Mild and Selective Deprotection of tert-Butyl(dimethyl)silyl Ethers with Catalytic Amounts of Sodium Tetrachloroaurate(III) Dihydrate

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Abstract  
A simple and mild method for the removal of tert-butyl(dimethyl)silyl (TBS) protecting groups with catalytic amounts of sodium tetrachloroaurate(III) dihydrate is described. The procedure permits selective deprotection of aliphatic TBS ethers in good to excellent yields in the presence of aromatic TBS ethers, aliphatic triisopropylsilyl ethers, aliphatic tert-butyl(diphenyl)silyl ethers, or sterically hindered aliphatic TBS ethers. Additionally, TBS ethers can also be transformed into 4-methoxybenzyl ethers or methyl ethers in one pot by using larger quantities of the catalyst and a higher reaction temperature.

Key words  
deprotection, silyl ethers, alcohols, ethers, catalysis, gold

Protection/deprotection strategies play important roles in modern organic synthesis.1,2 The tert-butyl(dimethyl)silyl (TBS) group is one of the most widely used protecting groups for alcohols because of its easy installation, its stability to various reaction conditions, and the selectivity of its cleavage reaction. Numerous methods are available for removal of TBS groups3–9 including the use of acidic,4 basic,5 reducing,6 oxidizing,7 or fluoride-based reagents8 among others.9 However, new mild and selective protocols for the deprotection of TBS ethers are still in great demand for use in syntheses of multifunctional compounds, particularly complex natural products.

Commercially available sodium tetrachloroaurate(III) dihydrate (NaAuCl4·2H2O) is the least expensive gold catalyst and has been used in several types of reaction, including nucleophilic addition to multiple bonds,10–13 nucleophilic substitution of propargylic alcohols,14,15 nonsymmetrical etherization,16 and others.17,18 In the course of an ongoing total-synthesis project, we serendipitously found that the TBS protecting group was cleanly removed in the presence of a small amount of NaAuCl4·2H2O. Inspired by this observation, we explored the possibility of using NaAuCl4·2H2O as an effective catalyst for the deprotection of TBS ethers.

First, we evaluated the effects of the solvent and the catalyst loading on the gold(III)-catalyzed desilylation of the TBS ether of 6-(benzyloxy)hexan-1-ol (Table 1). In the presence of 0.01 equivalents of sodium tetrachloroaurate(III) in methanol, deprotection of the TBS ether proceeded smoothly to give the corresponding alcohol in 95% yield after 3.5 hours at room temperature (Table 1, entry 1). The cleavage also proceeded in other polar solvents, but yields were much lower (entries 2–4). Alcohol was still obtained in excellent yields and in reasonable reaction times when the amount of catalyst was reduced to 0.005, 0.001, or even 0.0005 equivalents, (entries 5–7), but the desilylation became sluggish when 0.0001 equivalents of the catalyst were used (entry 8).

Next, we synthesized various aliphatic and aromatic TBS ethers to examine the substrate scope of our deprotection method. The deprotection reaction of the primary TBS

Table 1 Optimization of Conditions for the Sodium Tetrachloroaurate(III) Catalyzed Deprotection of TBS Ether 1

<table>
<thead>
<tr>
<th>Entry</th>
<th>Catalyst (equiv)</th>
<th>Solvent</th>
<th>Time (h)</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0.01</td>
<td>MeOH</td>
<td>3.5</td>
<td>95</td>
</tr>
<tr>
<td>2</td>
<td>0.01</td>
<td>THF</td>
<td>12</td>
<td>73</td>
</tr>
<tr>
<td>3</td>
<td>0.01</td>
<td>MeCN</td>
<td>12</td>
<td>53</td>
</tr>
<tr>
<td>4</td>
<td>0.01</td>
<td>acetone–H2O (1:1 v/v)</td>
<td>12</td>
<td>40</td>
</tr>
<tr>
<td>5</td>
<td>0.005</td>
<td>MeOH</td>
<td>7</td>
<td>96</td>
</tr>
<tr>
<td>6</td>
<td>0.001</td>
<td>MeOH</td>
<td>12</td>
<td>95</td>
</tr>
<tr>
<td>7</td>
<td>0.0005</td>
<td>MeOH</td>
<td>36</td>
<td>93</td>
</tr>
<tr>
<td>8</td>
<td>0.0001</td>
<td>MeOH</td>
<td>36</td>
<td>25 (72%)</td>
</tr>
</tbody>
</table>

