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# A NOVEL 1,3 O ⟶ C SILYL REARRANGEMENT IN CARBOHYDRATE CHEMISTRY: SYNTHESIS OF α-D-GLYCOPYRANOSYLTRIMETHYLSILANES

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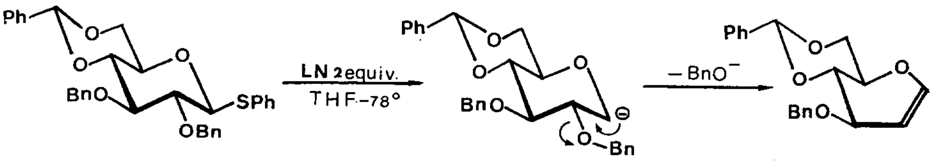
**Abstract**: Reductive lithiation of 2-*O*-trimethylsilyl derivatives of phenyl thio*gluco* and -*galacto*pyranosides gives rise to a 1,3 O ⟶ C silyl migration leading to α-D-*gluco* and -*galacto*pyranosyltrimethylsilanes in good yields. The expected β-elimination is observed to a small extent in the case of a 2,3-di-*O*-trimethylsilyl derivative of phenyl thio*gluco*pyranoside where a tandem 1,3 O ⟶ C, 1,4 O ⟶ O silyl rearrangement occurs, but becomes the only possible reaction in the case of an *O*-silylated derivative of phenyl thio*manno*pyranoside.

Unstabilized α-lithioethers can be conveniently prepared in tetrahydrofuran at -78° from α-(phenylthio)ethers by reductive lithiation with lithium naphthalenide (LN)[1]. This method has been applied to 2-deoxy phenyl thiohexopyranosides generating a reactive glycosyl-lithium species which was shown to couple at -78° with various electrophiles[2]. Moreover, phenyl thioglycopyranosides underwent reductive lithiation at C-1, followed by rapid elimination of the 2-substituent (acetal, ether, acetate) when treated with LN in tetrahydrofuran at low temperature[2,3]. Pyranoid glycals were obtained in excellent yields. A typical example (98% yield) is shown in Scheme 1. We now report on the unusual behavior of phenyl thioglycopyranosides having an *O*-trimethylsilyl ether function at C-2 when submitted to reductive lithiation.

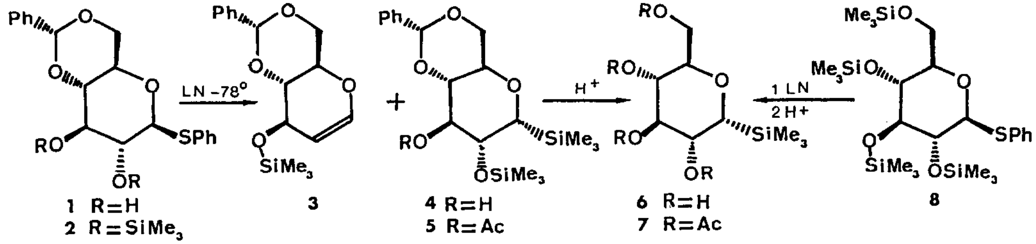
Scheme 1



The 2,3-di-*O*-trimethylsilyl derivative 2 of the known[4] diol, phenyl 4,6-*O*-benzylidene-1-thio-β-D-glucopyranoside 1, was reacted with LN (2 equiv.) in tetrahydrofuran at -78°. Two compounds were obtained (Scheme 2).

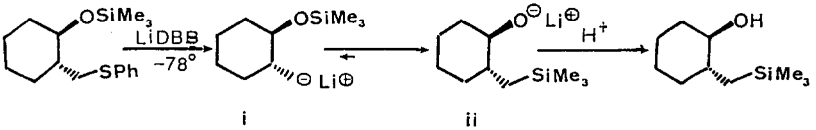
The minor one (12% yield) was shown to be glycal 3. Much to our surprise, the major reaction product was a crystalline compound 4, resulting from an unprecedented tandem 1,3 O ⟶ C; 1,4 O ⟶ O anionic silyl rearrangement! *O*-Acetylation of 4 gave a shift of the H-3 n.m.r. signal from δ 3.90 to 5.42 ppm, the H-2 signal being largely unaffected. Compound 4 has a $^4C_1$ conformation in chloroform solution, as shown by the *trans*-diaxial relationship of H-2 and H-3 ($J_{2,3}$ = 9 Hz, $J_{3,4}$ = 9.5 Hz); the anomeric silicon atom is axially oriented with an H-1 signal at δ 3.80 ($J_{1,2}$ 7.8 Hz).*

Scheme 2



Very fast anionic 1,4 O ⟶ C silyl migration has been observed by Rücker[6] under similar reaction conditions (Scheme 3). Owing to the high Si-O bond energy, silyl migrations in electroneutral molecules (reactions performed with *catalytic* amounts of base) usually occur in the direction from other atoms to oxygen[7]. In the case of anionic migration in the opposite direction described by Rücker, the equilibrium *i* ⇌ *ii* obviously lies far on the right side owing to the poor stabilization of the carbanion *i*. Besides, anionic 1,3 silyl migrations between oxygen and carbon atoms have been claimed to be observable only if the normally fast elimination of silyloxide (Peterson olefination) is retarded by various factors[8].

