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A novel and efficient method for the silylation of alcohols with methallylsilanes catalyzed by $Sc(OTf)_3$

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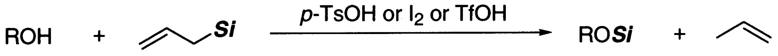
Abstract

Reaction of alcohols with methallylsilanes in the presence of a catalytic amount of $Sc(OTf)_3$ provides efficiently the corresponding alkyl silyl ethers. By using microencapsulated (MC) $Sc(OTf)_3$, which can be easily recovered and reused, yields of alkyl silyl ethers are improved and the work-up process after completion of the reaction is considerably simplified.

Keywords: silylation of alcohols; silyl ethers; catalytic; $Sc(OTf)_3$; MC $Sc(OTf)_3$; methallylsilanes; chemoselectivity.

Silyl ethers are the most popular and useful protecting groups of the hydroxy function in synthetic organic chemistry, and various types of silyl ethers have been developed.[1] Silyl ethers are usually obtained by the reaction of parent alcohols with the corresponding silyl halide in the presence of a stoichiometric amount of a base, such as imidazole, 4-dimethylaminopyridine, triethylamine, etc.[1] These silylation methods can give the corresponding silyl ethers in high yields, but require extraction or a careful filtration process to remove ammonium salts. On the contrary, metal-catalyzed dehydrogenative alcoholysis of hydrosilanes is a potent way to silyl ethers with no by-product,[2] but hydrosilylation or hydrogenation to a C–C double bond is an inevitable side-reaction, with the exception of the reaction using a tris(pentafluorophenyl)borane catalyst.[3] It was reported that allylsilane and silyl enol ether could silylate alcohols under the influence of a catalytic amount of *p*-toluenesulfonic acid,[4,5] iodine[6] or trifluoromethanesulfonic acid.[7] In the case where allylsilane was used, the reaction proceeded with evolution of propene and no other by-product, and did not need a work-up process, such as extraction, filtration and drying, but it was difficult to recover and reuse the catalysts (Scheme 1).



Scheme 1.

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On the other hand, scandium trifluoromethanesulfonate ($Sc(OTf)_3$), which is a stable Lewis acid in water, has been demonstrated in various useful reactions recently.[8] We expected that the coordination of the hydroxy function of alcohol to $Sc(OTf)_3$ would enhance the acidity of the hydroxy proton and it would behave as an acid catalyst itself in the silylation of alcohols using allyltrialkylsilanes.

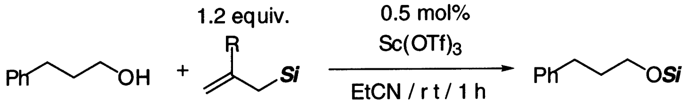
In this communication, we wish to report a practical and convenient method for the synthesis of trialkylsilyl ethers from the corresponding alcohols and methallylsilanes in the presence of a catalytic amount of $Sc(OTf)_3$.

To begin with, we examined the reaction of 3-phenylpropanol with allyl-*t*-butyldimethylsilane in the presence of 2 mol% of $Sc(OTf)_3$ in propionitrile (EtCN) and only a trace amount of the corresponding *t*-butyldimethylsilyl (TBS) ether was obtained (Table 1, Run 1). On the other hand, by using *t*-butylmethallyldimethylsilane,[9] which was presumably a more reactive nucleophile than unsubstituted allylsilane, the desired silyl ether was obtained in 98% isolated yield (Run 2). By using other types of methallylsilanes having a triethylsilyl (TES), triisopropylsilyl (TIPS), or *t*-butyldiphenylsilyl (TBDPS) moiety, the corresponding silyl ethers were similarly formed in high yields (Runs 4–6).

Representative and successful examples of synthesis of various alcohol TBS ethers are collected in Table 2. As well as primary alcohols, secondary alcohols were readily transformed into the corresponding TBS ethers in excellent yields (Runs 1–3). It should be noted that the TBS ether of a tertiary alcohol was also obtained in high yield in 0.5 h (Run 4). In the case of cinnamyl alcohol (Run 5) and phenols (Runs 6 and 7), although longer reaction times were required, the corresponding TBS ethers were obtained in >90% yields.

