselective method for trimethylsilylation of primary benzylic and aliphatic alcohols and for oxidation of the trimethylsilyl ethers obtained. High yields of the products, easy and clean work-up, and solvent-free reaction conditions are important advantages of this method, which make this procedure a useful and attractive addition to the currently available methods.

EXPERIMENTAL

Trimethylsilylation of Primary Alcohols: General Procedure

A mixture of the substrate (1 mmol), $Cu(NO_3)_2 \cdot 3\ H_2O$ (0.75 mmol, 0.181 g), and HMDS (1.3 mmol, 0.21 g) was shaken at room temperature for the specified time. The progress of the reaction was monitored by TLC. After completion of the reaction, the

Table 3 Oxidation of trimethylsilyl ethers[a,b]

Entry	Substrate	Product	Time (h)	Yield (%)	References
1	$PhCH_2OTMS$	$PhCHO$	0.2	91	Zolfigol et al. (2007)[27]
2	$2\text{-}ClC_6H_4CH_2OTMS$	$2\text{-}ClC_6H_4CHO$	0.3	88	Gholizadeh et al. (2004)[29]
3	$4\text{-}ClC_6H_4CH_2OTMS$	$4\text{-}ClC_6H_4CHO$	0.25	92	Zolfigol et al. (2007)[27]
4	$3,4\text{-}ClC_6H_3CH_2OTMS$	$3,4\text{-}ClC_6H_3CHO$	0.7	90	Zolfigol et al. (2007)[27]
5	$2\text{-}BrC_6H_4CH_2OTMS$	$2\text{-}BrC_6H_4CHO$	0.75	87	Gholizadeh et al. (2004)[29]
6	$4\text{-}BrC_6H_4CH_2OTMS$	$4\text{-}BrC_6H_4CHO$	0.4	91	Zolfigol et al. (2007)[27]
7	$2\text{-}MeC_6H_4CH_2OTMS$	$2\text{-}MeC_6H_4CHO$	0.3	90	Bagherzadeh (2003)[30]
8	$4\text{-}Me_3CC_6H_4CH_2OTMS$	$4\text{-}Me_3CC_6H_4CHO$	0.5	87	Gholizadeh et al. (2004)[29]
9	$2\text{-}NO_2C_6H_4CH_2OTMS$	$2\text{-}NO_2C_6H_4CHO$	2.5	85	Gholizadeh et al. (2004)[29]
10	$4\text{-}NO_2C_6H_4CH_2OTMS$	$4\text{-}NO_2C_6H_4CHO$	1.5	87	Zolfigol et al. (2007)[27]
11	$4\text{-}MeOC_6H_4CH_2OTMS$	$4\text{-}MeOC_6H_4CHO$	0.25	70	Zolfigol et al. (2007)[27]
12	$PhCH_2CH_2OTMS$	$PhCH_2CHO$	1	86	Zolfigol et al. (2007)[27]
13	$PhCH_2CH_2CH_2OTMS$	$PhCH_2CH_2CHO$	1.7	88	Tamami and Yeganeh (1999)[31]

[a] Products were identified spectroscopically.
[b] Isolated yields.

mixture was triturated with CH_2Cl_2 (10 mL) and then filtered. Evaporation of the solvent under reduced pressure gave almost pure product. Further purification was carried out using bulb-to-bulb distillation under reduced pressure, vacuum distillation, or recrystallization to afford pure silyl ether.

Oxidation of Trimethylsilyl Ethers: General Procedure

A mixture of the substrate (1 mmol), wet SiO_2 (0.5 g, 50% w:w), KBr (0.35 mmol, 0.042 g), and $Cu(NO_3)_2 \cdot 3\ H_2O$ (1 mmol, 0.241 g) was heated in an oil bath (90 °C). The progress of the reaction was monitored by TLC. After completion of the reaction, the mixture was triturated with CH_2Cl_2 (5 mL) and then filtered. The solid residue was washed with CH_2Cl_2 (5 mL). The filtrate was washed with a saturated solution of $NaHCO_3$ and H_2O and dried over $MgSO_4$. Evaporation of the solvent followed by column chromatography on silica gel gave the corresponding carbonyl compounds in excellent yields.

