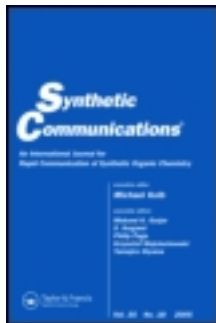


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Green and Efficient Procedure for the Trimethylsilylation of Hydroxy Groups and Their Regeneration Using Sulfamic Acid as Recyclable Catalyst

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GREEN AND EFFICIENT PROCEDURE FOR THE TRIMETHYLSILYLATION OF HYDROXY GROUPS AND THEIR REGENERATION USING SULFAMIC ACID AS RECYCLABLE CATALYST

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Structurally diverse alcohols and phenols were efficiently transformed into their corresponding trimethylsilyl ethers with hexamethyldisilazane (HMDS) in the presence of catalytic amounts of sulfamic acid (SA) at room temperature under both acetonitrile and solvent-free conditions. Deprotection of these trimethylsilyl ethers to their parent alcohols and phenols was also achieved using this catalyst in water at room temperature.

Keywords: Catalyst; detrimethylsilylation; hexamethyldisilazane; hydroxy groups; sulfamic acid; trimethylsilyl ether

INTRODUCTION

Functional group manipulations through protection and deprotection strategies are of interest in organic synthesis and widely used in the preparation of multifunctional target molecules. Protection of hydroxy groups through the formation of silyl ethers has been extensively utilized in organic synthesis.^[1] There are several methods available for the silylation of the hydroxy group.^[2] 1,1,1,3,3,3-Hexamethyldisilazane (HMDS) is a stable, cheap, and commercially available compound, which can be used for the preparation of trimethylsilyl (TMS) ethers from hydroxy compounds, giving ammonia as the only by-product. Even though the handling of this reagent is easy, its main drawback is its poor silylating ability, forceful conditions, and the long reaction time required.^[3] Therefore, for the activation of HMDS, a variety of catalysts have been reported.^[4–12] However, some of the reported methods suffer from one or more of the following disadvantages, such as expensive catalysts, hygroscopicity, and thermal instability of the catalysts, drastic reaction conditions, tedious workup, and formation of by-products. The main disadvantage of most of the existing methods is that the catalysts are destroyed in the work-up procedure and cannot be recovered or reused.

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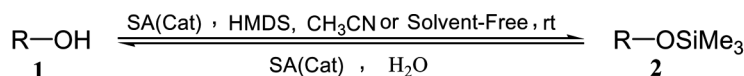
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Like protection, deprotection of the trimethylsilyl ethers constitutes an important process in the synthetic chemistry of polyfunctional molecules including the total synthesis of natural products. Although several methods have been reported for the deprotection of trimethylsilyl ethers,^[13–17] few of these catalysts can do both protection and deprotection of alcohols and phenols as trimethylsilyl ethers. Therefore, there is still a demand to develop new, mild, and ecofriendly catalysts for the trimethylsilylation of hydroxy groups and their regeneration in the presence of benchtop catalysts.

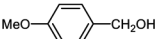
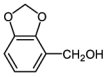
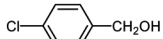
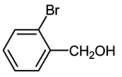
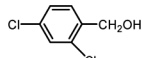
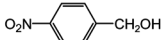
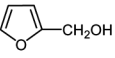
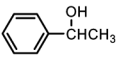
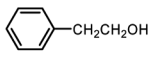
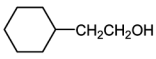
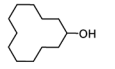
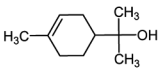
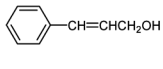
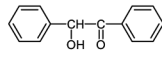
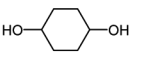
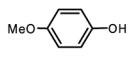
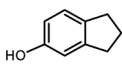

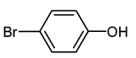
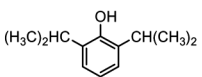


Although there is considerable interest in the use of solid acids as heterogeneous catalysts in organic synthesis,^[18] most of the used solid acid catalysts contain metal and are not green; therefore environmental pollution has limited their practical usage on a large scale, and they should be replaced by suitable catalysts.

