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The Synthesis of an *O,C*-Trisaccharide: The *O,C*-Analog of Methyl 4′-*O*-β-D-glucopyranosylgentiobioside

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This article is dedicated to Professeur Pierre Sinaÿ on the occasion of his 62nd birthday

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Abstract—The synthesis of an *O,C*-trisaccharide, namely methyl *O*-β-D-glucopyranosyl-(1→4)-*C*-β-D-glucopyranosyl-(1→6)-α-D-glucopyranoside, was achieved in 14 steps by way of the nitro–aldol coupling of hepta-*O*-acetyl-β-cellobiosylnitromethane and methyl 6-*aldehydo*-2,3,4-tri-*O*-benzyl-α-D-*gluco*-hexodialdo-1,5-pyranoside, followed by the elaboration of the coupling product. The resulting *O,C*-trisaccharide constitutes a potential inhibitor of the β-glucanases of the cellulase family. The perbenzylated derivative of cellobiosylnitromethane was also prepared. Both disaccharide-*C*-glycosides constitute useful starting materials for the preparation of higher mixed *O,C*-oligosaccharides.

Introduction

The *C*-analogs of disaccharides and higher oligosaccharides, i.e. analogs in which one or more interglycosidic oxygen atom is replaced by a methylene group, form a class of carbohydate mimics[1] of increasing importance: such compounds constitute useful glycosidase-resistant probes for the study, at the molecular level, of carbohydrate–protein interactions in lectins, antibodies and, possibly, enzymes. Of particular significance are the recent findings that methylene-bridged analogs retain the same affinity as the substrates for their macromolecular receptor in a number of cases: the *C,C*-analog of the H-type II human blood group antigenic trisaccharide for the lectin from *Ulex europaeus*,[2] a *C*-analog of a heparin-derived pentasaccharide for the antithrombin III protein,[3] and *C*-oligogalactosides of the $[-(1\rightarrow6)$-*C*-β-Gal$-]_n$ type for three monoclonal antigalactan antibodies.[4] In all cases, these results suggested that the interglycosidic oxygen atom(s) of the natural substrate is (are) not involved in an essential interaction with the receptor such as hydrogen bonding.

The synthesis of *C*-disaccharides has been the topic of intense research activity and several methods have been developed.[5] Examples of even more challenging higher *C*-oligosaccharides (*C,C*-trisaccharides) have also been reported,[6,7] in particular by Kishi and coworkers. The largest, fully methylene-bridged oligosaccharide analogs reported so far are *C,C,C*-tetrasaccharides: these remarkable compounds were prepared by iterative Wittig olefination (Dondoni et al.[8]) and by iterative lactone+acetylide couplings (Sinaÿ et al.[9]); the latter procedure was in fact the one that had been used by its authors to obtain the very first example of a *C*-disaccharide.[10] In comparison, few examples of mixed *O,C*-oligosaccharides have been described: a *C*-analog of the pentasaccharide corresponding to the antithrombin III binding domain of heparin,[3] and an *O,C*-analog of the Lewis^x trisaccharide.[11] Both of these compounds were generated by the glycosylation of a *C*-disaccharide.

We had reported[12] the synthesis of (1→1)- and (1→6)-linked *C*-disaccharides by way of the nitroaldol coupling of a glycosylnitromethane with a sugar aldehyde. This method remains one of the simplest and shortest procedures for the preparation of unbranched *C*-disaccharides and the modification recently proposed by Bednarski[13] should extend its scope. Since hexobiosylnitromethane derivatives had been reported to be readily available from the corresponding disaccharides,[14] we considered that such *C*-glycosyl compounds could serve as the precursors of *O,C*-trisaccharides using our methodology. We report in this article a new synthesis of cellobiosylnitromethane derivatives and an investigation of their utility in the synthesis of *O,C*-trisaccharides.

Results and Discussion

According to Petruš and coworkers,[14] hexobiosylnitromethanes can be generated from free disaccharides under the same conditions as β-D-glucopyranosylnitromethane

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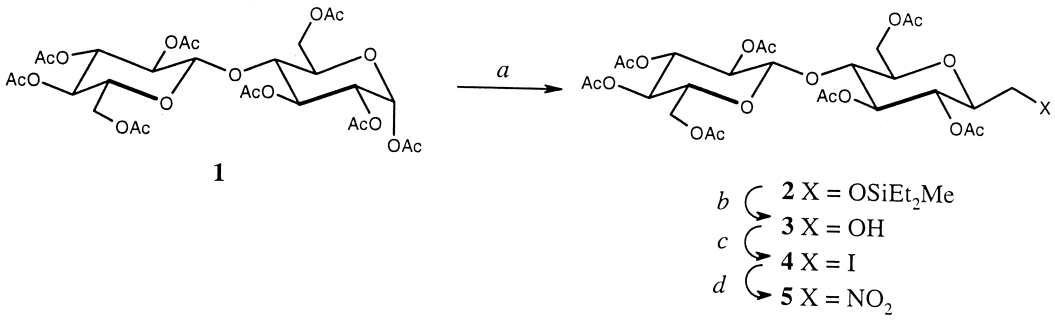


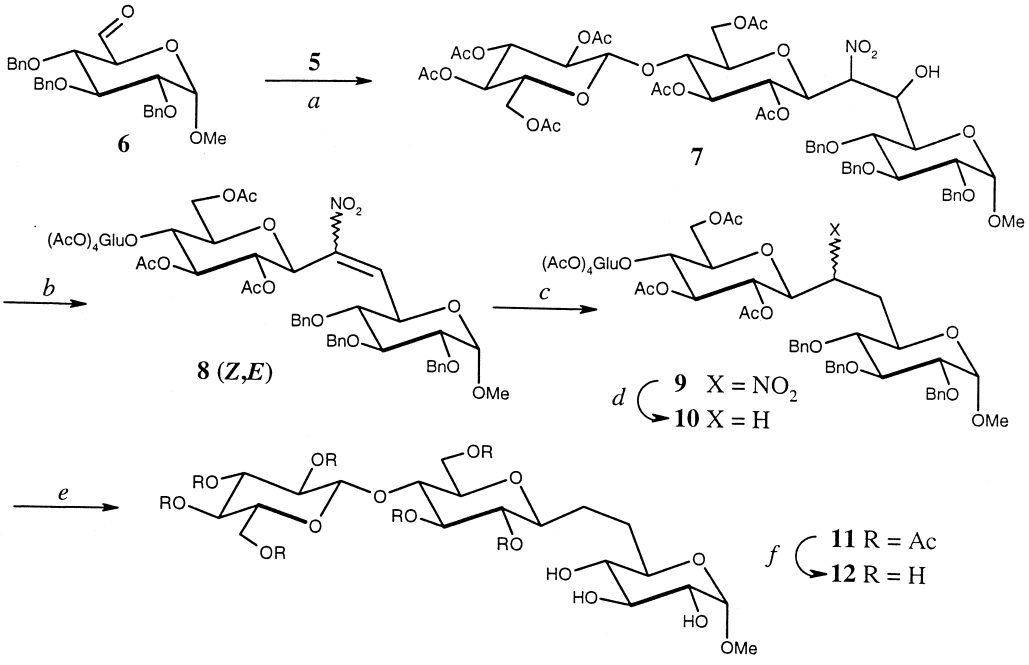
Scheme 1. (*a*) CO, $HSiEt_2Me$, cat $Co_2(CO)_8$; (*b*) THF/aq. HOAc; (*c*) Ph_3P, imidazole, I_2; (*d*) $NaNO_2$, DMSO/DMF.

