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# THE KOENIGS–KNORR REACTION OF METHYL 4,6-*O*-BENZYLIDENE-β-D-GLUCOPYRANOSIDE WITH 2,3,4,6-TETRA-*O*-ACETYL-α-D-GLUCOPYRANOSYL BROMIDE

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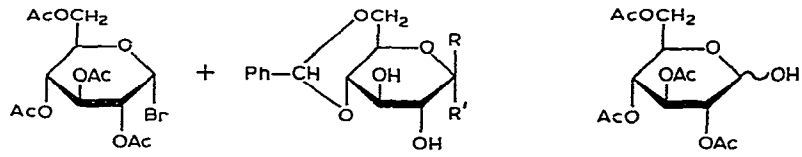
ABSTRACT

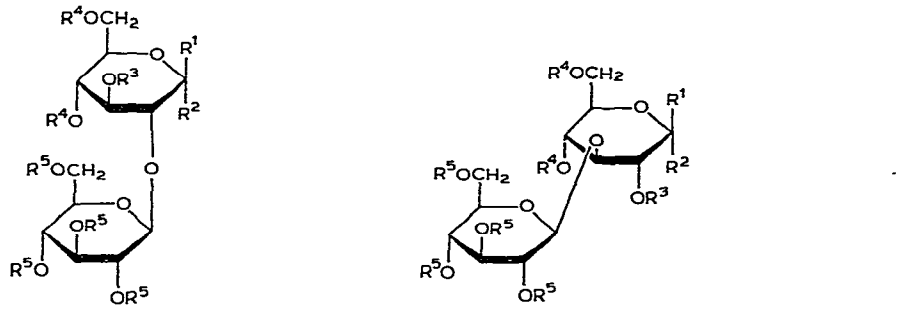
Condensation of methyl 4,6-*O*-benzylidene-β-D-glucopyranoside with 2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranosyl bromide in 1,1,2,2-tetrachloroethane in the presence of silver carbonate gave methyl 4,6-*O*-benzylidene-2-*O*- (**21**) and -3-*O*-(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl)-β-D-glucopyranoside (**24**), and a trisaccharide derivative, methyl *O*-(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl)-(1→3)-*O*-[2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl-(1→6)]-β-D-glucopyranoside (**28**). *O*-Deacetylation and removal of the benzylidene group of **21** and **24** gave methyl β-sophoroside and methyl β-laminarabioside, respectively. Compound **24** was found to be the precursor to **28**, and the mechanism leading to the formation of **28** is discussed.

## INTRODUCTION

In continuation of our studies on the chemistry of oligosaccharides[1,2], we were interested in the chemical modification of methyl 2-*O*-β-D-glucopyranosyl-α- (**6**) and -β-D-glucopyranoside (**7**) (methyl α- and β-sophorosides) and of methyl 3-*O*-β-D-glucopyranosyl-α- (**15**) and -β-D-glucopyranoside (**16**) (methyl α- and β-laminarabiosides). Since 2-*O*-β-D-glucopyranosyl-D-glucose (sophorose, **8**) and 3-*O*-β-D-glucopyranosyl-D-glucose (laminarabiose, **17**) are relatively inaccessible disaccharides, the preparation of the methyl glycosides starting from **8** and **17** is not practical. Recently, we reported[3] a convenient synthesis of **17** and some of its glycosides including **15** and **16**. Compound **6** is readily prepared by the Koenigs–Knorr condensation of 2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranosyl bromide (**1**) with methyl 4,6-*O*-benzylidene-α-D-glucopyranoside (**2**), followed by removal of the protecting groups[4,5]. In an attempt to synthesize **7**, methanolysis of the bromide[4,5] **9** having a nonparticipating β-D-glucopyranosyl group at C-2 resulted in the formation of a mixture of the methyl α- and β-glycosides **10** and **11**. The previous report[6] that the condensation of **1** with *p*-nitrophenyl 4,6-*O*-benzylidene-β-D-glucopyranoside (**3**) yields, after removal of the protecting groups, approximately equivalent amounts of *p*-nitrophenyl 3-*O*-(**12**) and 3-*O*-β-D-glucopyranosyl-β-D-glucopyranoside (**18**) suggested that, under comparable conditions, a similar reaction might prevail on condensing **1** with methyl 4,6-*O*-benzylidene-β-D-glucopyranoside (**4**). Thus, the desired **7** as well as **16** might