**With respect to the substrate 1.  
* Isolated yield of pure product.  
+ Recovery of substrate 1.

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ethers was conducted in the presence of 0.001–0.005 equivalents of sodium tetrachloroaurate(III) dihydrate in methanol at room temperature. Primary TBS ethers containing electron-donating or electron-withdrawing groups were readily deprotected to give the corresponding alcohols in high yields (Table 2, entries 1–5). Secondary and tertiary TBS ethers were also desilylated smoothly, although longer reaction times or greater catalyst loadings were required (entries 6 and 7). Although sodium tetrachloroaurate(III) dihydrate catalyzes addition reactions of alkenes or alkynes,10–13 the TBS protecting group of compound 9 was removed successfully under the current condition without any effect on the double bond (entry 8). Aromatic TBS ethers are usually deprotected by treatment with basic reagents or fluoride-based reagents that frequently produce unwanted side reactions, such as silyl migration.19 Gratifyingly, the cleavage of aromatic TBS ethers proceeded well in the presence of 0.05–0.1 equivalents of the catalyst in methanol at room temperature. Aromatic TBS ethers bearing electron-donating groups were much more reactive than those bearing electron-withdrawing groups (entries 9–12).

Next, we examined the selective deprotection of TBS ethers containing various sensitive functional groups under the optimized conditions (Table 3). On treatment with 0.005 equivalents of sodium tetrachloroaurate(III) dihydrate in methanol at room temperature, the TBS group in substrates 14–18 was selectively removed, whereas other

<table>
<thead>
<tr>
<th>Entry</th>
<th>Substrate</th>
<th>Catalyst (equiv)</th>
<th>Time (h)</th>
<th>Product</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>R = H (2)</td>
<td>0.005</td>
<td>8</td>
<td>R = H (2′)</td>
<td>95</td>
</tr>
<tr>
<td>2</td>
<td>R = OMe (3)</td>
<td>0.001</td>
<td>4</td>
<td>R = OMe (3′)</td>
<td>94</td>
</tr>
<tr>
<td>3</td>
<td>R = CF₃ (4)</td>
<td>0.005</td>
<td>15</td>
<td>R = CF₃ (4′)</td>
<td>91</td>
</tr>
<tr>
<td>4</td>
<td>OTBS</td>
<td>0.005</td>
<td>8</td>
<td>OH</td>
<td>97</td>
</tr>
<tr>
<td>5</td>
<td>OTBS</td>
<td>0.005</td>
<td>2</td>
<td>OH</td>
<td>96</td>
</tr>
<tr>
<td>6</td>
<td>OTBS</td>
<td>0.01</td>
<td>24</td>
<td>OH</td>
<td>92</td>
</tr>
<tr>
<td>7</td>
<td>OTBS</td>
<td>0.05</td>
<td>40</td>
<td>OH</td>
<td>93</td>
</tr>
<tr>
<td>8</td>
<td>OTBS</td>
<td>0.005</td>
<td>12</td>
<td>OH</td>
<td>86</td>
</tr>
<tr>
<td>9</td>
<td>R = All; R² = OMe (10)</td>
<td>0.05</td>
<td>7</td>
<td>R = All; R² = OMe (10′)</td>
<td>87</td>
</tr>
<tr>
<td>10</td>
<td>R = t-Bu; R² = OMe (11)</td>
<td>0.05</td>
<td>24</td>
<td>R = t-Bu; R² = OMe (11′)</td>
<td>92</td>
</tr>
<tr>
<td>11</td>
<td>R = NHAc; R² = OMe (12)</td>
<td>0.05</td>
<td>48</td>
<td>R = NHAc; R² = OMe (12′)</td>
<td>86</td>
</tr>
<tr>
<td>12</td>
<td>R = Ac; R² = H (13)</td>
<td>0.1</td>
<td>48</td>
<td>R = Ac; R² = H (13′)</td>
<td>21 (67%)</td>
</tr>
</tbody>
</table>

* With respect to the substrate.

* Isolated yield of pure product.

