Tetrahedron: *Asymmetry* 22 (2011) 399–405

Contents lists available at ScienceDirect

Tetrahedron: *Asymmetry*

journal homepage: www.elsevier.com/locate/tetasy

Conversion of fructose into a building block for the synthesis of carbocyclic mannose mimics

Clinton Ramstadius [a], Mikael Boklund [a], Ian Cumpstey [a,b,*]

[a] *Department of Organic Chemistry, The Arrhenius Laboratory, Stockholm University, 106 91 Stockholm, Sweden*
[b] *Institut de Chimie des Substances Naturelles, Centre National de la Recherche Scientifique, 91198 Gif-sur-Yvette Cedex, France*

ARTICLE INFO

Article history:
Received 4 November 2010
Revised 4 February 2011
Accepted 10 February 2011

ABSTRACT

Fructose was converted into C-1 diastereomeric carbocyclic building blocks resembling mannose using ruthenium-catalysed ring-closing metathesis as a key step. The potential use of the compounds in the synthesis of valienamine pseudodisaccharides is demonstrated using Mitsunobu coupling chemistry directly between a carbohydrate sulfonamide and the carbasugar C-1 alcohols.

1. Introduction

D-Fructose is amongst the most inexpensive of all known organic materials, which makes its utilisation as a starting material for synthesis attractive. Despite this, it has not been used as much as other carbohydrates.[1] D-Fructose **II** has an obvious structural similarity to D-mannose **I**, with it being oxidised at C-5 and reduced at C-1 (mannose numbering, Fig. 1).

We have been interested in the synthesis of C-5=C-5a unsaturated carbasugars **III** (valienamine derivatives) and their elaboration into pseudooligosaccharide structures **IV** (Fig. 1). Efficient and scalable routes to the benzyl-ether-protected building blocks mimicking D-glucose (i.e., D-*xylo* configured)[2] and D-galactose (i.e., L-*arabino* configured)[3] have been developed, starting from L-sorbose and lactose, respectively. We have reported the synthesis, from mannose, of a carbocyclic building block with OH-1 and OH-2 free, and used this for the synthesis of valienamines, notably 1,2-bis-*epi*-valienamine.[4] The relationship between D-glucose and L-sorbose is the same as that between D-mannose and D-fructose. Herein we report the results of our investigation into how D-mannose-mimicking (i.e., D-*lyxo* configured) unsaturated carbasugars may be synthesised from D-fructose using ring-closing metathesis as a key step.

Both of the C-1 diastereomeric *mono*-unprotected unsaturated carbasugars **9** and **10** are new compounds, but related compounds with different protecting group patterns have been synthesised before, starting from D-mannose[4–6] or quinic acid.[7,8] The areas of carbasugar synthesis in general,[9] ring-closing metathesis as a route to carbasugars from carbohydrates,[10] biological properties of valienamine and its epimers[11] and carbasugar pseudooligosaccharide synthesis[12] have all been recently reviewed.

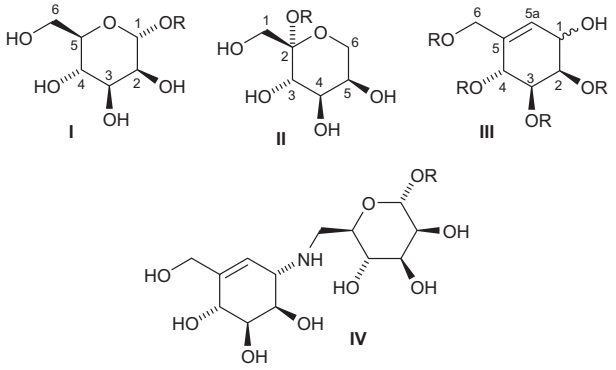


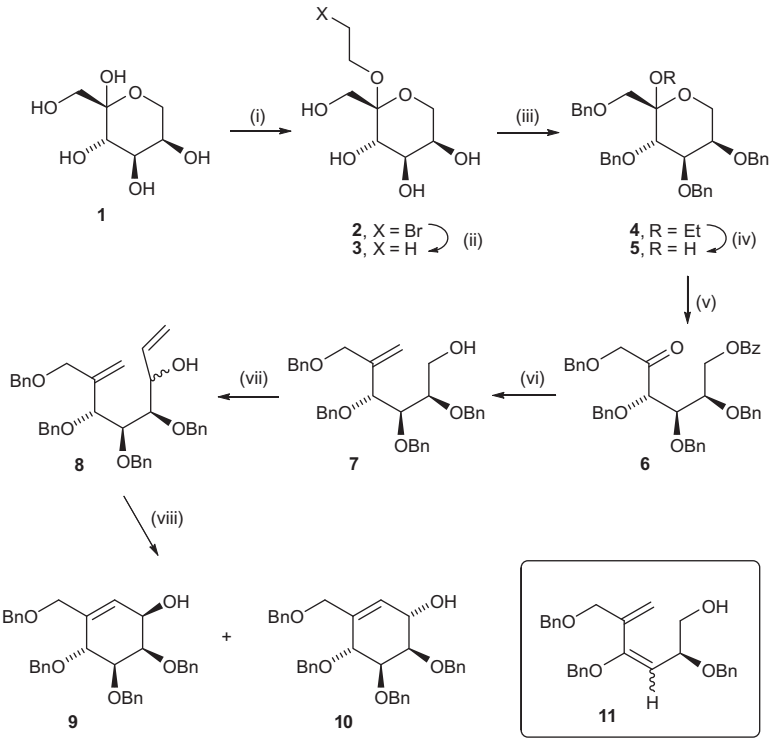
Figure 1. Structures of α-mannoside **I**; a β-fructopyranoside **II**, a selectively protected building block **III** for the synthesis of C-5=C-5 unsaturated carbocyclic mannose mimics, for example, *epi*-valienamines and a hydrolytically stable analogue **IV** of Man(α1→6)Man incorporating a 2-*epi*-valienamine moiety. The numbering of the aldose, ketose and carbasugar is also illustrated.