from D-glucose. However, in our hands, the base-catalyzed reaction of cellobiose with nitromethane followed by the dehydration and cyclization of the resulting nitroalditols did not afford more than traces of the desired β-cellobiosylnitromethane. This approach was therefore abandoned and an alternative method sought. As shown by Murai et al.,[15] glycosyl acetates are converted into the silyl ether of the corresponding glycosylmethanol derivatives in good yield and with a high degree of (β)-stereoselectivity in the *gluco* and *galacto* series, on treatment with CO and a trialkylsilane in the presence of cobalt octacarbonyl. As the hydroxymethyl group constitutes a convenient precursor of the nitromethyl group as well as of other functionalized C_1 units, we decided to investigate the siloxymethylation of cellobiose peracetate **1**. The reaction of **1** with $HSiMe_2Et/CO/Co_2(CO)_8$ was found to provide β-cellobiosylmethanol derivative **2** in good yield (66% isolated product on 10 g scale), and no α-epimer could be detected (Scheme 1). The best results were obtained using a recrystallized catalyst and taking the precaution of refilling the reaction flask with fresh CO every day (reaction time: 10–12 days). The Murai procedure, which involves a glycosylcobalt intermediate,[15,16] thus provides a convenient method for the direct *C*-glycosylation of disaccharide derivatives.

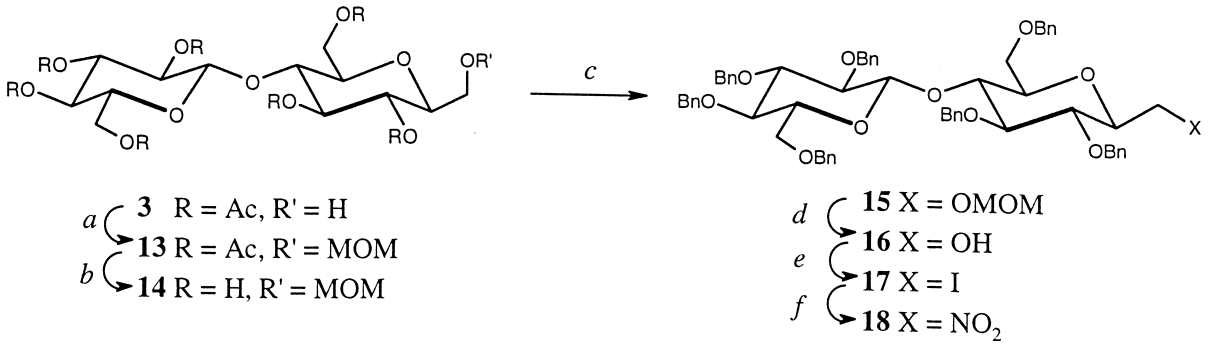
Compound **2** was then converted into β-cellobiosylnitromethane peracetate **5** in three steps and 58% overall yield: desilylation of **2** under mildly acidic conditions, to give **3**, replacement of the OH group of **3** by an iodine atom[17] (→**4**), and substitution of the iodide in **4** by the nitrite ion.[18] The β-configuration of the *C*-glycosidic linkage was clearly established by the NMR parameters of compounds **3**, **4**, and **5** ($J_{2,3}$=9.5–9.7 Hz).

The condensation of compound **5** with 6-*aldehydo*-glucopyranoside **6**[19] in the presence of KF in an aprotic medium afforded the desired pseudotrisaccharide **7** in 44% yield (Scheme 2). Some starting material (**5**) could be recovered and the yield of **7** based on consumed nitrosugar reached 73%. The coupling reaction is highly stereoselective: only one product could be isolated and the NMR analysis of this product revealed the presence of a single stereoisomer.

The coupling constants between the protons at positions 5,

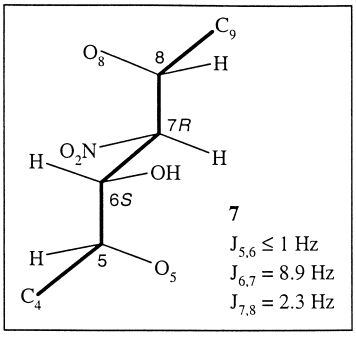


Scheme 2. (*a*) KF, 18-crown-6, CH_3CN, r.t.; (*b*) Ac_2O, py, 54 h; (*c*) $NaBH_4$, EtOH, 0°C; (d) Bu_3SnH, AIBN, toluene, refl., 30 min; (*e*) $H_2/Pd(OH)_2$, 1 atm., EtOH; (*f*) MeOH/MeONa.



Scheme 3. (a) $CH_3OCH_2OCH_3$, P_2O_5; (b) MeONa/MeOH; (c) NaH, BnBr, DMF; (d) 6M HCl, THF, Δ; (e) I_2, Ph_3P, imidazole; (f) $NaNO_2$, DMSO/DMF.

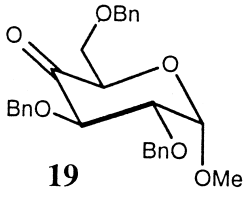
6, 7 and 8 in compound **7** indicate a *gauche* relationship between H-5 and H-6, *anti* between H-6 and H-7 and *gauche* between H-7 and H-8. On the basis of an analysis of the steric interactions in the conformations compatible with these relationships and of the fact that the carbon chain tends to preferentially adopt a zigzag arrangement in such systems,[20] we tentatively propose that the configuration at C-6 and C-7 in compound **7** is *S* and *R*, respectively. This structure is free of 1,3-diaxial-like interactions between substituents at C-5–C-8 and should be particularly favorable.



Compound **7** was further elaborated into a pseudotrisaccharide as follows: the nitroaldol product was dehydrated by acetylation and spontaneous elimination of acetic acid to afford a mixture of *E* and *Z* isomers of nitro alkene **8**. These sensitive compounds were rapidly treated with $NaBH_4$ to reduce the double bond, thus providing the 11-*O*-glucosylated 7-nitro-6,7-dideoxy-tridecose derivative **9** in 45% yield (~2:1 mixture of stereoisomers at C-7). The nitro group of **9** was then removed under radical conditions to give protected pseudotrisaccharide **10**. Deprotection of **10** by catalytic hydrogenation followed by deacetylation gave the free pseudotrisaccharide **12**, the methylene analog of methyl 4′-*O*-β-D-glucopyranosyl-α-gentiobioside. This compound constitutes a novel example of mixed *O*,*C*-oligosaccharide and the first one to have been made using as precursor a disaccharide *C*-glycoside. It is a potential inhibitor of the enzymes that cleave cellobiose and higher β-(1→4)-glucose oligomers (β-glucanases).

The possibility of using cellobiosylnitromethane for the synthesis of an *O*,*C*-analog of cellotriose was also investigated. However, attempts to couple **5** with a '4-ketoglucose' derivative (methyl 2,3,6-tri-*O*-benzyl-α-D-*xylo*-hexopyranosid-4-ulose, **19**) were not successful. In order to be able to use more vigorous coupling conditions, the perbenzylated derivative of cellobiosylnitromethane, compound **18**, was prepared (Scheme 3). For this purpose, compound **3** was converted into the MOM ether derivative **13** and the acetyl groups of **13** were replaced by benzyl groups under conventional conditions to give compound **15**. The MOM ether of **15** was then cleaved under acidic conditions and the OH group thus freed (compound **16)** was replaced by a nitro group by way of iodomethyl intermediate **17**, as described above for the synthesis of **5**. This sequence of reactions provided compound **18** in 26% overall yield from **3** (not optimized).