### Table 3 Selective Deprotection of Various Silyl Ethers Catalyzed by Sodium Tetrachloroaurate(III) in Methanol

<table>
<thead>
<tr>
<th>Entry</th>
<th>Substrate</th>
<th>Catalyst (equiv)</th>
<th>Time (h)</th>
<th>Product</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>R = All (14)</td>
<td>0.005</td>
<td>5</td>
<td>R = All (14')</td>
<td>95</td>
</tr>
<tr>
<td>2</td>
<td>R = Ac (15)</td>
<td>0.005</td>
<td>2</td>
<td>R = Ac (15')</td>
<td>94</td>
</tr>
<tr>
<td>3</td>
<td>R = MOM (16)</td>
<td>0.005</td>
<td>4</td>
<td>R = MOM (16')</td>
<td>97</td>
</tr>
<tr>
<td>4</td>
<td>R = MEM (17)</td>
<td>0.005</td>
<td>4</td>
<td>R = MEM (17')</td>
<td>95</td>
</tr>
<tr>
<td>5</td>
<td>ROOTBS</td>
<td>0.005</td>
<td>11</td>
<td>ROOH</td>
<td>96</td>
</tr>
<tr>
<td>6</td>
<td>TBDPSOOTBS</td>
<td>0.005</td>
<td>3</td>
<td>TBDPSOH</td>
<td>96</td>
</tr>
<tr>
<td>7</td>
<td>TBDPSOOTBS</td>
<td>0.005</td>
<td>7</td>
<td>TBDPSOH</td>
<td>97</td>
</tr>
<tr>
<td>8</td>
<td>TIPSOOTBS</td>
<td>0.005</td>
<td>2</td>
<td>TIPSOH</td>
<td>83 (7)c</td>
</tr>
<tr>
<td>9</td>
<td>TIPSOOTBS</td>
<td>0.005</td>
<td>7</td>
<td>TIPSOH</td>
<td>86 (5)c</td>
</tr>
<tr>
<td>10</td>
<td>TESOOTBS</td>
<td>0.001</td>
<td>0.5</td>
<td>TESOH</td>
<td>86 (8)c</td>
</tr>
<tr>
<td>11</td>
<td>TESOOTBS</td>
<td>0.001</td>
<td>1</td>
<td>TESOH</td>
<td>77 (18)c</td>
</tr>
<tr>
<td>12</td>
<td>TBSOOTBS</td>
<td>0.005</td>
<td>5</td>
<td>TBSOH</td>
<td>92</td>
</tr>
<tr>
<td>13d</td>
<td>ROOTBS</td>
<td>0.005</td>
<td>40</td>
<td>ROOH</td>
<td>93</td>
</tr>
<tr>
<td>14</td>
<td>TBSOOTBS</td>
<td>0.005</td>
<td>7</td>
<td>TBSOH</td>
<td>82 (9)c</td>
</tr>
<tr>
<td>15</td>
<td>TBSOOTBS</td>
<td>0.005</td>
<td>5</td>
<td>TBSOH</td>
<td>86 (5)c</td>
</tr>
</tbody>
</table>

---

*a* With respect to the substrate.

*b* Isolated yield of pure product.

*c* Yield of diol.

*d* EtOAc–MeOH (1:1, v/v) was used as the solvent.
common acid-labile protecting groups such as allyl, acetyl, methoxymethyl, (2-methoxyethoxy)methyl, and isopropyldiene were unaffected (Table 3, entries 1–5). The catalyst also showed good selectivity to various silyl protecting groups. Preferential cleavage of TBS ether groups in the presence of tert-butyl(diphenyl)silyl (TBDS) ether groups gave the monodeprotected products in high yields, and the corresponding diols were not obtained (entries 6 and 7). When a less-bulky trisopropylsilyl group (compared with TBDPS) and a TBS group were present together, the deprotection was less selective, but the desired monoalcohols were still obtained as the major products (≥83% yield) (entries 8 and 9). Moderate selectivity between triethylsilyl and TBS protecting groups was achieved by using 0.001 equivalents of the catalyst (entries 10 and 11). An aliphatic TBS ether group was selectively removed in the presence of tert-butyl(diphenyl)silyl (TBDS) ethers (entries 13–15). In all cases, the less-hindered one in good to excellent yield; this makes our method very useful in total syntheses of complicated, multifunctional, or sensitive molecules. In addition, by using larger amounts of catalyst and higher reaction temperatures, TBS ethers can also be transformed into 4-methoxybenzyl or methyl ethers in a one-pot process.

In conclusion, we have developed an effective protocol for the deprotection of TBS ethers by using a very small amount of sodium tetrachloroaurate(III) dihydrate as catalyst. Notable features of the protocol include mild conditions, low cost, easy operations, good functional group compatibility, and high selectivity. The method should therefore have widespread applications in syntheses of complex, multifunctional, or sensitive molecules. The catalyst used and the reaction temperature (Scheme 1).

\[ \text{Scheme 1: Transformation of TBS ethers into 4-methoxybenzyl or methyl ethers} \]

1H NMR and 13C NMR spectra were recorded in CDCl3 or CD3OD on a Bruker Avance 300 or Bruker Avance 400 instrument. Chemical shifts (δ) are referenced to internal TMS or CDCl3. High-resolution mass spectra were recorded on a Bruker maXis Impact mass spectrometer. Melting points were determined by using a Stuart Scientific SMP10 instrument and are uncorrected. IR spectra were recorded in the ATR mode on a Nicolet 6700 FT-IR Thermo Scientific spectrometer; only the more significant peaks are reported. All reagents and solvents obtained commercially and were used as received without further purification. Reactions were monitored by TLC on glass-backed plates coated with a 0.2 mm thickness of silica gel 60 F254; chromatograms were visualized by UV radiation (254 nm) or by staining with phosphomolybdic acid and H2SO4. Column chromatography was performed on 300–400 mesh silica gel.

