

# Photolabile arylsilyl group: application to the oxidation of C–Si bonds

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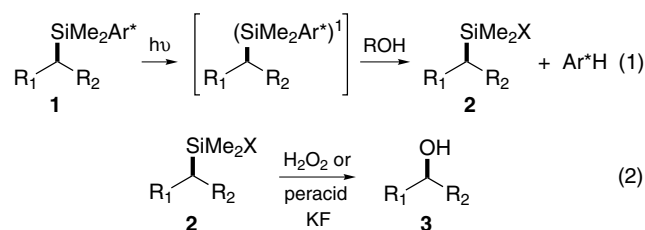
**Abstract**—(2,6-Dimethoxyphenyl)-dimethylsilyl group constitutes a new orthogonal masked hydroxyl group. Protodesilylation of this arylsilane occurs under photochemical conditions in the presence of alcohols such as hexafluoroisopropanol (HFIP) or isopropanol. These mild and neutral conditions thus allowed the oxidation of organosilicon compounds such as  $\beta$ -hydroxysilanes that are known to be prone to Peterson elimination.

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The oxidative cleavage of carbon–silicon bonds, discovered some twenty years ago is now part of the organic chemist armory and has enjoyed a widespread interest as illustrated by numerous examples in total synthesis of natural compounds.<sup>1,2</sup> The unmasking of a silicon group into the corresponding hydroxy group occurs with retention of configuration. The nature of the substituents at silicon dictates the outcome of the oxidation. Halo- and alkoxy-silanes are easily oxidized using  $H_2O_2$  in the presence of a fluorine source and such a transformation is usually compatible with many functionalities (Tamao conditions).<sup>1a,b</sup> Unfortunately, such organosilanes, although readily oxidized under mild conditions are sensitive, and not compatible with long synthetic sequences. In contrast, arylsilanes such as **1** are more robust and thus stable to a wide range of reaction conditions, but in turn, their oxidation requires more drastic conditions (Scheme 1).<sup>1c,d,2a</sup> Oxidation of arylsilanes is usually carried out through a two-step sequence involving a removal of the aryl group through protodesilylation, followed by peracid or  $H_2O_2$  oxidation of the remaining activated organosilanes **2** ( $X = F, OR, OAc, \dots$ ) (Fleming conditions). Protodesilylation which occurs under acidic conditions is usually the critical step, which may, depending on the substrate, lead to undesired by-products. Various solutions to this problem have been proposed, including the use of buffered conditions<sup>1d</sup> or the design of more labile arylsilanes.<sup>2b,c</sup>

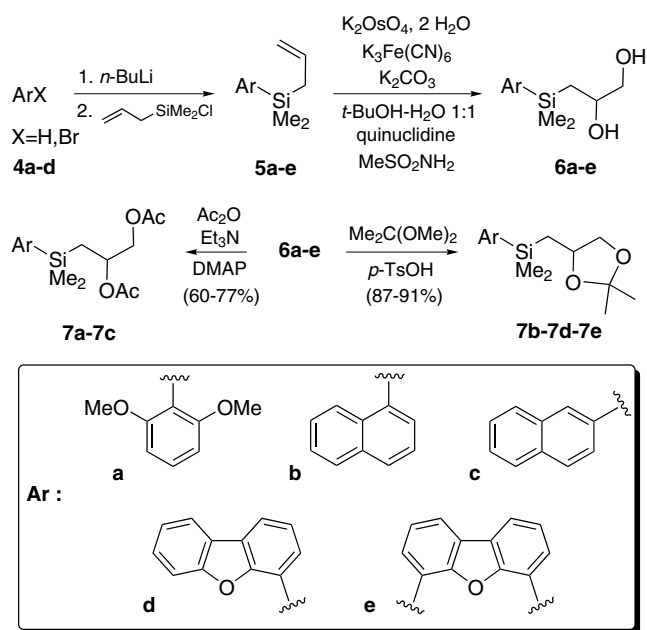
The need for new generation of masked hydroxyl groups thus prompts us to report here our preliminary studies on the development of arylsilane **1** that can be converted into **2** using light under neutral conditions (ROH).

