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Intramolecular Glycosidation: Stereocontrolled Synthesis of α-Glucosides from a 2-*O*-Alkoxysilyl Thioglucoside

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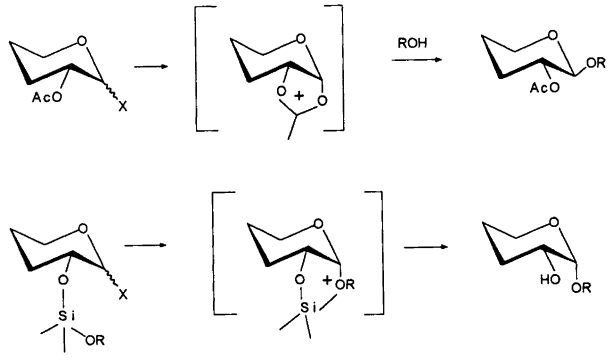
2-*O*-(Alkoxydimethyl)silylglucosyl piperidide, chloride and thiophenolate derivatives have been prepared, and intramolecular glycosidation of these derivatives was attempted. Reaction of phenyl 3,4,6-tri-*O*-acetyl-2-*O*-(octyloxy-, cyclohexyloxy-, *tert*-butoxy- and phenoxy-dimethyl)silyl-α-D-gluco-1-thiopyranoside with *N*-iodosuccinimide and trifluoromethanesulfonic acid gave stereospecifically the corresponding alkyl 3,4,6-tri-*O*-acetyl-α-D-glucopyranosides.

The effective synthesis of glycosides is an important problem in organic chemistry. Although tremendous research effort has been directed to this area during the last century no generally applicable method exists that is not critically dependent on the nature of the aglycone to be coupled.[1–5] The reason for this is a combination of two problems in nucleophilic substitution at the anomeric center: poor reactivity and stereoselectivity. Solving both problems has been very difficult. Generally S_N2-type processes that are stereospecific are too slow to be applicable for sterically hindered nucleophiles in limited concentrations, while S_N1-type processes have the reactivity, but at the expense of stereocontrol. The most general, though often not very effective, method of preparing glycosides has been the Koenigs–Knorr reaction[5] (Scheme 1) which uses S_N1 chemistry to generate a reactive carbonium ion intermediate at C-1 and neighboring-group participation from an ester at C-2 to control the stereochemistry. This permits the synthesis of 1,2-*trans*-glycosides. 1,2-*cis*-Glycosides are much less accessible.[6] However, from the observation in the Koenings–Knorr reaction that the five-membered acetoxonium ion can only be formed *cis* relative to the pyranoside ring, a stereocontrolled route to 1,2-*cis*-glycosides can be envisaged (Scheme 1). Thus, from an acetal-type derivative connecting the 2-hydroxy group and the aglycone, conversion of the anomeric center into a carbonium ion could result in the formation of a five-membered dioxolane ring that could open only to the 1,2-*cis*-glycoside. This can be termed intramolecular glycosidation. Recently this idea was successfully used to prepare β-D-mannosides from a phenylthio mannoside containing a 2-alkoxydimethylketal.[7] The basis of this method is that the dioxolane ring intermediate will open to the desired glycoside because a more stable carbonium ion will form at the dimethylketalic carbon. Since the formation of the ketal required several steps we believed that the method could be improved by using silylacetals. A number of methods for the preparation of unsymmetrical silylacetals of alcohols, including sugar alcohols, have been published.[8–11] In this paper we report that α-glucosides can be stereospecifically prepared from phenyl 2-alkoxydimethylsilyl-1-thioglucosides by intramolecular glycosidation with *N*-iodosuccinimide and a catalytic amount of trifluoromethanesulfonic acid.[12]

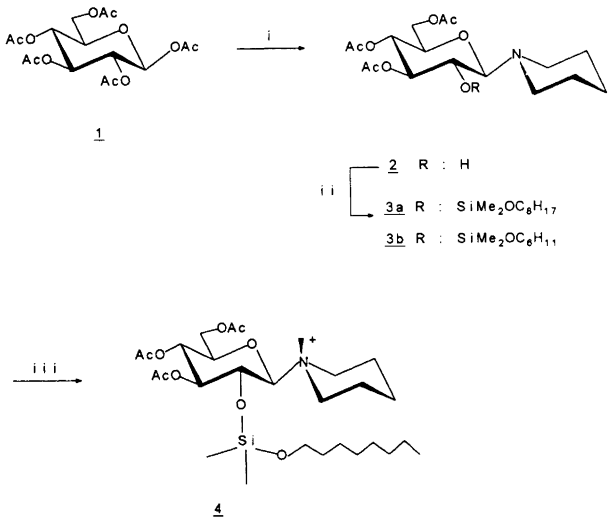


Scheme 1. Koenigs–Knorr.