Scheme 3



In the present case, we can postulate the following mechanism (Scheme 4): the unstable anomeric carbanion *i* will stabilize through either a β-elimination of LiOSiMe₃ to give glycal 3, or through a 1,3 O ⟶ C silyl

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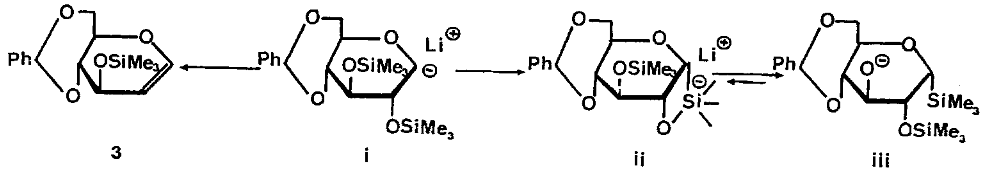
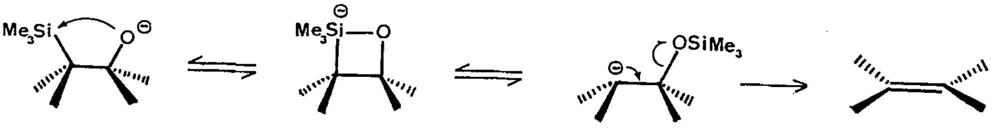
* (3,4,6-Tri-*O*-acetyl-2-deoxy-α-D-*arabino*-hexopyranosyl)trimethylsilane[5] which exists in CHCl₃ solution in a $^1C_4$ conformation has an H-1 n.m.r. signal at δ 3.65 ($J_{1,2ax}$ = 9.5 Hz, $J_{1,2eq}$ = 4.3 Hz).

Scheme 4



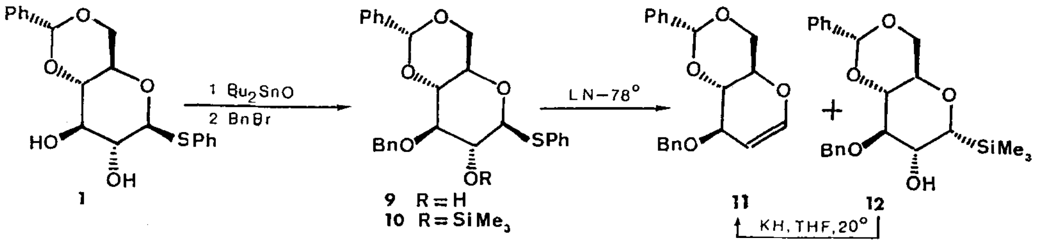
migration, a transient cyclic penta-coordinated species *ii* being a probable intermediate. The conversion of *ii* into *iii* then generates a more thermodynamically stable oxyanion. A pertinent question is: why should the cyclic intermediate *ii* not give rise to a concerted Peterson olefination and thus contribute to the formation of 3? Although the detailed mechanism of the Peterson reaction is not known, it appears that the elimination occurs more easily when the carbon atom carrying the silyl group has anion-stabilizing groups on it and when lithium cation is avoided[9]. On the other hand, theoretical calculations[10] have shown that fragmentation of an oxasiletanide-anion (such as *ii*) is a non-concerted process, with the C-Si cleavage being more advanced than the C-O cleavage. It could thus be that the mechanism of the Peterson olefination is actually a non-concerted fragmentation (Scheme 5).

Scheme 5

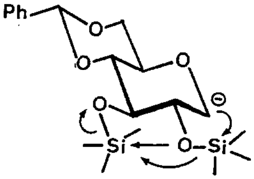


The instability of the anomeric glycosyl-lithium derivative generated in the reaction as described above is clearly a key factor. Once irreversibly produced from *i* (Scheme 4), the cyclic species *ii* does not fragment in a concerted manner, but is rather converted into the stable oxyanion *iii*.

Scheme 6



In order to find out if the tandem character of our reaction was a prerequisite for its viability, diol 1 was regioselectively converted into the 3-*O*-benzyl derivative 9 by the tin methodology[11], with a conventional *O*-trimethylsilylation then giving compound 10. When 10 was treated with LN (2 equiv.) in tetrahydrofuran at -78°, glycal 11 was obtained in 58% yield, and compound 12 resulting from the 1,3 O ⟶ C anionic silyl migration was isolated in only 40% yield (Scheme 6). Although not critical, the 3-*O*-trimethylsilyl group clearly favors the 1,3 O ⟶ C silyl migration, and the negative charge was transferred through the following pathway:



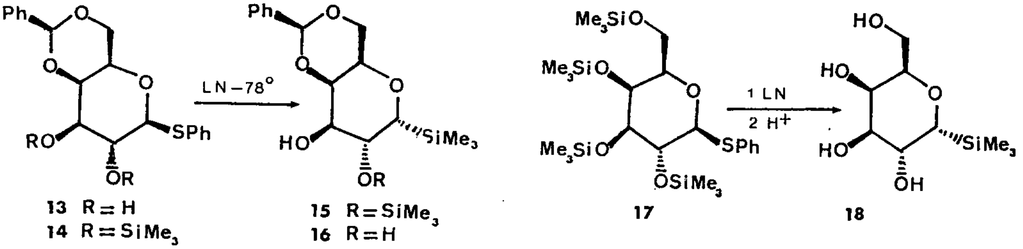
Compound 12 was perfectly stable at room temperature in the presence of *n*-butyllithium in THF, but was converted into glycal 11 (85% yield) by KH in THF at room temperature in 20 min (Peterson olefination).

