Oxidation of Sterically Hindered Alkoxysilanes and Phenylsilanes under Basic Conditions

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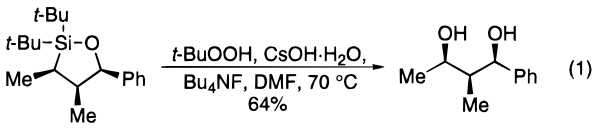
Since its discovery, the oxidation of silanes to alcohols has played an important role in organic synthesis.[1] This reaction permits the unique properties of organosilicon compounds to be employed in a reaction sequence, followed by oxidation of the carbon−silicon bond to provide a hydroxyl moiety.[2] However, the oxidation is restricted to silanes that are substituted with a heteroatom and to phenylsilanes that can be refunctionalized to install a heteroatom.[3,4] Hindered silicon groups are resistant to oxidation,[1,5] and many strategies for oxidizing phenylsilanes employ strongly electrophilic conditions, which limit functional group compatibility.[6] Conditions for oxidizing hindered silanes or phenylsilanes under nucleophilic conditions would complement current silane oxidation methods and improve the versatility of this important transformation. Herein we report new conditions for the oxidation of silanes that are successful in highly congested systems and for silyl groups that bear no heteroatoms.

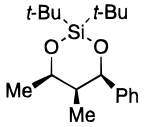
As part of our investigation of the insertion of aldehydes into silacyclopropanes, we prepared the oxasilacyclopentane **1**, which we reasoned could be oxidized to provide a synthesis of 1,3-diols.[7] Subjection of **1** to standard silane oxidation conditions (aqueous H_2O_2, $KHCO_3$, and KF) afforded only recovered starting material, presumably due to the steric hindrance at the silicon center. Furthermore, none of the other modifications of the oxidation proved effective.[1] These results are not surprising, since it has been demonstrated that alkoxysilanes bearing bulky substituents are unreactive.[1,5,8]

In contrast to the standard conditions,[1] we chose to employ polar aprotic media, a strong base, and 90% *tert*-butyl hydroperoxide to facilitate nucleophilic attack on silicon. Treatment of **1** with *t*-BuOOH, $CsOH·H_2O$, and tetrabutylammonium fluoride in DMF at 70 °C afforded the 1,3-diol **2** in 64% yield as a single diastereomer by ^1H and ^{13}C NMR spectroscopy. In the absence of a



1 **2** (1)

fluoride source or with less than 5 equiv of fluoride, both the diol **2** and the dioxasilacyclohexane **3** were isolated from the reaction mixture. Therefore, the fluoride source



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is important for deprotection of the oxidized silane, not for the oxidation itself. Proof that the reaction proceeded with retention of configuration[1] was obtained by comparing the X-ray structures of **1** and an acetal derivative of **2**.[9]

After the successful oxidation of **1**, the scope of the new oxidation conditions was examined. Hindered alkoxysilanes **4a**,**b** were prepared by treating the readily available chlorosilanes with the desired alcohol and triethylamine.[10,11] Treatment of silanes **4a**−**c** with *t*-BuOOH and base in DMF provided the alcohols in high yield (eq 2, Table 1).[12] Compared to previously reported condi-

$$\underset{\textbf{4a–c}}{R^1\text{–}SiR_3} \xrightarrow{[O]} \underset{\textbf{5}}{R^1OH} \qquad (2)$$

tions, improved yields were observed for diisopropoxysilanes **4a**,**c**[13] (entries 1, 3). Although *n*-decyl-*tert*-butoxydimethylsilane (**4b**) was resistant to the H_2O_2 oxidation, submission to the new conditions provided the alcohol in good yield (entry 2). Thus, even a hindered alkoxysilyl moiety is the functional equivalent of a hydroxyl group.[14]

A limitation of current methods for the oxidation of phenylsilanes is that treatment with HBF_4, Br_2, or $Hg(OAc)_2$ is required to install a heteroatom prior to oxidation.[3,4] Because the use of acidic or electrophilic reagents is incompatible with a variety of functional groups, including olefins and amines, other methods have been developed.[15−20] We have found that treatment of both primary and secondary phenylsilanes with *t*-BuOOH and KH provided good yields of the corresponding