Except for compound 8, 28, and 30, all TBS ethers were prepared according to the procedures reported in the literature.

3-[[tert-Butyl(dimethyl)silyl]oxy]-3-methylbutan-1-ol (8)

\[
\text{NaAuCl}_4 \cdot \text{H}_2\text{O} (4.0 \text{ mg}, 0.01 \text{ mmol, 0.005 equiv}) \text{ was added to a solution of } \text{diol 27} (665 \text{ mg, 2 mmol) in MeOH (4 mL) at r.t., and the mixture was stirred at r.t. for 7 h. The mixture was then diluted with } \text{EtOAc (10 mL), filtered through activated alumina, and concentrated in vacuo. The residue was purified by flash column chromatography [silica gel, EtOAc–PE (1:5)] to give a colorless oil; yield: 358 mg (82%).} \\
\text{IR (Kbr): 3355, 2945, 2857, 1468, 1420, 1041 cm}^{-1}. \\
\text{1H NMR (300 MHz, CDCl}_3\text{): } \delta = 3.82 (t, J = 5.9 \text{ Hz, 2 H}), 1.72 (t, J = 5.9 \text{ Hz, 2 H}), 1.31 (s, 6 \text{ H}), 0.87 (s, 9 \text{ H}), 0.13 (s, 6 \text{ H}). \\
\text{13C NMR (75 MHz, CDCl}_3\text{): } \delta = 75.31, 60.00, 45.70, 29.86, 25.79, 17.90, -2.01. \\
\text{MS (ESI, MeOH): } m/z = 241 [\text{M + Na}]^+. \\
\text{HRMS-ESI: } m/z [\text{M + Na}]^+ \text{ Calcd for C}_{11}\text{H}_{26}\text{NaO}_2\text{Si: 241.1600; found: 241.1612.} \\
\text{tert-Butyl}[1-((15\text{S,5R})-5-[[\text{tert-butyl(dimethyl)silyl]oxy}-4-methylyclohex-3-en-1-yl]-1-methylethoxy]dimethylsilane (28)} \\
\text{TBSOT (1.52 mL, 6.6 mmol) was added dropwise to a solution of diol 9} \text{(511 mg, 3 mmol) and 2,6-lutidine (0.76 mL, 6.6 mmol) in dry CH}_2\text{Cl}_2 (6 \text{ mL} \text{ at 0}^\circ\text{C, and the mixture was stirred for 5 h. H}_2\text{O (5 mL) and CH}_2\text{Cl}_2 (20 \text{ mL}) were added, and the organic layer was separated and washed successively with sat. aq NaHCO}_3 (5 \text{ mL}), \text{H}_2\text{O (2 × 5 mL), and brine (5 mL), then dried (MgSO}_4\text{) and filtered. The filtrate was concentrated in vacuo and the resulting residue was purified by flash column chromatography [silica gel, EtOAc–PE (1:25)] to give a colorless oil; yield: 1.065 g (89%).} \]
IR (KBr): 2960, 2920, 2861, 1475, 1368, 1256 cm⁻¹.

1HNMR (400 MHz, CDCl₃): δ = 5.52 (dd, J = 3.6, 1.6 Hz, 1 H), 4.01 (br s, 1 H), 2.11 (dt, J = 16.8, 5.6 Hz, 1 H), 1.88–1.78 (m, 2 H), 1.75–1.67 (m, 4 H), 1.37 (dt, J = 3.6, 13.2 Hz, 1 H), 1.21 (s, 3 H), 1.18 (s, 3 H), 0.91 (s, 9 H), 0.85 (s, 9 H), 0.10 (s, 6 H), 0.07 (s, 6 H).

13CNMR (75 MHz, CDCl₃): δ = 134.45, 125.05, 74.73, 69.46, 39.62, 33.58, 28.37, 27.57, 26.86, 25.95, 25.95, 21.25, 18.29, 18.15, –2.02 (2 C).

MS (ESI, MeOH): m/z = 421 [M + Na]⁺.

HRMS-ESI: m/z [M + Na]⁺ calcd for C₂₂H₄₆NaO₂Si₂: 421.2934; found: 421.2940.

