CHINESE JOURNAL OF CATALYSIS
Volume 32, Issue 4, 2011
Online English edition of the Chinese language journal

Available online at www.sciencedirect.com
ScienceDirect

Cite this article as: Chin. J. Catal., 2011, 32: 595–598.

RESEARCH PAPER

Protection of Hydroxyl Groups as a Trimethylsilyl Ether by 1,1,1,3,3,3-Hexamethyldisilazane Promoted by Aspartic Acid as an Efficient Organocatalyst

Arash GHORBANI-CHOGHAMARANI*, Masoomeh NOROUZI

Department of Chemistry, Faculty of Science, Ilam University, P.O. Box 69315516, Ilam, Iran

Abstract: A wide variety of alcohols and phenols were protected as trimethylsilyl ethers using 1,1,1,3,3,3-hexamethyl disilazane catalyzed by aspartic acid as a non-toxic, metal-free, and green organocatalyst at room temperature in acetonitrile under mild and heterogeneous conditions. The procedure is operationally simple and the silylated product was obtained in high yield and purity.

Key words: alcohol; phenol; 1,1,1,3,3,3-hexamethyldisilazane; trimethylsilylation; protection

The search for molecules that are able to catalyze reactions between other molecules is important to increase the efficiency of chemical reactions and to provide ecological and economical viable options for the consumption of chemicals [1]. When a chemical reaction is to be carried out selectively at one reactive site in a multifunctional compound the other reactive sites must be temporarily blocked [2]. Silyl ethers are a popular and promising protecting group of hydroxy functions in synthetic organic chemistry and a variety of silyl ethers have been developed to date [3–7]. However, the use of these silylating agents is limited by disadvantages such as harsh reaction conditions, scarcity and tedious purification processes. 1,1,1,3,3,3-Hexamethyldisilazane (HMDS) is a cost-effective and stable reagent and is one of the most widely used silylating agents for the trimethylsilylation of hydroxyl groups. The best advantage of this reagent is the quick isolation of the products from the reaction media because the by-product of the reaction is ammonia, which is easily removed from the reaction media. However, the low silylating power of HMDS is its main drawback. Therefore, to activate this reagent an appropriate catalyst should be used. Over the last decade many catalysts [8–15] have been used for this purpose but some of these procedures suffer from long reaction times, low product yields, heavy metal contamination, and catalyst toxicity.

1 Experimental

All chemicals and solvents were purchased from Fluka, Merck, or Aldrich and used without further purification. All the products are known and were characterized by a comparison of their spectral (IR, ^{1}H NMR, or ^{13}C NMR) and physical data with authentic samples.

To a mixture of 4-bromobenzyl alcohol (0.187 g, 1 mmol) and hexamethyldisilazane (0.129 g, 0.8 mmol) in CH_3CN (10 ml), aspartic acid (0.003 g, 0.02 mmol) was added and the mixture was stirred at room temperature for 7 min (reaction progress monitored by TLC). The reaction was then quenched with water (10 ml) and 20 ml of CH_2Cl_2 was added. The organic phase was then dried over Na_2SO_4 (3 g). Evaporation of the solvent gave pure (4-bromobenzyloxy)trimethylsilane in a 90% yield.

2 Results and discussion

In a continuation of our studies into the application of new catalysts in organic functional group transformations [16–22], we disclose here a new, efficient, and mild procedure for the trimethylsilylation of a wide variety of hydroxyl groups using HMDS in the presence of a catalytic amount of aspartic acid as

Received 24 November 2010. Accepted 6 February 2011.
*Corresponding author. Tel: +98-841-2227022; Fax: +98-841-2227022; E-mail: arashghch58@yahoo.com, a.ghorbani@mail.ilam.ac.ir
This work was supported by the research facilities of Ilam University, Ilam, Iran for financially supporting this research project.

DOI: 10.1016/S1872-2067(10)60210-0

an efficient organocatalyst under mild and heterogeneous conditions at room temperature.

Initially, to find an appropriate solvent for this procedure we screened different solvents for the trimethylsilylation of 4-bromobenzyl alcohol with HMDS in the presence of a catalytic amount of aspartic acid. As is evident from Table 1, 4-bromobenzyl alcohol was silylated in acetonitrile faster than in the other solvents. Consequently, we decided to use acetonitrile as a solvent for the protection of the hydroxyl group by HMDS and aspartic acid.

