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Oxidation of Carbon–Silicon Bonds: The Dramatic Advantage of Strained Siletanes

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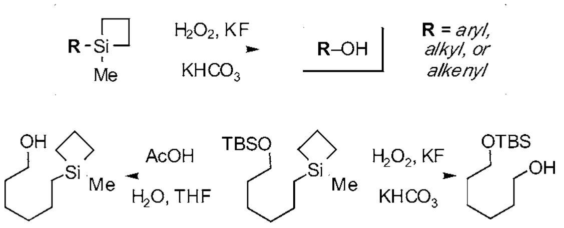
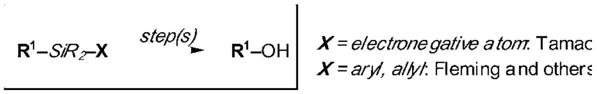
ABSTRACT



Herein we report on the use of siletanes as substrates for the oxidation of carbon–silicon bonds. These tetraalkylsilanes are easy to handle yet susceptible to rapid ring opening and oxidation upon exposure to aqueous fluoride and peroxide. This combination of stability and reactivity presents many practical benefits, including compatibility with silicon protecting groups and electron-rich aromatic rings.

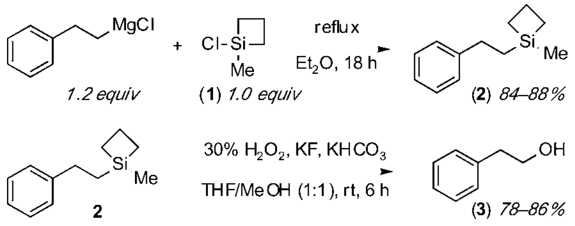
The Tamao oxidation of carbon−silicon bonds begat new uses of silicon in organic chemistry.[1] For this oxidation to occur, the silane must be further substituted with an electron-withdrawing heteroatom. Fleming showed that arylsilanes, which are compatible with a broader range of reaction conditions, serve as oxidation precursors via initial cleavage of the aryl group (Scheme 1).[2] The two-step Tamao−Fleming protocol has seen widespread use in organic chemistry,[3,4] particularly for the advantages inherent in employing silanes as latent hydroxyl groups.

Scheme 1. Tamao−Fleming Oxidation



Herein we report new substrates for the oxidation of carbon−silicon bonds that combine the high reactivity associated with heteroatom-substituted silanes with the ease of purification and handling of tetraalkylsilanes (Scheme 2). We also demonstrate their application to the synthesis of phenols and their orthogonality with silyl ether protecting

Scheme 2. Preparation and Oxidation of 1-Methyl-1-phenethylsiletane



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(1) Tamao, K.; Ishida, N.; Tanaka, T.; Kumada, M. *Organometallics* **1983**, *2*, 1694−1696. (b) Tamao, K.; Ishida, N.; Ito, Y.; Kumada, M. *Org. Synth.* **1990**, *69*, 96−105 and references therein.

(2) Fleming, I.; Henning, R.; Plaut, H. *J. Chem. Soc., Chem. Commun.* **1984**, 29−31. (b) Fleming, I.; Sanderson, P. E. J. *Tetrahedron Lett.* **1987**, *28*, 4229−4232. (c) Fleming, I.; Henning, R.; Parker, D. C.; Plaut, H.; Sanderson, P. E. J. *J. Chem. Soc., Perkin Trans. 1* **1995**, 317−337.

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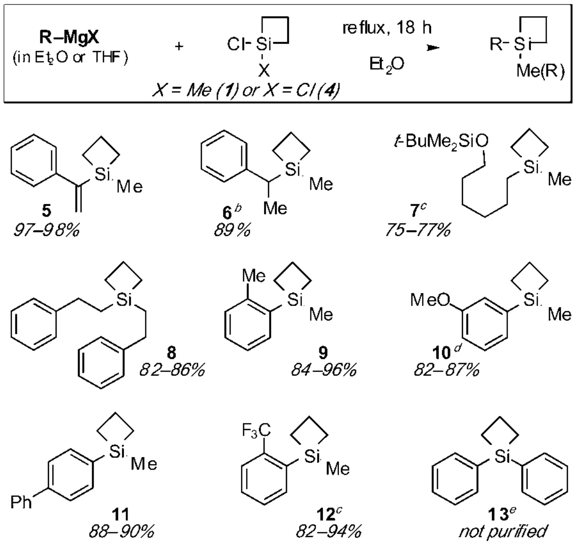
Scheme 3. Synthesis of Siletane Substrates[a]

