B(C$_6$F$_5$)$_3$-Catalyzed Silation of Alcohols: A Mild, General Method for Synthesis of Silyl Ethers

James M. Blackwell, Katherine L. Foster, Victoria H. Beck, and Warren E. Piers*

Department of Chemistry, University of Calgary, 2500 University Drive NW, Calgary, Alberta T2N 1N4, Canada

The commercially available borane tris(pentafluorophenyl)borane, B(C$_6$F$_5$)$_3$, is an effective catalyst for the dehydrogenative silation of alcohols using a variety of silanes, R$_3$SiH, R$_2$SiH$_2$, and R$_2$R′SiH. Generally, the reactions occur in a convenient time frame at room temperature using 2 mol % of the borane and are clean and high yielding, with dihydrogen as the only byproduct. Primary aliphatic alcohols are silated cleanly but slowly, with reaction times ranging from 20 to 144 h. Faster reaction times can be achieved by increasing the catalyst loading to 8 mol % or by heating the reaction to ∼60 °C. Secondary and tertiary alcohols react more rapidly, with most reactions being complete in 0.5–2 h. The reaction is tolerant of many functional groups including C=C, C≡C, −Br, aliphatic ketones, C(O)OR, lactones, furans, OBn, OMe, and NO$_2$; examples of each are given. Using the phenolic substrate 2,4,6-trimethylphenol, a number of different silanes were tested. Only the most bulky silanes (Bn$_3$SiH and Pr$^i_3$SiH) were not reactive under these conditions. The selectivity of the silation reactions are roughly governed by the relative basicity of the alcohols (and other functions in the molecule) with more basic groups being selectively silated. These observations are rationalized on the basis of a mechanism that invokes borane activation of the silane by hydride abstraction. The resulting intermediate silylium/hydridoborate ion pair then reacts with alcohols to give the observed silyl ether and dihydrogen products.

Introduction

Silyl ethers are employed widely as protecting groups for alcohols in organic synthesis.[1] Variation in the bulk of the alkyl substituents on silicon allows for acheivement of a balance between the stability of the silyl ether and the ease with which it can be removed at a later stage.[1,2] Silyl groups such as Bu^{t}Me$_2$Si− (TBDMS),[3] Bu^{t}Ph$_2$Si− (TBDPS),[4] Pr$^i_3$Si− (TIPS),[5] and Et$_3$Si− (TES) are among the most effective in striking this balance and are commonly encountered trialkylsilyl moieties for alcohol protection.

The standard method for introducing these groups involves treatment of the alcohol to be protected with a silyl chloride in the presence of an excess of a nitrogen Lewis base (such as imidazole) in a polar solvent (commonly DMF). In some instances, catalytic amounts of the strong base can be employed,[6] with Et$_3$N serving to neutralize the HCl byproduct. Verkade et al. have shown that DMF can be avoided in favor of less polar and more convenient solvents (CH$_3$CN or CH$_2$Cl$_2$) via the use of a superbase.[7] While generally effective, these methods for introducing silyl ether functions using silyl chlorides have some drawbacks. They often fail for the protection of tertiary or otherwise hindered alcohols, necessitating the use of more expensive silyl triflate reagents.[8] Alcohols with other, base-sensitive functions are difficult to protect chemoselectively. From an environmental perspective, the frequent need for the use of DMF and the production of stoichiometric quantities of ammonium hydrochloride byproducts is less than desirable.

Silanolysis of alcohols using R$_3$SiH[9] is an attractive alternative, since the only byproduct of the reaction is H$_2$ (eq 1). While thermodynamically quite favorable, this

$$R-OH \xrightarrow[\text{R'}_3\text{Si-H}]{\text{cat}} R-OSiR'_3 + H_2 \quad (1)$$
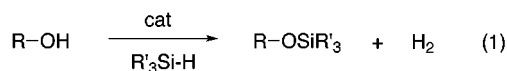
reaction requires a catalyst to occur at convenient rates, and many transition-metal-based catalysts have been reported that mediate the process.[10] None of them have enjoyed widespread use because they each suffer from one or more disadvantages, including poor functional group tolerance, slow rates with bulky (desirable) silanes and tertiary alcohols, the need for rigorously anaerobic and water-free conditions, and the lack of a commercial source for the catalyst.

Herein we report the use of the commercially available highly Lewis acidic borane tris(pentafluorophenyl)borane, B(C$_6$F$_5$)$_3$, as a catalyst for the silanolysis of alcohols.[11] In addition to being effective for primary, secondary, and tertiary alcohols alike, it is tolerant of a wide variety of

* To whom correspondence should be addressed. Phone: 403-220-5746. Fax: 403-289-9488. E-mail: wpiers@chem.ucalgary.ca.

(1) Greene, T. W.; Wuts, P. G. *Protective Groups in Organic Synthesis*, 2nd ed.; John Wiley and Sons: New York, 1991.