2. Results and discussion

The synthetic route began with the synthesis of the fructopyranose hemiacetal **5** from D-fructose **1** (Scheme 1). For sorbose, Fischer glycosylation with methanol gave the methyl α-L-pyranoside as a single diastereomer in excellent yield.[2] This reaction is not extendable to fructose. Treatment of D-fructose with HCl in methanol gave a mixture of glycosides, including pyranosides and furanosides. We found that the required methyl β-D-pyranoside could be isolated after perbenzylation of a partially purified glycoside mixture in only 21% yield over two steps, both involving

* Corresponding author. Tel.: +33(0)1 69 82 30 78; fax: +33(0)1 69 07 72 47.
E-mail addresses: ian.cumpstey@icsn.cnrs-gif.fr, ian.cumpstey@sjc.oxon.org (I. Cumpstey).

0957-4166/$ - see front matter © 2011 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tetasy.2011.02.013

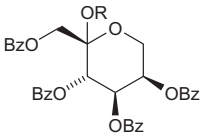


Scheme 1. Reagents and conditions: (i) 2-bromoethanol, 89%; (ii) Pd/C, H_2, $NaHCO_3$, H_2O, 50 °C; (iii) BnBr, NaH, DMF, 74% from **2**; (iv) AcOH, $HCl_{(aq)}$, 60 °C, 85%; (v) BzCl, py, 86%; (vi) (a) Ph_3PCH_3Br, ^tBuOK, PhMe, 0 °C; (b) NaOMe, MeOH, 84%; (vii) (a) $(COCl)_2$, Me_2SO, CH_2Cl_2, −78 °C, then Et_3N, −78 °C→rt; (b) vinylmagnesium chloride, THF, 0 °C, 76%; (viii) Hoveyda–Grubbs II, toluene, 60 °C; 28% **9** + 59% **10**.

difficult chromatographic separations. This problem has been solved by Chittenden et al., who developed a Fischer glycosylation in bromoethanol.[13] The crystalline β-fructopyranoside **2** precipitates from the reaction mixture, allowing an easy separation and high-yielding reaction. We found that this procedure worked very well, giving the fructopyranoside **2** in 89% yield, and was much more reliable than a similar procedure reported by Chittenden et al. using allyl alcohol,[14] which worked poorly in our hands. The bromide must be reduced before benzylation, and catalytic hydrogenolysis over palladium gave the ethyl glycoside **3**.[13] Benzylation gave the fully protected glycoside **4**, and hydrolysis gave the hemiacetal **5**.[15]

We then synthesised the carbocycles broadly following the pathway developed for the sorbose series.[2] The direct formation of the alkene **7** by Wittig methylenation of the hemiacetal **5** gave the desired product, but the competing formation of the elimination product **11** was always observed. For example, our best reaction conditions [pre-treatment of **5** with KHMDS (1 equiv) at 0 °C, then addition to the ylid suspension (8.2 equiv, formed using KHMDS) at rt in toluene] gave **7** in 45% yield, along with 23% of **11**. More commonly, **11** was the major or exclusive product. A higher-yielding, but longer route is via the open-chain ketone **6**, which was formed by treatment of the hemiacetal **5** with benzoyl chloride and pyridine.

The contrasting behaviour of the tetrabenzyl and tetrabenzoyl fructopyranose hemiacetals is noteworthy. It has been reported that the tetrabenzoyl compound **12** (Fig. 2) is acylated on the hemiacetal hydroxyl (O-2), giving a pyranose product **13** (with the addition of DMAP).[16] Here we have shown that the tetrabenzyl derivative **5** is acylated on the primary hydroxyl (O-1), giving an open-chain ketone **6**, as we found in the *sorbo* series.[2] This difference can be explained by considering the electronic properties of the protecting groups.[17] The benzoate esters are more electron-withdrawing than the benzyl ethers, hence the open-chain keto form of the benzoate protected sugar is more destabilised with respect to its cyclic hemiacetal form **12**, presumably to the extent that it is not present at all for acylation. It should be noted that in the NMR spectra of the benzyl-ether-protected hemiacetal **5**, only the hemiacetal and none of the keto form is seen, but presumably the rate of ring-opening to form the relatively stable benzyl-ether-protected keto form is higher than the rate of acylation of the hindered hemiacetal OH group, allowing acylation of the reactive primary OH group to occur.

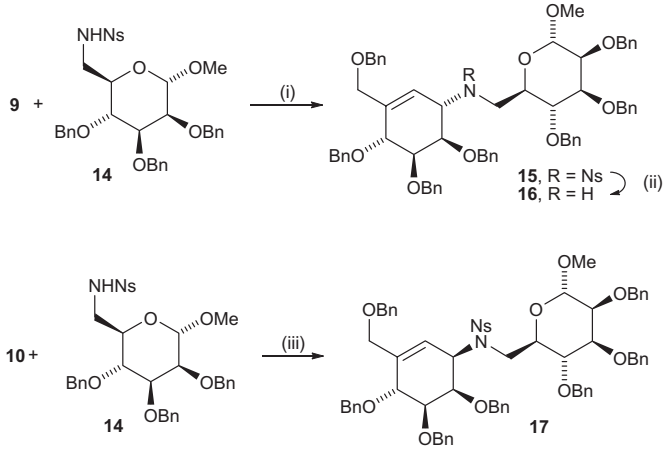


12, R = H
13, R = Bz

Figure 2.

Ketone **6** underwent a smooth Wittig methylenation, and methoxide-mediated deprotection of the benzoate ester from the crude product gave alkene **7**. In forming **8** with a Swern oxidation followed by Grignard addition, we did not attempt to optimise the diastereoselectivity. It is noteworthy that a slight difference between vinylmagnesium bromide (3:1) and chloride (2:1) was seen. Ring-closing metathesis with the Hoveyda–Grubbs II complex gave the carbocycles **9** and **10**, which were separable by chromatography. The stereochemistry of the ring-closed products was assigned by ^1H NMR $^3J_{1,2}$ coupling constants:[18] 4.2 Hz for **9** and 7.9 Hz for **10**, the latter being consistent with a *trans*-relationship and an $^3H_2$ conformation.