The coupling of the nitronate ion derived from **18** with keto sugar **19**, under various conditions, was unsuccessful; attempts to use the dianionic species generated by the treatment of **18** with 2 equiv. of BuLi, under the conditions described by Seebach,[21] also remained fruitless.



In spite of these results, compounds **5** and **18** themselves, as well as their precursors carrying a hydroxymethyl or an iodomethyl substituent, constitute very useful synthetic intermediates in the field of carbohydrate mimics: they should readily give access to *C*-analogs of disaccharide-derived glycoconjugates, a class of compound for which few direct synthetic routes are available.

Conclusion

The synthesis of the *O*,*C*-analog of methyl β-D-glucopyranosyl-(1→4)-β-D-glucopyranosyl-(1→6)-α-D-glucopyranoside was achieved in 14 steps from simple sugars by the nitroaldol coupling methodology using a cellobiosylnitromethane derivative as the key precursor. This is the first synthesis of a mixed *O*,*C*-oligosaccharide in which the *C*-glycosidic linkage is already built into a disaccharide precursor. The cellobiosylnitromethane derivatives prepared, and their synthetic precursors, provide useful intermediates for the synthesis of other pseudo-oligosaccharides

as well as of *C*-glycosidic analogs of disaccharide glycoconjugates.

Experimental

General methods

Melting points were obtained using a Fisher–Johns melting point apparatus and are uncorrected. Thin-layer chromatography was performed on 0.25 mm Merck silica gel plates ($60F_{254}$). The determination of spots was conducted by inspection under UV light (254 nm), as well as by spraying the developed plates with a solution of ammonium phosphomolybdate (H_2SO_4=100 mL/H_3PO_4=100 mL/H_2O=3.8 L/$(NH_4)_6Mo_7O_{24}$=100 g) and charring on a hot plate. Flash column chromatography was performed on silica gel 60 (230–400 mesh) from Merck. Optical rotations were measured with a Perkin–Elmer 243B polarimeter for solutions in a 0.1 dm cell at room temperature (20±3°C). ^1H and ^{13}C NMR spectra were recorded on a Bruker AM-360 spectrometer at 360 and 90 MHz, respectively. $CDCl_3$ was used as the solvent unless otherwise noted; chemical shifts are in ppm (δ) relative to tetramethylsilane (TMS) with TMS (δ=0.00 ppm) as the internal reference, unless indicated otherwise. Chemical shifts and coupling constants were obtained from the direct examination of spectra for all first-order spectra and all assignments of signals were verified by 2D correlation spectra. IR spectra were obtained using a Perkin–Elmer 1600 FT-IR instrument. Mass spectral analyses were carried out by Midwest Center for Mass Spectrometry, University of Nebraska, Lincoln, NE 68588. Elemental analyses were carried out by Atlantic Microlab, Inc., Norcross, GA 30091.

(Hepta-*O*-acetyl-β-D-cellobiosyl)methanol methyldiethylsilyl ether (2). For general procedure: see Ref. 16. The following precautions were followed: α-D-cellobiosyl octaacetate was dried at 100°C for 8 h under high vacuum. Et_2MeSiH was used straight from an ampoule or from reagent that was stored at 0°C under CO atmosphere in a desiccator. $Co_2(CO)_8$ (Strem Chemicals Co.) was recrystallized from hexane (room temperature to −25°C) and collected under CO atmosphere. The recrystallized $Co_2(CO)_8$ was stored under CO at 0°C in a desiccator. Caution: the purified crystals ignite spontaneously on exposure to air. The CO gas used (99.99% purity) was passed through an on-line desiccant. CO gas was stored in a helium-quality balloon that was connected to a three-neck reaction flask by a glass stopcock. The vessel was evacuated daily and refilled with CO in the course of the reaction.

Actual procedure

$Co_2(CO)_8$ (0.25 g; 0.73 mmol) was added to a three-neck flask under CO atmosphere. Et_2MeSiH (12.0 mL; 8.46 g; 82.7 mmol; 5.4 eq.) was then added and the mixture was stirred for 5 min. A solution of α-D-cellobiosyl octaacetate **1** (10.41 g; 15.34 mmol) in anhydrous CH_2Cl_2 (85 mL) was degassed (freeze–pump–thaw procedure) and then added using a syringe. After complete addition, the flask was evacuated and refilled (3×) with CO gas. The gas was added under the level of the solution. The reaction was stopped after 11 days of stirring at room temperature. The cobalt complex was precipitated by the dropwise addition of pyridine (2 mL) and then bubbling air through the solution for 15 min. The content of the flask was filtered through 5 cm of silica gel that was eluted with chloroform. The filtrate was evaporated and the residue subjected to flash chromatography (EtOAc/hexanes 1:2) that afforded 7.62 g (10.12 mmol; 66%) of white solid product **2**. $[\alpha]_D^{20}$ −10.3 (c 1.07, $CHCl_3$); mp 148.0–149.0°C; R_f 0.37 (EtOAc/hexanes 5:6); IR (film, cm^{-1}) 1748.6 (C=O); ^{13}C NMR: δ 170.39, 170.24, 170.11, 169.94, 169.60, 169.21, 168.96 (acetate COs), 100.72 (C-1′), 78.49 (C-2), 76.65 (C-5), 76.39 (C-6), 74.16 (C-4), 72.94 (C-3′), 71.88 (C-5′), 71.61 (C-2′), 69.03 (C-3), 67.84 (C-4′), 62.26 (C-1,7), 61.56 (C-6′), 20.69, 20.62, 20.54, 20.44 (acetate CH_3s), 6.54, 6.13, 6.10, −5.08 (silyl CHs); FABMS (3-NBA): *m/z* 773 $[M+Na]^+$; HR-FABMS: calcd for $C_{32}H_{50}NaO_{18}Si$ *m/z* 773.2664; found 773.2635.

(Hepta-*O*-acetyl-β-D-cellobiosyl)methanol (3). To a solution of compound **2** (1.62 g; 2.16 mmol) in THF (5.5 mL) at 0°C, HOAc (2.5 mL) and water (1.5 mL) were added. The reaction mixture was stirred for 9 h. The THF was then evaporated and the remaining suspension was diluted with CH_2Cl_2 (large excess). The solution was washed successively with saturated aqueous sodium bicarbonate and with a phosphate buffer (pH=7). The organic layer was then separated, dried over $MgSO_4$ and the solvent evaporated. The resultant compound was purified by flash chromatography (EtOAc/hexanes 1:1) to furnish **3** as a beige-white solid (1.29 g; 1.98 mmol, 92%). $[\alpha]_D^{20}$ −13.6 (c 0.96, $CHCl_3$); mp 198.0–198.5°C; R_f 0.15 (EtOAc/hexanes 2:1), 0.54 (EtOAc); IR (film, cm^{-1}) 3495.1 (O–H), 1748.6 (C=O); ^{13}C NMR δ 170.39, 170.32, 170.26, 170.11, 169.81, 169.21, 168.96 (acetate COs), 100.69 (C-1′), 77.87 (C-2), 76.64 (C-6), 76.49 (C-5), 73.54 (C-4), 72.87 (C-3′), 71.89 (C-5′), 71.56 (C-2′), 68.75 (C-3), 67.77 (C-4′), 62.15 (C-7), 61.53 (C-6′), 61.28 (C-1), 20.76, 20.55, 20.47, 20.42 (acetate CH_3s);^1H NMR: δ 5.23 (t, 1H, $J_{4,3}$=$J_{4,5}$=9.3 Hz, H-4), 5.15 (t, 1H, $J_{3',2'}$=$J_{3',4'}$=9.3 Hz, H-3′), 5.07 (t, 1H, $J_{4',5'}$=9.7 Hz, H-4′), 4.96 (t, 1H, $J_{3,2}$=9.7 Hz, H-3), 4.93 (t, 1H, H-2′), 4.52 (d, 1H, $J_{1',2'}$=8.0 Hz, H-1′), 4.51 (dd, 1H, $J_{7b,6}$=1.8 Hz, H-7b), 4.38 (dd, 1H, $J_{6'a,6'b}$=12.5 Hz, $J_{6'b,5'}$=4.3 Hz, H-6′b), 4.09 (dd, 1H, $J_{7a,7b}$=12.1, $J_{7a,6}$=5.3 Hz, H-7a), 4.05 (dd, 1H, $J_{6'a,5'}$=2.2 Hz, H-6′a), 3.75 (t, 1H, $J_{5,6}$=9.7 Hz, H-5), 3.71 (dd, 1H, $J_{1a,1b}$=12.4 Hz, $J_{1b,2}$=1.9 Hz, H-1b), 3.67 (ddd, 1H, H-5′), 3.61 (ddd, 1H, H-6), 3.54 (dd, 1H, $J_{1a,2}$=4.9 Hz, H-1a), 3.50 (ddd, 1H, H-2), 2.33 (s, broad, 1H, O–H), 2.15–1.90 (7s, 21H, acetate CH_3s). Anal. calcd for $C_{27}H_{38}O_{18}$: C, 49.85; H, 5.89; found: C, 50.42; H, 5.99.