(2) (a) Wilson, N. S.; Keay, B. A. *Tetrahedron Lett.* **1996**, *37*, 153. (b) Wilson, N. S.; Keay, B. A. *J. Org. Chem.* **1996**, *61*, 2918.

(3) Corey, E. J.; Venkateswarlu, A. *J. Am. Chem. Soc.* **1972**, *94*, 6190.

(4) Hanessian, S.; Lavallee, P. *Can. J. Chem.* **1975**, *53*, 2975.

(5) Ogilvie, K. K.; Thompson, E. A.; Quilliam, M. A.; Westmore, J. B. *Tetrahedron Lett.* **1974**, 2865.

(6) (a) Kim, S.; Chang, H. *Synth. Commun.* **1984**, *14*, 899. (b) Kim, S.; Chang, H. *Bull. Chem. Soc. Jpn.* **1985**, *58*, 3669. (c) Chaudhary, S. K.; Hernandez, O. *Tetrahedron Lett.* **1979**, *21*, 99.

(7) (a) D'Sa, B. A.; Verkade, J. G. *J. Am. Chem. Soc.* **1996**, *118*, 12832. (b) D'Sa, B. A.; McLeod, D.; Verkade, J. G. *J. Org. Chem.* **1997**, *62*, 5057.

(8) Corey, E. J.; Cho, H.; Rücker, C.; Hua, D. H. *Tetrahedron Lett.* **1981**, *22*, 3455.

(9) (a) Lukevics, F.; Dzintara, M. *J. Organomet. Chem.* **1985**, *295*, 265. (b) Corey, J. Y. In *Advances in Silicon Chemistry*; Larson, G., Ed.; JAI Press: Greenwich, CT, 1991; p 327.

functional groups and is effective for a number of different silanes, including some of the more commonly employed silyl ether protecting groups.

Results and Discussion

$B(C_6F_5)_3$-Catalyzed Silation of Alcohols. In general, the reactions reported here are carried out by adding the borane catalyst to a toluene or CH_2Cl_2 solution containing the substrate alcohol and the silane. The borane catalyst may be easily prepared[12] or purchased and used as received. In most instances, clean reactions (quantitative by ^1H NMR) occur and are signaled by an observable evolution of H_2. Isolated yields are high and workup procedures are trivial since the only byproduct is dihydrogen. Although we used scrupulously dried borane to effect the reactions reported, special treatment of the borane is not entirely necessary. When "off the shelf" borane is employed, this wet material is found to be only moderately less active, with typical reactivity being observed after an initial induction period over which time the water is silated to $R_3SiOSiR_3$. Since the presence of siloxane dimers can complicate product purification, we prefer to use dry borane. Similarly, although we generally used carefully dried solvents, use of conventionally distilled solvents or freshly opened bottles is not ultimately detrimental to the procedures reported.

As summarized in Table 1, the $B(C_6F_5)_3/R_3SiH$ reagent combination leads efficiently to the silation of primary, secondary, tertiary, and phenolic aliphatic alcohols. Unlike conventional base-mediated methods for alcohol silation, the relative reactivity order found in these studies follows an inverse trend with respect to alcohol size; that is, sterically bulky alcohols are silated more rapidly than less hindered alcohols. For instance, the triphenylsilation of decyl alcohol (Table 1, entry 1) requires significantly more time for the reaction to reach completion compared to cyclohexanol (Table 1, entry 4) for which vigorous hydrogen evolution occurs immediately upon addition of $B(C_6F_5)_3$ to the solution of alcohol