We examined Mitsunobu coupling as a method for forming the C–N bond in a pseudodisaccharide:[19–21] treatment of an almost equimolar mixture of the β-*lyxo* alcohol **9** and a mannose-6-sulfonamide nucleophile **14** with DIAD and triphenylphosphine resulted in the formation of a pseudodisaccharide product **15** as a single diastereomer (Scheme 2). The nosyl activating group was removed by a treatment with phenyl thiolate, to give the pseudodisaccharide **16**. Treating α-*lyxo* alcohol **10** with sulfonamide **14**, DIAD and triphenylphosphine also resulted in the formation of a single diastereomer of a pseudodisaccharide coupling product **17**, albeit in a much lower yield. Alternative degradation pathways competed successfully with coupling in this case. A major by-product, which was not isolated pure, appeared to be the product of elimination, a diene, arising from the loss of a proton from C-6 and of the leaving group from C-1, as judged by its ^{1}H NMR spectrum, in particular the appearance of three alkene protons at 5.72, 6.09, and 6.65 ppm.



Scheme 2. Reagents and conditions: (i) PPh_3, DIAD, toluene, 0 °C→rt; (ii) PhSH, K_2CO_3, DMF, 50 °C, 51% from **9**; (iii) PPh_3, DIAD, toluene, 0 °C→rt, 20%.

However, the, $^3J_{1,2}$ coupling constants for the pseudodisaccharides **15** and **16** could not be obtained due to spectral overlap. Nevertheless, since the reactions were stereospecific (i.e., **9** led only to **15**, and **10** led only to **17**), we assigned the stereochemistry of the pseudodisaccharides with inversion of configuration at C-1, as is expected for stereospecific (S_N2) Mitsunobu reactions. Moreover, the coupling constants that could be obtained for the carbocyclic rings were consistent with the assigned conformations. In **16**, $J_{2,3}$ (1.8 Hz) and $J_{3,4}$ (3.5 Hz) are both small values, consistent with the respective axial–equatorial and pseudodiequatorial relationships in the expected $^3H_2$ conformation.[4] In **17**, $J_{1,2}$ (<1 Hz) and $J_{2,3}$ (<1 Hz) are both small, which is consistent with the (pseudo)equatorial–axial relationships, while $J_{3,4}$ (8.6 Hz) is large, which is consistent with the pseudodiaxial relationship in the expected $^2H_3$ conformation.[4]

3. Conclusion

Carbocyclic mannose mimics, differentially unprotected at OH-1, are available from fructose in eight steps. The overall yield for the synthesis of the major diastereomer was 19%. These *epi*-valienol derivatives coupled with a carbohydrate sulfonamide to give *epi*-valienamine pseudodisaccharides. The coupling reaction of the β-*lyxo* C-1 alcohol to give the 1,2-*trans*-α-*lyxo* pseudodisaccharide is efficient. The α-*lyxo* alcohol underwent decomposition to a larger extent, although a pseudodisaccharide was formed in low yield; in fact this is the first time such a valienamine pseudodisaccharide with a β-*lyxo* configuration has been synthesised. The proposition that the pseudodisaccharide- or pseudotetrasaccharide-forming coupling reactions in validoxylamine and acarbose biosynthesis proceed via S_N reactions on valienol-derived allylic electrophiles with nucleotide diphosphates as C-1 leaving groups[22] makes the strategy reported in this paper for valienamine pseudodisaccharide synthesis bioreminiscent. We will report the results of our further studies on the coupling reactions of the building blocks in due course.

4. Experimental

4.1. General

Melting points were measured on a Stuart SMP3 device and are uncorrected. Proton nuclear magnetic resonance (^{1}H) spectra were recorded on a Bruker Avance II 500 (500 MHz) or a Bruker Avance II 400 (400 MHz) spectrometer; multiplicities are quoted as singlet (s), doublet (d), doublet of doublets (dd), doublet of doublet of doublets (ddd), triplet (t), apparent triplet (at), doublet of apparent triplets (dat), quartet (q), and multiplet (m). Carbon nuclear magnetic resonance (^{13}C) spectra were recorded on a Bruker Avance II 500 (125 MHz) or a Bruker Avance II 400 (100 MHz) spectrometer. ^{1}H and ^{13}C spectra and ^{13}C multiplicities were assigned using COSY, HSQC and DEPT experiments. All chemical shifts are quoted on the δ-scale in parts per million (ppm). Residual solvent signals or TMS were used as the internal reference. High-resolution (HRMS) electrospray (ESI^+) mass spectra were recorded using a Bruker Microtof instrument. Infra-red spectra were recorded on a Perkin–Elmer Spectrum One FT-IR spectrometer using the thin film method on NaCl plates. Optical rotations were measured on a Perkin–Elmer 241 polarimeter with a path length of 1 dm; concentrations are given in g/100 mL. Thin layer chromatography (TLC) was carried out on Merck Kieselgel sheets, pre-coated with $60F_{254}$ silica. Plates were visualised with UV light and developed using 10% sulfuric acid, or an ammonium molybdate (10% w/v) and cerium (IV) sulfate (2% w/v) solution in 10% sulfuric acid. Flash column chromatography was carried out on silica gel (35–70 μm, Grace). Dichloromethane was distilled from calcium hydride. THF and toluene were dried over molecular sieves and dispensed from a solvent purifier by VAC. Reactions performed under an atmosphere of hydrogen or argon were maintained by an inflated balloon.

