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Synthesis of a Symmetric Multivalent Molecule containing four Carbohydrate Substituents

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Summary. Starting with allyl- and pent-4-enyl-β-*D*-glucopyranosides **4–7**, different *D*-Glucose units (**8–15**) containing alkyl spacers of variable lenght and with different end groups can be prepared. Reaction of four equivalents of the caesium salt derived from propan-4-carboxy-1-yl-2,3,4,6-tetra-O-acetyl-β-*D*-glucopyranoside **15** with pentaerythrityltetrabromide yields the tetravalent molecule **16**.

Keywords. Carbohydrates; Dendrimers; Spacer.

Synthese eines symmetrischen multivalenten Moleküls mit vier Kohlenhydratsubstituenten

Zusammenfassung. Ausgehend von den Allyl- und Pent-4-enyl-β-*D*-glucopyranosiden **4–7** können die *D*-Glucosederivate **8–15** dargestellt werden, welche am anomeren Zentrum unterschiedlich lange Spacereinheiten mit verschiedenen Endgruppen besitzen. Bei Reaktion von vier Äquivalenten des Caesiumsalzes von Propan-4-carboxy-1-yl-2,3,4,6-tetra-O-acetyl-β-*D*-glucopyranosid **15** mit Pentaerythrityltetrabromid entsteht das tetravalente Molekül **16**.

Introduction

The synthesis and design of multivalent molecules became of considerable interest during the last years. These efforts include the construction of polymeric and quasipolymeric compounds containing different types of functional groups [1–4]. Especially the use of multivalent carbohydrate structures either as enzyme inhibitors [2, 3] or lectin- and antibody-binding structures [5, 6] has been investigated intensively. Among the quasipolymeric molecules, dendrimers [7, 8] and arborols [9] are known best. These compounds – also named cascade molecules – consist of branched compounds which are linked together by repeating reaction sequences and thus show an exponential increase in the number of functional groups on their surface [8]. Due to the remarkable physical and chemical properties [10–12] of these molecules, various functional groups have been placed on their surface, including hydroxyl-, carboxylate-, amino-, aromatic-, and even sialic acid residues [13–15].

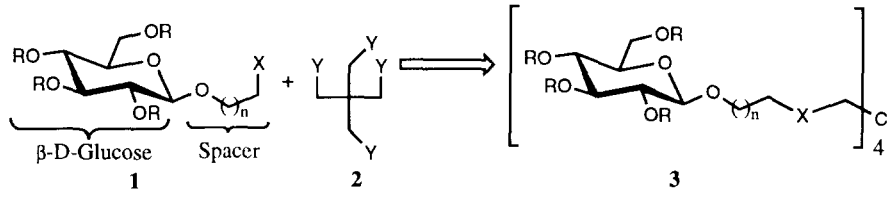
We report here the synthesis of a tetrameric molecule containing four carbohydrate units linked by an appropriate spacer to the surface of a simple dendrimeric unit.

Results and Discussion

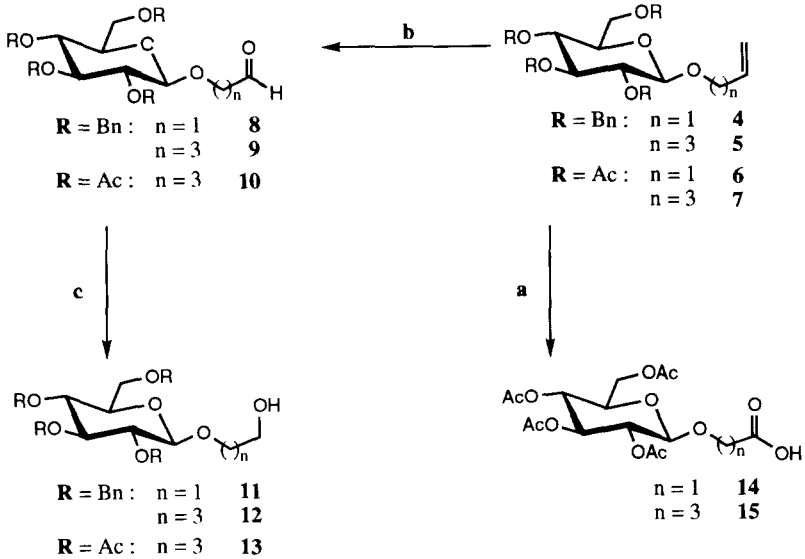
We choose a pentaerythrityl unit as the central molecule for the attachment of the carbohydrate moieties. These pentaerythrityl units have been used by *Tomalia et al.* [16] for the construction of dendrimers up to the third generation and are commercially available [17]. A direct attachment of the carbohydrate units has proven to be impossible because of sterical hindrance between the carbohydrate residues (Scheme 1).