Results and discussion

The intramolecular glucosidation strategy for the synthesis of α-glucosides outlined above demands as an additional requirement a free hydroxy group in the 2-position of the glycosyl donor, and evidently it would be a distinct advantage if such a glycosyl donor were readily available. *N*-Glucosyl derivatives have been used as glucosyl donors but were unreactive,[13,14] however, reaction with an intramolecular nucleophile might occur more readily. Therefore, 3,4,6-tri-*O*-acetyl-β-D-glucosyl piperidide (**2**) seemed attractive since it could be prepared in one step by the treatment of pentaacetylglucose (**1**) with piperidine.[15]

Chloro(dimethyl)octyloxysilane, chloro(cyclohexyloxy)-dimethylsilane, *tert*-butoxy(chloro)dimethylsilane and chloro(dimethyl)phenoxysilane were prepared accord-



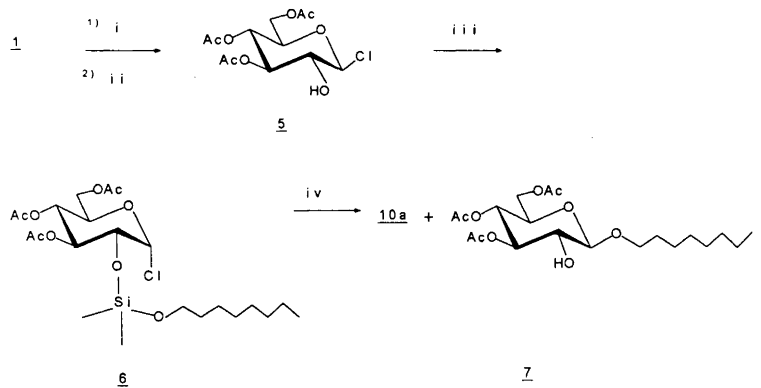
Scheme 2. i, piperidine, Ref. 14; ii, $R'OSiMe_2Cl$, pyridine, THF; iii, MeOTf, $MeNO_2$.

ing to the general procedure of Knoth and Lindsey (Scheme 2).[16] Reaction of piperidide **2** with chloro(dimethyl)octyloxysilane and Et_3N gave the disiloxane **3a** in 96% yield. Similarly, reaction of **2** with chloro(cyclohexyloxy)dimethylsilane and pyridine in THF gave **3b** in 85% yield. Compounds **3a** and **3b** were chromatographically stable. Activation of the glucosyl piperidide proved difficult. Although the glucosyl piperidides are known to be very labile under aqueous acidic conditions,[17] treatment of **3a** with Brønsted or Lewis acids in an aprotic solvent did not cleave the piperidide but rather the disiloxane. The stability of the glycosyl piperide was probably because the mechanism of hydrolysis which commences with ring opening not was possible. The piperidine nitrogen was easily alkylated with methyl triflate in nitromethane to the *N*-methylpiperidinium salt **4**. Compound **4** was, however, also very stable even at elevated temperatures. This is in contrast with 1-(*N*-methylmorpholinium) 2,3,4,6-tetra-*O*-benzyl-β-D-glucopyranoside which has been reported to react intermolecularly with methanol.[14] Recently, heptaacetyl-β-D-cellobiosyl piperidide was converted into the glycosyl bromide with *N*-bromosuccinimide (NBS).[18] Reaction of **3b** with NBS or *N*-chlorosuccinimide in chloroform did lead to cleavage of the carbon–nitrogen bond, but a complex mixture of products was formed which did not contain the desired glycoside.

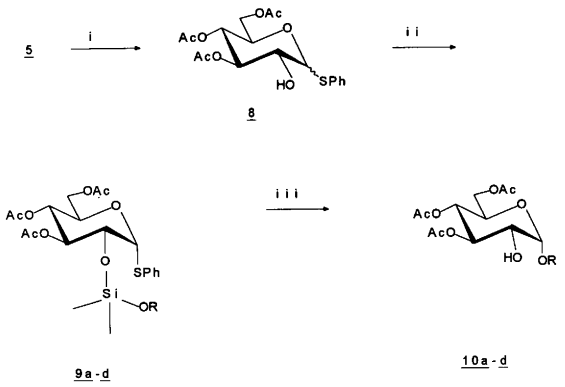
An alternative method was then studied using 3,4,6-tri-*O*-acetyl-β-D-glucopyranosyl chloride (**5**), available from **1** in two steps as described by Briegl.[19] The intermolecular reaction between trimethylsilylated alcohols and glycosyl chlorides in the presence of silver perchlorate has previously been carried out.[20] When the glucosyl chloride **5** was silylated with chloro(dimethyl)octyloxysilane and Et_3N a rapid anomerization occurred simultaneously, to give the α-chloride (Scheme 3) **6**. Compound **6** was not isolated but treated with $AgClO_4$ *in situ*. This did result in glycoside formation, but surprisingly a 1:1 mixture of the octyl α- and β-glycosides **10a** and **7** was isolated. It has been suggested however that this reaction involves oxygen–silicon fission caused by the electrophilic silver ion.[4]

Finally, the chloride **5** was converted into phenyl 3,4,6-tri-*O*-acetyl-α,β-D-gluco-1-thiopyranoside **8**, the α:β ratio of **8** being 6:1. Silylation of **8** with one equivalent of chloro(dimethyl)octyloxysilane and pyridine in THF gave the disiloxane **9a** in 75% yield. The thioglycoside **9a** did not react with either NBS or *N*-iodosuccinimide (NIS), but activating NIS with a catalytic amount of trifluoromethanesulphonic acid[21,22] led to an immediate reaction of **9a** with evolution of I_2, and the α-glucoside **10a** was obtained in 59% yield as the only product. No β-glucoside was observed. This stereocontrol was consistent with an intramolecular mechanism with the intermediate proposed in Scheme 1. The remainder of the siloxane was apparently lost during work-up. This was to be expected if the initial product of the reaction were an unstable silyl imide.

