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On a new catalyzed silylation of alcohols by phenylhydrosilanes

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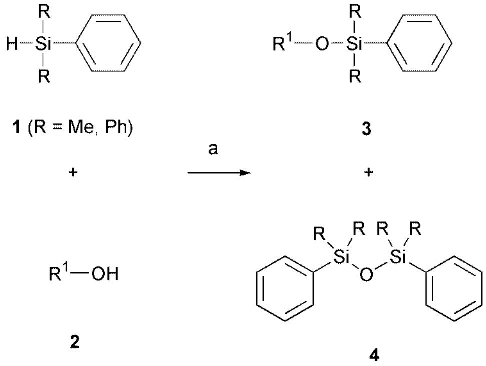
KOH–18-crown-6 ether is a valuable system for the catalyzed dehydrocoupling of alcohols with phenylhydrosilanes (Ph_3SiH and $PhMe_2SiH$).

The importance of silyl ethers in organic synthesis as protecting groups for alcohols has been discussed.[1,2] The most common route to these compounds involves the reaction of a silyl chloride (or the corresponding triflate for hindered alcohols) with an alcohol in the presence of an amine (pyridine, triethylamine, imidazole…). The stoichiometric amounts of ammonium salts produced as well as the cost[3] of the silylating reagents has led chemists to study the dehydrocoupling process involving hydrosilanes. This reaction has been reported using a wide range of catalytic species such as transition metal complexes, Lewis acids[4] and salts.[5,6] In this work, we show that a new method involving KOH–18-crown-6 ether is simple, inexpensive and is valuable for the catalyzed silylation of alcohols with phenylhydrosilanes.

When hydrosilanes **1** were added to a mixture of KOH (9% mol)–18-crown-6 ether (3% mol) and alcohols **2** in CH_2Cl_2 (Scheme 1), a gas evolution occurred. Apart from the desired silyl ether **3**, small amounts of siloxanes **4** were produced so that a slight excess of hydrosilanes (1.4 eq.) was therefore required for the total conversion of the alcohols.† It is noteworthy that the reactions are generally clean as judged by the ^1H NMR spectra of the crude reaction mixtures and that under the same reaction conditions, no conversion of the starting materials in the absence of 18-crown-6 ether was observed. Dichloromethane was chosen because of its low boiling point and for being a good solvent for the reagents used, but other solvents such as THF, benzene or ether are also appropriate.

We found that Et_3SiH is less reactive under these conditions than the phenylhydrosilanes as shown by its reaction with 4-methylbenzyl alcohol, which led to only 33% conversion. Among the phenylhydrosilanes, Ph_3SiH is more reactive than $PhMe_2SiH$ judging from their different abilities to transform tertiary alcohols (Table 1, entry 1). The reactions of other hindered alcohols such as 2-methylpropan-2-ol or 2-methylpentan-2-ol were also unsuccessful using $PhMe_2SiH$ even in boiling THF.



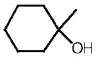
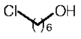
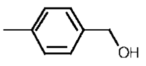
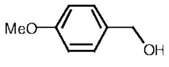
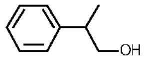
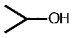
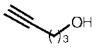
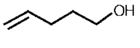
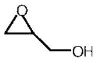
Scheme 1 a. KOH–18-crown-6 ether (9% : 3%), argon, 18 h, CH_2Cl_2, rt or CH_2Cl_2, Δ, 3 h.

A better knowledge of the course of this reaction was provided by examining different alcohols (Table 1). The presence of a strong withdrawing group close to the hydroxy function inhibits the reaction. For instance, 2-chloroethanol is not reactive under the conditions used to transform 6-chlorohexan-1-ol into the corresponding silyl ethers (Table 1, entry 2). Phenol or 4-methoxyphenol, which show a poor nucleophilic character in comparison with aliphatic alcohols, are not reactive while benzylic alcohols (Table 1, entries 3 and 4) or 2-phenylpropan-1-ol (Table 1, entry 5) are converted into the desired products in good yields. Saturated alcohols (entry 6) are good substrates for the reaction, as long as they do not provide a strong steric hindrance as mentioned above (entry 1). Compared to other transition metal catalysts,[7] the KOH–18-crown-6 ether system has the advantage of being compatible with unsaturated alcohols (entries 7 and 8). Furthermore, this system is convenient for the protection of hydroxy epoxide glycidol (entry 9) since it does not lead to the loss of the oxirane ring as mentioned for Lewis acid catalyzed reactions.[4]

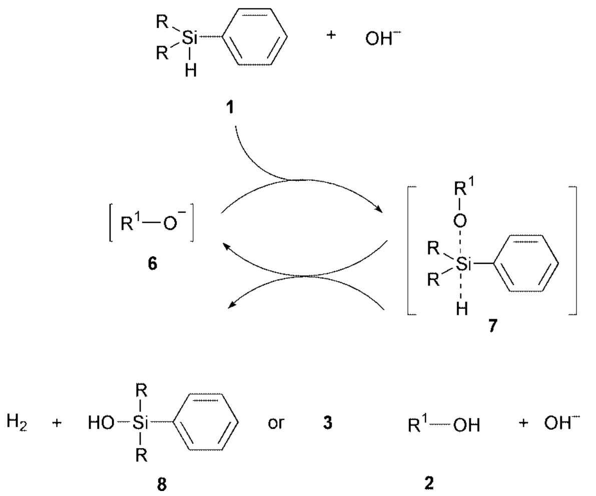
This reaction when performed on a larger scale (20 mmol of glycidol) gave the same yield of the desired product with $PhMe_2SiH$ as the silylating agent.