Next, we investigated the effect of microencapsulated (MC) $Sc(OTf)_3$[10,11] instead of monomeric $Sc(OTf)_3$ (Table 3). In all cases, the corresponding TBS ethers were obtained in high yields with no drop in the activity of $Sc(OTf)_3$. In the case of alcohols containing other functional groups, such as ketone, ether, ester, and acetal, yields of the corresponding TBS ethers were higher than that in the case of using monomeric $Sc(OTf)_3$ (Runs 2–5). Additionally, by using MC $Sc(OTf)_3$, work-up processes, such as extraction and drying, are excluded, and MC $Sc(OTf)_3$ can be easily recovered by a simple filtration.

Table 1
Silylation of 3-phenylpropanol



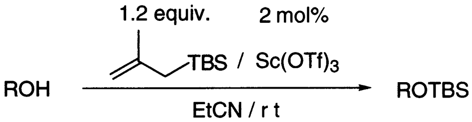
Run	R	Si	Yield[a] (%)
1	H	TBS	Trace
2	Me	TBS	98
3	Me	TBS	84[b]
4	Me	TES	83
5	Me	TIPS	84[c]
6	Me	TBDPS	85[c]

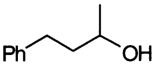
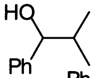
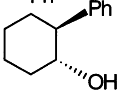
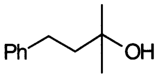
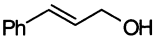
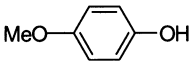
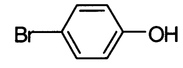
[a] Isolated yield.

[b] MeCN was used as the solvent.

[c] 5 mol% of $Sc(OTf)_3$ was used. Reaction time: 6 h.

Table 2
Synthesis of various TBS ethers from alcohols

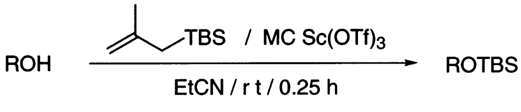


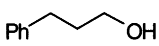
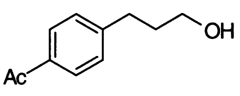
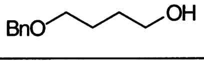
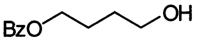
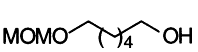
Run	ROH	Time / h	Yield[a] / %
1		0.5	93
2		0.5	97
3		0.5	98
4		0.5	88
5		6	91
6		2	94
7		2	94

a) Isolated yield.

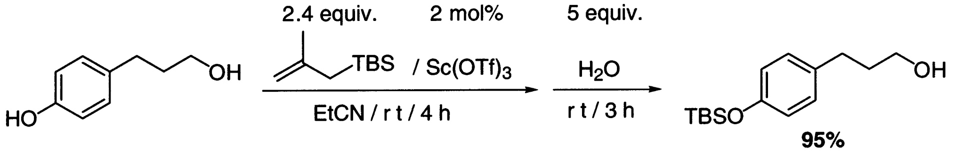
Previously, we reported a chemoselective deprotection of alkyl silyl ethers in the presence of aryl silyl ethers by Sc(OTf)$_3$ in water-containing acetonitrile.[12] Therefore, we attempted silylation of the aliphatic and aromatic hydroxyl functions and subsequent chemoselective desilylation in a one-pot procedure. After treating 3-(4-hydroxyphenyl)propanol with 2.4 equiv. of *t*-butylmethallyldimethylsilane in the presence of Sc(OTf)$_3$, 5 equiv. of H_2O were added and the solution was stirred for 3 h at room temperature. After the usual work-up of the reaction mixture, the mono TBS ether that was selectively silylated at the phenolic hydroxy function was obtained in 95% yield (Scheme 2).

Table 3
Synthesis of various TBS ethers using MC Sc(OTf)$_3$



Run	ROH	Yield[a] / %
1		98[b]
2		93 (59)[c]
3		92 (61)
4		95 (74)
5		85 (32)

a) Isolated yields. b) 0.5 mol% of MC Sc(OTf)$_3$ and 1.2 equiv. of methallylsilane were used. Reaction was performed for 1 h. c) Figures in parentheses are yields in the case of using monomeric Sc(OTf)$_3$.



Scheme 2.

In conclusion, we have succeeded in developing a new method for the silylation of alcohols using methallylsilanes catalyzed by $Sc(OTf)_3$.[13] In the case of using MC $Sc(OTf)_3$, the catalyst was readily recovered, and work-up processes, such as extraction and drying, were not required. This silylation method has not only an operational advantage, but it also exploits the utility of $Sc(OTf)_3$ in the activation of the hydroxy function. Further investigation to broaden the scope and synthetic applications of this efficient silylation is under way in our laboratory.

Acknowledgements

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