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Synthesis of L-glucose derivatives from D-glucose and L-arabinose

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Abstract. L-Glucose derivatives are prepared by two different routes. The first involves a modification of the previously reported multi-step approach by *Shiozaki*[8], starting from a D-glucurono-1,5-lactone derivative, resulting in the isolation of 2,3,4,6-tetra-*O*-benzyl-L-glucopyranose. The other route comprises the synthesis of penta-*O*-acetyl-L-glucopyranose via a highly stereoselective addition of [(phenyldimethylsilyl)methyl]magnesium chloride with 2,3,5-tri-*O*-benzyl-L-arabinofuranose.

Introduction

In earlier reports, *Tatsuda* et al.[1] showed that methyl α-L-glucopyranoside (**1a**) was a potentially useful synthon for the preparation of 2,6-dideoxy-L-sugars (*e.g.* L-olivose **2**) and 2,6-dideoxy-3*C*-branched carbohydrates (*e.g.* L-cladinose **3**) which, in turn, are glycosidic components of interesting antibiotics[2].

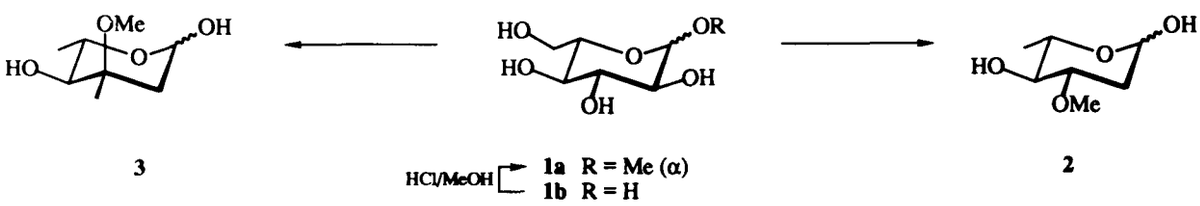
Thus far, several routes to the synthesis of L-glucose (**1b**), which can easily be converted into **1a**, have been published. For example, one century ago *Fischer* reported[3] the first chemical synthesis of **1b** from L-arabinose by the cyanohydrin Kiliany approach. Later on it was shown[4], that the accessibility of **1b** could be improved substantially by condensing L-arabinose with nitromethane (Nef reaction), followed by hydrolysis of the 1-deoxy-1-nitroalditol, and subsequent separation of the resulting L-glucose and L-mannose. On the other hand, an enantioselective synthesis of **1b** could be realized[5] without chain extension from D-glucose.

Recent studies from this laboratory revealed that hydroxymethylation of carbonyl functions with the reagents [(benzyloxy)methyl]lithium[6] (**7**) and [(phenyldimethylsilyl)methyl]magnesium chloride[7] (**22b**) proceeds with a high degree of stereoselectivity. Our need for an easy access to L-glucose derivatives urged us to investigate whether the above-mentioned hydroxymethylating reagents could be applied for this purpose.

We here report the preparation of L-glucose derivatives by two distinct routes of synthesis, the initial steps of which involve either hydroxymethylation of 2,3,4-tri-*O*-benzyl-6-*O*-(*tert*-butyldiphenylsilyl)-D-glucono-1,5-lactone (**9**) with **7** or 2,3,5-tri-*O*-benzyl-L-arabinofuranose (**21**) with **22b**.

Results and discussion

In 1991, *Shiozaki*[8] reported for the first time the conversion of 2,3,4,6-tetra-*O*-benzyl-D-glucono-1,5-lactone (**8**) into 2,3,4-tri-*O*-benzyl-6-*O*-(trimethylacetyl)-L-glucose (**18**) using [(methoxymethoxy)methyl]lithium (**6**), generated *in situ* from the corresponding tributylstannane derivative **4** with *n*-butyllithium, as the hydroxymethylating reagent. However, the particular choice of the two reactants was in several aspects not fully satisfactory. For example, the condensation (Scheme 1) of compound **8** with **6** to give **10** did not proceed in a stereoselective manner. Moreover, the presence of a benzyl protecting group at C–*O*-6 in the starting compound **8** entailed an elaborate deprotection procedure (*i.e.* **10** → **13**) which was required for the key oxidative decarboxylation of an α-oxy carboxylic acid via a diacyl peroxide intermediate (*i.e.* **15** → **18**). These drawbacks could be overcome using the known[9] 6-*O*-silyl-protected D-glucono-1,5-lactone **9** and reagent **7**, prepared[10] *in situ* by tin/lithium exchange of the tributylstannane derivative[11] **5** with *n*-butyllithium, as the starting compounds. Thus, addition of **9** to **7**, gave the anomerically pure α-D-*gluco*-heptulopyranose **11**. In the next tep, dehydroxylation of **11** with triethylsilane–boron-trifluoride-etherate was performed in