**tert-Butyl(dimethyl)[(3,4,5-trimethoxybenzyl)oxy]silane (30)**

A solution of alcohol 30[22] (396 mg, 2 mmol), imidazole (300 mg, 4.4 mmol), and TBSCl (332 mg, 2.2 mmol) in anhyd CH₂Cl₂ (4 mL) was stirred at overnight at r.t. When the starting material had disappeared (TLC), mixture was diluted with NaHCO₃ (5 mL), H₂O (2 × 5 mL), and brine (5 mL), then dried (MgSO₄) and filtered. The filtrate was concentrated in vacuo and resulting residue was purified by flash column chromatography [silica gel, EtOAc–PE (1:3)] to give a colorless oil; yield: 569 mg (91%).

1H NMR (300 MHz, CDCl₃): δ = 6.57 (s, 2 H), 4.69 (s, 2 H), 3.85 (s, 6 H), 3.83 (s, 3 H), 0.96 (s, 9 H), 0.11 (s, 6 H).

13CNMR (75 MHz, CDCl₃): δ = 153.16, 137.14, 136.78, 102.80, 64.86, 60.78, 55.96, 25.89, 18.36, –5.28.

MS (ESI, MeOH): m/z = 335 [M + Na]⁺.


**Protection of TBS Ethers; General Procedure**

A solution of the TBS ether (2 mmol) in MeOH (4 mL) was treated with NaAuCl₄·2H₂O (4.0 mg, 0.01 mmol, 0.005 equiv) at r.t. When the starting material had disappeared (TLC), mixture was diluted with EtOAc (10 mL) and filtered through activated alumina. The solution was then concentrated in vacuo and the resulting residue was purified by flash column chromatography (silica gel, EtOAc–PE (1:3)) to give a colorless oil; yield: 569 mg (91%).

1H NMR (300 MHz, CDCl₃): δ = 7.27 (d, J = 8.7 Hz, 2 H), 6.88 (d, J = 8.7 Hz, 4 H), 4.46 (s, 2 H), 3.80 (s, 3 H).

13CNMR (75 MHz, CDCl₃): δ = 159.11, 130.42, 129.27, 113.70, 71.37, 55.12.

MS (ESI, MeOH): m/z = 161 [M + Na]⁺.


**[4-(Trifluoromethyl)phenyl]methanol (4f)**

Prepared according to the general procedure from silyle ether 4[24] (581 mg), and purified by flash column chromatography [silica gel, EtOAc–PE (1:3)] as a colorless oil; yield: 237 mg (97%).

1H NMR (300 MHz, CDCl₃): δ = 7.62 (d, J = 8.1 Hz, 2 H), 7.47 (d, J = 8.1 Hz, 2 H), 4.77 (s, 2 H), 1.91 (br s, 1 H).

13CNMR (75 MHz, CDCl₃): δ = 145.67, 129.76 (q), 126.80, 124.42 (q), 122.78, 64.40.

MS (ESI, MeOH): m/z = 199 [M + Na]⁺.


2-Phenylethanol (5l)

Prepared according to the general procedure from silyle ether 5[25] (473 mg), and purified by flash column chromatography [silica gel, EtOAc–PE (1:3)] as a colorless oil; yield: 237 mg (97%).

1H NMR (300 MHz, CDCl₃): δ = 7.33–7.30 (m, 2 H), 7.24–7.22 (m, 3 H), 3.86 (t, J = 5.0 Hz, 2 H), 2.87 (t, J = 5.0 Hz, 2 H), 1.52 (br s, 1 H).

13CNMR (75 MHz, CDCl₃): δ = 138.48, 128.97, 128.51, 126.40, 63.58, 39.14.

MS (ESI, MeOH): m/z = 145 [M + Na]⁺.


(2)-trans-Cyclohexane-1,4-diyldimethanol (6v)

Prepared according to the general procedure from 2[26] (517 mg), and purified by flash column chromatography [silica gel, EtOAc–PE (2:1)] as a white solid; yield: 277 mg (96%); mp 63–65 °C.

1H NMR (300 MHz, CDCl₃): δ = 3.47 (d, J = 4.8 Hz, 4 H), 1.86–1.84 (m, 4 H), 1.46–1.44 (m, 4 H, including 1.46 (br s, 2 H)), 1.01–0.96 (m, 4 H).

13CNMR (75 MHz, CDCl₃): δ = 68.51, 40.57, 28.87.

MS (ESI, MeOH): m/z = 167 [M + Na]⁺.