Compound 4 was hydrolyzed by 80% aqueous acetic acid at 100° to give the crystalline (α-D-glucopyranosyl)trimethylsilane 6 which showed, in a $D_2O$ solution, a $^4C_1$ conformation with an H-1 n.m.r. signal at δ 4.03 (d, $J_{1,2}$ = 7 Hz). Its *O*-acetylated derivative 7 showed an important change of conformation with an H-1 signal at δ 3.92 (d, $J_{1,2}$ = 5.5 Hz) and $J_{2,3}$ = 7.3 Hz, $J_{3,4}$ = 7.8 Hz. The *syn* relationship between the axial anomeric trimethylsilyl group and the equatorial OH-2 in 6 explains its stability in an acidic medium[12].

(α-D-Glucopyranosyl)trimethylsilane 6 was also promptly obtained in gram amounts by per-*O*-trimethylsilylation of the known phenyl 1-thio-β-D-glucopyranoside[13], followed by reductive lithiation and acidic hydrolysis (61% overall yield, Scheme 2). This represents the first synthesis of a Si-glucoside to date.

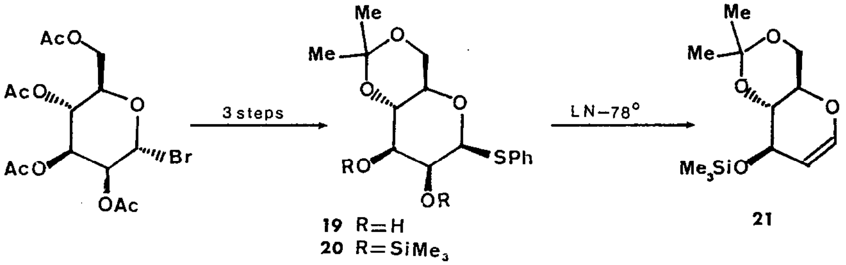
Reductive lithiation was also applied to the 2,3-di-*O*-trimethylsilyl derivative 14, prepared from the known[4] phenyl 4,6-*O*-benzylidene-1-thio-β-D-galactopyranoside 13 (Scheme 7). Compound 15 resulting from the tandem 1,3, O ⟶ C; 1,4 O ⟶ O silyl migration was isolated in 16% yield together with diol 16, resulting from easy hydrolysis of the 2-*O*-trimethylsilyl group during workup (23% yield). Unsaturated compounds were also present but could not be isolated owing to severe streaking on silica gel. The crystalline (α-D-galactopyranosyl)trimethylsilane 18 was best prepared in 50% overall yield from phenyl 1-thio-β-D-galactopyranoside[14] through the already described sequence: silylation-reductive lithiation-acidic hydrolysis.

Scheme 7

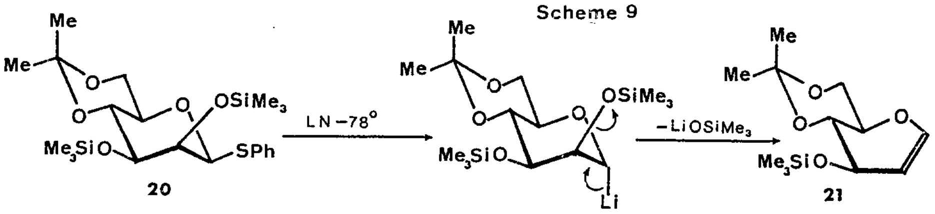


Finally, we investigated the influence of the stereochemistry at C-2 upon the outcome of the reaction. Phenyl 1-thio-β-D-mannopyranoside, prepared from acetobromomannose by treatment with sodium thiophenoxide in HMPA[15], followed by *O*-deacetylation, was converted into the 4,6-*O*-isopropylidene derivative 19. The 2,3-di-*O*-trimethylsilyl derivative 20, when submitted to reductive lithiation, was transformed into glycal 21 (68% yield) (Scheme 8). Since glycosyl-lithium species have been shown[2] to be α-oriented, no 1,3 O⟶C silyl rearrangement was possible for steric reasons, and *anti*-elimination of $LiOSiMe_3$ occurred exclusively (Scheme 9).

Scheme 8



Scheme 9



In conclusion, this work provides a straightforward entry to a novel class of cabohydrate derivatives which may have interesting chemical and biochemical properties. It is also of mechanistic interest in connection with the Peterson olefination reaction.

## EXPERIMENTAL

Melting points are uncorrected. Optical rotations were measured at 20±2° with a Perkin-Elmer Model 241 polarimeter. Elemental analyses were performed at Université Pierre et Marie Curie (Paris VI). $^1$H-N.m.r. spectra were recorded with a Cameca 250 and a Bruker AM-400 spectrometer for solutions in $CDCl_3$ or $C_6D_6$ ($Me_4Si$ as internal standard). $^{29}$Si-N.m.r. spectra were recorded at 79.424 MHz with a Bruker AM-400 spectrometer for solutions in $CDCl_3$ ($Me_4Si$ as internal standard) or $D_2O$ (DSS as internal standard). Reactions were monitored by t.l.c. on Silica Gel 60 $F_{254}$ (Merck) and detection by charring with sulfuric acid. Flash column chromatography was performed on Silica Gel 60 (230-400 mesh, Merck).