(Hepta-*O*-acetyl-β-D-cellobiosyl)iodomethane (4). A mixture of compound **3** (1.33 g; 2.04 mmol), triphenylphosphine (0.83 g; 3.2 mmol), imidazole (0.45 g; 6.6 mmol) and iodine (0.78 g; 3.1 mmol) in THF (35 mL) was stirred under reflux for 3.5 h. THF was then evaporated, the crude product was dissolved in CH_2Cl_2 (100 mL) and solids were removed by filtration. An equal volume of saturated aqueous sodium bicarbonate was added and the mixture was stirred for 10 min. Iodine was added in portions and when the organic phase remained iodine-colored, the mixture was stirred for an additional 10 min. Excess iodine was destroyed by the

addition of saturated aqueous sodium thiosulfate. The organic layer was diluted with CH_2Cl_2 (100 mL), separated, washed with water (100 mL), dried over $MgSO_4$, and concentrated to afford a solid residue. The product was purified by flash chromatography (EtOAc/hexanes, 1:3→1:1 gradient), thus affording compound **4** (1.38 g, 1.82 mmol, 89%). $[\alpha]_D^{20}$ −32.5 (c 0.94, $CHCl_3$); mp 211.0–212.0°C; R_f 0.40 (EtOAc/hexanes 1:1); ^{13}C NMR δ 170.44, 170.29, 170.16, 169.83, 169.62, 169.25, 169.00 (acetate COs), 100.79 (C-1′), 76.69 (C-5), 76.65 (C-6), 76.60 (C-2), 73.34 (C-4), 72.90 (C-3′), 72.32 (C-3), 71.97 (C-5′), 71.58 (C-2′), 67.78 (C-4′), 61.88 (C-7), 61.55 (C-6′), 20.90, 20.68, 20.63, 20.50 (acetate CH_3s), 3.54 (C-1); ^1H NMR: δ 5.18 (t, 1H, $J_{4,3}=J_{4,5}=9.2$ Hz, H-4), 5.15 (t, 1H, $J_{3',2'}=J_{3',4'}=9.3$ Hz, H-3′), 5.07 (t, 1H, $J_{4',5'}=9.5$ Hz, H-4′), 4.93 (t, 1H, H-2′), 4.85 (t, 1H, $J_{3,2}=9.50$ Hz, H-3), 4.52 (dd, 1H, $J_{7b,7a}=12.0$ Hz, $J_{7b,6}=2.0$ Hz, H-7b), 4.50 (d, 1H, $J_{1',2'}=7.9$ Hz, H-1′), 4.39 (dd, 1H, $J_{6'a,6'b}=12.5$ Hz, $J_{6'b,5'}=4.3$ Hz, H-6′b), 4.12 (dd, 1H, $J_{7a,6}=5.4$ Hz, H-7a), 4.04 (dd, 1H, $J_{6'a,5'}=2.3$ Hz, H-6′a), 3.75 (t, 1H, $J_{5,6}=9.3$ Hz, H-5), 3.66 (ddd, 1H, H-5′), 3.63 (ddd, 1H, H-6), 3.37 (ddd, 1H, $J_{2,1a}=7.1$ Hz, $J_{2,1b}=2.7$ Hz, H-2), 3.29 (dd, 1H, $J_{1b,1a}=11.1$ Hz, H-1b), 3.10 (dd, 1H, H-1a), 2.15–1.95 (7s, 21H, acetate CH_3s). Anal. Calcd for $C_{27}H_{37}O_{17}I$: C, 42.64; H, 4.90; I, 16.69; found: C, 42.94; H, 5.07; I, 16.48.

(Hepta-*O*-acetyl-β-D-cellobiosyl)nitromethane (5). Compound **4** (0.65 g; 0.86 mmol) was dissolved in a mixture of DMSO (2 mL) and DMF (6 mL). Phloroglucinol dihydrate (0.08 g; 0.49 mmol) and sodium nitrite (0.26 g; 3.8 mmol) were added and the mixture was stirred for 3 days at r.t. The solution was then poured onto ice (50 g) and the mixture was stored in a freezer for 10 min. The suspension was allowed to warm up slightly, the precipitate was filtered (Büchner) and washed with ice–water until the filtrate remained clear. The precipitate was dried and submitted to flash chromatography (EtOAc/hexanes 1:1) to furnish white solid **5** (0.41 g; 0.60 mmol; 71% yield). $[\alpha]_D^{20}$ −26.2 (c 1.09, $CHCl_3$); mp 215.0–216.0°C; R_f 0.24 (EtOAc/hexanes 1:1); IR (film, cm^{-1}) 1560.6, 1369.7 (NO_2); ^{13}C NMR: δ 170.32, 170.06, 169.76, 169.57, 169.18, 168.89 (acetate COs), 100.61 (C-1′), 76.81 (C-5′), 76.10 (C-5), 75.62 (C-1), 74.08 (C-2), 73.17 (C-4), 72.80 (C-3′), 71.96 (C-6), 71.51 (C-2′), 69.42 (C-3), 67.87 (C-4′), 61.67 (C-6′), 61.60 (C-7), 20.55, 20.51, 20.37 (acetate CH_3s); ^1H NMR: δ 5.23 (t, 1H, $J_{4,3}=J_{4,5}=9.1$ Hz, H-4), 5.14 (t, 1H, $J_{3',2'}=J_{3',4'}=9.3$ Hz, H-3′), 5.06 (t, 1H, $J_{4',5'}=9.4$ Hz, H-4′), 4.92 (t, 1H, H-2′), 4.87 (t, 1H, $J_{3,2}=9.5$ Hz, H-3), 4.50 (d, 1H, $J_{1',2'}=7.9$ Hz, H-1′), 4.50–4.34 (overlapping dd, 4H, H-1a,1b,6′b,7b), 4.22 (qd, 1H, $J_{2,1a\text{ or }1b}=2.9$ Hz, $J_{2,1b\text{ or }1a}=9$ Hz, H-2), 4.12 (dd, 1H, $J_{7a,7b}=12.1$, $J_{7b,6}=5.3$ Hz, H-7a), 4.05 (dd, 1H, $J_{6'a,6'b}=12.4$, $J_{6'a,5'}=2.1$ Hz, H-6′a), 3.77 (t, 1H, $J_{5,6}=9.5$ Hz, H-5), 3.66 (m, 1H, H-6), 3.65 (m, 1H, H-5′), 1.9–2.2 (7s, 21H, acetate CH_3s). Anal. calcd for $C_{27}H_{37}NO_{19}$: C, 47.72; H, 5.49; N, 2.06; found: C, 47.94; H, 5.63; N, 2.00.