While several photocleavable OH protecting groups have been developed,<sup>3</sup> oxidation of the C–Si bond based on a photochemical removal of a substituent at silicon (a furyl group) has been exploited only once by Kocienski et al.<sup>4</sup> to carry out a critical oxidation of the C–Si bond of an allylsilane. During this oxidation, the furyl group was lost upon photooxygenation. The methodology we planned to develop is quite different since the arene at silicon would be removed through photoprotonation and thus theoretically reusable. Based on some early work by Desvergne<sup>5</sup> and McClelland,<sup>6</sup> it was anticipated that light-sensitive aromatic groups ( $Ar^*$  in **1**) on the silicon center might be cleaved selectively through protodesilylation under photochemical activation in the presence of alcohols.<sup>7</sup> Using photoactivation, it was



Scheme 1.

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Scheme 2.

effectively shown that alcohols such as MeOH, *t*-BuOH or hexafluoroisopropanol (HFIP) were acidic enough to protonate an arene in its singlet excited state, and at the same time nucleophilic enough to finally form the alkoxy-silane intermediate **2** (Scheme 1, X = OR). The authors suggested that protodesilylation involved an associative process in which the cleavage of the C–Si bond and the formation of the Si–OR bond were concerted.

Several arenes **4a–d** were thus chosen as potent photolabile aryl silicon substituents (Scheme 2). Polynuclear arenes **4b–c** and heteroarenes **4d–e** were selected based on the known stability of their silicon derivatives and their UV absorption at longer wavelengths.  $\beta$ -hydroxysilanes were used as model compounds for our oxidation as their C–Si bond oxidation is often difficult, due to Peterson  $\beta$ -elimination<sup>8</sup> that may occur under both acidic and basic conditions.<sup>2a,b</sup>

Arenes **4a–d** were easily coupled through metallation with commercially available allyldimethylchlorosilane to provide the desired arylallylsilanes **5a–e** in good yield (Table 1).<sup>9</sup> With arene **4a**, metallation then silylation occurred regioselectively between the two methoxy groups.<sup>9a</sup> With dibenzofurane, mono- and bis-silylation occurred (i.e., **5d–e**), as reported, *ortho* to the furanyl group.<sup>9d</sup> Dihydroxylation of the latter under sharpless conditions<sup>10</sup> led to the corresponding diols **6a–e** that were then protected as their acetones **7b**, **7d–e** or bis-acetates **7a**, **7c**, using standard procedures.

Irradiation of precursors **7a–e** was carried out in quartz glassware using a medium pressure mercury lamp in various non degassed alcohols (distilled prior to irradiation) at room temperature under an air atmosphere. A cooling bath was generally used to maintain the temperature close to 20 °C. The product of the reaction was then simply recovered after evaporation of the solvent under reduced pressure. Preliminary experiments (Table 2, entries 1 and 2) were carried out using **7a**, which upon irradiation in HFIP, unexpectedly provided disiloxane **8a** (PG = OAc) and none of the desired alkoxy-silane, as indicated by <sup>1</sup>H NMR and mass spectrometry.<sup>11</sup> It is worthy of note that 1,3-dimethoxybenzene could also be recovered and may thus be recycled. In some cases, small amounts of silanol **9** (**9a**, PG = OAc) were detected, indicating that water was present in the medium.<sup>12</sup> Different attempts to remove water using 3 Å molecular sieves and a nitrogen atmosphere were however unsuccessful. On the contrary, addition of 10% (vol.) of water led to similar results, indicating that water likely catalyzes the formation of siloxane **8a**<sup>13</sup> through dimerization of silanol **9a** (PG = OAc).

Although we were able to recover expensive HFIP through distillation, other solvents were tested as possible alternatives. Isopropanol led to encouraging results (entries 4 and 5), although the reaction was much slower than that with HFIP. Methanol led to mixtures of **8a** and starting material (entry 3) and trifluoroethanol (entry 6) led to decomposition. Under these conditions,  $\alpha$ - and  $\beta$ -naphthylsilanes **7b** and **7c** led to no reaction

Table 1. Preparation of model compounds **5a–e** and **6a–e** (Scheme 2)