*Phenyl 4,6-O-benzylidene-2,3-di-O-trimethylsilyl-1-thio-β-D-glucopyranoside* (2). -- To a solution of phenyl 4,6-*O*-benzylidene-1-thio-β-D-glucopyranoside 1[4] (3.6 g, 10 mmoles) in dry pyridine (50 mL) were added in succession hexamethyldisilazane (19 mL, 90 mmoles) and chlorotrimethylsilane (8 mL, 63 mmoles) at room temperature under argon. After stirring at 60° for 20 min, the reaction mixture was evaporated at 40-50° under good vacuum. Carbon tetrachloride (50 mL) was added to the residue and $NH_4Cl$ was removed by filtration. The filtrate was washed with cold water, dried ($MgSO_4$), and concentrated to give 2 (4.8 g, 95%) as a colorless syrup, $[\alpha]_D$ −49° (*c* 1, $CHCl_3$); $^1$H-n.m.r. ($CDCl_3$): δ 7.60-7.10 (10 H, arom.), 5.50 (s, PhCH), 4.71 (d, $J_{1,2}$ = 10 Hz, H-1), 4.32 (dd, $J_{5,6a}$ = 4 Hz, $J_{6a,6b}$ = 10 Hz, H-6a), 3.76 (m, 2 H), 3.63 (dd, $J_{2,3}$ = 8 Hz, H-2), 3.46 (m, 2 H), 0.22 and 0.06 (2 s, 2 $SiMe_3$).

*Anal.* Calc. for $C_{25}H_{36}O_5SSi_2$: C, 59.48; H, 7.19. Found: C, 59.70; H, 7.25.

*1,5-Anhydro-4,6-O-benzylidene-2-deoxy-3-O-trimethylsilyl-D-*arabino*-hex-1-enitol* (3) and *(4,6-O-benzylidene-2-O-trimethylsilyl-α-D-glucopyranosyl)trimethylsilane* (4). -- Small chips of lithium (694 mg, 100 mmoles), previously washed with dry hexane, were added under argon at room temperature to a solution of naphthalene (12.8 g, 100 mmoles) in anhydrous THF (100 mL), distilled over Na benzophenone. The mixture was stirred (glass-coated magnetic bar) overnight at room temperature under argon. The resulting dark-green solution of lithium naphthalenide could be stored for a few days under argon in the refrigerator.

The ≤1 M lithium naphthalenide solution (≥20 mL) was transferred dropwise under argon by standard syringe techniques to a solution of the phenyl thioglycoside 2 (5 g, 10 mmoles) in anhydrous THF (50 mL) at −78° with stirring. The reaction was accompanied by a change of color (from dark-green to light-brown) of the solution, and was monitored by t.l.c.

(toluene-EtOAc, 9:1). Two new compounds soon became detectable at $R_F$ 0.75 (unsaturated product) and 0.55. The addition of lithium naphthalenide was stopped when the starting material ($R_F$ 0.85) disappeared. The mixture was allowed to warm to 0° and carefully neutralized by dropwise addition of THF-AcOH (4:1, ≅ 6 mL). After evaporation, dichloromethane (100 mL) was added to the residue and insoluble material was removed by filtration. The filtrate was washed with water, dried ($MgSO_4$), and evaporated. Flash chromatography of the residue (toluene-EtOAc, 19:1) gave first **3** (367 mg, 12%) as a syrup, $^1$H-n.m.r. ($CDCl_3$): δ 7.60-7.30 (5 H, arom.), 6.38 (dd, $J_{1,2}$ = 6.1 Hz, $J_{1,3}$ = 1.2 Hz, H-1), 5.68 (s, PhCH), 4.72 (dd, $J_{2,3}$ = 1.8 Hz, H-2), 4.56 (ddd, $J_{3,4}$ = 7 Hz, H-3), 4.40 (m, H-5), 4.00-3.80 (m, H-4,6a,6b), 0.16 (s, $SiMe_3$).

Next eluted was **4** (2.4 g, 61%) which was crystallized from hexane, m.p. 141-143°; $[\alpha]_D$ +24° (*c* 1, $CHCl_3$); $^1$H-n.m.r. ($CDCl_3$): δ 7.60-7.40 (5 H, arom.), 5.58 (s, PhCH), 4.32 (dd, $J_{5,6a}$ = 4.5 Hz, $J_{6a,6b}$ = 10.5 Hz, H-6a), 4.10 (dd, $J_{1,2}$ = 7.8 Hz, $J_{2,3}$ = 9 Hz, H-2), 3.90 (dd, $J_{3,4}$ = 9.5 Hz, H-3), 3.80 (d, H-1), 3.68 (dd, $J_{5,6b}$ = 10 Hz, H-6b), 3.46 (m, H-4,5), 2.46 (s, OH), 0.20 and 0.19 (2 s, 2 $SiMe_3$); $^{29}$Si-n.m.r. ($CDCl_3$): $\delta_{TMS}$ 19.64 ($OSiMe_3$) and 2.29 ($CSiMe_3$).

*Anal.* Calc. for $C_{19}H_{32}O_5Si_2$: C, 57.54; H, 8.13. Found: C, 57.45; H, 8.02.

Compound **4** (13 mg) was treated for 90 min at room temperature with acetic anhydride (0.5 mL), pyridine (1 mL), and a catalytic amount of *N,N*-dimethylaminopyridine. Methanol (0.5 mL) was added and the solution was evaporated in the presence of toluene to give **5** as a syrup (15 mg); $^1$H-n.m.r. ($CDCl_3$): δ 7.50-7.30 (5 H, arom.), 5.52 (s, PhCH), 5.42 (dd, $J_{2,3}$ = 9 Hz, $J_{3,4}$ = 9 Hz, H-3), 4.32 (dd, $J_{5,6a}$ = 4 Hz, $J_{6a,6b}$ = 10 Hz, H-6a), 4.19 (dd, $J_{1,2}$ = 8 Hz, H-2), 3.79 (d, H-1), 3.67 (dd, $J_{5,6b}$ = 10 Hz, H-6b), 3.51 (m, H-4,5), 2.13 (s, OAc), 0.23 and 0.13 (2 s, 2 $SiMe_3$).