4.2. 2′-Bromoethyl β-D-fructopyranoside 2

D-Fructose **1** (6.04 g, 33.5 mmol) was suspended in 2-bromoethanol (35 mL) under Ar. After 16 h, an off-white precipitate had formed, and Et_3N (0.25 mL) was added. The solid material was filtered and washed with cold EtOH (10 mL), EtOH–Et_2O (1:10, 15 mL) and Et_2O (15 mL) to yield the β-pyranoside **2** (8.53 g, 89%) as a white powder, which could be recrystallised from water containing 5% NaOAc; mp 140–142 °C (decomp.) (lit.[13] 126–129 °C (decomp.)); $[\alpha]_D^{26} = -114$ (*c* 1.0, H_2O) [lit.[13] −131.5 (H_2O)]; δ_H (500 MHz, D_2O) 3.58–3.63 (2H, m), 3.72–4.04 (9H, m); δ_C (100 MHz, D_2O) 34.5 (t, CH_2CH_2Br), 64.2, 64.4, 67.1 (3 × t, C-1, C-6, CH_2CH_2Br), 71.2, 72.0, 72.4 (3 × d, C-3, C-4, C-5), 103.5 (s, C-2); *m*/*z* (ESI^+) Isotope distribution 325.1 ($M+K^+$, 26), 323.1 ($M+K^+$, 27), 311.0 ($M+Na^+$, 98), 309.0 ($M+Na^+$, 100%); HRMS (ESI^+) calcd for $C_8H_{15}O_6BrNa$ ($M+Na^+$) 308.9944; found 308.9949.

4.3. Ethyl 1,3,4,5-tetra-*O*-benzyl-β-D-fructopyranoside 4

2′-Bromoethyl β-D-fructopyranoside (8.98 g, 31.9 mmol), $NaHCO_3$ (4.1 g, 38.5 mmol) and Pd/C (675 mg, 10%, 0.63 mmol)

were suspended in water (75 mL). The suspension was degassed and refilled with $H_{2(g)}$, and the mixture heated to 50 °C. After 22 h, the reaction mixture was allowed to cool to rt. Further Pd/C (245 mg, 0.23 mmol) was added, and the suspension was degassed and refilled with $H_{2(g)}$. The reaction mixture was stirred at 50 °C for a further 17 h, after which the mixture was allowed to cool and then filtered through cotton wool and sand. The resulting clear solution was concentrated in vacuo to yield the crude ethyl glycoside **3**[13] as a white solid (11 g, containing salts), which was used without further purification; δ_H (400 MHz, D_2O) 1.16 (3H, t, *J* 7.0 Hz, OCH_2CH_3), 3.57–3.67 (2H, m), 3.74–3.88 (4H, m), 3.95–3.97 (2H, m), 4.05 (1H, m); δ_C (100 MHz, D_2O) 14.6 (q, CH_3), 56.7, 61.3, 63.8 (3 × t, C-1, C-6, CH_2CH_3), 71.2, 72.0, 72.4 (3 × d, C-3, C-4, C-5), 103.5 (s, C-2); *m*/*z* (ESI^+) 439 ($2M+Na^+$, 59), 231 ($M+Na^+$, 100%); HRMS (ESI^+) calcd for $C_8H_{16}O_6Na$ ($M+Na^+$) 231.0839; found 231.0828; calcd for $C_{16}H_{32}O_{12}Na$ ($2M+Na^+$) 439.1786; found 439.1763.

Crude ethyl β-D-fructopyranoside **3** (11 g, 31.9 mmol) was suspended in DMF (150 mL) under Ar, and benzyl bromide (23 mL, 194 mmol) was added. The resulting suspension was cooled to 0 °C, and NaH (60% in oil, 10.2 g, 255 mmol) was added portionwise over the course of 6 h. After a further 15 h, TLC (pentane–EtOAc, 3:1) indicated the complete consumption of starting material (R_f ~0) and the formation of a major product (R_f 0.7). The reaction was quenched by the addition of MeOH (25 mL), and the mixture was transferred to a separatory funnel, diluted with Et_2O (200 mL) and washed with brine (200 + 100 mL). The combined aqueous phases were extracted with Et_2O (3 × 100 mL). The combined organic extracts were dried ($MgSO_4$), filtered and concentrated in vacuo. The crude product was purified by flash column chromatography (pentane–EtOAc, 10:1→8:1→6:1→4:1) to yield the tetrabenzyl derivative **4** (13.5 g, 74% over two steps) as a colourless oil, which could be recrystallised from Et_2O–heptane to give white crystals; mp 52–54 °C (Et_2O–heptane); $[\alpha]_D^{21} = -45.4$ (*c* 1.0, $CHCl_3$); δ_H (400 MHz, $CDCl_3$) 1.17 (3H, t, *J* 7.1 Hz, CH_2CH_3), 3.49–3.66 (4H, m, H-1, H-6, CH_2CH_3), 3.78–3.81 (2H, m, H-1′, H-5), 3.87 (1H, dd, $J_{5,6'}$ 1.9 Hz, $J_{6,6'}$ 12.5 Hz, H-6′), 4.00 (1H, dd, $J_{4,5}$ 3.3 Hz, $J_{3,4}$ 10.1 Hz, H-4), 4.37 (1H, d, $J_{3,4}$ 10.1 Hz, H-3), 4.41 (1H, d, *J* 11.9 Hz, PhCHH′), 4.60–4.69 (4H, m, $PhCH_2$, PhCHH′, PhCHH′), 4.72, 4.78 (2H, 2 × d, *J* 12.6 Hz, $PhCH_2$), 4.93 (1H, d, *J* 11.3 Hz, PhCHH′), 7.20–7.41 (20 H, m, Ar-H); δ_C (100 MHz, $CDCl_3$) 15.9 (q, CH_3), 56.6 (t, CH_2CH_3), 61.1 (t, C-6), 70.3 (t, C-1), 71.2, 72.3, 73.6, 75.7 (4 × t, 4 × $PhCH_2$), 73.9 (d, C-5), 76.4 (d, C-3), 79.0 (d, C-4), 101.8 (s, C-2), 127.4, 127.5, 127.5, 127.7, 127.8, 127.8, 128.2, 128.3, 128.3, 128.3, 128.6 (11 × d, Ar-CH), 138.2, 138.7, 138.9, 139.1 (4 × s, 4 × Ar-C); *m*/*z* (ESI^+) 607 ($M+K^+$, 5), 591 ($M+Na^+$, 100%); HRMS (ESI^+) calcd for $C_{36}H_{40}O_6Na$ ($M+Na^+$) 591.2717; found 591.2714.

