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Synthetic Methods

# Synthesis and Applications of Silyl 2-Methylprop-2-ene-1-sulfinates in Preparative Silylation and GC-Derivatization Reactions of Polyols and Carbohydrates

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**Abstract:** Trimethylsilyl, triethylsilyl, *tert*-butyldimethylsilyl, and triisopropylsilyl 2-methylprop-2-ene-1-sulfinates were prepared through $(CuOTf)_2{\cdot}C_6H_6$-catalyzed sila-ene reactions of the corresponding methallylsilanes with $SO_2$ at 50 °C. Sterically hindered, epimerizable, and base-sensitive alcohols gave the corresponding silyl ethers in high yields and purities at room temperature and under neutral conditions. As the byproducts of the silylation reaction ($SO_2$ + isobutylene) are volatile, the workup was simplified to solvent evaporation. The developed method can be employed for the chemo- and regioselective semiprotection of polyols and glycosides and for the silylation of unstable aldols. The high reactivity of the developed reagents is shown by the synthesis of sterically hindered per-*O*-*tert*-butyldimethylsilyl-α-D-glucopyranose, the X-ray crystallographic analysis of which is the first for a per-*O*-silylated hexopyranose. The per-*O*-silylation of polyols, hydroxy carboxylic acids, and carbohydrates with trimethylsilyl 2-methylprop-2-ene-1-sulfinate was coupled with the GC analysis of nonvolatile polyhydroxy compounds both qualitatively and quantitatively.

## Introduction

The selective semiprotection of polyols, phenols, carboxylic acids, and other compounds containing hydroxy groups is of great importance in modern organic synthesis.[1] Silyl ethers and derivatives[4] are recognized as the most valuable protecting group because of their stability toward basic and acidic hydrolysis,[2] high specificity for fluoride-mediated cleavage,[3] and solubility in nonpolar solvents. In addition, the silylation of hydroxy-containing compounds is frequently used in analytical chemistry because this reaction converts compounds with low volatility into volatile and thermally more stable derivatives, thus facilitating analysis by GC and MS techniques.[5] Silyl derivatization is useful for the structural characterization and quantification of compounds of interest.[6,7] The most common silylation procedures in preparative organic synthesis react compounds containing hydroxy groups with silyl halides or triflates and a stoichiometric amount of a Lewis base in polar aprotic solvents.[8] Approaches that deal with GC derivatization frequently use *N*,*O*-bis(trimethylsilyl)acetamide (BSA), *N*,*O*-bis(trimethylsilyl)trifluoroacetamide (BSTFA), *N*-trimethylsilylimidazole (TMSIM), *N*-(*tert*-butyldimethylsilyl)-*N*-methyltrifluoroacetamide (MTBSTFA), and others.[9] Other methods are based on the $S_N2$ substitution of Si–O,[10] Si–N,[11] Si–S,[12] or Si–C[13] compounds or on catalyzed dehydrogenative silanolysis with $R_3SiH$ reagents.[14]

Although these methods offer good reliability, they may fail because of low reactivity, difficult removal of excess base and byproducts, and/or their ability to epimerize or destroy base-sensitive compounds.[15] The synthesis of complicated natural products and analogues of biological interest often requires the chemo- and regioselective semiprotection of polyols, an operation that can be costly in terms of synthetic steps and reagents. There is a need for better semiprotection protocols that are simpler, are less costly, and minimize waste production.

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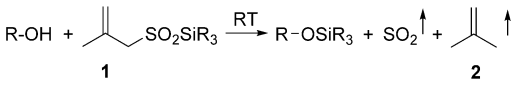
On the other hand, the success of GC and GC-MS analysis is dictated by the efficiency of the procedures employed prior to injection of the sample. Therefore, the rate of silylation may play an important role because on many occasions only the comparison of several empirically developed recipes leads to an appropriate rate of silylation.[7,16] Frequently, these procedures employ mixtures of reagents that include up to three components (e.g., BSTFA + TMSCl + TMSIM).[9] In the GC analysis of carbohydrates, oxime formation followed by silylation is often required for the reliable determination of their concentration.[17]

As part of our program on the development of the organic chemistry of sulfur dioxide,[18] we have described the use of silyl 2-methylprop-2-ene-1-sulfinates **1** as a new and efficient class of agent for the silylation of alcohols, phenols, and carboxylic acids (Scheme 1).[19] The reactions are fast, generally on



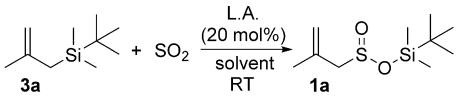

**Scheme 1.** Silylation of alcohols with silyl 2-methylprop-2-ene-1-sulfinates.

a timescale of minutes at 20 °C, and the silylated products are obtained in high yields and purities. Our conditions are neutral, thus requiring neither acid nor base as catalysts or coreagents. Because the byproducts are volatile ($SO_2$ + isobutylene), the silylated compounds can be purified by simple evaporation of the solvent in many instances. This approach is particularly advantageous when temporary protection with trimethylsilyl (TMS) groups, which are easily removed during aqueous workup, is envisioned.

Herein, we describe an improved and high-yielding synthetic route for the preparation of a variety of silyl 2-methylprop-2-ene-1-sulfinates **1** and their utilization for the protection of isomerizable, base-sensitive, or sterically hindered alcohols. The chemo- and regioselective semiprotection of polyols and glycosides is reported. Our neutral silylation method is demonstrated to be especially useful for the protection of unstable aldols and also allows a user-friendly access to fully *O*-silylated hexopyranoses and their first X-ray analysis. Finally, our silylation procedure was adapted for the qualitative and quantitative analysis of multicomponent mixtures by using GC-MS.

## Results and Discussion

Originally silyl sulfinates **1** were prepared by trimethylsilyl trifluoromethanesulfonate (TMSOTf)-catalyzed sila-ene reactions of the corresponding methallylsilanes **3** with sulfur dioxide.[19a,20] Further development lead to the reaction between $SO_2$ and methallyltrimethylsilane catalyzed by *N*-trimethylsilyl bis(trifluoromethanesulfonyl)imide ($TMSNTf_2$; formed in situ from $Tf_2NH$ and $H_2C{=}C(Me)CH_2TMS$) in toluene at ambient pressure.[18i,j,19b] However, the latter advancement worked only for the mentioned combination. The TMSOTf-catalyzed processes lead to low yields (20–54%) and required high loading of the catalyst (up to 20% mol).[19a,20] Our efforts were first to improve the reaction conditions and to elaborate a simpler and more efficient route for the preparation of silyl 2-methylprop-2-ene-1-sulfinates on a larger preparative scale. Therefore, we explored the role of Lewis acids, solvent, and temperature. *tert*-Butyldimethyl(2-methylprop-2-en-1-yl)silane (**3a**), as the least reactive starting material, was used as a test substrate and the reactions were carried out in sealed NMR tubes with an excess of $SO_2$ and toluene as an internal reference (Scheme 2). The results of our screening are shown in Table 1.




**Scheme 2.** Synthesis of *tert*-butyl-dimethylsilyl 2-methylprop-2-ene-1-sulfinate (**1a**) by a Lewis acid (LA)-catalyzed sila-ene reaction between *tert*-butyl-dimethyl-(2-methylprop-2-en-1-yl)silane (**3a**) and sulfur dioxide.

**Table 1.** Catalyst screening for the sila-ene reaction between *tert*-butyl-dimethyl-(2-methylprop-2-en-1-yl)silane (**3a**) and sulfur dioxide according to Scheme 2.

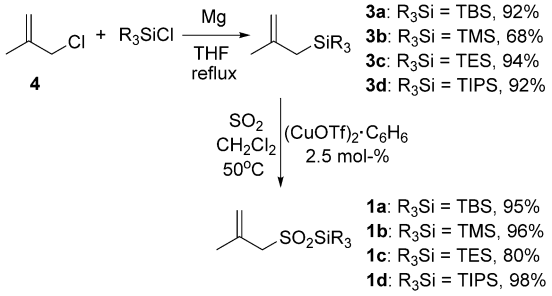
| Entry | Solvent | Lewis acid | Reaction time [h] | Conversion [%][a] |
|---|---|---|---|---|
| 1 | $CD_3CN$ | $AlCl_3$ | 5 | quant. |
| 2 | $CD_2Cl_2$ | $AlCl_3$ | 5 | 87 |
| 3 | $CD_3CN$ | $SbCl_5$ | 5 | 98 |
| 4 | $CD_2Cl_2$ | $SbCl_5$ | 7 | 98 |
| 5 | $CD_2Cl_2$ | $Al(OTf)_3$ | 5 | 14[b] |
| 6 | $CD_2Cl_2$ | $SbCl_3$ | 5 | 17[b] |
| 7 | $CD_2Cl_2$ | $Cu(OTf)_2$ | 5 | 23[b] |
| 8 | $CD_2Cl_2$ | $ScCl_3$ | 5 | 9[b] |
| 9 | $CD_2Cl_2$ | $Zn(OTf)_2$ | 5 | 2[b] |
| 10 | $CD_2Cl_2$ | $ZnCl_2$ | 5 | –[b] |
| 11 | $CD_2Cl_2$ | AgOTf | 20 | quant. |
| 12 | $CD_3CN$ | AgOTf | 20 | 43[b] |
| 13 | $CD_2Cl_2$ | $(CuOTf)_2{\cdot}C_6H_6$ | 5 | quant. |
| 14 | $CD_3CN$ | $(CuOTf)_2{\cdot}C_6H_6$ | 5 | 65[b] |

[a] Determined by $^1H$ NMR spectroscopic analysis and toluene was used as an internal reference. [b] Decomposition of the reaction mixture occurs.