The reaction was also attempted with a secondary and a tertiary alcohol (Scheme 4). Silylation of **8** with chloro(cyclohexyloxy)dimethylsilane or with *tert*-butoxy(chloro)dimethylsilane and pyridine gave the siloxanes **9b** and **9c** in 74% and 76% yield, respectively. Reaction of



Scheme 3. i, PCl_5; ii, NH_3; iii, $ClSiMe_2OC_8H_{17}$, THF, pyridine: iv, $AgClO_4$.



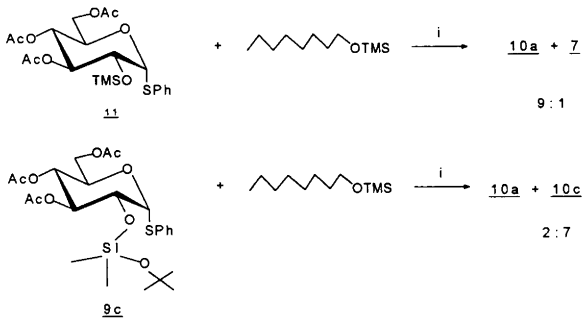
a: R = octyl
b: R = cyclohexyl
c: R = *tert*-butyl
d: R = phenyl

Scheme 4. i, PhSK, MeOH; ii, $ClSiMe_2OR$, pyridine, THF; iii, NIS, TfOH (cat.), CH_2Cl_2.

9b with NIS (2.5 equivalents) and CF_3SO_3H (0.2 equivalents) in CH_2Cl_2 led to the immediate formation of the α-glucoside **10b**, isolated in 62% yield. Similarly, **9c** was converted into the tertiary alkyl α-glucoside **10c** in 61% yield. In neither reaction was the possible β-glucoside observed. It is interesting that the primary, secondary and tertiary alkyl glycosides **10a**, **10b** and **10c** were formed in virtually identical yields. This indicates that the reaction is independent of steric hindrance. It is in perfect agreement with an intramolecular reaction and is in contrast with classical intermolecular glycosidations.

Finally the synthesis of a phenolic glycoside was attempted. The thioglycoside **8** was silylated with chloro(dimethyl)phenoxysilane to give the disiloxane **9d**. Although this reaction proceeded without problems, **9d** was somewhat unstable on silica gel, and thus a lower yield, 54%, was obtained after chromatography. Reaction of **9d** with NIS and CF_3SO_3H gave, as in the previous cases, exclusively the α-glucoside **10d** in 72% yield.

To verify further whether the stereocontrol observed was a result of an intramolecular reaction, an intermolecular equivalent of the reaction was devised. The thioglycoside **8** was converted into the 2-*O*-trimethylsilyl ether **11** in 89% yield with TMSCl–pyridine. Treatment of **11** with 1 equivalent of trimethylsilyloctan-1-ol and NIS (2.5 equiv.)/CF_3SO_3H (0.2 equiv.), at exactly the same concentration as for the reaction of **9a**, gave the anomeric glycosides **10a** and **7** in the ratio 9:1. The 2-*O*-trimethylsilyl group was apparently lost during work-up. Although 10% of the β-anomer was formed in this reaction, while the corresponding intramolecular reaction had at least α:β > 20:1, the extremely high α-selectivity[23] cast some doubt on whether the rearrangement **9a** to **10a** actually occurred intramolecularly. It is possible that octanol was delivered from another molecule of **9a**, which, as a chiral glycosyl acceptor, might increase the stereoselectivity. Therefore a competition experiment was carried out. The intramolecular glycosidation of **9c** was performed in the presence 1 equivalent of trimethyl(octyloxy)silane. If an intramolecular reaction did not take place, the oxtyloxyglycoside should have prevailed in the product since the primary silyl ether would be expected to be the more reactive; if not, the *tert*-butylglycoside should prevail. The result of the experiment was a 2:7 ratio between **10a** and **10c** meaning that at least the majority of the reaction was intramolecular (Scheme 5).



Scheme 5. i, NIS (2.5 equiv.), TfOH (cat.), CH_2Cl_2.

In conclusion we believe that the reaction of the 2-alkoxysilyl thioglycosides with NIS–TfOH took place intramolecularly for the following reasons: (1) the stereocontrol in the reaction, (2) the fact that steric hindrance in the aglycone did not affect the yield of the reaction, (3) that lower stereoselectivity was observed in the corresponding intermolecular reaction, and (4) the fact that a competition experiment gave mainly the product from the intramolecular reaction. The intramolecular method for preparing α-glucosides described in this paper may be of value, especially in sterically hindered cases or in cases where the stereoselectivity of the intermolecular reaction is poor.

