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An expedient route to acylated glucosyl halides with a free 2-OH group

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Abstract

The carbonyl group of 3,4,6-tri-*O*-benzoyl-α-D-*arabino*-hexosyl-2-ulose bromide (**8**), readily accessible from the hydroxyglycal ester, can be reduced by cyanoborohydride without affecting the anomeric bromine; exclusive axial attack of the hydride affords the benzoylated glucosyl bromide **6** with a free 2-OH group (72%). This amounts to a five-step synthesis from D-glucose, free from chromatography, in 55% overall yield. Bromide **6**, or the more reactive α-iodide **7**, smoothly generated from **6** by halogen exchange, readily undergoes α- or β-selective glycosidations, emphasizing their potential as glycosyl donors for the generation of (1 → 2)-linked oligosaccharides.

1. Introduction

Aside from D-*gluco*-oligosaccharides with an α-(1 → 2)-connection [1], glucosides with further sugar residues at O-2 have increasingly been uncovered in Nature, as, for example, in saponins [2], flavonoids [3], antibiotics [4], teichoic acids [5], and lipopolysaccharides [6]. Suitable glucosyl donors for their synthesis have to carry either an O-2 protecting group which can be selectively removed after glycosidation or, alternatively, have a free 2-OH function from the beginning. The former approach has repeatedly been pursued for the generation of β-D-mannosides [7]; the latter alternative, using 3,4,6-*O*-blocked glucosyl halides, has hardly been followed, despite the fact that six compounds of this type, **1**–**6**, have been reported [8–12]. Reasons for this are undoubtedly the rather modest yields (24–40%) obtained in glycosylations by **1** [11a,13], and the fact that only two of these glucosyl halides are reasonably accessible, namely, **1** (28% in 3 steps from D-glucose [8]) and **4** (38% over 7 steps [9]). The availability of the others, particularly the anomerically more reactive α-bromides **5** and **6**, leaves much to be

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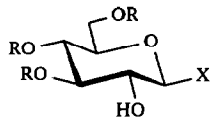
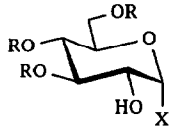
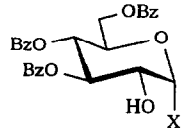
desired. The triacetate **5**, although preparable from D-glucose in two steps (25% overall yield [11a]), could be characterized only as a rapidly degrading syrup, whereas access to the tribenzoate **6**, albeit crystalline and stable, required six steps from D-glucose with a 10% overall yield [12].



	R	X
1	Ac	Cl
2	Bn	F



	R	X
3	Ac	Cl
4	Bn	Cl
5	Ac	Br



6 X = Br
7 X = I

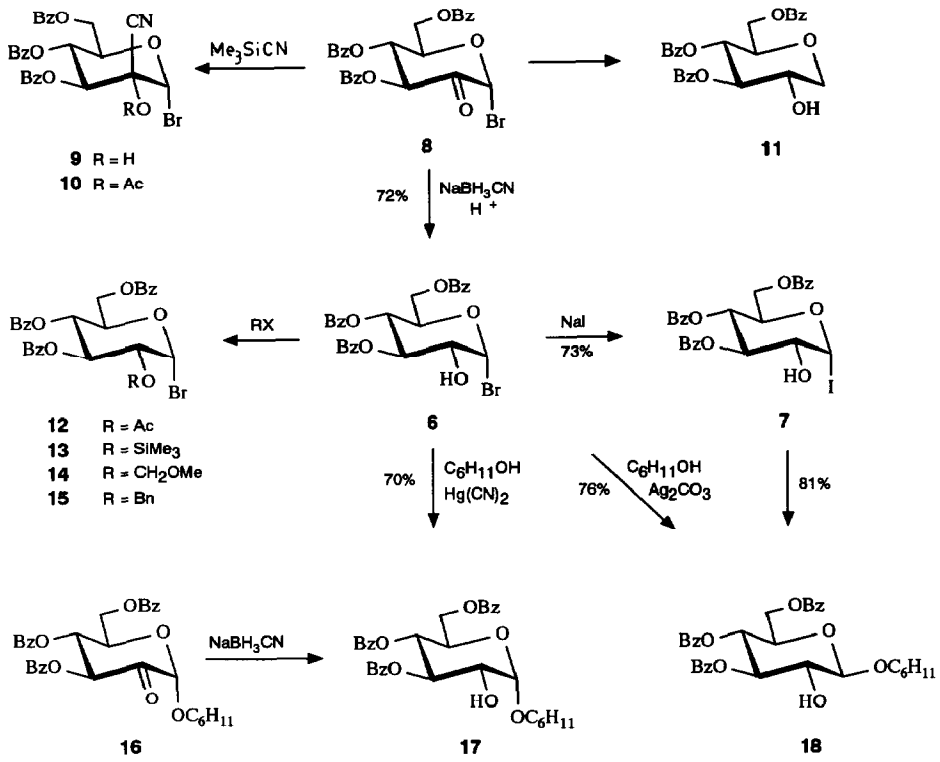
We report here a novel approach to the 3,4,6-tri-*O*-benzoyl-α-D-glucosyl bromide (**6**) and iodide (**7**), entailing five and six steps, respectively, from D-glucose in overall yields of over 50%, and provide evidence for their suitability for α- and β-selective glycosylations.

