



An efficient synthesis of silyl ethers of primary alcohols, secondary alcohols, phenols and oximes with a hydrosilane using InBr_3 as a catalyst

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ABSTRACT

An efficient method for the preparation of silyl ethers by InBr_3 catalyzed silylation of primary alcohols, secondary alcohols, phenols and oxime with a hydrosilane is described.

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Silyl ether is an important protecting group for the hydroxyl functionality in a multi-step organic synthesis¹ and silyl ethers are generally prepared by reacting an alcohol and a chlorosilane using a base such as pyridine in stoichiometric quantity. The major disadvantages of this method are: (a) it involves an unwanted side reaction of an acid and a base producing salt as an effluent in stoichiometric quantity and (b) chlorosilanes are highly moisture sensitive and corrosive reagents and are not convenient for handling and storage.

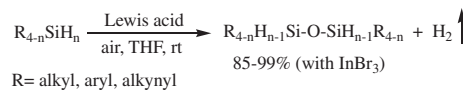
An attractive 'green' approach for the preparation of silyl ethers is by catalytic *O*-silylation of alcohols using hydrosilanes (R_3SiH , R = alkyl or aryl), which are stable, non-corrosive and convenient for handling and storage. In this reaction, hydrogen is the only side product and no effluent is produced. This dehydrogenative *O*-silylation reaction has been extensively studied in literature using a variety of metal catalysts such as $[\text{Rh}(\text{diphos})\text{ClO}_4]$,² $\text{Rh}(\text{II})$ carboxylates,³ anchored $\text{Rh}(\text{I})$ catalyst,⁴ alumina-supported gold nanoparticles,⁵ colloidal palladium nanoparticles,⁶ $\text{Re}_2(\text{CO})_{12}$,⁷ Grubbs' catalyst $[\text{Cl}_2(\text{PCy}_3)_2\text{Ru}=\text{CHPh}]$,⁸ iridium complexes,⁹

$\text{Cu}(\text{I})$ complexes,¹⁰ $[\text{RuCl}(\textit{p}\text{-cymene})_2]$ ¹¹ and $(\text{Ru}/\text{AlO}(\text{OH}))$.¹² Most of these methods found limited practical utility as the catalysts are either highly expensive or not readily accessible commercially or involve a complex procedure for preparation. Hence, development of a simple and efficient method for the synthesis of silyl ethers from alcohols using hydrosilanes is highly desired.

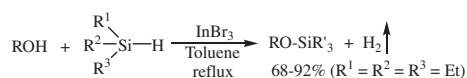
In our recent study,¹³ we found that hydrosilanes undergo catalytic air oxidation to symmetrical disiloxanes in the presence of a

Lewis acid such as InBr_3 and in this process, hydrogen is evolved as a side product as shown in Scheme 1.

In the light of this observation, we envisaged that hydrosilane could possibly react with a protic substrate such as an alcohol or phenol in the presence of InBr_3 as a catalyst under oxygen-free conditions to produce silyl ether. Since studies on *O*-silylation of alcohols with hydrosilanes using Lewis acids such as InBr_3 are so far not known in the literature, we have investigated the formation of silyl ethers by reaction of a hydrosilane with an alcohol using Lewis acid as a catalyst. Herein we report for the first time an efficient method for the *O*-silylation of alcohols, phenols and oximes with hydrosilanes using InBr_3 as a catalyst as shown in Scheme 2.



Scheme 1. Lewis acid catalyzed air oxidation of hydrosilanes to symmetrical disiloxanes.

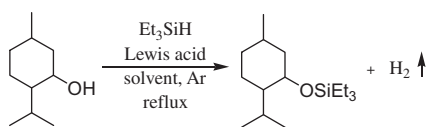


ROH = primary alcohol, secondary alcohol, phenol or oxime
 $\text{R}^1 = \text{R}^2 = \text{R}^3$ = alkyl or aryl

Scheme 2. InBr_3 catalyzed *O*-silylation of an alcohol with a hydrosilane.

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Table 1
Lewis acid catalyzed *O*-silylation of menthol with triethylsilane



Entry	Catalyst ^a	Solvent	Reaction time (h)	Yield ^b (%)
1	InBr ₃	Toluene	2	80
2 ^c	InBr ₃	Toluene	2	N.R.
3	InBr ₃	Tetrahydrofuran	12	60
4	InBr ₃	Acetonitrile	24	24
5	InBr ₃	Dichloromethane	16	N.R.
6	InBr ₃	1,2-Dichloroethane	16	N.R.
7	InBr ₃	Diethyl ether	16	N.R.
8	InCl ₃	Toluene	24	30
9	In(OTf) ₃	Toluene	16	N.R.
10	ZnCl ₂	Toluene	16	N.R.
11	Gd(OTf) ₃	Toluene	24	10
12	Yt(OTf) ₃	Toluene	24	5
13	Fe(BF ₄) ₃ ·H ₂ O	Toluene	24	10
14	SbCl ₃	Toluene	24	22
15	CuCl ₂ ·2H ₂ O	Toluene	24	28
16	BF ₃ ·Et ₂ O	Toluene	16	N.R.
17	FeCl ₃	Toluene	16	N.R.
18	AlCl ₃	Toluene	16	N.R.
19	NbCl ₅	Toluene	16	N.R.
20	Sc(OTf) ₃	Toluene	16	N.R.
21	I ₂	Toluene	16	N.R.