Methyl 9,10,13-tri-*O*-acetyl-11-*O*-(tetra-*O*-acetyl-β-D-glucopyranosyl)-8,12-anhydro-2,3,4-tri-*O*-benzyl-7-deoxy-7-nitro-α-D-*arabino*-D-*manno*-D-*gluco*-trideco-1,5-pyranoside (7). To a solution of aldehydo-sugar **6** (Ref. 19) (2.03 g; 4.34 mmol; 1.5 eq.) in dry CH_3CN (30 mL) were added nitro sugar **5** (1.99 g; 2.93 mmol), KF (0.26 g; 4.82 mmol; 1.7 eq.) and 18-crown-6 ether (0.14 g; 0.05 mmol). The mixture was stirred for 6 h at r.t. The solution was then concentrated to dryness and the residue dissolved in CH_2Cl_2 (100 mL). The solution was then washed with water (2×40 mL), dried over Na_2SO_4, and concentrated. The residual product was submitted to flash chromatography (EtOAc/hexanes 5:6) which afforded compound **7** (1.46 g, 1.28 mmol; 44% yield) as a white solid (single stereoisomer). Some starting material (**5**) could be recovered (yield based on nitro sugar consumed: 73%). $[\alpha]_D^{20}$ −3.2 (c 4.0, $CHCl_3$); mp 237.0–238.0°C; R_f 0.18 (EtOAc/hexanes 1:1); IR (film, cm^{-1}) 3483.3 (OH), 1754.5 (CO), 1552.8 and 1367.2 (NO_2); ^{13}C NMR: δ 170.44, 170.18, 170.12, 170.02, 169.24, 168.99, 168.86 (acetate COs), 138.54, 137.99 (2)(ArCs), 128.77, 128.49, 128.39, 128.05, 128.00, 127.95, 127.66 (ArCHs), 100.80 (C-1′), 98.86 (C-1), 84.32 (C-7), 81.51 (C-3), 79.49 (C-2), 77.19 (C-12), 76.34 (C-4), 76.05 (C-11), 75.79, 74.79, 73.48 (3 benzyl CH_2s), 74.13 (C-3′), 74.13 (C-8), 72.87 (C-10), 72.03 (C-5′), 71.59 (C-9), 69.38 (C-5), 68.56 (C-2′), 67.76 (C-4′), 66.18 (C-6), 61.51 (C-6′), 61.30 (C-13), 55.83 (CH_3), 20.59, 20.51, 20.46, 20.25 (acetates CH_3s); ^1H NMR: δ 7.22–7.45 (m, 15H, ArHs), 5.15, 5.14 (2t, 2H, J=9.4, 9.0 Hz, H-3′,10), 5.09 (t, 1H, $J_{3',4'}=J_{4',5'}=9.7$ Hz, H-4′), 4.97 (d, 1H, J=10.4 Hz), 4.88 (d, 1H, J=11.1 Hz), 4.81 (d, 1H, J=12.5 Hz), 4.81 (d, 1H, J=10.4 Hz), 4.71 (d, 1H, J=11.4 Hz) and 4.62 (d, 1H, J=12.7 Hz) (3AB, 3 CH_2Ph), 4.95 (t, 1H, H-9), 4.92 (t, 1H, H-2′), 4.70 (dd, 1H, $J_{7,8}=2.3$, $J_{7,6}=8.9$ Hz, H-7), 4.65 (dd, 1H, $J_{13b,13a}=12.1$, $J_{13b,12}=2.3$ Hz, H-13b), 4.59 (broad m, 1H, H-6), 4.55 (d, 1H, $J_{1,2}=3.5$ Hz, H-1), 4.51 (d, 1H, $J_{1',2'}=7.9$ Hz, H-1′), 4.36 (dd, 1H, $J_{6'a,6'b}=12.6$, $J_{6'b,5'}=4.3$ Hz, H-6′b), 4.12 (dd, 1H, $J_{8,9}=10.3$ Hz, H-8), 4.03 (dd, 1H, $J_{6'a,5'}=2.2$ Hz, H-6′a), 3.98 (2dd, 2H, $J_{13a,12}=5$, $J_{3,4}=8$ Hz, H-3,13a), 3.74 (t, 1H, $J_{10,11}=J_{11,12}=9.6$ Hz, H-11), 3.65 (ddd, 1H, H-5′), 3.62 (distorted dd, 1H, $J_{3,4}=8.1$, $J_{4,5}=10$ Hz, H-4), 3.58 (br distorted d, $J_{5,6}\leq 1$ Hz, H-5), 3.57 (ddd, 1H, H-12), 3.45 (dd, 1H, $J_{2,3}=9.7$ Hz, H-2), 3.27 (s, 3H, OCH_3), 1.90–2.20 (several s, 21H, acetate CH_3s); FABMS (3-NBA+Na^+): *m/z* 1164 $[M+Na]^+$; HR-FABMS: calcd for $C_{55}H_{67}NNaO_{25}$ *m/z* 1164.3900; found 1164.3867.

***Z*- and *E*-Methyl 9,10,13-tri-*O*-acetyl-11-*O*-(tetra-*O*-acetyl-β-D-glucopyranosyl)-8,12-anhydro-2,3,4-tri-*O*-benzyl-6,7-dideoxy-7-nitro-α-D-*glycero*-D-*gulo*-D-*gluco*-tridec-6-eno-1,5-pyranoside (8).** To a solution of compound **7** (780.0 mg; 0.683 mmol) in CH_2Cl_2 (5 mL) at 0°C was added freshly distilled Ac_2O (1.2 mL; 13 mmol) and pyridine (0.75 mL; 9.3 mmol). The mixture was allowed to warm up to r.t. and maintained in absence of light for 54 h. The reaction mixture was then diluted with CH_2Cl_2 (100 mL) and washed successively with 1M aq HCl (2×10 mL), aq $NaHCO_3$ (5% w/v; 2×20 mL) and water (2×20 mL). The solution was then dried over Na_2SO_4 and concentrated. Flash chromatography (EtOAc/hexanes 2:3) of the residue afforded 99.1 mg of *E*-**8**, 104.4 mg of *Z*-**8**, and 442.7 mg of a mixture of *E*-**8** and *Z*-**8**; total yield: 86%. *Z*-**8**: mp 174.5–175.5°C, light yellow solid; R_f 0.29 (EtOAc/hexanes 2:3); ^1H NMR: δ 6.15 (dd, 1H, $J_{6,5}=9.7$ Hz, $^4J_{6,8}=1.4$ Hz, H-6), 3.87 (dd, 1H, $J_{8,9}=9.8$ Hz, H-8); FABMS (3-NBA+Na^+): *m/z* 1146 $[M+Na]^+$, also