*(α-D-Glucopyranosyl)trimethylsilane* (**6**). -- (a) A solution of **4** (2 g) in acetic acid (40 mL) and water (10 mL) was heated at 100° for 10 min, then cooled and evaporated in the presence of toluene. The residue was crystallized from EtOAc to give **6** (0.88 g, 74%), m.p. 171-173°, $[\alpha]_D$ +44° (*c* 1, MeOH); $^1$H-n.m.r. (pyridine-$d_5$ + $D_2O$): δ 4.30 (dd, $J_{1,2}$ = 7 Hz, $J_{2,3}$ = 8.5 Hz, H-2), 4.29 (dd, $J_{5,6a}$ = 2.5 Hz, $J_{6a,6b}$ = 12 Hz, H-6a), 4.16 (dd, $J_{3,4}$ = 9 Hz, H-3), 4.06 (dd, $J_{5,6b}$ = 6 Hz, H-6b), 4.03 (d, H-1), 3.88 (dd, H-4), 3.78 (m, H-5), 0.12 (s, $SiMe_3$); $^{29}$Si-n.m.r. ($D_2O$): $\delta_{DSS}$ +0.361 ($SiMe_3$).

*Anal.* Calc. for $C_9H_{20}O_5Si$: C, 45.74; H, 8.53. Found: C, 45.87; H, 8.54.

A portion of compound **6** (55 mg) was conventionally acetylated to give **7** as a syrup (92 mg); $^1$H-n.m.r. ($CDCl_3$): δ 5.31 (dd, $J_{2,3}$ = 7.3 Hz, $J_{3,4}$ = 7.8 Hz, H-3), 5.23 (dd, $J_{1,2}$ = 5.5 Hz, H-2), 4.99 (dd, $J_{4,5}$ = 8 Hz, H-4), 4.36 (dd, $J_{5,6a}$ = 6.5 Hz, $J_{6a,6b}$ = 12 Hz, H-6a), 4.11 (dd, $J_{5,6b}$ = 3 Hz, H-6b), 3.92 (d, H-1), 3.20 (ddd, H-5), 2.09 (4 OAc), 0.17 (s, $SiMe_3$).

(*b*) Phenyl 1-thio-β-D-glucopyranoside[13] (2.7 g, 10 mmoles) was silylated by treatment with hexamethyldisilazane (41 mL, 194 mmoles) and chlorotri-methylsilane (17 mL, 134 mmoles) in dry pyridine (100 mL) for 15 min at 60°. The reaction mixture was processed as described for 2 to give 8 as a solid mass very sensitive to moisture (5.4 g, 96%); $^1$H-n.m.r. ($CDCl_3$): δ 7.56-7.18 (m, 5 H, arom.), 4.62 (m, H-1), 3.78 (dd, $J_{5,6a}$ = 2 Hz, $J_{6a,6b}$ = 11 Hz, H-6a), 3.60 (dd, $J_{5,6b}$ = 6.5 Hz, H-6b), 3.50-3.24 (m, H-2,3,4,5), 0.18, 0.10 and 0.04 (4 $SiMe_3$).

A solution of 8 (5.4 g) in anhydrous THF (50 mL) was treated with a 1 M lithium naphthalenide solution in THF (≅20 mL) at -78° as described for 2. The addition of lithium naphthalenide was stopped when the starting material disappeared as verified by t.l.c. ($CH_2Cl_2$). Several products corresponding to partial de-*O*-silylation were detectable. The reaction mixture was allowed to warm to room temperature, acidified with THF-AcOH-water (4:1:1, 30 mL), stirred at room temperature for 20 h, and evaporated in the presence of toluene. The residue was extracted with water, and the aqueous extract was washed with $CH_2Cl_2$, then evaporated. Flash chromatography (acetone-EtOAc, 1:1), followed by crystallization from EtOAc, gave a product identical to 6 (1.44 g, 61% overall yield).

*Phenyl 3-O-benzyl-4,6-O-benzylidene-1-thio-β-D-glucopyranoside* (9). -- A mixture of 1 (3.6 g, 10 mmoles), $Bu_2SnO$ (3 g, 12 mmoles), powdered 4 Å molecular sieves (10 g) in dry acetonitrile (100 mL) was heated at reflux for 4 h, then cooled at room temperature under argon. Tetrabutylammonium bromide (3.2 g, 10 mmoles) and benzyl bromide (2.9 mL, 24 mmoles) were added, and the mixture was heated at reflux for 13 h, then cooled, filtered, and concentrated. Flash chromatography of the residue (toluene-EtOAc, 57:3) gave 9 (2.16 g, 48%) which was crystallized from ether-hexane, m.p. 120.5-121.5°, $[\alpha]_D$ -41° (*c* 1, $CHCl_3$); $^1$H-n.m.r. ($CDCl_3$): δ 7.60-7.30 (m, 15 H, arom.), 5.62 (s, PhCH), 5.00 and 4.82 (2 d, $J_{gem}$ = 11.5 Hz, $PhCH_2$), 4.66 (d, $J_{1,2}$ = 9.5 Hz, H-1), 4.43 (dd, $J_{5,6a}$ = 5 Hz, $J_{6a,6b}$ = 10.5 Hz, H-6a), 3.84 (dd, $J_{2,3}$ = 10 Hz, H-2), 3.72 (m, H-3,4), 3.56 (m, H-5,6b), 2.58 (d, $J_{2,OH}$ = 2 Hz, OH).