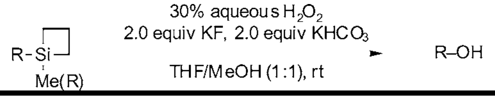


[a] See Supporting Information for details. Unless otherwise noted, substrates were prepared by treatment of 1.0 equiv of **1**[13] (0.5 equiv of **4**[13] for siletanes **8** and **13**) with 1.0−1.3 equiv of Grignard reagent and purified on silica gel. [b]Prepared by hydrogenation of **5** with diimide. [c]Prepared in THF at 40 °C. [d]1.1 equiv of siletane **1**, *t* = 2 h; yield based on Grignard. [e]Literature yield: 81%.[13b]

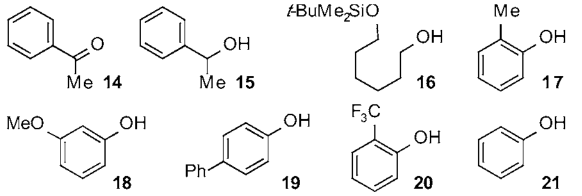
groups, two traditional limitations of carbosilane oxidation chemistry.

Siletanes (silacyclobutanes)[5] and other strained silacycles[6] have begun to receive more attention for their unique "strain-release" Lewis acidic properties. Mukaiyama aldol reactions[7] and aldehyde allylations,[8,9] for example, proceed in the absence of external catalysts when traditional silanes are replaced with siletanes. In a series of reports, Denmark revealed that siletanes also serve as precursors to silanols for Hiyama-type cross-coupling reactions,[5] and the ring strain has also been exploited to effect insertions (ring expansions) into siliranes[10] and siletanes,[11] respectively.

Table 1. Oxidation of Siletanes to the Corresponding Alcohols[a]



entry	siletane	time (h)	R–OH	yield (%)[b]
1	**2**	2	**3**	46[c]
2	**2**	5	**3**	62[c]
3	**2**	17	**3**	64[c]
4	**2**	6	**3**	78–86
5	**5**	6	**14**[d]	72–78
6	**6**	6	**15**	72–74
7	**7**	6	**16**	82–85
8	**8**	6	**3**	77–81
9	**9**	6	**17**	68–74
10	**10**	6	**18**	74–78
11	**11**	6	**19**	87–88
12	**12**	6	**20**	n.d.[e]
13	**13**	6	**21**	75–78[f]



[a] See Supporting Information for details. [b] Isolated yield of at least 100 mg of sample from two independent experiments unless noted. [c] Small-scale, exploratory experiments. [d] Obtained as keto tautomer (acetophenone). [e] Exact yield not determined due to volatility of the product alcohol. [f] Overall yield based on PhMgBr and siletane **4**.

In our nascent research program aimed at identifying novel applications of siletane chemistry, we have found that these stable, easy-to-handle silanes can be oxidized under remarkably mild conditions, *competitive with even the most reactive heteroatom-substituted silanes* (vide infra).

We prepared a series of siletanes as shown in Scheme 3. Yields were uniformly high and refer to purified material isolated following two independent experiments. Arenes with varying steric and electronic properties are easily introduced (**9**−**13**), as are alkyl (**2**, **7**−**8**) and alkenyl (**5**) groups. We obtained α-phenethylsiletane **6** by hydrogenation of **5**.[12]

Table 1 summarizes the oxidation of the siletanes. Oxidation occurs under the standard, mild conditions recommended by Tamao[1] for heteroatom-substituted silanes: aqueous hydrogen peroxide is added to the reaction mixture, which is stirred open to the air. In entries 1−4, siletane **2** was consumed shortly after addition of peroxide (but not immediately), and the yield of phenethyl alcohol (**3**) maximized within 6 h.[14]

In general, the alcohols were obtained in good yields. Entries 4 and 6−8 demonstrate the preparation of aliphatic alcohols. In entry 5, an alkenylsiletane (**5**) yields the corresponding ketone product (acetophenone, **14**). Entries 8 and 13 illustrate a more economical variant in which symmetrical siletanes provide two equivalents of the desired

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(3) Recent reviews: (a) Tamao, K. Oxidative Cleavage of the Carbon−Silicon Bond: Development, Mechanism, Scope, and Limitations. In *Advances in Silicon Chemistry*; Larson, G. L., Ed.; JAI Press: Greenwich, CT, 1996; Vol. 3, pp 1−62. (b) Fleming, I. *Chemtracts: Org. Chem.* **1996**, 1−64. (c) Jones, G. R.; Landais, Y. *Tetrahedron* **1996**, *52*, 7599−7662.