4.4. 1,3,4,5-Tetra-*O*-benzyl-α,β-D-fructopyranose 5

Ethyl glycoside **4** (5.25 g, 9.2 mmol) was dissolved in AcOH (25 mL) and HCl (1 M aq, 2 mL) was added. The resulting solution was heated to 60 °C. After 3.5 h, TLC (pentane–EtOAc, 3:1) indicated complete consumption of the starting material (R_f 0.7) and the formation of a minor (R_f 0.6) and a major product (R_f 0.2). The reaction mixture was allowed to cool to rt and then partitioned between EtOAc (150 mL) and H_2O (200 mL). Solid $NaHCO_3$ was added until the resulting evolution of gas ceased. The aqueous phase was re-extracted with EtOAc (2 × 100 mL). The combined organic extracts were dried ($MgSO_4$), filtered and concentrated in vacuo. The crude product was purified by flash column chromatography (pentane–EtOAc, 4:1→5:2→2:1) to yield the hemiketal **5** (4.23 g, 85%, α:β, 1:5) as a yellow oil;[15] selected data for β-anomer: δ_H (400 MHz, $CDCl_3$) 3.46, 3.53 (2H, 2 × d, $J_{1,1'}$ 10.0 Hz, H-1, H-1′), 4.78 (1H, d, *J* 12.6 Hz, PhCHH′), 4.94 (1H, d, *J* 12.6 Hz, PhCHH′); δ_C (125 MHz, $CDCl_3$) 61.0 (t, C-6), 71.3, 72.1, 72.2, 73.9, 75.6 (5 × t, C-1, 4 × $PhCH_2$), 73.3, 75.9, 79.0 (3 × d, C-3, C-4, C-5), 98.2 (s, C-2), 137.8, 138.2, 138.5, 138.5 (4 × s, 4 × Ar-C); selected data for α-anomer: δ_C (125 MHz, $CDCl_3$) 57.4 (t, C-6), 71.6, 73.6, 73.9, 74.2 (4 × t, 4 × $PhCH_2$, C-1), 71.8, 74.5, 74.6 (3 × d, C-3, C-4, C-5), 97.5 (s, C-2), 137.2, 137.9, 138.2, 138.2 (4 × s, 4 × Ar-C); *m*/*z* (ESI^+) 1103 ($2M+Na^+$, 15), 563 ($M+Na^+$, 100%); HRMS (ESI^+) calcd for $C_{34}H_{36}O_6Na$ ($M+Na^+$) 563.2404; found 563.2378.

4.5. 1,3,4,5-Tetra-*O*-benzyl-6-*O*-benzoyl-D-fructose 6

Hemiketal **5** (3.0 g, 5.55 mmol) was dissolved in pyridine (10 mL) and BzCl (1.6 mL, 13.8 mmol) was added, which resulted in the solution turning brown. After 17 h, TLC (pentane–EtOAc, 4:1) indicated complete consumption of the starting material (R_f 0.1) and formation of a major product (R_f 0.3). The reaction mixture was diluted with EtOAc (150 mL) and washed with HCl (1 M aq, 3 × 50 mL). The combined aqueous phases were extracted with EtOAc (2 × 50 mL). The combined organic extracts were washed with $NaHCO_3$ (satd aq, 2 × 50 mL), dried ($MgSO_4$), filtered and concentrated in vacuo. The crude product was purified by flash column chromatography (pentane–EtOAc, 7:1→6:1→5:1) to yield the open-chain ketone **6** (3.06 g, 86%) as a yellow oil; $[\alpha]_D^{21} = -4.2$ (*c* 1.0, $CHCl_3$); ν_{max}/cm^{-1} 1720 (C=O); δ_H (500 MHz, $CDCl_3$) 3.97 (1H, ddd, $J_{5,6'}$ 2.6 Hz, $J_{5,6}$ 3.8 Hz, $J_{4,5}$ 7.8 Hz, H-5), 4.22–4.28 (2H, m, H-4, PhCHH′ or H-1), 4.33–4.54 (8H, m, H-3, H-6, 2 × $PhCH_2$, PhCHH′ or H-1, PhCHH′ or H-1′), 4.54, 4.60 (2H, 2 × d, *J* 10.8 Hz, $PhCH_2$), 4.73 (1H, d, *J* 11.3 Hz, PhCHH′ or H-1′), 4.96 (1H, dd, $J_{5,6'}$ 2.6 Hz, $J_{6,6'}$ 12.3 Hz, H-6′), 7.21–7.32 (20H, m, Ar-H), 7.47 (2H, m, Ar-H), 7.60 (1H, m, Ar-H), 8.05 (2H, m, Ar-H); δ_C (125 MHz, $CDCl_3$) 62.2 (t, C-6), 71.8, 73.4, 74.3, 74.5, 75.0 (5 × t, C-1, 4 × $PhCH_2$), 76.7 (d, C-5), 79.4 (d, C-4), 84.4 (d, C-3), 128.1, 128.3, 128.3, 128.5, 128.5, 128.5, 128.5, 128.7 (8 × d, Ar-CH), 129.8, 133.2 (2 × d, Ar-CH), 130.1 (s, Ar-C), 136.9, 137.3, 137.4, 137.8 (4 × s, Ar-C), 166.4 (s, OC=O), 208.5 (s, C-2); *m*/*z* (ESI^+) 683 ($M+K^+$, 27), 667 ($M+Na^+$, 100%); HRMS (ESI^+) calcd for $C_{41}H_{40}O_7Na$ ($M+Na^+$) 667.2666; found 667.2697.