(10) (a) Chang, S.; Scharrer, E.; Brookhart, M. *J. Mol. Catal. A* **1998**, *130*, 107. (b) Wang, X., Ellis, W. W.; Bosnich, B. *Chem. Commun.* **1996**, 2561. (c) Lorenz, C.; Schubert, U. *Chem. Ber.* **1995**, *128*, 1267. (d) Gregg, T. B.; Cutler, A. R. *Organometallics* **1994**, *13*, 1039. (e) Burn, M. J.; Bergman, R. G. *J. Organomet. Chem.* **1994**, *472*, 43. (f) Barber, D. E.; Lu, Z.; Richadson, T.; Crabtree, R. H. *Inorg. Chem.* **1992**, *31*, 4709. (g) Bedard, T. C.; Corey, J. Y. *J. Organomet. Chem.* **1992**, *428*, 315. (h) Barton, D. H. R.; Kelly, M. J. *Tetrahedron Lett.* **1992**, *33*, 5041. (i) Doyle, M. P.; High, K. G.; Bagher, V.; Pieters, R. J.; Lewis, P. J.; Pearson, M. M. *J. Org. Chem.* **1990**, *55*, 6082. (j) Luo, X.; Crabtree, R. H. *J. Am. Chem. Soc.* **1989**, *111*, 2527. (k) Yamamoto, K.; Takemae, M. *Bull. Chem. Soc. Jpn.* **1989**, *62*, 2111. (l) Caseri, W.; Pregosin, P. S. *Organometallics* **1988**, *7*, 1373. (m) Oehmichen, U.; Singer, H.; *J. Organomet. Chem.* **1983**, *243*, 199. (n) Davies, J. A.; Hartley, F. R.; Murray, S. G.; Marshall, G. *J. Mol. Catal.* **1981**, *10*, 171. (o) Blackburn, S. N.; Haszeldine, R. N.; Parish, R. V.; Stchfi, J. H. *J. Organomet. Chem.* **1980**, *192*, 329. (p) Haszeldine, R. N.; Parish, R. V.; Riley, B. F. *J. Chem. Soc., Dalton Trans.* **1980**, 705. (q) Archer, N. J.; Haszeldine, R. N.; Parish, R. V. *J. Chem. Soc., Dalton Trans.* **1979**, 695. (r) Corriu, R. J. P.; Moreau, J. J. E. *J. Organomet. Chem.* **1977**, *127*, 7. (s) Corriu, R. J. P.; Moreau, J. J. E. *J. Organomet. Chem.* **1976**, *120*, 337. (t) Corriu, R. J. P.; Moreau, J. J. E. *J. Organomet. Chem.* **1976**, *114*, 135. (u) Ojima, I.; Kogure, T.; Nihonyanagi, M.; Kono, H.; Inaba, S.; Nagai, Y. *Chem. Lett.* **1973**, 501. (v) Chalk, A. J. *J. Chem. Soc. Chem. Commun.* **1970**, 847.

(11) Other applications of $B(C_6F_5)_3$ in organic synthesis: (a) Ishihara, K.; Hananki, N.; Yamamoto, H. *Synlett* **1993**, 577. (b) Ishihara, K.; Funahasi, M.; Hanaki, N.; Miyata, M.; Yamamoto, H. *Synlett* **1994**, 963. (c) Ishihara, K.; Hananki, N.; Yamamoto, H. *Synlett* **1995**, 721. (d) Ishihara, K.; Hanaki, N.; Funahasi, M.; Miyata, M.; Yamamoto, H. *Bull. Chem. Soc. Jpn.* **1995**, *68*, 1721. (e) Gevorgyan, V.; Liu, J.-X.; Yamamoto, Y. *J. Org. Chem.* **1997**, *62*, 2963.

(12) Massey, A. G.; Park, A. J. *J. Organomet. Chem.* **1966**, *5*, 218.

Table 1. $B(C_6F_5)_3$-Catalyzed Silation of Unfunctionalized Alcohols

$$R-OH \xrightarrow[\substack{R'_3SiH \\ Conditions}]{B(C_6F_5)_3} R-OSiR'_3$$

E	ROH	Silane	Cond[a]	Time[b]	Yield[c]
1	(decyl alcohol, chain of 4) OH	Ph_3SiH	A	24	80
2	(benzyl alcohol) OH	Ph_3SiH	A	20	93
3	(phenethyl alcohol) OH	Ph_3SiH	A	144	87
4	(cyclohexanol) OH	Ph_3SiH	A	1	95
5	(2,4-dimethyl-3-pentanol) OH	Ph_3SiH	A	2	95
6	(1-phenethyl alcohol) OH	Ph_3SiH	A	48	87
7	(2,6-dimethylphenol type) OH	Ph_3SiH	A	2	75
8	(1-methylcyclohexanol) OH	Et_3SiH	B	<1	91
9	(1-adamantanol) OH	Et_3SiH	B	<1	79

[a] Conditions **A**: ROH (5 mmol), $B(C_6F_5)_3$ (0.1 mmol), toluene, rt. Conditions **B**: ROH (5 mmol), $B(C_6F_5)_3$ (0.05 mmol), toluene, rt. [b] Time (h). [c] Isolated yield (%).

and triphenylsilane. The sluggishness of primary alcohols toward silation is also demonstrated by benzyl alcohol and 1-phenethyl alcohol (Table 1, entries 2 and 3). The reaction times required for less active substrates can be lowered significantly by increasing the catalyst loading (8%) or heating (50−60 °C) gently.

Tertiary alcohols are highly reactive under typical silation conditions, but for these substrates, use of Ph_3-SiH leads to mixtures of products that consist of the desired silyl ether contaminated with significant quantities of olefinic side products. However, silyl ether formation is favored cleanly when Et_3SiH is employed (Table 1, entries 8 and 9). Addition of as little as 1 mol % of $B(C_6F_5)_3$ to a toluene solution of triethylsilane and 1-methylcyclohexanol or 1-adamantol resulted in immediate evolution of hydrogen, which subsided after a few minutes. The high rate of reactivity of tertiary alcohols vs secondary and primary substrates is not entirely unprecedented[10g] and has mechanistic implications that will be discussed below.