1 2 R = H, R′ = OMe; 3 R = $OC_6H_4NO_2$ (p), R′ = H; 4 R = OMe, R′ = H 5



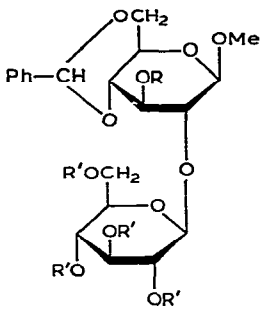
6 $R^1 = R^3 = R^4 = R^5 = H, R^2 = OMe$
7 $R^1 = OMe, R^2 = R^3 = R^4 = R^5 = H$
8 $R^1, R^2 = H, OH, R^3 = R^4 = R^5 = H$
9 $R^1 = H, R^2 = Br, R^3 = R^4 = R^5 = Ac$
10 $R^1 = H, R^2 = OMe, R^3 = R^4 = R^5 = Ac$
11 $R^1 = OMe, R^2 = H, R^3 = R^4 = R^5 = Ac$
12 $R^1 = OC_6H_4NO_2(p), R^2 = R^3 = R^4 = R^5 = H$
13 $R^1 = OMe, R^2 = R^3 = R^4 = H, R^5 = Ac$
14 $R^1 = OMe, R^2 = R^4 = H, R^3 = R^5 = Ac$

15 $R^1 = R^3 = R^4 = R^5 = H, R^2 = OMe$
16 $R^1 = OMe, R^2 = R^3 = R^4 = R^5 = H$
17 $R^1, R^2 = H, OH, R^3 = R^4 = R^5 = H$
18 $R^1 = OC_6H_4NO_2(p), R^2 = R^3 = R^4 = R^5 = H$
19 $R^1 = OMe, R^2 = R^3 = R^4 = H, R^5 = Ac$
20 $R^1 = OMe, R^2 = R^4 = H, R^3 = R^5 = Ac$

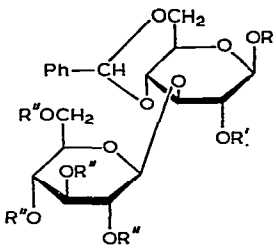
be straightforwardly obtained after appropriate deblocking, and this prompted us to investigate the reaction of **1** with **4** under the classical Koenigs–Knorr conditions using silver carbonate as the acid acceptor[7].

## RESULTS AND DISCUSSION

Because **4** is sparingly soluble in such solvents as acetonitrile, benzene, chloroform, dichloromethane, and nitromethane that are commonly used in the Koenigs–Knorr condensation[8], alternative solvents were examined. Compound **4** is soluble in acetone, 1,4-dioxane, *N*,*N*-dimethylformamide, and tetrahydrofuran; however, an attempt to condense **1** with **4** in each of these solvents, in the presence of silver carbonate and Drierite, showed sluggish reactions, and led to decomposition of **1**.



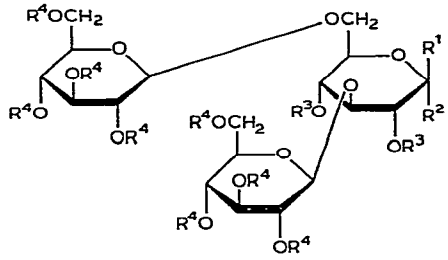
21 R = H, R′ = Ac
22 R = R′ = H
23 R = R′ = Ac



24 R = Me, R′ = H, R″ = Ac
25 R = Me, R′ = R″ = H
26 R = Me, R′ = R″ = Ac
27 R = $CH_2Ph$, R′ = H, R″ = Ac

Subsequently, it was found that 1,1,2,2-tetrachloroethane, in which **4** is moderately soluble (~1 g/40 ml at 30°), was an effective solvent for the condensation.