observed: 1206 $[M+HOAc+Na]^+$; HR-FABMS: calcd for $C_{55}H_{65}NNaO_{24}$ *m/z* 1146.3794; found 1146.3824. ***E*-8**: $[\alpha]_D^{20}$+15.0 (c 1.8, $CHCl_3$); mp 80.5–81.5°C, white solid; R_f 0.37 (EtOAc/hexanes 2:3); IR (film, cm^{-1}) 1538 and 1367 (NO_2); ^{13}C NMR: δ 171.0–169.0 (acetate COs), 148.56 (C-7), 137.90, 137.80, 137.05 (ArCs), 136.60 (C-6), 128.5–127.0 (ArCHs), 100.88 (C-14), 98.84 (C-1), 81.32, 80.01, 79.54, 77.04, 75.95, 75.78, 75.06, 73.69, 73.50, 72.93, 72.21, 72.00, 71.62, 70.33, 67.71, 65.91, 61.48, 61.37, 56.49 (OCH_3), 20.9–20.1 (acetate CH_3s); ^1H NMR: δ 6.86 (d, 1H, $J_{6,5}$=6.5 Hz, H-6); FABMS (3-NBA+Na^+): *m/z* 1146 $[M+Na]^+$; HR-FABMS: calcd for $C_{55}H_{65}NNaO_{24}$ *m/z* 1146.3794; found 1146.3805.

Methyl 9,10,13-tri-*O*-acetyl-11-*O*-(tetra-*O*-acetyl-β-D-glucopyranosyl)-8,12-anhydro-2,3,4-tri-*O*-benzyl-6,7-dideoxy-7-nitro-α-D-*erythro*-(L-*talo* and L-*galacto*)-D-*gluco*-trideco-1,5-pyranoside (9). To a solution of compound **8** (*E*,*Z* mixture; 442.7 mg; 0.403 mmol) in CH_2Cl_2 (2 mL) at 0°C was added a solution of $NaBH_4$ (0.07 g; 1.9 mmol; 4.7 eq.) in EtOH (10 mL). The mixture was stirred for 13 h. The solution was then diluted with EtOAc (100 mL), washed with water (2×25 mL), dried over Na_2SO_4 and concentrated. Flash chromatography of the residue (EtOAc/hexanes 5:6) furnished a homogeneous mixture of 7(*R*) and 7(*S*) epimers (white solid; 199 mg; 45% yield). R_f 0.42 (EtOAc/hexanes 1:1); IR (film, cm^{-1}) 1560 and 1368.5 (NO_2);^{13}C NMR (mixture of epimers, all signals are given): δ 170.4–169.0 (acetate COs), 138.53, 138.23, 138.03, 137.94 (ArCs), 128.5–127.0 (ArCHs), 100.84, 100.69 (C-14s), 98.03 (C-1s), 86.40, 82.82, 81.63, 81.54, 81.38 (2C), 79.89, 79.78, 77.05, 76.78, 76.14 (2C), 75.80, 75.67, 74.83, 73.89, 73.53, 73.30, 72.85, 72.07, 71.58, 70.18, 68.94, 67.80, 66.29, 61.87, 61.60, 55.69, 55.42 (OCH_3s), 31.18, 30.57 (C-6s), 20.6–20.3 (acetate CH_3s); FABMS (3-NBA+Na^+): *m/z* 1148 $[M+Na]^+$; HR-FABMS: calcd for $C_{55}H_{67}NNaO_{24}$ *m/z* 1148.3951; found 1148.3973.

Methyl 9,10,13-tri-*O*-acetyl-11-*O*-(tetra-*O*-acetyl-β-D-glucopyranosyl)-8,12-anhydro-2,3,4-tri-*O*-benzyl-6,7-dideoxy-α-D-*glycero*-D-*gulo*-D-*gluco*-trideco-1,5-pyranoside (10). A solution of tridecoside (**9**) (199 mg; 0.182 mmol) in dry toluene was purged with dry, deoxygenated N_2 and then heated under reflux. To this hot solution was added a solution of Bu_3SnH (0.255 mL; 0.948 mmol) and AIBN (16 mg; 0.097 mmol) in degassed toluene (10 mL). The resulting solution was stirred under reflux for 30 min. The toluene was then removed under vacuum. The resulting residue was dissolved in a minimum amount of $CHCl_3$ and applied to a column of silica gel; the column was flushed with several volumes of hexane (to remove tin by-products) and then eluted with EtOAc/hexanes (1:2) to afford 106 mg (0.1 mmol) of white solid product (56% yield). $[\alpha]_D^{20}$ −7.6 (c 5.5, $CHCl_3$); mp 168–169°C; R_f 0.32 (EtOAc/hexanes 1:1); IR (film, cm^{-1}) 1755.2 (C=O); ^{13}C NMR: δ 170.39, 170.25, 170.11, 169.87, 169.78, 169.22, 168.99 (acetate COs), 138.70, 138.17, 138.14 (ArCs), 128.7–127.5 (ArCHs), 100.77 (C-1′), 97.74 (C-1), 82.07 (C-4), 81.92 (C-3), 80.09 (C-2), 77.70 (C-8), 76.85 (C-11), 76.46 (C-12), 75.69 (benzyl CH_2), 75.19 (benzyl CH_2), 74.09 (C-3′), 73.24 (benzyl CH_2), 72.95 (C-10), 72.30 (C-9), 71.91 (C-5′), 71.62 (C-2′), 70.27 (C-5), 67.86 (C-4′), 62.43 (C-13), 61.59 (C-6′), 54.93 (OCH_3), 27.77 (C-6), 27.17 (C-7), 20.67, 20.61, 20.55, 20.46 (acetate CH_3s); ^1H NMR: δ 7.43–7.22 (m, 15H, ArH's), 5.14 (t, 1H, $J_{3',2'}$=$J_{3',4'}$=9.3 Hz, H-3′), 5.12 (t, 1H, $J_{10,9}$=$J_{10,11}$=9.3 Hz, H-10), 5.06 (t, 1H, $J_{4',5'}$=9.6 Hz, H-4′), 4.96 (d, 1H, *J*=10.9 Hz), 4.87 (d, 1H, *J*=10.9 Hz), 4.79 (d, 1H, *J*=10.7 Hz), 4.78 (d, 1H, *J*=12 Hz), 4.65 (d, 1H, *J*=12.1 Hz) and 4.59 (d, 1H, *J*=10.8 Hz) (3 AB, 3 OCH_2Ph), 4.92 (dd, 1H, $J_{1',2'}$=8.2, $J_{2',3'}$=9 Hz, H-2′), 4.76 (t, 1H, $J_{9,8}$=9.5 Hz, H-9), 4.51 (d, 1H, $J_{1,2}$=4.1 Hz, H-1), 4.49 (d, 1H, $J_{1',2'}$=8.3 Hz, H-1′), 4.43 (dd, 1H, $J_{13b,13a}$=11.9, $J_{13b,12}$=1.7 Hz, H-13b), 4.37 (dd, 1H, $J_{6'b,6'a}$=12.5 Hz, $J_{6'b,5'}$=4.3 Hz, H-6′b), 4.04 (m, 2H, H-6′a,13a), 3.93 (t, 1H, $J_{3,2}$=$J_{3,4}$=9.2 Hz, H-3), 3.71 (t, 1H, $J_{11,12}$=9.6 Hz, H-11), 3.64 (ddd, 1H, $J_{5',6'a}$=2.4 Hz, H-5′), 3.55 (m, 1H, H-5), 3.51 (m, 1H, H-12), 3.48 (dd, 1H, H-2), 3.34 (m, 1H, H-8), 3.315 (s, 3H, OCH_3), 3.13 (t, 1H, $J_{4,5}$=9.2 Hz, H-4), 2.1–1.9 (several s, 21H, acetate CH_3s), 2.08 (m, 1H, H-6b), 1.72 (m, 1H, H-7b), 1.36 (m, 1H, H-7a), 1.30 (m, 1H, H-6a); FABMS (3-NBA+Na^+): *m/z* 1103 $[M+Na]^+$; HR-FABMS: calcd for $C_{55}H_{68}NaO_{22}$ *m/z* 1103.4100; found 1103.4067. Anal. calcd for $C_{55}H_{68}O_{22}$: C, 61.10; H, 6.34; found: C, 60.91; H, 6.27.