We therefore investigated the coupling between a pentaerythrityl unit (**2**) and *D*-glucose units (**1**) containing aliphatic spacer groups of different length linked *via* the anomeric center on one side and containing a reactive group *X* on the other side of the spacer. Thus, the tetravalent molecule **3** should be accessible. Carbohydrate spacer units similar to **1** have been prepared by *Lemieux et al.* [18] by condensation of glycosylbromides with ethyl-9-hydroxynonanoate, but this method did not allow an easy access towards different reactive end groups *X*.

The synthesis started from the pent-4-enyl- and prop-2-enyl-glycosides **4**–**7** which could be prepared in large quantities in a simple reaction sequence starting from penta-O-acetyl-β-*D*-glycopyranose [19] (Scheme 2).



Scheme 1



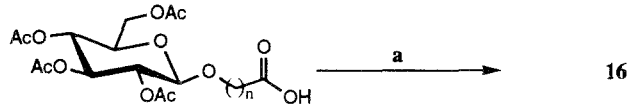
(a) $NaIO_4/KMnO_4/H_2O$, ethanol, 'butanol; (b) O_3, PPh_3; (c) $LiAlH_4$ or $NaBH_4/THF$

Scheme 2

Ozonization of **4**, **5**, and **7**, followed by reductive treatment with triphenylphosphine, yielded the aldehydes **8–10** which could be further transformed to the corresponding alcohols by reduction with lithium aluminiumhydride (**11**, **12**) and $NaBH_4$ in *THF* (**13**). Coupling of these carbohydrate spacer compounds **11–13** with pentaerythrityltetrabromide (*Pe*Br_4) *via* the corresponding oxonucleophiles generated with potassiumhydride in different solvents did not yield the desired tetrasubstituted product (as shown in Scheme 1; R = Ac or Bn; $n = 1$ or 3; Y = Br; X = O).

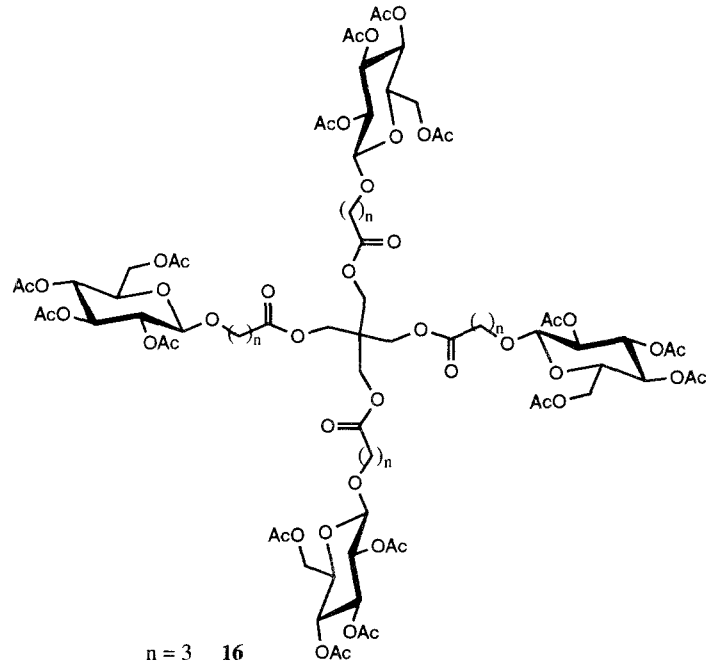
Oxidative cleavage of the double bond [20] present in derivatives **6** and **7** with $NaIO_4$ and a catalytic amount of $KMnO_4$ yielded the corresponding acids **14** and **15** in 39% and 78% yield, respectively. This reaction was performed in a mixture of water, ethanol, and *tert.* butanol. The fraction of solvents has proven to be critical for obtaining the desired products (see Experimental). When using *THF*/water mixtures, mostly the aldehydes were obtained in low yields.

