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Note

Syntheses of oligosaccharides having the β-D-Glc*p*NAc-(1 → 4)-D-Glc- structure

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In this work directed toward the synthesis of oligosaccharide fragments of hyaluronic acid, we report the synthesis of a protected derivative of the tetrasaccharide β-D-Glc*p*NAc-(1 → 4)-β-D-Glc*p*-(1 → 3)-β-D-Glc*p*NAc-(1 → 4)-β-D-Glc. Two basic assumptions were made throughout the entire synthetic plan. Firstly, owing to the poor nucleophilicity of an OH-4 in a D-glucopyranosyl derivative, glycosylation reactions directed toward the formation of a β-D-(1 → 4) linkage were carried out in the early phase of the synthesis to yield disaccharide building blocks. Then the relatively high-yielding (1 → 3) coupling could be performed late in the synthesis to conserve valuable intermediates. Secondly, the low yield in glycosylation reactions caused by neighboring uronic acid ester groups, also reported by Nakahara and Ogawa[1], was circumvented by use of D-glucose instead of D-glucuronic acid and selective blockage of the primary hydroxyl group in each D-glucose unit. The idea is to deesterify and oxidize the residues later to yield the analogous tetrasaccharide containing two residues of D-glucuronic acid.

Following the more classical route (Scheme 1), methyl 2,3-di-*O*-benzyl-α-D-glucopyranoside (**1**) could be blocked selectively by silylation[2] at O-6 at −30°C to give the glycosyl acceptor **2** in 66% yield. This, in turn, could be coupled to the per-*O*-acetylated *N*-phthalimidoglucosyl bromide **3** (ref 3) in the presence of mercuric cyanide to give an acceptable yield (56%) of the disaccharide building block **4**. However, subsequent work showed that this route has certain drawbacks, because an extensive amount of protecting-group chemistry is necessary at the disaccharide level to obtain a precursor unblocked at the OH-3′ position. Additionally, removal of the anomeric methoxy group was shown to interfere with

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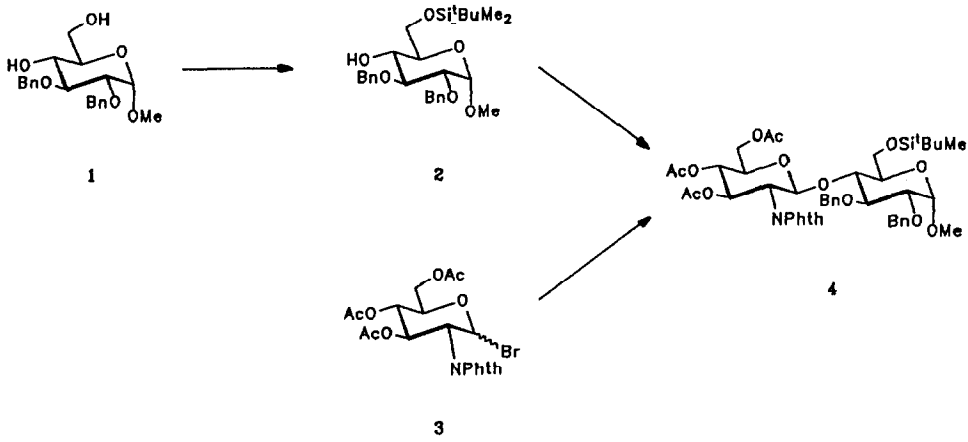


Scheme 1.

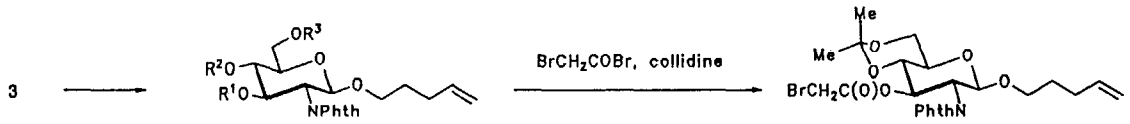
either the benzyl or silyl ethers. These disadvantages made it necessary to switch to an alternative synthetic strategy.