Treatment of **4** with 1.1 mol. equiv. of **1** in 1,1,2,2-tetrachloroethane at 30°, in the presence of silver carbonate and Drierite, gave a mixture showing five well-defined spots in t.l.c. The second-fastest-moving was identified as 2,3,4,6-tetra-*O*-acetyl-D-glucopyranose (**5**), which arose from the hydrolysis of **1**, and the slowest as unreacted **4**. Extraction of the reaction mixture with boiling water removed most of **4** and **5**, and the resulting residue was fractionated on a column of silica gel. The first-eluted component (obtained in crystalline form in 17% yield) was shown to be methyl 4,6-*O*-benzylidene-2-*O*-(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl)-β-D-glucopyranoside (**21**) by *O*-deacetylation of **21** to give crystalline **22**, which on treatment with hot, aqueous acetic acid to remove the benzylidene group afforded known[9] **7**. The second component to be eluted from the column was residual **5**. The third component to be eluted (obtained as an amorphous powder in 16% yield) was methyl 4,6-*O*-benzylidene-3-*O*-(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl)-β-D-glucopyranoside (**24**), as shown by *O*-deacetylation to give crystalline methyl 4,6-*O*-benzylidene-3-*O*-β-D-glucopyranosyl-β-D-glucopyranoside (**25**) which was debenzylidenated into the known[10] **16**. The fourth component eluted from the column was residual **4**. To the component of lowest mobility, obtained in crystalline form in 7% yield, was assigned the structure methyl *O*-(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl)-(1→3)-*O*-[2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl-(1→6)]-β-D-glucopyranoside (**28**) on the basis of the following observations: The n.m.r. spectrum of **28** in chloroform-*d* showed a 3-proton singlet at δ 3.55 for a methoxyl group and overlapping singlets at δ 2.08–1.98 for acetyl groups, and the absence of signals due to the benzylidene group. The ratio of the intensity of acetyl to methyl protons in the n.m.r. spectrum, combined with the results of the elemental analysis, suggested an octa-*O*-acetylated trisaccharide having two free hydroxyl groups. Acetylation of **28** gave the crystalline deca-*O*-acetyl derivative **29**. To determine the position of the free hydroxyl groups, **28** was methylated with diazomethane–boron trifluoride



28 $R^1$ = OMe, $R^2$ = $R^3$ = H, $R^4$ = Ac
29 $R^1$ = OMe, $R^2$ = H, $R^3$ = $R^4$ = Ac
30 $R^1$ = OMe, $R^2$ = H, $R^3$ = Me, $R^4$ = Ac
31 $R^1$ = OMe, $R^2$ = $R^3$ = $R^4$ = H
32 $R^1$, $R^2$ = H, OH, $R^3$ = $R^4$ = OH

etherate[11] to give the octa-*O*-acetyl-di-*O*-methyl derivative **30**. G.l.c. examination of the methanolyzate of **30** as *O*-trimethylsilyl derivatives showed the presence of methyl α,β-D-glucopyranoside and a methyl di-*O*-methyl-D-glucopyranoside in a ratio of 2:1. Successive *O*-deacetylation of **30**, hydrolysis, reduction with sodium borohydride, and acetylation gave a 1:2 mixture of the peracetates of 2,4-di-*O*-methyl-D-glucitol and D-glucitol (g.l.c.). These data indicate that the free hydroxyl groups in **28** are located at C-2 and -4, and that **28** is a branched trisaccharide derivative containing (1→3)- and (1→6)-interglycosidic linkages. *O*-Deacetylation of **28** afforded the crystalline free sugar **31**, which on partial acid hydrolysis gave a mixture, in which **17** and gentiobiose were identified by p.c., confirming the interglycosidic linkages in **28**. The n.m.r. spectrum of **31** in deuterium oxide showed three 1-proton doublets at δ 4.72 (*J* 7.5 Hz), 4.51 (*J* 7.5 Hz), and 4.42 (*J* 8.0 Hz), which were assigned to one anomeric and two inter-sugar anomeric protons, but they could not be differentiated. The magnitude of the coupling constants of the inter-sugar anomeric protons indicated β-D-(1→3)- and β-D-(1→6)-linkages.

Condensation of **4** with 2.2 mol. equiv. of **1** under the aforementioned conditions, followed by the same procedure described earlier to remove **4** and **5** and fractionation of the resulting residue by column chromatography, gave **21**, **24**, and **28** in 30%, 19%, and 13% yield, respectively. Thus, the use of 2.2 mol. equiv. of **1** in the reaction with **4** led to an about two-fold increase in the yield of **21** and **28**, and a slight increase in the yield of **24**, as compared to the reaction of **4** with 1.1 mol. equiv. of **1**.