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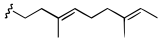
Table 1. Oxidation of Alkoxysilanes 4

entry	compd	R^1	SiR_3	yield of **5** (%)[a]	yield of **5** (%) (lit. procedure)[b]
1	**4a**	*n*-decyl	$SiMe(O\text{-}i\text{-}Pr)_2$	81	75
2	**4b**	*n*-decyl	$SiMe_2(O\text{-}t\text{-}Bu)$	90	0
3	**4c**		$SiMe(O\text{-}i\text{-}Pr)_2$	94[c,d]	44

[a] *t*-BuOOH, $CsOH{\cdot}H_2O$, DMF, 70 °C unless otherwise noted. [b] H_2O_2, $KHCO_3$, KF, 1:1 THF/MeOH, reflux. [c] *t*-BuOOH, KH, TBAF, DMF, 23 °C. [d] Reference 13.

Table 2. Oxidation of Silanes 6

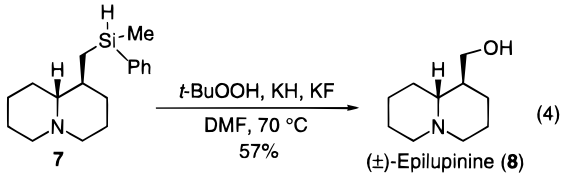
entry	compd	R	SiR_3	yield of **5** (%)[a]
1	**6a**	*n*-decyl	$SiMePh_2$	84
2	**6b**	*n*-decyl	$SiMe_2Ph$	82
3	**6c**	cyclododecyl	$SiMe_2Ph$	80[b]
4	**6d**	*n*-decyl	$SiMe_2H$	82
5	**6e**	*n*-decyl	$SiMe_3$	37[c]

[a] *t*-BuOOH, KH, NMP, 70 °C unless otherwise noted. [b] *t*-BuOOH, KH, NMP, TBAF, 70 °C. [c] *t*-BuOOH, KH, 1:1:2 THF/toluene/NMP, 120 °C.

alcohols in one step (eq 3, Table 2). Since the nonpolar

$$\underset{\textbf{6a–e}}{R^1\text{–}SiR_3} \xrightarrow{[O]} \underset{\textbf{5}}{R^1OH} \qquad (3)$$

starting materials were only marginally soluble in DMF, *N*-methylpyrrolidinone (NMP) was employed as the solvent. The stronger base KH was necessary for consumption of all starting material. Both mono- and diphenylsilanes were oxidized under the conditions in good yield (entries 1−3). The yield of the oxidation of the secondary phenylsilane **6c** (80%) is comparable to that obtained (77%) by following the Fleming protocol (HBF_4 and then H_2O_2, $KHCO_3$, KF).[3] The utility of these basic oxidation conditions for the oxidation of phenylsilanes is illustrated by an application in a natural product synthesis. The silane **7**, prepared by Molander and Nichols using an organoyttrium-promoted cyclization/silylation reaction, could not be oxidized under acidic conditions.[21] However, when **7** was submitted to these basic conditions, (±)-epilupinine (**8**) was provided in 57% isolated yield (eq 4).[21] This result demonstrates that tertiary amines are compatible with this protocol.



(4)

The unfunctionalized silanes **6d**,**e** were also found to oxidize under the new conditions (Table 2). For these substrates, use of THF as a cosolvent was necessary for dissolution of the starting material. When silane **6d** was treated with *t*-BuOOH and KH in 1:1 THF/NMP, *n*-decanol was obtained in 82% yield. In fact, treatment of *n*-decyltrimethylsilane (**6e**) with *t*-BuOOH and KH in 1:1:2 THF/toluene/NMP afforded decanol in 37% yield (50% conversion by ^1H NMR spectroscopy), demonstrating that even tetraalkylsilanes can be oxidized. Attempts to increase conversion by varying the reaction temperature, number of equivalents of reagents, and solvent systems and by addition of fluoride ion were unsuccessful.