Therefore, we decided to adopt the pentenyl glycosylation technique recently devised by Fraser-Reid and co-workers[4–8]. The goal was to modify the glycosyl donor in an early phase of the synthesis whilst having the anomeric pentenyl group already in place. Starting from the easily accessible glycosyl bromide **3** (Scheme 2), silver triflate–collidine mediated glycosylation of 4-penten-1-ol in dichloromethane gave the fully acetylated β-D-glycoside **5** (ref 7). As the yield for this step was 72%, and the workup was less tedious, it was much more preferable than the tin(IV) chloride-mediated glycosylation of the corresponding 1,3,4,6-tetra-*O*-acetyl-2-deoxy-2-*N*-phthalimido-β-D-glucohexopyranose according to the procedure described by Campos-Valdez et al.[9], which in our hands led to intractable emulsions during the extraction process.

The pentenyl glycoside **5** was then deesterified by the Zemplén method to give triol **6** in an almost quantitative yield. Treatment with 2,2-dimethoxypropane in the presence of a trace of camphorsulfonic acid in anhyd acetone yielded the intermediate 4,6-*O*-isopropylidene compound **7**, which in turn was bromoacetylated at OH-3 to give the fully blocked glycosyl donor **8** in 55% yield. The modest yield was due to the need for repeated column chromatography after each step in order to separate the sugar from deep brown-colored byproducts.

The glycosyl acceptor **10** was obtained in two steps, including a final chromatographic purification, from methyl 4,6-*O*-benzylidene-α-D-glucopyranoside, in a 76% overall yield. After cleavage of the benzylidene acetal in **9**, the intermediate diol was selectively bromoacetylated at −40°C to yield acceptor **10** with unblocked OH-4 ready for disaccharide formation.

The acceptor **10** and donor **8** were coupled in the presence of a 1.2-fold molar excess of *N*-iodosuccinimide and a catalytic ammount of silver triflate, under strict

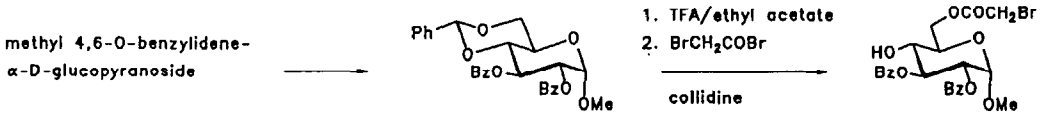


5 $R^1 = R^2 = R^3 = OAc$

6 $R^1 = R^2 = R^3 = H$

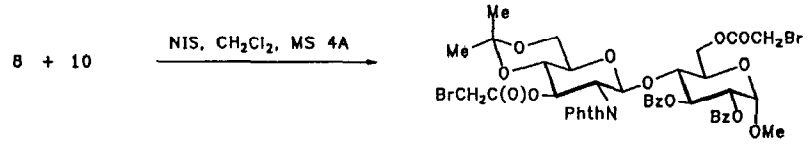
7 $R^1 = H$, R^2, R^3 = isopropylidene

8



9

10



11

Scheme 2.