Removal of the benzylidene group of **21** and **24** afforded crystalline methyl 2-*O*- (**13**) and 3-*O*-(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl)-β-D-glucopyranoside (**19**), respectively. Acetylation of **21** and **24** gave the crystalline 3- (**23**) and 2-*O*-acetyl (**26**) derivatives, respectively, which were debenzylidenated into crystalline 3,2′,3′,4′,6′- (**14**) and 2,2′,3′,4′,6′-penta-*O*-acetyl derivatives (**20**), respectively. In a simplified synthesis of **21** and **26**, the product obtained by treatment of **4** with 2.2 mol. equiv. of **1** was extracted with boiling water, and the residue gave a crystalline

mixture of **21** and **28**. Attempts to separate the mixture by fractional crystallization failed, because **21** and **28** have a strong tendency to co-crystallize. Chromatographic fractionation of the mixture readily furnished **21** in 28% yield. The mother liquor from **21** and **28** was acetylated to give **26** in 16% yield. Compounds **13**, **14**, **21**, and **23**, and **19**, **20**, **24**, and **26** are useful intermediates for the introduction of a wide range of functional groups into a specific position of **7** and **16**, respectively.

The formation of a trisaccharide derivative in the condensation of **1** with **3** was not reported earlier[6]. However, Klemer and Homberg[12] observed that treatment of **1** with benzyl 4,6-*O*-benzylidene-β-D-glucopyranoside in the presence of silver oxide, followed by deblocking reactions, gives a trisaccharide, 3,6-di-*O*-(β-D-glucopyranosyl)-D-glucopyranose (**32**) besides **8** and **17**. The formation of the derivative of **32** was explained by a migration of the benzylidene acetal group from O-4,6 to O-2,4 in **27** to form a trisaccharide intermediate in $^1C_4$ conformation, which in turn was transformed into the derivative of **32** in $^4C_1$ conformation[12]. Since no formation of a trisaccharide was observed[4,5] in the reaction between the corresponding α-D anomer **2** with **1**, it is possible that, in the β-D series, the $^4C_1$ conformation is somewhat destabilized due to the anomeric effects which increase the relative stability of the $^1C_4$ conformation, necessary for the formation of the product of migration[13]. Indeed, the absence of trisaccharide derivative among the products obtained by the reaction between **1** and **2** was demonstrated[14]. The yields of **21**, **24**, and **28** (obtained by treatment of **4** with 1.1 or 2.2 mol. equiv. of **1**) suggest that, once formed, **24** could be transformed into **28** on further treatment with **1**. Thus, treatment of **24** with 1.2 mol. equiv. of **1** gave **28** in 35% yield, whereas **26** did not react under the same conditions. In the former experiment, no debenzylidenation of **24** to **19** was observed. This result demonstrates that **24**, and not **19**, was the precursor to **28**, in agreement with the suggestion of Klemer and Homberg[12]. No intermediate having a trisaccharide structure leading to **28** was detected by monitoring with t.l.c. the reaction between **1** and **4** or **24**. However, the observation that no debenzylidenation of **24** occurred during the reaction and that the presence of free OH-2 in **24** was essential for the production of **28** suggests that a synchronous mechanism similar to that proposed[12] for the reaction between **1** and **27** was also present for the reaction between **1** and **24**. It had been assumed[12] that the 2,4-*O*-benzylidene group in the trisaccharide derivative of **32** was cleaved during partial hydrogenolysis of the reaction product under controlled conditions to remove the aglycone residue. The absence of a benzylidene group in **28** was indicated, however, by n.m.r. spectroscopy. Therefore, it may be assumed that consecutive liberation of hydrogen bromide and water during the reaction cleaved, even in the presence of Drierite, the unstable benzylidene group to give a trisaccharide intermediate in the energetically unfavorable $^1C_4$ conformation, which in turn gave **28** in $^4C_1$ conformation.