(4) For a recent example and leading references, see: Angelaud, R.; Landais, Y. *Tetrahedron* **2000**, *56*, 2025−2036.

(5) Denmark, S. E.; Sweis, R. F. *Acc. Chem. Res.* **2002**, *35*, 835−846 and references therein.

(6) Franz, A. K.; Woerpel, K. A. *Acc. Chem. Res.* **2000**, *33*, 813−820.

(7) Myers, A. G.; Kephart, S. E.; Chen, H. *J. Am. Chem. Soc.* **1992**, *114*, 7922−7923. (b) Denmark, S. E.; Griedel, B. D.; Coe, D. M.; Schnute, M. E. *J. Am. Chem. Soc.* **1994**, *116*, 7026−7043.

(8) Matsumoto, K.; Oshima, K.; Utimoto, K. *J. Org. Chem.* **1994**, *59*, 7152−7155.

(9) Leighton achieved enantioselective allylations using strained five-membered silacycles derived from chiral amino alcohols or diamines; see: (a) Kinnaird, J. W. A.; Ng, P. Y.; Kubota, K.; Wang, X.; Leighton, J. L. *J. Am. Chem. Soc.* **2002**, *124*, 7920−7921. (b) Kubota, K.; Leighton, J. L. *Angew. Chem., Int. Ed.* **2003**, *42*, 946−948. (c) Berger, R.; Rabbat, P. M. A.; Leighton, J. L. *J. Am. Chem. Soc.* **2003**, *125*, 9596−9597.

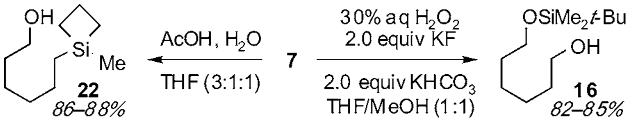
(10) Driver, T. G.; Franz, A. K.; Woerpel, K. A. *J. Am. Chem. Soc.* **2002**, *124*, 6524−6525.

(11) Takeyama, Y.; Oshima, K.; Utimoto, K. *Tetrahedron Lett.* **1990**, *31*, 6059−6062.

(12) Pasto, D. J.; Taylor, R. T. *Org. React.* **1991**, *40*, 91−155.

(13) Commercially available from Aldrich. (b) Auner, N.; Grobe, J. *J. Organomet. Chem.* **1980**, *188*, 25−52.

Scheme 4. Divergent Chemoselectivity of Silyloxyhexylsiletane **7**

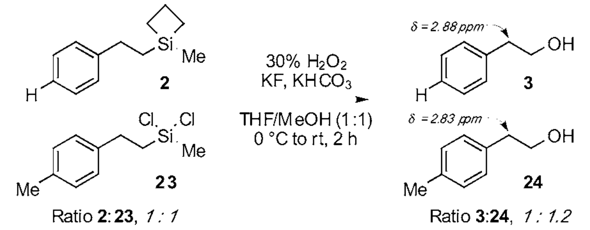


alcohols. Entries 9−13 cover the synthesis of phenols from a range of *ortho*-, *meta*-, and *para*-substituted arylsiletanes, including electron-rich (entry 10) and electron-deficient (entry 12) species.

Note that many of the more widely used Tamao−Fleming substrates require initial arene protonolysis (or other cleavage, e.g., with bromine) to set up the oxidation reaction.[3] This complicating factor must be addressed if one wishes to *oxidize* an aryl group.[15,16] That the siletanes readily give way to phenols with no evidence of arene protodesilylation[17] is a key feature of this chemistry. Indeed, phenol synthesis is not a trivial process, and this siletane oxidation may constitute an attractive option.