3 HCl/MeOH → **1a** R = Me (α), **1b** R = H **2**

the solvent 1,2-dichloroethane instead of acetonitrile to yield exclusively the D-*glycero*-D-*gulo*-heptitol derivative **12**. The relatively high yield of **12** may be attributed to the fact that the occurrence of the now well-established[12] addition reaction of acetonitrile with a transiently formed oxocarbenium ion was excluded. Removal of the 7-*O*-silyl protecting group from **12** with fluoride ions afforded the partially protected 2,6-anhydroheptitol derivative **14** in an excellent yield. Conversion of **14** into the heptonic acid methyl esther **17** could be realized by oxidation with chromic acid followed by methylation of crude **16** with diazomethane, to give homogeneous **17** in 81% for the two steps. In his respect, it is of interest to note that the two-step oxidation (*i.e.* Swern followed by *Sharpless*[13]) of **13**, as reported by *Shiozaki*[8], resulted in a low recovery of the heptonic acid **15**. Saponification of **17** and subsequent treatment of **16** with 3-chloroperoxybenzoic acid and DCC gave the fully protected L-glucose derivative **19**, which was finally saponified to the target molecule **20**.

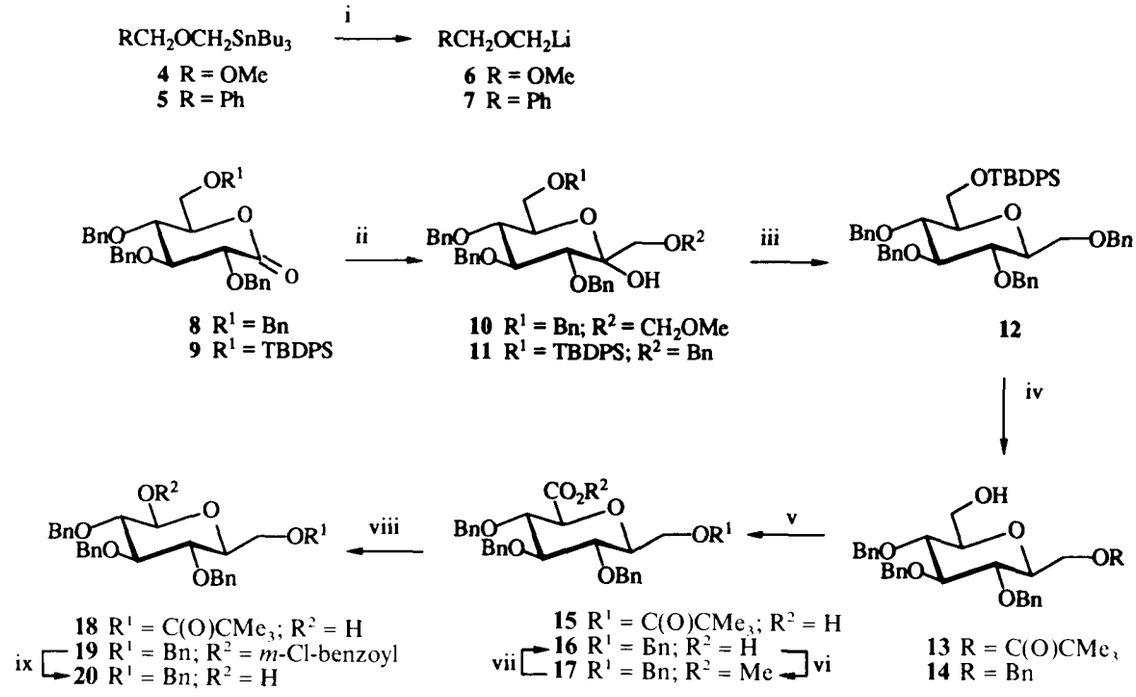
It is evident that the original approach of *Shiozaki*, despite the improvements here described does not give ready access to L-glucose or derivatives thereof. Recently, *Singh* et al.[14] reported that the reaction of organomagnesium nucleophiles with the masked aldehyde function of 2,3-*O*-isopropylidene derivatives of furanoses proceeds in a highly stereoselective manner, resulting in products with an *anti*-relationship[15] between the newly created chiral centre and the old C-2 of the sugar. The latter intriguing finding goaded us to investigate in detail the stereochemical outcome of the addition reaction of the conformationally less rigid 2,3,5-tri-*O*-benzyl-L-arabinofuranose[16] (**21**) with the earlier mentioned Grignard reagent **22b**, prepared *in situ* (see Scheme 2) by treating commercially available (phenyldimethylsilyl)lmethyl chloride **22a** with magnesium. First of all, it was observed that the condensation of **21** with **22b** only proceeded in an acceptable rate at elevated temperature. Thus, TLC analysis of the reaction mixture, after 4 h at 60°C, revealed the presence of one product having a higher R_f value than the starting compound **21**. Work-up and purification afforded a product, the ^{1}H- and ^{13}C-NMR data of which were in good accordance with the structure of one of the possible two diastereoisomers; *i.e.* the 2,3-*anti* (**23**) or 2,3-*syn* (**24**) isomer. The stereochemistry of the condensation product was unambiguously ascertained by executing the following sequence of reactions. Benzylation[7] of **24** (**23**) and subsequent unmasking[7] of the silane function in **25** gave **26**, the exposed primary hydroxyl group of which was converted to the aldehyde derivative **27** by Swern oxidation. Finally, hydrogenolysis of the benzyl groups and acetylation of **1b**, resulted in the isolation of L-glucose derivative **28**, as evidenced by proton nuclear magnetic resonance and specific rotation measurements. Furthermore, high-performance liquid chromatography of **1b**, obtained after saponification of **28**, showed that the product was not contaminated with L-mannose having a retention time of 17.5 min (*cf.* **1b**: 15.5 min). Thus, the condensation of the L-arabinofuranose derivative **21** with the Grignard reagent **22b** proceeds stereoselectively with *syn*-selectivity (*i.e.* exclusive formation of the L-glucitol **24** instead of the L-mannitol derivative **23**). Furthermore, the conversion of **21** into L-glucose derivative **28** promises to be, in terms of overall yield (*i.e.* 26% based on **21**), an attractive route for the future synthesis of valuable L-sugar synthons.