With optimal conditions in hand, we report here the protection of alcohols as trimethylsilyl ethers using HMDS in the presence of a catalytic amount of aspartic acid in acetonitrile at room temperature with good to excellent yields (Table 2).

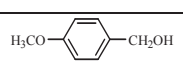
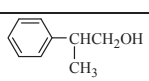
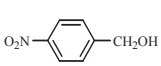
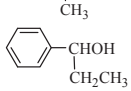
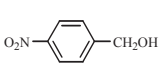
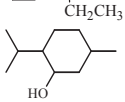
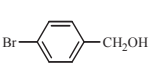
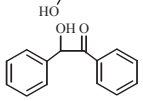
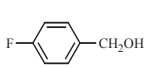
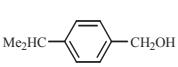
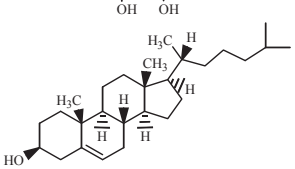
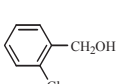
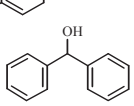
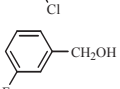
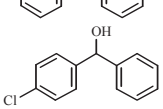
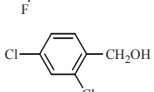
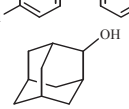
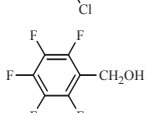
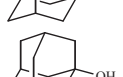
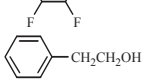
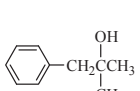
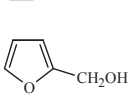
The trimethylsilylated product was obtained in good to high yield and the work-up procedure is very simple. Aspartic acid is easily isolated by filtration and the pure product can be obtained by a simple distillation of the reaction solvent. As shown in Table 2, the amount of HMDS and catalyst depends on the nature of the alcohol.

Table 1 Trimethylsilylation of 4-bromobenzyl alcohol using HMDS and catalytic amounts of aspartic acid at room temperature in different solvents

Entry	Solvent	Time (h)	Yield[a] (%)
1	acetonitrile	0.12	90
2	chloroform	24	66
3	dichloromethane	12	87
4	*n*-hexane	24	—[b]
5	ethyl acetate	20	77
6	acetone	24	87

Reaction conditions: substrate 1 mmol, HMDS 0.8 mmol, aspartic acid 0.02 mmol. [a]Isolated yield. [b]Trace conversion.

Table 2 Trimethylsilylation of alcohols **1a–1v** to the corresponding trimethylsilyl ethers **2a–2v** using HMDS in the presence of a catalytic amount of aspartic acid in CH_3CN at room temperature

Entry		Substrate	HMDS (mmol)	Catalyst (mmol)	Time (min)	Yield[a] (%)	Entry		Substrate	HMDS (mmol)	Catalyst (mmol)	Time (min)	Yield[a] (%)
1	**1a**		0.8	0.02	8	95	13	**1l**		0.8	0.02	3	88
2	**1b**		0.8	0.02	50	91	14	**1m**		0.8	0.02	4	98
3	**1b**		0.8	—	300	72[b]	15	**1n**		0.8	0.02	25	84
4	**1c**		0.8	0.02	7	90	16	**1o**		0.8	0.02	60	96
5	**1d**		0.8	0.02	3	91	17	**1p**		1.6	0.02	10	80
6	**1e**		0.8	0.02	6	98	18	**1q**		1.0	0.02	17	97
7	**1f**		0.8	0.02	10	88	19	**1r**		0.8	0.02	60	90
8	**1g**		0.8	0.02	3	97	20	**1s**		0.8	0.02	3	96
9	**1h**		0.8	0.02	50	94	21	**1t**		1.0	0.02	25	94
10	**1i**		0.8	0.02	5	92	22	**1u**		0.8	0.02	90	85
11	**1j**		0.8	0.02	3	98	23	**1v**		2.0	0.20	840	87
12	**1k**		0.8	0.02	5	86							

[a]Isolated yield. [b]In the absence of catalyst.