2. Results and discussion

Glycosyl-2-ulose bromides of type **8** have recently become easily accessible, requiring only a four-step sequence from the parent mono- and di-saccharides and allowing overall yields in the 60% range [14,15]. They are shelf-stable, crystalline substances of comparatively low anomeric reactivity, relative to benzobromoglucose for example, as shown by their recovery from a methanol solution at ambient temperature, methanolysis occurring only on heating.

The low anomeric reactivity of acylated glycosylulose bromides is also evident in the addition of cyanide and of hydride to the carbonyl group, both being feasible, under the appropriate conditions, with retention of the bromine. Accordingly, exposure of **8** to cyanation with BF_3–trimethylsilyl cyanide in nitromethane led in an instantaneous reaction to the cyanohydrin **9** (Scheme 1), isolable in crystalline form in 87% yield; its acetate **10** proved to be a suitable substrate for the anomeric C-homologation, silver triflate-promoted reaction with the trimethylsilyl enol ether of acetophenone cleanly affording the corresponding β-glucosylacetophenone [16]. The configuration at the tertiary C-2 of **9** was inferred by analogy. Hydride addition to the carbonyl group of **8** proceeds from the β-side with high selectivity to give the glucosyl bromide **6** (vide infra), whose configuration was readily proved by ^1H NMR. Attack of the more bulky cyanide would certainly not be expected to occur from the α-side, i.e., the side of the anomeric bromine, but should follow an analogous steric course.

Acid-catalyzed cyanoborohydride reduction [17], when applied to **8** in dioxane solution, resulted in an essentially stereospecific hydride addition from the side opposite to the anomeric substituent, to give the glucosyl bromide **6** in 72% yield (Scheme 1). With $TiCl_4$ as the catalyst, the reaction was complete within 5 min; a



Scheme 1.

strongly acidic ion-exchanger required 12 h but workup was simpler. Only on longer reaction times, with excess of reductant, and, increasingly, in dichloromethane as the solvent, both hydride addition and reductive debromination occurred, to afford the 3,4,6-tribenzoate of 1,5-anhydro-D-glucitol (**11**), isolable in 60% yield.

The 2-OH group in **6** may be protected without affecting the anomeric bromine, e.g., acetylation (→ **12**, 69%), silylation (→ **13**, 78%), and methoxymethylation (→ **14**, 73%) yield the respective 2-*O* derivatives. Alkylation, however, appears problematic, since the slightly basic conditions result in anomeric hydrolysis. Even when employing a method used previously for the benzylation of partially acylated glycoses [18], i.e., benzyl triflate–2,6-di-*tert*-butylpyridine, a mixture of products was obtained, from which the 2-benzyl ether **15** could be isolated in only 22% yield.

Direct β-glycosylation by the glucosyl bromide **6** was readily achievable. Koenigs–Knorr conditions provided β-glucosides with high preference, as exemplified by the silver carbonate-promoted conversion of **6** with cyclohexanol in dichloromethane (12 h, 25°C) into a 1:10 mixture of **17** and **18**, from which the major product, β anomer **18**, was easily separable in 76% yield. The glucosyl

iodide **7**, smoothly generated by treatment of **6** with sodium iodide in acetone and characterized in crystalline form, proved to be a considerably more reactive glucosyl donor, since the glycosidation with cyclohexanol was complete within 2 h. However, the α/β-selectivity (1:10) remained the same.