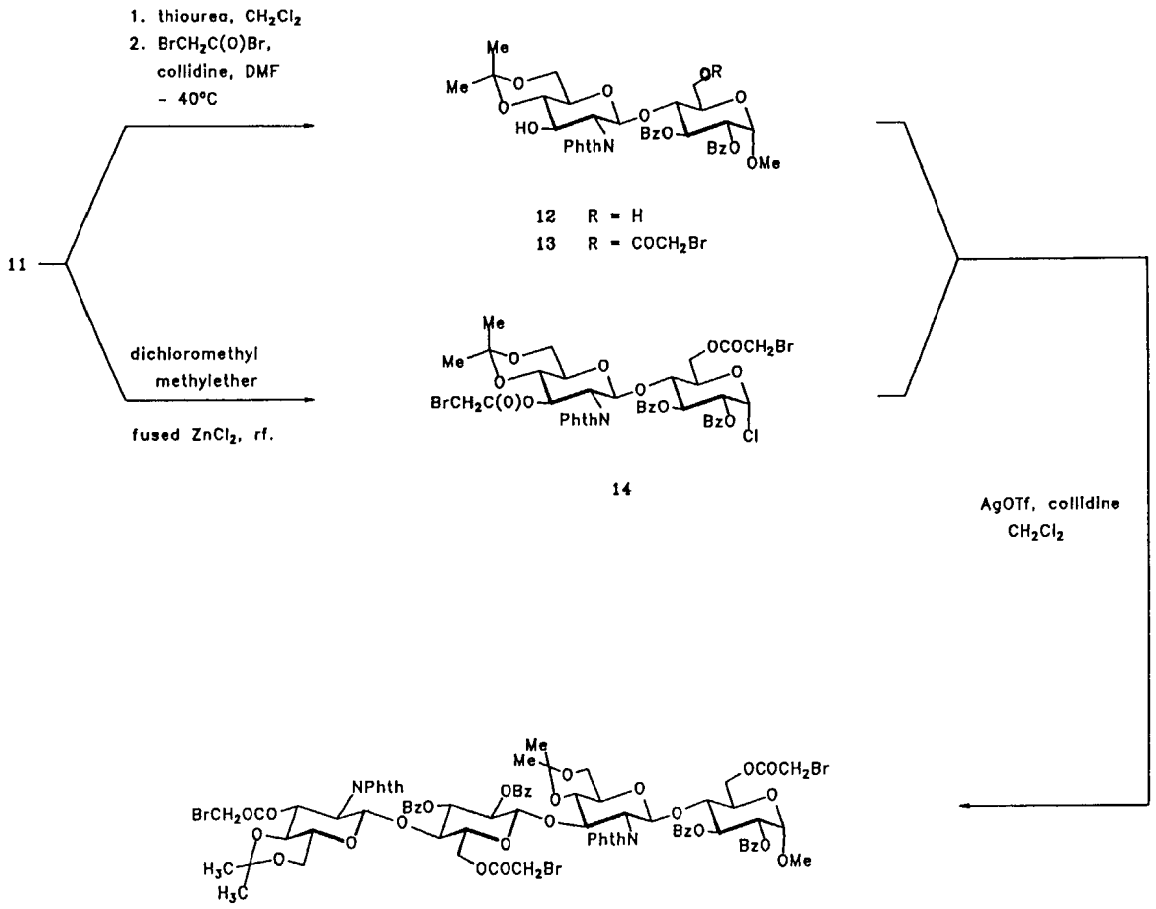
exclusion of moisture and light, to give the β-linked disaccharide **11**, which was isolated in 68% yield after chromatography. The small $J_{1,2}$ and the large $J_{1',2'}$ couplings of 3.5 and 8.5 Hz, respectively, clearly demonstrate the methyl glycoside to be α and the interglycosidic bond to be β-linked. This disaccharide occupied a key position in the synthetic strategy. Not only could it serve as a glycosyl acceptor, but it could also serve as the precursor of the disaccharide glycosyl donor **14** for the synthesis of tetrasaccharide **15** (Scheme 3). Thus, **11** was completely debromoacetylated by treatment with thiourea in methanol[10,11] at 50°C to yield **12** in 91% yield, and subsequently protected again selectively at OH-6 by bromoacetylation, leaving a free OH-3 of the nonreducing residue. The acceptor sugar alcohol **13** was isolated in 53% yield after chromatography.

The conversion of **11** into the donor **14** was achieved by treating the methyl glycoside with dichloromethyl methyl ether and freshly fused zinc chloride[12,13]. As the glucosyl chloride **14** was fairly unstable, the excess ether was evaporated off, the residue taken up in dry toluene, and insoluble salt was filtered off. In order to remove moisture, the crude product was twice coevaporated with toluene to leave a yellow syrup. This was dissolved under a nitrogen atmosphere in anhyd dichloromethane and added to a 1.5-fold molar excess of both acceptor disaccharide **13** and 2,4,6-trimethylpyridine. To this solution silver triflate was added at −50°C, and, after the reagent had completely dissolved, the mixture was stirred and allowed to reach room temperature. This procedure yielded 41% of the tetrasaccharide **15**, the structure of which was proven by a homonuclear ^1H–^1H COSY experiment. The signals for the anomeric protons where found to have one small and three large couplings, confirming the presence of a single α and three β linkages. The synthesis was easily carried out to provide about 50 mg of product.