The anhydrous Lewis acids $AlCl_3$ and $SbCl_5$ in $CD_3CN$ or $CD_2Cl_2$ catalyzed the sila-ene reaction efficiently (Table 1, entries 1–4). Unfortunately, the purification of silyl sulfinate **1a** was unsuccessful due to the formation of stable oligomeric sulfinic $AlCl_3$ complexes[18c] or due to the high acidity of $SbCl_5$ that degraded **1a** during distillation. $Al(OTf)_3$, $SbCl_3$, $Cu(OTf)_2$, $ScCl_3$, $Zn(OTf)_2$, and $ZnCl_2$ also catalyzed the reaction, but led to lower conversion rates because of concurrent degradation of the methallylsilane (Table 1, entries 4–10). Because of the low solubility of $ZnCl_2$, $Zn(OTf)_2$ and $ScCl_3$ in the reaction media, very slow reactions were observed. High conversion rates were obtained by applying the commercially available triflates AgOTf and $(CuOTf)_2{\cdot}C_6H_6$ as catalysts in $CD_2Cl_2$ (Table 1, entries 11 and 13). Lower yields were observed for both catalysts in $CD_3CN$ (Table 1, entries 12 and 14), and the copper

complex led to the fastest reaction. Optimization experiments showed that the amount of the $(CuOTf)_2{\cdot}C_6H_6$ catalyst could be decreased to 2.5% at 50 °C.

We applied our optimized conditions to prepare TBS, TMS, TES, and TIPS 2-methylprop-2-ene-1-sulfinates **1a–d**. Methallylsilanes **3a–d** were obtained by using Barbier–Calas reactions[21] of methallyl chloride (**4**) with the corresponding trialkylsilyl chlorides in the presence of magnesium (Scheme 3). These

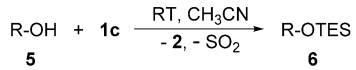



**Scheme 3.** Synthesis of silyl methallylsulfinates **1a–d** on a preparative scale (yields are given after purification by distillation). TBS = *tert*-butyldimethylsilyl, TES = triethylsilyl, TIPS = triisopropylsilyl, TMS = trimethylsilyl.

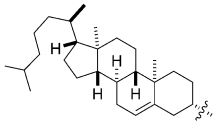
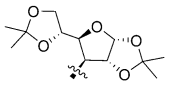
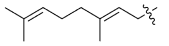
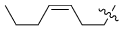
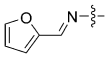
products were purified by distillation under reduced pressure and obtained in yields of 68–95%. Further, a stainless-steel autoclave containing the catalyst (2.5 mol% of $(CuOTf)_2{\cdot}C_6H_6$ complex) was cooled to −78 °C and charged with liquid $SO_2$ followed by the addition of a solution of the corresponding methallyl silane **1a–d** in $CH_2Cl_2$. The ene reactions were completed after 12 hours at 50 °C. Excess $SO_2$ and $CH_2Cl_2$ were evaporated under slightly reduced pressure. This solvent/reagent mixture can be reused in the next sila-ene reaction. The resulting residue was collected by distillation under reduced pressure, thus giving the pure silyl sulfinates **1** in 80–98% yield. The process was reproducible in high yields and on a scale of 40 gram for the methallyl silanes.

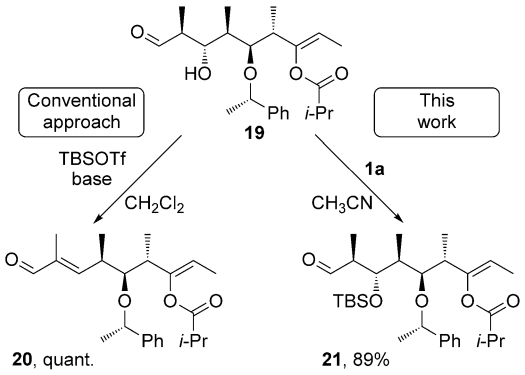
As a test of the usefulness of our reagents, we carried out the silylation of different alcohols with triethylsilyl 2-methylprop-2-ene-1-sulfinate (**1c**). The silylation reactions were conducted in acetonitrile at 20 °C (the results are summarized in Table 2). Secondary alcohols, such as cholesterol (**5a**) and 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose (**5b**), were silylated in a few minutes with one equivalent of **1c** to give silyl ethers **6a** and **6b** in 98 and 93% yield, respectively (purification was carried out by filtration through a plug of silica gel; Table 2, entries 1 and 2). Allylic and *cis*-homoallylic alcohols **5c** and **5d** were protected by conversion into **6c** and **6d** in 93 and 91% yield, respectively (Table 2, entries 3 and 4). Silylation of the Roche ester **5e** gave the epimerizable silyl ether **6e** without loss of enantiomeric purity. The silylation of pent-4-en-2-ol (**5f**), which might be prone to water elimination,[22] was performed under solvent-free conditions in excellent yield (Table 2, entry 6). Similarly, sterically hindered 1,1-diethylpropanol (**5g**) was silylated with **1c** to form **6g** in a high yield of 90%. Silyl sulfinate **1c** was also effective for the protection of oxime **5h** by conversion into the *O*-silyl derivative **6h** (98%).

**Table 2.** User-friendly synthesis of triethylsilyl ethers from reactions between triethylsilyl 2-methylprop-2-ene-1-sulfinate **1c** and selected alcohols in $CH_3CN$ at 20 °C.




5 6

| Entry | Substrate | R | Product | Yield [%] |
|---|---|---|---|---|
| 1 | **5a** |  | **6a** | 98 |
| 2 | **5b** |  | **6b** | 93 |
| 3 | **5c** |  | **6c** | 93 |
| 4 | **5d** |  | **6d** | 91 |
| 5 | **5e** |  | **6e** | 92 |
| 6 | **5f** |  | **6f** | 88 |
| 7 | **5g** |  | **6g** | 90 |
| 8 | **5h** |  | **6h** | 96 |

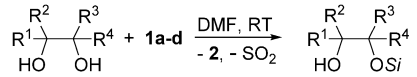


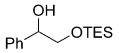
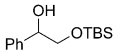
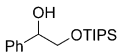
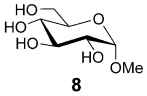
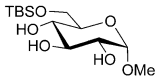
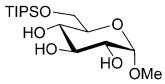
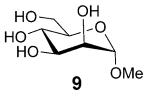
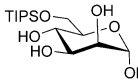
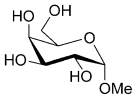
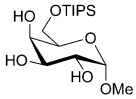
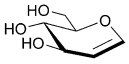
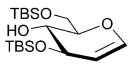
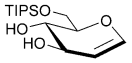
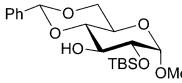
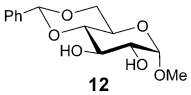
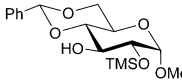
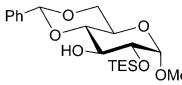
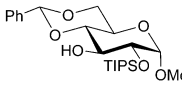

**Scheme 4.** Comparison of the conventional silylation conditions used for unstable aldols and the use of silyl 2-methylprop-2-ene-1-sulfinate **1a**. OTf = trifluoromethanesulfonate.

We further tested our neutral silylation method for the protection of base-sensitive aldols (Scheme 4). Whereas all our attempts to protect aldol **19** as a silyl ether by applying the classical methods failed and led exclusively to β-elimination of water, thus giving enal **20**, the use of TBS sulfinate **1a** permitted us to obtain β-silyloxy aldehyde **21** in 89% yield.

