Anilinosilanes/TBAF Catalyst: Mild and Powerful Agent for the Silylation of Sterically Hindered Alcohols

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Abstract: We developed an efficient method for the silylation of alcohols using anilinosilane with tetrabutylammonium fluoride (TBAF) catalyst, wherein TMS, TES and TBS groups were smoothly introduced into silylation-resistant hindered alcohols under mild conditions.

Key words: alcohols, silylation, anilinosilane, TBAF, catalyst

The silylation of alcohols is an essential process in the various organic synthesis fields, especially as the most reliable protective method.1 Silyl ethers are commonly obtained by the reacting parent alcohols with the corresponding trialkylsilyl halides or triflates in the presence of stoichiometric amounts of bases, such as trialkylamine and imidazole. Despite these well-established methods, there remains a need for improved efficiency in view of process chemistry and natural product synthesis. Our and Johnson’s groups independently reported a nearly neutral and effective method for silylation systems using silazanes,2a,3 hydrosilanes or disilanes2b together with catalytic tetrabutylammonium fluoride (TBAF). Silazanes are also efficient silylation agents for alcohols or phenols promoted by the PyH+·OTf– catalyst,4 and for ketones or aldehydes giving enol silyl ethers catalyzed by NaH or DBU.5

Consistent with the study of these mild, catalytic, and practical silylations systems, we report herein a nearly neutral and powerful method utilizing a novel agent, anilinosilanes 1–TBAF catalyst (Scheme 1). The present method covers three types of silylation (TMS, TES, TBS) against sterically uncrowded and crowded alcohols under mild conditions.

Initially, trimethylsilylation was examined using 1-octanol to check the inherent reactivity of several available silazanes with gas chromatography monitoring. (Table 1, Method A). Silazanes are placed in the order of reactivity (entries 1–14) except anilinotrimethylsilane 1a (entries 15 and 16). Next, comparable experiment was guided using very sterically crowded (silylation-resistant) terpine-4-ol in the presence of TBAF catalyst (0.02 equiv) (Method B), because this catalytic method was generally very powerful due to the utilization of reactive hypervalent silicate intermediates.2a Scheme 2 illustrates the relative order of reactivity of methods A and B. It should be noted that this order is not necessarily same and the case using 1a exhibits clear contrast. This result indicates that TBAF acts as a highly effective trigger for the present trimethylsilylation using 1a (the reaction completed within 30 min even at –20°C (entry 16).

Scheme 1

Scheme 2
Anilinosilanes 1 are commercially available (TMS; 1a) or easily prepared (TES; 1b and TBS; 1c) by the reported method6 from aniline and the corresponding hydrosilanes with a Pd/C catalyst in good yields (Scheme 3).

Scheme 3

This hydrosilylation method to give 1b and 1c was originally utilized for silyl protection of amino groups and performed in gram-scale preparation. TBS analog 1c is considerably moisture-insensitive (see experimental section).

Table 2 lists the results of the silylations (TMS, TES, and TBS) for various alcohols. Not only primary and secondary alcohols, but also sterically crowded tertiary alcohols were successfully silylated in good to excellent isolated yields (entries 1–20). Cl atom, THP and methyl ester functions tolerated the reaction conditions (entries 21–26). p-Cresol was also trimethylsilylated, however, with a much lower reaction speed (entry 27). TES and TBS were not introduced into p-cresol.

A plausible reaction mechanism is shown in Scheme 4, which is similar to a previously reported method.2a The TBAF catalyst first attacks the anilinosilane to form the reactive pentavalent silicate A,7 which in turn condenses with an alcohol to form alkoxy(fluoro)silicate B with eliminating aniline. The fluoride anion is transferred from B to the remaining anilinosilane to release the silyl ether by reforming A. A slight excess of anilinosilane completes the catalytic cycle.

In conclusion, we developed a mild, practical, and powerful method for the preparation of various silyl (TMS, TES, TBS) ethers using readily available anilinosilanes and catalytic TBAF.