To obtain a picture of the functional group tolerance of the silation conditions, a variety of functionalized alcohols were protected as their triphenylsilyl ethers using $B(C_6F_5)_3$ catalysis, Table 2. The first three examples demonstrate that alkene and alkyne functionality is not affected under these conditions. This is an important distinction from several of the transition-metal-based catalysts for this reaction, for which competitive alkene and alkyne hydrosilation is often observed.[10] Furthermore, $B(C_6F_5)_3$-catalyzed hydrostannation of alkynes has been recently reported.[13] As entry 3 of Table 2 shows, sluggish reactions can be encouraged with higher catalyst loadings. Halogens are also tolerated (Table 2, entries 4

Table 2. B(C₆F₅)₃-Catalyzed Silation of Functionalized Alcohols

E	ROH	Silane	Cond[a]	Time[b]	Yield[c]
1	⌇⌇OH	Ph₃SiH	A	72	78
2	⌇⌇OH	Ph₃SiH	B	4	95
3	≡⌇OH	Ph₃SiH	A	2	95
4	Br⌇⌇OH	Ph₃SiH	A	1	93
5	Br⌇⌇OH	Ph₃SiH	A	16	85
6	NC⌇⌇OH	Ph₃SiH	A	84	55
7	OH O ⌇OEt	Ph₃SiH	A	1	86
8	O=⌇ HO	Ph₃SiH	C	2	83
9	⌇OH	Ph₃SiH	A	2	93
10	O Ph OH	Et₃SiH	C	20	86

[a] Conditions **A**: ROH (5 mmol), B(C₆F₅)3 (0.1 mmol), toluene, rt. Conditions **B**: ROH (5 mmol), B(C₆F₅)₃ (0.4 mmol), toluene, rt. Conditions **C**: ROH (2.5 mmol), B(C₆F₅)₃ (0.125 mmol), CH₂Cl₂, rt. [b] Time (h). [c] Isolated yield (%).

and 5), but nitrile functions prove problematic in that reactions are inconveniently slow, even with higher catalyst loadings (Table 2, entry 6). An independent NMR tube experiment revealed that no competing processes involving the nitrile group were occurring during the reaction, even with heating. Although for this particular nitrile-substituted substrate the reaction proceeded to completion, the isolated yield was consistently low, perhaps a result of losses/decomposition during purification of the silyl ether by column chromatography. Again, primary alcohols are silated comparatively slowly, although, curiously, propargyl alcohol and 2-bromoethanol are silated much more rapidly than the other primary alcohols (vide infra).

Silation of alcohols can also be carried out in the presence of functionalities that are known to be reactive under B(C₆F₅)₃/R₃SiH conditions.[14] Entries 7 and 8 of Table 2 demonstrate tolerance of the ester functionality, including a lactone, which also illustrates the suitability of this protocol for base-sensitive substrates. Despite the observed propensity of the silating reagents to ring open tetrahydrofuran,[15] selective alcohol silation of 3-hydroxytetrahydrofuran is observed (Table 2, entry 9). The protocol cannot be extended to include smaller oxygen-containing heterocycles, however. For example, attempted protection of the hydroxy epoxide glycidol resulted in competitive ring-opening of the epoxide[11c] in addition to silyl ether formation. Finally, nonphenolic hydroxy groups are selectively silated in the presence of

(13) Gevorgyan, V.; Liu, J.-X.; Yamamoto, Y. *Chem. Commun.* **1998**, 37.

(14) Parks, D. J.; Piers, W. E. *J. Am. Chem. Soc.* **1996**, *118*, 9440.

(15) Parks, D. J. Ph.D. Dissertation, University of Calgary, 1998.

Table 3. B(C₆F₅)₃-Catalyzed Silation of Functionalized Phenols

E	X	Y	cond[a]	time[b]	yield[c]
1	OMe	H	A	20	95
2	OBn	H	A	20	92
3	CO₂Me	H	A, B	20	87
4	H	NO₂	A	2	91
5	CH₂C≡N	H	A, B	240	12
6	C(O)H	H	C		d
7	C(O)Me	H	C		d
8	H	C(O)H	C		d
9	H	C(O)Me	C		d

[a] Conditions **A**: ROH (2.5 mmol), B(C₆F₅)₃ (0.125 mmol), toluene or CH₂Cl₂, rt. Conditions **B**: same as **A**, except 40 °C (refluxing CH₂Cl₂). Conditions **C**: ROH (0.1 mmol), B(C₆F₅)₃ (0.005 mmol), CDCl₃, rt. [b] Time (h). [c] Isolated yield (%). [d] Competitive reduction of X or Y groups.

ketone carbonyl groups (Table 2, entry 10); since this substrate is a tertiary alcohol, the use of triethylsilane was necessary (vide supra).