Entry	ArX	Conditions <sup>a</sup>	% Yield <sup>c</sup> <b>5a–e</b>	% Yield <sup>c</sup> <b>6a–e</b>
1	<b>4a</b> (X = H)	<i>n</i> -BuLi (1 equiv), TMEDA Hexane, 0 °C to rt, 22 h	<b>5a</b> (84)	<b>6a</b> (99)
2	<b>4b</b> (X = Br)	<i>t</i> -BuLi (2 equiv), THF –78 °C, 5 h	<b>5b</b> (75)	<b>6b</b> (98)
3	<b>4c</b> (X = Br)	<i>t</i> -BuLi (2 equiv), THF –78 °C, 5 h	<b>5c</b> (99)	<b>6c</b> (91)
4	<b>4d</b> (X = H)	<i>n</i> -BuLi (1 equiv), THF rt, <sup>b</sup> 22 h	<b>5d</b> (77) <sup>d</sup>	<b>6d</b> (100) <sup>f</sup>
5	<b>4d</b> (X = H)	<i>n</i> -BuLi (2 equiv), THF rt, <sup>b</sup> 22 h	<b>5e</b> (35) <sup>e</sup>	<b>6e</b> (95) <sup>f</sup>

<sup>a</sup> Allyldimethylchlorosilane was added after metallation and the reaction mixture stirred for the period reported above.

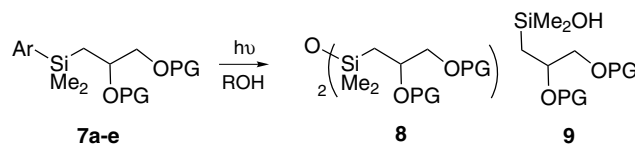
<sup>b</sup> The reaction mixture was refluxed after the addition of allyldimethylchlorosilane.

<sup>c</sup> Isolated yields unless otherwise mentioned.

<sup>d</sup> 11% of bis-silylated product **5e** was also isolated.

<sup>e</sup> 57% of monosilylated product **5d** was also isolated.

<sup>f</sup> Crude yield.

**Table 2.** Irradiation of model compounds **7a–e**

Entry	Arylsilane	ROH <sup>a</sup>	Time (h) <sup>b</sup>	% Yield <sup>c</sup>
1	<b>7a</b>	HFIP	14	<b>8a</b> (quant.)
2	<b>7a</b>	HFIP–MeOH (22 equiv)	44	<b>8a</b> (quant.)
3	<b>7a</b>	MeOH	26	— <sup>d</sup>
4	<b>7a</b>	<i>i</i> -PrOH	25	<sup>e</sup>
5	<b>7a</b>	<i>i</i> -PrOH	56	<b>8a</b> (quant.)
6	<b>7a</b>	CF <sub>3</sub> CH <sub>2</sub> OH	27	decomp.
7	<b>7b</b>	HFIP	48	<b>7b</b> (quant.)
8	<b>7c</b>	HFIP (40 equiv)–MeOH	26	<b>7c</b> (quant.)
9	<b>7d</b>	HFIP	28	<b>7d</b> (quant.)
10	<b>7e</b>	HFIP	28	<b>7e</b> (quant.)

<sup>a</sup> Arylsilanes **7a–e** were dissolved in the indicated solvent (C = 10–20 mmol/l) and irradiated at 20 °C using a medium pressure mercury lamp.

<sup>b</sup> Irradiation time.

<sup>c</sup> Crude yields after evaporation of the solvent.

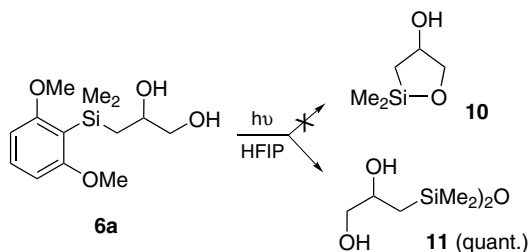
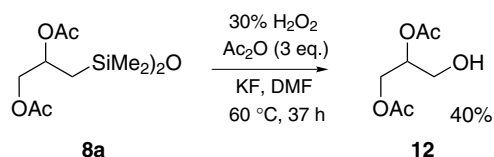
<sup>d</sup> A 56:44 mixture of **7a/8a** was estimated from <sup>1</sup>H NMR of the crude reaction mixture.

<sup>e</sup> A 58:42 mixture of **7a/8a** was estimated from <sup>1</sup>H NMR of the crude reaction mixture.

and surprisingly starting materials were recovered unchanged, whatever the conditions (entries 7 and 8). Similarly, dibenzofuranylsilanes **7d** and **7e** were also recovered unchanged after irradiation for 28 h in HFIP (entries 9 and 10).