Direct coupling of acids **14** and **15** with pentaerythritol using activating reagents like *DCC*, *EDC* [21], or *via* the corresponding acid chlorides using oxalylchlorid or triphenylphosphine/CCl_4 [22] was not successful. Reaction on the *in situ* prepared caesiumcarboxylate of **15** with 0.24 equiv. *Pe*Br_4 in *DMF* at 65 °C [23] resulted in clean formation of **16** after four days (Scheme 3).



n = 1 **14**
n = 3 **15**

(a) $C(CH_2Br)_4$, 0.5 equiv. Cs_2CO_3, DMF, 65 °C



n = 3 **16**

Scheme 3

The structure of this compound could be proven unambiguosly applying NMR and mass spectrometric methods. The ^{1}H as well as the ^{13}C NMR-spectrum turned out to be simple in contrast to the complex structure of **16**, proving its four-fold symmetry. The signal of the central carbon atom of the pentaerythrityl unit could only be detected using long relaxation delays. In the TOF mass-spectrum the molecule-ion-matrix peak could be detected at 1951.10 *m/e* (calcd.: 1951.84 *m/e*) when using matrix assisted desorption [24] (3-transpyridylacrylic acid as matrix).

When reacting $PeBr_4$ with the caesium salt derived from **14** – in which the spacer is shortened by two carbon atoms relativèly to **15** – under the developed conditions, the tetrasubstituted product similar to **16** ($n = 1$) could not be obtained. This might be due to increased sterical hindrance because of the reduced spacer length in **14** *vs.* **15**.

In summary, we have succeeded in synthesizing a tetravalent molecule containing four *D*-glucose units linked *via* a C-4 spacer to a pentaerythrityl unit as the central molecule. A caesium carboxylate has proven to be effective as reactive group at the end of the alkyl-spacers. However, the length of the carbon chain is critical for the attachment of four carbohydrate residues. Further investigations concerning the coupling of the developed carbohydrate spacer molecules with dendrimers containing more functional groups on their surface are under progress.

Experimental

General

Chemicals were purchased from Aldrich and were reagent grade. Analytical thin layer chromatography was performed on Merck plates (silica gel F_{254}, 0.25 mm thick). Compounds were visualized by spraying with a solution of 3% $Ce(SO_4)_2$ in 2 *N* H_2SO_4 followed by heating to 200 °C. Flash chromatography was performed using Merck silica gel 60 (0.04–0.063 mm).

NMR spectra were recorded on a BRUKER AM 250 spectrometer unless indicated otherwise (internal *TMS*, δ in ppm). In the spectroscopic data given we used superscripts to denote atoms or groups in glycosides and to refer to the individual sugar residues and aglycons, respectively. They are serially indicated beginning with the non-reducing residue. For example, in **7** (Pent-4-enyl-2,3,4,6-tetra-O-acetyl-β-*D*-glucopyranoside), the Gluc residue has no superscript and the pent-4-enyl aglycon is indicated with (').

Mass spectra were recorded on a BioIon 20 ^{252}Cf-plasma desorption time-of-flight mass spectrometer using *trans*-3-(3-pyridyl)-acrylic acid (*PAA*) as matrix for the peracetylated products. Abbreviations used are as follows: hexane (*PE*), ethyl acetate (*EA*), dichloromethane (*MC*), methanol (MeOH).

Prop-2-enyl-2,3,4,6-tetra-O-benzyl-β-D-glucopyranoside (**4**)

0.5 g (2.27 mmol) of prop-2-enyl-β-*D*-glycopyranoside (**6**) were dissolved in 50 ml *DMF*. 450 mg (9.5 mmol) NaH (as suspension in oil) was washed three times with *PE*, dried, and added to the above solution. After five minutes, 1.15 ml (9.1 mmol) benzylbromide was slowly added and the solution was stirred overnight at room temperature. After TLC (*PE/EA* = 2/1) indicated completion of the reaction, the solvent was removed *in vacuo* and the residue dissolved in 50 ml of *MC* and 50 ml of water. The organic layer was separated and dried over Na_2SO_4, followed by removal of the solvent by

evaporation. The crude product was purified by chromatography over silica gel (*PE/EA* = 5/1) to yield 1.1 g (83%) of **4** as a white solid.

^{1}H NMR ($CDCl_3$): δ = 3.40–3.78 (m, 6H), 4.15 (dd, 1H, J = 6.0, 12.9 Hz), 4.40–4.61 (m, 5H), 4.73, 4.79, 4.83, 4.93, 4.98 (d, 5H, J = 11.0 Hz), 5.20 (dd, 1H, J = 1.4, 10.5 Hz), 5.35 (dd, 1H, J = 1.6, 17.3 Hz), 5.98 (m, 1H), 7.0–7.50 (m, 20H); ^{13}C NMR ($CDCl_3$): δ = 138.53, 138.37, 138.05 (2C), 133.98, 128.44, 128.24, 128.09, 127.83, 127.75, 127.64, 127.54, 127.47, 125.36, 117.09, 102.63, 84.61, 82.18, 77.78, 75.56, 74.86, 74.78, 74.75, 73.35, 70.16, 68.85.