## EXPERIMENTAL

*General methods.* — Melting points were determined with a Yanagimoto hot-

stage microscope and are uncorrected. Optical rotations were measured with an Ohyo Denki automatic polarimeter, Model MP-1T. N.m.r. spectra were recorded with a Varian A-60A spectrometer; tetramethylsilane (in chloroform-*d* and dimethyl sulfoxide-$d_6$) and 2,2-dimethyl-2-silapentane-5-sulfonate (in deuterium oxide) were the internal standards. Gas-liquid chromatography was performed with a Hitachi gas chromatogram 063 using the following columns: (*A*) 5% silicone SE-30 on 80–100 mesh Chromosorb W (operating temperature 170°) and (*B*) 3% ECNSS-M on 100–120 mesh Gas-Chrom Q (operating temperature 180°), with nitrogen as carrier gas at a flow rate of 60 ml/min. Retention times are quoted relative to methyl β-D-glucopyranoside for methyl glycosides, and to 1,5-di-*O*-acetyl-2,3,4,6-tetra-*O*-methyl-D-glucitol for *O*-acetyl-*O*-methyl alditols. T.l.c. was performed on Silica gel No 7731 (Merck); spots were detected by spraying the plates with 5% sulfuric acid in ethanol, followed by heating. Column chromatography was performed on Silica gel No 7734 (Merck) in the following solvent systems (v/v): (*A*) 3:2, (*B*) 1:1, and (*C*) 2:1 ethyl acetate–benzene. Descending paper chromatography was performed on Whatman No 1 paper in 4:1:5 (v/v) 1-butanol–ethanol–water (upper phase), and detection with aniline hydrogen phthalate. Unless otherwise stated, solutions were evaporated at a temperature <40° under reduced pressure.

*Condensation of methyl 4,6-O-benzylidene-β-D-glucopyranoside* (**4**) *with 1.1 mol. equiv. of 2,3,4,6-tetra-O-acetyl-α-D-glucopyranosyl bromide* (**1**). — Compound **4** (5 g) was dissolved by heating in anhydrous 1,1,2,2-tetrachloroethane (200 mL), and the solution was cooled to 30°. Dry silver carbonate (7 g) and ground Drierite (15 g) were added, and the mixture was stirred for 2 h at 30° in the dark with exclusion of moisture. Iodine (1 g) and **1** (8.01 g, 1.1 mol. equiv.) were added, and stirring was continued for 30 h at 30°, when t.l.c. (solvent *A*) showed the presence of five spots having $R_F$ values of 0.59 (**21**), 0.50 (**5**), 0.41 (**24**), 0.25 (**4**), and 0.13 (**28**), respectively. The reaction mixture was filtered through a bed of Celite, and the inorganic solids were washed extensively with chloroform. The combined filtrate and washings were evaporated, and the remaining solvent was coevaporated with water *in vacuo* at 80° to give a syrup, which was extracted with boiling water (2 × 200 mL) to remove **4** and **5**. The resulting residue was fractionated on a column of silica gel (400 g) with solvent *B*. The first fraction gave methyl 4,6-*O*-benzylidene-2-*O*-(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl)-β-D-glucopyranoside (**21**) (1.84 g, 17%), m.p. 194–195° (ethanol), $[\alpha]_D^{24}$ −29.7° (*c* 1.5, chloroform); n.m.r. (dimethyl sulfoxide-$d_6$): δ 5.58 (s, 1 H, benzylic-H), 5.35 (d, 1 H, $J_{3,OH-3}$ 5.0 Hz, exchangeable with $D_2O$, OH-3), 3.42 (s, 3 H, OMe), 1.97, 1.96, 1.92, and 1.91 (s, each 3 H, 4 OAc).

*Anal.* Calc. for $C_{28}H_{36}O_{15}$: C, 54.90; H, 5.92. Found: 54.78; H, 6.01.

The second fraction afforded residual **5** and was not collected.

The third fraction gave methyl 4,6-*O*-benzylidene-3-*O*-(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl)-β-D-glucopyranoside (**24**) as an amorphous powder (1.73 g, 16%), $[\alpha]_D^{24}$ −30.7° (*c* 2.5, chloroform); n.m.r. (dimethyl sulfoxide-$d_6$): δ 5.62 (s, 1 H, benzylic-H), 5.43 (d, 1 H, $J_{2,OH-2}$ 5.0 Hz, exchangeable with $D_2O$, OH-2), 3.43 (s, 3 H, OMe), 2.02 (s, 3 H, OAc), 1.98 (s, 6 H, 2 OAc), and 1.93 (s, 3 H, OAc).

*Anal.* Calc. for $C_{28}H_{36}O_{15}$: C, 54.90; H, 5.92. Found: C, 54.82; H, 5.81.

The fourth fraction gave residual **4** and was not collected.

The fifth fraction afforded methyl *O*-(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl)-(1→3)-*O*-[2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl-(1→6)]-β-D-glucopyranoside (**28**) (1.05 g, 7%), m.p. 226–228° (ethanol), $[\alpha]_D^{24}$ −13.3° (*c* 2.0, chloroform).

*Anal.* Calc. for $C_{35}H_{50}O_{24}$: C, 49.18; H, 5.90. Found: C, 49.31; H, 5.78.

