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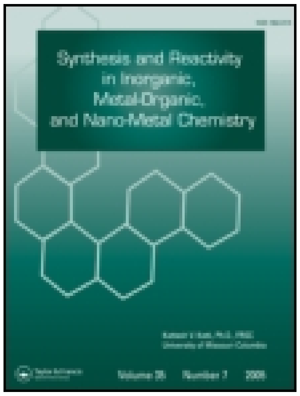

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P_2O_5/SiO_2 as an Efficient and Mild Catalyst for Trimethylsilylation of Alcohols Using Hexamethyldisilazane

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P_2O_5/SiO_2 as an Efficient and Mild Catalyst for Trimethylsilylation of Alcohols Using Hexamethyldisilazane

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The protection of alcohols with hexamethyldisilazane (HMDS) in the presence of P_2O_5/SiO_2 at very mild and ambient condition with short reaction times is accomplished in excellent yields. P_2O_5/SiO_2 catalyst is an efficient solid acid and heterogeneous catalyst for this transformation and easily recovered and reused for several times without significant decrease in its activity. Selectivity studies showed competitive reaction of primary alcohols over secondary alcohols and phenols.

Keywords HMDS, hydroxyl group, protection, trimethylsilylation

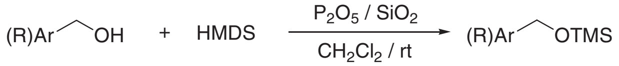
INTRODUCTION

Trimethysilylation of hydroxyl groups is one of the most important strategy for the protection of alcohols.[1] Organosilyl ethers are stable under various conditions, soluble in nonpolar solvents, have high thermal stability, and can be easily converted to corresponding alcohols under acid or base hydrolytic conditions.[2] They help to increase the volatility for analysis in gas-chromatography and mass spectrometry.[3]

On the other hand, the increasing interest in heterogeneous catalytic systems have made them important in industry and organic chemistry.[4] These systems have many advantages such as simple experimental procedures, mild reaction conditions, and minimum chemical wastes in comparison with liquid-phase reactions.[5] Solid acid catalysts are easier to handle, holding more acidity, and their separation from the products is easier.

Although there are some silylating agents for protection of hydroxyl group,[6–11] the use of hexamethyldisilazane (HMDS) as a silylating agent removes some of the difficulties that a researcher may focus with them. HMDS is nearly neutral, stable, inexpensive, and easy to handle. The only byproduct is ammonia, which can be easily removed. A variety of catalysts are used to enhance the silylating power of this reagent such as silica chloride,[12] $Al(HSO_4)_3$,[13] $Al(OTf)_3$,[14] $ZrCl_4$,[15] $CuSO_4.5H_2O$,[16] $Cu(OTf)_2$,[17] $LiClO_4$,[18] $Mg(OTf)_2$,[19] sulfonic acid-functionalized nanoporous silica,[20] iodine,[21] and $LaCl_3$.[22]

Considering these reports and in continuation of our previous works,[23–30] we decided to study the application of P_2O_5/SiO_2 as an inexpensive and easily prepared solid acid catalyst on the protection of alcohols by HMDS as silylating agents (Scheme 1).



SCH. 1. P_2O_5/SiO_2 (1.75 mole %).

EXPERIMENTAL

Protection of Benzyl Alcohol (Typical Procedure)

P_2O_5/SiO_2 (5 mg, 1.75 mole% based on benzyl alcohol) was added to a solution of benzyl alcohol (1 mmol, 0.108 g) and HMDS (0.7 mmol, 0.113 g) in dry CH_2Cl_2 (5 ml). The mixture was stirred for 5 min. at room temperature and then filtered. The column chromatography of the filtrate on silica gel using n-hexane: ethyl acetate (7:3) as eluent yielded the silylated alcohol in 99% yield.

RESULTS AND DISCUSSION

P_2O_5/SiO_2 was prepared according to our previous published method.[31] During this research, in order to get an insight into the solvent effect on the yields and the reaction times, we performed a set of preliminary experiments on the silylation of benzyl alcohol as a model experiment in different solvents such as THF, CH_3CN, CH_2Cl_2, $CHCl_3$, MeOH, and EtOH. The best results (99% yield in 5 min reaction time) were achieved when CH_2Cl_2 was used as the reaction media (Table 1).

