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Synthesis of Kojitriose using Silicon-Tethered Glycosidation

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Reaction of 3,4,6-tri-*O*-acetyl-β-D-glucopyranosyl chloride (**1**) with potassium phenylselenate gave phenyl 3,4,6-tri-*O*-acetyl-1-seleno-α,β-D-glucopyranoside (**2**) in 59% yield. Silylation of benzyl 3,4,6-tri-*O*-benzyl-β-D-glucopyranoside (**4**) with ethyl 3,4,6-tri-*O*-benzyl-2-*O*-chlorodimethylsilyl-1-thio-β-D-glucopyranoside gave benzyl 2-*O*-(3,4,6-tri-*O*-benzyl-1-*S*-ethyl-1-thio-β-D-glucopyranos-2-*O*-yldimethylsilyl)-3,4,6-tri-*O*-benzyl-β-D-glucopyranoside (**5**) in 35% yield. Reaction of **5** with *N*-iodosuccinimide in nitromethane gave benzyl 2-*O*-(3,4,6-tri-*O*-benzyl-α-D-glucopyranosyl)-3,4,6-tri-*O*-benzyl-β-D-glucopyranoside (**6**) in 45% yield. Chlorodimethylsilylation of phenyl 3,4,6-tri-*O*-acetyl-1-seleno-α-D-glucopyranoside (**2α**) and reaction with **6** gave benzyl 2-*O*-[2-*O*-(3,4,6-tri-*O*-acetyl-1-*Se*-phenyl-1-seleno-α-D-glucopyranos-2-*O*-yldimethylsilyl)-3,4,6-tri-*O*-benzyl-α-D-glucopyranosyl]-3,4,6-tri-*O*-benzyl-β-D-glucopyranoside (**7**) in 82% yield. Intramolecular glycosidation of **7** using *N*-iodosuccinimide in nitromethane gave benzyl 2-*O*-[2-*O*-(3,4,6-tri-*O*-acetyl-α-D-glucopyranosyl)-3,4,6-tri-*O*-benzyl-α-D-glucopyranosyl]-3,4,6-tri-*O*-benzyl-β-D-glucopyranoside (**8**) in 45% yield. Deprotection of **8** gave kojitriose (**9**) in quantitative yield. Chlorodimethylsilylation of 1,3,4,6-tetra-*O*-benzyl-α,β-D-fructofuranose (**10**) with dimethyldichlorosilane and pyridine followed by reaction with ethyl 3,4,6-tri-*O*-benzyl-1-thio-β-D-glucopyranoside (**3**) gave ethyl 2-*O*-(1,3,4,6-tetra-*O*-benzyl-α,β-D-fructofuranosyloxydimethylsilyl)-3,4,6-tri-*O*-benzyl-1-thio-β-D-glucopyranoside (**11**) in 85% yield. Chlorodimethylsilylation of 1,3,4,6-tetra-*O*-benzoyl-α-D-fructofuranose (**12**) with dimethyldichlorosilane and triethylamine followed by reaction with phenyl 3,4,6-tri-*O*-acetyl-1-thio-α-D-glucopyranoside (**13**) gave phenyl 2-*O*-(1,3,4,6-tetra-*O*-benzoyl-α-D-fructofuranosyloxydimethylsilyl)-3,4,6-tri-*O*-acetyl-1-thio-α-D-glucopyranoside (**14**) in 62% yield. Both **11** and **14** failed to undergo intramolecular glycosidation.

Synthesis of *O*-glycosidic bonds is a long-standing and important area of research in organic chemistry. It is vital for chemists who wish to prepare carbohydrate biomaterials to be able to make these bonds. In the chemical synthesis of *O*-glycosides the chemist has, ever since the emergence of this discipline, had to deal with the problems of stereochemistry in the reaction.

A number of approaches to stereoselective synthesis of glycosides have emerged over the years (Fig. 1). The most important one is the Koenigs–Knorr procedure that employs neighbouring group participation of a 2-acyloxy group to obtain 1,2-*trans* stereochemistry of the product glycoside.[1] This is usually a highly selective process and is the method of choice for that group of compounds. A method for synthesising pyranosides having the 1-substituent axial was invented by Lemieux[2] and relies on *in situ* epimerisation of 1-halo sugars and careful kinetic control of the substitution so that only the more reactive equatorial halide reacts. Though stereochemically relatively reliable and simple to carry out this method suffers somewhat from the drawback that unstable 1-halo sugars have to be employed. At the moment one of the most popular ways of trying to control stereochemistry, when the Koenigs–Knorr method cannot be used, is therefore through solvent effects. The solvent effects are generally that a non-polar solvent tends to give mostly axial 1-substituents while particularly acetonitrile tends to give equatorial substituents.[3] However, these effects are unreliable.