RESULTS AND DISCUSSION

Sulfamic acid (SA, $\text{H}_2\text{NSO}_3\text{H}$) is a common inorganic acid with a mild acidity that is nonvolatile, noncorrosive, and utilized as a stable, low-cost, and commercially



R= benzylic, allylic, linear, cyclic, heterocyclic, aryl

a 	b 	c 	d 
e 	f 	g 	h 
i 	j $\text{CH}_3(\text{CH}_2)_6\text{CH}_2\text{OH}$	k 	l $\text{CH}_3(\text{CH}_2)_4\text{CH}(\text{OH})\text{CH}_3$
m 	n 	o 	p 
q 	r 	s 	t 
u 	v 	w 	x 

Scheme 1. Trimethylsilylation of hydroxy groups and their regeneration catalyzed by SA.

available reagent. Because of its zwitterionic property, this heterogeneous catalyst can be readily recycled and reused through simple filtration and washing. More important, its water resistance and incapability for formation of complexes make it an outstanding alternative to metal catalysts, in different areas of organic synthesis, as an efficient, green heterogeneous catalyst.^[19–26]

In continuation of our studies to develop new synthetic methodologies,^[27–30] we decided to report the use of readily available HMDS for the trimethylsilylation of alcohols and phenols in the presence of a catalytic amount of SA under both solution and solvent-free conditions. Also, the desilylation of the corresponding trimethylsilyl ethers using this catalyst in water has been investigated (Scheme 1).

As shown in Table 1, the trimethylsilylation of benzylic alcohols, including electron-donating, electron-withdrawing, and acid-sensitive groups, proceeded efficiently with good isolated yields (entries 1–8). Primary, secondary, and tertiary aliphatic alcohols were also converted into their corresponding trimethylsilyl ethers in almost quantitative yields (entries 9–14). This method was also found to be useful for the trimethylsilylation of allylic alcohols, acyloins, and diols (entries 15, 16, and

Table 1. Trimethylsilylation of alcohols and phenols using HMDS catalyzed with SA under both CH₃CN (I) and solvent-free (II) conditions at room temperature

Entry	Substrate	Product ^a	Time (h)		HMDS/SA		Yield (%) ^b	
			I	II	I	II	I	II
1	1a	2a	0.5	0.3	0.7/0.05	1.5/0.05	95	94
2	1b	2b	2	0.9	0.7/0.1	1.5/0.05	95	94
3	1c	2c	1	0.75	0.7/0.05	1.5/0.05	94	95
4	1d	2d	0.75	0.5	0.7/0.05	1.5/0.05	95	94
5	1e	2e	0.3	0.25	0.7/0.05	1.5/0.05	95	92
6	1f	2f	7.5	1	0.7/0.05	1.5/0.05	88	85
7	1g	2g	12	3.5	0.7/0.1	1.5/0.05	60	90
8	1h	2h	2	1.5	1.5/0.1	1.5/0.05	92	90
9	1i	2i	1.8	1.5	1.5/0.1	1.5/0.1	93	92
10	1j	2j	3	2	1.5/0.15	1.5/0.1	84	72
11	1k	2k	2.3	1.5	1.5/0.15	1.5/0.1	91	90
12	1l	2l	2.5	1.6	1.5/0.15	1.5/0.1	84	79
13	1m	2m	2	1.2	1.5/0.15	1.5/0.1	88	88
14	1n	2n	72	48	15/0.4	15/0.4	95	94
15	1o	2o	30	15	1.5/0.1	1.5/0.05	95	96
16	1p	2p	15	7	0.7/0.15	1.5/0.05	70	95
17	1q	2q	2	1.3	1.5/0.15	1.5/0.1	95	93
18	1r	2r	1.5	1	0.7/0.05	1.5/0.05	95	96
19	1s	2s	1.7	1	0.7/0.05	1.5/0.05	95	94
20	1t	2t	0.9	0.7	0.7/0.05	1.5/0.05	95	95
21	1u	2u	0.7	0.2	0.7/0.05	1.5/0.05	95	95
22	1v	2v	15	15	2.5/0.15	5/0.25	0	0
23	1w	2w	15	15	2.5/0.15	5/0.25	0	0
24	1x	2x	15	15	2.5/0.15	5/0.25	0	0

^aAll products were characterized by comparison of their spectral data (¹H NMR, IR spectroscopy) with those of authentic samples.