Preferential α-glycosylation by **6** could either be affected via the in situ anomerization procedure (EI_4NBr in dichloromethane) or under Helferich conditions [$Hg(CN)_2$ in nitromethane], each affording ca. 5:1 α/β-anomeric mixtures, from which the α-glucoside **17** could be secured in 70% yield. The same product, incidentally, was also formed, in 84% yield, by acid-catalyzed cyanoborohydride reduction of the anomerically pure cyclohexyl glycosidulose **16**, hydride addition being essentially stereospecific.

In conclusion, the relative neglect of glucosyl donors with a free 2-OH group in oligosaccharide synthesis is likely to change with the accessibility of 3,4,6-tri-*O*-benzoyl-α-D-glucosyl bromide in five steps from D-glucose in high overall yield (55%) and adaptable to a large scale. Extension of this methodology to other glycosylulose bromides, particularly those derived from D-galactose, 6-deoxy sugars, and disaccharides is in progress, as well as the use of the corresponding glycosyl donors for the straightforward generation of oligosaccharides with a 2-*O*-glycosyl branch. As of now, the benzoylated glycosylulose bromides appear to be more selective in their cyanoborohydride reductions than their acetyl and pivaloyl analogues.

3. Experimental

General methods.—Melting points were determined with a Bock hot-stage microscope and are not corrected. Optical rotations were measured at 20°C with a Perkin–Elmer 241 polarimeter. NMR spectra were recorded with a Bruker WM 300 spectrometer at 300 (^1H) and 75.5 MHz (^{13}C), respectively. A Varian MAT 311A spectrometer was used to obtain mass spectra. TLC on Kieselgel F_{254} plastic sheets (Merck, Darmstadt) was used to monitor the reactions and to ascertain the purity of the products. Developers employed: *A*, 10:1 toluene–EtOAc; *B*, 2:1 toluene–EtOAc; *C*, 2:1 hexane–EtOAc. The spots were visualized by UV light or by spraying with aq 50% H_2SO_4 and charring at 120°C for 5 min. Column chromatography was performed on Kieselgel 60 (Merck, 63–200 μm).

*3,4,6-Tri-*O*-benzoyl-α-D-glucopyranosyl bromide* (**6**).—(*a*) *Acid-catalyzed cyanoborohydride reduction of 3,4,6-tri-*O*-benzoyl-α-D-arabino-hexopyranosyl-2-ulose bromide* (**8**). To a solution of **8** [14] (10.0 g, 18 mmol) in dry dioxane (100 mL) was added strongly acidic ion-exchange resin (Amberlite IR-120, H^+-form, 10 g) and $NaBH_3CN$ (1.15 g, 18 mmol), and the mixture was stirred at ambient temperature for 20 h, followed by filtration over Celite and evaporation of the filtrate in vacuo. The syrupy residue crystallized on trituration with 2:1 ether–hexane (75 mL). Recrystallization from EtOAc gave 7.2 g (72%) of **6** as colorless needles; mp 149–150°C (dec); R_f (in *A*) 0.30; $[\alpha]_D$ +128.5° (*c* 1.2, $CHCl_3$); lit. [12a]: mp 157–158°C, $[\alpha]_D^{23}$ +126.8° (*c* 2.7, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 2.72 (br d, 1 H, OH), 3.92 (m, 1 H, H-2), 4.48 (dd, 1 H, H-6b), 4.65 (m, 2 H, H-5,6a), 5.78 (m, 2 H,

H-3,4), 6.64 (d, 1 H, H-1), 7.34–8.08 (m, 15 H, 3 C_6H_5); $J_{1,2}$ 3.8, $J_{2,3}$ 9.3, $J_{4,5a}$ 2.8, $J_{5,6b}$ 5.1, $J_{6a,6b}$ 12.8 Hz; ^{13}C NMR ($CDCl_3$): δ 61.93 (C-6), 67.25 (C-4), 71.86 (C-5), 72.85 (C-3), 74.20 (C-2), 94.20 (C-1). MS (FD) data: m/z 554, 556 (M^+), 476 (M − Br + 1). Anal. Calcd. for $C_{27}H_{23}BrO_8$ (555.4): C, 58.39; H, 4.17. Found: C, 58.42; H, 4.08.