Recently intramolecular glycosidation has emerged as a new approach to obtain stereoselectivity in glycosidation reactions.[4–15] In this approach the glycosyl acceptor is tethered to a hydroxy group of the glycosyl donor before glycosidic bond formation is carried out (Fig. 1). When the 2-OH group of the glycosyl donor is used for tethering with a one-atom tether, the reaction is completely stereoselective leading to the 1,2-*cis* glycoside,[4–12] while linking to other hydroxy groups and other tether lengths lead to varying stereo- and regioselectivity.[13–15]

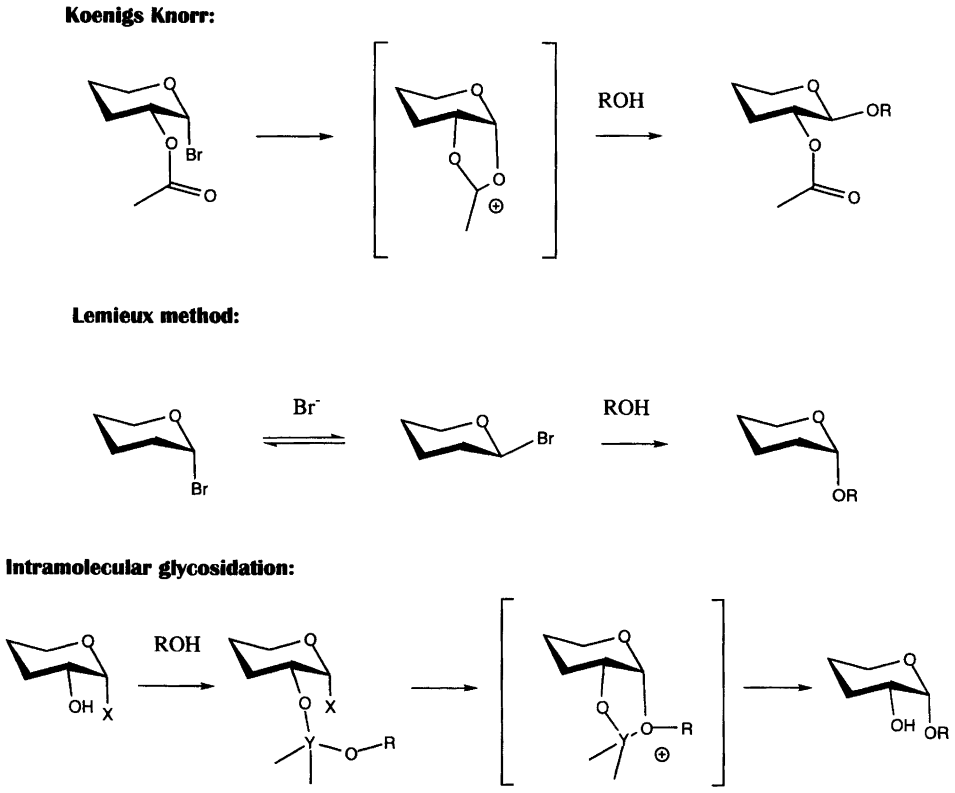


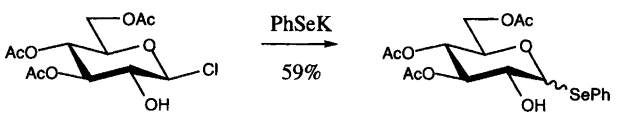
Fig 1.

2-OH-group-tethered intramolecular glycosidation is potentially a powerful method for synthesis of oligosaccharides containing the α-D-Glu(1→2)-α-D-Glu(1→2)-type linkages such as the kojitri-,[16] tetra-,[17] penta-[17] and hexa-oses,[18] and for the synthesis of the notoriously difficult α-D-Glu(1→1)-β-D-Fru linkage. In the present paper we have investigated these targets to probe the scope of this novel type of glycosidation method.

Results and discussion

We planned to test the previously developed methods[8–11,13] for the synthesis of targets kojitriose and sucrose; however in addition to the previously employed thioglycoside glycosyl donors we tried to include a selenoglycoside, which might be more reactive and easier to activate. Selenoglycoside glycosyl donors have been successfully employed in intermolecular glycosidation,[19,20] including with *N*-iodosuccinimide activation.[21,22]

Accordingly, we prepared phenyl 3,4,6-tri-*O*-acetyl-1-seleno-α,β-D-glucopyranoside (**2**). This was done by substitution of the Briegl glucosyl chloride **1**[23] with potassium phenylselenate, a reaction that smoothly gave

