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Trimethylsilylation of Alcohols and Phenols using KBr as an Efficient and Reusable Catalyst

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Trimethylsilylation of Alcohols and Phenols using KBr as an Efficient and Reusable Catalyst

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Rasht, Iran

Abstract: KBr acts as an efficient and reusable catalyst for the selective and efficient trimethylsilylation of benzylic, primary and secondary aliphatic alcohols and phenols with hexamethyldisilazane. All reactions were performed at room temperature under mild and completely heterogeneous conditions in good to high yields.

Keywords: Alcohols, hexamethyldisilazane, KBr, phenols, trimethylsilylation

The hydroxy group is one of the versatile functional groups in organic molecules, and its controlled manipulation is of great value in multistep syntheses.

The conversion of hydroxy functional groups to their corresponding trimethylsilyl ethers is a widely used method for protection of alcohols and phenols.[1,2] Among the several reagents that have been used for this purpose,[3–5] hexamethyldisilazane (HMDS), as a cheap, stable, and commercially available reagent, has found a special position. Its handling does not require special precautions, silylation using this reagent is nearly neutral, and workup is not tim consuming. However, the low silylating power of this reagent is the main drawback of its application, which needs forceful conditions and long reaction times in many instances.[6] To improve the silylating power of HMDS, a variety of reagents have been reported; of them sulfonic acid,[7] zirconium sulfophenyl phosphonate,[8] K-10 montmorilonite,[9]

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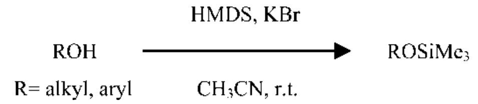
Me_3SiCl[10] and silica chloride[11] are examples. Although these procedures provide an improvement, in most cases low selectivity, forceful conditions, and long reaction times have been observed.[6,12]

In continuation of our ongoing effort to develop new methods for the protection of the hydroxyl group,[13–15] herein we report a mild and efficient method for trimethylsilylation of alcohols and phenols using hexamethyldisilazane in the presence of KBr, as a neutral, reusable, and heterogeneous catalyst (Scheme 1).

Different types of alcohols were subjected to trimethylsilylation using this method at room temperature under completely heterogeneous reaction conditions (Table 1). Trimethylsilylation of benzylic alcohols including acid sensitive and electron-donating or withdrawing groups proceeded efficiently with high isolated yields (Table 1, entries 1–14). Primary and secondary aliphatic alcohols were also successfully converted to their corresponding silyl ethers in almost quantitative yields at room temperature (Table 1, entries 18–22). This method was found to be useful for trimethylsilylation of diols and acyloins (Table 1, entries 15–17). No elimination and rearrangement by-products were observed at all. Phenols also undergo silylation easily using this method, and their corresponding silyl ethers can be isolated in good to high yields (Table 1, entries 26–30). As shown in Table 1, tertiary alcohols are resistant to this reagent system and remained intact in the reaction mixture (Table 1, entries 23–25). Therefore, this methodology shows selectivity and is suitable for the selective trimethylsilylation of benzylic, primary and secondary aliphatic alcohols and phenols in the presence of tertiary ones. This is exemplified by the competitive reactions between 4-methoxybenzyl alcohol and *tert*-butanol, between cyclohexanol and 1-adamantaol, and between 4-phenyl phenol and triphenyl methanol (Table 1, entries 32–34). This method is not useful for silylation of allylic alcohols (Table 1, entry 31).

We have found that KBr is a reusable catalyst, and even after five runs for the silylation of alcohols and phenols with HMDS, the catalytic activity of KBr was almost the same as that of the fresh catalyst.

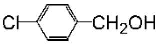
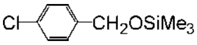
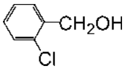
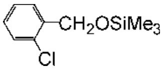
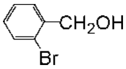
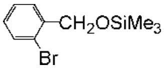
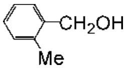
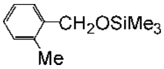
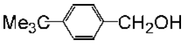
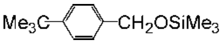
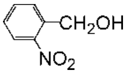
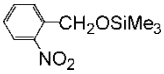
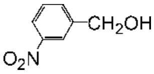
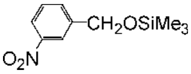
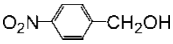
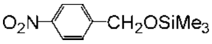
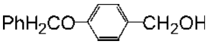
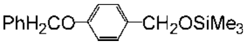
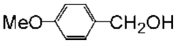
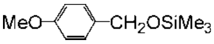
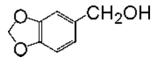
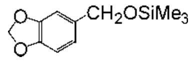
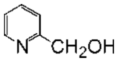
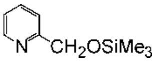
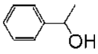
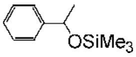
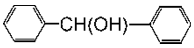
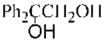
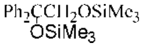
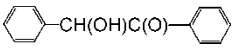
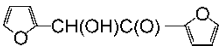
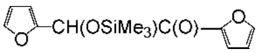
The mechanism of the reaction is not clear, but the fast evolution of NH_3 gas from the reaction mixture and the reusability of the catalyst directed us to accept the mechanism shown in Scheme 2 as a most probable one. This mechanism shows that the first step of the reaction is the probable production of the reactive intermediate **1**, by the polarization of the Si-N bond in HMDS by KBr. A rapid reaction with alcohol then



$$\underset{R = \text{alkyl, aryl}}{ROH} \xrightarrow[CH_3CN,\ r.t.]{HMDS,\ KBr} ROSiMe_3$$

Scheme 1.