(R)-(-)-Menthol (7)⁵⁶

NaAuCl₄·2H₂O (8.0 mg, 0.02 mmol, 0.01 equiv) was added to a solution of silyl ether ⁶⁷ (541 mg, 2 mmol) in MeOH (4 mL) at r.t., and the mixture was stirred at r.t. for 24 h. The mixture was then diluted with EtOAc (10 mL), filtered through activated alumina, and concentrated in vacuo. The residue was purified by flash column chromatography [silica gel, EtOAc–PE (2:1)] to give a white solid; yield: 293 mg (86%); mp 166–168 °C.


4-tert-Butylphenol (11)⁶⁷

NaAuCl₄·2H₂O (39.8 mg, 0.1 mmol, 0.05 equiv) was added to a solution of silyl ether ¹¹ (529 mg, 2 mmol) in MeOH (4 mL) at r.t., and the mixture was stirred at r.t. for 24 h. The mixture was then diluted with EtOAc (10 mL), filtered through activated alumina, and concentrated in vacuo. The residue was purified by flash column chromatography [silica gel, EtOAc–PE (1:5)] to give a white solid; yield: 277 mg (92%); mp 97–99 °C.


N-(4-Hydroxyphenyl)acetamide (12)²³

NaAuCl₄·2H₂O (39.8 mg, 0.1 mmol, 0.05 equiv) was added to a solution of acetamide ¹² (531 mg, 2 mmol) in MeOH (4 mL) at r.t., and the mixture was stirred at r.t. for 48 h. The mixture was then diluted with EtOAc (10 mL), filtered through activated alumina, and concentrated in vacuo. The residue was purified by flash column chromatography [silica gel, EtOAc–PE (2:1)] to give a white solid; yield: 260 mg (86%); mp 166–168 °C.


1-(4-Hydroxyphenyl)ethaneone (13)⁶⁷

NaAuCl₄·2H₂O (79.6 mg, 0.2 mmol, 0.1 equiv) was added to a solution of hydroxy ketone ¹³ (501 mg, 2 mmol) in MeOH (4 mL) at r.t., and the mixture was stirred at r.t. for 48 h. The mixture was then diluted with EtOAc (10 mL), filtered through activated alumina, and concentrated in vacuo. The residue was purified by flash column chromatography [silica gel, EtOAc–PE (1:5)] to give a white solid; yield: 57 mg (21%); mp 109–110 °C.

6-(Allyloxy)hexan-1-ol (14)\textsuperscript{33}
Prepared according to the general procedure from 14\textsuperscript{34} (545 mg), and purified by flash column chromatography [silica gel, EtOAc–PE (3:1)] as a colorless oil; yield: 301 mg (95%).

\begin{itemize}
  \item[1\textsuperscript{H} NMR (300 MHz, CDCl\textsubscript{3})]: \(\delta = 5.98-5.85\) (m, 1 H), 5.27 (dd, \(J = 1.7, 17.3\) Hz, 1 H), 5.17 (dd, \(J = 1.1, 10.4\) Hz, 1 H), 3.97 (d, \(J = 4.2\) Hz, 2 H), 3.65 (t, \(J = 4.1\) Hz, 2 H), 3.44 (t, \(J = 5.0\) Hz, 2 H), 1.62–1.56 (m, 4 H), 1.41–1.38 (m, 5 H).
  \item[13C NMR (75 MHz, CDCl\textsubscript{3})]: \(\delta = 134.93, 116.64, 71.69, 70.24, 62.64, 32.56, 29.58, 25.89, 25.51.\)
  \item[MS (ESI, MeOH)]: \(m/z = 181\) [M + Na\textsuperscript{+}].
  \item[HRMS-ESI]: \(m/z\) [M + Na\textsuperscript{+}] calcd for C\textsubscript{8}H\textsubscript{15}NaO\textsubscript{2}: 181.1204; found: 181.1198.
\end{itemize}

6-Hydroxyhexyl Acetate (15)\textsuperscript{36}
Prepared according to the general procedure from 15\textsuperscript{46} (549 mg), and purified by flash column chromatography [silica gel, EtOAc–PE (1:1)] as a colorless oil; yield: 301 mg (94%).

\begin{itemize}
  \item[1\textsuperscript{H} NMR (300 MHz, CDCl\textsubscript{3})]: \(\delta = 4.06\) (t, \(J = 5.0\) Hz, 2 H), 3.64 (t, \(J = 4.8\) Hz, 2 H), 2.05 (s, 3 H), 1.64–1.58 (m, 4 H), 1.40–1.38 (m, 4 H).
  \item[13C NMR (75 MHz, CDCl\textsubscript{3})]: \(\delta = 171.20, 64.40, 62.59, 32.49, 28.49, 25.63, 25.31, 20.87.\)
  \item[MS (ESI, MeOH)]: \(m/z = 183\) [M + Na\textsuperscript{+}].
  \item[HRMS-ESI]: \(m/z\) [M + Na\textsuperscript{+}] calcd for C\textsubscript{8}H\textsubscript{15}NaO\textsubscript{2}: 183.0997; found: 183.0990.
\end{itemize}