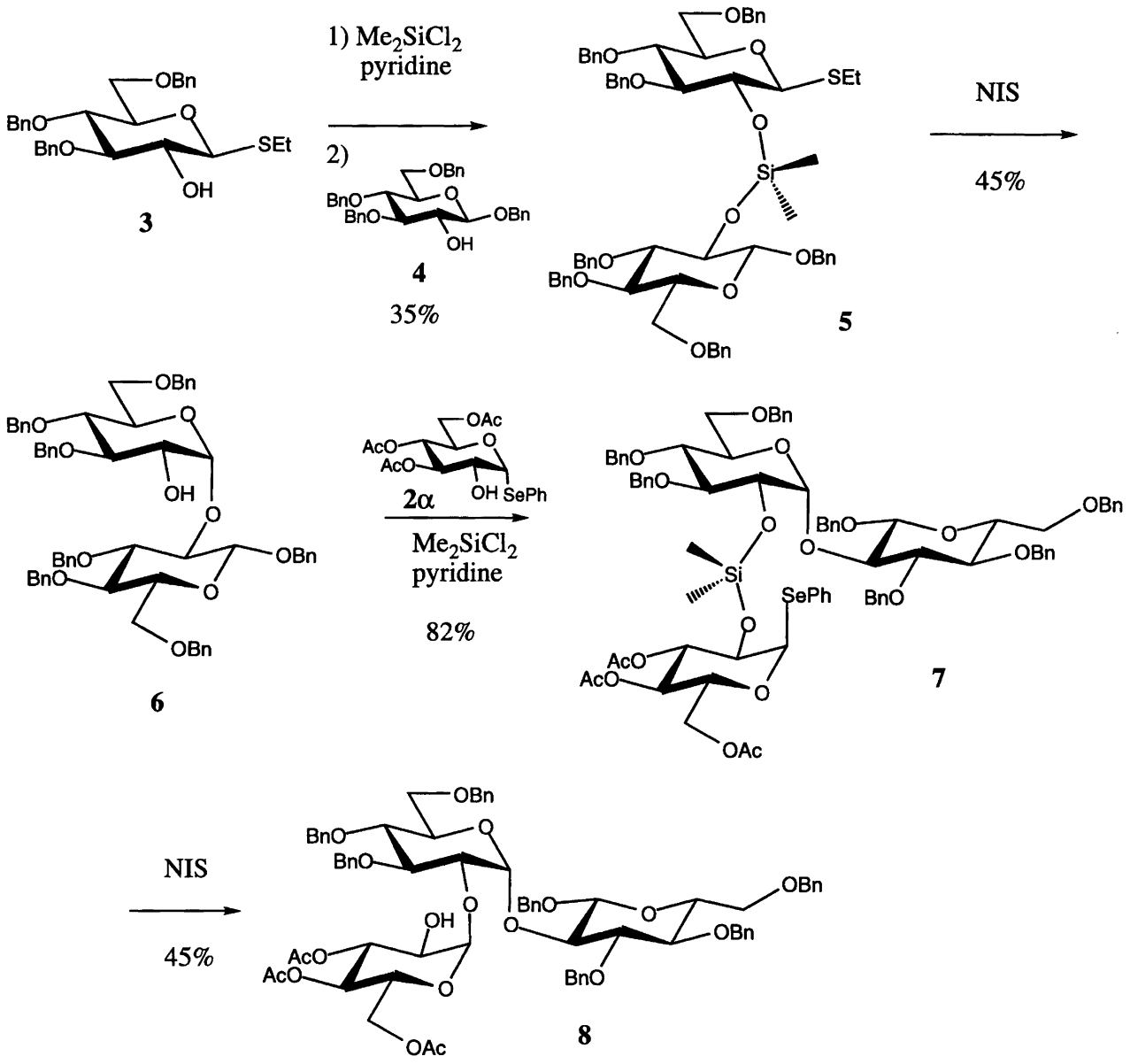


1 **2**

2 in 59% yield as a syrup and mixture of anomers with an α/β ratio of ≈1:3. The minor α-isomer was obtained crystalline from the mixture. Potassium phenylselenate was obtained by hypophosphoric acid reduction of diphenyl diselenide to selenophenol[20] followed by treatment *in situ* with potassium methoxide. Initially we attempted to prepare sodium phenylselenate *in situ* from sodium borohydride reduction of diphenyl diselenide in ethanol,[24] but the sodium phenylselenate solution obtained in this manner gave extensive deacetylation or transesterification of **1** and/or **2**.

Kojitriose is a constituent of intracellular teichoic acids with RNA binding properties and is obtained from streptococci.[25]

For the synthesis of kojitriose we used known[17] 1,3,4,6,3′,4′,6′-hepta-*O*-benzylkojibiose (**6**) as an intermediate, and prepared this intermediate by intramolecular glycosidation of 1,3,4,6-tetra-*O*-benzyl-β-D-glucopyranoside[17] (**4**) with glycosyl donor **3**.[10] We did not anticipate any problems since intramolecular α-glucosidation had previously successfully been carried out between donor **3** and the 2-OH group of a glucoside acceptor.[11] However, several attempted reactions of a solution of ethyl 2-*O*-chlorodimethylsilyl-3,4,6-tri-*O*-benzyl-1-thio-β-D-glucopyranoside (prepared from **3**, excess dichlorodimethylsilane and pyridine as previously described)[11] with **4** and pyridine failed to give high yields of silylacetal-tethered disaccharide **5**. The best yield of **5** was 35%, unlike reaction of this silyl chloride with methyl



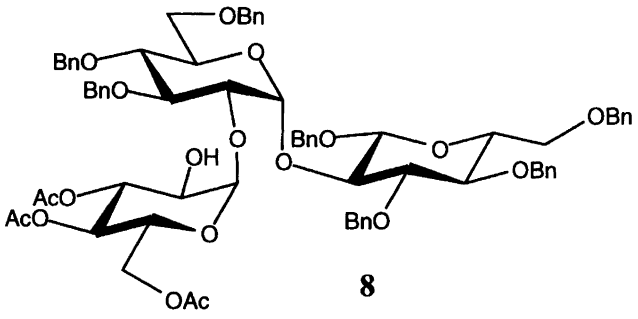
4,6-*O*-benzylidene-3-*O*-methyl-β-D-glucopyranoside which gave the silylacetal product in 93% yield.[11] Reaction of **5** with *N*-iodosuccinimide (NIS) in nitromethane gave stereospecifically α-glucoside **6** in 45% yield, with the remaining fraction of **5** being transformed into **4**. The thioglucoside part of this fraction could not be found. Again this was disappointing, compared with reaction of the dimethylsilylacetal between **3** and methyl 4,6-*O*-benzylidene-3-*O*-methyl-β-D-glucopyranoside with NIS which gave the α-glucoside in 67% yield. The comparatively low yields in these two reactions are probably due to greater steric hindrance from the neighbouring benzyl groups relative to methyl groups on the acceptor.