EXPERIMENTAL

General procedures. —^1H NMR spectra were recorded with Bruker AM 300 or AM 400 spectrometers at the frequencies indicated, applying standard pulse angles. If doubtful, coupled protons were assigned by ^1H–^1H COSY. All reactions were monitored by TLC on silica gel plates (GF_{254}, E. Merck) and detected by either UV absorption or charring with 5% H_2SO_4 in EtOH and subsequent heating to 500°C. Column chromatography was performed on Silica Gel 60 (230–400 mesh, E. Merck) with solvents listed below.

*Methyl 2,3-di-*O*-benzyl-6-*O*-(*tert*-butyldimethylsilyl)-α-*D*-glucopyranoside* (**2**).—To a solution of methyl 2,3-di-*O*-benzyl-α-D-glucopyranoside (**1**) (ref. 14) (970 mg, 2 mmol) and imidazole (330 mg, 4 mmol) in anhyd DMF (10 mL) was added slowly at −30°C a solution of *tert*-butylchlorodimethylsilane (362 mg, 2.4 mmol) in the same solvent (5 mL). After 40 min TLC (2:1 hexane–EtOAc) showed the disappearance of the starting material in favour of a faster moving spot. The mixture was treated with CH_2Cl_2 (30 mL) and washed with 10% aq $NaHCO_3$ (20 mL). The aqueous phase was extracted twice with CH_2Cl_2 (10 mL), the combined organic


1. thiourea, CH_2Cl_2
2. $BrCH_2C(O)Br$,
collidine, DMF
- 40°C
11
dichloromethyl
methylether
fused $ZnCl_2$, rf.
12 R = H
13 R = $COCH_2Br$
14
AgOTf, collidine
CH_2Cl_2
15

Scheme 3.

layers washed with water (20 mL), dried ($MgSO_4$), and concentrated before being purified by column chromatography (3:1 hexane–ETOAc) to give **2** (650 mg, 66%); $[\alpha]_D^{20}$ −14.3° (*c* 1.0, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$) δ 7.39–7.25 (m, 10 H, Ar), 4.98 (d, CH-H), 4.76 (2 × d, 2 H, CH_2), 4.64 (d, CH-H), 4.60 (d, H-1), 3.79 (mc, 3 H, H-5,6a,6b), 3.54 (mc, 2 H, H-3, H-4), 3.48 (dd, H-2), 3.37 (s, 3 H, OCH_3), 2.60 (d, OH-4), 0.89 (s, 9 H, ^{t}Bu), and 0.09 (s, 6 H, $Si(CH_3)_3$); $J_{1,2}$ 3.5, $J_{2,3}$ 9.8, $J_{3,4}$ 9.7, and $J_{4,4\text{-OH}}$ 1.8 Hz. *Anal.* Calcd. for $C_{27}H_{40}O_6Si$ (488.70): C, 66.36; H, 8.25. Found: C, 66.39; H, 8.20.