^bIsolated yields.

17). Phenols were also transformed into their corresponding trimethylsilyl ethers in good to high yields (entries 18–22). We observed that amines and thiols were not converted to the corresponding trimethylsilyl ethers under same conditions (entries 23 and 24). No eliminations and rearrangements were observed during the all reactions.

Organic reactions in water have received much attention, because water is a cheap, safe, and environmentally benign solvent. However, we investigated the possibility of deprotection of trimethylsilyl ethers using SA as catalyst in water. It was found that the trimethylsilyl group could be removed efficiently in the presence of a catalytic amount of SA in water at room temperature in good to excellent yields (Table 2).

We used this procedure for the selective trimethylsilylation of *n*-octanol (as a model for primary alcohols) or cyclododecanol (as a model for secondary alcohols) in the presence of α -terpinol (as a model for tertiary alcohols). The only observed products were *n*-octyl trimethylsilyl ether or cyclododecanyl trimethylsilyl ether in 100% conversion (Scheme 2).

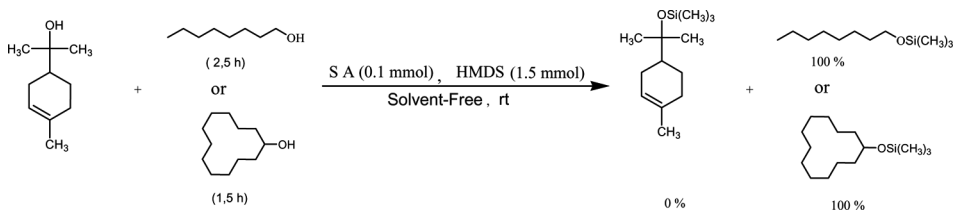
The catalyst can be easily separated by dispersing the reaction mixture in diethyl ether. As in the previous studies, the reusability of SA has been investigated for the trimethylsilylation of alcohols and phenols with HMDS. We have found that SA is a reusable catalyst even after four runs.

On the basis of the previously reported mechanisms for applying SA in organic synthesis,^[20–25] one idea for these process is that SA may act as a source for the

Table 2. Deprotection of trimethylsilyl ethers in the presence of a catalytic amount of SA (0.05–0.1 mmol) in H₂O (3 mL) at room temperature

Entry	Substrate	Product	Time (h)	Yield (%)
1	2a	1a	2	93
2	2b	1b	0.9	93
3	2c	1c	1.7	92
4	2d	1d	1.2	92
5	2e	1e	0.3	93
6	2f	1f	1.5	90
7	2g	1g	2	85
8	2h	1h	3	90
9	2i	1i	1.5	89
10	2j	1j	3	77
11	2k	1k	3.5	85
12	2l	1l	6.5	63
13	2m	1m	2.3	88
14	2n	1n	24	0
15	2o	1o	24	0
16	2p	1p	8	92
17	2q	1q	4.5	91
18	2r	1r	1	95
19	2s	1s	2.5	93
20	2t	1t	1	94
21	2u	1u	0.84	94

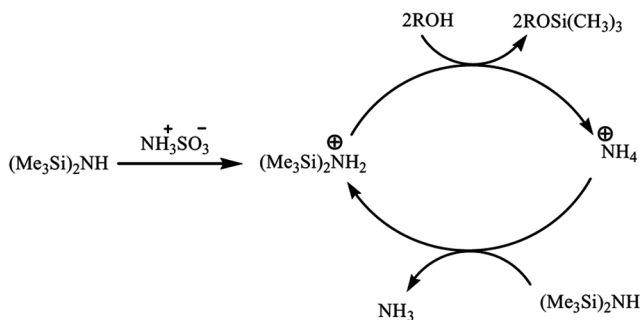
^aIsolated yields.