The results summarized in Table 3 further probe the selectivity of this reaction using a series of phenolic substrates. Both methyl and benzyl ethers (Table 3, entries 1 and 2) did not interfere with alcohol silation, although we have observed facile cleavage of these ethers under typical reaction conditions in the absence other functionality.[16] Again, ester groups do not compete for silane, as the efficient protection of the phenolic OH of methyl 4-hydroxybenzoate demonstrates (Table 3, entry 3). The presence of a nitro group did not interfere with silyl ether formation, but the nitrile group again hindered the reaction by slowing the reaction to impractical rates. A more functionalized substrate is also cleanly protected, showing again tolerance for an ester and also the commonly employed acetonide protecting group, eq 2.

(2)

74%
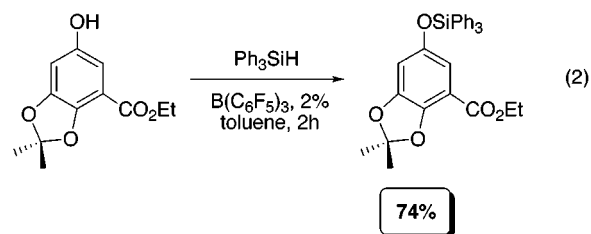
For phenolic substrates, the presence of ketone or aldehyde functions in the 4-position of the ring resulted in poor chemoselectivity using the B(C₆F₅)₃/Ph₃SiH reagent combination. Indeed, when monitored by NMR spectroscopy, it is clear that the major products are derived from carbonyl hydrosilation (Table 3, entries 6 and 7). Because the para substitution pattern results in increased basicity of the carbonyl groups with a concomitant decrease in the basicity of the phenolic oxygen, we also investigated the meta-substituted isomers; however, taking the carbonyl groups out of resonance with the phenolic −OH has no effect on the selectivity of the reaction.
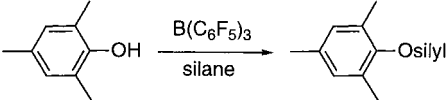
With the exception of the deployment of Et₃SiH for tertiary substrates, triphenylsilane was used because of

(16) The products of these reactions are a silyl ether and either methane or toluene depending on the ether used. We are exploring the B(C₆F₅)₃/R₃SiH system as a deprotection protocol for these groups.

Table 4. B(C$_6$F$_5$)$_3$-Catalyzed Silation of 2,4,6-Trimethylphenol with Various Silanes

E	silane	cond[a]	time[b]	yield[c]
1	HSiEt$_3$	**A**	2	95
2	HSiPh$_3$	**A**	2	72
3	HSiMe$_2$t-Bu	**A**	12	95
4	HSiMe$_2$Ph	**A**	1	80
5	HSiMe$_2$Cl	**A**	2	79
6	H$_2$SiPh$_2$	**A**	<1	95[d]
7	HSiBn$_3$	**B**		
8	HSii-Pr$_3$	**B**		

[a] Conditions **A**: ROH (5 mmol), B(C$_6$F$_5$)$_3$ (0.1 mmol), toluene, rt. Conditions **B**: ROH (5 mmol), B(C$_6$F$_5$)$_3$ (0.1 mmol), toluene, 110 °C. [b] Time (h). [c] Isolated yield (%). [d] Crude yield.

the stability of the silyl ether products and the ease with which they can be handled. However, the triphenylsilyl group is not the most widely used protecting group in synthetic chemistry, and to more fully demonstrate the scope of this silation method, the silation of 2,4,6-trimethyl phenol was carried out with a number of silanes. The results are summarized in Table 4. Of the eight silanes examined, six of them were shown to be effective for the silation of this phenol. In addition to the triphenylsilyl and triethylsilyl groups, TBDMS and di-methylphenylsilyl groups were easily installed using B(C$_6$F$_5$)$_3$ and the appropriate silane. However, the more sterically bulky silanes triisopropylsilane and tribenzyl-silane were not reactive even under forcing conditions with this particular substrate (Table 4, entries 7 and 8).

Entries 5 and 6 of Table 4 show that difunctional silanes can also be employed; i.e., both dimethylchlorosi-lane (possessing a functionalizable Si−Cl bond) and diphenylsilane reacted cleanly to give the corresponding silyl ether. The use of diphenylsilane offers the potential for further reactivity involving the remain Si−H bond and another group. Equations 3 and 4 offer illustrations of this principle for two diols that can be protected as cyclic siloxanes in moderate yield as shown. These

(3)

61%

(4)

56%
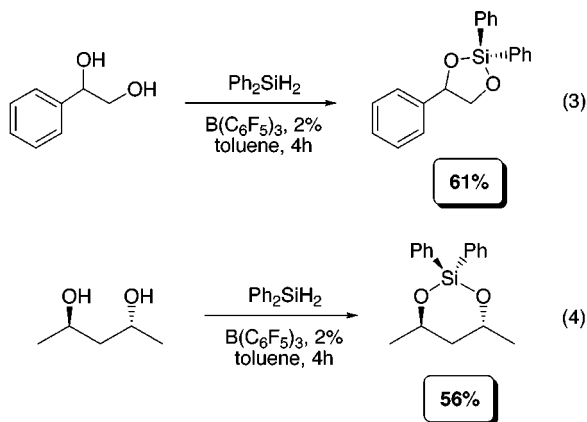
procedures have not as yet been optimized, but the lower yield stems mainly from the instability of the products toward our purification procedures. The experiments illustrate the potential of the B(C$_6$F$_5$)$_3$/R$_3$SiH system for tandem protection of 1,2-diols and, in connection with other protocols,[17] should be effective in protecting second-ary alcohols in the presence of primary −OH functions.