Next, we employed silyl sulfinates **1a–d** for the regioselective protection of the primary alcohol moieties of diol **7**, methyl hexopyranosides **8–10**, **12** and glucal (**11**) in DMF at 20 °C. All reactions led to high yields (Table 3, entries 1–9). Thus, 1-phenylethane-1,2-diol (**7**) was selectively protected with TMS, TES, or TIPS protecting groups to afford **13a–c** in

**Table 3.** Regioselective preparative silylations of 1-phenylethane-1,2-diol and monosaccharides by using trialkylsilyl methallylsulfinates **1a–d**.




| Entry | Substrate | Silyl sulfonate | Product | | Yield [%] |
|---|---|---|---|---|---|
| 1 | | **1c** |  | **13a** | 95 |
| 2 |  **7** | **1a** |  | **13b** | 80 |
| 3 | | **1d** |  | **13c** | 98 |
| 4 |  **8** | **1a** |  | **14a** | 97 |
| 5 | | **1d** |  | **14b** | 98 |
| 6 |  **9** | **1d** |  | **15** | 99 |
| 7 |  **10** | **1d** |  | **16** | 86 |
| 8 |  **11** | **1a**[a] |  | **17a** | 96 |
| 9 | | **1d** |  | **17b** | 98 |
| 10 | | **1a** |  | **18a** | 96 |
| 11 |  **12** | **1b** |  | **18b** | 83 |
| 12 | | **1c** |  | **18c** | 97 |
| 13 | | **1d** |  | **18d** | 95 |

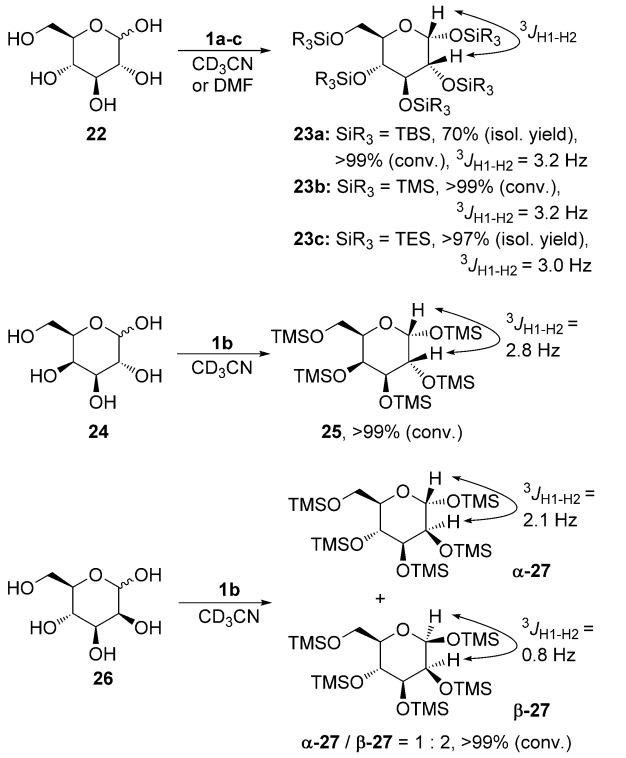
[a] Two equivalents of **1a** were used.

95, 80, and 98% yield, respectively. Methyl α-D-glucopyranoside (**8**) was treated with one equivalent of sulfinates **1a** and **1d**, thus selectively giving the corresponding 6-*O*-silylated monosaccharides **14a** and **14b** in excellent yields of 97 and 98%, respectively. Similarly, methyl α-D-mannopyranoside (**9**) and methyl α-D-galactopyranoside (**10**) were converted into monosilyl ethers **15** and **16** (99 and 86%, respectively), in which only their primary alcohol moiety is protected as a TIPS ether group. D-Glucal (**11**) with one equivalent of TBS sulfinate **1a** gave a mixture of products due to the competitive silylation of the 6-*O*- and 3-*O* centers. However, **11** reacted with two equivalents of **1a** to chemo- and regioselectively give the 3,6-*O*-bis[(*tert*-butyl)dimethylsilyl] derivative **17a** in 96% yield of the isolated product. D-Glucal (**11**) with one equivalent of TIPS sulfinate **1d** regioselectively gave 6-*O*-triisopropylsilyl-D-glucal (**17b**) in 98% yield, whereas the 2-*O*-protected glucopyranosides **18a–d** were obtained in high yields (83–97%) by the reaction of the D-glucose-derived diol **12** and silyl sulfinates **1a–d**.

The higher reactivity of the "super-armed" silylated glycosyl donors was explained by an inversion of the chair conformations from $^4C_1$ to $^1C_4$ and by a simultaneous change of the positions of the substituents from the equatorial to axial or pseudoaxial positions.[23] This concept has found important applications in sequential chemoselective oligosaccharide synthesis. Gervay-Hague and co-workers reported the use of per-*O*-trimethylsilylated monosaccharides in the synthesis of the corresponding glycosyl iodides, which were further applied in a one-pot stereoselective glycosylation protocol.[24] Other applications include protecting-group manipulations that start from per-*O*-silylated carbohydrates,[26] such as the regioselective silyl/acetate exchange of either per-*O*-silylated monosaccharides[24f] or disaccharides, thus providing advanced glycosyl donor and acceptor precursors.[26] In addition, the per-*O*-silylation of saccharides has been established as one of the most popular derivatization techniques in GC and GC-MS analysis.[29] The important limitations of the currently used silylation reactions of carbohydrates imply the formation of complex mixtures due to the different tautomeric forms of glycosides or the necessity for rigorous sample drying because of the high moisture sensitivity of the silylation reagents.[27]

The efficiency of silyl sulfinates **1** as derivatization agents for the formation of "super-armed" persilylated glycosyl donors and their conformational analysis is further demonstrated. By applying our new silylation method, persilylated glycosides **23**, **25**, and **27** were obtained in one-step and with excellent conversions, as analyzed by using GC-MS, NMR spectroscopy, and X-ray studies (Scheme 5). For example, the reaction of D-glucose (**22**) with silylating reagent **1a** showed quantitative conversion (GC-MS analysis) into per-*O*-silylated α-glucopyranoside **23a** ($^3J_{H1-H2}$ = 3.2 Hz), which was isolated in 70% yield.

The molecular structure and conformation of product **23a** was unambiguously established by X-ray structural analysis of monocrystals obtained from a mixture of $CD_3CN/CDCl_3$ at room temperature. This single-crystal X-ray analysis was the first that has ever been carried out on any per-*O*-silylated hexopyranose. The crystals of persilylated α-D-glucopyranoside **23a** form the asymmetric unit, which contains two independent conformers **23a-1** and **23a-2** (Figure 1). Conformers **23a-1** and **23a-2** differ only by rotation of the TBSO substituents. Atoms C2 and C5 deviate from the least-squares plane calculated for the other four atoms of the pyranose ring (i.e., O, C1, C3, C4) by 0.64 and 0.60 Å, respectively, in conformer **23a-1**. The pyranose cycle of conformer **23a-2** is virtually superimpos-




**Scheme 5.** Synthesis and analysis by using GC-MS and NMR spectroscopy of per-*O*-silylated monosaccharides.

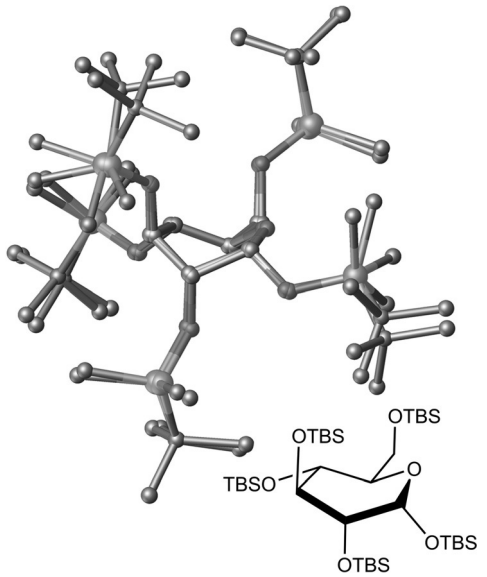



**Figure 1.** Superposition of two conformations of pentasilylated α-glucopyranoside **23a-1** and **23a-2** obtained by X-ray studies. The hydrogen atoms have been omitted for clarity. Selected bond lengths [Å] and angles [°] for **23a-1**: C1-O1 1.39(1), C2-O2 1.41(1), C3-O3 1.42(1), C4-O4 1.42(1), C6-O5 1.39(1), C1-O1-Si1 120.3(6), C2-O2- Si2 125.7(6), C3-O3- Si3 127.4(6), C4-O4-Si4 126.5(5), C6-O5-Si5 125.3(6), Si1-O1 1.705(7), Si2-O2 1.639(7), Si3-O3 1.658(6), Si4-O4 1.645(7), Si5-O5 1.632(6).

able with the pyranose ring of conformer **23a-1**, in which atoms C2 and C5 deviate from the least-squares plane of the other atoms by 0.69 and 0.61 Å, respectively. On the other hand, the truncated Fourier formalism introduced by Haasnoot[29] provides a description of six-membered-ring conformations in terms of three ring-puckering coordinates derived from the endocyclic torsion angles. Most surprisingly, the calculated ring-puckering parameters $P_2 \approx 343$, $\theta \approx 88$, and $Q \approx 64^\circ$ for monosaccharide **23a** define its pyranose-ring conformation as a transition between the $^0S_2$ (skew-boat) and $B_{2,5}$ (boat) conformations. The related thioglucosides were proposed to adopt twisted-boat or $^1C_4$ chair conformations in solution.[24] The observed $^0S_2$ (skew-boat)/$B_{2,5}$ (boat) conformation of **23a** orients the silylated C2 and C3 hydroxy groups in pseudoaxial positions and the C4 and C5 substituents into pseudoequatorial positions. The lengths the of Si–O bonds in **23a** vary from 1.622(6) to 1.705(7) Å. It is interesting to note that the glycosidic substituents in both conformers possess the longest Si–O bonds of 1.705(7) and 1.670(8) Å, respectively.