Also, to obtain the best molar ratio of catalyst, the model reaction performed with different amounts of catalyst. The obtained results showed using 5 mg of catalyst (1.75 mole %) per 1 mmol of substrate obtained the best yield.

Various substituted alcohols were subjected into the reaction conditions in the presence of 5 mg of P_2O_5/SiO_2 in CH_2Cl_2 as solvent to give the desired protected compounds 1–14. All

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TABLE 1
The optimization of solvent on time and yield of the typical reaction of benzyl alcohol and HMDS[a]

Entry	Solvent	Time (min)	Yield[b] (%)
1	THF	30	80
2	CH_3CN	40	85
3	CH_2Cl_2	5	99
4	$CHCl_3$	10	95
5	MeOH	60	75
6	EtOH	50	80

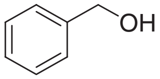
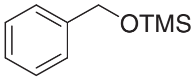
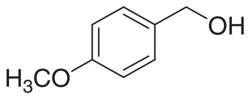
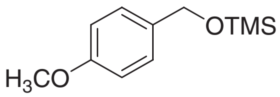
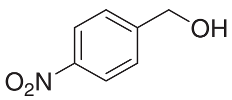
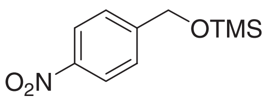
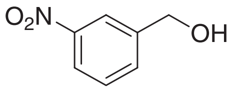
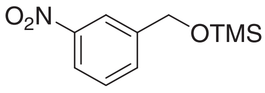
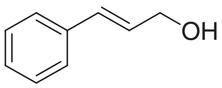
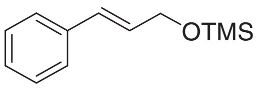
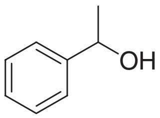
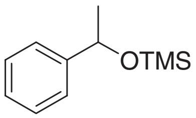
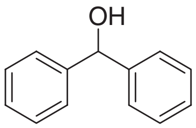
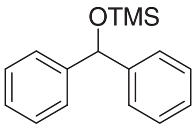
[a] Benzyl alcohol (1 mmol), HMDS (0.7 mmol), and catalyst (5 mg, 1.75 mole %) in CH_2Cl_2 (5 mL).

[b] Isolated yields.

the substrates depicted in Table 2 were successfully reacted at room temperature in a relatively short period of time, giving the excellent yield of product.

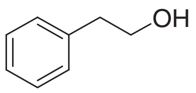
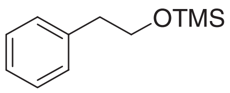
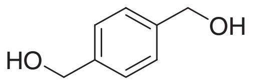
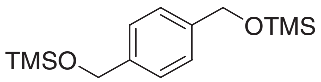
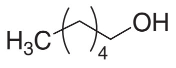
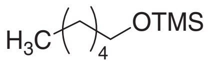
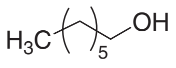
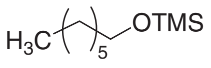
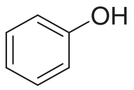
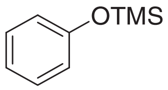
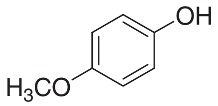
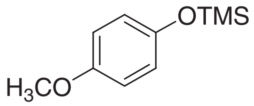
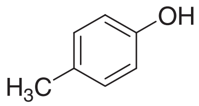
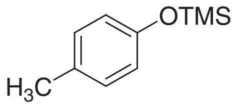
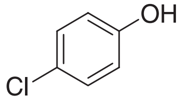
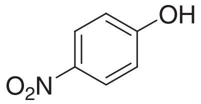
The results showed the efficiency of this method. The substrates that were trimethylsilylated by this method are primary, secondary, allylic, benzylic, and hindered alcohols. Generally, in the case of primary alcohols, the reactions were completed within less than 15 min in CH_2Cl_2 at room temperature with excellent yields. This method is also applicable for protecting of relatively unreactive and steric-hindered alcohols such as benzhydrol (entry 7). In this method, phenol and its electron-donating derivatives were converted into their corresponding trimethylsilylated products in low yield while phenols with electron-withdrawing substituents failed in this reaction (entries 12–16).