Scheme 1
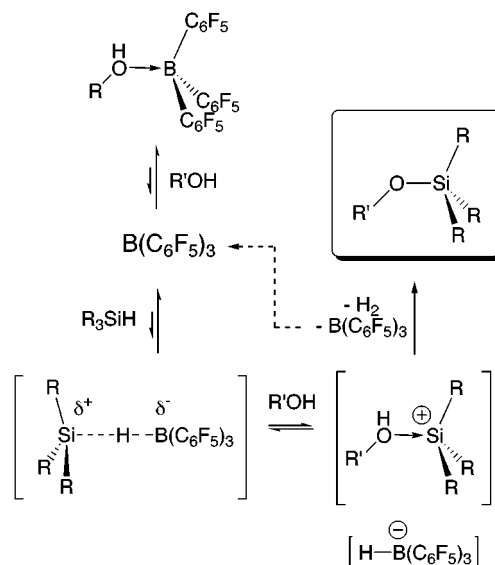
Furthermore, the second group need not be limited to ROH; we have performed examples of directed carbonyl reductions using B(C$_6$F$_5$)$_3$/Ph$_2$SiH$_2$ and keto alcohol sub-strates.

Finally, the scalability of the reaction was tested by performing a silation of 2,6-dimethylphenol on a 0.1 molar scale. This experiment was performed by dropwise addition of Et$_3$SiH to a toluene solution of the phenol containing 5% B(C$_6$F$_5$)$_3$ catalyst. The rate of hydrogen evolution was controlled by modulating the rate of silane addition, which was complete in 5 min. Workup led to a 95% isolated yield of the silyl ether product.

Mechanistic Considerations. In the foregoing dis-cussion, we have focused primarily on the utility of this B(C$_6$F$_5$)$_3$-catalyzed reaction rather than on the mecha-nistic aspects of the process. Although we have not engaged in extensive mechanistic studies on this par-ticular reaction, the qualitative evidence strongly sug-gests that the mechanism is related to that observed in the B(C$_6$F$_5$)$_3$-catalyzed hydrosilation of carbonyl func-tions, a reaction we have studied in detail from a mechanistic perspective.[14,15] In that study, kinetic, isotope labeling, and computational studies indicate that, while the borane readily forms adducts with carbonyl contain-ing substrates,[18] it is borane activation of the silane (via hydride abstraction) that is the key step in the addition of Si−H to C=O.

Thus, while the ROH substrates undoubtedly form adducts with B(C$_6$F$_5$)$_3$[19] (either through the alcohol func-tion or another, more basic group in the molecule), it is likely that dissociation of the borane is necessary so that it can interact with R$_3$SiH and effect silation of the ROH functionality (Scheme 1). This notion is consistent with the qualitative observation that primary alcohols are

(17) Tanino, K.; Shimizu, T.; Kuwahara, M.; Kuwajima, I. *J. Org. Chem.* **1998**, *63*, 2422.
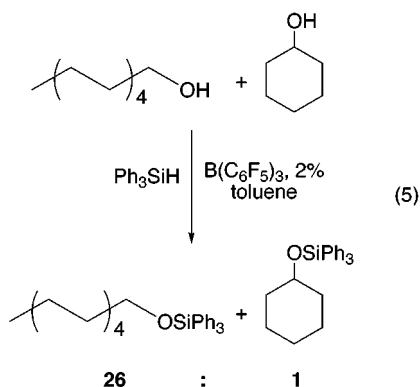
(18) Parks, D. J.; Piers, W. E.; Parvez, M.; MacQuarrie, D. C.; Zaworotko, M. J. *Organometallics* **1998**, *17*, 1369.

(19) While we have not studied these adducts in any detail, they have been claimed as olefin polymerization cocatalysts and cationic initiators: Siedle, A. R.; Lamanna, W. M. (3M) U.S. Pat. 5416177, 1995. Additionally, the water adduct of B(C$_6$F$_5$)$_3$ has recently been re-ported: Danopoulos, A. D.; Galsworthy, J. R.; Green, M. L. H.; Cafferkey, S.; Doerrer, L. H.; Hursthouse, M. B. *Chem Commun.* **1998**, 2529.