At present, we are studying in detail the scope of the highly stereoselective *syn*-addition of the Grignard reagent **22b** with other furanose derivatives. The results of this study will be published in due course.

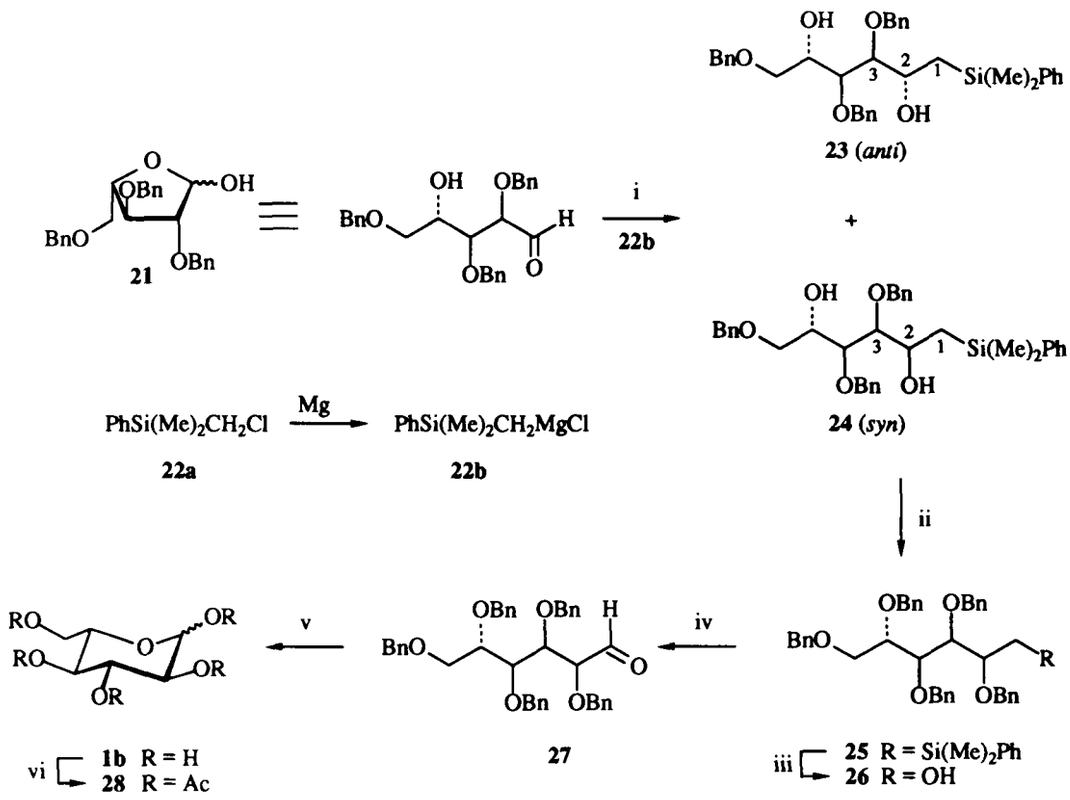
Experimental

General methods and materials

Dioxane and pyridine were dried by refluxing with CaH_2 (5 g/l) for 6 h and then distilled. Dichloromethane, 1,2-dichloroethane and