TABLE 2
Trimethylsilylation of various alcohols with P_2O_5/SiO_2[a]

Entry/Compound Numbers	Substrate	Product	Time (min)	Yield (%)[b]
1			10	99
2			5	98
3			15	96
4			10	98
5			15	95
6			20	95
7			30	88

(*Continued on next page*)

TABLE 2
Trimethylsilylation of various alcohols with P_2O_5/SiO_2[a] (*Continued*)

Entry/Compound Numbers	Substrate	Product	Time (min)	Yield (%)[b]
8			5	97
9[c]			15	90
10			20	94
11			20	92
12			120	30
13			100	45
14			120	35
15		No reaction	—	—
16		No reaction	—	—

[a] Reaction conditions: substrate (1 mmol), HMDS (0.7 mmol), P_2O_5/SiO_2 (5 mg per 1 mmol of substrate), CH_2Cl_2 (5 mL).
[b] Isolated yield.
[c] Reaction performed with 1 mmol of substrate and 2 mmol of HMDS.

To explore the selectivity of this method, we have studied the competitive reaction for trimethylsilylation with a mixture of primary and secondary alcohols. The reaction was performed with benzyl alcohol, 1-phenyl-1-ethanol, HMDS (1 mmol of each substrates), and P_2O_5/SiO_2. The result showed benzyl alcohol as a primary alcohol was protected while 1-phenyl-1-ethanol as secondary alcohol was intact.

One of the special features of the P_2O_5/SiO_2 catalyst is its insolubility in organic solvents, which makes its recovery very convenient. Therefore, the reusability of the catalyst was also examined under the optimized reaction conditions with benzyl alcohol and HMDS as a model reaction. For each of the repeated reactions, the catalyst was recovered and washed with ethyl acetate consecutively, and dried before being used for the next

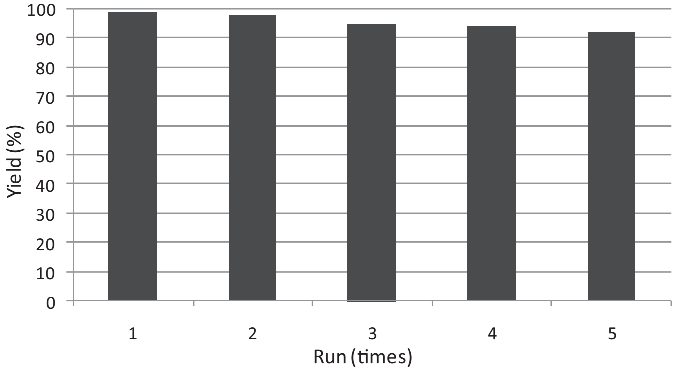


FIG. 1. Recycling of P_2O_5/SiO_2 catalyst in the protection of benzyl alcohol with HMDS.

silylation reaction. It is important to note that the catalyst was reused four times without significant any loss of activity and selectivity as shown in Figure 1.

CONCLUSION

In summary, this method provides a useful alternative for preparation of trimethylsilylated alcohols. P_2O_5/SiO_2 is an effective solid acid catalyst for this transformation. The advantages of this method are chemoselectivity, mild reaction conditions, simple procedure, irreversibility, high yield, and stability of the catalyst. Further investigation on the other aspects of this heterogeneous catalyst in the synthesis of heterocyclic compounds is in progress in our laboratory.