The combined yield of **6** for the two steps was only 16%, which is less than the previous intermolecular synthesis of this compound, even though that synthesis was stereochemically unselective.[17] In that work **4** was condensed with 2-*O*-allyl-3,4,6-tri-*O*-benzyl-α-D-glucopyranosyl chloride and silver perchlorate to give a mixture of anomers which after separation gave 32% α-glucoside. Deallylation of this compound gave 86% **6** so that the combined yield for the two steps was 27%.[17]

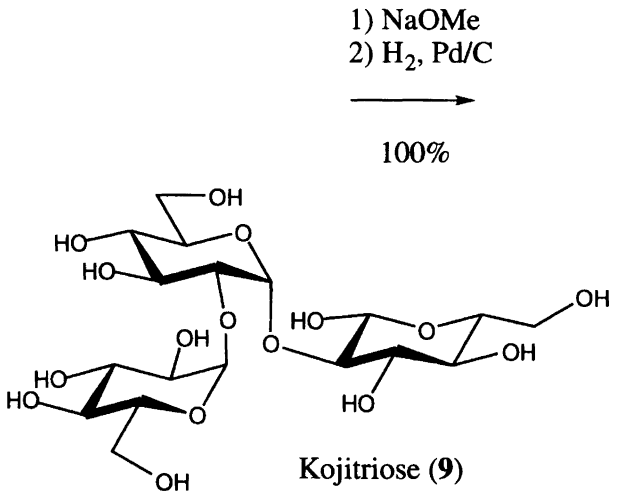
Reaction of **2α** with dichlorodimethylsilane–pyridine and removal of the excess reagent by distillation gave a solution of the 2-*O*-chlorodimethylsilyl ether of **2α**, which was reacted, in the presence of pyridine, with **6** to give silyl-tethered trisaccharide **7** in excellent yield. However, attempts to couple **3** instead of **2α** with **6** were unsuccessful, which confirmed that steric hindrance was a problem when **3** was used as the donor molecule.

Internal glycosidation of **7** with NIS in nitromethane gave a 1:1 mixture of two products: trisaccharide **8** and aglycone **6**. After chromatographic separation, **8** was isolated in 45% yield.

The deprotection of **8** was performed by deacetylation



8



Kojitriose (**9**)

with catalytic NaOMe in methanol, followed by hydrogenolysis of the benzyl groups using 1 atm hydrogen-pressure and 10% palladium-on-carbon as catalyst. The product kojitriose (**9**) was obtained in quantitative yield, and had an identical ^{1}H NMR spectrum with the previously published one.[16]

We also investigated the synthesis of sucrose. This disaccharide is notoriously difficult to synthesise, and in fact only a handful of syntheses of this compound have been published.[26–30] The stereochemistry at both anomeric centres has to be controlled; one centre is controlled by intramolecular glycosidation and the other by the result of silylation of the anomeric OH of fructose. For the latter purpose it was desirable to employ a 1,3,4,6-tetraprotected fructofuranose derivative which had the β-configuration in the crystalline state. Silylation of such a derivative would be expected to occur without much mutarotation so that only the β-silyl ether would be obtained. 1,3,4,6-Tetra-*O*-benzylfructofuranose (**10**) seemed to be such a derivative since evidence suggested that it crystallised as the β-anomer.[31] We were, however, not able to obtain **10** crystalline, but the syrupy material was a 1:2 mixture of α- and β-anomers. The anomeric configuration of both **10** and the fructose-derivatives obtained below, was easily determined from the ^{13}C NMR chemical shift of C-2, since the chemical shift of an α-fructofuranose anomer is 3–5 ppm higher (approx. 106 ppm) than the β-anomer (approx. 102–103 ppm).

This material was first reacted with an excess of dichlorodimethylsilane–pyridine to give a 2-*O*-chlorosilane that was then reacted with **3**. The product silylacetal **11** was obtained in 85% yield as a mixture of **11**α and **11**β. The two anomers could be separated chromatographically to give 33% pure **11**β and 18% **11**α.

'Prosucrose' silylacetal **11**β was subjected to treatment with NIS in nitromethane. Reaction occurred, but no disaccharides were formed after conversion of the starting material.