Pent-4-enyl-2,3,4,6-tetra-O-benzyl-β-D-glucopyranoside (**5**)

1.5 g (6.0 mmol) pent-4-enyl-β-*D*-glucopyranoside (**7**) were treated with 1.31 g NaH (30.24 mmol) and 3.61 ml (30.24 mmol) benzylbromide as described for compound **4**. After analogous workup and purification by flash chromatography (*PE/EA* = 10/1) 1.7 g (44%) of **5** were obtained as white foam.

^{1}H NMR ($CDCl_3$): δ = 1.79 (pent, 2H, J = 6.9 Hz), 2.20 (q, 2H, J = 8.0 Hz), 3.45–3.81 (m, 8H), 4.00 (dt, J = 6.6, 9.6 Hz), 4.42 (d, J = 7.7 Hz), 4.53–4.63 (m, 3H), 4.75 (d, 1H, J = 11.0 Hz), 4.81 (d, 1H, J = 11.0 Hz), 4.84 (d, 1H, J = 10.7 Hz), 4.96 (d, 1H, J = 10.7 Hz), 4.98–5.11 (m, 2H), 5.85 (tq, 1H, J = 6.6, 10.2 Hz), 7.10–7.40 (m, 20H); ^{13}C NMR ($CDCl_3$): δ = 138.59, 138.44, 138.16, 138.07, 138.00, 128.30, 128.08, 127.92, 127.81, 127.70, 127.59, 127.53, 114.87, 103.60, 84.68, 82.24, 77.88, 75.62, 74.94, 74.82, 74.77, 73.42, 69.30, 68.94, 30.20, 28.96.

Prop-2-enyl-2,3,4,6-tetra-O-acetyl-β-D-glucopyranoside (**6**)

To a solution of 2.0 g (5.12 mmol) penta-O-acetyl-β-*D*-glucopyranose [19] and 0.42 ml (6.16 mmol) of allylalcohol in 50 ml of absolute *MC*, 0.6 ml (5.12 mmol) of tin(IV)chloride were added. This reaction mixture was treated further as described for compound **7**. After crystallization from *PE/EA*, 1.2 g (60.3%) of **6** were obtained as white solid.

^{1}H NMR ($CDCl_3$): δ = 1.96, 1.98, 2.01, 2.05 (s, 12H, acetyl-CH_3), 3.65 (ddd, 1H, J = 2.5, 4.7, 9.6 Hz, H-5), 4.0–4.13 (m, 2H, H-6a, H-1a′), 4.21 (dd, 1H, J = 12.4, 4.7 Hz, H-6b), 4.26–4.34 (m, 1H, H-1b′), 4.51 (d, 1H, J = 8.0 Hz, H-1), 4.98 (dd, 1H, J = 7.7, 8.7 Hz, H-2), 5.05 (t, 1H, J = 8.8 Hz, H-4), 5.13–5.28 (m, 3H, H-3, H-3′); 5.80 (m, 1H, H-2′); ^{13}C NMR ($CDCl_3$): δ = 170.60, 170.22, 169.33, 169.25, 133.24, 117.58, 99.49, 72.79, 71.72, 71.22, 69.95, 68.37, 61.88, 20.67, 20.60, 20.54 (2C).

1.2 g (3.1 mmol) of **6** were deacetylated in dry methanol using a catalytic amount of sodium methoxide. After 10 h Dowex 50 H^+ was added to neutralize the mixture. The resin was then filtered off and the solvents were evaporated to yield 670 mg (98%) of prop-2-enyl-β-*D*-glucopyranoside as colorless oil.

^{1}H NMR (D_2O): δ = 3.26, 3.38, 3.42 (t, 3H, J = 8.8 Hz, H-3, H-2, H-4), 3.45 (m, 1H, H-5), 3.69 (dd, 1H, J = 5.5, 12.4 Hz, H-6a), 3.89 (dd, 1H, J = 2.0, 12.4 Hz, H-6b), 4.20 (dd, 1H, J = 6.6, 12.9 Hz, H-1a′), 4.37 (dd, 1H, J = 5.8, 12.9 Hz, H-1b′), 4.48 (d, 1H, J = 8.0 Hz, H-1), 5.26 (dd, 1H, J = 0.8, 10.2 Hz, H-3a′), 5.36 (dd, 1H, J = 1.4, 17.3 Hz, H-3b′), 5.96 (tq, 1H, J = 6.0, 10.5 Hz, H-2′); ^{13}C-NMR (D_2O): δ = 133.67, 119.09, 101.54, 76.26, 76.15, 73.47, 70.97, 70.02, 61.12.