NMR spectra were recorded on a JEOL DELTA 300 spectrometer, operating at 300 MHz for 1H NMR and 75 MHz for 13C NMR. Chemical shifts (δ) in CDCl3 are reported downfield from TMS (0 ppm) or CHCl3 (7.26 ppm) for 1H NMR. For 13C NMR, chemical shifts (δ) were reported in the scale relative to CDCl3 (77.00 ppm) as an internal reference. IR spectra were recorded on JASCO FT/IR-5300 spectrophotometer. Flash column chromatography analyses were performed with silica gel Merck 60 (230–400 mesh ASTM) according to the method of Still.8 GC data were obtained on a Simazu GC-17A [column: Widebore DB-1701; Φ: 0.53 mm × 30 m; oven temperature: 50 °C–250 °C (20 °C/min); injection/detection (FID) temperature: 250 °C; carrier gas: N2].

**Anilinotriethylsilane (1b)**

Aniline (5.0 g, 50 mmol) and Et3SiH (7.6 g, 65 mmol) were successively added to a stirred suspension of 10% Pd-C (3.5 g, 2.5 mmol) in toluene (100 mL) at 25 °C under an Ar atmosphere. After stirring at reflux for 12 h, the mixture was filtered through the celite with glass filter and the filtrate was concentrated in reduced pressure. The obtained crude product was purified by distillation to give the...
Table 2  Silylations of Various Alcohols Using Anilinosilanes (1a,b,c) with TBAF Catalyst

<table>
<thead>
<tr>
<th>Entry</th>
<th>Alcohol</th>
<th>Anilinosilane</th>
<th>Time (min)</th>
<th>Silyl ether</th>
<th>Yield (%)a</th>
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<td>5</td>
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<td>2a 96</td>
</tr>
<tr>
<td>2</td>
<td>ROH</td>
<td>1b</td>
<td>5</td>
<td>ROH OSi</td>
<td>2b 96</td>
</tr>
<tr>
<td>3</td>
<td>ROH</td>
<td>1c</td>
<td>5</td>
<td>ROH OSi</td>
<td>2c 99</td>
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<tr>
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<td>5</td>
<td>ROH OSi</td>
<td>3a 96</td>
</tr>
<tr>
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<td>3b 94</td>
</tr>
<tr>
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<td>1a</td>
<td>210</td>
<td>ROH OSi</td>
<td>14a 81b</td>
</tr>
</tbody>
</table>

a Isolated yield.

b Anilinosilane 1a (2.5 equiv) was used.

desired product (9.44 g, 91%); colorless oil; bp 96–97 °C/2.1 mmHg.
IR (neat): 3381, 2953, 1601, 1499, 1292, 889 cm–1.
1H NMR (300 MHz, CDCl3): δ = 0.72–0.82 (m, 6 H), 0.94–1.03 (m, 9 H), 3.34 (br s, 1 H), 6.65–6.74 (m, 3 H), 7.10–7.18 (m, 2 H).
13C NMR (75 MHz, CDCl3): δ = 4.63, 7.00, 116.03, 117.35, 129.18, 147.73.
Anal. Calcd for C12H21NSi: C, 69.5; H, 10.2; N, 6.8. Found: C, 69.1; H, 9.9; N, 6.6.

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Anilinos(tert-butyldimethyl)silane (1c)

Colorless oil.
IR (neat): 3399, 2955, 1603, 1499, 1292, 897 cm–1.
1H NMR (300 MHz, CDCl3): δ = 0.27 (s, 6 H), 0.98 (s, 9 H), 3.34 (br s, 1 H), 6.62–6.77 (m, 3 H), 7.09–7.20 (m, 2 H).
13C NMR (75 MHz, CDCl3): δ = –4.23, 17.95, 26.37, 116.54, 117.52, 129.14, 147.65.
Silylations of 1-Octanol Using Anilinotrimethylsilane (1a); Typical Procedure
TBAF (1 M THF solution; 0.02 mL, 0.02 mmol) was added to a stirred solution of 1-octanol (130 mg, 1.0 mmol) and PhNHTMS (1a; 248 mg, 1.5 mmol) in DMF (2.0 mL) at 20–25 °C under an Ar atmosphere. After stirring at the same temperature for 5 min, the mixture was quenched with water (5.0 mL), which was extracted with Et2O. The combined organic phase was washed with water, brine, dried (Na2SO4) and concentrated. The obtained crude product was purified by SiO2 column chromatography (hexane) to give 1-(trimethylsiloxy)octane (2a)11 (194 mg, 96%); colorless oil.