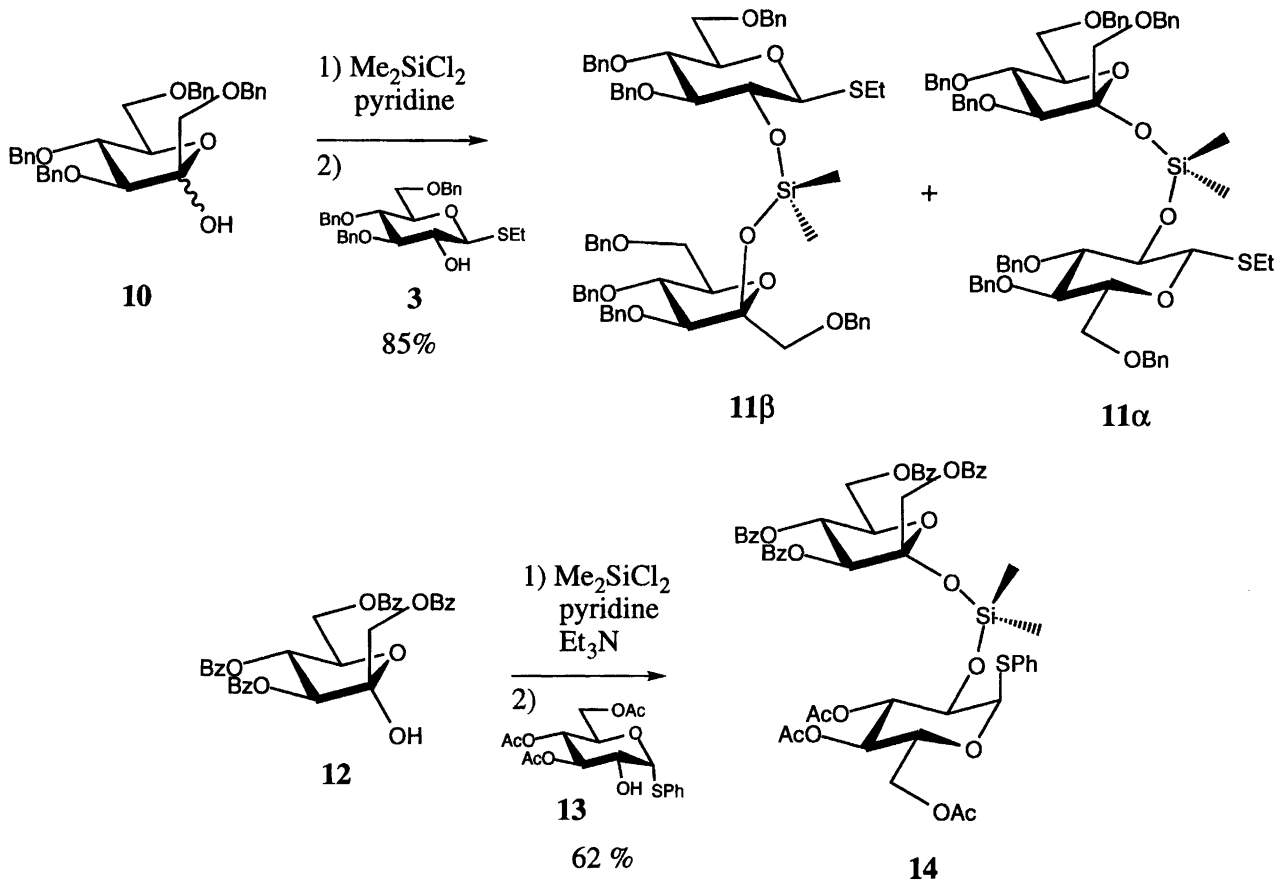
As an alternative, the protection-group pattern was varied. Crystalline 1,3,4,6-tetra-*O*-benzoyl-α-D-fructofuranose[32] (**12**) was reacted with dichlorodimethylsilane and triethylamine to the 2-*O*-chlorosilane and then condensed with phenylthio-3,4,6-tri-*O*-acetyl-α-D-glucopyranoside[10] (**13**) to give the silylacetal disaccharide **14** in 62% yield. The reaction gave almost entirely the α-anomer even though **12** was allowed to mutarotate. Like **11**β, **14** resisted all attempts to make it successfully undergo intramolecular glycosidation.

This work has revealed that silicon-tethered glycosidation can be employed for oligosaccharide synthesis but has limitations similar to conventional glycosidations. Silicon-tethered glycosidation seems to be invariably stereoselective, but it is difficult to predict the success of this method, and it does seem to be hampered by steric hindrance. These results complement the discoveries of Barresi and Hindsgaul regarding carbon-tethered glycosidation.[6] Kojitriose was successfully synthesised; unlike previous syntheses the new synthesis was highly stereoselective, however in terms of yield it was not an improvement compared with the syntheses based on conventional glycosidation reactions.

Experimental

General.^{13}C NMR and ^{1}H NMR spectra were recorded on Bruker AC 200, AC 250 and AM 500 instruments. When $CDCl_3$ was used as solvent TMS and $CDCl_3$ (^{13}C NMR: δ 76.93) were used as references. Mass spectra were obtained on a VG TRIO-2 instru ment. Melting points were uncorrected. Optical rotations were measured on a Perkin Elmer 141 polarimeter. Microanalysis was carried out by Leo Microanalytical Laboratory. Concentrations were performed on a rotary evaporator at a temperature below 40 °C. All reactions were performed under an atmosphere of inert gas (nitrogen or argon).

*Phenyl 3,4,6-tri-*O*-acetyl-1-seleno-α,β-*D*-glucopyranoside (**2**).* A solution of selenophenol in CH_2Cl_2 was prepared by refluxing diphenyl diselenide (4.0 g, 12.8 mmol) with