We have recently shown that KOH–18-crown-6 ether was an efficient system for catalyzed hydrosilylation and the

Table 1 Silylation of a number of alcohols in the presence of a catalytic amount of KOH–18-crown-6 ether: reactions were performed in CH_2Cl_2 at rt under argon for 18 h and isolated yields calculated following flash chromatography, unless otherwise stated.

	2	R	**3** (cond.)
1		Me Ph	—[a] 87%
2		Me Ph	73% 100%[b]
3		Me Ph	94% 100%[b]
4		Me Ph	80%[c] 78%
5		Me Ph	90% 100%[b]
6		Me Ph	90% 100%[bd]
7		Me Ph	68% 57%
8		Me Ph	72% 100%[d]
9		Me Ph	50%[c] 93%

[a] No reaction even with THF, Δ. [b] Inseparable mixture of **3** and **4**, total conversion of **2** according to the ^1H NMR spectrum of the crude reaction mixture. [c] CH_2Cl_2, Δ, 3 h. [d] Reaction performed in CD_2Cl_2, rt, 18 h.



Scheme 2 A possible mechanism for the catalyzed silylation of alcohols.

Tishchenko reaction of aromatic aldehydes.[8] The KOH–18-crown-6 ether catalyzed reaction of 4-methylbenzyl alcohol with $PhMe_2SiH$ was therefore conducted with a stoichiometric amount of *p*-anisaldehyde, a good substrate in the hydrosilylation process.[8] The ^1H NMR spectrum of the crude reaction mixture showed 12% conversion of the aldehyde and 82% of the alcohol, thus demonstrating that the dehydrocoupling reaction predominates over hydrosilylation.

From a mechanistic standpoint, the catalytic cycle could be easily explained in terms of the anionic activation of the Si–H bond first reported by Corriu *et al.* for various salts.[5] Thus, it can be proposed that the Si–H bond is labilized by anionic coordination of the alcoholate **6** (or OH^-) to give the pentacoordinate intermediate **7** (Scheme 2). This activated species could give the desired product **3** or the silanol **8**, a possible precursor for the isolated siloxane **4**.

Thus we show above that KOH–18-crown-6 ether is an efficient system for the catalyzed silylation of nucleophilic alcohols with Ph_3SiH and $PhMe_2SiH$. The lack of reactivity towards non-nucleophilic and hindered alcohols could be profitable for the use of these phenylsilyl ethers as selective protecting groups in organic synthesis. Compared to most other catalyzed silylation reactions, this method has the advantage of being compatible with double or triple bonds, carbonyl functions, chlorine and oxirane.

A mechanistic study of this reaction is being undertaken. The role of OH^- in the catalytic cycle remains to be elucidated.

Notes and references

† *Typical procedure*: reaction vessels were dried under vacuum and the reactions carried out under argon. The silane (1.4 mmol) was added at rt to a solution of the alcohol (1 mmol) and KOH–18-crown-6 ether (5 mg : 6 mg) in CH_2Cl_2 (0.75 mL). After stirring for 18 h, the reaction mixture was concentrated and the residue was purified by flash chromatography or crystallization to give the silyl ether (see Table 1). All products were characterized by the usual spectroscopic techniques or compared with data reported in the literature.

1 T. W. Greene and P. G. M. Wutz, *Protective Groups in Organic Synthesis*, Wiley, 2nd edn., New York, 1991, p. 50.
2 P. J. Kocienski, *Protecting Groups*, ed. D. Enders, R. Noyori and B. M. Trost, Thieme, Stuttgart, New York, 1994, p. 28.
3 For instance, the cost (Aldrich) per mmol of Ph_3SiCl (respectively $PhMe_2SiCl$) is 1.46 euros (respectively 1.18 euros for $PhMe_2SiH$) compared with 0.60 euros for Ph_3SiH (respectively 0.50 euros for $PhMe_2SiH$)
4 J. M. Blackwell, K. L. Foster, V. H. Beck and W. E. Piers, *J. Org. Chem.*, 1999, **64**, 4887 and references cited therein.
5 R. J. P. Corriu, R. Perz and C. Reye, *Tetrahedron*, 1983, **39**, 999.
6 Y. Tanabe, H. Okumura, A. Maeda and M. Murakami, *Tetrahedron Lett.*, 1994, **35**, 8413.
7 Schubert *et al.* recently reported a good copper hydride complex which allows the hydrosilylation of alcohols without reduction of double or triple bonds present in the molecule: C. Lorenz and U. Schubert, *Chem. Ber.*, 1995, **128**, 1267.
8 F. Le Bideau, T. Coradin, D. Gourier, J. Henique and E. Samuel, *Tetrahedron Lett.*, 2000, **41**, 5215.