Pent-4-enyl-2,3,4,6-tetra-O-acetyl-β-D-glucopyranoside (**7**)

To a solution of 2.0 g (5.12 mmol) penta-O-acetyl-β-*D*-glucopyranose [19] and 1.01 ml (6.24 mmol) of 4-penten-1-ol in 50 ml of absolute *MC*, 0.60 ml (5.12 mmol) of tin(IV)chloride were added dropwise. After consumption of the starting material (DC: *PE/EA* = 2/1), 10 g of $MgSO_4 \cdot 7H_2O_{(s)}$ and 10 g of $NaHCO_{3(s)}$ were added and stirred until neutral *pH* was reached. The solids were then removed by filtration over celite and washed with 150 ml of *MC*. The combined organic phases were dried over Na_2SO_4 and the solvent was evaporated under reduced pressure. The residue was purified by flash chromatography (*PE/EA* = 4/1) to yield 1.49 g (70%) of **7** as a white solid.

^{1}H NMR ($CDCl_3$): δ = 1.55–1.71 (m, 2H, H-2'), 1.96, 1.98, 2.00, 2.04 (s, 14H, acetyl-CH_3, H-3'), 3.45 (dt, 1H, J = 6.9, 9.6 Hz, H-1a'), 3.64 (ddd, 1H, J = 2.2, 4.4, 9.6 Hz, H-5), 3.83 (dt, 1H, J = 6.0, 9.6 Hz, H-1b'), 4.08 (dd, 1H, J = 12.1, 2.2 Hz, H-6a), 4.23 (dd, 1H, J = 12.4, 4.7 Hz, H-6b), 4.45 (d, 1H, J = 8.0 Hz, H-1), 4.93 (m, 3H, H-5', H-2), 5.04 (t, 1H, J = 9.6 Hz, H-4), 5.16 (t, 1H, J = 9.3 Hz, H-3), 5.74 (tq, 1H, J = 6.6, 10.2 Hz, H-4'); ^{13}C NMR ($CDCl_3$): δ = 170.63, 170.26, 169.35, 169.23, 137.75, 115.04, 100.78, 72.83, 71.70, 71.31, 69.28, 68.43, 61.94, 29.77, 28.52, 20.68, 20.60 (2C), 20.57.

700 mg (1.68 mmol) of **7** were deacetylated in methanol using a catalytic amount of sodium methoxid. After consumption of the starting material, Dowex 50 H^+ was added and the mixture was filtered. The solvent was then removed by evaporation to yield 410 mg (98.2%) of pent-4-enyl-β-*D*-glucopyranoside after purification by flash chromatography (MeOH/*MC* = 1/7).

^{1}H NMR (D_2O): δ = 1.70 (m, 2H), 2.13 (m, 2H), 3.24 (t, 1H, J = 8.8 Hz), 3.37–3.51 (m, 3H), 3.70 (m, 2H), 3.90 (m, 2H), 4.45 (dd, 1H, J = 0.8, 8.0 Hz), 4.90–5.13 (m, 2H), 5.90 (m, 1H); ^{13}C NMR (D_2O): δ = 139.15, 115.16, 102.55, 76.24, 76.14, 73.50, 70.26, 70.01, 61.11, 29.69, 28.35.

Methan-2-carboxy-1-yl-2,3,4,6-tetra-O-acetyl-β-D-glucopyranoside (**14**)

1.104 g (5.15 mmol) of $NaIO_4$ and 122 mg (0.77 mmol) $KMnO_4$ were stirred in a mixture of 200 ml of water and 40 ml of ethanol at 40 °C for 10 min. Then 720 mg (5.15 mmol) of K_2CO_3 and a solution of 2.0 g (5.15 mmol) of **6** in 40 ml *tert.* butanol were added and the mixture was stirred for 10 h at 50 °C. Aqueous HCl was then added until the solution became strongly acidic. The mixture was then extracted five times with 50 ml portions of *EA*. The combined organic phases were extracted three times with 80 ml portions of a 10% Na_2CO_3 solution. The combined aqueous phases were again acidified with aqueous HCl and were reextracted five times with 60 ml portions of *EA*. The combined organic phases were then dried with Na_2SO_4 and the solvent was removed by evaporation to yield 820 mg (39%) of **14** as a colorless oil.