Experimental

General methods. NMR spectra were recorded in $CDCl_3$ (internal Me_4Si) with a Bruker AC-250 instrument unless otherwise specified. Melting points were measured on a Büchi apparatus and are uncorrected. Optical rotations were measured with a Perkin-Elmer PE241 instrument. Microanalyses were performed by the Leo Microanalytical Laboratory. Column chromatography was performed on Kieselgel 60 (Merck 0.4–0.63 mm), using the flash technique. TLC was performed on Kieselgel 60 F_{254} (Merck) using detection with 1% cerium sulfate and 1.5% molybdic acid in aqueous 10% H_2SO_4 at 200°C for 5 min. Evaporations were carried out *in vacuo* at 40°C, unless otherwise specified.

*N-{3,4,6-Tri-*O*-acetyl-2-*O*-[dimethyl(octyloxy)silyl]-*β*-*D*-glucopyranosyl}piperidine* (**3a**). To a solution of

N-[3,4,6-tri-*O*-acetyl-β-D-glucopyranosyl]piperidine[15] (**2**, 1.0 g, 2.7 mmol) and chloro(dimethyl)octyloxysilane[24] (0.68 g, 3.0 mmol) in CH_2Cl_2 (10 ml) at 0°C was added Et_3N (0.28 g, 0.38 ml, 2.7 mmol), and the mixture was stirred at 0°C for 3 h. CH_2Cl_2 (50 ml) was added, and the solution was washed with ice–water (2 × 50 ml). Drying ($MgSO_4$) and concentration left the title compound **3a** as a clear syrup (1.45 g, 96%). $[\alpha]_D^{20}$: +11.1 (*c* 2.1, CH_2Cl_2). ^{13}C NMR ($CDCl_3$): δ 170.7, 170.1 and 169.9 (Ac's), 95.9 (C-1), 76.7, 72.7, 68.9 and 68.8 (C-2, C-3, C-4, C-5), 62.6 and 62.4 (C-6, CH_2O), 48.8 (2 C, CH_2N), 32.4, 31.7, 29.3, 29.2, 25.6 (2 C), 24.4, 22.5 (2 C) (CH_2's), 20.9, 20.7, 20.6 (Ac's), 14.0 (CH_3), −2.3, −2.4 (CH_3Si's). Anal. Calc. for $C_{27}H_{49}NO_9Si$: C, 57.93; H, 8.82. Found: C, 58.40; H, 9.01.

*N-{3,4,6-Tri-*O*-acetyl-2-*O*-[cyclohexyloxy(dimethyl)silyl]-*β*-D-glucopyranosyl}piperidine* (**3b**). To a solution of **2** (373 mg, 1 mmol) in THF (8 ml) and pyridine (2 ml) was added cyclohexyloxy(dimethyl)silyl chloride[25] (0.4 g, 2 mmol). After 1.5 h of stirring at 25°C, Et_2O (100 ml) was added, and the organic layer was washed with H_2O (10 ml) and NaCl (sat. 10 ml). Drying and concentration left a clear syrup (699 mg) that was flash chromatographed to give **3b** (452 mg, 85%). $[\alpha]_D^{20}$: +21.1° (*c* 0.4, CH_2Cl_2). ^{13}C NMR ($CDCl_3$): δ 170.5, 170.0 and 198.8 (Ac's), 96.1 (C-1), 76.9, 72.5, 70.6, 69.1, 68.5 (C-2, C-3, C-4, C-5, CH-O), 62.4 (C-6), 48.7 (2 C, CH_2N's), 35.5, 35.5, 25.8 (2 C), 25.3, 24.4, 24.1 (2 C, 8 CH_2), 20.8, 20.6, 20.5 (Ac's), −1.4 and −1.5 ($SiMe_2$). Anal. Calc. for $C_{25}H_{43}NO_9Si$: C, H.

Methylation of **3a** *with methyl triflate.* To a solution of **3a** (1.0 g, 1.8 mmol) in dry $MeNO_2$ (20 ml) was added MeOTf (0.20 ml, 0.29 g, 1.8 mmol), and the solution was refluxed 30 min. ^{13}C NMR spectroscopy showed complete conversion into the methylpiperidinium salt **4**. ^{13}C NMR [$MeNO_2$ (ref. 62.5 ppm)]: δ 171.2, 170.6 and 170.5 (Ac's), 92.2 (C-1), 75.8, 75.4, 70.2, 68.3 (C-2, C-3, C-4, C-5), 63.3, 61.6, 61.4 (C-6, CH_2O, CH_2N's), 44.9 (NMe), 32.3, 32.0, 29.4 (2 C), 25.9, 25.8, 22.7, 20.9, 20.6 (9 CH_2), 19.8 (2 C), 19.7 (Ac's), 13.5 (Me), −3.6, −3.7 ($SiMe_2$).