*Methyl 4,6-O-benzylidene-2-O-β-D-glucopyranosyl-β-D-glucopyranoside* (**22**). — A solution of **21** (1.5 g) in anhydrous methanol (20 mL) was treated with methanolic 0.5M sodium methoxide (1 mL). The solution was stirred for 1 h at room temperature, neutralized with Amberlite IR-120 ($H^+$) cation-exchange resin, filtered, and evaporated to give a crystalline mass, which on recrystallization from ethanol gave **22** (992 mg, 91%), m.p. 217–218°, $[\alpha]_D^{24}$ −77.2° (*c* 1.3, pyridine); n.m.r. (dimethyl sulfoxide-$d_6$): δ 5.60 (s 1 H, benzylic H).

*Anal.* Calc. for $C_{20}H_{28}O_{11}$: C, 54.05; H, 6.35. Found: C, 53.90; H, 6.28.

*Methyl 2-O-β-D-glucopyranosyl-β-D-glucopyranoside* (**7**). — A solution of **22** (800 mg) in acetic acid (8 mL) was heated to 100°, water (5.3 mL) was added in small portions within a few min, and the mixture was kept for 15 min at 100°. The solvents were evaporated and the last traces of volatile compounds were removed by repeated codistillation with toluene to give a solid, which was recrystallized from ethanol to afford **7** (558 mg, 87%), m.p. 195–196°, $[\alpha]_D^{24}$ −38.4° (*c* 1.5, water); lit.[9] m.p. 194.5–195.5° (95% ethanol), $[\alpha]_D^{27}$ −36.03° (*c* 1.693, water).

*Methyl 4,6-O-benzylidene-3-O-β-D-glucopyranosyl-β-D-glucopyranoside* (**25**). — *O*-Deacetylation of **24** (1.5 g), as described for **21**, gave **25** (1.01 g, 93%), m.p. 240–242° (methanol), $[\alpha]_D^{24}$ −75.2° (*c* 1.7, pyridine); n.m.r. (dimethyl sulfoxide-$d_6$): δ 5.60 (s, 1 H, benzylic-H).

*Anal.* Calc. for $C_{20}H_{28}O_{11}$: C, 54.05; H, 6.35. Found: C, 54.14; H, 6.39.

*Methyl 3-O-β-D-glucopyranosyl-β-D-glucopyranoside* (**16**). — Treatment of **25** (800 mg) in acetic acid (8 mL) with water (5.3 mL) at 100°, as described for **22**, afforded **16** (583 mg, 91%), m.p. 164–165° (ethanol–ether), $[\alpha]_D^{24}$ −28.5° (*c* 1.5, water); lit.[10] m.p. 165–166° (ethanol–ether), $[\alpha]_D^{19}$ −28° (*c* 2.5, water).

*Methyl 2,4-di-O-acetyl-O-(2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyl)-(1→3)-O-[2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyl)-(1→6)]-β-D-glucopyranoside* (**29**). — Conventional acetylation of **28** (100 mg) with 1:1 (v/v) pyridine–acetic anhydride (1 mL) overnight at room temperature, and isolation in the usual way gave **29** (86 mg, 78%), m.p. 231–232° (ethanol), $[\alpha]_D^{24}$ −40.0° (*c* 1.3, chloroform); n.m.r. (chloroform-*d*): δ 3.45 (s, 3 H, OMe) and 2.13–1.97 (overlapping singlets, 30 H, 10 OAc).

*Anal.* Calc. for $C_{39}H_{54}O_{26}$: C, 49.89; H, 5.80. Found: C, 49.76; H, 5.85.

*Methyl 2,4-di-O-methyl-O-(2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyl)-(1→3)-O-[2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyl-(1→6)]-β-D-glucopyranoside* (**30**). — To a solution of **28** (500 mg) in dry dichloromethane (5 mL) maintained at −5° was added boron trifluoride–etherate (0.05 mL), followed by a solution of diazomethane in dichloromethane until a faint yellow color persisted. The mixture was kept for 1 h at room temperature, polymethylene was filtered off, and the solution was washed

successively with water, aqueous sodium hydrogencarbonate and water, dried ($Na_2SO_4$), and evaporated. Crystallization of the residue from ethanol gave **30** (428 mg, 83%), m.p. 139–150° (broad), $[\alpha]_D^{24}$ −24.5° (*c* 2.7, chloroform); n.m.r. (chloroform-*d*): δ 3.48 (s, 6 H, 2 OMe), 3.52 (s, 3 H, OMe), and 2.08–1.90 (overlapping singlets, 24 H, 8 OAc).