In conclusion, a new set of conditions for the oxidation of the C−Si bond has been developed. The conditions (excess *t*-BuOOH and KH or $CsOH{\cdot}H_2O$ in DMF or NMP) have been shown to be more reactive than the standard protocol for hindered alkoxysilanes.[1] The procedure is also applicable to the oxidation of arylsilanes, permitting the oxidation of these compounds in one step and providing an alternative to the known conditions.[3,4] Silanes containing functional groups such as phenyl rings, alkenes, and tertiary amines,[21] which can be incompatible with acidic or electrophilic reagents, can be oxidized by using the new method. Consequently, hindered phenyl and alkylsilanes may find broadened use as hydroxyl equivalents in organic synthesis.

Experimental Section

General. All reactions were carried out under an atmosphere of nitrogen in glassware which had been flame-dried under a stream of nitrogen. Liquid chromatography was performed using forced flow (flash chromatography) of the indicated solvent system on EM Reagents silica gel (SiO_2) 60 (230−400) mesh. Coupling constants for ^1H NMR spectra are reported in hertz. THF was distilled from sodium and benzophenone ketyl. DMF was distilled from CaH_2 and stored over 4 Å molecular sieves. NMP was stirred over $CaSO_4$, filtered, distilled, and stored over 4 Å molecular sieves. Silanes were purchased from United Chemical Technologies and used without further purification. The preparation of silanes **4a**, **6b**, **6c**, and **6e** is provided as supporting information. Microanalyses were performed by Atlantic Microlab (Atlanta, GA).

***tert*-Butoxy-*n*-decyldimethylsilane (4b).**[11] To a stirred solution of chloro-*n*-decyldimethylsilane (7.4 mL, 0.030 mol) in 8 mL of toluene were added *t*-BuOH (14.0 mL, 0.076 mol) and triethylamine (10.6 mL, 0.153 mol). The reaction was heated at reflux for 20 h. After the reaction was cooled to 25 °C, 100 mL of saturated aqueous NH_4Cl was added, and the mixture was extracted with 3 × 100 mL of Et_2O. Combined organic layers were washed with 50 mL of brine, dried (Na_2SO_4), and concentrated *in vacuo* to afford a yellow liquid, which was purified by flash chromatography (3:97 EtOAc/hexanes) to yield the product as a colorless liquid. Further purification by bulb-to-bulb distillation (0.05 mmHg, 85 °C) afforded the product as a colorless liquid (4.91 g, 60%): ^1H NMR ($CDCl_3$, 500 MHz) δ 1.29 (m, 16H), 1.24 (s, 9H), 0.88 (t, 3H, J = 7.0), 0.54 (m, 2H), 0.09 (s, 6H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 71.9, 33.6, 32.1, 32.0, 29.73, 29.67, 29.44, 29.40, 23.5, 22.7, 18.8, 14.1, 0.95; IR (neat) 2959, 2923, 2854, 1462, 1388, 1363, 1249, 1200, 1051, 1024, 839, 776 cm^{-1}; HRMS (CI/isobutane) m/z calcd for $C_{16}H_{37}OSi$ $(M + H)^+$ 273.2610, found 273.2613. Anal. Calcd for $C_{16}H_{36}OSi$: C, 70.51; H, 13.31. Found: C, 70.57; H, 13.36.

***n*-Decyldiphenylmethylsilane (6a).** To a cooled (0 °C) solution of *n*-decyldimethylchlorosilane (5.2 mL, 20 mmol) in 20 mL of THF was added phenylmagnesium chloride (2.0 M solution in THF, 40 mL, 80 mmol) by syringe. The reaction mixture was stirred for 36 h. The thick tan slurry was diluted with 30 mL of saturated aqueous NH_4Cl and concentrated *in vacuo*. The resultant white slurry was extracted with 4 × 30 mL of Et_2O. The combined organic layers were washed with 10 mL of brine, dried (Na_2SO_4), and concentrated *in vacuo* to afford 6.1 g of a golden oil, which was flushed through a pad of SiO_2 (hexanes) to give 5.01 g of a clear, colorless liquid. Purification