The reaction mixtures obtained in the silylation experiments of monosaccharides **22**, **24**, and **25** with reagent **1b** were analyzed in parallel by using $^1$H NMR spectroscopy and GC-MS to double check each analytical method. The derivatization of glucose (**22**) by using silyl sulfinates **1b** and **1c** also exclusively provided α anomers of per-*O*-trimethylsilyl **23b** ($J_{H1-H2} = 3.2$ Hz, 99% conv.; ref. [24a]: $^3J_{H1-H2} = 3.0$ Hz ($CD_2Cl_2$)) and per-*O*-triethylsilyl **23c** ($^3J_{H1-H2} = 3.0$ Hz, 97% yield of the isolated product; Scheme 5). It is interesting to note that an alternative GC derivatization of glucose with hexamethyldisilazane (HMDS) and catalytic amounts of TMSOTf gave an α/β ratio of 3.5:1,[25a] whereas BSTFA provided a mixture of α and β anomers.[27c] D-Galactose (**24**) gave also only α anomer **25** ($^3J_{H1-H2} = 2.8$ Hz ($CD_3CN$); ref. [24a]: $J_{H1-H2} = 2.2$ Hz ($CD_2Cl_2$)) upon treatment with **1b**, whereas alternative methods have given a mixture of anomers.[25a] Per-*O*-silylation of D-mannose (**26**) with **1b** in $CH_3CN$ (GC-MS analysis) and $CD_3CN$ (NMR spectroscopy) resulted in a mixture of α and β anomers of α-**27** ($^3J_{H1-H2} = 2.1$ Hz) within the ratio of 2:1 (ref. [24f]: $^3J_{H1-H2} = 2.4$ and 0.8 Hz for α-**27** and β-**27** ($CDCl_3$), respectively; ref. [24g]: $^3J_{H1-H2} \rightarrow 0$ Hz for β-**27** ($CDCl_3$)).

We further used our simple, mild, and fast silylation method for the qualitative analysis of complex mixtures of compounds by means of GC-MS analysis. For example, after the treatment of a mixture of D-glucose (**22**), D-galactose (**24**), and D-mannose (**26**) with TMS sulfinate **1b** for 4 hours in $CH_3CN$ at 70 °C, a straightforward GC-MS analysis was performed and a clean mixture of per-*O*-silylated glucopyranose (**23b**: $t_R = 10.78$ min), galactopyranose (**25**: $t_R = 10.61$ min), and mannopyranose (α-**27**: $t_R = 10.33$; β-**27**: $t_R = 10.86$ min) was obtained (see the GC-MS traces presented in Figure 2). Furthermore, we performed the GC separation of the nine-component mixture of **28**–**36** obtained after treatment of the corresponding alcohols with trimethylsilyl sulfinate **1b** in MeCN (Figure 3). The subsequent submission of the mixture of **28**–**36** to GC provided a clean GC trace, with a good baseline separation of peaks.

Finally, we used our silylation technique for the purpose of quantitative GC-MS analysis of thermally unstable hydroxy compounds with low volatility. Calibration curves (i.e., concentration $c$ [mg mL$^{-1}$] vs. GC mass-selective-detector correlation area) were constructed for trimethylsilylated glycerol (**30**), tar-

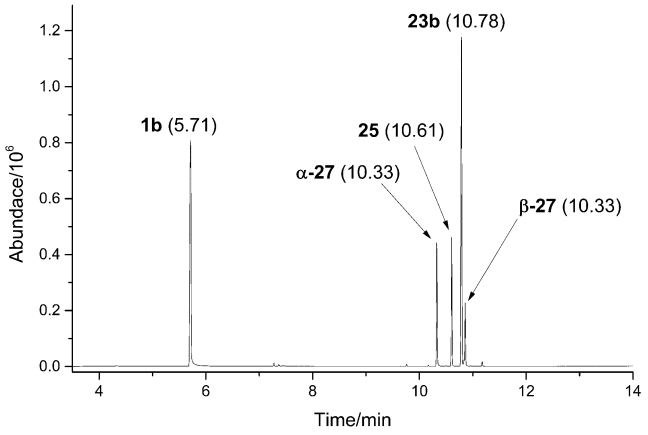



**Figure 2.** GC-MS traces of a mixture of per-*O*-silylated glucopyranose (**23**), galactopyranose (**25**), and mannopyranose (α-**27** and **β-27**; $t_R$ = 10.78, 10.61, 10.33, 10.86 min, respectively). Capillary column: HP-5MS (5% phenylmethylsiloxane) 30 m × 0.25 μm; injector temperature = 250 °C; eluent = He; flow rate = 0.8 mL min$^{-1}$; split injection = 600:1; injection volume = 0.2 μL; temperature regime = 70 °C for 2 min, 20 °C min$^{-1}$ until 310 °C; MS detector (ESI, 70 eV): MS Quad 150 °C; MS source = 230 °C.

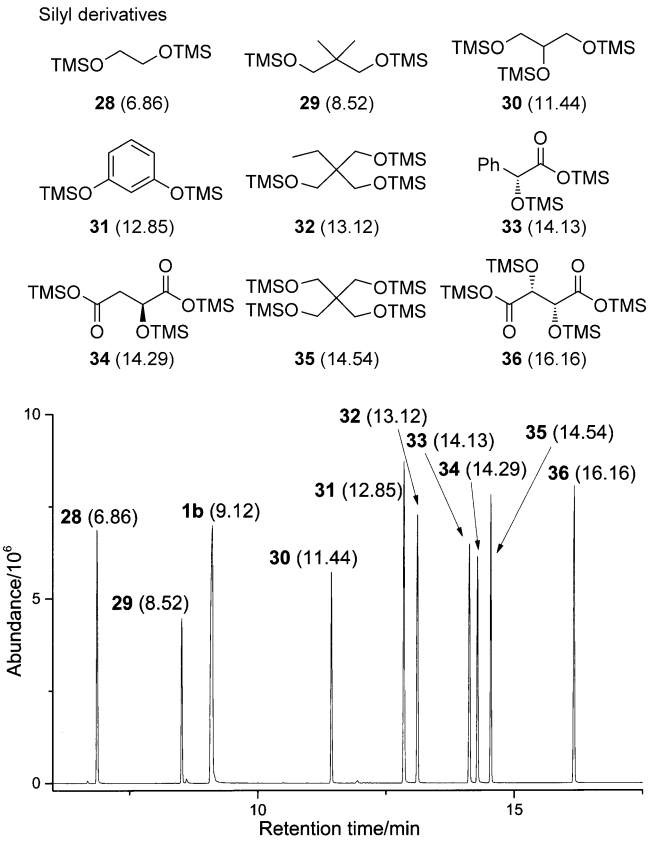



**Figure 3.** GC-MS traces of a mixture of *O*-silylated polyhydroxy compounds and their retention times given in parenthesis [min]. Capillary column HP-5MS (5% phenylmethylsiloxane) 30 m × 0.25 mm × 0.25 μm; injector temperature = 250 °C; eluent = He, flow rate = 0.8 mL min$^{-1}$; split injection = 100:1; injection volume = 0.2 μL; temperature regime = 50 °C for 2 min, 10 °C min$^{-1}$ until 310 °C; MS detector (ESI, 70 eV): MS Quad 150 °C; MS source = 230 °C.

taric acid (**36**), and D-mannose (**27**) obtained in situ (Figure 4). The experimental error of the developed technique was estimated to be 0.7, 0.5, and 1.0% for **30**, **36**, and **27** by comparing with the measurements and the control samples. In addition to their applications for the silylation of polyols and glycosides, silyl sulfinates **1a–d** can be thus used as new derivatization reagents for qualitative and quantitative GC analysis.