*Methyl β-*D*-glucopyranosyl)-2,3-di-*O*-benzyl-6-*O*-(*tert*-butyldimethylsilyl)-4-*O*-(2,3,6-tri-*O*-acetyl-2-deoxy-2-phthalimido-α-*D*-glucopyranoside* (**4**).—A solution of **2** (676 mg, 1.38 mmol) and **3** (900 mg, 1.8 mmol) in anhyd acetonitrile (5 mL) and CH_2Cl_2 (5 mL) was equilibrated over powdered 4A molecular sieves under an N_2 atmosphere for 0.5 h at room temperature. $Hg(CN)_2$ (300 mg, 1.2 mmol) was added, the mixture stirred for 2 h, then diluted with diethyl ether, and the salt was filtered off. The filtrate was washed with a satd aq NaI, and the organic layer was dried over $MgSO_4$ and concentrated. After chromatography (2:1 toluene–ETOAc) **4** was eluted in the second fraction to yield a colourless foam (700 mg, 56%); $[\alpha]_D^{20}$ 22.5° (*c* 1.2, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$) δ 7.84 and 7.73 (each q, each 2 H, phthalimidoyl), 7.43–7.14 (m, 10 H, aromatic), 5.73 (dd, H-4′), 5.68 (d, H-1′), 5.14 (dd, H-1), 5.00, 4.91, 4.86, and 4.55 (each d, each 1 H, 2 × $-CH_2-$), 4.46 (d, H-1), 4.25 (dd, H-2′), 4.14 (dd, H-6a′), 3.83 (mc, 3 H, H-6b′,6a,6b), 3.57 (mc, H-2, H-5,5′), 3.48–3.47 (m, 3 H, H-2,3,4), 3.25 (s, 3 H, OCH_3), 2.00, 1.98, and 1.81 (each s, each 3 H, OAc), 0.83 (s, 9 H, ^{t}Bu), and 0.08 (s, ~6 H, $Si(CH_3)_3$); $J_{1,2}$ 3.5, $J_{1',2'}$ 8.5, $J_{2',3'}$ 10.5, and $J_{3',4'}$ 9.2 Hz. *Anal.* Calcd. for $C_{47}H_{60}NO_{15}Si$ (907.09): C, 62.23; H, 6.67. Found: C, 62.19; H, 6.80.

*4-Pentenyl 3-*O*-bromoacetyl-2-deoxy-4,6-*O*-isopropylidene-2-phthalimido-β-*D*-glucopyranoside* (**8**).—A solution of **7** (ref. 7) (1.64 g, 3.9 mmol) in anhyd DMF (20 mL), maintained under an N_2 atmosphere and cooled to −40°C, was treated with collidine (0.67 mL, 5.07 mmol), followed by dropwise addition of a solution of bromoacetyl bromide (0.44 mL, 5.07 mmol) in anhyd toluene (3 mL). The temperature was maintained for 4 h and then allowed to reach room temperature. After 16 h water was added (50 mL), the mixture extracted with CH_2Cl_2 (3 × 50 mL), and the organic layers were combined and washed with water (100 mL), dried over $MgSO_4$, and concentrated in vacuo to leave a yellow syrup. Column chromatography (3:1 hexane–EtOAc) yielded **8** (1.39 g, 68%) as a colorless oil, which after storage at −10°C yielded an amorphous solid; $[\alpha]_D^{20}$ −41.9° (*c* 0.6, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$) δ 7.83 and 7.21 (each q, each 2 H, phthalimidoyl), 5.77 (dd, H-3), 5.54 (dec ~ dddd, 1 H, pentenyl), 5.32 (d, H-1), 4.73 (m, 2 H, pentenyl), 4.28 (dd, H-2), 4.02 (dd, H-6a), 3.55–3.86 (m, 3 H, H-4,5,6b), 3.66 (s, 2 H, bromoacetyl), 3.55 and 3.42 (each sx, each 1 H, pentenyl), 1.84 (qt, 2 H, pentenyl), 1.50 (qt, 2 H, pentenyl), 1.84 and 1.38 (each s, each 3 H, isopropylidene); $J_{1,2}$ 8.3, $J_{2,3}$ 10.5, $J_{3,4}$ 9.2, $J_{5,6a}$ 5.5, and $J_{6a,6b}$ 10.5 Hz. *Anal.* Calcd. for $C_{24}H_{28}BrNO_8$ (538.40): C, 53.54; H, 5.24. Found: C, 53.76; H, 5.85.