hypophosphoric acid (40 ml, 60%) for 8 h, extracting the weakly yellow solution with CH_2Cl_2 twice (10 ml each), washing the organic extract with water twice (10 ml each) and drying them with $MgSO_4$. The solution was added to a solution of potassium (0.39 g, 10 mmol) in methanol (10 ml), and 3,4,6-tri-*O*-acetyl-β-D-glucopyranosyl chloride[23] (**1**, 3.0 g, 9.2 mmol) was added. The solution was stirred for 2 days and concentrated, redissolved in CH_2Cl_2 (50 ml), washed twice with NaOH (0.1 M, 20 ml each) and twice with water (20 ml each). The organic layer was dried with $MgSO_4$, filtered and concentrated to give a syrup (3.67 g). Flash-chromatography in EtOAc–pentane 1:3 followed by 1:2 followed by 1:1 gave compound **2** (2.41 g, α/β-ratio 1:3, 59%). The α-anomer could be crystallised from EtOAc-pentane. α-anomer: M.p. 145–148 °C, $[\alpha]_D^{22}$ +286° (*c* 0.32, CH_2Cl_2), ^1H NMR ($CDCl_3$): δ 7.6 (m, 2 H, Ph), 7.25 (m, 3 H, Ph), 5.95 (d, 1 H, $J_{1,2}$ 5.5 Hz, H-1), 5.05 (m, 2 H, H-3, H-4), 4.4 (m, 1 H, H-5), 4.3 (dd, 1 H, $J_{6'}$ 12 Hz, $J_{5,6}$ 5 Hz, H-6), 4.0 (dd, 1 H, $J_{5,6'}$ 2 Hz, H-6'), 3.9 (m, 1 H, H-2), 2.6 (d, 1 H, *J* 8 Hz, OH), 2.1 (s, 3 H, Ac), 2.0 (s, 6 H, 2 Ac). ^{13}C NMR ($CDCl_3$): δ 169–173, 134.2, 129.2, 128.1 (Ph), 89.8 (C-1), 74.8, 70.9, 70.6, 67.5 (C-2, C-3, C-4, C-5), 61.8 (C-6), 20.7 (Ac), 20.5 (2 Ac). β-anomer: ^{13}C NMR ($CDCl_3$): δ 169–173, 134.2, 129.2, 128.0 (Ph), 90.0 (C-1), 74.4, 72.8, 71.0, 67.9 (C-2, C-3, C-4, C-5), 60.8 (C-6), 20.7 (2Ac), 20.6 (Ac). Anal. $C_{18}H_{22}O_7Se$: C, H.

Benzyl 2-O-(1-S-ethyl-3,4,6-tri-O-benzyl-1-thio-β-D-glucopyranos-2-O-yl)dimethylsilyl-3,4,6-tri-O-benzyl-β-D-glucopyranoside (**5**). A solution of ethyl 3,4,6-tri-*O*-benzyl-2-*O*-(chlorodimethylsilyl)-1-thio-β-D-glucopyranoside in toluene–pyridine (62.5 ml, 8.9 mmol, 1.2 equiv.) was prepared from **3**[11] (4.7 g), toluene (63 ml), pyridine (16 ml) and dimethylsilyl dichloride (5.7 ml) as previously described,[11] and added to **4**[17] (4.0 g, 7.4 mmol). The resulting solution was stirred for 18 h, ether (100 ml) was added and the solution was washed with water (25 ml) and NaCl-solution (saturated, 25 ml), dried with Na_2SO_4 and concentrated to a syrup (9.83 g). Flash chromatography in EtOAc–pentane 1:10 followed by 1:6 followed by 1:4 gave **5** (2.8 g, 35%). ^{13}C NMR ($CDCl_3$): δ 137.3–138.7 (Ph *ipso*-Cs), 127.2–128.2 (Ph CH), 102.1 (C-1), 87.0, 86.0, 85.6, 78.9, 77.8, 77.7, 75.3, 75.2, 75.0, 74.7, 74.4, 73.3, 73.2, 71.0, 68.9, 68.7 (C-2–C-6, C-1'–C-6', Bn), 24.5, 15.0 (SEt), −1.5, −1.6 (SiMe).

Benzyl 2-O-(3,4,6-tri-O-benzyl-α-D-glucopyranosyl)-3,4,6-tri-O-benzyl-β-D-glucopyranoside (**6**). **5** (122 mg, 0.11 mmol) was dissolved in nitromethane (3 ml) and *N*-iodosuccinimide (252 mg) was added. The mixture was stirred at 25 °C for 18 h, ether (50 ml) was added and the solution was washed with $NaHCO_3$-solution (saturated, 20 ml) and $Na_2S_2O_3$-solution (saturated, 20 ml), dried with Na_2SO_4 and concentrated to a residue (120 mg) containing a 1:1 mixture of **6** and **4**. Flash-

chromatography in EtOAc–pentane 1:10 followed by 1:6 followed by 1:4 gave crystalline **6** (49 mg, 45%). M.p. 116–118 °C (Lit.[17] 120 °C). ^{13}C NMR ($CDCl_3$): δ 136.2–138.5 (Ph *ipso*-C), 127.1–128.1 (Ph CH), 101.3 (C-1), 98.5 (C-1′), 83.3, 82.9, 67.7–77.7 (C-2–C-6, C-2′–C-6′, Bn).

Benzyl 2-O-[2-O-(3,4,6-tri-O-acetyl-1-Se-phenyl-1-seleno-α-D-glucopyranos-2-O-yl)dimethylsilyl-3,4,6-tri-O-benzyl-α-D-glucopyranosyl]-3,4,6-tri-O-benzyl-β-D-glucopyranoside (7). To a solution of **2α** (300 mg, 0.67 mmol, 1.3 equiv.) in toluene (10 ml) and pyridine (1.5 ml) was added dichlorodimethylsilane (0.4 ml, 0.43 g, 3.35 mmol). The mixture was stirred for 0.5 h, after which excess reagent was removed by distillation until the temperature of the distillate revealed that it was pure toluene. After cooling, **6** (500 mg, 0.51 mmol) and pyridine (1 ml) were added to the solution in the distillation flask. The resulting solution was stirred for 18 h, ether (50 ml) was added and the solution was washed twice with NaCl-solution (saturated, 20 ml each), dried with Na_2SO_4 and concentrated to a syrup (908 mg). Flash-chromatography in EtOAc–pentane 1:6 followed by 1:4 followed by 1:3 gave **7** (619 mg, 82%). $[\alpha]_D^{22}+111°$ (*c* 2.3, CH_2Cl_2). ^{1}H NMR ($CDCl_3$): δ 7.5 (m, 2 H, Ph), 7.2–7.3 (m, 34 H, Ph), 7.0 (m, 4 H, Ph), 6.0 (d, 1 H, $J_{1'',2''}$ 5.5 Hz, H-1″), 5.5 (d, 1 H, $J_{1',2'}$ 3.5 Hz, H-1′), 5.25 (t, 1 H, *J* 9 Hz) and 4.95 (t, 1 H, *J* 9 Hz, H-3″ and H-4″), 4.0–4.9 (m, 19 H), 3.3–3.9 (m, 12 H), 2.0, 2.0, 1.9 (3 s, 9 H, 3 Ac), 0.05, −0.05 (2 s, 6 H, SiMe). ^{13}C NMR ($CDCl_3$): δ 169–173 (3 Ac), 137.5–138.5, 133.6 (Ph *ipso*-C), 127.3–129.0 (Ph CH), 102.6 (C-1), 96.9 (C-1′), 85.6, 83.6, 81.7, 78.4, 78.0, 75.9, 75.2, 74.7, 74.0, 73.3, 72.7, 70.8, 70.0, 69.9, 69.5, 68.5, 68.2 (C-2–C-6, C-2′–C-6′, C-1″–C-5″, Bn), 62.0 (C-6″), 20.6–20.9 (Ac), −1.7, −1.9 (SiMe).