Scheme 1. i) BuLi, THF, 7 min; ii) **6** *and* **8**, *−78°C, 30 min (*__10__*, 74%), or* **7** *and* **9**, *−80°C, 20 min (*__11__*, 85%); iii) Et_3SiH, $BF_3 \cdot Et_2O$, 1,2-dichloroethane, 20°C, 30 min (81%); iv) Bu_4NF, 1,4-dioxane, 55°C, 2 h (93%); v) $K_2Cr_2O_7/H_2SO_4$, acetone, 55°C, 2 h; vi) CH_2N_2, methanol, 20°C (81%, based on* **14***); vii) LiOH in methanol/water, 0°C, 24 h; viii)* m-*chloroperbenzoic acid, DCC, CH_2Cl_2, 0–5°C, 30 min (43%, based on* **17***); ix) LiOH, methanol/water, 20°C, 2 h (59%).*



Scheme 2. i) THF, −20 → 60 °C, 4 h (70%); ii) NaH, BnBr, Bu_4NI, DMF, RT, 2 h; iii) CH_3CO_3H, NaBr, NaOAc, AcOH, AcOH, 0 °C, 1 h (70%, based on **24***); iv) Swern oxidation (90%); v) H_2, Pd/C, 45 °C, 1 h; vi) Ac_2O/pyridine, 1/1, RT, 1 h (60%, based on* **27***).*

toluene were distilled from P_2O_5. DMF was stirred with CaH_2 at room temperature for 16 h and distilled under reduced pressure. Diethyl ether and tetrahydrofuran were distilled from $LiAlH_4$. Dioxane, tetrahydrofuran and pyridine were stored over molecular sieves 4 Å (Aldrich). Toluene and diethyl ether were stored over sodium wire, dichloromethane and 1,2-dichloroethane over Alumina.

Schleicher and Schüll DC Fertigfolien F1500 LS 254 were used for TLC analysis. The following eluents were used: System A (100% dichloromethane), System B dichloromethane/methanol, 98/2, v/v), System C (dichloromethane/methanol, 99/1, v/v), System D (toluene/ethylacetate, 60/40, v/v), System E (diethylether/*n*-hexane, 1/2, v/v), System F (diethylether/*n*-hexane, 2/1, v/v), System G (diethylether/*n*-hexane, 1/1, v/v), System H (ethylacetate/methanol/water, 5/3/2, v/v/v). Compounds were detected by charring with 20% sulfuric acid in methanol. Optical rotations were recorded at 20 °C with a Perkin-Elmer 241 polarimeter. Column chromatography was performed on silica gel 60, 70–230 mesh (Merck).

NMR spectra were recorded with a JEOL JNM-FX 200 (^{13}C, 50.1 MHz, internal standard chloroform or methanol) and a Bruker WM-300 spectrometer equipped with an Aspect-2000 computer (^1H, 300 MHz, internal standard Me_4Si).

High-Performance Liquid Chromatography was performed using a Carbopac^{TM} PA1 (Dionex) column (4 × 250 mm; eluent: 14mM NaOH, isocratic; flow: 1.0 ml/min; pressure: 63 bar) with a Dionex Pulsed Amperometric Detector II (E_1 +0.1 V, t_1 500 ms; E_2 +0.6 V, t_2 80 ms; E_3 −0.6 V, t_3 50 ms).

*1,3,4,5-Tetra-O-benzyl-7-O-(*tert*-butyldiphenylsilyl)-α-D-*gluco*-heptulopyranose* (**11**)