Methyl 2,3-di-O-benzoyl-6-O-bromoacetyl-α-D-glucopyranoside (**10**).—Compound **9** (ref. 15) was dissolved in a mixture of 5:1 EtOAc–trifluoroacetic acid (100 mL) and stirred for 4 h at 40°C. The solvents were removed by evaporation, and the syrupy residue was redissolved in EtOAc (50 mL) and neutralized by washing with 10% aq $NaHCO_3$ (200 mL). After separation, the organic layer was dried over $MgSO_4$ and evaporated. Purification by flash chromatography (1:1 toluene–EtOAc) removed the benzaldehyde to yield, after evaporation, a colorless solid material, which was then completely dissolved in anhyd DMF (50 mL), cooled to −30°C and treated with collidine (1.75 mL, 133 mmol). A solution of bromoacetyl bromide (1.15 mL, 13.3 mmol) in anhyd toluene (15 mL) was added dropwise, and the temperature was maintained for 2 h before the mixture was allowed to reach room temperature. After dilution with CH_2Cl_2 (100 mL), the reaction was worked up similar to the procedure described for **8**. Column chromatography (2:1 toluene–EtOAc) yielded **10** as a colorless foam (3.31 g, 62%): $[\alpha]_D^{20}$ +112.4° (*c* 1.0, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$) δ 7.94, 7.45 and 7.33 (each m, 10 H, Ar), 5.75 (dd, H-3), 5.21 (dd, H-2), 5.10 (d, H-1), 4.55 (dd, H-6a), 4.50 (dd, H-6b), 4.02 (ddd, H-5), 3.90 (s, 2 H, bromoacetyl), 3.86 (m, H-4), 3.60 (d, br, 4-OH), and 3.40 (s, 3 H, OCH_3); $J_{1,2}$ 3.5, $J_{2,3}$ 10.0, $J_{3,4}$ 9.0, $J_{4,4\text{-OH}}$ 5.5, $J_{5,6a}$ 2.5, $J_{5,6b}$ 4.5, and $J_{6a,6b}$ 12.0 Hz. *Anal.* Calc. for $C_{23}H_{23}BrO_9$ (523.35): C, 52.79; H, 4.43. Found: C, 52.40; H, 4.32.

Methyl 2,3-di-O-benzoyl-6-O-bromoacetyl-4-O-(3-O-bromoacetyl-2-deoxy-4,6-O-isopropylidene-2-phthalimido-β-D-glucopyranosyl)-α-D-glucopyranoside (**11**).—Compound **8** (520 mg, 0.99 mmol) and **10** (785 mg, 1.5 mmol) were dissolved in anhyd acetonitrile (5 mL) and CH_2Cl_2 (5 mL) at 0°C. The solution was treated with *N*-iodosuccinimide (338 mg, 1.5 mmol) and a catalytic amount of silver triflate (4 mg, 0.015 mmol). Completion of the reaction was monitored by TLC (2:1 toluene–EtOAc) by the disappearance of starting material **8** (R_f 0.7). The mixture was treated with $CHCl_3$ (20 mL), washed twice with 10% aq $Na_2S_2O_3$ (100 mL) and dried over $MgSO_4$. After column chromatography (2:1 toluene–EtOAc) a mixture of starting material **10** and product **11** (R_f 0.4) was obtained, and the latter was further purified by column chromatography (3:1 toluene–ETOAc) to yield pure **11** (657 mg, 68%) as the second fraction; $[\alpha]_D^{20}$ −21.2° (*c* 1.0, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$) δ 7.95, 7.87, 7.49, and 7.34 (each m, 14 H, Ar), 5.77 (dd, H-3′), 5.46 (dd, H-3), 5.40 (d, H-1′), 5.04 (dd, H-2), 5.77 (d, H-1), 4.54 (m ~ 2 × dd, H-6a,6b), 4.35 (dd, H-2′), 4.03 (dd, H-6a′), 3.92 (s, 2 H, CH_2Br), 3.84 (m, ~ ddd and dd, 2 H, H-5′,6b′), 3.72 (ddd, H-5), 3.62 (s, 2 H, CH_2Br), 3.59 (mc, 2 H, H-4,4′), 3.15 (s, 3 H, OCH_3), 1.48 and 1.37 (each s, each 3 H, isopropylidene); $J_{1,2}$ 3.5, $J_{2,3}$ 10.0, $J_{3,4}$ 9.0, $J_{4,5}$ 9.2, $J_{5,6a}$ 2.5, $J_{5,6b}$ 4.5, $J_{6a,6b}$ 12.0, $J_{1',2'}$ 8.5, $J_{2',3'}$ 10.0, $J_{3',4'}$ 9.5, $J_{5',6a'}$ 5.5, and $J_{6a',6b'}$ 11.0 Hz. *Anal.* Calcd. for $C_{42}H_{41}Br_2NO_{16}$ (975.61): C, 51.71; H, 4.24. Found: C, 52.42; H, 4.66.