^a 5 mol %.

^b Isolated yields.

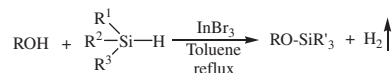
^c In the presence of radical scavenger (20 mol % benzophenone).

In our preliminary experiments, we have studied the reaction of triethylsilane and (–)-menthol under argon atmosphere using InBr₃ as a catalyst under reflux in tetrahydrofuran and obtained corresponding silyl ether in 60% yield along with dimethyl ether as a side reaction product in 10% yield in 12 h. This reaction has been studied also in other aprotic solvents such as toluene, acetonitrile, dichloromethane, 1,2-dichloroethane and diethyl ether under reflux condition and obtained silyl ether selectively in good yields (80%) in 2 h using toluene as a solvent. We have also studied this reaction using Lewis acids such as InCl₃, ZnCl₂, Gd(OTf)₃, Y(OTf)₃, Fe(BF₄)₃·H₂O, Sc(OTf)₃, SbCl₃, CuCl₂·2H₂O, BF₃·Et₂O, FeCl₃, AlCl₃, NbCl₅ and I₂ under reflux in toluene and found these catalysts to be not as effective as InBr₃ in promoting the *O*-silylation of menthol with triethylsilane and the results are shown in Table 1.

Next, we reacted triethylsilane with a variety of alcohols, phenols and oximes using InBr₃ as a catalyst by refluxing in toluene under argon atmosphere to obtain corresponding silyl ethers in 70–95% yields¹⁴ and the representative results are shown in Table 1. In this study, however, tertiary alcohols such as *t*-butanol (entry 6, Table 2) and 1-methyl cyclohexanol (entry 7, Table 2) could not react with triethylsilane under the reaction conditions. A variety of bulky hydrosilanes such as Ph₃SiH, (*i*-Pr)₃SiH, (*n*-Oct)₃SiH, Et₂(Me)-SiH, Me₂(Et)SiH and (*n*-Pr)₃SiH were also found to give silyl ethers with phenol (entries 19–22) in high yields (>83%) and the results are shown in Table 2.

The mechanism of the present reaction is not clear. In our earlier work (Scheme 1), we found hydrosilanes to undergo efficient dehydrogenative air oxidation in the presence of a Lewis acid as a catalyst, producing symmetrical disiloxanes in high

Table 2
InBr₃ catalyzed *O*-silylation of alcohols, phenols and oximes with a hydrosilane



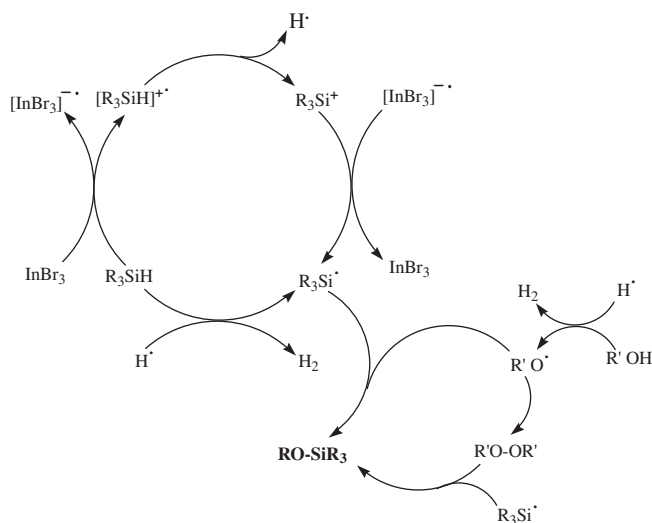
Entry	R-OH	Hydrosilane	Product	Reaction time (h)	Yield (%) ^a
1	Ph-CH=CH-CH ₂ -OH	Et ₃ SiH	Ph-CH=CH-CH ₂ -OSEt ₃	2.5	76
2	Ph-CH ₂ -CH ₂ -CH ₂ -OH	Et ₃ SiH	Ph-CH ₂ -CH ₂ -CH ₂ -OSEt ₃	2.0	80
3	CH ₂ =CH-CH ₂ -OH	Et ₃ SiH	CH ₂ =CH-CH ₂ -OSEt ₃	2.0	85
4	Menthol	Et ₃ SiH	Menthol-OSEt ₃	2.0	80
5	1-Methylcyclohexanol	Et ₃ SiH	1-Methylcyclohexanol-OSEt ₃	2.0	82
6	<i>t</i> -Butanol	Et ₃ SiH	N.R.	15.0	N.R.
7	1-Methylcyclohexanol	Et ₃ SiH	N.R.	15.0	N.R.
8	4-Nitrophenol	Et ₃ SiH	4-Nitrophenol-OSEt ₃	1.0	90
9	Phenol	Et ₃ SiH	Phenol-OSEt ₃	2.0	86
10	1-Naphthol	Et ₃ SiH	1-Naphthol-OSEt ₃	1.5	85
11	2,4-Dimethoxyphenol	Et ₃ SiH	2,4-Dimethoxyphenol-OSEt ₃	2.5	68
12	4-Bromophenol	Et ₃ SiH	4-Bromophenol-OSEt ₃	2.5	82