n-Butyllithium (1.6M in *n*-hexane, 5.7 ml) was added over a period of 5 min, to a cooled (−80 °C) solution of compound **5** (3.82 g, 9.3 mmol) in dry THF (100 ml). After stirring the mixture for 7 min under an argon atmosphere, compound **9** (2.5 g, 3.6 mmol) in dry THF (10 ml) was added. Stirring was continued for 20 min at −80 °C, when TLC analysis (System A) showed complete conversion of **9**. The reaction was quenched with aq. NH_4Cl (20%, 100 ml) and diluted with diethyl ether (100 ml). The organic layer was washed with water (3 × 30 ml), dried ($MgSO_4$) and concentrated. The residue was purified by column chromatography on silica gel (eluent: dichloromethane/*n*-hexane, 0/1 to 1/1, v/v) to yield pure **11** (2.47 g, 85%) as a colourless oil; R_f 0.41 (System A). ^{13}C NMR data ($CDCl_3$): δ 138.4–137.7 (C-quat., arom.); 134.6–135.8 (C-arom., TBDPS); 133.6, 133.0 (C-quat., TBDPS); 127.3–129.4 (C-arom.); 97.4 (C-2); 72.4, 77.6, 79.4, 83.3 (C-3, C-4, C-5, C-6); 73.7–75.7 (CH_2-benzyl); 72.4 (C-1); 26.7 (CH_3, TBDPS); 19.2 (C-quat., TBDPS).

*2,6-Anhydro-1,3,4,5-tetra-O-benzyl-7-O-(*tert*-butyldiphenylsilyl)-D-*glycero*-D-gulo-heptitol* (**12**)

$BF_3 \cdot Et_2O$ (0.37 ml) was added to a solution of **11** (2.72 g, 3.36 mmol) and triethylsilane (0.91 ml, 5.7 mmol) in 1,2-dichloroethane (100 ml) under a nitrogen atmosphere. After stirring for 30 min at 20 °C, TLC analysis (System A) showed complete conversion of **11**. The reaction mixture was diluted with ethyl acetate (50 ml), washed with water (100 ml) and aq. $NaHCO_3$ (10%, 100 ml). The organic layer was dried ($MgSO_4$) and concentrated. The residue was purified on silica gel (eluent: dichloromethane/hexane, 0/1 to 1/3, v/v) to give **12** (2.17 g, 81%); R_f 0.59 (System A). ^{13}C NMR data ($CDCl_3$): δ 138.3–138.6 (C-quat., arom.); 134.7–135.9 (C-arom., TBDPS); 133.6, 133.0 (C-quat., TBDPS); 127.4–129.5 (C-arom.); 87.1 (C-2); 78.0, 78.6, 78.9, 79.6 (C-3, C-4, C-5, C-6); 73.6–76.4 (CH_2-benzyl); 69.6 (C-1); δ 62.8 (C-7); δ 26.5, 26.8 (CH_3, TBDMS); 19.3 (C-quat., TBDPS).

*2,6-Anhydro-1,3,4,5-tetra-O-benzyl-D-*glycero*-D-gulo-heptitol* **14**)

Compound **12** (2.9 g, 3.66 mmol) was co-evaporated with 1,4-dioxane (2 × 25 ml) and subsequently redissolved in 1,4-dioxane (10 ml). Tetrabutylammonium fluoride (0.5M in 1,4-dioxane, 7.4 ml) was added to this solution. The mixture was stirred for 4 h at 55 °C, when TLC analysis (System B) showed complete reaction. The reaction mixture was diluted with dichloromethane (100 ml) and washed with water (100 ml). The organic layer was

dried ($MgSO_4$) and concentrated *in vacuo*. The residue was chromatographed on silica gel (eluent: dichloromethane/hexane, 1/3, v/v to dichloromethane/methanol, 96/4, v/v) giving pure **14** (1.9 g, 93%); R_f 0.39 (System B). ^{13}C NMR data ($CDCl_3$): δ 137.5–138.3 (C-quat., arom.); δ 127.2–128.0 (C-atom.); δ 86.6 (C-2); δ 77.7, 77.8, 78.1, 79.3 (C-3, C-4, C-5, C-6); δ 73.0–75.0 (CH_2-benzyl); δ 68.6 (C-1); δ 61.3 (C-7).

*Methyl 2,6-anhydro-3,4,5,7-tetra-O-benzyl-L-*glycero-*L-*gulo*-heptanoate* (**17**)

Potassium dichromate (1.28 g, 4.35 mmol) in sulfuric acid (6.3 ml, 3.6N) was added to a solution of **14** (1.6 g, 2.88 mmol) in acetone (50 ml). The mixture was stirred for 2 h at 55°C, when TLC analysis (System B) showed the reaction to be complete. The reaction mixture was diluted with ice water (25 ml) and dichloromethane (50 ml). The organic layer was washed with water (2 × 30 ml), dried ($MgSO_4$) and concentrated. The residue was dissolved in methanol (50 ml) and to this solution was added diazomethane (0.5M in diethyl ether, 8 ml). After 10 min, TLC analysis (System B) showed complete conversion of **16**. Excess diazomethane was destroyed with acetic acid/methanol (1/9, v/v, 5 ml). The mixture was concentrated *in vacuo* and the residue was purified on silica gel (eluent: dichloromethane/*n*-hexane, 1/1 to 1/0) to give **17** (1.3 g, 81%); R_f 0.48 (System B). ^{13}C NMR data ($CDCl_3$): δ 169.0 (C-7); δ 137.6–138.1 (C-quat., arom.); δ 127.3–128.0 (C-arom.); δ 86.0 (C-2); δ 77.4, 78.0, 79.2, 79.6 (C-3, C-4, C-5, C-6); δ 73.0–75.2 (CH_2-benzyl); δ 68.4 (C-1); δ 51.9 (CH_3).