*Anal.* Calc. for $C_{26}H_{26}O_5S$: C, 69.31; H, 5.82. Found: C, 69.42; H, 5.80.

Pure EtOAc eluted unchanged 1 (1 g, 28%).

*Phenyl 3-O-benzyl-4,6-O-benzylidene-2-O-trimethylsilyl-1-thio-β-D-glucopyranoside* (10). -- Compound 9 (1.8 g, 4 mmoles) was silylated by treatment with hexamethyldisilazane (9.5 mL, 45 mmoles) and chlorotrimethylsilane (4 mL, 31.5 mmoles) in dry pyridine (20 mL) for 30 min at 60°. The reaction mixture was processed as usual and the residue was submitted to flash chromatography (hexane-acetone, 93:7) to give 10 as a syrup (2.05 g, 98%), $[\alpha]_D$ -56° (*c* 1, $CHCl_3$).

*Anal.* Calc. for $C_{29}H_{34}O_5SSi$: C, 66.63; H, 6.56. Found: C, 66.58; H, 6.70.

*1,5-Anhydro-3-O-benzyl-4,6-O-benzylidene-2-deoxy-*D-arabino-*hex-1-enitol* (11) and *(3-O-benzyl-4,6-O-benzylidene-α-*D*-glucopyranosyl)trimethylsilane* (12). -- (a) A solution of 10 (523 mg, 1 mmole) in anhydrous THF (6 mL) was treated with a 1 M lithium naphthalenide solution in THF (≅2 mL) at -78° under argon. The addition of lithium naphthalenide was stopped when 10 disappeared as verified by t.l.c. ($CH_2Cl_2$, $R_F$ 0.66); two new compounds were detectable at $R_F$ 0.59 (unsaturated product) and 0.51. The reaction mixture was processed as usual and the residue was submitted to flash chromatography. Toluene eluted first naphthalene, then $CH_2Cl_2$ eluted 11 (184 mg, 58%) which was crystallized from hexane, m.p. 103-104°, $[\alpha]_D$ -43.5° (*c* 1, $CHCl_3$); $^1$H-n.m.r. ($C_6D_6$): δ 7.60-7.10 (m, 10 H, arom.), 6.12 (dd, $J_{1,2}$ = 6.2 Hz, $J_{1,3}$ = 1.6 Hz, H-1), 5.30 (s, PhCH), 4.78 and 4.62 (2 d, $J_{gem}$ = 12.5 Hz, $PhCH_2$), 4.72 (dd, $J_{2,3}$ = 2 Hz, H-2), 4.28 (ddd, $J_{3,4}$ = 7.5 Hz, H-3), 4.15 (dd, $J_{5,6a}$ = 5.2 Hz, $J_{6a,6b}$ = 10.4 Hz, H-6a), 3.95 (dd, $J_{4,5}$ =10 Hz, H-4), 3.72 (ddd, $J_{5,6b}$ = 10.2 Hz, H-5), 3.50 (dd, H-6b).

*Anal.* Calc. for $C_{20}H_{20}O_4$: C, 74.06; H, 6.22. Found: C, 73,69; H, 6.18. Hexane-EtOAc 1:1 eluted 12 (166 mg, 40%) as a syrup. $^1$H-N.m.r. ($CDCl_3$): δ 7.60-7.40 (m, 10 H, arom.), 5.64 (s, PhCH), 5.06 and 4.78 (2 d, $J_{gem}$ = 11.6 Hz, $PhCH_2$), 4.32 (dd, $J_{5,6a}$ = 5 Hz, H-6a), 4.13 (dd, $J_{1,2}$ = 8 Hz, $J_{2,3}$ = 10 Hz, H-2), 3.91 (d, H-1), 3.72 (m, H-3,4,6b), 3.44 (m, H-5), 2.32 (d, $J_{2,OH}$ = 2 Hz, OH).

(b) A solution of 12 (162 mg, 0.5 mmole) in dry THF (5 mL) was added under argon at room temperature to KH (108 mg of a 50% dispersion in oil, 1.3 mmole, previously washed three times with dry hexane). The mixture was stirred at room temperature for 20 min, then cooled at 0°; a saturated aqueous solution of $NH_4Cl$ was added cautiously; the solution was diluted with ether (20 mL), washed with water, dried ($MgSO_4$), and evaporated. Flash chromatography of the residue (toluene as eluant) gave 11 (138 mg, 85%), identical to the product described above.

*Phenyl 4,6-O-benzylidene-2,3-di-O-trimethylsilyl-1-thio-β-*D*-galactopyranoside* (14). -- Phenyl 4,6-*O*-benzylidene-1-thio-β-D-galactopyranoside 13[4] was silylated as described for 1 to give 14 (92%), m.p. 140-141°, $[\alpha]_D$ -14.5° (*c* 1, $CHCl_3$); $^1$H-n.m.r. ($CDCl_3$): δ 7.75-7.24 (m, 10 H, arom.), 5.54 (s, PhCH), 4.59 (d, $J_{1,2}$ = 9 Hz, H-1), 4.44 (dd, $J_{5,6a}$ = 1.5 Hz, $J_{6a,6b}$ = 12.5 Hz, H-6a), 4.15 (dd, $J_{3,4}$ = 3.5 Hz, $J_{4,5}$ < 1 Hz, H-4), 4.14 (dd, $J_{5,6b}$ = 1.5 Hz, H-6b), 4.05 (dd, $J_{2,3}$ = 9 Hz, H-2), 3.78 (dd, H-3), 3.50 (m, H-5), 0.23 and 0.15 (2 s, 2 $SiMe_3$).