4.6. (3*R*,4*R*,5*R*) 1,3,4,5-Tetra-*O*-Benzyl-2-methylene-hexane-1,3,4,5,6-pentaol 7

4.6.1. Method 1: from the open-chain ketone 6

Triphenylmethylphosphonium bromide (4.0 g, 11.2 mmol) was suspended in dry toluene (20 mL) under Ar, and potassium *tert*-butoxide (1.2 g, 10.7 mmol) was added. The resulting suspension was heated to 80 °C, and after a few minutes, the suspension turned yellow. After a further 45 min, the suspension containing the ylid was allowed to cool to rt, and then cooled to 0 °C. Ketone **6** (3.03 g, 4.70 mmol) was dissolved in dry toluene (10 + 5 mL) and added to the ylid by cannula. After 10 min, TLC (pentane–EtOAc, 4:1) indicated complete consumption of the starting material (R_f 0.4) and the formation of a major product (R_f 0.7). Next, MeOH (0.5 mL) was added to the reaction mixture, and after a further 2 h, no change was observed according to TLC. The reaction mixture was diluted with toluene–EtOAc (1:1, 50 mL), filtered through Celite and concentrated in vacuo.

The crude residue was dissolved in MeOH (15 mL). Sodium (65 mg, 2.8 mmol) was added to MeOH (8 mL), and the resulting solution was added to the carbohydrate solution by pipette. After 22 h, TLC (pentane–EtOAc, 3:1) indicated the complete consumption of the starting material (R_f 0.8) and the formation of a major product (R_f 0.3). Next, HCl (1 M aq, 4 mL) was added, and the mixture was concentrated in vacuo. The resulting residue was dissolved in EtOAc (100 mL) and washed with HCl (1 M aq, 100 mL). The aqueous phase was re-extracted with EtOAc (50 mL), and the combined organic extracts were washed with $NaHCO_3$ (satd aq,

2 × 100 mL). The aqueous phases were combined and extracted with EtOAc (50 mL). The combined organic phases were dried ($MgSO_4$), filtered and concentrated in vacuo. The crude product was purified by flash column chromatography (CH_2Cl_2–Et_2O, 50:1→40:1→30:1) to yield the alkene **7** (2.12 g, 84%) as a colourless oil; $[\alpha]_D^{22} = -6.5$ (*c* 1.0, $CHCl_3$); δ_H (500 MHz, $CDCl_3$) 2.26 (1H, at, *J* 6.2 Hz, OH-6), 3.66 (1H, m, H-5), 3.79–3.81 (2H, m, H-6, H-6′), 3.89 (1H, at, *J* 5.3 Hz, H-4), 4.03, 4.08 (2H, 2 × d, $J_{1,1'}$ 12.7 Hz, H-1, H-1′), 4.19 (1H, d, $J_{3,4}$ 5.1 Hz, H-3), 4.28, 4.40 (2H, 2 × d, *J* 11.5 Hz, PhCH_2), 4.32, 4.61 (2H, 2 × d, *J* 11.7 Hz, PhCH_2), 4.51, 4.55 (2H, 2 × d, *J* 11.5 Hz, PhCH_2), 4.70, 4.73 (2H, 2 × d, *J* 11.1 Hz, PhCH_2), 5.41 (1H, br s, H-2a), 5.47 (1H, m, H-2a′), 7.21–7.38 (20H, m, Ar-H); δ_C (125 MHz, $CDCl_3$) 60.9 (t, C-6), 70.6 (t, C-1), 71.0, 71.6, 72.9, 75.3 (4 × t, 4 × PhCH_2), 79.2 (d, C-5), 80.5 (d, C-4), 81.2 (d, C-3), 116.6 (t, C-2a), 127.8, 128.3, 128.4, 128.4, 128.5, 128.5, 128.5 (7 × d, Ar-CH), 138.3, 138.4 (2 × s, Ar-C), 142.8 (s, C-2); *m*/*z* (ESI^+) 1099 (2M+Na^+, 32), 561 (M+Na^+, 100%); HRMS (ESI^+) calcd. for $C_{35}H_{38}O_5Na$ (M+Na^+) 561.2612; found 561.2612.

4.6.2. Method 2: directly from the hemiketal 5

Triphenylmethylphosphonium bromide (1.25 g, 3.50 mmol) was suspended in dry toluene (2 mL) under Ar and cooled to 0 °C. Potassium bis(trimethylsilyl)amide (5.15 mL, 3.40 mmol, 15% solution in toluene by weight) was added, upon which the resulting suspension turned yellow. After 55 min, hemiketal **5** (225 mg, 0.416 mmol) was dissolved in toluene (1.5 mL) under Ar and cooled to 0 °C. Potassium bis(trimethylsilyl)amide (620 μL, 0.410 mmol) was added to this hemiketal solution. After 5 min, the hemiketal solution was transferred to the ylid suspension by cannula (rinsing with 0.5 mL toluene). The resulting reaction mixture was maintained at 0 °C for 1 h, after which it was slowly allowed to warm to rt. After 12 h 40 min, TLC (CH_2Cl_2–Et_2O, 30:1) indicated the complete consumption of starting material (R_f 0.4) and the formation of the desired alkene (R_f 0.3) and of the undesired diene (R_f 0.2). The mixture was filtered through Celite, eluting with toluene–EtOAc (10:1) and the filtrate was concentrated in vacuo. The crude residue was purified by flash column chromatography (CH_2Cl_2–Et_2O, 50:1→40:1→30:1→20:1) to yield **7** (100 mg, 45%) as a colourless oil identical to that described above and elimination product **11** (42 mg, 23%) as a colourless oil. Data for **11**: δ_H (400 MHz, $CDCl_3$) 2.12 (1H, s, OH-6), 3.39–3.50 (2H, m, H-6, H-6′), 4.19 (2H, m, H-1, H-1′), 4.28, 4.51 (2H, 2 × d, *J* 11.7 Hz, PhCH_2), 4.43 (1H, ddd, *J* 3.9 Hz, *J* 7.6 Hz, $J_{4,5}$ 9.1 Hz, H-5), 4.59 (2H, s, PhCH_2), 4.69, 4.75 (2H, 2 × d, *J* 11.4 Hz, PhCH_2), 5.15 (1H, d, $J_{4,5}$ 9.1 Hz, H-4), 5.50 (1H, d, *J* 1.3 Hz, H-2a), 5.61 (1H, d, *J* 1.4 Hz, H-2a′), 7.28–7.40 (15H, m, Ar-H); δ_C (100 MHz, $CDCl_3$) 65.3 (t, C-6), 70.5, 72.4, 73.5 (3 × t, 3 × PhCH_2), 70.6 (t, C-1), 74.7 (d, C-5), 113.7 (d, C-4), 117.1 (t, C-2a), 137.0, 138.1, 138.6, 138.9, 155.8 (5 × s, C-2, C-3, 3 × Ar-C).