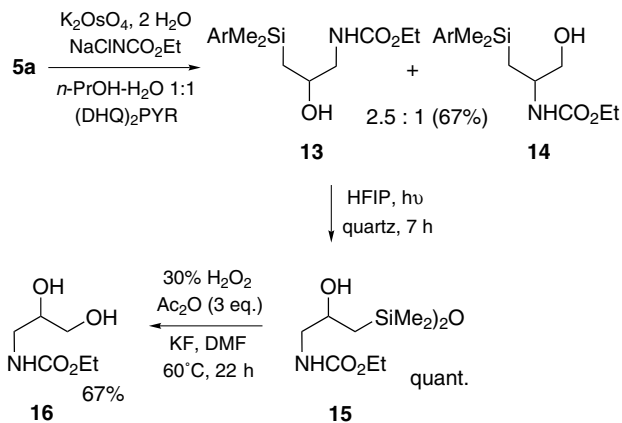
As water likely assists the protodesilylation<sup>6</sup> to form the silanol (i.e., **9**) which then dimerizes, it was decided to carry out the reaction on a precursor such as **6a**, having an hydroxyl group close to silicon that could approach the silicon center to form siloxane **10** and thus prevent the nucleophilic attack by water (Scheme 3). Irradiation of **6a** was thus carried out as above, but disiloxane **11** was the only product of the reaction with none of the expected cyclic siloxane **10** formed.

These results suggest that disiloxanes are the thermodynamically favored compounds due to the formation of two strong Si–O bonds. Therefore, it was decided to test the oxidation on **8a** as it is easily obtained in quantitative yield. Different conditions were thus tested that led consistently to complex mixtures of polysiloxanes. Finally, when the oxidation was conducted in the presence of acetic anhydride, 30% H<sub>2</sub>O<sub>2</sub> and KF in DMF,<sup>1a,b</sup> the desired alcohol **12** was obtained, albeit in modest yield (Scheme 4). The role of acetic anhydride is not clear. Siloxanes are difficult to oxidize and their

**Scheme 3.****Scheme 4.**

reactions under the usual Tamao conditions probably lead to siloxanes and polysiloxanes, through dimerization of silanols formed in situ. Acetic anhydride might react with the latter and thus prevent the formation of siloxanes, through the formation of acetoxysilanes which are easier to oxidize.

The study was then extended to related hydroxycarbamate **13** which is also prone to Peterson elimination. **13** was prepared from allylsilane **5a** using sharpless amino-hydroxylation (AA) protocol.<sup>14</sup> This led to a 2.5:1 mixture of regioisomers **13** and **14** (Scheme 5),

**Scheme 5.**

which were easily separated by chromatography.<sup>15</sup> **13** was then irradiated as above to provide disiloxane **15**<sup>16</sup> in quantitative yield. Oxidation of crude **15** under the optimized conditions above led to diol **16**<sup>15,17</sup> in a satisfying 67% yield.

These results thus unambiguously show that the 2,6-dimethoxyphenylsilyl group can be considered as a new potent masked hydroxyl group. It is stable under basic conditions and in mildly acidic medium.<sup>18</sup> It is cleaved under neutral conditions which should be compatible with the presence of other arylsilyl groups. One could then envisage a selective oxidation of this aryl group in the presence of other aryl dimethylsilanes such as PhMe<sub>2</sub>Si,<sup>2a,b</sup> *p*-TolMe<sub>2</sub>Si<sup>19</sup> or the recently developed (Ph<sub>2</sub>CH)Me<sub>2</sub>Si group.<sup>20</sup> Interestingly, when treated under buffered Fleming conditions<sup>1c,d</sup> (AcOOH, AcONa, KBr, rt, 88 h), **7a** led to **12** with only 50% conversion and did not produce the desired alcohol under Tamao conditions<sup>1a,b</sup> (30% H<sub>2</sub>O<sub>2</sub>, K<sub>2</sub>CO<sub>3</sub>, KF, THF–MeOH, rt, 73 h).

In summary, we devised a photolabile arylsilicon group that can be used for the C–Si bond oxidation. Protodesilylation occurs under neutral conditions, generating a siloxane that may then be oxidized under standard conditions. Our preliminary results demonstrate that the methodology is useful for the oxidation of acid and base sensitive organosilanes. Application of this sequence to more complex organosilanes is under way and will be reported in due course.