6-(Methoxymethoxy)hexan-1-ol (16)\textsuperscript{1}\nPrepared according to the general procedure from 16\textsuperscript{6} (553 mg), and purified by flash column chromatography [silica gel, EtOAc–PE (1:2)] as a colorless oil; yield: 315 mg (97%).

\begin{itemize}
  \item[1\textsuperscript{H} NMR (300 MHz, CDCl\textsubscript{3})]: \(\delta = 4.62\) (s, 2 H), 3.65 (t, \(J = 6.5\) Hz, 3 H), 3.53 (t, \(J = 6.5\) Hz, 2 H), 3.36 (s, 3 H), 1.75–1.52 (m, 4 H), 1.42–1.39 (m, 4 H).
  \item[13C NMR (75 MHz, CDCl\textsubscript{3})]: \(\delta = 96.38, 67.72, 62.84, 55.06, 32.67, 29.66, 25.99, 25.53.\)
  \item[MS (ESI, MeOH)]: \(m/z = 185\) [M + Na\textsuperscript{+}].
  \item[HRMS-ESI]: \(m/z\) [M + Na\textsuperscript{+}] calcd for C\textsubscript{8}H\textsubscript{15}NaO\textsubscript{2}: 185.1145; found: 185.1148.
\end{itemize}

6-([2-Methoxyethoxy]methoxy)hexan-1-ol (17)\textsuperscript{1}\nPrepared according to the general procedure from 17\textsuperscript{9} (641 mg), and purified by flash column chromatography [silica gel, EtOAc–PE (1:3)] as a colorless oil; yield: 392 mg (95%).

\begin{itemize}
  \item[1\textsuperscript{H} NMR (300 MHz, CDCl\textsubscript{3})]: \(\delta = 4.71\) (s, 2 H), 3.75–3.62 (m, 4 H), 3.60–3.51 (m, 4 H), 3.40 (s, 3 H), 1.75–1.53 (m, 4 H), 1.46–1.39 (m, 4 H).
  \item[13C NMR (75 MHz, CDCl\textsubscript{3})]: \(\delta = 95.43, 71.80, 67.77, 66.68, 62.79, 58.95, 32.65, 29.59, 25.95, 25.49.\)
  \item[MS (ESI, MeOH)]: \(m/z = 229\) [M + Na\textsuperscript{+}].
  \item[HRMS-ESI]: \(m/z\) [M + Na\textsuperscript{+}] calcd for C\textsubscript{10}H\textsubscript{19}NaO\textsubscript{2}: 229.1416; found: 229.1413.
\end{itemize}

1.2.3.4-Bis-O-(1-Methylbicyclo[2.2.2]octyl)-α-d-galactopyranose (18)\textsuperscript{8b}
Prepared according to the general procedure from 18\textsuperscript{8a} (749 mg), and purified by flash column chromatography [silica gel, EtOAc–PE (2:1)] as a colorless oil; yield: 500 mg (96%).

\begin{itemize}
  \item[1\textsuperscript{H} NMR (300 MHz, CDCl\textsubscript{3})]: \(\delta = 5.57\) (d, \(J = 5.0\) Hz, 1 H), 4.62 (dd, \(J = 7.9, 2.2\) Hz, 1 H), 4.34 (m, 1 H), 4.29 (d, \(J = 6.3\) Hz, 1 H), 3.95–3.83 (m, 2 H), 3.79–3.72 (m, 1 H), 2.10 (dd, \(J = 9.6, 3.0\) Hz, 1 H), 1.54 (s, 3 H), 1.46 (s, 3 H), 1.34 (s, 6 H).
  \item[13C NMR (75 MHz, CDCl\textsubscript{3})]: \(\delta = 109.20, 108.45, 96.10, 71.22, 70.57, 70.43, 68.17, 61.79, 25.82, 25.75, 24.76, 24.18.\)
  \item[MS (ESI, MeOH)]: \(m/z = 283\) [M + Na\textsuperscript{+}].
  \item[HRMS-ESI]: \(m/z\) [M + Na\textsuperscript{+}] calcd for C\textsubscript{18}H\textsubscript{26}NaO\textsubscript{9}: 283.1158; found: 283.1153.
\end{itemize}
(4-[[[4-Butyl(dimethyl)silyloxy]methyl]phenyl]methanol (23)\textsuperscript{25}\textsuperscript{1}