(*b*) *$TiCl_4$-catalyzed cyanoborohydride reduction of* **8**. To a stirred solution of **8** [14] (2.0 g, 3.6 mmol) in dry dioxane (50 mL) was added $NaBH_3CN$ (390 mg, 6 mmol) and $TiCl_4$ (0.1 mL, 1 mmol), and the mixture was stirred for 15 min and subsequently quenched by pouring into cooled (−5°C), satd aq NaCl (30 mL). Extraction with CH_2Cl_2 (100 mL), drying of the extract ($MgSO_4$), and removal of the solvent in vacuo gave a syrup, which crystallized from ether–hexane. Recrystallization from EtOAc gave **8** (1.42 g, 71%) identical in all respects with the product described above.

*3,4,6-Tri-*O*-benzoyl-α-*D*-glucopyranosyl iodide* (**7**).—A solution of bromide **6** (600 mg, 1.08 mmol) in acetone (20 mL) was added to a suspension of 300 mg (2 mmol) of NaI in acetone (10 mL) and the mixture was stirred for 30 min at room temperature. Subsequent removal of the solvent in vacuo, extraction of the residue with CH_2Cl_2 (2 × 30 mL), and evaporation to dryness in vacuo left a dark-brown residue which crystallized from 1:1 EtOAc–hexane: 340 mg (53%) of **7** as light-yellow needles; mp 126–127°C (dec); $[\alpha]_D$ +161.9° (*c* 0.9, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 2.84 (d, 1 H, OH), 3.15 (ddd, 1 H, H-2), 4.41 (ddd, 1 H, H-5), 4.48 (dd, 1 H, H-6a), 4.63 (dd, 1 H, H-6b), 5.66 (dd, 1 H, H-4), 5.78 (dd, 1 H, H-3), 7.01 (d, 1 H, H-1), 7.2–8.1 (m, 15 H, 3 C_6H_5); $J_{1,2}$ 4.0, $J_{2,3}$ 9.4, $J_{2,OH}$ 9.7, $J_{3,4}$ 9.5, $J_{4,5}$ 9.6, $J_{5,6a}$ 4.7, $J_{5,6b}$ 2.4, $J_{6a,6b}$ 12.3 Hz. MS (FD) data: m/z 602 (M^+), 475 (M − I). Anal. Calcd for $C_{27}H_{23}IO_8$ (602.4): C, 53.84; H, 3.85. Found: C, 54.02; H, 3.90.

*3,4,6-Tri-*O*-benzoyl-2-cyano-α-*D*-glucopyranosyl bromide* (**9**).—A solution of bromide **8** [14] (2.5 g, 47 mmol), trimethylsilyl cyanide (0.85 mL, 1.5 mol equiv), and $BF_3 \cdot Et_2O$ (0.7 mL, 1.3 mol equiv) in CH_2Cl_2 (30 mL) was stirred at ambient temperature for 2 h. Subsequent dilution with CH_2Cl_2 (100 mL), washing with satd aq $NaHCO_3$ and water, drying (Na_2SO_4), and concentration in vacuo gave a syrup which crystallized on trituration with $CHCl_3$–hexane: 2.29 g (87%) of **9** as colorless crystals; mp 178–180°C; $[\alpha]_D$ +81.4° (*c* 0.9, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 4.49 (dd, 1 H, H-6a), 4.66 (m, 3 H, H-5,6b, OH), 5.94 (d, 1 H, H-3), 6.08 (t, 1 H, H-4), 6.64 (s, 1 H, H-1), 7.45–8.11 (m, 15 H, 3 C_6H_5); $J_{3,4} = J_{4,5} = 9.7$, $J_{5,6a}$ 4.4, $J_{6a,6b}$ 13.2 Hz. MS (FD) data: m/z 579, 581 (M^+). Anal. Calcd for $C_{28}H_{22}BrNO_8$ (580.4): C, 57.94; H, 3.82; N, 17.23. Found: C, 57.85; H, 3.90; N, 17.16.