REFERENCES

1. Goldschmidt, A. G. T. German Patent 2 758884.
2. Zhang, Z. H.; Li, T. S.; Yang, F.; Fu, C. G. *Synth. Commun.* **1998,** 28, 3105–3114.
3. Curini, M.; Epifano, F.; Marcotullio, M. C.; Rosati, O.; Costantino, U. *Synth. Commun.* **1999,** 29, 541–546.
4. Gautret, P.; El-Ghamarti, S.; Legrand, A.; Couturier, D.; Rigo, B. *Synth. Commun.* **1996,** 26, 707–713.
5. Shirini, F.; Zolfigol, M. A.; Mohammadi, K. *Phosphorus Sulfur Silicon Relat. Elem.* **2003,** 178, 1567–1570.
6. Shirini, F.; Zolfigol, M. A.; Abedini, M. *Bull. Chem. Soc. Jpn.* **2005,** 78, 1982–1985.
7. Shirini, F.; Zolfigol, M. A.; Abri, A. *Monatsh. Chem.* **2008,** 139, 17–20.
8. Shirini, F.; Mollarazi, E. *Catal. Commun.* **2007,** 8, 1393–1396.
9. Firuozabadi, H.; Iranpoor, N.; Amani, K.; Nowrouzi, F. *J. Chem. Soc. Perkin Trans 1* **2002,** 2601–2604.

10. Shirini, F.; Zolfigol, M. A.; Abedini, M. *Monatsh. Chem.* **2009,** 140, 61–64.
11. Zareyee, D.; Karimi, B. *Tetrahedron Lett.* **2007,** 48, 1277–1280.
12. Khazaei, A.; Zolfigol, M. A.; Rostami, A.; Ghorbani Choghamarani, A. *Catal. Commun.* **2007,** 8, 543–547.
13. Akhlaghinia, B.; Tavakoli, S. *Synthesis* **2005,** 1775–1778.
14. Firouzabadi, H.; Iranpoor, N.; Sobhani, S.; Gassemipour, S.; Amoozgar, Z. *Tetrahedron Lett.* **2003,** 44, 891–893.
15. Khazaei, A.; Zolfigol, M. A.; Tanbakouchian, Z.; Shiri, M.; Rostami, A. *J. Braz. Chem. Soc.* **2007,** 18, 239–242.
16. Khazaei, A.; Zolfigol, M. A.; Tanbakouchian, Z.; Shiri, M.; Niknam, K.; Saien, J. *Catal. Commun.* **2007,** 8, 917–920.
17. Narsaiah, A. V. *J. Organomet. Chem.* **2007,** 692, 3614–3617.
18. Ghorbani-Choghamarani, A.; Zolfigol, M. A.; Hajjami, M.; Jafari, S. *J. Chin. Chem. Soc.* **2008,** 55, 1208–1213.
19. Ghorbani-Choghamarani, A.; Cheraghi-Fathabad, N. *Chin. J. Catal.* **2010,** 319, 1103–1106.
20. Hou, J. T.; Chen, H. L.; Zhang, Z. H. *Phosphorus Sulfur Silicon Relat. Elem.* **2011,** 186, 88–93.
21. Ghorbani-Vaghei, R.; Malaekehpoor, S. M. *Phosphorus Sulfur Silicon Relat. Elem.* **2010,** 185, 582–587.
22. Khazaei, A.; Rostami, A.; Mamtashlo, F. *Phosphorus Sulfur Silicon Relat. Elem.* **2009,** 184, 2288–2296.
23. Shaterian, H. R.; Khorami, F.; Doostmahammadi, R.; Amirzadeh, A. Ghashang, M. *Phosphorus Sulfur Silicon Relat. Elem.* **2009,** 184, 2227–2237.
24. Heravi, M. M.; Bakhtiari, K.; Tehrani, M. H.; Oskooie, H. A. *Synth. Commun.* **2007,** 37, 1121–1126.
25. Rajagopal, G.; Lee, H.; Kim, S. S. *Tetrahedron* **2009,** 65, 4735–4741.
26. Kadam, S. T.; Kim, S. S. *J. Organomet. Chem.* **2009,** 694, 2562–2566.
27. Zolfigol, M. A.; Shirini, F.; Ghorbani-Choghamarani, A.; Kolvari, E. *J. Mol. Catal. A: Chem.* **2007,** 265, 272–275.
28. Desai, U. V.; Pore, D. M.; Tamhankar, B. V.; Jadhav, S. A.; Wadgaonkar, P. P. *Tetrahedron Lett.* **2006,** 47, 8559–8561.
29. Gholizadeh, M.; Mohammadpoor-Baltork, I.; Kharamesh, B. *Bull. Korean Chem. Soc.* **2004,** 25, 566–568.
30. Bagherzadeh, M. *Tetrahedron Lett.* **2003,** 44, 8943–8945.
31. Tamami, B.; Yeganeh, H. *Eur. Poly. J.* **1999,** 35, 1445–1450.