*Anal.* Calc. for $C_{25}H_{36}O_5SSi_2$: C, 59.48; H, 7.19. Found: C, 59.85; H, 7.35.

*Reductive lithiation of* 14. -- A solution of 14 (253 mg, 0.5 mmole) in dry THF (5 mL) was treated at -78° under argon with a ≅1 M lithium naphthalenide solution in THF (≅1 mL). Severe streaking was observed by t.l.c. (toluene-EtOAc, 7:1). Nevertheless, flash chromatography (toluene-EtOAc, 7:1, then EtOAc) allowed the isolation of two compounds **15** and **16**.

*(4,6-O-Benzylidene-2-O-trimethylsilyl-α-D-galactopyranosyl)trimethylsilane* (**15**) (32 mg, 16%) was a crystalline mass very sensitive to moisture; $^1$H-n.m.r. ($CDCl_3$): δ 7.58-7.42 (m, 5 H, arom.), 5.58 (s, PhCH), 4.26 (2 dd, $J_{3,4}$ = 4 Hz, $J_{4,5}$ = 1 Hz, $J_{5,6a}$ = 1.5 Hz, $J_{6a,6b}$ = 12.5 Hz, H-4,6a), 4.23 (dd, $J_{1,2}$ = 8 Hz, $J_{2,3}$ = 10 Hz, H-2), 4.04 (dd, $J_{5,6b}$ = 2 Hz, H-6b), 3.90 (d, H-1), 3.77 (ddd, $J_{3,OH}$ = 9.5 Hz, H-3), 3.43 (m, H-5), 2.28 (d, OH), 0.15 and 0.13 (2 s, 2 $SiMe_3$).

*(4,6-O-Benzylidene-α-D-galactopyranosyl)trimethylsilane* (**16**) (37 mg, 23%) was a crystalline mass; $^1$H-n.m.r. ($CDCl_3$ + $CCl_3CONCO$): δ 8.68 and 8.38 (2 s, 2 NH), 7.60-7.42 (m, 5 H, arom.), 5.79 (dd, $J_{1,2}$ = 6.5 Hz, $J_{2,3}$ = 8.5 Hz, H-2), 5.60 (s, PhCH), 5.38 (dd, $J_{3,4}$ = 3 Hz, H-3), 4.68 (dd, $J_{4,5}$ = 2.5 Hz, H-4), 4.56 (d, H-1), 4.38 (dd, $J_{5,6a}$ < 1 Hz, $J_{6a,6b}$ = 13.5 Hz, H-6a), 4.14 (dd, $J_{5,6b}$ = 2 Hz, H-6b), 3.70 (ddd, H-5), 0.20 (s, $SiMe_3$).

Unsaturated products were detectable by t.l.c. but could not be isolated in a pure state.

*(α-D-Galactopyranosyl)trimethylsilane* (**18**). -- Phenyl 1-thio-β-galactopyranoside[14] (2.7 g, 10 mmoles) was silylated as described above to give **17** as a syrup sensitive to moisture (5.2 g, 93%); $^1$H-n.m.r. ($CDCl_3$): δ 7.54-7.16 (5 H, arom.), 4.50 (d, $J_{1,2}$ = 9.5 Hz, H-1), 3.88 (dd, $J_{2,3}$ = 9 Hz, H-2), 3.40 (dd, $J_{3,4}$ = 2.5 Hz, H-3), 0.1-0.0 (4 s, 4 $SiMe_3$). A solution of **17** (5.2 g) in dry THF (50 mL) was treated first with lithium naphthalenide, then with aqueous acetic acid as for **8**. The crude product was purified by flash chromatography ($CH_2Cl_2$-MeOH, 6:1), then by gel filtration over Sephadex LH-20 ($CHCl_3$-MeOH, 1:1) to remove silicic acid. Compound **18** (1.28 g, 54%) was crystallized from EtOAc, m.p. 131-133°, $[\alpha]_D$ +11.5° (*c* 1, MeOH); $^1$H-n.m.r. (pyridine-$d_5$ + $D_2O$): δ 4.84 (dd, $J_{3,4}$ = 3.5 Hz, $J_{4,5}$ = 3.5 Hz, H-4), 4.79 (dd, $J_{1,2}$ 5 Hz, $J_{2,3}$ = 6.8 Hz, H-2), 4.66 (dd, $J_{5,6a}$ = 7 Hz, $J_{6a,6b}$ = 11.5 Hz, H-6a), 4.49 (2 dd, $J_{5,6b}$ = 4.5 Hz, H-3,6b), 4.37 (m, H-1,5), 0.39 (s, $SiMe_3$); $^{29}$Si-n.m.r. ($D_2O$): $\delta_{DSS}$ +0.386 ($SiMe_3$).

*Anal*. Calc. for $C_9H_{20}O_5Si$: C, 45.74; H, 8.53. Found: C, 45.97; H, 8.63.