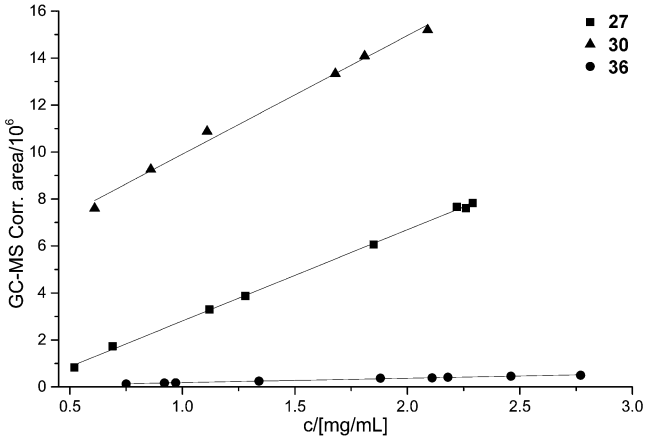



**Figure 4.** GC-MS calibration curves for trimethylsilylated D-mannose (**27**, ■), glycerol (**30**, ▲), and tartaric acid (**36**, ●) after their derivatization in situ with **1b**. Data were fitted by using a linear-fitting model $y = a + bx$: **27**: $a = -1.07 \pm 0.08$, $b = 3.89 \pm 0.05$; **30**: $a = 4.86 \pm 0.03$, $b = 5.05 \pm 0.02$; **36**: $a = -0.006 \pm 0.001$, $b = 0.19 \pm 0.01$ (standard error values are given).

## Conclusion

We have found a new catalytic system for the sila-ene reaction of allylsilanes **3a–d** with $SO_2$. The utilization of $(CuOTf)_2 \cdot C_6H_6$ as a catalyst (2.5% mol) permitted the preparation of powerful silylation reagents, namely, silyl sulfinates **1a–d**, on a multigram scale. By employing **1a–d**, the silylation of sterically hindered systems, such as tertiary alcohols and unstable aldols that readily eliminate water, was performed in high yields on a minute timescale. In most cases, the purification of the silylated products could simply be carried out by solvent evaporation because the byproducts ($SO_2$ + isobutylene) of the reaction are volatile. The regioselective semiprotection of polyols, including carbohydrate derivatives, and the direct one-step per-*O*-silylation of monosaccharides has also been developed. To the best of our knowledge, this report has also given the first fully described synthesis and analysis of the molecular structure and pyranose conformation of per-*O*-*tert*-butyldimethylsilyl-α-D-glucopyranose,[25d] which was possible due to high reactivity of *tert*-butyldimethylsilyl-2-methylprop-2-ene-1-sulfinate (**1a**). Silyl sulfinates were also used for silyl derivatization prior to the qualitative and quantitative GC analysis of polyhydroxyated compounds. Thus, silyl sufinates **1a–d** are new silylation reagents that should find wide applications in the synthesis of complicated natural products, as analogues of biological interest, and in analytical derivatization prior to GC analysis. Further studies will be directed toward the synthesis and conformational analysis of variously silylated glycosides by means of NMR spectroscopic analysis and X-ray crystal diffraction studies and will be coupled to computational methods.

## Experimental Section

### General

Commercial reagents (Fluka, Aldrich) were used without purification, if not noted differently. Solvents were distilled prior to use: THF, dioxane, and toluene from Na and benzophenone; MeOH from Mg and $I_2$; acetonitrile, DMF, DMSO, 1,1,3,3-tetramethylurea (TMU), *N*-methylpyrrolidone (NMP), and $CH_2Cl_2$ from $CaH_2$. Deuterated solvents were distilled prior to use: $CD_2Cl_2$ and $CDCl_3$ from $CaH_2$. $SO_2$ was dried by passing through a column filled with $P_2O_5$ (Fluka 06400) and $Al_2O_3$ for drying ($Al_2O_3$ basic activated type 5016A Brockman I; Aldrich 19,944-3). The solutions after the reactions and extractions were evaporated on a rotatory evaporator under reduced pressure. Liquid/solid flash chromatography (FC) was carried out on columns of silica gel (0.040–0.63 mm, Merck no. 9385, silica gel 60, 240–400 mesh). The eluent was a mixture of light petroleum ether (PE) and ethyl acetate (EtOAc), if not stated otherwise. TLC analysis for reaction monitoring was carried out on Merck silica gel 60 F254 plates with detection by UV light, the Pancaldi reagent ($(NH_4)_6MoO_4$, $Ce(SO_4)_2$, $H_2SO_4$, and $H_2O$) or $KMnO_4$. IR spectra were recorded on a Varian 800 FTIR spectrometer. $^1$H NMR spectra were recorded on Bruker ARX-300 or ARX-400 spectrometers (300 or 400 MHz) and the $\delta$(H) signals are given in ppm relative to the residual solvent signals as an internal reference ($CDCl_3$: $\delta$(H) = 7.27, $CD_2Cl_2$: $\delta$(H) = 5.30, [$D_6$]DMSO: $\delta$(H) = 2.50, [$D_7$]DMF: $\delta$(H) = 2.90 ppm). $^{13}$C NMR spectra were recorded on the same instrument as for the $^1$H NMR spectra (75.5 or 100.6 MHz), and $\delta$(C) signals are given in ppm relative to the signal of the solvent as an internal reference ($CDCl_3$: $\delta$(C) = 77.1, $CD_2Cl_2$: $\delta$(C) = 53.5, [$D_6$]DMSO: $\delta$(C) = 39.4, [$D_7$]DMF: $\delta$(C) = 31.0 ppm). The *J*(H,H) coupling constants were obtained by means of selective irradiation experiments. HRMS was performed on Jeol AX-505 spectrometer. GC-MS analysis of the TMS derivatives, their mixtures, and standards for calibration were carried out on a Hewlett–Packard Agilent 6890 system, equipped with a mass-selective detector system. The capillary column was an Agilent 19091 J-433 HP-5 5% phenyl methyl siloxane, 30 m × 0.25 mm i.d. with a film thickness of 0.25 μm. The injector temperature was maintained at 250 °C. The maximum temperature of the capillary column was 325 °C. The carrier gas was helium at a constant flow rate of 0.8 mL min$^{-1}$. Data were fitted by using OriginPro 9.0 SR 2 (OriginLab Corporation). CCDC contains the supplementary crystallographic data for this paper. These data are provided free of charge by The Cambridge Crystallographic Data Centre.

**General procedure for the synthesis of trialkylyl(2-methylallyl)silane reagents 3 a–d**: A few drops of iodine were added to a mixture of magnesium (7 g, 0.29 mol) in anhydrous THF (20 mL) to initiate the reaction. A solution of 3-chloro-2-methylpropene (18.11 g, 0.20 mol) and trialkylsilyl chloride (0.15 mol) in THF (130 mL) was dropwise added over 5 h to the reaction mixture at reflux in an argon atmosphere. The reaction mixture was heated to reflux for an additional 12 h when the addition was complete. The precipitate was filtrated and the residue was extracted with petroleum ether. The combined filtrate and extracts were distilled in a Vigreux column under atmospheric pressure to remove the excess of organic solvents. Trialkylyl(2-methylallyl)silanes were obtained by distillation under reduced pressure. The spectral data for **3 a–d** are in agreement with those data previously reported for these compounds.[19a]

***tert*-Butyldimethyl(2-methylallyl)silane (3 a)**:[19a] Colorless oil, 92% yield (23.51 g, 0.137 mol); b.p. 140 °C at 1 atm; $^1$H NMR ($CDCl_3$, 400 MHz): $\delta$ = 4.62 (br s, 1H; H-C(3)), 4.51 (br s, 1H; H-C(3)), 1.74 (s, 3H; Me-C(2)), 1.57 (s, 2H-C(1)), 0.91 (s, 9H; H-C(1′)), 0.01 ppm (s, 6H; H-C(3′)).

**General procedure for the preparation of trialkylsilyl-2-methylprop-2-ene-1-sulfinates 1 a–d**: $(CuOTf)_2PhH$ (1.07 g, 2.14 mmol, 2.5 mol%) in dry dichloromethane (15 mL) was placed in an autoclave. $SO_2$, dried over a column of $P_2O_5$ and alumina oxide, was poured to the solution at −78 °C, and the solution was stirred for 30 min. (2-Methylallyl)silane **3 a–d** (85.30 mmol) was added by syringe in the autoclave, which was heated at 50 °C for 12 h. The excess of $SO_2$ and $CH_2Cl_2$ were evaporated under reduced pressure (30 Torr) at −20 °C. The resulting solution was transferred into a flask and distilled under reduced pressure to give pure silyl methallylsulfinate. The spectral data for **1 a–c** are in agreement with those data previously reported for these compounds.[19a]

***tert*-Butyldimethylsilyl-2-methylprop-2-ene-1-sulfinate (1 a)**[19a] Colorless oil, 95% yield (19.02 g, 81.14 mmol); b.p. 64 °C at 0.4 Torr; $^1$H NMR ($CDCl_3$, 400 MHz): $\delta$ = 5.09 (br s, 1H; H-C(3)), 4.99 (br s, 1H; H-C(3)), 3.39 (s, 2H; C(1)), 1.89 (s, 3H; Me-C(2)), 0.96 (s, 9H; H-C(1′)), 0.27 (br s, 3H; Me-Si), 0.29 ppm (br s, 3H; Me-Si).