*2-*O*-Acetyl-3,4,6-tri-*O*-benzoyl-2-cyano-α-*D*-glucopyranosyl bromide* (**10**).—To a suspension of cyanohydrin **9** (1.16 g, 2 mmol) in Ac_2O (10 mL) was added a few drops of $BF_3 \cdot Et_2O$. The mixture was stirred at room temperature for 3 h and then poured into cold (0°C) aq $NaHCO_3$ with vigorous stirring. The precipitate formed was filtered off after 1 h, dissolved in ether, and treated with hexane. Standing at 5°C caused **10** to separate as a chromatographically uniform solid; R_f 0.45 (TLC in *C*); mp 157–158°C; $[\alpha]_D$ +43.9° (*c* 1.1, $CHCl_3$). MS (FD) data: m/z 623 (M + 1), 621 (M − 1). Anal. Calcd for $C_{30}H_{24}BrNO_9$ (622.4): C, 57.89; H, 3.92; N, 2.25. Found: C, 57.80; H, 4.03; N, 2.31.

*1,5-Anhydro-3,4,6-tri-*O*-benzoyl-*D*-glucitol* (**11**).—A mixture of bromide **8** [14] (1.0 g, 1.8 mmol), Amberlite IR-120 (H^+-form, 1.2 g), $NaBH_3CN$ (330 mg, 3 mol equiv), and CH_2Cl_2 (40 mL) was stirred at room temperature for 24 h and then filtered over Celite. The filtrate was taken to dryness in vacuo and the syrupy residue was purified by elution from a column (2 × 20 cm) of silica gel with 6:1 toluene–EtOAc. Evaporation of the fractions of R_f 0.35 (solvent system *B*) and trituration of the remaining syrup with ether resulted in crystallization: 485 mg (59%) of **11** as colorless needles; mp 147–148°C; $[\alpha]_D^{20}$ −8.5° (*c* 1, $CHCl_3$); lit.: mp 152–153°C, $[\alpha]_D^{20}$ −8.2° (*c* 1, $CHCl_3$) [19]; mp 145–146°C, $[\alpha]_D^{23}$ −7.0° (*c* 1, $CHCl_3$) [20]; ^{1}H NMR ($CDCl_3/D_2O$): δ 3.49 (dd, 1 H, H-1*ax*), 3.94 (ddd, 1 H, H-5), 4.05 (ddd, 1 H, H-2), 4.22 (dd, 1 H, H-1*eq*), 4.40 (dd, 1 H, H-6b), 4.58 (dd, 1 H, H-6a), 5.38 (dd, 1 H, H-3), 5.57 (dd, 1 H, H-4), 7.5–8.1 (m, 15 H, 3 C_6H_5); $J_{1ax,1eq}$ 11.3, $J_{1ax,2}$ 10.4, $J_{1eq,2}$ 5.6, $J_{2,3}$ 9.2, $J_{3,4}$ 9.6, $J_{4,5}$ 9.9, $J_{5,6a}$ 2.8, $J_{5,6b}$ 5.3, $J_{6a,6b}$ 12.2 Hz. MS (FD) data: *m/z* 477 (M + 1). Anal. Calcd for $C_{27}H_{24}O_8$ (476.5): C, 68.06; H, 5.08. Found: C, 67.94; H, 5.14.

*2-*O*-Acetyl-3,4,6-tri-*O*-benzoyl-α-*D*-glucopyranosyl bromide* (**12**).—Acetic anhydride (5 mL) and Amberlite IR-120 (H^+-form, 1 g) was added to a CH_2Cl_2 solution of glucosyl bromide **6** (1.0 g, 1.8 mmol in 10 mL), and the mixture was kept at ambient temperature for 24 h. Filtration, evaporation to dryness in vacuo, followed by several re-evaporations from toluene gave a residue which crystallized from ether to give **12** (570 mg, 53%) as colorless needles; mp 135–136°C; $[\alpha]_D$ +100.1° (*c* 1.5, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 2.03 (s, 3 H, $COCH_3$), 4.47 (dd, 1 H, H-6b), 4.63 (dd, 1 H, H-6a), 4.67 (m, 1 H, H-5), 5.13 (dd, 1 H, H-2), 5.73 (dd, 1 H, H-4), 6.09 (dd, 1 H, H-3), 6.72 (d, 1 H, H-1), 7.45–8.07 (m, 15 H, 3 C_6H_5); $J_{1,2}$ 4.0, $J_{2,3}$ 10.0, $J_{3,4}$ 9.8, $J_{4,5}$ 10.0, $J_{5,6a}$ 2.4, $J_{5,6b}$ 4.6, $J_{6a,6b}$ 12.7 Hz; ^{13}C NMR ($CDCl_3$): δ 20.61 ($COCH_3$), 61.95 (C-6), 68.13 (C-4), 70.52 (C-2), 70.90 (C-5), 72.63 (C-3), 86.72 (C-1), 169.89 ($COCH_3$). MS (FD) data: *m/z* 596, 598 (M^+), 552, 554 (M − Ac − 1), 517 (M − Br). Anal. Calcd for $C_{29}H_{25}BrO_9$ (597.4): C, 58.30; H, 4.22. Found: C, 58.55; H, 4.28.