^{1}H NMR ($CDCl_3$): δ = 1.97, 1.98, 2.02, 2.05 (s, 12H, acetyl-CH_3), 3.69 (ddd, 1H, J = 2.2, 4.4, 9.9 Hz, H-5), 4.09 (dd, 1H, J = 2.5, 12.1 Hz, H-6a), 4.21 (dd, 1H, J = 4.7, 12.4 Hz, H-6b), 4.28 (s, 2H, H-1'), 4.62 (d, 1H, J = 7.7 Hz, H-1), 5.00 (dd, 1H, J = 7.9, 9.6 Hz, H-2), 5.05 (t, 1H, J = 9.9 Hz, H-4), 5.20 (t, 1H, J = 9.6 Hz, H-3); ^{13}C NMR ($CDCl_3$): δ = 173.10, 170.81, 170.25, 169.72, 169.47, 100.13, 72.36, 71.90, 70.87, 68.17, 64.85, 61.70, 20.61, 20.58, 20.49 (2C).

Propan-4-carboxy-1-yl-2,3,4,6-tetra-O-acetyl-β-D-glucopyranoside (**15**)

1.0 g (2.4 mmol) of pent-4-enyl-2,3,4,6-tetra-O-acetyl-β-*D*-glucopyranoside **7** was treated with 5.14 g (24 mmol) $NaIO_4$, 76 mg (0.48 mmol) $KMnO_4$, and 331 mg (2.4 mmol) K_2CO_3 in a mixture of 100 ml water, 20 ml ethanol, and 20 ml *tert.* butanol as described for compound **14**. Analogous workup yielded 736 mg (70.4%) of **15**.

^{1}H NMR ($CDCl_3$): δ = 1.85 (m, 2H, H-2'), 1.97, 1.99, 2.01, 2.03 (s, 12H, acetyl-CH_3), 2.39 (t, 2H, J = 7.1 Hz, H-3'), 3.52 (dt, 1H, J = 5.8, 9.6 Hz, H-1a'), 3.65 (ddd, 1H, J = 2.2, 4.4, 9.6 Hz, H-5), 3.88 (dt, 1H, J = 5.8, 9.9 Hz, H-1b'), 4.09 (dd, 1H, J = 2.5, 12.4 Hz, H-6a), 4.22 (dd, 1H, J = 4.7, 12.1 Hz, H-6b), 4.46 (d, 1H, J = 7.8 Hz, H-1), 4.49 (dd, 1H, J = 8.0, 9.6 Hz, H-2), 5.04 (t, 1H, J = 9.6 Hz, H-3), 5.16 (t, 1H, J = 9.3 Hz, H-4); ^{13}C NMR ($CDCl_3$): δ = 178.54, 170.76, 170.30, 169.42, 100.67, 72.76, 71.72, 71.21, 68.52, 68.35, 61.88, 30.07, 24.43, 20.67 (2C), 20.56 (2C).

Eth-2-al-1-yl-2,3,4,6-tetra-O-benzyl-β-D-glucopyranoside (**8**)

1.0 g (1.72 mmol) of **4** was dissolved in 50 ml *MC* and ozone was bubbled through this solution at −78 °C until a blue colour persisted. The solution was sparged with argon and 0.54 g (2.06 mmol) triphenylphosphine were added. The mixture was allowed to warm to room temperature (DC: *PE*/*EA* = 1/1) and the solvents were removed by evaporation. After purification by flash chromatography (*PE*/*EA* = 1/1), 700 mg (70%) of **8** were obtained as colorless oil.

^{1}H NMR ($CDCl_3$): δ = 3.40–3.72 (m, 6H), 4.26 (dd, 2H, J = 2.4, 3.3 Hz), 4.44 (d, 1H, J = 7.4 Hz), 4.50, 4.54, 4.56, 4.77, 4.81, 4.83, 4.93, 4.98 (d, 8H, J = 11.0 Hz), 7.12–7.43 (m, 20H), 9.76 (t, 1H, J = 1.1 Hz); ^{13}C NMR ($CDCl_3$): δ = 200.59, 138.44, 138.23, 137.96 (2C), 128.37, 128.08, 127.92, 127.81, 127.72, 127.66, 127.61, 103.93, 84.44, 82.00, 77.47, 75.68, 75.00, 74.96, 74.92, 74.55, 73.49, 68.57.

But-4-al-1-yl-2,3,4,6-tetra-O-benzyl-β-D-glucopyranoside (**9**)

2.0 g (3.3 mmol) of **5** were treated with ozone and triphenylphosphine as described for compound **8**. Purification by flash chromatography (PE/EA = 1/1) yielded 1.5 g (75%) of **9**.