Methyl 2,3-di-O-benzoyl-4-O-(2-deoxy-4,6-O-isopropylidene-2-phthalimido-β-D-glucopyranosyl)-α-D-glucopyranoside (**12**).—To solution of **11** (360 mg, 0.36 mmol) in MeOH (5 mL) was added at 40°C a solution of thiourea (140 mg, 1.84 mmol) in

MeOH (2 mL). After 4 h the reaction mixture was diluted with EtOAc (15 mL), treated with NaCl, and washed with water (50 mL). The organic layer was separated, dried over $MgSO_4$ and, after concentration, subjected to column chromatography (1:1 hexane–EtOAc, followed by elution with EtOAc). The product **12** (243 mg, 92%) was eluted first, to give upon evaporation of the solvent, a colourless syrup, which after storage for several weeks at −10°C turned into a transparent glass; $[\alpha]_D^{20}$ −20.8° (*c* 1.1, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$) δ 7.95–7.29 (m, 14 H, Ar), 5.48 (dd, H-3), 5.30 (d, H-1′), 5.06 (dd, H-2), 4.80 (d, H-1), 4.46 (ddd, H-3′), 4.25 (dd, H-2′), 3.98 (dd, H-6a′), 3.85 (dd, H-6b′), 3.71 (mc, 3 H, H-6a,6b,5), 3.62 (mc, 2 H, H-4′,5′), 3.58 (dd, H-4), 3.18 (s, 3 H, OCH_3), 2.76 (d, OH-6), 2.48 (d, br, 3-OH), 1.50 and 1.43 (each s, each 3 H, isopropylidene); $J_{1,2}$ 3.6, $J_{2,3}$ 10.0, $J_{3,4}$ 9.5, $J_{4,5}$ 9.8, $J_{1',2'}$ 8.3, $J_{2',3'}$ 10.5, $J_{3',4'}$ 10.5, $J_{3',OH\text{-}3'}$ 2.5, $J_{5',6a'}$ 5.5, $J_{5',6b'}$ 2.7, and $J_{6a',6b'}$ 11.0 Hz. *Anal.* Calcd. for $C_{38}H_{39}NO_{14}$ (773.74): C, 62.21; H, 5.36. Found: C, 62.10; H, 5.42.

*Methyl 2,3-di-*O*-benzoyl-6-*O*-bromoacetyl-4-*O*-(2-deoxy-4,6-*O*-isopropylidene-2-phthalimido-β-*D*-glucopyranosyl)-α-*D*-glucopyranoside* (**13**).—A solution of **12** (200 mg, 0.27 mmol) and collidine (35.5 μL, 0.35 mmol) in anhyd DMF (5 mL), was cooled to −30°C and slowly treated with a solution of bromoacetyl bromide (30.4 μL, 0.35 mmol) in anhyd toluene (5 mL), while the temperature was maintained for 4 h, before the mixture was allowed to reach room temperature. Dichloromethane (5 mL) was added and workup was performed as described for compound **8**. After column chromatography (1.5:1 toluene–EtOAc) **13** was obtained as a transparent yellow syrup (120 mg, 52%); $[\alpha]_D^{20}$ −12.7° (*c* 1.0, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$) δ 7.90–7.26 (m, 14 H, Ar), 5.42 (dd, H-3), 5.21 (d, H-1′), 5.07 (dd, H-2), 4.77 (d, H-1), 4.51 (m, br, ~ ddd, H-3′), 4.25 (dd, H-2′), 4.00 (dd, H-6a′), 3.91 (s, 2 H, CH_2Br), 3.87 (dd, H-6b′), 3.75 (m, 3 H, H-5,6a,6b), 3.68 (ddd, H-5′), 3.57 (mc, 2 H, H-4,4′), 3.18 (s, 3 H, OCH_3), 1.51 and 1.42 (each s, each 3 H, isopropylidene); $J_{1,2}$ 3.5, $J_{2,3}$ 10.2, $J_{3,4}$ 9.2, $J_{1',2'}$ 8.3, $J_{2',3'}$ 9.8, $J_{3',4'}$ 9.5, $J_{3',OH\text{-}3'}$ 3.3, $J_{5',6a'}$ 5.4, $J_{5',6b'}$ 2.9, and $J_{6a',6b'}$ 11.1 Hz. *Anal.* Calcd. for $C_{40}H_{40}BrNO_{25}$ (854.67): C, 56.21; H, 4.72. Found: C, 56.26; H, 4.85.