Benzyl 2-O-[2-O-(3,4,6-tri-O-acetyl-α-D-glucopyranosyl)-3,4,6-tri-O-benzyl-α-D-glucopyranosyl]-3,4,6-tri-O-benzyl-β-D-glucopyranoside (8). **7** (247 mg, 0.17 mmol) was dissolved in nitromethane (5 ml) and N-iodosuccinimide (378 mg, 1.68 mmol, 10 equiv.) was added. The mixture was stirred at 25 °C for 5 h and then heated to 100 °C for 5 min. CH_2Cl_2 (50 ml) was added and the solution was washed with HCl (1 M, 20 ml), $NaHCO_3$-solution (saturated, 20 ml) and $Na_2S_2O_3$-solution (saturated, 20 ml), dried with Na_2SO_4 and concentrated to a residue (203 mg) that contained a 1:1 mixture of **8** and **6**. Flash-chromatography in EtOAc-pentane 1:6 followed by 1:4 followed by 1:3 followed by 1:2 followed by 1:1 gave pure **8** (96 mg, 45%). $[\alpha]_D^{22}+80.4°$ (*c* 0.5, CH_2Cl_2). ^{1}H NMR ($CDCl_3$): δ 7.3–7.4 (m, 28 H, Ph), 7.2 (m, 3 H, Ph), 7.1 (m, 4 H, Ph), 5.7 (d, 1 H, $J_{1',2'}$ 3.5 Hz, H-1′), 5.25 (t, 1 H, *J* 9.5 Hz), 4.4–5.1 (m, 18 H), 3.3–4.1 (m, 16 H), 2.2, 2.1, 1.95 (3 s, 9 H, 3 Ac). ^{13}C NMR ($CDCl_3$): δ 169–173 (3 Ac), 137.1–138.1 (Ph *ipso*-C), 127.2–128.3 (PhCH), 102.8 (C-1), 94.7, 93.8 (C-1′, C-1″), 83.1, 80.0, 78.6–67.2 (C-2–C-6, C-2′–C-6′, C-2″–C-5″, Bn), 61.2 (C-6″), 20.5–20.9 (Ac).

Kojitriose (9). **8** (146 mg, 0.116 mmol) was dissolved in 10 ml methanol and 0.2 ml of a solution of 0.8 M NaOMe in methanol was added. After 5 min at 25 °C, TLC-analysis revealed the reaction to be complete with the formation of a single product (R_f 0.6 in EtOAc). The solution was neutralised by addition of solid CO_2, and then concentrated. The residue was extracted with EtOAc (25 ml), filtered and the filtrate was concentrated. Methanol (10 ml), water (2 ml), acetic acid (0.1 ml) and palladium on carbon (100 mg, 10%) was added, and mixture was hydrogenolysed at 1 atm H_2-pressure for 3 days. Filtration and concentration gave syrupy **9**[16,17] (62 mg, 100% with 1 mol water). ^{1}H NMR (D_2O).[17] δ 5.56 (d, 1 H, *J* 3.5 Hz, β-anomer), 5.41 (d, 1 H, *J* 3.5 Hz, α-anomer), 5.26 (d, 1 H, *J* 3.5 Hz, α-anomer), 5.14 (d, 1 H, *J* 3.5 Hz, β-anomer), 5.06 (d, 1 H, *J* 3.5 Hz, α-anomer), 4.74 (d, 1 H, *J* 7.0 Hz, β-anomer), 3.3–4.1 (m, 18H). ^{13}C NMR (D_2O): δ 103.5, 103.2, 102.4, 101.7, 100.6, 96.4 (C-1, C-1′, C-1″, αβ-anomers), 85.4, 82.9, 82.8, 82.6, 81.3, 79.8, 78.8, 78.7, 78.6, 78.4, 78.3, 78.1, 76.7, 76.5, 76.4, 76.3, 76.1, 67.7, 67.5, 67.3, 67.1.