IR (neat): 1260, 1095, 845, 785 cm–1.

1H NMR (300 MHz, CDCl3): δ = 0.46 (m, 10 H), 3.72–3.82 (m, 1 H).

13C NMR (75 MHz, CDCl3): δ = 13.45, 26.02, 26.37, 39.52, 60.35, 124.12, 124.42, 131.52, 136.83.

1-(Triethylsiloxy)octane (2b)11
Colorless oil.

IR (neat): 1475, 1245, 1105, 1015 cm–1.

1H NMR (300 MHz, CDCl3): δ = 0.80 (t, J = 6.5 Hz, 3 H), 0.86–0.99 (m, 3 H), 0.96 (t, J = 7.9 Hz, 9 H), 1.19–1.38 (m, 10 H), 1.47–1.58 (m, 2 H), 3.59 (t, J = 6.5 Hz, 2 H).

13C NMR (75 MHz, CDCl3): δ = 4.45, 6.76, 14.09, 22.68, 25.85, 29.33, 29.45, 31.85, 32.96, 63.00.

1-(tert-Butyldimethylsiloxy)octane (2c)12
Colorless oil.

IR (neat): 2932, 1464, 1253, 1101, 846, 783 cm–1.

1H NMR (300 MHz, CDCl3): δ = 0.05 (s, 6 H), 0.87–0.91 (m, 3 H), 0.88 (s, 9 H), 1.24–1.33 (m, 10 H), 1.46–1.56 (m, 2 H), 3.60 (t, J = 6.5 Hz, 2 H).

13C NMR (75 MHz, CDCl3): δ = 5.24, 14.11, 18.39, 22.68, 25.70, 26.00, 29.33, 29.43, 31.85, 32.91, 63.37.

2-(Trimethylsiloxy)octane (3a)13
Colorless oil.

IR (neat): 2930, 2858, 1250, 1082, 841 cm–1.

1H NMR (300 MHz, CDCl3): δ = 0.11 (s, 9 H), 0.85–0.91 (m, 3 H), 1.12 (d, J = 6.2 Hz, 3 H), 1.19–1.46 (m, 10 H), 3.70–3.80 (m, 1 H).

13C NMR (75 MHz, CDCl3): δ = 0.25, 14.09, 22.66, 23.90, 25.97, 29.35, 31.91, 39.66, 68.61.

2-(Triethylsiloxy)octane (3b)11
Colorless oil.

IR (neat): 2957, 1460, 1075, 1013, 739 cm–1.

1H NMR (300 MHz, CDCl3): δ = 0.59 (q, J = 7.9 Hz, 6 H), 0.85–0.99 (m, 3 H), 0.96 (t, J = 7.9 Hz, 9 H), 1.13 (d, J = 6.2 Hz, 3 H), 1.23–1.41 (m, 10 H), 3.72–3.82 (m, 1 H).

13C NMR (75 MHz, CDCl3): δ = 4.69, 6.88, 14.09, 22.64, 23.84, 25.81, 29.41, 31.91, 39.87, 68.53.

2-(tert-Butyldimethylsiloxy)octane (3c)12
Colorless oil.

IR (neat): 1260, 1095, 845, 785 cm–1.

1H NMR (300 MHz, CDCl3): δ = 0.05 (s, 6 H), 0.86–0.90 (m, 3 H), 0.89 (s, 9 H), 1.11 (d, J = 6.2 Hz, 3 H), 1.24–1.46 (m, 10 H), 3.71–3.82 (m, 1 H).

13C NMR (75 MHz, CDCl3): δ = 4.45, 6.79, 32.14, 34.47, 62.14, 125.64, 128.26, 128.42, 142.24.
1-(tert-Butyldimethylsiloxy)-3-phenylpropane (6c)

Colorless oil.
1H NMR (300 MHz, CDCl3): δ = 0.06 (s, 6 H), 0.92 (s, 3 H), 1.80–1.89 (m, 2 H), 2.66–2.71 (m, 2 H), 3.64 (t, J = 6.5 Hz, 2 H), 7.15–7.31 (m, 5 H).