2,3,4,6-Tetra-O-benzyl-1-O-(3-chlorobenzoyl)β-L-glucopyranose (**19**)

Compound **17** (0.1 g, 0.17 mmol) was dissolved at 0°C in a solution of lithium hydroxide in methanol/water (3/1, v/v, 0.25M, 3.4 ml). After stirring the mixture for 18 h at 0°C, Dowex WX4 (Na^+) was added and after stirring for 5 min the mixture was filtered and concentrated. The crude **16** thus obtained was dissolved in dichloromethane (4 ml) and cooled to 0°C. To this solution was added 3-chloroperbenzoic acid (40.6 mg) and 1,3-dicyclohexylcarbodiimide (50.7 mg). After stirring for 30 min at room temperature, TLC analysis (System C) showed complete conversion of the starting material **16**. The reaction mixture was filtered over Celite, diluted with dichloromethane (10 ml) and washed with TEAB (10 ml), dried ($MgSO_4$) and concentrated. The residue was purified on silica gel (eluent: dichloromethane/hexane, 1/1, v/v) to give compound **19** as an oil; R_f 0.85 (System C). ^{13}C NMR data ($CDCl_3$) of **19**: δ 163.7 (C=O); δ 137.6–138.3 (C-quat., arom.); δ 134.6 (C–Cl, 3-chlorobenzoyl); δ 133.5, 131.0 (C–H, 3-chlorobenzoyl); δ 127.7–130.0 (C-arom.); δ 94.8 (C-1); δ 75.6, 77.1, 80.6, 84.9 (C-2, C-3, C-4, C-5); δ 73.5–76.4 (CH_2-benzyl); δ 68.0 (C-6). ^{13}C NMR data ($CDCl_3$) of **16**: δ 171.8 (C-1); δ 138.1–138.8 (C-quat., arom.); δ 128.3–128.9 (C-arom.); δ 86.6 (C-6); δ 78.1, 78.7, 79.4, 80.5 (C-2, C-3, C-4, C-5); δ 69.2–76.2 (CH_2-benzyl); δ 69.2 (C-7).

2,3,4,6-Tetra-O-benzyl-L-glucopyranose (**20**)

Lithium hydroxide in methanol/water 3/1, v/v, 0.25M, 4 ml) was added to a cooled (0°C) solution of compound **19** (50 mg, 0.07 mmol) in methanol (1 ml). After stirring the mixture for 2 h at ambient temperature, TLC analysis (System C) indicated the reaction to be complete. The reaction mixture was neutralized with 1N HCl and concentrated. The residue was redissolved in dichloromethane (10 ml) and washed with water (10 ml). The organic layer was dried ($MgSO_4$) and evaporated to dryness. The residue was purified by silica gel chromatography (eluent: dichloromethane to dichloromethane/methanol, 98/2, v/v) to give pure **20** (23 mg, 59%) as a white solid; R_f 0.42 (System C); $[\alpha]_D$ −18.6 (*c* 0.3, $CHCl_3$); m.p. 148°C. ^{13}C NMR data ($CDCl_3$): δ 137.6–138.3 (C-quat., arom.); δ 128.2–129.1 (C-arom.); δ 98.1 (β-C-1); δ 91.9 (α-C-1); δ 70.8, 75.2, 78.3–85.1 (C-2, C-3, C-4, C-5); δ 73.8–77.6 (CH_2-benzyl); δ 69.2, 69.5 (C-6).