Reaction of **6** *with silver perchlorate.* To a mixture of the glucosyl chloride **5** (100 mg, 0.31 mmol), CH_2Cl_2 (5 ml), chloro(dimethyl)octyloxysilane[24] (9.1 mg, 0.41 mmol) and powdered 4 Å molecular sieves was added Et_3N (0.36 mmol) under N_2 at 0°C. After 15 min* at 0°C, $AgClO_4$ (150 mg, 0.72 mmol) was added. The mixture was stirred for 1.5 h, and, on addition of CH_2Cl_2 (25 ml), filtered, washed with H_2O (25 ml), dried ($MgSO_2$) and concentrated to a residue (130 mg) which contained **7**, **10a** and α-**5** (1:1:1). Flash chromatography (EtOAc–pentane 1:2) gave first a 1:1 mixture of the anomeric glycosides **7** and **10a** (41 mg, 32%) and as a slower moving fraction α-**5** (19 mg, 19%). ^{13}C NMR (**7**, $CDCl_3$): δ 102.7 (C-1), 74.2, 72.2, 71.6, 70.5, 68.3 (C-2, C-3, C-4, C-5, CH_2O), 62.0 (C-6).

*Phenyl 3,4,6-tri-*O*-acetyl-α-D-gluco-1-thiopyranoside* (**8**). Potassium (0.4 g, 10 mmol) dissolved in dry methanol (10 ml) was cooled to −78°C, and thiophenol (4.2 ml, 4.54 g, 41 mmol) was added. After 5 min 3,4,6-tri-*O*-acetyl-β-D-glucopyranosyl chloride[19] (**5**, 3.25 g, 10 mmol) was added, and the mixture was stirred at 25°C for 4 h. Filtration and concentration (40°C, 1 mmHg) left a residue that was taken up in $CHCl_3$ (50 ml) and washed with sat. $NaHCO_3$ (50 ml). Drying ($MgSO_4$) and concentration left a residue (4.18 g) that was purified by flash chromatography (EtOAc–pentane 1:2 followed by 1:1) to give **8** as a solid (2.53 g, α:β ~ 6:1, 63%). Recrystallization from ether–pentane gave 1.66 g of pure **8** (42%) with the following data: m.p. 128–131°C, $[\alpha]_D^{20}$ +252° (*c* 0.7, CH_2Cl_2). ^{13}C NMR ($CDCl_3$): δ 171.0, 170.5 and 169.5 (Ac's), 133.3 (Ar), 131.8, 129.1 and 127.8 (Ar), 90.1 (C-1), 73.7, 70.4, 68.7, 67.9 (C-2, C-3, C-4, C-5), 61.9 (C-6), 20.4–20.7 (Ac's). Anal. $C_{18}H_{22}O_8S$: C, H.

Silylation procedure for **8**. Phenyl 3,4,6-tri-*O*-acetyl-α-D-gluco-1-thiopyranoside (**8**, 100 mg, 0.25 mmol) was stirred under N_2 in THF (2 ml) and pyridine (0.5 ml), and the alkoxychlorodimethylsilane (0.50 mmol) was added. The mixture was stirred for 2 h. Diethyl ether (50 ml) was added, and the solution was washed with water (10 ml) and saturated aqueous NaCl (10 ml). Drying (Na_2SO_4), concentration and flash chromatography (EtOAc–pentane 1:10 followed by 1:4) gave the desired disiloxane.

*Phenyl 3,4,6-tri-*O*-acetyl-2-*O*-[dimethyl(octyloxy)silyl]-α-D-gluco-1-thiopyranoside* (**9a**). From dimethyl(octyloxy)silyl chloride[24] (0.13 ml, 118 mg, 0.53 mmol) the desired siloxane **9a** was isolated as a clear syrup (110 mg, 75%). $[\alpha]_D^{20}$ +137.0° (*c* 0.2, CH_2Cl_2). ^1H NMR ($CDCl_3$): δ 7.3–7.5 (m, 5 H, Ph), 5.66 (d, J_{12} = 5.5 Hz, H-1), 5.29 and 5.01 (2 t, all J = 9.5 Hz, H-3, H-4), 4.58 (ddd, J_{56} = 5 Hz, $J_{56'}$ = 2 Hz, H-5), 4.29 (dd, $J_{66'}$ = 12 Hz, H-6), 4.24 (dd, H-2), 3.98 (dd, H-6'), 3.64 (t, J = 6.5 Hz, CH_2O), 2.05 (3 s, 9 H, Ac's), 1.50 (m, 2 H), 1.25 (m, 10 H), 0.85 (t, CH_3), 0.15 (s, 6 H, SiMe's). ^{13}C NMR ($CDCl_3$): δ 170.5, 169.9, 169.8 (Ac's), 133.5 (Ar-*ipso*), 131.5, 128.9, 127.2 (Ar), 88.3 (C-1), 73.3, 70.3, 68.5, 68.0 (C-2, C-3, C-4, C-5), 62.8, 62.0 (C-6, CH_2O), 32.4, 31.7, 29.3, 29.2, 25.6, 22.6 (CH_2's), 20.6, 20.9 (Ac's), 14.0 (CH_3), −2.7 and −3.0 (Me_2Si). Anal. Calc. for $C_{28}H_{44}O_9SSi$: C, 57.51; H, 7.58. Found: C, 57.09; H, 7.64.