^{1}H NMR ($CDCl_3$): δ = 1.95 (pent., 2H, J = 6.3 Hz), 2.54 (t, 2H, J = 7.4 Hz), 3.42 (m, 2H), 3.52–3.74 (m, 5H), 3.95 (dt, 1H, J = 6.3, 9.6 Hz), 4.36 (m, 1H, J = 7.7 Hz), 4.49–4.62 (m, 3H), 4.70–4.90 (m, 4H), 7.10–7.30 (m, 20H), 9.73 (t, 1H, J = 1.4 Hz); ^{13}C NMR ($CDCl_3$): δ = 201.85, 138.55, 138.44, 138.11, 138.06, 129.65, 128.35, 128.34, 128.08, 127.93, 127.91, 127.82, 127.73, 127.64, 127.60, 127.57, 103.49, 84.68, 82.25, 77.80, 75.61, 74.94, 74.81, 74.79, 73.43, 68.86, 68.69, 40.60, 22.37.

But-4-al-1-yl-2,3,4,6-tetra-O-acetyl-β-D-glucopyranoside (**10**)

1.0 g (2.4 mmol) of **7** were treated with ozone and triphenylphosphine as described for compound **8**. After purification by flash chromatography (PE/EA = 2/1), 716 mg (71%) of **10** were obtained as colorless oil.

^{1}H NMR ($CDCl_3$): δ = 1.80–1.95 (m, 2H, H-2'), 1.96, 1.99, 2.02, 2.06 (s, 12H, acetyl-CH_3), 2.47 (m, 2H, H-3'), 3.50 (ddd, 1H, J = 5.5, 7.1, 9.6 Hz, H-1a'), 3.65 (ddd, 1H, J = 2.5, 4.7, 10.0 Hz, H-5), 3.87 (dt, 1H, J = 6.0, 9.6 Hz, H-1b'), 4.08 (dd, 1H, J = 2.5, 12.1 Hz, H-6a), 4.22 (dd, 1H, J = 4.7 Hz, H-6b), 4.45 (d, 1H, J = 8.0 Hz, H-1), 4.94 (dd, 1H, J = 7.7, 9.3 Hz, H-2), 5.03 (t, 1H, J = 9.6 Hz, H-3), 5.16 (t, 1H, J = 9.3 Hz, H-4), 9.71 (t, 1H, J = 1.4 Hz, H-4'); ^{13}C NMR ($CDCl_3$): δ = 201.74, 170.61, 170.20, 169.29 (2C), 100.64, 72.74, 71.77, 71.17, 68.70, 68.35, 61.86, 40.32, 22.17, 20.67 (2C), 20.55 (2C).

2-Hydroxyeth-1-yl-2,3,4,6-tetra-O-benzyl-β-D-glucopyranoside (**11**)

2.4 g (4.1 mmol) of **8** were dissolved in 50 ml of dry diethyl ether, and 155 mg (4.1 mmol) of lithium aluminium hydride were added. After 10 min (TLC: PE/EA = 1/1), 100 ml of a saturated aqueous NH_4Cl solution was added and the mixture was stirred for additional three hours. The organic phase was then separated and the aqueous phase was extracted three times with 60 ml portions of diethyl ether. The combined organic layers were dried over Na_2SO_4 and the solvent was removed by evaporation to yield 2.15 g (90%) of **11**.

^{1}H NMR ($CDCl_3$): δ = 3.10 (s, broad, 1H, OH), 3.46–3.80 (m, 7H), 3.81–4.01 (m, 3H), 4.44 (d, 1H, J = 7.7 Hz), 4.53 (d, 1H, J = 11.0 Hz), 4.56–4.60 (m, 2H), 4.75–4.88 (t, 1H, J = 11.3 Hz), 4.93 (d, 1H, J = 11.0 Hz), 4.96 (d, 1H, J = 11.0 Hz), 7.10–7.32 (m, 20H); ^{13}C NMR ($CDCl_3$): δ = 138.42, 138.27, 137.85, 137.76, 128.33, 127.96, 127.93, 127.81, 127.79, 127.69, 127.64, 127.58, 104.15, 84.62, 82.21, 77.78, 75.62, 74.92 (2C), 74.49, 73.54, 73.41, 68.79, 62.39.

4-Hydroxybut-1-yl-2,3,4,6-tetra-O-benzyl-β-D-glucopyranoside (**12**)

1.5 g (2.46 mmol) of **9** were treated with 0.25 g (6.58 mmol) of lithium aluminium hydride as described for compound **11**. After analogous workup, 1.26 g (84%) of **12** were obtained as colorless oil.