*3,4,6-Tri-*O*-benzoyl-2-*O*-trimethylsilyl-α-*D*-glucopyranosyl bromide* (**13**).—Trimethylsilyl chloride (6.3 mL, 5 mmol) and hexamethyldisilazane (0.85 mL, 4 mmol) was added to a CH_2Cl_2 solution of glucosyl bromide **6** (2.5 g, 4.5 mmol, in 30 mL), and the mixture was stirred at ambient temperature for 20 h. Filtration, washing of the filtrate with ice–water (2 × 20 mL), drying ($MgSO_4$), evaporation to dryness, and crystallization of the residue from EtOAc gave **13** (2.1 g, 74%) as colorless needles; mp 158–159°C; $[\alpha]_D$ +106.9° (*c* 1, $CHCl_3$); ^{1}H NMR data ($CDCl_3$): δ 0.05 (s, 9 H, 3 $SiCH_3$), 3.97 (dd, 1 H, H-2), 4.47 (dd, 1 H, H-6b), 4.62 (dd, 1 H, H-6a), 4.68 (ddd, 1 H, H-5), 5.64 (dd, 1 H, H-4), 5.91 (dd, 1 H, H-3), 6.40 (d, 1 H, H-1), 7.30–8.10 (m, 15 H, 3 C_6H_5); $J_{1,2}$ 3.9, $J_{2,3}$ 9.3, $J_{3,4}$ 9.5, $J_{4,5}$ 9.9, $J_{5,6a}$ 2.7, $J_{5,6b}$ 4.7, $J_{6a,6b}$ 12.3 Hz; ^{13}C NMR data ($CDCl_3$): δ 62.17 (C-6), 68.09 (C-4), 71.47 (C-5), 72.45 (C-3), 73.19 (C-2), 91.56 (C-1). MS (FD) data: *m/z* 626, 628 (M^+), 611, 613 (M − CH_3), 547 (M − HBr). Anal. Calcd for $C_{30}H_{31}BrO_8Si$ (627.6): C, 57.42; H, 4.98. Found: C, 57.75; H, 4.90.

*3,4,6-Tri-*O*-benzoyl-2-*O*-methoxymethyl-α-*D*-glucopyranosyl bromide* (**14**).—To an intensely stirred solution of glucosyl bromide **6** (1.65 g, 3 mmol) and formaldehyde

dimethyl acetal (10 mL) in CH_2Cl_2 (50 mL) was added P_4O_{10} (0.5 g) and, after 1 h, another 0.5-g portion. After a total of 2 h stirring, the mixture was filtered through Celite, the filtrate was washed with aq 5% $NaHCO_3$ and water, dried ($MgSO_4$), and evaporated to dryness in vacuo. The resulting syrup crystallized from 1:1 ether–hexane to give **14** (1.30, 73%) as colorless needles; mp 111°C; $[\alpha]_D$ +99.1° (*c* 0.8, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 3.35 (s, 3 H, OCH_3), 3.94 (dd, 1 H, H-2), 4.46 (dd, 1 H, H-6b), 4.62 (dd, 1 H, H-6a), 4.64 and 4.71 (2 d, each 1 H, OCH_2O), 4.66 (ddd, 1 H, H-5), 5.68 (dd, 1 H, H-4), 6.03 (dd, 1 H, H-3), 6.64 (d, 1 H, H-1), 7.40–8.00 (m, 15 H, 3 C_6H_5); $J_{1,2}$ 3.8, $J_{2,3}$ 9.8, $J_{3,4}$ 9.8, $J_{4,5}$ 10.0, $J_{5,6a}$ 2.7, $J_{5,6b}$ 4.7, $J_{6a,6b}$ 12.6 Hz; ^{13}C NMR ($CDCl_3$): δ 56.6 (CH_3), 62.0 (C-6), 68.1 (C-4), 71.8 (C-5), 72.5 (C-3), 76.7 (C-2), 90.1 (C-1), 97.3 (OCH_2). MS (FD) data: *m/z* 598, 600 (M^+), 567, 569 ($M - OCH_3$), 519 ($M - Br$). Anal. Cacld for $C_{29}H_{27}BrO_9$ (599.4): C, 58.14; H, 4.54. Found C, 58.06; H, 4.58.