REFERENCES

1. (a) Lalonde, E.; Chem, T.H. Use of organosilicon reagents as protective groups in organic synthesis. *Synthesis* **1985**, 817–845. (b) Suzuki, T.; Watahiki, T.; Oriyama, T. A novel and efficient method for the silylation of alcohols with methallylsilanes catalyzed by $Sc(OTf)_3$. *Tetrahedron Lett.* **2000**, *41*, 8903–8906.
2. Shirakawa, E.; Hironaka, K.; Otsuka, H.; Hayashi, T. Palladium-catalyzed silylation of alcohols with hexamethyldisilane. *Chem. Commun.* **2006**, 3927–3929.
3. Tullberg, I.; Peetra, I.B.; Smith, B.E. Structural investigation of phenols and alcohols using silylation and gas chromatography. *J. Chromatogr. A.* **1976**, *120*, 103–113.
4. Corma, A. Solid acid catalysts. *Curr. Opin. Solid State Mater. Sci.* **1997**, *2*, 63–75.
5. Clark, J.H.; Rhodes, C.N. Clean synthesis using porous inorganic solid catalysts and supported reagents, Cambridge: Royal Society of Chemistry; **2000**.
6. Lissel, M.; Weiffen, J. Phase transfer catalysis for the preparation of trimethylsilyl and tert-butyldimethylsilyl ethers. *Synth. Commun.* **1981**, *11*, 545–549.
7. Pinnick, H.W.; Bal, B.S.; Lajis, N.H. A new preparation of trimethylsilyl ethers. *Tetrahedron Lett.* **1978**, *19*, 4261–4262.
8. (a) Morita, T.; Okamaoto, Y.; Sakutai, H. Use of allylsilanes as a new type of silylating agent for alcohols and carboxylic acids. *Tetrahedron Lett.* **1980**, *21*, 835–838. (b) Olah, G.A.; Gupta, B.G. B.; Salem, G.F.; Narang, S.C. Synthetic methods and reactions. Silylations with in situ generated trimethylsilyl triflate reagent systems. *J. Org. Chem.* **1981**, *46*, 5212–5214.
9. Chirakul, P.; Hampton, P.D.; Duelser, E.N. Synthesis and crystal structure of an O-silylated hexahomotriazacalix[3]arene. *Tetrahedron Lett.* **1998**, *39*, 5473–5476.
10. Corey, E.J.; Venkateswarlu, A. Protection of hydroxyl groups as tert-butyldimethylsilyl derivatives. *J. Am. Chem. Soc.* **1972**, *94*, 6190–6191.
11. Kita, Y.; Haruta, J.; Segawa, J.; Tamura, Y. Palladium-catalyzed cross-coupling reaction of allyl acetates with pinacol aryl- and vinylboronates. *Tetrahedron Lett.* **1979**, *44*, 4311–4314.
12. Shirini, F.; Zolfigol, M.A.; Mohammadi, K. A mild and efficient method for chemoselective silylation of alcohols using hexamethyldisilazane in the presence of silica chloride. *Phosphorous Sulfur Silicon* **2003**, *178*, 1567–1570.
13. Shirini, F.; Zolfigol, M.A.; Abedini, M. Silylation and tetrahydropyranylation of alcohols catalyzed by $Al(HSO_4)_3$. *Bull. Chem. Soc. Jpn.* **2005**, *78*, 1982–1985.
14. Firouzabadi, H.; Iranpoor, N.; Sobhani, S.; Gassamipour, S. Aluminium triflate $[Al(OTf)_3]$ as a recyclable catalyst for the conversion of α-hydroxyphosphonates, alcohols and phenols to their corresponding O-silylated products with hexamethyldisilazane (HMDS). *Synthesis* **2005**, 595–599.
15. Shirini, F.; Mollarazi, E. Efficient trimethylsilylation of alcohols and phenols in the presence of $ZrCl_4$ as a reusable catalyst. *Catal. Commun.* **2007**, *8*, 1393–1396.
16. Akhlaghinia, B.; Tavakoli, S. An efficient method for the protection of alcohols and phenols by using hexamethyldisilazane in the presence of cupric sulfate pentahydrate under neutral reaction conditions. *Synthesis* **2005**, 1775–1778.
17. Firouzabadi, H.; Iranpoor, N.; Sobhani, S.; Gassamipour, S.; Amoozgar, Z. Copper triflate $[Cu(OTf)_2]$ is an efficient and mild catalyst for the silylation of α-hydroxyphosphonates to α-trimethylsilyloxyphosphonates with HMDS at room temperature. *Tetrahedron Lett.* **2003**, *44*, 891–893.
18. Bandgar, P.K.; Kasture, S.P. Chemoselective protection of hydroxyl groups and deprotection of silyl ethers. *Monatsh. Chem.* **2001**, *132*, 1101–1104.
19. Firouzabadi, H.; Iranpoor, N.; Sobhani, S.; Gassamipour, S. Magnesium triflate $[Mg(OTf)_2]$ a highly stable, non-hygroscopic and a recyclable catalyst for the high yielding preparation of diethyl α-trimethylsilyloxyphosphonates from diethyl α-hydroxyphosphonates by HMDS under solventless conditions. *J. Organomet. Chem.* **2004**, *689*, 3197–3202.
20. Zareyee, D.; Karimi, B. A novel and highly efficient method for the silylation of alcohols with hexamethyldisilazane (HMDS) catalyzed by recyclable sulfonic acid-functionalized ordered nanoporous silica. *Tetrahedron Lett.* **2007**, *48*, 1277–1280.
21. Karimi, B.; Golshani, B. Mild and highly efficient method for the silylation of alcohols using hexamethyldisilazane catalyzed by iodine under nearly neutral reaction conditions. *J. Org. Chem.* **2000**, *65*, 7228–7230.
22. Narsaiah, A.V. Lanthanum trichloride: an efficient catalyst for the silylation of hydroxyl groups by activating hexamethyldisilazane (HMDS). *J. Organomet. Chem.* **2007**, *692*, 3614–3618.
23. Eshghi, H.; Hassankhani, A. Phosphorus pentoxide supported on silica gel and alumina (P_2O_5/SiO_2, P_2O_5/Al_2O_3) as useful catalysts in organic synthesis. *J. Iran. Chem. Soc.* **2012**, *9*, 467–482.
24. Bakavoli, M.; Shiri, A.; Ebrahimpour, Z.; Rahimizadeh, M. Clean heterocyclic synthesis in water: I_2/KI catalyzed one-pot synthesis of quinazolin-4(3H)-ones. *Chin. Chem. Lett.* **2008**, *19*, 1403–1406.
25. Rahimizadeh, M.; Bakavoli, M.; Shiri, A.; Eshghi, H.; Saberi, S. 3,3,9,9-Tetramethyl-1,5,7,11-tetraoxaspiro [5.5]undecane as a new and efficient reagent for protection of carbonyl compounds. *J. Chem. Res.* **2008**, 704–706.
26. Eshghi, H.; Rahimizadeh, M.; Saberi, S. Selective monotetrahydropyranylation of symmetrical diols using P_2O_5/SiO_2 under solvent-free conditions and their depyranylation. *Chin. Chem. Lett.* **2008**, *19*, 1063–1067.