*Anal.* Calc. for $C_{37}H_{54}O_{24}$: C, 50.34; H, 6.17. Found: C, 50.21; H, 6.29.

Methanolysis of a portion of **30**, followed by *O*-trimethylsilylation of the product gave compounds that had the retention times of methyl 2,4-di-*O*-methyl-D-glucoside (*T* 0.34, 33%) and methyl D-glucosides (*T* 0.91 and 1.00, 66%) on column *A*. *O*-Deacetylation of a portion of **30**, followed by hydrolysis, reduction with sodium borohydride, and acetylation gave compounds that had the retention times of the peracetates of 2,4-di-*O*-methyl-D-glucitol (*T* 5.10, 33%) and D-glucitol (*T* 10.53, 66%) on column *B*.

*Methyl* O-*β*-D-*glucopyranosyl*-(*1*→*3*)-O-[*β*-D-*glucopyranosyl*-(*1*→*6*)]-*β*-D-*glucopyranoside* (**31**). — *O*-Deacetylation of **28** (411 mg), as described for the preparation of **22**, gave **31** (219 mg, 90%), m.p. 144–146° (ethanol), $[\alpha]_D^{24}$ −38.4° (*c* 1.7, water).

*Anal.* Calc. for $C_{19}H_{34}O_{16}$: C, 44.02; H, 6.51. Found: C, 44.15; H, 6.63.

A solution of **31** (20 mg) in 25mM sulfuric acid (2 mL) was heated for 8 h at 100°, neutralized with barium carbonate, filtered, and evaporated to a syrup, in which **17** ($R_{Glc}$ 0.64) and gentiobiose ($R_{Glc}$ 0.27) were identified by p.c.

*Methyl* 2-O-(*2,3,4,6-tetra*-O-*acetyl*-*β*-D-*glucopyranosyl*)-*β*-D-*glucopyranoside* (**13**). — Treatment of **21** (600 mg) in acetic acid (6 mL) with water (3.75 mL) at 100°, as described for **22**, afforded **13** (427 mg, 83%), m.p. 153–154° (ether–benzene–methanol), $[\alpha]_D^{24}$ −11.0° (*c* 2.4, chloroform); n.m.r. (chloroform-*d*); δ 2.08, 2.07, 2.04, and 2.01 (s, each 3 H, 4 OAc).

*Anal.* Calc. for $C_{21}H_{32}O_{15}$: C, 48.09; H, 6.15. Found: C, 48.15; H, 6.22.

*Methyl* 3-O-(*2,3,4,6-tetra*-O-*acetyl*-*β*-D-*glucopyranosyl*)-*β*-D-*glucopyranoside* (**19**). — Treatment of **24** (420 mg) in acetic acid (4 mL) with water (2.7 mL) at 100°, as described for **22**, gave **19** (330 mg, 92%) as an amorphous powder, $[\alpha]_D^{24}$ +2.3° (*c* 1.8, chloroform); n.m.r. (chloroform-*d*): δ 2.09, 2.05, 2.03, and 2.00 (s, each 3 H, 4 OAc).

*Anal.* Calc. for $C_{21}H_{32}O_{15}$: C, 48.09; H, 6.15. Found: C, 48.19; H, 6.23.

*Methyl* 3-O-*acetyl*-4,6-O-*benzylidene*-2-O-(*2,3,4,6-tetra*-O-*acetyl*-*β*-D-*glucopyranosyl*)-*β*-D-*glucopyranoside* (**23**). — Conventional acetylation of **21** (1.7 g) with 1:1 (v/v) acetic anhydride–pyridine (16 mL) overnight at room temperature gave **23** (1.63 g, 90%), m.p. 195–196° (ethanol), $[\alpha]_D^{24}$ −46.1° (*c* 1.6, chloroform).

*Anal.* Calc. for $C_{30}H_{38}O_{16}$: C, 55.04; H, 5.85. Found: C, 55.11; H, 5.80.

*Methyl* 2-O-*acetyl*-4,6-O-*benzylidene*-3-O-(*2,3,4,6-tetra*-O-*acetyl*-*β*-D-*glucopyranosyl*)-*β*-D-*glucopyranoside* (**26**). — Acetylation of **24** (1 g) with 1:1 (v/v) acetic anhydride–pyridine (10 mL) afforded **26** (983 mg, 92%), m.p. 228–229° (ethanol), $[\alpha]_D^{24}$ −67.9° (*c* 1.3, chloroform).