**General procedure for the silylation of alcohols 5 a–h**: Triethylsilyl-2-methylprop-2-ene-1-sulfinate (**1 c**; 91 mg, 0.388 mmol, 1 equiv) was added to a stirred solution of alcohol **5 a**–**h** (0.388 mmol) in $CH_3CN$ (1 mL) in an argon atmosphere at RT. After the full conversion was confirmed by TLC analysis, the reaction mixture was concentrated under reduced pressure and filtrated though a plug of silica gel.

**3-*O*-(Triethylsilyl)cholesterol (6 a)**: White solid, 98% yield (191 mg, 0.38 mmol); $R_f$ = 0.37 (EP/diethyl ether = 10:1); $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ = 5.36 (d, *J* = 5.0 Hz, 1H; H-C(6)), 3.48 (sept, *J* = 11.0, 4.5 Hz, 1H; H-C(3)), 2.30 (dd, *J* = 4.5, 13.0 Hz, 1H; H-C(4a)), 2.24 (ddd, *J* = 13.0, 2.0 Hz, 1H; H-C(4b)), 2.05–1.92 (m, 2H; H-7a, H-C(12a)), 1.89–1.83 (m, 2H; H-1a, H-C(16)), 1.72 (m, 1H; H-2b), 1.62–1.1 (22H; all residual protons, except methyl groups), 1.02 (s, 3H; H-C(19)), 0.90 (d, *J* = 6.5 Hz, 3H; H-C(21)), 0.96 (t, *J* = 8.0 Hz, 9H; H-C(2′)), 0.7 (s, 3H; H-C(18)), 0.56 and 0.53 ppm (q, *J* = 8.0 Hz, 6H; H-C(1′)); the spectroscopic data for **6 a** are in agreement with those data previously reported for this compound.[28b]

**General procedure for the silylation of 1-phenylethanediol (7)**: Trialkylsilyl-2-methylprop-2-ene-1-sulfinate **1 a**, **1 c**, or **1 d** (0.29 mmol, 1 equiv) was added in an argon atmosphere at RT to a stirred solution of 1-phenylethanediol (**7**; 40 mg, 0.29 mmol) in [$D_7$]DMF (0.7 mL) containing toluene as an internal reference. After full conversion was confirmed by $^1$H NMR spectroscopic analysis, the reaction mixture was concentrated under reduced pressure and filtrated though a plug of silica gel.

**1-Phenyl-2-[(triethylsilyl)oxy]ethanol (13 a)**:[19a] Colorless oil, 93% yield, (68 mg, 0.27 mmol); $R_f$ = 0.29 (EP/diethyl ether = 10:3); $^1$H NMR ($CDCl_3$, 400 MHz): $\delta$ = 7.49–7.27 (m, 5H; aromatic), 4.80 (dd, *J* = 8.9, *J* = 3.9 Hz, 1H; H-C(1)), 3.78 (dd, *J* = 10.2, 3.9 Hz, 1H; H-C(2)), 3.57 (dd, *J* = 10.2, 8.9 Hz, 1H; H-C(2)), 3.09 (s, 1H; H-O), 0.99 (t, *J* = 8.3 Hz, 9H; $SiCH_2CH_3$), 0.66 ppm (q, *J* = 8.3 Hz, 6H; $SiCH_2CH_3$).

**General procedure for the silylation of methyl-α-D-pyranosides 8–10**: Trialkylsilyl-2-methylprop-2-ene-1-sulfinate **1 a** or **1 d** (0.515 mmol, 1 equiv) was added to a NMR tube containing a solution of a methyl-α-D-pyranoside (100 mg, 0.515 mmol) in [$D_7$]DMF (1.5 mL) containing toluene as an internal reference. The reaction was followed by $^1$H NMR spectroscopic analysis at RT. The reaction was finished after 15 min and the obtained reaction mixture was quenched with buffer (pH 7), extracted with $CH_2Cl_2$, dried over $Na_2SO_4$, and evaporated under reduced pressure. The resulting oil was purified by filtration though a plug of silica gel.

**Methyl-6-*O*-(*tert*-butyldimethylsilyl)-α-D-glucopyranoside (14a)**: White powder, 97% yield (154 mg, 0.50 mmol); $^1$H NMR ([D$_7$]DMF, 400 MHz): $\delta$ = 5.17 (d, $J$ = 4.8 Hz, 1H; OH-C(4)), 5.08 (d, $J$ = 4.5 Hz, 1H; OH-C(3)), 4.85 (d, $J$ = 6.5 Hz, 1H; OH-C(2)), 4.80 (d, $J$ = 3.4 Hz, 1H; H-C(1)), 4.12 (dd, $J$ = 11.0, 2.1 Hz, 1H; H-C(6a)), 3.95 (dd, $J$ = 11.0, $J$ = 6.2 Hz, 1H; H-C(6b)), 3.78 (ddd, $J$ = 4.5, 8.5, 3.8 Hz, 1H; H-C(3)) 3.67 (m, $J$ = 3.8, 2.1, 4.8 Hz, 1H; H-(5)), 3.52 (s, 3H; OCH$_3$), 3.50 (t, $J$ = 3.8 Hz, 1H; H-C(2)), 3.44–3.38 (ddd, $J$ = 4.5, 8.5, 5.1 Hz, 1H; H-C(4)), 1.08 (s, 9H; H-*t*BuSi), 0.26 ppm (s, 6H; H-MeSi); the spectroscopic data for **14a** are in agreement with those data previously reported for this compound.[28h]

**General procedure for the silylation of α-D-glucal (11)**: Trialkylsilyl-2-methylprop-2-ene-1-sulfinate **1a** (1.36 mmol, 2 equiv) or **1d** (0.68 mmol, 1 equiv) was added to a NMR tube containing a solution of D-glucal (**11**; 100 mg, 0.68 mmol) in [D$_7$]DMF (0.6 mL) containing toluene as an internal reference. The reaction was followed by $^1$H NMR spectroscopic analysis. The obtained reaction mixtures were quenched with water buffer (pH 7), extracted with $CH_2Cl_2$, dried over $Na_2SO_4$, and evaporated under reduced pressure. The resulting oil was purified by filtration though a plug of silica gel.

**3,6-Bis-*O*-(*tert*-butyldimethylsilyl)-D-Glucal (17a)**: White powder, 96% yield (243 mg, 0.65 mmol); $[\alpha]_D^{25} = -30.2$ ($c$ = 0.75 in CHCl$_3$); $^1$H NMR (CDCl$_3$, 400 MHz): $\delta$ = 6.31 (dd, $J$ = 1.7, 6.1 Hz, 1H; H-C(1)), 4.65 (dd, $J$ = 2.4, 6.1 Hz, 1H; H-C(2)), 4.24 (dt, $J$ = 6.1, 1.7 Hz, 1H; H-C(3)), 4.00 (dd, $J$ = 4.8, 11.1 Hz, 1H; H-C(6a)), 3.92 (dd, $J$ = 3.7, 11.1 Hz, 1H; H-C(6b)), 3.88–3.84 (ddd, $J$ = 3.7, 4.8 Hz, $J$ = 8.5 Hz, 1H; H-C(5)), 3.80 (dd, $J$ = 6.5, 8.5 Hz, 1H; H-C(4)), 2.55 (br s, 1H; C(4)-OH), 0.94 (d, $J$ = 1.7 Hz, 18H; H-C(1′)), 0.15 (d, $J$ = 1.0 Hz, 6H; H-C(3′)), 0.12 ppm (d, $J$ = 1.0 Hz, 6H; H-C(3′)); the spectroscopic data for **17a** are in agreement with those data previously reported for this compound.[28i]

**General procedure for the silylation of methyl-4,6-*O*-benzylidene-α-D-glucopyranoside (12)**: Trialkylsilyl-2-methylprop-2-ene-1-sulfinate **1a**–**d** (0.354 mmol, 1 equiv) was added to a stirred solution of methyl-4,6-*O*-benzylidene-α-D-glucopyranoside (100 mg, 0.354 mmol) in DMF (1.5 mL) in an argon atmosphere at RT. The reaction was followed by TLC analysis (petroleum ether/ethyl acetate = 10:2). At the end of the reaction, the reaction mix was quenched with water buffer (pH 7), extracted with $CH_2Cl_2$, and dried over $Na_2SO_4$. The obtained solution was evaporated under reduced pressure and purified by filtration though a plug of silica gel (petroleum ether/ethyl acetate = 10:2).