Table 1. Trimethysilylation of alcohols and phenols

Entry	Substrate	Product	Time (min)	Yield (%)[a,b]
1			14	98
2			14	95
3			15	85
4			5	95
5			3	95
6			40	90[c]
7			18	95
8			17	97
9			16	95[c]
10			5	95
11			60	75
12			14	75
13			3	87
14			13	95
15	 $Ph_2\underset{OH}{C}CH_2OH$	 $Ph_2\underset{OSiMe_3}{C}CH_2OSiMe_3$	70	80
16			70	95
17			75	80
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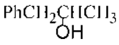
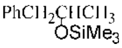
19	 $PhCH_2\underset{OH}{C}HCH_3$	 $PhCH_2\underset{OSiMe_3}{C}HCH_3$	5	92

(*continued*)

Table 1. Continued

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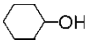
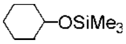
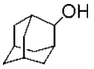
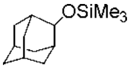
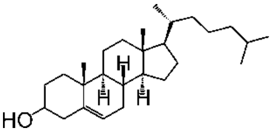
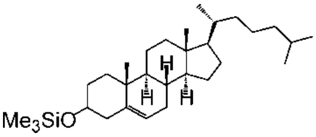
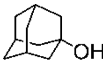
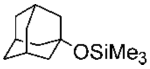
20			10	95
21			30	90
22			20	85
23			60	0^{d}
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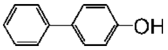
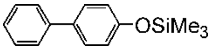
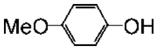
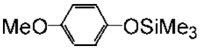
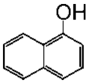
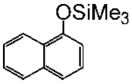
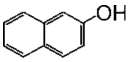
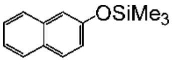
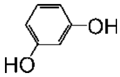
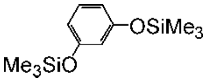
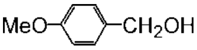
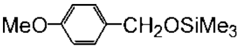
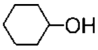
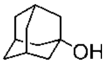
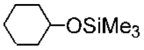
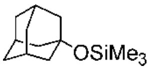
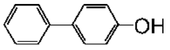
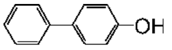
26			30	80
27			15	80
28			8	85
29			8	95
30			30	70^{e}
31	$PhCH{=}CHCH_2OH$	$PhCH{=}CHCH_2OSiMe_3$	30	—^{f}
32	 + Me_3COH	 + $Me_3COSiMe_3$	5	100^{g} + 0^{g}
33	 + 	 + 	10	100^{g} + 0^{g}

(*continued*)

Table 1. Continued

Entry	Substrate	Product	Time (min)	Yield (%)[a,b]
34	 + Ph_3COH	 + $Ph_3COSiMe_3$	30	90[g] + 0[g]

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

[b] Isolated yields.

[c] KBr 0.15 mmol is used.

[d] Starting material was recovered unchanged.

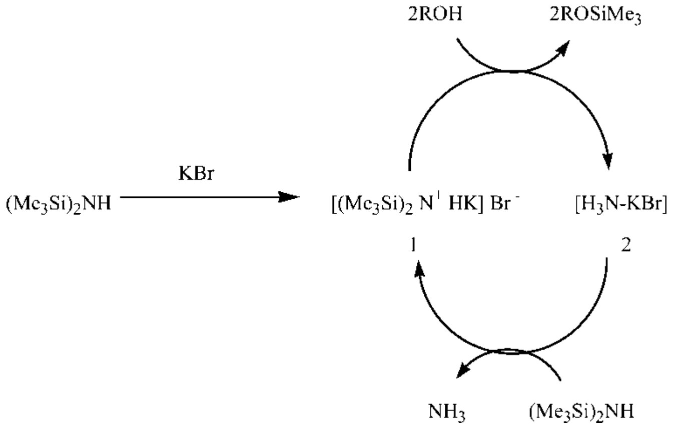
[e] HMDS 1.4 mmol is used.

[f] Unidentified products.

[g] GC yield.

ensues, leading to the unstable ammonia–KBr complex **2**. Irreversible cleavage of **2** leads to the fast evolution of NH_3 and release of KBr, which reenters to the catalytic cycle.

In conclusion, we have reported a mild and efficient method for the preparation of silyl ethers using hexamethyldisilazane catalyzed by KBr. The method offers several advantages including selectivity, short reaction times, high yields of the products, cleaner reactions, and an inexpensive reagent, which makes the reaction convenient and more economical.



Scheme 2.

EXPERIMENTAL

All of the products were characterized by comparison of their physical and spectral data with those of known samples. All yields refer to isolated products.

General Procedure for Trimethylsilylation of Alcohols and Phenols

HMDS (0.7 mmol) was added dropwise to a mixture of the substrate (1 mmol) and KBr (0.1 mmol, 0.012 g) in CH_3CN (3 mL) for 2 min with stirring at room temperature. The reaction was monitored by TLC. After completion of the reaction, the solvent was evaporated under reduced pressure. n-Hexane (5 mL) was added, and the catalyst was recovered by filtration and washed with n-hexane (5 mL). The filtrate was washed with water (10 mL), and the organic layer was dried over $MgSO_4$. Evaporation of the solvent under reduced pressure afforded the silylated compounds in high purity. Further purification proceeded by vacuum distillation or recrystallization to afford the pure silyl ethers in good to high yields.

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