*Phenyl 3,4,6-tri-*O*-acetyl-2-*O*-[cyclohexyloxy(dimethyl)-silyl]-α-D-gluco-1-thiopyranoside* (**9b**). From cyclohexyl-

* Silylation of **5** (10 mg) with $ClSiMe_2OOct$ (10 µl) and Et_3N (4 µl) in $CDCl_3$ (0.5 ml) was found to be complete in < 5 min, as seen in the ^1H NMR spectrum from the lowering of the $OSiMe_2Cl$ signal (0.45 ppm, s) and appearance of a $OSiMe_2O$ signal (0.1 ppm, s). Anomerization was slower: after 25 min, an α/β ratio of 1:2 was observed.

oxy(dimethyl)silyl chloride[25] (0.10 ml, 100 mg, 0.52 mmol) the desired siloxane **9b** was isolated as a clear syrup (103 mg, 74%). $[\alpha]_D^{20} + 148°$ (*c* 0.2, CH_2Cl_2). ^1H NMR ($CDCl_3$): δ 7.2–7.6 (m, 5 H, Ph), 5.67 (d, $J_{12} = 5.5$ Hz, H-1), 5.28 and 5.01 (2 t, all $J = 9.5$ Hz, H-3, H-4), 4.58 (ddd, $J_{56} = 5.5$ Hz, $J_{56'} = 2.0$ Hz, H-5), 4.30 (dd, $J_{66'} = 12.0$ Hz, H-6), 4.25 (dd, H-2), 3.98 (dd, H-6'), 3.7 (m, CH-O), 2.0 (3s, 9 H, Ac's), 1.8 (m, 4 H), 1.5 (m, 1 H), 1.2 (m, 5H), 0.2 (s, 6 H, Me_2Si). ^{13}C NMR ($CDCl_3$): δ 169.8–170.5 (Ac's), 133.5 (Ar-*ipso*), 131.5, 128.9, 127.2 (Ar), 88.4 (C-1), 73.4, 71.1, 70.2, 68.6, 68.0 (CH, C-2, C-3, C-4, C-5), 62.0 (C-6), 35.7, 35.6, 25.3, 24.1, (CH_2's), 20.6–20.8 (Ac's), −1.7 and −2.2 (Me_2Si). Anal. $C_{26}H_{38}O_9SSi$: C, H.

Phenyl 3,4,6-tri-O-*acetyl-2*-O-*[*tert-*butoxy(dimethyl)-silyl]*-α-D-*gluco-1-thiopyranoside* (**9c**). From 103 mg of **8** (0.26 mmol) and *tert*-butoxy(dimethyl)silyl chloride[26] (0.1 ml, 88 mg, 0.53 mmol) the desired siloxane **9c** was isolated as a clear syrup (104 mg, 76%). $[\alpha]_D^{20} + 180°$ (*c* 1.2, CH_2Cl_2). ^1H NMR ($CDCl_3$): δ 7.2–7.5 (m, 5 H, Ar), 5.69 (d, $J_{12} = 5.5$ Hz, H-1), 5.29 and 5.01 (2 t, all $J = 9.5$ Hz, H-3, H-4), 4.59 (ddd, $J_{56} = 5.0$ Hz, $J_{56'} = 2.0$ Hz, H-5), 4.30 (dd, $J_{66'} = 12.0$ Hz, H-6), 4.24 (dd, H-2), 3.98 (dd, H-6'), 2.0–2.1 (3 s, 9 H, Ac's), 1.25 (s, 9 H, CMe_3), 0.15 (s, 6 H, Me_2Si). ^{13}C NMR ($CDCl_3$): δ 169.7–170.5 (Ac's), 133.5 (Ar-*ipso*), 131.7, 128.8, 127.2 (Ar), 88.5 (C-1), 73.3, 72.8, 70.2, 68.6, 67.9 (C-2, C-3, C-4, C-5, CMe_3), 62.0 (C-6), 31.7 (Me's), 20.5–20.7 (Ac's), 0.5 and 0.3 (Me_2Si). Anal. $C_{24}H_{36}O_9SSi$: C, H.

Phenyl 3,4,6-tri-O-*acetyl-2*-O-*[dimethyl(phenoxy)silyl]*-α-D-*gluco-1-thiopyranoside* (**9d**). From dimethyl-(phenoxy)silyl chloride[27] (0.089 ml, 97 mg, 0.52 mmol) the desired siloxane **9d**, which was somewhat unstable during chromatography, was isolated as a colorless syrup (74 mg, 54%). $[\alpha]_D^{20} + 112°$ (*c* 0.5, CH_2Cl_2). ^1H NMR ($CDCl_3$): δ 6.8–7.5 (m, 10 H, Ar's), 5.58 (d, $J_{12} = 5.5$ Hz, H-1), 5.34 and 5.01 (2 t, all $J = 9.5$ Hz, H-3, H-4), 4.59 (ddd, $J_{56} = 5.0$ Hz, $J_{56'} = 2.0$ Hz, H-5), 4.35 (dd, H-2), 4.29 (dd, $J_{66'} = 12.0$ Hz, H-6), 3.97 (dd, H-6'). ^{13}C NMR ($CDCl_3$): δ 169.8–170.5 (Ac's), 133.1, 131.6, 129.5, 128.9, 127.3, 121.9, 119.5 (Ar's), 88.1 (C-1), 73.2, 70.6, 68.5, 68.0 (C-2, C-3, C-4, C-5), 61.9 (C-6), 20.6 (Ac's), −2.2 and −2.4 (Me_2Si). Anal. $C_{26}H_{32}O_9SSi$: C, H.