*3,4,6-Tri-*O*-benzoyl-2-*O*-benzyl-α-*D*-glucopyranosyl bromide* (**15**).—A solution of trifluoromethanesulfonic anhydride (1 mL, 6 mmol) in CH_2Cl_2 (25 mL) was cooled in a dry ice-bath (−70°C) and, with stirring, a mixture of benzyl alcohol (0.63 mL, 6 mmol) and 2,6-di-*tert*-butylpyridine (1.5 mL, 6 mmol) in CH_2Cl_2 (8 mL) was gradually added, followed by dropwise addition of glucosyl bromide **6** (1.65 g, 3 mmol) in CH_2Cl_2 (10 mL). The mixture was then allowed to warm to room temperature and stirring was continued for 12 h. Subsequent washing with water (2 × 20 mL), drying ($MgSO_4$), and removal of the solvent in vacuo left a residue that was purified by fast elution from a short column of silica gel with toluene. Evaporation of the eluates to dryness left a syrup which crystallized from 2:1 ether–pentane to give **15** (290 mg, 22%) as colorless needles; mp 67–69°C; R_f 0.43 (in *A*); $[\alpha]_D$ +67.5° (*c* 1, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 3.77 (dd, 1 H, H-2), 4.42 (dd, 1 H, H-6a), 4.54–4.67 (m, 4 H, H-5,6b, $PhCH_2$), 5.59 (dd, 1 H, H-4), 6.01 (dd, 1 H, H-3), 6.46 (d, 1 H, H-1), 7.21–8.02 (m, 20 H, 4 C_6H_5); $J_{1,2}$ 3.8, $J_{2,3}$ 9.7, $J_{3,4}$ 9.5, $J_{4,5}$ 9.8, $J_{5,6a}$ 4.8, $J_{6a,6b}$ 12.3 Hz. MS (FD) data: *m/z* 644, 646 (M^+), 564 ($M - HBr$). Anal. Calcd for $C_{34}H_{29}BrO_8$ (645.5): C, 63.26; H, 4.53. Found C, 63.25; H, 4.49.

*Cyclohexyl 3,4,6-tri-*O*-benzoyl-α-*D*-*arabino*-hexopyranosid-2-ulose* (**16**).—Silver triflate (510 mg, 2 mmol) was added to a solution of 1.11 g (2 mmol) of bromide **8** [14] and 0.21 mL (2 mmol) of cyclohexanol in CH_2Cl_2 (20 mL), resulting in immediate precipitation of AgBr. The mixture was stirred at room temperature for 30 min and then filtered with suction through Celite. Washing of the filtrate with aq 10% $Na_2S_2O_3$ and water, drying (Na_2SO_4), and evaporation to dryness gave 375 mg (34%) of **16** as fine needles; mp 165–166°C; $[\alpha]_D$ +40.7° (*c* 0.5, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 1.1–2.1 (m, 10 H, 5 cyclohexyl-CH_2), 3.76 (tt, 1 H, cyclohexyl-CH), 4.50 (dd, 1 H, H-6a), 4.68 (dd, 1 H, H-6b), 4.86 (ddd, 1 H, H-5), 5.14 (s, 1 H, H-1), 5.86 (dd, 1 H, H-4), 6.17 (d, 1 H, H-3), 7.3–8.1 (m, 15 H, 3 C_6H_5); $J_{3,4} = J_{4,5} = 10.2$, $J_{5,6a}$ 5.8, $J_{5,6b}$ 2.6, $J_{6a,6b}$ 12.2 Hz. MS (FD) data: *m/z* 573 (M^+), 489 ($M - C_6H_{11}$). Anal. Calcd for $C_{33}H_{32}O_9$ (572.7): C, 69.21; H, 5.64. Found: C, 69.15; H, 5.58.