### Acknowledgements

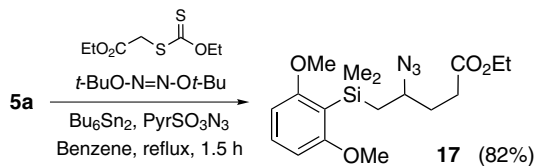
The authors gratefully acknowledged the CNRS, Région Aquitaine and the *Institut Universitaire de France* for financial support. We also thank Dr. Dario Bassani and Dr. Jean-Pierre Desvergne (Université Bordeaux I, ISM) for fruitful discussions.

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- Stirring of the organosilanes in HFIP in the absence of irradiation led to no reaction, indicating that the conjunction of alcohol and the irradiation was necessary for the protodesilylation to occur.
- Alkoxysilanes may be isolated under strictly anhydrous conditions,<sup>6</sup> which are not really suitable for preparative chemistry.
- General procedure for photoprotonation of 2,6-dimethoxyphenylsilyl group*: The solution of the arylsilane (0.3 mmol) in HFIP (14 ml) was irradiated over a period of 14 h. After evaporation of the solvent and 1,3-dimethoxybenzene, the crude siloxane was obtained as a yellow oil that was not purified further, but used directly in the next step. **8a**: <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>): δ 5.26–5.14 (m, 1H), 4.24–4.19 (m, 1H), 3.91 (dd, *J* = 7.0 Hz, 11.9 Hz, 1H), 2.02 (s, 3H), 2.00 (s, 3H), 1.01–0.86 (m, 2H), 0.11 (s, 3H), 0.09 ppm (s, 3H). <sup>13</sup>C NMR: (75.5 MHz, CDCl<sub>3</sub>): δ 170.8, 70.4, 69.6, 66.9, 21.3, 20.9, 20.8, 1.4, 0.9 ppm. MS (LSIMS, FAB<sup>+</sup>) *m/z*: 235 (34%); 265 (8%); 281 (6%); 413 (10%); 473 ([M+Na]<sup>+</sup>, 100%).
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- Compound 15*: <sup>1</sup>H NMR (250 MHz, CDCl<sub>3</sub>): δ 5.38 (br s, 1H), 4.08 (quart, *J* = 6.8 Hz, 2H), 3.94–3.90 (m, 1H), 3.33–3.24 (m, 1H), 3.03–2.91 (m, 1H), 1.21 (t, *J* = 7.0 Hz, 3H), 1.06–0.71 (m, 2H), 0.26 (d, 3H), 0.18–0.05 ppm (m, 3H). <sup>13</sup>C NMR: (75.5 MHz, CDCl<sub>3</sub>): δ 157.6, 68.8, 61.1, 49.6, 24.9, 14.7, 1.6, 1.2 ppm.
- General procedure for the disiloxane oxidation*: To a solution of disiloxane (0.2 mmol) in DMF (2.2 ml) was added at room temperature, KF (1 mmol) and then at 0 °C acetic anhydride (1 mmol) and a 30% aqueous solution of H<sub>2</sub>O<sub>2</sub> (10 mmol). The reaction mixture was stirred at 60 °C for 36 h, then quenched with a 25% Na<sub>2</sub>S<sub>2</sub>O<sub>3</sub> solution. After the addition of a 0.5% solution of HCl (5 ml), the reaction mixture was extracted with diethylether (3×) and dried over Na<sub>2</sub>SO<sub>4</sub>. Evaporation of the solvent in vacuo and purification of the residue by column chromatography led to the desired alcohol. *Compound 16*:<sup>15</sup> <sup>1</sup>H NMR (250 MHz, CDCl<sub>3</sub>): δ 5.56 (br s, 1H), 4.11 (quart,

$J = 7.0$  Hz, 2H), 3.95 (s, 1H), 3.74 (m, 2H), 3.65–3.49 (m, 2H), 3.37–3.16 (m, 2H), 1.23 ppm (t,  $J = 7.0$  Hz, 3H).  
 $^{13}\text{C}$  NMR: (62.4 MHz,  $\text{CDCl}_3$ ):  $\delta$  158.1, 71.4, 63.9, 61.4, 43.3, 14.7 ppm.

18. The 2,6-dimethoxyphenylsilyl group is also stable to thermal radical conditions as illustrated by the carboazidation of allylsilane **5a**:



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