Intramolecular glucosidation procedure. To a dry solution of phenyl 3,4,6-tri-*O*-acetyl-2-*O*-[alkoxy(dimethyl)silyl]-α-D-gluco-1-thiopyranoside (0.02 M) and *N*-iodo-succinimide (0.05 M) in CH_2Cl_2 under N_2 was added a catalytic amount of trifluoromethanesulfonic acid (0.4 µl per ml solution). After 10 min EtOAc (50 ml) was added, and the solution was washed with $NaHCO_3$ (10 ml) and $Na_2S_2O_3$ (10 ml). Drying (Na_2SO_4), concentration, and flash chromatography in EtOAc–pentane 1:3 followed by 1:2 gave the desired α-glucoside.

Octyl 3,4,6-tri-O-*acetyl*-α-D-*glucopyranoside* (**10a**). From **9a** (74 mg, 0.127 mmol) the α-glycoside **10a** was isolated as a clear syrup (31 mg, 59%). $[\alpha]_D^{20} + 116°$ (*c* 0.2, CH_2Cl_2), ^1H NMR ($CDCl_3$): δ 5.24 and 5.02 (2 t, all $J = 9.5$ Hz, H-3, H-4), 4.92 (d, $J_{12} = 4.0$ Hz, H-1), 4.28 (dd, $J_{56} = 5.0$ Hz, $J_{66'} = 12.0$ Hz, H-6), 4.07 (dd, $J_{56'} = 2.0$ Hz, H-6), 3.97 (ddd, H-5), 3.74 (dt, $J_{vic} = J_{vic} = 6.5$ Hz, $J_{gem} = 10.0$ Hz, O–CH–*H*), 3.68 (dd, H-2), 3.50 (dt, $J_{vic} = J_{vic} = 6.5$ Hz, OCH–*H*), 2.1, 2.1 and 2.05 (3 s, 9 H, Ac's), 1.6 (m, 2 H), 1.3 (m, 10 H), 0.9 (b t, 3 H). ^{13}C NMR ($CDCl_3$): δ 171.0, 170.6 and 169.5 (Ac's), 98.0 (C-1), 73.5, 70.8, 68.8, 67.9, 67.5 (C-2, C-3, C-4, C-5, CH_2O), 61.9 (C-6), 31.7, 29.3 (2 C), 29.1, 26.0, 22.5 (CH_2's), 20.8, 20.6, 20.6 (Ac's) and 14.0 (CH_3). MS (CI, NH_3): *m/z* 436 $(M + NH_4)^+$.

Cyclohexyl 3,4,6-tri-O-*acetyl*-α-D-*glucopyranoside* (**10b**). From **9b** (99 mg, 0.179 mmol) the α-glycoside **10b** was obtained as a clear syrup (43 mg, 62%). $[\alpha]_D^{20} + 132°$ (*c* 0.4, CH_2Cl_2), ^1H NMR ($CDCl_3$): δ 5.22 and 5.00 (2 t, all $J = 9.5$ Hz, H-3 and H-4), 5.06 (d, $J_{12} = 4.0$ Hz, H-1), 4.26 (dd, $J_{56} = 5.0$ Hz, $J_{66'} = 13.0$ Hz, H-6), 4.1 (m, 2 H, H-5, H-6'), 3.66 (dd, *H*-2), 3.61 (m, CH), 2.83 (s, OH), 2.1 (s, 6 H, Ac's), 2.05 (s, 3 H, Ac), 1.9 (m, 3 H), 1.8 (m, 2 H), 1.5 (m, 1 H), 1.3 (m, 4 H). ^{13}C NMR ($CDCl_3$): δ 171.0, 170.6, 169.6 (Ac's), 96.8 (C-1), 77.5 (CH), 73.5, 70.6, 68.1, 67.6 (C-2, C-3, C-4, C-5), 62.0 (C-6), 33.4, 31.7, 25.3, 24.1, 23.9 (CH_2's), 20.8, 20.6, 20.6 (Ac's). Anal. $C_{18}H_{28}O_9$: C, H.