NaAuCl\textsubscript{4}·2H\textsubscript{2}O (0.8 mg, 0.002 mmol, 0.001 equiv) was added to a solution of disilyl ether 23\textsuperscript{3} (733 mg, 2 mmol) in MeOH (4 mL) at r.t., and the mixture was stirred at r.t. for 0.5 h. The mixture was then diluted with EtOAc (10 mL), filtered through activated alumina, and concentrated in vacuo. The residue was purified by flash column chromatography [silica gel, EtOAc-PE (1:5)] to give a colorless oil; yield: 435 mg (86%).

\[ \text{HRMS-ESI: } m/z = 275 \text{ [M + Na]}^+ \]

HRMS-ESI: m/z [M + Na]\textsuperscript{+} calcd for C\textsubscript{14}H\textsubscript{30}NaO\textsubscript{2}Si: 317.1913; found: 317.1912.

(2)-trans-5-1-[[[4-Butyl(dimethyl)silyloxy]-1-methylthethyl]-2-methylcyclohex-2-en-1-ol (28)\textsuperscript{26}

Prepared according to the general procedure from 28 (798 mg), and purified by flash column chromatography [silica gel, EtOAc-PE (1:5)] as a colorless oil; yield: 489 mg (86%).

IR (KBr): 3550, 2969, 2922, 2857, 1468, 1379, 1250 cm\textsuperscript{-1}.

HRMS-ESI: m/z [M + Na]\textsuperscript{+} calcd for C\textsubscript{10}H\textsubscript{14}NaO\textsubscript{4}: 221.0790; found: 221.0790.

(3,4,5-Trimethoxyphenyl)methanol (30)\textsuperscript{27}

Prepared according to the general procedure from 30 (625 mg), and purified by flash column chromatography [silica gel, EtOAc-PE (1:5)] as a white solid; yield: 361 mg (91%); mp: 36–38°C.

HRMS-ESI: m/z [M + Na]\textsuperscript{+} calcd for C\textsubscript{10}H\textsubscript{14}NaO\textsubscript{4}: 221.0790; found: 221.0790.

1-((6-Benzylloxy)hexyl)oxy)methyl-4-methoxybenzene (29)\textsuperscript{28}

NaAuCl\textsubscript{4}·2H\textsubscript{2}O (398 mg, 0.1 mmol, 0.05 equiv) was added to a solution of silyl ether 1 (645 mg, 2 mmol) and 4-MeOC\textsubscript{6}H\textsubscript{4}CH\textsubscript{2}OH (3) (1.24 mL, 10 mmol) in THF (4 mL) and the mixture was refluxed for 8 h. The mixture was then cooled to r.t., diluted with EtOAc (10 mL), filtered through activated alumina, and concentrated in vacuo. The residue was purified by flash column chromatography [silica gel, EtOAc-PE (1:10)] to give a colorless oil; yield: 394 mg (60%).

IR (KBr): 3550, 2969, 2922, 2857, 1468, 1379, 1250 cm\textsuperscript{-1}.

HRMS-ESI: m/z [M + Na]\textsuperscript{+} calcd for C\textsubscript{10}H\textsubscript{14}NaO\textsubscript{4}: 351.1936; found: 351.1939.
1,2,3-Tris(methoxymethyl)benzene (31)

NaAlCl₂ · 2H₂O (39.8 mg, 0.1 mmol, 0.05 equiv) was added to a solution of silyl ether 30 (624 mg, 2 mmol) in MeOH (4 mL), and the mixture was refluxed for 24 h. The mixture was then cooled to rt., diluted with EtOAc (10 mL), filtered through activated alumina, and concentrated in vacuo. The residue was purified by flash column chromatography [silica gel, EtOAc–PE (1:10)] to give a colorless oil; yield: 266 mg (63%).

1H NMR (300 MHz, CDCl₃): δ = 6.57 (s, 2 H), 4.39 (s, 2 H), 3.87 (s, 6 H), 3.84 (s, 3 H), 3.41 (s, 3 H).

13C NMR (75 MHz, CDCl₃): δ = 153.26, 137.46, 133.85, 104.61, 74.85, 60.76, 58.11, 56.05. MS (ESI, MeOH): m/z = 235 [M + Na]⁺.

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References
(3) For a recent review, see: Crouch, R. D. Tetrahedron 2013, 69, 2383; and references therein.

This article differs from the e-first online version only in its layout; no content has been changed.