(continued on next page)

Table 2 (continued)

Entry	R-OH	Hydrosilane	Product	Reaction time (h)	Yield (%) ^a
13		Et ₃ SiH		1.5	92
14		Et ₃ SiH		2.5	76
15		Et ₃ SiH		2.0	85
16		Et ₃ SiH		2.0	85
17		Et ₃ SiH		2.0	82
18	PhOH	Et ₃ SiH	PhOSiEt ₃	1.5	90
19	PhOH	Ph ₃ SiH	PhOSiPh ₃	1.0	83
20	PhOH	(i-Pr) ₃ SiH	PhOSi(i-Pr) ₃	1.5	86
21	PhOH	(n-Oct) ₃ SiH	PhOSi(n-Oct) ₃	2.0	85
22	PhOH	Et ₂ (Me)SiH	PhOSi(Me)Et ₂	1.0	92
23		Et ₃ SiH		2.5	82
24		Et ₃ SiH		2.5	80

^a Isolated yields. All products gave satisfactory ¹H and ¹³C NMR, IR and mass spectral data.



Scheme 3. Plausible mechanism for formation of a silyl ether.

yields. Earlier to this observation, Berberova¹⁵ observed the formation of symmetrical disiloxane with evolution of hydrogen from electrochemical oxidation of a hydrosilane. In this reaction, hydrosilane radical cation [R₃SiH^{•+}] is produced in the initial step, which eventually splits into silyl cation [R₃Si⁺] and hydrogen [H[•]] and reacts with air to form disiloxane. Since Lewis acids (metal halides) are known to induce single electron oxidations reactions,¹⁶ we believe that air oxidation of hydrosilane to siloxane involves SET pathway as the initial step of the process (Scheme 1) and a similar mechanism is possibly operative also in the present dehydrogenative O-silylation reaction. In our study, radical scavenger (benzophenone) completely inhibited O-silylation of menthol with triethylsilane under InBr₃ catalysis (entry 2, Table 1), which asserts that the present reaction proceeds through a radical mechanism and here, we consider that the initial SET process between InBr₃ and R₃SiH possibly helps the splitting of R₃SiH into R₃Si[•] and H[•] radicals, which react with alcohol forming silyl ether and hydrogen as shown in Scheme 3.

In conclusion, we have shown an unprecedented and efficient method for silylation of primary and secondary alcohols, phenols and oximes with hydrosilanes using InBr₃ as a catalyst under reflux in toluene. In this method, bulky hydrosilanes also gave silyl ethers in excellent yields.

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- Typical procedure for O-silylation with a hydrosilane using InBr₃ as a catalyst*: (–)-Menthol (1.0 g, 6.4 mmol), triethylsilane (0.7 g, 6.4 mmol) and toluene (10 ml) were taken into a 50 ml two neck round-bottomed flask fitted with a condenser, rubber septa and an argon balloon. InBr₃ (0.1 g, 0.32 mmol) was added to the contents in the flask under purge of argon and the mixture was refluxed for 2 h under argon atmosphere. Progress of the reaction was by TLC and after completion of the reaction, the reaction mixture was cooled to room temperature and solvent was removed under reduced pressure. The crude product was extracted with ethyl acetate (2 × 5 ml) and the combined organic layer was washed with water (1 × 3 ml) and saturated NaCl solution (1 × 3 ml) and dried over anhyd. Na₂SO₄. Next, the solvent was removed under reduced pressure and the crude product was purified by normal column chromatography (Silica gel (60–120 mesh, hexane) to obtain (menthyl)oxytriethylsilane (0.136 g, 80%) in the form of a colourless oil and it was characterized by the following spectral data: ¹H NMR (300 MHz, CDCl₃): δ = 3.33–3.39 (m, 1H), 2.16–2.24 (m, 1H), 1.81–1.86 (m, 1H), 1.55–1.64 (m, 2H), 1.25–1.39 (m, 1H), 1.06–1.12 (m, 1H), 0.93–0.97 (t, 9H, J = 7.82 Hz), 0.88–0.91 (m, 9H), 0.71–0.73 (d, 3H, J = 6.84 Hz), 0.55–0.61 (q, 6H, J = 7.82 Hz); ¹³C NMR (75 MHz, CDCl₃): δ = 72.32, 50.20, 45.55, 34.54, 31.72, 25.05, 22.81, 22.35, 21.30, 15.82, 6.98, 5.27; IR (neat): ν 2955, 2918, 2874, 1457, 1413, 1376, 1237, 1107, 1008, 738 cm⁻¹; EIMS (m/z): 270 (M⁺), 255, 241, 185, 139, 115, 103; Exact mass observed for C₁₆H₃₄O₂: 270.2369 (calculated: 270.2379).
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