**(+)-Methyl-4,6-*O*-benzylidene-2-*O*-(*tert*-butyldimethylsilyl)-α-D-glucopyranoside (18a)**: White powder, 96% yield (134 mg, 0.34 mmol); $R_f$ = 0.57; $[\alpha]_D^{25} = +57.8$ ($c$ = 1.1 in CHCl$_3$); $^1$H NMR (CDCl$_3$, 400 MHz): $\delta$ = 5.56 (s, 1H; PhCH), 4.68 (d, $J$ = 3.5 Hz, 1H; H-C(1), 4.33 (dd, $J$ = 10.0, 5.0 Hz, 1H; H-C(6a)), 4.03 (t, $J$ = 9.5 Hz, 1H; H-C(3)), 3.90–3.84 (ddd, $J$ = 9.0, 5.0, 3.5 Hz, 1H,H-C(5)), 3.76 (t, $J$ = 10.0 Hz, 1H; H-C(6b)), 3.72 (dd, $J$ = 3.5, 9.5 Hz, 1H; H-C(2)), 3.52 (t, $J$ = 9.0 Hz, 1H; H-C(4)), 3.46 (s, 3H; MeO), 0.95 (s, 9H; H-*t*BuSi), 0.16 ppm (d, $J$ = 1.5 Hz, 6H; MeSi); the spectroscopic data for **18a** are in agreement with those data previously reported for this compound.[28i]

**(−)-(1*Z*,2*S*,3*S*,4*R*,5*E*)-1-Ethylidene-2,4,6-trimethyl-7-oxo-3-[(1*S*)-1-phenylethoxy]hept-5-en-1-yl 2-methylpropanoate (20)**: This product resulted from the silylation of **19** in basic media. Procedure with triethylamine as the base: Triethylamine (21 μL, 0.15 mmol, 2.2 equiv) was added to a solution of aldehyde **19** (21 mg, 0.05 mmol, 1 equiv) in dichloromethane (2 mL). The reaction mixture was cooled to −15 °C, treated with TBSOTf (14 μL, 0.06 mmol, 1.2 equiv), and allowed to reach RT over 5 h. The mixture was poured into saturated aqueous NaHCO$_3$ solution (1 mL). Extraction with dichloromethane, washing the combined organic layer with aqueous NaCl, drying, evaporation, and purification by flash chromatography (petroleum ether/ethyl acetate = 9:1) afforded the pure elimination product **20**. Colorless oil, quant. yield (20 mg, 0.05 mmol); $R_f$ = 0.75 (petroleum ether/ethyl acetate = 9:1); $[\alpha]_D^{25} = -22$ ($c$ = 0.3 in CHCl$_3$); $^1$H NMR (CDCl$_3$, 400 MHz): $\delta$ = 8.98 (s, 1H; CHO), 7.32–7.28 (m, 5H; arom), 5.99 (d, $J$ = 10.1 Hz, 1H; H-C(5)), 5.13 (q, $J$ = 6.8 Hz, 1H; H-C(1′)), 4.39 (q, $J$ = 6.5 Hz, 1H; H-C(1″)), 3.25 (t, $J$ = 5.9 Hz, 1H; H-C(3)), 2.75 (2 m, 2H; H-C(4), H-C(2)), 2.59 (sept, $J$ = 7.0 Hz, 1H; (CH$_3$)$_2$*CH*COO-C(1)), 1.55 (s, 3H; H$_3$C-C(6)), 1.39 (d, $J$ = 7.0 Hz, 3H; H-C(2″)), 1.37 (d, $J$ = 6.8 Hz, 3H; H-C(2′)), 1.18–1.16 (2 d, $J$ = 7.0 Hz, 6H; (*CH*$_3$)$_2$CHCOO-C(1)), 1.03 (d, 3H; $J$ = 7.1 Hz, CH$_3$-C(2)), 0.91 ppm (d, $J$ = 6.8 Hz, 3H; CH$_3$-C(4)); $^{13}$C NMR (CDCl$_3$, 100.6 MHz): $\delta$ = 195.6, 174.3, 149.5, 143.2, 128.4, 128.0, 127.1, 112.4, 79.2, 77.1, 40.1, 34.8, 34.2, 29.7, 23.6, 19.2, 19.1, 14.9, 12.6, 10.8 ppm; IR (film): $\tilde{\nu}$ = 2964, 2924, 2851, 1750, 1690, 1639, 1454, 1414, 1386, 1264, 1096, 1020, 865, 797, 702 cm$^{-1}$; MS (CI; NH$_3$): $m/z$ (%) 404(21) $[M+18]^+$, 307(31), 283(38), 265(34), 212(37), 195(90), 105(100); HRMS (MALDI): $m/z$ calcd for $C_{24}H_{34}O_4Na$: 409.2354; found: 409.2349 $[M+Na]^+$.

**(+)-(1*Z*,2*S*,3*S*,4*S*,5*S*,6*S*)-5-{[(*tert*-Butyl(dimethyl)silyl]oxy}-1-ethylidene-2,4,6-trimethyl-7-oxo-3-[(1*S*)-1-phenylethoxy)heptyl 2-methylpropanoate (21)**: *tert*-Butyldimethylsilyl methallylsulfinate (11.3 mg, 0.148 mmol, 1.2 equiv) was added to a solution of alcohol **19** (50 mg, 0.123 mmol, 1 equiv) in CH$_3$CN (1 mL). The reaction mixture was stirred until total conversion, as monitored by TLC analysis. Evaporation of the solvent gave the pure product **21**. Colorless oil, 89% yield, (68 mg, 0.11 mmol); $R_f$ = 0.52 (petroleum ether/ethyl acetate = 9:1); $[\alpha]_D^{25} = +7$ ($c$ = 0.25 in CHCl$_3$); $^1$H NMR (CDCl$_3$, 400 MHz): $\delta$ = 9.72 (d, $J$ = 2.5 Hz, 1H; CHO), 7.37–7.28 (m, 5H; arom), 5.21 (q, $J$ = 7.0 Hz, 1H; H-C(1′)), 4.43 (q, $J$ = 6.8 Hz, 1H; H-C(1″)), 3.47 (d, 1H; H-C(5)), 3.25 (dd, $J$ = 4.6, 2.7 Hz, 1H; H-C(3)), 2.93 (quint, $J$ = 5.5 Hz, 1H; H-C(2)), 2.55 (sept, $J$ = 7.1 Hz, 1H; (CH$_3$)$_2$*CH*COO-C(1)), 2.26 (q, $J$ = 6.9 Hz, 1H; H-C(4)), 1.88 (dquint, $J$ = 7.2, 2.6 Hz, 1H; H-C(6)), 1.47 (d, $J$ = 6.6 Hz, 3H; H-C(2′)), 1.41 (d, $J$ = 6.8 Hz, 3H; H-C(2″)) 1.19–1.16 (2 d, $J$ = 7.1 Hz, 6H; (*CH*$_3$)$_2$CHCOO-C(1)), 1.09 (d, $J$ = 7.3 Hz, 3H; CH$_3$-C(2)), 0.93 (d, $J$ = 7.2 Hz, 3H; CH$_3$-C(6)), 0.82 (s, 9H; TBS), 0.79 (d, $J$ = 6.9 Hz, 3H; CH$_3$-C(4)), −0.07 (s, 3H; TBS), −0.08 ppm (s, 3H; TBS); $^{13}$C NMR (CDCl$_3$, 100.6 MHz): $\delta$ = 205.2, 174.2, 150.4, 143.1, 128.4, 127.8, 127.1, 111.8, 78.3, 75.6, 75.2, 48.2, 40.0, 39.4, 41.2, 25.7, 23.9, 19.2, 19.1, 13.2, 11.5, 10.8, 10.4, −4.3, −5.1 ppm; IR (film): $\tilde{\nu}$ = 2964, 2930, 2857, 2360, 2342, 1748, 1728, 1716, 1471, 1456, 1386, 1258, 1113, 1081, 1024, 912, 836 cm$^{-1}$; MS (CI; NH$_3$): $m/z$ (%): 518(8) $[M]^+$, 391(52), 253(100), 251(67), 235(20), 207(32), 104(10); HRMS (MALDI): $m/z$ calcd for $C_{30}H_{50}O_5SiNa$: 542.3358; found: 542.33592 $[M+Na]^+$.