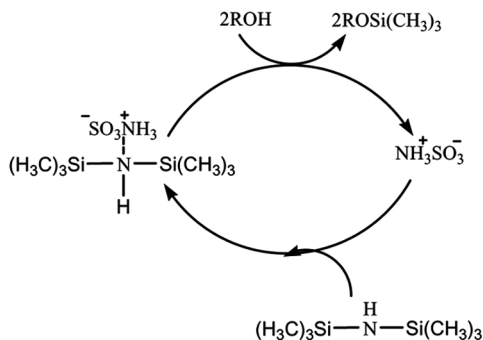
Scheme 2. Selective trimethylsilylation of *n*-octanol or cyclododecanol in presence of α -terpinol catalyzed by SA.

formation of H^+ , which may be the actual catalyst for trimethylsilylation/detrimethylsilylation reaction (as a protic acid). Another idea is that SA may polarize the Si–N bond in HMDS or Si–O bond in TMS ether to form a zwitterionic species, making the HMDS or TMS ether susceptible to nucleophilic attack by hydroxy group. Therefore, the mechanisms shown in Scheme 3 are proposed. However, at this time the precise role of SA is not clear and the actual role of this reagent should be studied in detail.

Mechanism 1



Mechanism 2



Scheme 3. Proposed mechanisms for the trimethylsilylation of hydroxy groups using HMDS catalyzed by SA.

EXPERIMENTAL

General Procedure for the Trimethylsilylation of Alcohols and Phenols Using HMDS Catalyzed with SA Under Solvent-Free Conditions

Alcohols or phenols (1 mmol) were added to a mixture of HMDS (1.5 mmol) and SA (0.05–0.1 mmol), and then the mixture was stirred at room temperature for the specified time (see Table 1). The progress was monitored by thin-layer chromatography (TLC). After the completion of the reaction, diethyl ether (15 mL) was added and filtered to recover the catalyst. Then 10% aqueous NaHCO_3 (20 mL) was added to destroy the extra amount of HMDS. The organic layer was dried over anhydrous Na_2SO_4 (0.5 g). Evaporation of the diethyl ether under reduced pressure gave the pure product without further purification. The filtered catalyst could be washed with diethyl ether, activated at 70 °C for 2 h, and reused for subsequent runs.

General Procedure for Trimethylsilylation of Alcohols and Phenols Using HMDS Catalyzed with SA in Solution

Alcohols or phenols (1 mmol) were added to a mixture of HMDS (0.7–1.5 mmol) and SA (0.05–0.1 mmol) in CH_3CN (3 mL), and then the mixture was stirred at room temperature for the specified time (Table 1). After the completion of the reaction, as indicated by TLC, the reaction mixture was diluted with diethyl ether and filtered to recover the catalyst. Then 10% aqueous NaHCO_3 (10 mL) was added to destroy the extra amounts of HMDS, and the organic layer was dried over anhydrous Na_2SO_4 (0.3 g). Evaporation of the diethyl ether under reduced pressure gave the pure product without further purification.

General Procedure for the Deprotection of Trimethylsilyl Ethers Catalyzed by SA

SA (0.05–0.1 mmol) was added to a mixture of TMS ethers (1 mmol) in H_2O (3 mL), and then the mixture was stirred at room temperature for the specified time (see Table 2). The progress of the reaction was monitored by TLC. After completion of the reaction, the reaction mixture was extracted with diethyl ether (3×10 mL). The combined organic layers were dried over anhydrous Na_2SO_4 (0.7 g). Evaporation of the diethyl ether under reduced pressure gave the pure product without further purification.

CONCLUSION

The advantages or the characteristic aspects of the described method in this communication in comparison with other previously reported catalysts are the following:

1. Sulfamic acid (SA) has several advantages. It is cost-effective, has no moisture sensitivity, is easy to handle, and is recyclable. It is a green alternative to metal-containing acidic materials.