(21) Molander and Nichols have employed the oxidation protocol reported here as their final step of an expeditious synthesis of epilupinine in the accompanying paper: Molander, G. A.; Nichols, P. J. *J. Org. Chem.* **1996**, *61*, 6040−6043.

by bulb-to-bulb distillation (120−160 °C, 0.05 mmHg) afforded the product as a colorless liquid (4.99 g, 74%): ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.50 (m, 4H), 7.32 (m, 6H), 1.29 (m, 16H), 1.05 (m, 2H), 0.87 (t, 3H, J = 6.7), 0.53 (s, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 137.5, 134.4, 129.0, 127.7, 33.6, 31.9, 29.63, 29.58, 29.3, 29.2, 23.8, 22.7, 14.2, 14.1, −4.5; IR (neat) 3068, 3048, 2955, 2923, 2853, 1465, 1427, 1250, 1190, 1169, 787, 730, 699 cm^{-1}; HRMS (CI/isobutane) m/z calcd for $C_{23}H_{33}Si$ $(M - H)^+$ 337.2352, found 337.2367. Anal. Calcd for $C_{23}H_{34}Si$: C, 81.56; H, 10.14. Found: C, 81.64; H, 10.12.

***n*-Decyldimethylsilane (6d).** $LiAlH_4$ (0.377 g, 20.2 mmol) was added to 20 mL of THF. Chloro-*n*-decyldimethylsilane (2.5 mL, 10.1 mmol) was added to the $LiAlH_4$ suspension dropwise by syringe over 2 min. The resultant suspension was stirred at room temperature for 12 h. After the suspension was cooled to 0 °C, excess $LiAlH_4$ was quenched by successive addition of 0.77 mL of H_2O, 0.77 mL of 15% NaOH, and 2.3 mL of H_2O. The resultant white slurry was filtered through celite, washing with Et_2O. The filtrate was concentrated *in vacuo* to a colorless liquid. Purification by bulb-to-bulb distillation (0.05 mmHg, 80 °C) afforded the product as a colorless liquid (1.62 g, 80%): ^{1}H NMR ($CDCl_3$, 300 MHz) δ 3.83 (septet, 1H, J = 3.5), 1.38 (m, 16H), 0.86 (t, 3H, J = 6.5), 0.56 (m, 2H), 0.05 (d, 3H, J = 3.5); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 33.3, 32.0, 29.7, 29.6, 29.44, 29.40, 24.4, 22.7, 14.2, 14.1, −4.4; IR (neat) 2957, 2923, 2854, 2112, 1466, 1249, 887, 835, 768 cm^{-1}; HRMS (CI/isobutane) m/z calcd for $C_{12}H_{27}Si$ $(M - H)^+$ 199.1882, found 199.1888. Anal. Calcd for $C_{12}H_{28}Si$: C, 71.93; H, 14.10. Found: C, 72.03; H, 14.06.

Representative Oxidation Procedure: Oxidation of Cyclododecylphenyldimethylsilane 6c to Cyclododecanol. To a cooled (0 °C) solution of KH (0.335 g, 2.92 mmol, 35% dispersion in mineral oil washed with 3 × 5 mL of hexanes) in 1.5 mL of NMP was added *tert*-butyl hydroperoxide (90%, 0.320 mL, 2.90 mmol) dropwise. After the solution was warmed to 25 °C, a solution of **6c** (0.144 g, 0.476 mmol) in 3.0 mL of NMP was added dropwise. After 10 min, *n*-Bu_4NF (0.267 g, 1.02 mmol, hydrate lyophilized from benzene) was added. The reaction mixture was heated at 70 °C for 10 h. After the mixture was cooled to 25 °C, 1.0 g of $Na_2S_2O_3$ was added, followed by 3 mL of H_2O. The mixture was washed with 4 × 10 mL of *t*-BuOMe. The combined organic layers were washed with 4 × 1 mL of H_2O, 2 × 2 mL of NaOH, and 5 mL of brine, dried ($MgSO_4$), and concentrated *in vacuo* to afford a tan solid. Purification by flash chromatography (hexanes to 10:90 EtOAc/hexanes) afforded the product as a white solid (0.070 g, 80%). ^{1}H and ^{13}C NMR spectra, GC, and TLC were consistent with those of an authentic sample of cyclododecanol.