Ethyl 3,4,6-tri-O-benzyl-2-O-(1,3,4,6-tetra-O-benzyl-α,β-D-fructofuranosyloxydimethylsilyl)-1-thio-β-D-glucopyranoside (11). 1,3,4,6-tetra-*O*-benzyl-α,β-D-fructofuranose[31] (**10**, 0.72 g, 1.33 mmol) was dissolved in dry toluene (9 ml) and pyridine (2.2 ml, 27 mmol), dichlorodimethylsilane (0.8 ml, 6.6 mmol, 5 equiv.) was added, and the mixture was stirred for 1 h, and then subjected to distillation until the temperature in the distillate revealed that only toluene was distilling. To the recooled distillation-flask were added pyridine (1 ml) and **3** (500 mg, 1 mmol) and the mixture was stirred for 3 days. Ether (50 ml) was added and the solution was washed with water (10 ml) and NaCl-solution (saturated, 10 ml), dried with Na_2SO_4 and concentrated to a syrup (1.36 g). Flash-chromatography in EtOAc–pentane 1:10 gave first a mixture of **11α** and **11β** (781 mg, 1:1 ratio) and then some pure **11β** (160 mg) Combined yield: 85%. Repeated flash-chromatography of the mixed fraction in EtOAc–pentane 1:15 followed by 1:12 followed by 1:10 allowed the isolation of pure **11α** (198 mg), a mixed fraction (293 mg) and more **11β** (207 mg). **11β**: ^{1}H NMR ($CDCl_3$): δ 7.2 (m, 33 H, Ph), 6.95 (m, 2 H, Ph), 4.9 (d, 1 H, *J* 12 Hz), 3.9–4.7 (m, 17 H), 3.3–3.7 (m, 10 H), 2.55 (m, 2 H, SCH_2), 1.15 (t, 3 H, CH_3), 0.15, 0.1 (2 s, 6 H, SiMe). ^{13}C NMR ($CDCl_3$): δ 137.9–138.8 (Ph *ipso*-C), 127.0–128.0 (Ph CH), 103.2 (C-2), 87.1, 86.0, 83.4, 83.2 (C-3–C-5, C-1′), 78.9, 78.4, 77.9, 74.9, 74.7, 74.3, 73.6, 73.3, 73.2, 73.0, 72.1, 71.1, 69.0 (C-1, C-6, C-2′, C-3′, C-4′, C-5′, C-6′, Bn), 24.5, 15.0 (SEt), 0.8 (SiMe). **11α**: ^{13}C NMR ($CDCl_3$): δ 106.1 (C-2), 89.4, 85.7, 82.9, 82.4 (C-3–C-5. C-1′), 70.4–79.7 (C-1, C-6, C-2′–C-6′, Bn), Ph, SiMe and SEt as β-anomer.

Phenylthio 2-O-(1,3,4,6-tetra-O-benzoyl-α-D-fructofuranosyloxy)dimethylsilyl-3,4,6-tri-O-acetyl-1-thio-α-D-glucopyranoside (14). 1,3,4,6-tetra-*O*-benzoyl-α-D-fructofuranose[32] (**12**, 0.60 g, 1 mmol) was dissolved in dry

benzene (10 ml), Et_3N (0.16 ml, 0.12 g, 1.2 mmol) was added and the solution kept for 30 min to allow the sugar to mutarotate. A solution of dichlorodimethylsilane (0.36 ml, 3 mmol) in benzene (1 ml) was added, and the mixture was allowed to react for 4 h. It was then concentrated, redissolved in dry ether (10 ml), filtered and concentrated. To the residue (611 mg) were added THF (4 ml), pyridine (1 ml) and phenyl 3,4,6-tri-*O*-acetyl-1-thio-α-D-glucopyranoside (**13**, 200 mg, 0.5 mmol) and the mixture was stirred for 18 h. Ether (50 ml) was added and the solution was washed with water (10 ml) and NaCl-solution (saturated, 10 ml), dried with Na_2SO_4 and concentrated to a syrup (908 mg). Flash-chromatography in EtOAc–pentane 1:4 followed by 1:3 followed 1:2 gave **14** (328 mg, 62%). $[\alpha]_D^{22} + 78.9°$ (*c* 2.2, CH_2Cl_2). ^1H NMR ($CDCl_3$): δ 7.8–8.0 (m, 8 H, Ph), 7.0–7.5 (m, 17 H, Ph), 5.85 (d, 1 H, $J_{2,3}$ 3.0 Hz, H-3), 5.7 (d, 1 H, $J_{1',2'}$ 5.5 Hz, H-1'), 5.5 (m, 2 H, H-4, H-5), 5.2 (t, 1 H, *J* 9.5 Hz, H-3'), 4.8 (t, 1 H, *J* 9.5 Hz, H-4'), 4.4–4.75 (m, 5 H), 4.2 (m, 1 H, H-5'), 4.05 (dd, 1 H, $J_{5',6'}$ 5.0 Hz, $J_{6',6a'}$ 12.0 Hz, H-6'), 3.8 (dd, 1 H, $J_{5',6a'}$ 2.0 Hz, H-6a'), 1.9, 1.9, 1.85 (3 s, 9 H, 3 Ac), 0.25, 0.2 (2 s, 6 H, SiMe). ^{13}C NMR ($CDCl_3$): δ 170.3, 169.7 (Ac), 166, 165.5, 165 (Bz), 127.1–133.4 (Ph), 105.9 (C-2), 87.5 (C-1'), 81.9, 80.9, 77.7 (C-3–C-5), 73.2, 70.6, 68.7, 67.8 (C-2'–C-5'), 64.7, 63.8, 62.1 (C-1, C-6, C-6'), 20.5–20.7 (Ac), −0.2, −1.1 (SiMe).

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