Methyl 8,12-anhydro-6,7-dideoxy-11-*O*-(β-D-glucopyranosyl)-α-D-*glycero*-D-*gulo*-D-*gluco*-trideco-1,5-pyranoside (12). To a solution of compound **10** (51.2 mg; 0.0486 mmol) in EtOH (40 mL) was added $Pd(OH)_2$ (20% on C, 70 mg) and AcOH (0.05 mL). The mixture was degassed and then hydrogenated (H_2, 1 atm) for 2 days at r.t. under vigorous stirring. The mixture was then diluted with EtOH (50 mL) and the catalyst removed by filtration through a nylon membrane (0.45 μm). The filtrate was concentrated and the resultant clear syrupy product (**11**) was used in the next step without further purification. ^{13}C NMR of **11** (CD_3OD): δ 172.58, 172.21, 172.12, 171.64, 171.22, 171.01, 101.85, 101.13, 79.03, 78.44, 77.90, 75.75 (2C), 75.14, 74.50, 73.99, 73.73, 73.16, 72.90, 72.39, 69.37, 64.12, 62.88, 55.50, 28.92, 28.59, 21.00, 20.78, 20.66, 20.62, 20.53. To a solution of crude **11** obtained above in MeOH (40 mL) was added a 0.3M solution of MeONa in MeOH (4 mL). The mixture was stirred for 30 h, then neutralized with Amberlite IR-120 (H^+) resin and treated with activated charcoal (spatula tip). The suspension was filtered and the solvent evaporated. The residual syrup was then redissolved in H_2O (10 mL) by brief sonication, the solution washed with CH_2Cl_2 (3×10 mL) and concentrated under high vacuum to afford compound **12** (24.2 mg; 97%) as a light yellow syrup. $[\alpha]_D^{20}$+37.6 (c 1.17, CH_3OH); R_f 0.64 ($CHCl_3$/EtOAc/MeOH/H_2O 3.5:3.5:8:2); IR (film, cm^{-1}) 3364 (v br O–H); ^{13}C NMR (CD_3OD): δ 104.64, 101.10, 81.42, 81.05, 80.16, 78.12 (2C), 77.88, 75.77, 75.35, 75.10, 74.96, 73.76, 72.73, 71.40, 62.46, 62.36, 55.50, 29.14, 28.77; ^1H NMR (CD_3OD): δ 4.56 (d, 1H, $J_{1,2}$=3.7 Hz, H-1), 4.34 (d, 1H, $J_{1',2'}$=7.8 Hz, H-1′); FABMS [(−)-ions, glycerol+thioglycerol]: *m/z* 515 $[M-H]^-$; HR-FABMS (−): calcd for $C_{20}H_{35}O_{15}$ *m/z* 515.1976; found 515.1969.

(Hepta-*O*-acetyl-β-D-cellobiosyl)methanol methoxymethyl ether (13). Dimethoxymethane (20 mL; 230.0 mmol) was added to compound **3** (1.45 g; 2.23 mmol) followed by $CHCl_3$ (27 mL) and phosphorus

pentoxide (3 g). The reaction mixture was vigorously stirred for 1 h. The mixture was then cooled in an ice bath, neutralized with aqueous Na_2CO_3, transferred to a separating funnel and extracted with ether (3×100 mL). The organic phases were combined, washed with brine (3×10 mL), and the solvent was evaporated. The residual solid was then redissolved in CH_2Cl_2, the solution dried over Na_2SO_4 and concentrated to yield a yellowish-white solid (1.44 g; 93%). The protected disaccharide was used without further purification in the next step. A sample was purified by flash chromatography (EtOAc/hexanes 2:1): $[\alpha]_D^{20}$ −18.5 (c 1.49, $CHCl_3$); mp 168.5–169.5°C; R_f 0.45 (EtOAc/hexanes 2:1); ^{13}C NMR: δ 170.39, 170.22, 170.09, 169.89, 169.63, 169.20, 168.97, 100.79, 96.66 (MOM-CH_2), 77.01, 76.66, 76.57, 74.07, 72.95, 71.96, 71.62, 69.10, 67.85, 66.04, 62.26, 61.59, 55.27, 20.79, 20.60, 20.55, 20.48. Anal. calcd for $C_{29}H_{42}O_{19}$: C, 50.14; H, 6.09; found: C, 50.16; H, 6.08.

(Hepta-*O*-benzyl-β-D-cellobiosyl)methanol (16). To a suspension of compound **13** (1.35 g; 1.94 mmol) in dry MeOH (95 mL) was added a 5.2M solution of MeONa in MeOH (5 mL). The reaction was vigorously stirred for 24 h. The solution was then neutralized with Amberlite IR-120(H^+) resin (prewashed by refluxing with MeOH in a Soxhlet extractor), the resin was removed by filtration and the solvent was evaporated. The residual solid was then dissolved in CH_2Cl_2, the solution dried over Na_2SO_4, and concentrated to yield crude (β-D-cellobiosyl)methanol methoxymethyl ether (**14**) as a clear syrup in essentially quantitative yield: R_f 0.65 ($CHCl_3$/EtOAc/CH_3OH/H_2O 3.5/3.5/8/2); ^{13}C NMR (D_2O): δ 102.59, 96.30 (MOM-CH_2), 78.82, 78.47, 77.94, 76.05, 75.91, 75.58, 73.24, 69.69, 69.52, 66.97, 60.65, 60.36, 55.20. DMF (40 mL) was added to crude **14** (0.86 g; 2.2 mmol). To the resulting, vigorously stirred suspension was added hexane-washed NaH (60% dispersion in mineral oil, 0.91 g) followed, after cooling to 0°C, by BnBr (2.2 mL; 18.5 mmol). The ice bath was removed and the mixture was stirred for 29 h at r.t. The reaction was quenched by the addition of MeOH (10 mL) and the mixture was stirred for an additional 20 min. The solution was then concentrated to about one-third of its original volume and the product precipitated by pouring the solution onto ice-water (200 mL). The precipitate was then collected on a ice-cooled Büchner funnel, washed with water and then with cold MeOH. The beige-white solid was allowed to dry in the open air. The product was dissolved in CH_2Cl_2, the solution dried over Na_2SO_4 and concentrated to give crude (hepta-*O*-benzyl-β-D-cellobiosyl)methanol methoxymethyl ether (**15**) (2.34 g, ≈100%; syrup). This product was used without further purification in the next step. (**15**): R_f 0.49 (EtOAc/hexanes 1:2); ^{13}C NMR: δ 139.4–138.2 (ArCs), 130.9–127.1 (ArCHs), 102.46, 96.74 (MOM-CH_2), 85.40, 84.97, 82.80, 79.22, 78.89, 78.16, 77.80, 77.20, 76.65, 75.62, 75.10, 74.99 (2C), 74.81, 73.27 (2C), 69.05, 68.17 (2C), 66.99, 55.24. Crude **15** (2.50 g; 2.46 mmol) was dissolved in a mixture of THF (20 mL), H_2O (5 mL) and 6M aq HCl (26 mL). The reaction was stirred under reflux for 12 h. The mixture was then neutralized by adding an equal volume of saturated aqueous sodium bicarbonate. The solution was extracted with CH_2Cl_2 (3×50 mL), the organic phases were combined, washed with H_2O (3×10 mL), dried over $MgSO_4$ and concentrated. Purification of the residual product by flash chromatography (EtOAc/hexanes, 1:3→1:1) afforded compound **16** as a slightly opaque syrup (1.23 g; 1.26 mmol; 51%). $[\alpha]_D^{21}$ +18.3 (c 0.93, $CHCl_3$); R_f 0.25 (EtOAc/hexanes 1:2); IR (film, cm^{-1}) 3448 (OH); ^{13}C NMR: δ 139.4, 138.63, 138.59, 138.44, 138.30, 138.19, 138.00 (ArCs), 128.4–127.2 (ArCHs), 102.47 (C-1′), 85.19 (C-2), 84.95 (C-4′), 82.80 (C-3′), 79.28 (C-2′), 78.99 (C-5), 78.16 (C-5′), 77.66 (C-6), 76.73 (C-3), 75.62 (benzyl CH_2), 75.20 (C-4), 75.14, 75.05, 75.00, 74.81, 73.33 (benzyl CH_2s), 69.08 (C-6′), 68.30 (C-7), 62.53 (C-1); FABMS (3-NBA+Na^+): *m/z* 1009 $[M+Na]^+$; HR-FABMS: calcd for $C_{62}H_{66}NaO_{11}$ *m/z* 1009.4503; found 1009.4484.