*Anal.* Calc. for $C_{30}H_{38}O_{16}$: C, 55.04; H, 5.85. Found: 54.96; H, 5.87.

*Methyl* 3-O-*acetyl*-2-O-(*2,3,4,6-tetra*-O-*acetyl*-*β*-D-*glucopyranosyl*)-*β*-D-*gluco*-

*pyranoside* (**14**). — Treatment of **23** (1 g) in acetic acid (10 mL) with water (6.3 mL) at 100°, as just described, gave **14** (780 mg, 90%), m.p. 136–137° (ethanol–ether), $[\alpha]_D^{24}$ −18.5° (*c* 1.5, chloroform).

*Anal.* Calc. for $C_{23}H_{34}O_{16}$: C, 48.76; H, 6.05. Found: C, 48.70; H, 6.11.

*Methyl 2-O-acetyl-3-O-(2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyl)-β-D-glucopyranoside* (**20**). — Treatment of **26** (600 mg) in acetic acid (6 mL) with water (3.7 mL), as just described, gave **20** (478 mg, 92%), m.p. 185–187° (ethanol), $[\alpha]_D^{24}$ −34.9° (*c* 1.5, chloroform).

*Anal.* Calc. for $C_{23}H_{34}O_{16}$: C, 48.76; H, 6.05. Found: C, 48.69; H, 6.15.

*Condensation of* **4** *with 2.2 mol. equiv. of* **1**. — (*a*). Treatment of **4** (5 g) with **1** (16.02 g, 2.2 mol. equiv.) in 1,1,2,2-tetrachloroethane (200 mL) for 30 h at 30°, in the presence of silver carbonate (14 g), Drierite (20 g), and iodine (1 g), followed by processing as just described earlier, gave a syrupy product, which was extracted with boiling water (3 × 200 mL). The resulting residue was eluted from a column of silica gel (400 g) with solvent *B* to give **21** (3.29 g, 30%), **24** (2.11 g, 19%), and **28** (1.97 g, 13%).

(*b*). The product obtained by condensation of **4** (5 g) with **1** (16.02 g), under the same conditions as in (*a*), was extracted with boiling water, and the residue was crystallized from ethanol to give a crystalline mixture of **21** and **28**, which on fractionation on a column of silica gel (100 g) with solvent *C* afforded **21** (3.06 g, 28%), m.p. and mixed m.p. 194–195°, $[\alpha]_D^{24}$ −29.8° (*c* 2.0, chloroform). Compound **28** was not isolated. The mother liquor from **21** and **28** was evaporated to a syrup, which was acetylated with 1:1 (v/v) acetic anhydride–pyridine (30 mL) overnight at room temperature. After isolation in the usual way, the resulting solid was crystallized three times from ethanol to give **26** (1.9 g, 16%), m.p. and mixed m.p. 228–229°, $[\alpha]_D^{24}$ −68.0° (*c* 2.0, chloroform).

*Condensation of* **24** *with 1.2 mol. equiv. of* **1**. — A mixture of **24** (200 mg), silver carbonate (280 mg), and Drierite (600 mg) in 1,1,2,2-tetrachloroethane (5 mL) was stirred for 2 h at 30°, and iodine (30 mg) and **1** (161 mg, 1.2 mol. equiv.) were added. Stirring was continued for 20 h at 30°, and the mixture was processed as described earlier. The resulting syrupy residue was extracted with boiling water (2 × 5 mL), and the residue was eluted from a column of silica gel (30 g) with solvent *B* to give starting material **24** (128 mg), $[\alpha]_D^{24}$ −30.5° (*c* 0.8, chloroform) and **28** (77 mg, 35%), m.p. and mixed m.p. 226–228°, $[\alpha]_D^{24}$ −13.2° (*c* 0.8, chloroform).

*Treatment of* **26** *with 1.2 mol. equiv. of* **1**. — Compound **26** (100 mg) was treated with **1** (81 mg, 1.2 mol. equiv.) in 1,1,2,2-tetrachloroethane (3 mL) for 20 h at 30°, in the presence of silver carbonate (100 mg), Drierite (300 mg), and iodine (20 mg), as just described, after which t.l.c. (solvent *A*) indicated that **26** had not reacted.

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