**1,2,3,4,6-Penta-*O*-tert-butyldimethylsilyl-α-D-glucopyranose (23a)**: *tert*-Butyldimethylsilyl-2-methylprop-2-ene-1-sulfinate (**1b**; 122.0 mg, 0.52 mmol, 15 equiv) was added to a stirred suspension of D-glucose (**22**; 6.3 mg, 0.035 mmol, 1 equiv) in a mixture of CD$_3$CN (0.6 mL) and CDCl$_3$ (0.6 mL) at ambient temperature. The resulting reaction mixture was heated at 60 °C for 24 h (monitored by NMR and GC-MS). The conversion of 99% was established by $^1$H NMR spectroscopic analysis by using toluene as an internal reference. MeOH (0.5 mL) was added and the volatiles were evaporated under reduced pressure. The oily residue was purified by preparative TLC (hexane/dichloromethane = 4:1). Crystals were isolated from a mixture of CD$_3$CN (0.6 mL) and CDCl$_3$ (0.2 mL). Yield = 70% (18.3 mg, 0.025 mmol); $^1$H NMR (CD$_3$CN + CDCl$_3$, 300 MHz): $\delta$ = 5.16 (d, $J$ = 3.2 Hz, 1H; H-C(1)), 4.02–3.95 (m, 1H; H-C(5)), 3.85 (bd, $J$ = 3.8 Hz, 1H; H-C(4)), 3.83–3.68 (m, 4H; H-C(2), H-C(3), H-C(6)), 0.91, 0.90, 0.88 (3 s, 45H; 15 × CH$_3$), 0.11–0.04 ppm (m, 30H; 10 × CH$_3$); $^{13}$C NMR (CD$_3$CN + CDCl$_3$, 75.5 MHz,): $\delta$ = 91.6, 77.3, 76.7, 73.4, 72.7, 63.5, 26.5, 26.4, 26.3, 26.2, 26.0, 0.06 (2C), −0.04 (2C), −0.1 ppm;

crystal data for **23a** ($C_{36}H_{82}O_6Si_5$): $M_r = 751.47$, monoclinic, $P2_1$, $a = 12.1077(1)$, $b = 36.4878(5)$, $c = 12.1834(3)$ Å, $\beta = 112.7115(8)^\circ$, $V = 4965.07(15)$ Å$^3$, $T = 173(2)$ K, $Z = 4$, $\mu(Mo_{K\alpha}) = 0.178$ mm$^{-1}$, 21172 reflections measured, 21172 independent reflections, $R_{1(obs)} = 0.093$, $wR_{1(obs)} = 0.191$, $R_{1(all)} = 0.233$, $wR_{1(all)} = 0.244$, $S = 1.01$.

**Monosaccharides 23b, 25, and 27**: $CD_3CN$ (1 mL) and silyl sulfinate **1b** (10 equiv) were added to monosaccharides **22**, **24**, or **26** measured in a GC vial, and the resulting mixture was stirred in an argon atmosphere for 18 h at 60 °C. The GC-MS and NMR spectroscopic analyses were performed and revealed full conversion into the corresponding products **23b**, **25**, or **27**, respectively. The samples of silylated monosaccharides were injected into the gas chromatograph in the split mode (100:1; injection volume = 1.00 μL). The oven temperature was held at 70 °C for 2 min, increased to 310 °C at 20 °C min$^{-1}$, and held at 310 °C for 2 min.

**Silylation of a mixture of monosaccharides**: $CH_3CN$ (1 mL) and silyl sulfinate **1b** (255 mg, 227 μL, 10 equiv) were added to monosaccharides D-(+)-glucose (**22**; 13.46 mg, 0.075 mmol), D-(+)-galactose (**24**; 4.45 mg, 0.025 mmol), and D-(+)-mannose (**26**; 5.99 mg, 0.033 mmol) measured into a GC vial. The resulting mixture was stirred in an argon atmosphere for 4 h at 70 °C and GC-MS analysis was then carried out. The mixture of silylated monosaccharides were injected into the gas chromatograph in the split mode (600:1; injection volume = 0.20 μL). The oven temperature was held at 70 °C for 2 min, increased to 310 °C at 20 °C min$^{-1}$, and held at 310 °C for 2 min (the GC-MS traces are depicted in Figure 2).

**Silylation of a mixture of polyhydroxy compounds and analysis of the silylated forms 28–36**: $CH_3CN$ (1 mL) and TMS sulfinate **1b** (200 mg, 180 μL, 1.041 mmol) were added to ethane-1,2-diol (4.16 mg, 0.067 mmol), 2,2-dimethylpropane-1,3-diol (2.74 mg, 0.026 mmol), glycerol (2.38 mg, 0.026 mmol), resorcinol (5.82 mg, 0.053 mmol), 2-ethyl-2-(hydroxymethyl)propane-1,3-diol (3.73 mg, 0.0278 mmol), (*R*)-2-hydroxy-2-phenylacetic acid (5.64 mg, 0.037 mmol), L-(−)-malic acid (4.30 mg, 0.032 mmol), pentaerythritol (3.05 mg, 0.022 mmol), and L-(+)-tartaric acid (5.79 mg, 0.039 mmol) measured into a GC vial. The resulting mixture was stirred in an argon atmosphere for 4 h at 50 °C, and GC-MS analysis was then performed. The sample containing the silylated polyhydroxyates **28**–**36** was injected into a gas chromatograph in the split mode (split ratio = 100:1, injection volume = 0.20 μL). The oven temperature was held at 50 °C for 3 min, increased to 120 °C at 10 °C min$^{-1}$, increased to 310 °C at 100 °C min$^{-1}$, and held at 310 °C for 3 min (the GC-MS traces are depicted in Figure 3).

**General procedure to obtain calibration curves for 1,2,3,4,6-penta-*O*-trimethylsilyl-D-mannopyranose (27), tris-*O*-trimethylsilyl glycerol (30), and per-*O*-trimethylsilylated tartaric acid (36) generated in situ**: The samples of D-mannose (**26**), glycerol or L-(+)-tartaric acid were precisely weighed in a volumetric flask (10 or 20 mL) and diluted with anhydrous $CH_3CN$. Trimethylsilyl sulfinate **1b** (2 equiv per OH group) was added, the volumetric flask was filled to the mark, and the resulting solution was left for 3 h. The samples were transferred into GC vials and analyzed 3× each. The samples were injected into the gas chromatograph in a splitless mode (injection volume = 0.20 μL). The oven temperature was held at 50 °C for 2 min, increased to 310 °C at 100 °C min$^{-1}$, and held at 310 °C for 2 min (the calibration curves are depicted in Figure 4).

**Calibration curve for 1,2,3,4,6-penta-*O*-trimethylsilyl-D-mannopyranose (27) generated in situ**: The following aliquots of D-mannose were measured into a volumetric flask (10 mL), derivatized, and analyzed as described above: 5.17 mg (0.52 mg mL$^{-1}$), 6.89 mg (0.69 mg mL$^{-1}$), 9.31 mg (0.93 mg mL$^{-1}$), 11.21 mg (1.12 mg mL$^{-1}$), 12.79 mg (1.28 mg mL$^{-1}$), 18.54 mg (1.85 mg mL$^{-1}$), 22.23 mg (2.22 mg mL$^{-1}$), 22,63 mg (2.26 mg mL$^{-1}$), and 22.87 mg (2.29 mg mL$^{-1}$).

**Calibration curve for tris-*O*-trimethylsilyl glycerol (30) generated in situ**: The following samples of glycerol were weighted into a volumetric flask (20 mL), derivatized, and analyzed as described above: 12.25 mg (0.61 mg mL$^{-1}$), 17.17 mg (0.86 mg mL$^{-1}$), 22.27 mg (1.11 mg mL$^{-1}$), 33.69 mg (1.68 mg mL$^{-1}$), 36.14 mg (1.81 mg mL$^{-1}$), 41.84 mg (2.09 mg mL$^{-1}$).

**Calibration curve for per-*O*-trimethylsilylated tartaric acid (36) generated in situ**: The following aliquots of L-(+)-tartaric acid were measured into a volumetric flask (10 mL), derivatized, and analyzed as described above: 7.50 mg (0.75 mg mL$^{-1}$), 9.21 mg (0.92 mg mL$^{-1}$), 9.73 mg (0.97 mg mL$^{-1}$), 13.51 mg (1.35 mg mL$^{-1}$), 18.83 mg (1.88 mg mL$^{-1}$), 21.06 mg (2.11 mg mL$^{-1}$), 21.80 mg (2.18 mg mL$^{-1}$), 24.61 mg (2.46 mg mL$^{-1}$), and 27.70 mg (2.77 mg mL$^{-1}$).

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