4.7. (3*R*,4*R*,5*R*,6*RS*)-1,3,4,5-Tetra-*O*-benzyl-1,3,4,5,6-pentahydroxy-2-methylene-oct-7-ene 8a,b

Oxalyl chloride (0.65 mL, 7.6 mmol) was dissolved in CH_2Cl_2 (5 mL, freshly distilled) under Ar at −78 °C. Next, Me_2SO (1.15 mL, 16.2 mmol) was dissolved in CH_2Cl_2 (20 mL, freshly distilled) under Ar at −78 °C and then transferred to the oxalyl chloride solution by cannula. After 45 min, a solution of alcohol **7** (1.18 g, 2.19 mmol) in CH_2Cl_2 (8 + 4 mL) was transferred to the reaction vessel at −78 °C. After 30 min, Et_3N (2.9 mL, 20.9 mmol) was added to the reaction mixture at −78 °C, and the mixture was then allowed to warm to rt. After an additional 15 min, TLC (pentane–EtOAc, 3:1) indicated the complete consumption of starting material (R_f 0.3) and the formation of a major product (R_f 0.8). The reaction mixture was diluted with CH_2Cl_2 (100 mL), transferred to a separatory funnel and washed with H_2O (100 mL). The aqueous phase was re-extracted with CH_2Cl_2 (2 × 30 mL). The combined organic extracts were dried (Na_2SO_4), filtered and concentrated in vacuo, to yield the crude aldehyde (6.8 g) as a yellow solid.

The crude aldehyde was dissolved in THF (10 mL), and cooled to 0 °C under Ar. Vinylmagnesium chloride (2.4 mL, 4.1 mmol) was added. After 15 min, TLC (pentane–EtOAc, 3:1) indicated the complete consumption of aldehyde (R_f 0.8) and the formation of a major product (R_f 0.7). The reaction was quenched by the addition of NH_4Cl (satd aq, 6 mL). The mixture was diluted with EtOAc (100 mL) and washed with saturated NH_4Cl (satd aq, 100 mL). The aqueous phase was extracted with EtOAc (2 × 50 mL) and the combined organic extracts were dried ($MgSO_4$), filtered and concentrated in vacuo. The crude product was purified by flash column chromatography (pentane–EtOAc, 6:1→5:1) to yield the dienes **8a**,**b** (941 mg, dr 2:1, 76% over two steps), an inseparable mixture of diastereomers, as a yellow oil; Selected data for major diastereomer: δ_H (400 MHz, $CDCl_3$) 3.04 (1H, d, $J_{OH,6}$ 7.7 Hz, OH-6), 3.74 (1H, dd, $J_{5,6}$ 1.9 Hz, $J_{4,5}$ 6.8 Hz, H-5); δ_C (125 MHz, $CDCl_3$) 70.7, 70.7, 72.9, 73.4, 75.3 (5 × t, C-1, 4 × PhCH_2), 71.4 (d, C-6), 79.9 (d, C-5), 80.4 (d, C-3), 80.7 (d, C-4), 115.1 (t, C-8), 116.4 (t, C-2a), 139.2 (d, C-7), 142.8 (s, C-2); Selected data for minor diastereomer: δ_H (400 MHz, $CDCl_3$) 2.92 (1H, br s, OH-6), 3.66 (1H, dd, *J* 5.2 Hz, *J* 5.9 Hz, H-5); δ_C (125 MHz, $CDCl_3$) 70.8, 70.9, 72.9, 73.1, 74.9 (5 × t, C-1, 4 × PhCH_2), 73.1 (d, C-6), 81.0, 81.9, 82.3 (3 × d, C-5), 115.9 (t, C-8), 116.9 (t, C-2a), 142.9 (s, C-2); *m*/*z* (ESI^+) 587 (M+Na^+, 100%); HRMS (ESI^+) calcd for $C_{37}H_{40}O_5Na$ (M+Na^+) 587.2768; found 587.2803.

4.8. 2,3,4,6-Tetra-*O*-benzyl-5a-carba-β-D-*lyxo*-hex-5(5a)-enopyranose 9 and 2,3,4,6-tetra-*O*-benzyl-5a-carba-α-D-*lyxo*-hex-5(5a)-enopyranose 10