2. The trimethylsilylation of alcohols and phenols was performed in the presence of other functional groups under both solution and solvent-free conditions. Also, the desilylation of the corresponding trimethylsilyl ethers occurred in water at room temperature.
3. The workup is simple and clean, and the product yields are good to excellent.

These advantages make the protocol environmentally benign.

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REFERENCES

1. Greene, T. W.; Wuts, P. G. M. *Protective Groups in Organic Synthesis*, 3rd ed.; John Wiley: New York, 1999.
2. Look, G. V.; Simchen, G.; Heberle, J. *Silylation Agents*; Fluka: Buchs, Switzerland, 1995.
3. Dsa, B. A.; Verkade, J. G. P(MeNCH₂CH₂)₃N: An efficient silylation catalyst. *J. Am. Chem. Soc.* **1996**, *118*, 12832–12833.
4. 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*, 2228–2144.
5. Firouzabadi, H.; Iranpoor, N.; Amani, K.; Nowrouzi, F. Tungstophosphoric acid (H₃PW₁₂O₄₀) as a heterogeneous inorganic catalyst: Activation of hexamethyldisilazane (HMDS) by tungstophosphoric acid for efficient and selective solvent-free O-silylation reactions. *J. Chem. Soc., Perkin Trans. 1* **2002**, 2601–2604.
6. 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.
7. Jin, T.-S.; Lin, R.-F.; Zhao, Y.; Li, T.-S. Silica sulfate, an efficient catalyst for the trimethylsilylation of alcohols. *Synth. Commun.* **2006**, *36*, 1823–1828.
8. Shirakawa, E.; Hironaka, K.; Otsuka, H.; Hayashi, T. Palladium-catalyzed silylation of alcohols with hexamethyldisilane. *Chem. Commun.* **2006**, 3927–3929.
9. Jadhav, V. H.; Kumar, K. S. A.; Chaudhari, V. D.; Dhavale, D. D. Facile method for trimethylsilylation of alcohols using hexamethyldisilazane and ammonium thiocyanate under neutral conditions. *Synth. Commun.* **2007**, *37*, 1363–1370.
10. Shaterian, H. R.; Shahrekipoor, F.; Ghashang, M. Silica-supported perchloric acid (HClO₄-SiO₂): A highly efficient and reusable catalyst for the protection of hydroxyl groups using HMDS under mild and ambient conditions. *J. M. Catal. A: Chem.* **2007**, *272*, 142–151.
11. Moghadam, M.; Tangestaninejad, S.; Mirkhani, V.; Mohammadpoor-Baltork, I.; Chahardahcheric, S.; Tavakoli, Z. Rapid and highly efficient trimethylsilylation of alcohols and phenols with hexamethyldisilazane (HMDS) catalyzed by reusable zirconyl triflate, [ZrO(OTf)₂]. *J. Organometal. Chem.* **2008**, *693*, 2041–2046.
12. Shirini, F.; Zolfigol, M. A.; Abedini, M. Chemoselective trimethylsilylation of alcohols catalyzed by saccharin sulfonic. *Monatsh. Chem.* **2009**, *140*, 61–64.
13. Yu, Z.; Verkade, J. G. P(MeNCH₂CH₂)₃N: An efficient catalyst for the desilylation of *tert*-butyldimethylsilyl ethers. *J. Org. Chem.* **2000**, *65*, 2065–2068.