^{1}H NMR ($CDCl_3$): δ = 1.60–1.85 (m, 5H), 3.47 (m, 2H), 3.55–3.75 (m, 6H), 4.00 (dt, J = 5.8, 11.3 Hz), 4.41 (d, J = 7.7 Hz), 4.50–4.67 (m, 4H), 4.74, 4.81, 4.83, 4.94, 4.95 (d, 5H, J = 11.0 Hz), 7.10–7.50 (m, 20H); ^{13}C NMR ($CDCl_3$): δ = 138.55, 138.45, 138.08, 138.03, 128.72, 128.43, 128.29, 127.95, 127.90, 127.77, 127.72, 127.68, 127.58, 127.55, 127.52, 127.48, 126.86, 125.43, 103.52, 84.65, 82.20, 77.83, 75.58, 74.91, 74.70 (2C), 73.39, 69.85, 68.89, 62.40, 29.43, 26.18.

(4-Hydroxy-but-1-yl)-tetra-O-acetyl-β-D-glucopyranoside (**13**)

2.0 g (4.7 mmol) of **10** were dissolved in 100 ml of dry *THF* and 180 mg (4.7 mmol) of $NaBH_4$ were added. After 10 min at room temperature (DC: *PE/EA* = 1/1), 50 ml of a 10% aqueous NH_4Cl solution were added and the mixture was stirred for 2 hours. The organic layer was separated and the aqueous phase was extracted three times with 40 ml portions of *MC*. The combined organic phases were dried over Na_2SO_4. After filtration the solvent was evaporated to yield 1.7 g (85%) of **13**.

^1H NMR ($CDCl_3$): δ = 1.55–1.70 (m, 4H, H-2′, H-3′), 1.97, 2.00, 2.02, 2.06 (s, 12H, 4x acetyl-CH_3), 3.50 (dt, 1H, J = 5.8, 9.9 Hz, H-1a′), 3.57–3.73 (m, 4H, H-5, H-4′, OH), 3.90 (dt, 1H, J = 3.6, 9.3 Hz, H-1b′), 4.12 (dd, 1H, J = 2.5, 11.3 Hz, H-6a), 4.22 (dd, 1H, J = 4.7, 12.4 Hz, H-6b), 4.48 (d, 1H, J = 8.0 Hz, H-1), 4.95 (dd, 1H, J = 8.0, 9.6 Hz, H-2), 5.05 (t, 1H, J = 9.6 Hz, H-3), 5.18 (t, 1H, J = 9.3 Hz, H-4); ^{13}C NMR ($CDCl_3$). δ = 170.68, 170.27, 169.38 (2C), 100.76, 72.81, 71.79, 71.32, 69.95, 68.44, 62.30, 61.91, 29.29, 25.84, 20.71, 20.63, 20.58 (2C).

Synthesis of compound **16**

To a solution of 150 mg (0.34 mmol) of **15** in 10 ml of dry *DMF*, 33.4 mg (0.085 mmol) pentaerythrityl-tetrabromide and 56 mg (0.17 mmol) Cs_2CO_3 were added and the mixture was heated to 65–70 °C. After 5–6 days (TLC: *EA/PE* = 4/1), *DMF* was removed by vacuum distillation and the resulting residue was dissolved in 50 ml of *MC* and 50 ml of water. The organic layer was separated and dried over Na_2SO_4. After filtration, the solvent was removed by evaporation to yield 150 mg (96%) of **16** as yellowish oil.

^1H NMR (400 MHz, $CDCl_3$): δ = 1.80–1.92 (m, 2H, H-2′), 1.99, 2.01, 2.04, 2.08 (s, 12H, acetyl-CH_3), 2.38 (t, 2H, J = 7.4 Hz, H-3′), 3.53 (dt, 1H, J = 9.8, 5.9 Hz, H-1a′), 3.70 (ddd, 1H, J = 2.0, 9.8, 4.4 Hz, H-5), 3.89 (dt, 1H, J = 5.9, 9.8 Hz, H-1b′), 4.08–4.14 (m, 3H, J = 12.3, 8.4, 2.5 Hz, H-6a, OCH_2), 4.50 (d, 1H, J = 7.9 Hz, H-1), 4.96 (dd, 1H, J = 7.9, 9.4 Hz, H-2), 5.07 (t, 1H, J = 9.8 Hz, H-4*), 5.19 (t, 1H, J = 9.8 Hz, H-3*); ^{13}C NMR ($CDCl_3$): δ = 172.46, 170.63, 170.23, 169.38, 169.29, 100.69, 72.79, 71.78, 71.22, 68.65, 68.39, 61.90 (2C), 42.10, 30.34, 24.69, 20.71, 20.63, 20.58, 20.57; MS (70 eV): 1951.1 ($(M + PAA + H)^+$, 100%), calcd.: 1951.84.

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