Entry 7 presents another key advantage of the siletane reagents: oxidation of a carbon−silicon bond in the presence of a silyl ether. To the best of our knowledge, such selectivity is unique for a tetraalkylsilane oxidation with Tamao's standard conditions.[18,19] In fact, although examples are known,[3] Tamao−Fleming protocols are rarely conducted in the presence of silyl ethers.[20] Furthermore, cleavage of the silyl ether with mild acid leaves the siletane untouched (Scheme 4). This selectivity would likely be impossible with the more labile heteroatom-substituted silanes required for the traditional Tamao oxidation.

Scheme 5. Competition between a Siletane and a Dichlorosilane



This remarkable *selectivity* inspired us to challenge the siletanes against heteroatom-substituted silanes in terms of *reactivity*. For the sake of comparison, we conducted the competition experiment outlined in Scheme 5. Phenethylsiletane **2** and (4-methylphenethyl)silyl dichloride **23** were mixed in equimolar ratios and subjected to the reaction conditions for 2 h.

Importantly, neither oxidation was complete within 2 h, at which time we analyzed the crude mixture by ^{1}H NMR spectroscopy. The observed ratio of product alcohols **3** and **24** (1:1.2) indicates that the oxidation of the siletane is virtually as fast as the analogous dichloride, despite being much less prone to incidental hydrolysis.

In conclusion, we report our initial findings on the facile oxidation of easy to handle siletanes. This chemistry, which merges the mildness and efficiency of the standard Tamao oxidation with the practicality of tetraalkylsilanes, capitalizes on the unique reactivity of strained silacycles. We are currently looking at a broader range of substrates, at alternative means of their preparation, and at employing the siletanes in multistep synthetic sequences. We will report our findings in due course.

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Supporting Information Available: Full experimental detail and characterization data for all compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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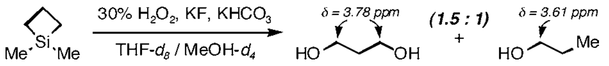
(14) The siletane ring reacts rapidly, followed by oxidation of the pendant alkyl groups. In a reaction monitored by ^{1}H NMR spectroscopy, 1,1-dimethylsiletane[13] was oxidized to propanediol and propanol in a 1.5:1 ratio. Presumably double oxidation of the siletane ring generates propanediol, whereas hydrolysis followed by oxidation produces propanol.



(15) For prior examples of arylsilane oxidations that yield phenols, see ref 4 and Suginome, M.; Matsunaga, S.; Ito, Y. *Synlett* **1995**, 941−942. (b) For a recent study on the protonolysis of arylsilanes, see: Utimoto, K.; Otake, Y.; Yoshino, H.; Kuwahara, E.; Oshima, K.; Matsubara, S. *Bull. Chem. Soc. Jpn.* **2001**, *74*, 753−754.

(16) Woerpel's anhydrous, basic conditions (*t*-BuOOH, KH, Δ) may effect arylsilane oxidations without initial arene protonolysis, although the isolation of phenols is not specifically mentioned: Smitrovich, J. H.; Woerpel, K. A. *J. Org. Chem.* **1996**, *61*, 6044−6046. We thank a referee for bringing this report to our attention.

(17) In particular, no evidence was found for the formation of anisole in entry 10 or biphenyl in entry 11 (TLC or ^{1}H NMR of crude reaction mixture).

(18) For the oxidation of a trialkylsilyl hydride with hydrogen peroxide in the presence of a silyl ether under more forcing conditions, see: Tamao, K.; Yamauchi, T.; Ito, Y. *Chem. Lett.* **1987**, 171−174. (b) 2-Pyridylsilanes can be oxidized with hydrogen peroxide by heating under similar conditions, but tolerance of silyl protecting groups has not been demonstrated; see: Itami, K.; Kamei, T.; Mitsudo, K.; Nokami, T.; Yoshida, J. *J. Org. Chem.* **2001**, *66*, 3970−3976.

(19) For examples of multistep, one-pot dearylation/oxidations, see: (a) Fleming, I.; Ghosh, S. K. *J. Chem. Soc., Chem. Commun.* **1992**, 1775−1777. (b) Hunt, J. A.; Roush, W. R. *J. Org. Chem.* **1997**, *62*, 1112−1124.

(20) For a detailed study in which tetraalkylsilanes ultimately proved incompatible with a silyl ether protecting group, see: Barrett, A. G. M.; Head, J.; Smith, M. L.; Stock, N. S.; White, A. J. P.; Williams, D. J. *J. Org. Chem.* **1999**, *64*, 6005−6018.