3,4,6-Tri-O-benzyl-1-deoxy-1-(phenyldimethylsilyl)-L-glucitol (**24**)

2,3,5-Tri-*O*-benzyl-L-arabinose[16] **21** (420 mg, 1 mmol) was co-evaporated with toluene (3 × 15 ml) and redissolved in dry tetrahydrofuran (10 ml). To the cooled (−20°C) mixture was added a solution of [(phenyldimethylsilyl)methyl]magnesium chloride[7] **22b** (0.5M in THF, 6 ml). After 30 min, the reaction mixture was allowed to reach room temperature and stirring was continued for 4 h at 60°C. The reaction mixture was quenched with aq. NH_4Cl (20%, 10 ml) and diluted with dichloromethane (50 ml). The organic layer was washed with water (3 × 30 ml), dried ($MgSO_4$) and concentrated. The residue was purified by column chromatography on silica gel (eluent: toluene/ethyl-acetate, 85/15, v/v to 60/40, v/v) resulting in the isolation of compound **24** (400 mg, 70%) and the recovery of unreacted **21** (105 mg, 25%). Compound **24**: R_f 0.6 (System D); $[\alpha]_D$ −6.1 (*c*, 3, $CHCl_3$). ^{13}C NMR data ($CDCl_3$): δ 139.2, 137.9, 137.7 (C-quat., arom.); δ 127.4–133.4 (C-arom.); δ 68.4, 70.5, 78.1, 83.9 (C-2, C-3, C-4, C-5); δ 73.0, 73.3, 74.4 (3 CH_2-benzyl); δ 71.0 (C-6); δ 21.6 (C-1); δ −1.9, −2.7 (2 × CH_3–Si). ^1H NMR data ($CDCl_3$): δ 7.1–7.6 (m, 20 H, H-arom.); δ 4.45–4.7 (m, 6H, CH_2-benzyl); δ 3.97–4.05, 3.4–3.7 (2 m, 6 H, H-2, H-3, H-4, H-5, H-6, H-6″); δ 1.08–1.17 (AB, 1 H, $J_{1,2}$ 9.9 Hz, $J_{1,1\#}$ 14.6 Hz, H-1); δ 0.95–1.02 (AB, 1 H, $J_{1\#,2}$ 4.5 Hz, $J_{1,1\#}$ 14.6 Hz, H-1); δ 0.30, 0.34 (2 s, 6 H, CH_3–Si). Anal. calcd. for $C_{35}H_{42}O_5Si$: C 73.65, H 7.42; found: C 73.76, H 7.59%.

2,3,4,5,6-Penta-O-benzyl-1-deoxy-1-(phenyldimethylsilyl)-L-glucitol (**25**)

Compound **24** (380 mg, 0.67 mmol) was dissolved in dry DMF (3 ml). To the cooled (0°C) solution was added tetrabutylammonium iodide (25 mg, 0.067 mmol), sodium hydride (40 mg, 1.67 mmol) and benzyl bromide (0.2 ml, 1.67 mmol). The mixture was stirred for 2 h at room temperature, at which time TLC analysis (System E) showed the reaction to be complete. The reaction mixture was quenched with methanol (0.5 ml), diluted with ethyl acetate (40 ml) and washed with water (2 × 25 ml). The organic layer was dried ($MgSO_4$), filtered and concentrated *in vacuo*. The residue was purified on silica gel (eluent: diethyl-ether/*n*-hexane, 1/3 to 1/2, v/v) to give **25** (530 mg, 100%); R_f 0.8 (System E). ^{13}C NMR data ($CDCl_3$): δ 138.9–139.1 (C-quat., arom.); δ 127.1–133.6 (C-arom.); δ 77.2, 79.0, 80.1, 81.4 (C-2, C-3, C-4, C-5); δ 70.3–74.4 (5 CH_2-benzyl, C-6); δ 18.2 (C-1); δ −1.6, −2.2 (2 CH_3–Si).

2,3,4,5,6-Penta-O-benzyl-L-glucitol (**26**)

Sodium acetate (656 mg, 8 mmol) and sodium bromide (82 mg, 0.8 mmol) were added to a solution of compound **25** (530 mg, 0.67 mmol) in acetic acid (3 ml). The mixture was cooled to 0°C and stirred under a nitrogen atmosphere with exclusion of light. To this mixture, peracetic acid (4.5 ml, 32% solution in dilute acetic acid) was added. After stirring for 1 h at 0°C, TLC analysis (System F) revealed the reaction to be complete. The mixture was diluted with dichloromethane (50 ml) and washed with 10% aq. $Na_2S_2O_3$ (2 × 25 ml) and water (2 × 25 ml). The organic layer was concentrated and the remaining oil was coevaporated with toluene (2 × 25 ml) and ethanol (25 ml). The residue was purified by silica gel column chromatography (eluent: diethyl-ether/*n*-hexane, 1/2 to 2/1, v/v) to give pure **26** (310 mg, 70%); R_f 0.3 (System F); $[\alpha]_D$ +0.5 (*c*, 3, $CHCl_3$). ^{13}C NMR data ($CDCl_3$): δ 138.1–138.5 (C-quat., arom.); δ 127.3–128.1 (C-arom.); δ 78.5–79.2 (C-2, C-3, C-4, C-5); δ 71.7–74.4 (5 CH_2-benzyl); δ 69.5 (C-6); δ 61.5 (C-1). ^1H NMR data ($CDCl_3$): δ 7.2–7.5 (m, 25 H, H-arom.); δ 4.4–4.8 (m, 10 H, 5 CH_2-benzyl); δ 3.4–4.0 (m, 8 H, 2 H-1, H-2, H-3, H-4, H-5, 2 H-6).