27. Rahimizadeh, M.; Bakavoli, M.; Shiri, A.; Eshghi, H. Iodine-catalyzed synthesis of spiroorthcarbonates under neutral conditions. *Bull. Korean Chem. Soc.* **2009**, *30*, 1699–1700.
28. Bakavoli, M.; Rahimizadeh, M.; Eshghi, H.; Shiri, A.; Ebrahimpour, Z.; Takjoo, R. Synthesis, characterization and structure of DBUhydrobromide-perbromide: a novel oxidizing agent for oxidation of alcohols to carbonyl compounds. *Bull. Korean Chem. Soc.* **2010**, *31*, 949–952.
29. Rahimizadeh, M.; Rajabzadeh, G.; Khatami, S.-M.; Eshghi, H.; Shiri, A. TiO_2 nanoparticles and preyssler-type heteropoly acid modified nano-sized TiO_2: a facile and efficient catalyst for the selective oxidation of sulfides to sulfones and sulfoxides. *J. Mol. Cat. A: Chem.* **2010**, *323*, 59–64.
30. Rahimizadeh, M.; Bazazan, T.; Shiri, A.; Bakavoli, M.; Hassani, H. Preyssler-type heteropoly acid: a new, mild and efficient catalyst for protection of carbonyl compounds. *Chin. Chem. Lett.* **2011**, *22*, 435–438.
31. Eshghi, H.; Hassankhani, A. P_2O_5/SiO_2-catalyzed one-pot synthesis of amides from ketones via Schmidt reaction under microwave irradiation in dry media. *Synth. Commun.* **2006**, *36*, 2211–2216.