*Phenyl 4,6-O-isopropylidene-1-thio-β-D-mannopyranoside* (**19**). -- Sodium hydride (1.6 g of a 60% dispersion in oil, 40 mmoles) was added gradually at room temperature under argon to a solution of 2,3,4,6-tetra-*O*-acetyl-α-D-mannopyranosyl bromide[16] (4.12 g, 10 mmoles) and thiophenol (4.1 mL, 40 mmoles) in HMPA (50 mL); the mixture was stirred for 30 min at room temperature until the hydrogen evolution stopped, then poured into ice-cold water (1 L), then extracted three times with EtOAc. The extract was washed with 0.1 M aqueous hydrochloric acid, then water until neutral, dried ($MgSO_4$), and concentrated to give nearly pure phenyl 2,3,4,6-tetra-*O*-acetyl-1-thio-β-D-mannopyranoside (4.14 g, 94%) as a syrup; $^1$H-n.m.r. ($CDCl_3$): δ 7.62–7.18 (m, 5 H, arom.), 5.74 (dd, $J_{1,2}$ = 1 Hz, $J_{2,3}$ = 3.5 Hz, H-2), 5.34 (dd, $J_{3,4}$ = 10 Hz, $J_{4,5}$ = 10 Hz, H-4), 5.10 (dd, H-3), 4.95 (d, H-1), 4.34 (dd, $J_{5,6a}$ = 6.5 Hz, $J_{6a,6b}$ = 12 Hz, H-6a), 4.22 (dd, $J_{5,6b}$ = 2.5 Hz, H-6b), 3.74 (ddd, H-5), 2.24, 2.12, 2.01 and 2.00 (4 s, 4 OAc). Treatment with 0.2 M NaOMe in MeOH (35 mL) for 1 h at room temperature gave phenyl 1-thio-β-D-mannopyranoside (2.33 g, 91%) as a foam; $^1$H-n.m.r. ($D_2O$): δ 7.90–7.68 (m, 5 H, arom.), 5.48 (d, $J_{1,2}$ = 1 Hz, H-1), 4.52 (dd, $J_{2,3}$ = 1.5 Hz, H-2), 4.24 (dd, $J_{5,6a}$ = 2.5 Hz, $J_{6a,6b}$ = 12.5 Hz, H-6a), 4.06 (dd, $J_{5,6b}$ = 6 Hz, H-6b), 4.00–3.90 (m, H-3,4), 3.76 (m, H-5). The product (2.3 g, 8.4 mmoles) was then treated with 2-methoxypropene (1.6 mL, 17 mmoles) and *dl*-camphorsulfonic acid (43 mg) in dry DMF (70 mL) at room temperature for 15 min. Sodium carbonate (12 g) was added, and the mixture was stirred for 2 h, then filtered and concentrated. Flash chromatography of the residue (EtOAc with 0.1% $NEt_3$) gave **19** (1.5 g, 58%) which crystallized from EtOAc, m.p. 164–165°, $[\alpha]_D$ −99° (*c* 1, MeOH); $^1$H-n.m.r. (DMSO-$d_6$): δ 7.46–7.22 (m, 5 H, arom.), 5.37 (d, *J* = 6 Hz, OH), 5.19 (d, $J_{1,2}$ = 1 Hz, H-1), 5.05 (d, *J* = 6.5 Hz, OH), 3.92 (m, H-2), 3.83 (dd, $J_{5,6a}$ = 8 Hz, $J_{6a,6b}$ = 11 Hz, H-6a), 3.78 (dd, $J_{5,6b}$ = 5.5 Hz, H-6b), 3.70 (dd, $J_{3,4}$ = 10 Hz, $J_{4,5}$ = 11 Hz, H-4), 3.58 (m, H-3), 3.31 (m, H-5), 1.43 and 1.30 (2 s, $CMe_2$).

*Anal.* Calc. for $C_{15}H_{20}O_5S$: C, 57.67; H, 6.45. Found: C, 57.59; H, 6.36.

*Phenyl 4,6-O-isopropylidene-2,3-di-O-trimethylsilyl-1-thio-β-D-mannopyranoside* (**20**). — Compound **19** was silylated as described for **1** to give **20** (83%), m.p. 92–94°, $[\alpha]_D$ −80° (*c* 1, $CHCl_3$); $^1$H-n.m.r. ($CDCl_3$): δ 7.44–7.18 (m, 5 H, arom.), 5.16 (d, $J_{1,2}$ = 1 Hz, H-1), 4.09 (dd, $J_{2,3}$ = 3.5 Hz, H-2), 3.88–3.73 (m, H-4,6a,6b), 3.51 (dd, $J_{3,4}$ = 9.5 Hz, H-3), 3.12 (m, H-5), 1.37 and 1.27 (2 s, $CMe_2$), 0.50 and 0.0 (2 s, 2 $SiMe_3$).

*Anal.* Calc. for $C_{21}H_{36}O_5SSi_2$: C, 55.22; H, 7.94. Found: C, 55.32; H, 7.88.

*Reductive lithiation of* **20**. — A solution of **20** (228 mg, 0.5 mmole) in dry THF (5 mL) was treated at −78° under argon with a ≅1 M lithium naphthalenide solution in THF (≅1 ML). Only one product with some streaking was detectable by t.l.c. ($CH_2Cl_2$). Flash chromatography (hexane–$CH_2Cl_2$, 9:1, containing 0.5% $NEt_3$) gave *1,5-anhydro-4,6-O-isopropylidene-3-O-trimethylsilyl-*D-arabino-*hex-1-enitol* (**21**) (88 mg, 68%) as an oil; $^1$H-n.m.r. ($CDCl_3$): δ 6.20 (dd, $J_{1,2}$ = 6 Hz, $J_{1,3}$ = 1.5 Hz, H-1), 4.53 (dd, $J_{2,3}$ = 2 Hz, H-2), 4.22 (m, H-3), 3.88–3.56 (m, H-4,5,6a,6b), 1.39 and 1.29 (2 s, $CMe_2$), 0.0 (s, $SiMe_3$).

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