Penta-O-benzyl-aldehydo-*L-glucose* (**27**)

Dimethyl sulfoxide (1.92M in dichloromethane, 0.57 ml) was added to a cooled (−70°C) and stirred solution of oxalyl chloride (0.055 ml, 0.57 mmol) in dichloromethane (2 ml). After 5 min, a solution of compound **26** (280 mg, 0.42 mmol) in dichloromethane (2 ml) was added dropwise. After stirring for 30 min at −70°C, triethylamine (0.3 ml, 2.15 mmol) was added and the solution was allowed to warm-up to 20°C. The mixture was diluted with dichloromethane (50 ml), washed with water (2 × 25 ml), dried ($MgSO_4$) and concentrated *in vacuo*. The remaining oil was purified on silica gel (eluent: diethyl ether/*n*-hexane, 1/2 to 1/1, v/v) to yield pure **27** (200 mg, 70%) as an oil; R_f 0.7 (System G). ^{13}C NMR data ($CDCl_3$): δ 200.6 (C-1); δ 137.4–138.6 (C-quat., arom.); δ 127.6–128.4 (C-arom.); δ 77.3, 78.2, 80.1, 80.9 (C-2, C-3, C-4, C-5); δ 71.7–74.1 (5 CH_2-benzyl); δ 68.6 (C-6).

Penta-O-acetyl-L-glucopyranose (**28**)

Palladium on charcoal (200 mg) was added to a degassed solution of compound **27** (190 mg, 0.287 mmol) in ethanol/acetic-acid (9/1, v/v, 10 ml) and the mixture was stirred under a gentle stream of hydrogen. TLC analysis (System H, R_f 0.85), after 1 h at 50°C, revealed the reaction to be complete. The reaction mixture was degassed, filtered over Celite and concentrated. The residue was dissolved in acetic-anhydride/pyridine (1/1, v/v, 5 ml) and the solution was stirred for 1 h at room temperature, when TLC analysis (System F) showed the reaction to be complete. The reaction mixture was diluted with toluene (20 ml) and concentrated *in vacuo*. The residue was co-evaporated with toluene (3 × 20 ml) and ethyl alcohol (20 ml). The resulting oil was purified on silica gel (eluent: diethyl-ether/*n*-hexane, 2/1, v/v) to give **28** as a mixture of anomers (68 mg, 60%, α/β 4/5); R_f 0.5 (System F); $[\alpha]_D$ −54.5 (*c*, 1.1, $CHCl_3$). ^{13}C NMR data ($CDCl_3$): δ 91.27 (β-C-1); δ 88.65 (α-C-1). ^1H NMR data ($CDCl_3$): δ 6.32 (d, 1 H, $J_{1,2}$ 3.7 Hz, α-H-1); δ 5.72 (d, H, $J_{1,2}$ 8.2 Hz, β-H-1).

Penta-*O*-acetyl-β-D-glucopyranose. ^{13}C NMR data ($CDCl_3$): δ 91.36 (β-C-1). ^1H NMR data ($CDCl_3$): δ 5.71 (d, 1 H, $J_{1,2}$ 8.3 Hz, β-H-1); $[\alpha]_D$ +4 ($CHCl_3$); α-isomer: $[\alpha]_D$ +102 ($CHCl_3$).

Penta-*O*-acetyl-D-mannopyranose. ^{13}C NMR data ($CDCl_3$): δ 90.28, 90.14 (α,β-C-1). ^1H NMR data ($CDCl_3$): δ 6.09 (d, 1 H, $J_{1,2}$ 2.0 Hz, a-H-1); δ 5.87 (d, 1 H, $J_{1,2}$ 1.0 Hz, β-H-1); β-isomer: $[\alpha]_D$ −25.3 (*c*, 1, $CHCl_3$); α-isomer: $[\alpha]_D$ +55 (*c*, 1.1, $CHCl_3$). High-performance liquid chromatography: v_t D- or L-glucose (**1b**): 15.5 min; v_t D-mannose: 17.5 min.

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