Methyl O*-(3-*O*-bromoacetyl-2-deoxy-4,6-*O*-isopropylidene-2-phthalimido-β-*D*-glucopyranosyl)-(1 → 4)-*O*-(2,3-di-*O*-benzoyl-6-*O*-bromoacetyl-β-*D*-glucopyranosyl)-(1 → 3)-*O*-(2-deoxy-4,6-*O*-isopropylidene-2-phthalimido-β-*D*-glucopyranosyl)-(1 → 4)-2,3-di-*O*-benzoyl-6-*O*-bromoacetyl-α-*D*-glucopyranoside* (**15**). —To a solution of **11** (80 mg, 0.08 mmol) in dichloromethyl methyl ether (10 mL) was added freshly fused $ZnCl_2$ (5 mg), and the mixture was heated for 5 h at 80°C. The solvent was evaporated, the crude residue was taken up in anhyd toluene, the insoluble salt was filtered off, and the eluate was coevaporated with toluene (2 × 10 mL). This left a yellow syrup, which was dried in vacuo for 1 h before being dissolved in anhyd CH_2Cl_2 (10 mL) and treated with **13** (100 mg, 0.12 mmol) and collidine (16 μL, 0.12 mmol). At −50°C, silver triflate (31 mg, 0.12 mmol) was added under N_2, and the mixture was allowed to reach room temperature after the reagent was completely dissolved. The reaction mixture was stirred for 5 h, diluted with

CH_2Cl_2 (10 mL), washed with 10% aq $NaHCO_3$, water (each 15 mL), and dried over $MgSO_4$. After filtration, evaporation gave a brown syrup, which was purified by column chromatography (1:1 toluene–EtOAc) to give **15** (54 mg, 39%) as a slightly yellow oil. This compound decomposed quickly when stored in light at room temperature by loss of the bromoacetyl groups and extensive deglycosylation. However, it could be kept for 6–8 weeks at −10°C. No constant optical rotation could be determined. ^1H NMR (400 MHz, $CDCl_3$) δ 7.90–7.26 (m, ~28 H, Ar), 5.89 (dd, H-3′), 5.50 (mc, ~2 × dd, 2 H, H-3,3″), 5.42 (d, H-1′), 5.39 (d, H-1‴), 5.05 (mc, ~2 × dd, H-2,2″), 4.82 (d, H-1″), 4.79 (d, H-1), 3.85, 3.82 and 3.75 (3 × s, each 2 H, CH_2Br), 3.18 (s, 3 H, OCH_3), and 1.50–1.40 (m, ~4 × s, 12 H, isopropylidene); $J_{1,2}$ 3.5, $J_{2,3}$ 10.1, $J_{1',2'}$ 8.1, $J_{1'',2''}$ 8.4, and $J_{1''',2'''}$ 8.0 Hz. *Anal.* Calcd. for $C_{81}H_{77}Br_2N_2O_{30}$ (1718.34): C, 56.62; H, 4.52. Found: C, 56.18; H, 4.30.

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