(1*R,2*S**,3*R**)-1-Phenyl-2-methyl-1,3-butanediol (2).** To a cooled (0 °C) solution of *tert*-butyl hydroperoxide (90%, 0.207 g, 2.30 mmol) in 1.3 mL of DMF was added $CsOH \cdot H_2O$ (0.331 g, 1.97 mmol). After the mixture was warmed to 25 °C, a solution of oxasilacyclopentane **1** (0.050 g, 0.164 mmol) in 0.8 mL of DMF was added dropwise by syringe. After 10 min, *n*-Bu_4NF (0.214 g, 0.82 mmol, hydrate, lyophilized from benzene) was added. The reaction mixture was heated at 75 °C for 8 h. After the mixture was cooled to 25 °C, $Na_2S_2O_3$ was added, and the solvent was removed *in vacuo*. The resultant oily solid was partitioned between 5 mL of H_2O and 10 mL of Et_2O. The layers were separated, and the aqueous layer was extracted with 2 × 10 mL of Et_2O. The combined organic layers were washed with 10 × 1 mL of H_2O and 5 mL of brine, dried ($MgSO_4$), and concentrated *in vacuo* to afford 0.057 g of a yellow oil. The oil was purified by flash chromatography (25:75 to 35:65 EtOAc/hexanes) to yield the product as a colorless oil (0.019 g, 64%): ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.36−7.24 (m, 5H), 5.04 (d, 1H, J = 1.7), 3.83 (quintet, 1H, J = 6.3) 3.15 (br s, 1H), 2.56 (br s, 1H), 1.84 (m, 1H), 1.31 (d, 3H, J = 6.2), 0.82 (d, 3H, J = 7.0); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 142.6, 128.0, 127.0, 126.1, 75.0, 70.9, 45.5, 21.9, 11.5; IR (thin film) 3355, 2975, 2896, 1453, 1380, 1199, 1144, 1102, 1072, 1000, 974, 926, 887, 742, 702 cm^{-1}; HRMS (CI/isobutane) m/z calcd for $(M + H)^+$ 181.1228, found 181.1225. Anal. Calcd for $C_{11}H_{16}O_2$: C, 73.30; H, 8.95. Found: C, 73.09; H, 9.04.

(1*R,2*S**,3*R**)-1,2-Dioxa-4,5-dimethyl-6-phenyl-2-di-*tert*-butylsilacyclohexane (3)**. Using the procedure given for **2** with oxasilacyclopentane **1** (0.050g, 0.164 mmol), *tert*-butyl hydroperoxide (90%, 0.080 mL, 0.740 mmol), KH (0.126 g, 0.820 mmol, 26% dispersion washed with 3 × 1 mL of hexanes), and *n*-Bu_4NF (0.043 g, 0.164 mmol) afforded the product as a white solid (0.028 g, 53%): mp 69−70 °C; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.21−7.36 (m, 5H), 5.48 (d, 1H, J = 2.7), 4.69 (dq, 1H, J = 6.4, 2.4), 1.82 (m, 1H), 1.23 (d, 3H, J = 6.7), 1.13 (s, 9H), 1.12 (s, 9H), 0.67 (d, 3H, J = 7.2); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 143.5, 127.9, 126.4, 125.2, 78.7, 73.3, 43.3, 28.8, 27.9, 23.6, 22.0, 20.8, 4.6; IR (KBr) 3064, 2970, 2861, 1474, 1449, 1388, 1366, 1209, 1155, 1004, 967, 846, 732, 651 cm^{-1}; HRMS (CI/isobutane) m/z calcd for $C_{19}H_{33}O_2Si$ $(M + H)^+$ 321.2250, found: 321.2249. Anal. Calcd for $C_{19}H_{32}O_2Si$: C, 71.18; H, 10.08. Found: C, 70.97; H, 9.98.

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Supporting Information Available: Preparation of silanes **4a**, **6b**, **6c**, and **6e**; experimental procedure for oxidation of **7** to **8** (3 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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