(Hepta-*O*-benzyl-β-D-cellobiosyl)iodomethane (17). Compound **16** (1.21 g; 1.24 mmol) was dissolved in THF (35 mL). Iodine (0.51 g; 2.0 mmol), imidazole (0.27 g; 4.0 mmol) and triphenylphosphine (0.50 g; 1.9 mmol) were added to the solution. The mixture was vigorously stirred under reflux for 24 h. Additional amounts of each reagent were added after 8 h (total number of equivs. of reagents added: 3.0, 6.0, and 3.0, respectively). The solvent was then evaporated and the solid dissolved in CH_2Cl_2 (100 mL). The reaction mixture was processed by slowly adding an equal volume of saturated aqueous sodium bicarbonate, followed by iodine in portions until the organic phase remained iodine-colored; the mixture was stirred for 10 min. Excess iodine was destroyed by the addition of saturated aqueous sodium thiosulfate. The organic layer was separated, dried over $MgSO_4$ and concentrated. The residue was submitted to flash chromatography (EtOAc/hexanes, 1:10→1:5) which afforded white solid **17** (0.78 g; 0.92 mmol; 74%). $[\alpha]_D^{21}$ +51.5 (c 1.24, $CHCl_3$); mp 113.0–114.0°C; R_f 0.66 (EtOAc/hexanes 1:2); ^{13}C NMR: δ 138.66, 138.43 (2C), 138.29 (2C), 138.17 (2C) (ArCs), 128.4–127.3 (ArCHs), 102.45 (C-1′), 84.99 (C-4′), 84.87 (C-3′), 82.88 (C-2′), 80.97 (C-5′), 79.49 (C-6), 78.19 (C-4), 77.57 (C-2), 76.66 (C-5), 75.64, 75.34, 75.21 (benzyl CH_2s), 75.16 (C-3), 75.04, 74.83, 73.35 (2C) (benzyl CH_2s), 69.06 (C-6′), 67.93 (C-7), 7.61 (C-1). Anal. calcd. for $C_{62}H_{65}IO_{10}$: C, 67.88; H, 5.97; Found: C, 68.01; H, 6.10; FABMS (3-NBA+Na^+): *m/z* 1119 $[M+Na]^+$; HR-FABMS: calcd for $C_{62}H_{65}INaO_{10}$ *m/z* 1119.3520; found 1119.3521.

(Hepta-*O*-benzyl-β-D-cellobiosyl)nitromethane (18). Compound **17** (0.76 g; 0.67 mmol) was dissolved in a mixture of DMSO (5 mL) and DMF (25 mL). To the solution were added $NaNO_2$ (0.14 g; 2.0 mmol) and phloroglucinol dihydrate (0.15 g; 1.0 mmol). The mixture was stirred at r.t. for 4 days. In the course of the reaction, additional amounts of reagents were added (total amount of $NaNO_2$, 4 mmol; phloroglucinol, 1.4 mmol). Approximately 15 mL of DMF was then evaporated under high vacuum. The mixture was poured onto ice-water (300 mL). The resulting precipitate was collected on a cooled Büchner funnel and dried in the open air for 24 h. The product was then purified by flash chromatography (EtOAc/hexanes 1:4), to afford white solid **18** (0.51 g; 75% yield). $[\alpha]_D^{21}$ −1.7 (c 1.18, $CHCl_3$); mp 142.5–143.5°C; R_f 0.60 (EtOAc/hexanes 1:2); IR (film, cm^{-1}) 1557.0, 1360.8 (NO_2); ^{13}C NMR: δ 138.95, 138.57,

138.54, 138.29, 138.25, 137.92, 137.51 (ArCs), 128.6–127.3 (ArCHs), 102.37 (C-1′), 85.12 (C-4), 84.90 (C-3′), 82.78 (C-2′), 79.29 (C-6), 78.09 (C-4′), 77.18 (C-3), 76.35 (C-1), 76.06 (C-5), 75.70 (C-2), 75.19 (C-5′), 69.06 (C-6′), 67.49 (C-7), 75.61, 75.31, 75.04, 74.80 (2C), 73.29 (2C) (benzyl CH_2s); ^{1}H NMR: δ 7.42–7.14 (m, 35H, ArHs), 5.22 (d, 1H, J=11.2 Hz), 4.96–4.69 (several d, 6H) and 4.57–4.37 (several d, 7H) (7 OCH_2Ph), 4.50 (d, 1H, H-1′), 4.43 (dd, 1H, H-1b), 4.22 (dd, 1H, $J_{1b,1a}$=13.1, $J_{1a,2}$=8.9 Hz, H-1a), 4.07 (t, 1H, $J_{5,4}$=$J_{5,6}$=9.5 Hz, H-5), 3.97 (td, 1H, $J_{1b,2}$=1.6, $J_{2,3}$=10 Hz, H-2), 3.82 (dd, 1H, $J_{7b,7a}$=11.4, $J_{7b,6}$=3.1 Hz, H-7b), 3.73 (dd, 1H, $J_{6'b,6'a}$=11.0, $J_{6'b,5'}$=1.9 Hz, H-6′b), 3.67 (t, 1H, J=8.8 Hz, H-4), 3.60 (t, 1H, $J_{4',3'}$=$J_{4',5'}$=9.0 Hz, H-4′), 3.57 (m, 1H, H-7a), 3.54 (m, 1H, H-6′a), 3.53 (t, 1H, J=9.0 Hz, H-3′), 3.39 (dd, 1H, $J_{1',2'}$=7.9, $J_{2',3'}$=8.7 Hz, H-2′), 3.34 (ddd, 1H, H-5′), 3.29 (m, 1H, H-6), 3.27 (dd, 1H, H-3). Anal. calcd for $C_{62}H_{65}NO_{12}$: C, 73.28; H, 6.45; N, 1.38; found: C, 73.10; H, 6.57; N, 1.28.

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