tert-*Butyl 3,4,6-tri*-O-*acetyl*-α-D-*glucopyranoside* (**10c**). From **9c** (48 mg, 0.091 mmol) the α-glycoside **10c** was obtained as a clear syrup (20 mg, 61%). $[\alpha]_D^{20} + 134°$ (*c* 0.4, CH_2Cl_2), ^1H NMR ($CDCl_3$): δ 5.21 and 4.98 (2 t, all $J = 9.5$ Hz, H-3, H-4), 5–20 (d, $J_{12} = 4.0$ Hz, H-1), 4.28 (dd, $J_{56} = 5.0$ Hz, $J_{66'} = 12.0$ Hz, H-6), 4.13 (ddd, $J_{56'} = 2.0$ Hz, H-5), 4.01 (dd, H-6'), 3.64 (m, H-2), 2.1 (s, 6 H, Ac's), 2.05 (s, 3 H, Ac), 1.3 (s, 9 H, Me's). ^{13}C NMR ($CDCl_3$): δ 171.1, 170.6, 169.6 (Ac's), 92.7 (C-1), 73.6, 70.5, 68.2, 67.1 (C-2, C-3, C-4, C-5), 62.1 (C-6), 28.4 (3 C, Me's), 20.9–20.5 (Ac's). MS (CI, NH_3): *m/z* 380 $(M + NH_4)^+$.

Phenyl 3,4,6-tri-O-*acetyl*-α-D-*glucopyranoside* (**10d**). From **9d** (48 mg, 0.088 mmol) the α-glycoside **10d** was obtained as a colorless syrup (24 mg, 72%). $[\alpha]_D^{20} + 170°$ (*c* 0.5, CH_2Cl_2), ^1H NMR ($CDCl_3$): δ 7.3 (m, 2 H, Ph), 7.1 (m, 3 H, Ph), 5.62 (d, $J = 4.0$ Hz, H-1), 5.46 and 5.12 (2 t, all $J = 9.5$ Hz, H-3, H-4), 4.28 (dd, $J_{56} = 4.0$ Hz, $J_{66'} = 12.0$ Hz, H-6), 4.08 (m, H-5), 4.04 (dd, $J_{56'} = 2.0$ Hz), 3.9 (m, H-2), 2.05 (9 H, Ac's). ^{13}C NMR ($CDCl_3$): δ 168.9–169.5 (Ac's), 138.5 (C-*ipso*), 129.6 (C-*meta*), 123.2 (C-*para*), 116.5 (C-*ortho*), 96.8 (C-1), 73.2, 70.8, 68.3, 67.6 (C-2, C-3, C-4, C-5), 61.6 (C-6), 20.6–20.8 (Ac's). MS (CI, NH_3): *m/z* 400 $(M + NH_4)^+$.

Phenyl 3,4,6-tri-O-*acetyl-2*-O-*trimethylsilyl*-α-D-*gluco-pyranoside* (**11**). The thioglycoside **8** (202 mg, 0.51 mmol) was, using the above procedure, silylated with trimethylsilyl chloride (0.129 ml, 111 mg, 1.02 mmol) in

THF (4 ml) and pyridine (1 ml) to give the silyl ether **11** (212 mg, 89%) as a clear syrup. $[\alpha]_D^{20} + 199°$ (*c* 1.2, CH_2Cl_2). ^{13}C NMR ($CDCl_3$): δ 170.3, 169.7 (2 C, Ac's), 133.3, 131.7, 128.8, 127.2, (Ph), 88.5 (C-1), 73.3, 70.6, 68.4, 67.9 (C-2, C-3, C-4, C-5), 61.9 (C-6), 20.6, 20.5 (2 C, Ac's), −0.2 (Me_3Si). Anal. $C_{21}H_{30}O_8SSi$: C, H.

Intermolecular glycosidation of **11** *with octyloxy-(trimethyl)silane.* To a solution of **11** (84 mg, 0.18 mmol), octyloxy(trimethyl)silane (36 mg, 0.18 mmol) and NIS (100 mg, 0.45 mmol) in CH_2Cl_2 (9 ml) was added TfOH (4 µl, 6.8 mg, 0.046 mmol). After 15 min of stirring at 25°C, addition of EtOAc (50 ml), washing with $NaHCO_3$ (sat., 10 ml) and $Na_2S_2O_3$ (10%, 10 ml), drying ($MgSO_4$), and concentration gave a residue (113 mg) containing the α-glycoside **10a** and its β-anomer **7** in the ratio 9:1. Flash chromatography in EtOAc–pentane 1:4 followed by 1:2 gave a mixture of glycosides (41 mg, 55%, α:β 9:1).

Intramolecular glycosidation of **9c** *in the presence of octyloxy(trimethyl)silane.* To **9c** (23 mg, 0.044 mmol), octyloxy(trimethyl)silane (9 mg, 0.044 mmol) and NIS (25 mg, 0.11 mmol) in CH_2Cl_2 (2 ml) was added TfOH (1 µl, 1.71 mg, 0.011 mmol). After 10 min EtOAc (50 ml) was added, the solution was washed with $NaHCO_3$ (sat., 10 ml) and $Na_2S_2O_3$ (10%, 10 ml), dried (Na_2SO_4) and concentrated to a residue. ^{13}C NMR spectroscopy showed the glycoside **10a** and **10c** in the ratio 2:7.

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