Scheme 2
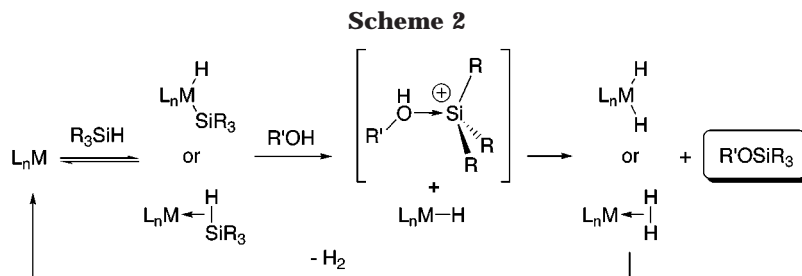
silated more slowly by B(C$_6$F$_5$)$_3$ than secondary or tertiary, a trend that has also been observed in certain transition-metal catalysts.[10j] Since primary alcohols are more basic toward sterically significant Lewis acids than the more bulky secondary or tertiary substrates, there is less free borane present to activate the silane via hydride abstraction. Indeed, this mechanistic picture of the reaction is not unlike what has been proposed (and in some instances strongly substantiated) for the general mechanism of transition-metal-catalyzed alcohol silation reactions (Scheme 2).[10a,d,h,j,v] Instead of a transition-metal center activating the Si−H bond (either via oxidative addition or by formation of a σ-complex[20]), the highly electrophilic borane center is able to fulfill this role. The polarization induced in the Si−H bond upon electrophilic activation renders the silicon center susceptible to nucleophilic attack by the alcohol in both mechanisms, giving essentially an alcohol adduct of a trialkyl-substituted silylium cation.[21] Subsequent proton transfer from this acid to the "M − H" species (in the case of the B(C$_6$F$_5$)$_3$-catalyzed reaction, [HB(C$_6$F$_5$)$_3$]$^-$, Scheme 1) completes the cycle, releasing dihydrogen and regenerating the catalyst.

An interesting aspect of this mechanism is that while more basic substrates react more slowly than less basic functions, it is the more basic groups that are favored in terms of selectivity. Thus, although 1-decanol is silated over the course of 24 h as opposed to less than 2 h for cyclohexanol (Table 1), in a competition experiment it is the primary substrate that is silated almost to the exclusion of the secondary alcohol (eq 5).

This arises because a key step in the process is coordination of the substrate to the silicon atom in the silylium ion formed from borane abstraction of H$^-$ from the silane. In competition, it will be the most basic group that prevails in this task.[22] The overall rate, however, is governed by the level of free borane present, which in turn is dependent on the basicity of the substrate, i.e., the position of the equilibrium between B(C$_6$F$_5$)$_3$ and ROH and the alcohol adduct of B(C$_6$F$_5$)$_3$. Lower chemoselectivity is observed when other functions in the substrate reach a comparable basicity to the alcohol moiety, as in the phenolic substrates with ketone or aldehyde functionality present[23] (Table 3, entries 6−9).

It is unclear at present why substrates with nitrile functions perform so poorly in this reaction (Table 2, entry 5, and Table 3, entry 5). While the nitrile group is known to coordinate relatively strongly to B(C$_6$F$_5$)$_3$[24] it should be labile enough to allow for reaction. Either these substrates sequester too much borane, lowering its effectiveness, or the long reaction times and higher temperatures required lead to catalyst degradation. For example, treatment of B(C$_6$F$_5$)$_3$ with Et$_3$SiH at 60 °C for 3 days is a preparative route to bis-pentafluorophenyl-borane, HB(C$_6$F$_5$)$_2$.[25] This borane reacts rapidly with ROH to form borinate esters ROB(C$_6$F$_5$)$_2$, which are significantly poorer Lewis acids and do not activate silanes effectively.

In conclusion, the use of B(C$_6$F$_5$)$_3$ for the formation of silyl ethers from a wide variety of alcohols has been demonstrated. Many features of this reaction, including the ready availability of the catalyst, the high functional group tolerance, and the easy workup procedures involved, make this method an attractive alternative to traditional procedures for protecting alcohols as silyl ethers.

Experimental Section

General Considerations. NMR spectra were recorded (^{1}H NMR, 200 MHz; ^{13}CNMR, 50 MHz) using deuterated chloroform as the solvent. ^{13}C NMR and ^{1}H NMR spectra were referenced to the deuterated chloroform resonance at δ 77.0 and 7.24, respectively. IR spectra were recorded neat. The

(20) Crabtree, R. H. *Angew. Chem., Int. Ed. Engl.* **1993**, *32*, 789.

(21) It should be noted that the trityl cation (which is isoelectronic to B(C$_6$F$_5$)$_3$) is an effective reagent for abstracting H$^-$ from trialkyl silanes to form silylium ions in the condensed phase: Lambert, J. B.; Zhang, S.; Ciro, S. M. *Organometallics* **1994**, *13*, 2430. Furthermore, coordination of an Si−H bond to a borane center has recently been conclusively demonstrated: Wrackmeyer, B.; Tok, O. L.; Bubnov, Y. N. *Angew. Chem., Int. Ed. Engl.* **1999**, *38*, 124.