14. Wu, Y. J.; Huang, H.; Shen, X.; Hu, Q.; Tang, C.-J.; Li, L. Facile cleavage of triethylsilyl (TES) ethers using *o*-iodoxybenzoic acid (IBX) without affecting *tert*-butyldimethylsilyl (TBS) ethers. *Org. Lett.* **2002**, *4*, 2141–2144.
15. Lakouraj, M. M.; Akbari, A. Sulfuric acid supported on silica gel: An efficient catalyst for silylation of hydroxyl groups with HMDS and their convenient deprotection under nonaqueous condition. *Ind. J. Chem. Sect. B* **2003**, *42*, 1165–1167.
16. Levin, J. I.; Du, M. T.; Park, K. Practical sulfonylation of amines with 4-hydroxybenzenesulfonyl chloride: In situ silylation–desilylation. *Synth. Commun.* **2004**, *34*, 2773–2781.
17. Crouch, R.; Williams, A. Rapid, acid-mediated deprotection of silyl ethers using microwave heating. *Synth. Commun.* **2006**, *36*, 959–964.
18. Clark, J. H. Solid acids for green chemistry. *Acc. Chem. Res.* **2002**, *35*, 791–797.
19. Wang, B. Sulfamic acid: A very useful catalyst. *Synlett* **2005**, 1342–1343.
20. Wang, B.; Gu, Y.; Song, G.; Yang, T.; Yang, L.; Suo, J. An efficient procedure for protection of carbonyls catalyzed by sulfamic acid. *J. Mol. Catal. A: Chem.* **2005**, *233*, 121–126.
21. Tao, L.; Zou, J.; Zhang, L. L.; Zhang, Y. Sulfamic acid-catalyzed Michael addition of indoles and pyrrole to electron-deficient nitroolefins under solvent-free condition. *Tetrahedron Lett.* **2007**, *48*, 4297–4300.
22. Kamal, A.; Rajendra-Prasad, B.; Malla-Reddy, A.; Naseer, M.; Khan, A. Sulfamic acid as an efficient and recyclable catalyst for the ring opening of epoxides with amines and anilines: An easy synthesis of β -amino alcohols under solvent-free conditions. *Catal. Commun.* **2007**, *8*, 1876–1880.
23. Li, Z.; Sun, Y.; Ren, X.; Wei, P.; Shi, Y.; Ouyang, P. Sulfamic acid-catalyzed direct condensation of aldehydes, amines, and TMSCN to α -aminonitriles at ambient temperature. *Synlett* **2007**, 803–805.
24. Upadhyaya, D. J.; Barge, A.; Stefania, R.; Cravotto, G. Efficient, solventless *N*-Boc protection of amines carried out at room temperature using sulfamic acid as recyclable catalyst. *Tetrahedron Lett.* **2007**, *48*, 8318–8322.
25. Heravi, M. M.; Ranjbar, L.; Derikvand, F.; Bamoharram, F. F. Sulfamic acid as a cost-effective catalyst instead of metal-containing acids for the one-pot synthesis of β -acetamido ketones. *J. Mol. Catal. A: Chem.* **2007**, *276*, 226–229.
26. Mitragotri, S. D.; Pore, D. M.; Desai, U. V.; Wadgaonkar, P. P. Sulfamic acid: An efficient and cost-effective solid acid catalyst for the synthesis of α -aminophosphonates at ambient temperature. *Catal. Commun.* **2008**, *9*, 1822–1826.
27. Khazaei, A.; Rostami, A.; Raiatzadeh, A.; Mahboubifar, M. *N*-Bromosuccinimide (NBS)-selective and effective catalyst for trimethylsilylation of alcohols and phenols using hexamethyldisilazane and their regeneration under mild and neutral reaction conditions. *Can. J. Chem.* **2007**, *85*, 336–340.
28. Khazaei, A.; Rostami, A.; Mahboubifar, M. *N,N'*-Dibromo-*N,N'*-1,2-ethanediybis(benzene sulfonamide) as a novel *N*-bromo reagent catalyzed tetrahydropyranylation/depyranylation of alcohols and phenols under mild conditions. *Catal. Commun.* **2007**, *8*, 383–388.
29. Rostami, A.; Khazaei, A.; Mahboubifar, M.; Rahmati, S. Convenient trimethylsilylation of hydroxy groups with hexamethyldisilazane under solvent-free conditions. *Org. Prep. Proc. Inter.* **2008**, *40*, 303–306.
30. Rostami, A.; Rahmati, S.; Khazaei, A. A highly efficient and ecofriendly procedure for tetrahydropyranylation of alcohols and phenols in the presence of in-situ-generated I_2 under heterogeneous and neutral conditions. *Monatsh. Chem.* **2009**, *140*, 663–667.