*Cyclohexyl 3,4,6-tri-*O*-benzoyl-α-*D*-glucopyranoside* (**17**).—(*a*) *By glycosylation with glucosyl bromide* **6**. A mixture of nitromethane (20 mL), cyclohexanol (0.2 mL,

2 mmol), $Hg(CN)_2$ (250 mg, 1 mmol), and 4A molecular sieve (1.5 g) was stirred at room temperature for 30 min, followed by the addition of **6** (550 mg, 1 mmol) and stirring was continued for another 30 min. Filtration through Celite and removal of the solvent in vacuo gave a syrupy 5:1 α/β-mixture of anomers (^{1}H NMR), which was fractionated by elution from a column (3 × 30 cm) of silica gel with 10:1 toluene–EtOAc. The fraction eluted first (R_f 0.34 in *A*) was freed from the solvent in vacuo and the residue was crystallized from EtOAc to give **17** (390 mg, 69%); mp 162–163°C; $[\alpha]_D$ +60.1° (*c* 0.7, $CHCl_3$); ^{1}H NMR ($CDCl_3/D_2O$): δ 1.2–2.1 (m, 10 H, 5 cyclohexyl-CH_2), 3.67 (m, 1 H, cyclohexyl-CH), 5.16 (d, 1 H, H-1), 5.31 (dd, 1 H, H-4), 5.71 (dd, 1 H, H-3), 7.32–8.08 (m, 15 H, 3 C_6H_5); $J_{1,2}$ 4.0, $J_{2,3}$ 9.8, $J_{3,4}$ 9.7, $J_{4,5}$ 9.6 Hz. MS (FD) data: *m/z* 575 (M + 1), 574 (M^+). Anal. Calcd for $C_{33}H_{34}O_9$ (574.6): C, 68.98; H, 5.93. Found: C, 68.73; H, 5.96.

(*b*) *By hydride reduction of hexosidulose* **16**. A CH_2Cl_2 solution of **16** (250 mg in 10 mL) was stirred with $NaBH_3CN$ and Amberlite IR-120 (H^+-form) for 3.5 h at ambient temperature and then filtered. Washing of the filtrate with water, drying ($MgSO_4$), and removal of the solvent in vacuo gave a residue that crystallized from ether to give **17** (210 mg, 84%), identical in all respects with the product described under (*a*).

Cyclohexyl 3,4,6-tri-O-benzoyl-β-D-glucopyranoside (**18**).—Silver carbonate (1.0 g, 3.6 mmol) and 4A molecular sieve (2 g) were added to a solution of glucosyl bromide **6** (1.0 g, 1.8 mmol) and cyclohexanol (0.5 mL, 5 mmol) in 10 mL of CH_2Cl_2, and the mixture was stirred in the dark at room temperature for 24 h. Filtration over Celite, washing of the filtrate with water, drying ($MgSO_4$), and removal of the solvent in vacuo gave a ca. 10:1 mixture of β (**18**) and α anomers (**17**), based on the intensity of anomeric protons. Separation was achieved by elution from a column (2 × 30 cm) of silica gel with 10:1 toluene–EtOAc: concentration of the fractions eluted first (R_f 0.34 in *A*) and crystallization of the residue from EtOAc gave **17** (60 mg, 6%) of mp 162–163°C, identical with the product described above. The major fraction eluted second (R_f 0.25 in *A*) gave, upon evaporation to dryness and crystallization of the syrup from 2:1 ether–hexane, β anomer **18** (680 mg, 66%) as colorless needles; mp 138–140°C; $[\alpha]_D$ −39.8° (*c* 0.6, $CHCl_3$); ^{1}H NMR ($CDCl_3/D_2O$): δ 1.16–2.06 (m, 10 H, 5 cyclohexyl-CH_2), 3.70 (m, 1 H, cyclohexyl-CH), 3.79 (dd, 1 H, H-2), 4.06 (ddd, 1 H, H-5), 4.48 (dd, 1 H, H-6b), 4.56 (dd, 1 H, H-6a), 4.66 (d, 1 H, H-1), 5.53 (dd, 1 H, H-4), 5.63 (dd, 1 H, H-3), 7.32–8.02 (m, 15 H, 3 C_6H_5); $J_{1,2}$ 7.8, $J_{2,3}$ 9.3, $J_{3,4}$ 9.5, $J_{4,5}$ 9.6, $J_{5,6a}$ 3.5, $J_{5,6b}$ 6.1, $J_{6a,6b}$ 12.0 Hz. MS (FD) data: *m/z* 575 (M + 1), 574 (M^+). Anal. Calcd for $C_{33}H_{34}O_9$ (574.6): C, 68.98; H, 5.93. Found: C, 69.07; H, 6.05.

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