(22) The anomolously high rates observed for the silation of propargyl alcohol and 2-bromoethanol may be due to the lower basicity of these substrates relative to the other primary alcohols studied. Alternatively, the presence of donor groups in these positions may aid in hydridoborate displacement from the silicon by chelation, i.e., hypercoordinate silicon.

(23) Relative basicity can be approximated by comparison of the pK_a's of the conjugate acids. pK_a for PhOH$_2^+$ = −6.7; pK_a for PhC(= OH)CH$_3^+$ = −6.2; pK_a for PhC(=OH)H$^+$ = −7.1. Although basicity toward acids other than proton is largely dictated by steric factors, to the extent that these functions are sterically similar, the pK_a values suggest that they have very similar inherent basicities, accounting for the poor chemoselectivity observed in these cases. pK_a values taken from: Streitwieser, A.; Heathcock, C. H.; Kosower, E. M. *Introduction to Organic Chemistry,* 4th ed.; Macmillan: New York, 1992; p A−6.

(24) Li, L.; Marks, T. J. *Organometallics* **1998**, *17*, 3996.

(25) Parks, D. J.; Piers, W. E.; Yap, G. P. A. *Organometallics* **1998**, *17*, 5492.

silanes were purchased from Aldrich−Sigma and degassed before use. B(C$_6$F$_5$)$_3$ was purchased from Boulder Scientific and was dried by stirring with excess Me$_2$ClSiH for ~20 min. The silane was removed under vacuum and the borane purified by sublimation at 80 °C under full dynamic vacuum. This procedure was generally carried out on 5−10 g batches that were then stored in a drybox. Alcohol substrates were purchased from Aldrich−Sigma; solids were used as received, while liquid alcohols were generally passed through basic alumina prior to use. Allyl alcohol, benzyl alcohol, and cyclohexanol were dried over CaH$_2$ and then distilled. Toluene was purified by the Grubbs method[26] and stored over titanocene[27] in an evacuated bomb. Methylene chloride was dried over CaH$_2$ and vacuum transferred to the reaction vessel. All reactions were performed under an atmosphere of argon, and yields refer to the amount of isolated product unless otherwise noted.

General Procedure for the B(C$_6$F$_5$)$_3$-Catalyzed Silation of Alcohols. To a solution of equimolar quantities of the alcohol and silane in toluene or dichloromethane (0.1−1.0 M) at room temperature was added B(C$_6$F$_5$)$_3$ (1−8%) as a solid under a purge of argon. In many cases, visible hydrogen evolution ensued upon borane addition. The reactions were monitored by either GC−MS, TLC, or ^{1}H NMR spectroscopy for the absence of either alcohol or silane. Typical workup procedures involved concentration of the reaction mixture followed immediately by purification using flash column chromatography, recrystallization, or a combination thereof. Silyl ether products were identified using NMR spectroscopy, mass spectrometry, elemental analysis, and comparison to literature data where available. In the Supporting Information, data for each product is given along with more specific

information concerning the conditions employed in each individual case. Refer to Tables 1−4 for reaction times and isolated yields.

Scaled-Up Synthesis of 2,6-Dimethyl-1-triethylsiloxybenzene. To a mixture of 2,6-dimethylphenol (12.24 g, 0.10 mol) and B(C$_6$F$_5$)$_3$ (2.57 g, 0.005 mol) was added 100 mL of dry toluene. Et$_3$SiH (16.0 mL, 0.10 mol) was immediately added by syringe over the course of 5 min. Vigorous evolution of H$_2$ and gentle warming was noted, but a cautious rate of addition kept the exotherm in check. After completion of silane addition, the reaction was stirred for 30 min, at which time TLC analysis showed the starting phenol to be completely consumed. The reaction mixture was concentrated to ~50 mL, and a portion of silica gel was added to the solution. The slurry was pumped to dryness, and the resulting white powder was poured into a large column containing hexanes−packed silica; the product was eluted with 2% ethyl acetate/hexanes. The fractions were concentrated in vacuo leading to 22.4 g (95%) of the silyl ether product in >95% purity as judged by ^{1}H NMR spectroscopy and gas chromatography.

Supporting Information Available: Complete characterization data (^{1}H, ^{13}C{^{1}H}, IR, elemental analysis) for all the compounds prepared in this study. This material is available free of charge via the Internet at http://pubs.acs.org.

JO9903003

(26) Pangborn, A. B.; Giardello, M. A.; Grubbs, R. H.; Rosen, R. K.; Timmers, F. J. *Organometallics* **1996**, *15*, 1518.

(27) Marvich, R. H.; Brintzinger, H. H. *J. Am. Chem. Soc.* **1971**, *93*, 2046.