13C NMR (75 MHz, CDCl3): δ = –5.28, 18.33, 25.97, 32.10, 34.47, 62.37, 125.66, 128.26, 128.47, 142.28.

3,7-Dimethyl-3-(trimethylsiloxy)-1,6-octadiene (7a)

Colorless oil.
1H NMR (300 MHz, CDCl3): δ = 0.12 (s, 9 H), 1.29 (s, 3 H), 1.42–1.52 (m, 4 H), 1.67 (s, 3 H), 1.70–1.81 (m, 2 H), 3.56 (t, J = 6.9 Hz, 2 H), 3.54 (t, J = 6.9 Hz, 2 H).

13C NMR (75 MHz, CDCl3): δ = –0.48, 28.77, 32.18, 33.89, 36.14, 75.52, 119.34, 133.49.

1-((tert-Butyldimethylsiloxy)-3-methyl-1-isopropyl-4-phenyltricyclo[3.3.1.1^3.7]decane (9a)

Colorless oil.
1H NMR (300 MHz, CDCl3): δ = 0.01 (s, 3 H), 0.08 (s, 3 H), 0.89 (s, 3 H), 1.80–1.89 (m, 2 H), 2.66–2.71 (m, 2 H), 3.64 (t, J = 6.5 Hz, 2 H), 7.15–7.31 (m, 5 H).

13C NMR (75 MHz, CDCl3): δ = 0.10 (s, 18 H), 1.27–1.34 (m, 8 H), 1.57–1.60 (m, 6 H), 2.57, 26.80, 31.74, 133.49.

8-Chloro-1-(tert-butyldimethylsiloxy)ocetane (10a)

Colorless oil.
1H NMR (300 MHz, CDCl3): δ = 0.01 (s, 6 H), 0.89 (s, 3 H), 1.25–1.55 (m, 10 H), 1.71–1.81 (m, 2 H), 3.56 (t, J = 6.5 Hz, 2 H), 3.54 (t, J = 6.9 Hz, 2 H).

13C NMR (75 MHz, CDCl3): δ = –0.48, 28.77, 32.18, 33.89, 36.14, 75.52, 119.34, 133.49.

1,8-Bis(trimethylsiloxy)octane (11a)

Colorless oil.
1H NMR (300 MHz, CDCl3): δ = 0.10 (s, 18 H), 1.27–1.34 (m, 8 H), 1.45–1.58 (m, 4 H), 3.56 (t, J = 6.5 Hz, 4 H).

13C NMR (75 MHz, CDCl3): δ = –0.48, 28.77, 32.18, 33.89, 36.14, 75.52, 119.34, 133.49.
1-Methyl-6-(tert-butylidimethylsiloxy)hexanoate (13c)\textsuperscript{29}

Colorless oil.

IR (neat): 2961, 1613, 1510, 1250, 918, 845 cm\textsuperscript{-1}.

\textsuperscript{1}H NMR (300 MHz, CDCl\textsubscript{3}): \(\delta = 0.04\) (s, 6 H), 0.89 (s, 9 H), 1.22–1.41 (m, 2 H), 1.46–1.69 (m, 4 H), 2.31 (t, \(J = 7.6\) Hz, 2 H), 3.60 (t, \(J = 6.5\) Hz, 2 H), 3.66 (s, 3 H).

\textsuperscript{13}C NMR (75 MHz, CDCl\textsubscript{3}): 26.44, 33.92, 51.44, 62.95, 174.19.

4-Methyl-1-(trimethylsiloxy)benzene (14a)\textsuperscript{30}

Colorless oil.

IR (neat): 2955, 2932, 2361, 1746, 1472, 1256, 1073, 837 cm\textsuperscript{-1}.

\textsuperscript{1}H NMR (300 MHz, CDCl\textsubscript{3}): \(\delta = -5.30, 18.34, 24.78, 25.43, 25.95, 32.45, 34.09, 51.44, 62.95, 174.19\).

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References