Dienes **8a**,**b** (941 mg, 1.67 mmol) were dissolved in dry toluene (60 mL) under Ar. Next, Hoveyda–Grubbs' 2nd generation complex (10 mg, 0.016 mmol) was added, and the dark green reaction mixture was heated to 60 °C. After 4.5 h, TLC (toluene–EtOAc, 6:1) indicated the presence of the starting material (R_f 0.6) and the formation of two major products (R_f's 0.3 and 0.1). An additional portion of Hoveyda–Grubbs' 2nd generation complex (5 mg, 0.008 mmol) was added, and after a further 2 h 15 min, TLC indicated complete consumption of the starting material and the formation of the products. The reaction mixture was allowed to cool to rt and DMSO (90 μL, 50 equiv vs Hoveyda–Grubbs' complex) was added. After 16 h, the reaction mixture was concentrated in vacuo and the residue was purified by flash column chromatography (toluene→toluene–EtOAc, 20:1→15:1→10:1) to yield carbocycle **9** (251 mg, 28%) as a white solid, which was recrystallised; mp 72–73 °C (Et_2O–pentane); $[\alpha]_D^{24} = -56.0$ (*c* 1.0, $CHCl_3$); ν_{max}/cm^{-1} 3525 (OH); δ_H (400 MHz, $CDCl_3$) 3.03 (1H, d, $J_{OH,1}$ 11.1 Hz, OH-1), 3.87–3.93 (2H, m, H-3, H-6), 3.96 (1H, dd, $J_{2,3}$ 1.8 Hz, $J_{1,2}$ 4.2 Hz, H-2), 4.18–4.27 (3H, m, H-1, H-4, H-6′), 4.37 (1H, d, *J* 11.9 Hz, PhC*H*H′), 4.49–4.52 (2H, m, PhCH*H*′, PhC*H*H′), 4.58 (1H, d, *J* 11.2 Hz, PhCH*H*′), 4.64, 4.72 (2H, 2 × d, *J* 11.9 Hz, PhCH_2), 4.77 (2H, s, PhCH_2), 5.92 (1H, d, *J* 5.9 Hz, H-5a), 7.19–7.39 (20H, m, Ar-H); δ_C (125 MHz, $CDCl_3$) 65.8 (d, C-1), 70.5 (t, C-6), 71.8, 72.0, 73.2, 73.9 (4 × t, 4 × PhCH_2), 75.3 (d, C-2 and C-4), 79.4 (d, C-3), 127.7, 127.8, 127.9, 128.0, 128.0, 128.2, 128.5, 128.5, 128.6, 128.6 (10 × d, Ar-CH), 129.0 (d, C-5a), 135.1, 138.0, 138.2, 138.3, 138.5 (5 × s, C-5, 4 × Ar-C); *m*/*z* (ESI^+) 1095 (2M+Na^+, 17), 559 (M+Na^+, 100%); HRMS (ESI^+) calcd for $C_{35}H_{36}O_5Na$ (M+Na^+) 559.2455; found 559.2427; calcd for $C_{70}H_{72}O_{10}Na$ (2M+Na^+) 1095.5018; found 1095.4967.

And carbocycle **10** (532 mg, 59%) as a colourless oil; $[\alpha]_D^{23} = +10.4$ (*c* 1.0, $CHCl_3$); ν_{max}/cm^{-1} 3435 (OH); δ_H (400 MHz, $CDCl_3$) 2.22 (1H, s, OH-1), 3.73 (1H, dd, $J_{1,2}$ 7.9 Hz, $J_{2,3}$ 2.2 Hz,

H-2), 3.89–3.92 (2H, m, H-3, H-6), 4.07 (1H, d, $J_{3,4}$ 3.1 Hz, H-4), 4.17 (1H, dat, J_{at} 1.4 Hz, $J_{6,6'}$ 12.4 Hz, H-6′), 4.38 (1H, d, J 11.8 Hz, PhC*H*H′), 4.46 (2H, s, PhCH_2), 4.51 (1H, d, J 11.8 Hz, PhCH*H*′), 4.58–4.60 (4H, m, H-1, PhCH_2, PhC*H*H), 4.66 (1H, d, J 12.4 Hz, PhCH*H*′), 5.87 (1H, m, H-5a), 7.21–7.23 (2H, m, Ar-H), 7.30–7.37 (18H, m, Ar-H); δ_C (125 MHz, $CDCl_3$) 68.2 (d, C-1), 70.6 (t, C-6), 71.8, 72.1, 72.6, 73.6 (4 × t, 4 × PhCH_2), 74.1 (d, C-3), 74.9 (d, C-4), 80.5 (d, C-2), 127.9, 127.9, 127.9, 128.0, 128.0, 128.1, 128.4, 128.5, 128.5, 128.6 (10 × d, Ar-CH), 129.5 (d, C-5a), 134.3, 138.3, 138.4, 138.4, 138.5 (5 × s, C-5, 4 × Ar-C); m/z (ESI^+) 559 (M+Na^+, 100%); HRMS (ESI^+) calcd for $C_{35}H_{36}O_5Na$ (M+Na^+) 559.2455; found 559.2454.

4.9. Methyl 6-*N*-[2,3,4,6-tetra-*O*-benzyl-5a-carba-α-D-*lyxo*-hex-5(5a)-enopyranosyl]-6-amino-2,3,4-tri-*O*-benzyl-6-deoxy-6-*N*-(2-nitrobenzenesulfonyl)-α-D-mannopyranoside 15

Alcohol **9** (31 mg, 0.058 mmol) and sulfonamide **14** (46 mg, 0.071 mmol) were dissolved in toluene (2 mL) under Ar. Triphenylphosphine (60 mg, 0.23 mmol) was added, and the resulting yellowish solution was cooled to 0 °C. Next, DIAD (50 μL, 0.26 mmol) was added, and the reaction mixture was left to warm slowly to rt. After 5.5 h, TLC (toluene–EtOAc, 4:1) indicated the formation of a major product (R_f 0.6) and the presence of some remaining alcohol (R_f 0.4) and sulfonamide (R_f 0.5) starting materials. The reaction mixture was concentrated in vacuo and the crude residue was purified twice by flash column chromatography (toluene→toluene–EtOAc, 30:1→15:1→10:1) to yield pseudodisaccharide **15** (41 mg, slightly contaminated by DIAD residue) as a yellow oil; δ_H (500 MHz, $CDCl_3$) 3.16 (3H, s, OCH_3), 3.64–3.77 (4H, m, H-2^I, H-6^I, H-6′^{I}), 3.85–3.91 (3H, m), 4.00–4.03 (2H, m), 4.09–4.14 (2H, m, H-2^{II}), 4.23 (2H, m, PhCH_2), 4.33 (1H, d, J 11.8 Hz, PhC*H*H′), 4.44–4.71 (11H, m, H-1^I, 4 × PhCH_2, PhC*H*H′, PhCH*H*′), 4.95–4.97 (2H, m, H-1^{II}, PhCH*H*′), 5.80 (1H, s, H-5a^{II}), 7.11–7.44 (38H, m, Ar-H), 7.90 (1H, d, J 7.9 Hz, Ar-H); δ_C (125 MHz, $CDCl_3$) 47.7* (t, C-6^I), 55.4 (q, OCH_3), 57.3* (d, C-1^{II}), 70.4, 70.7, 71.4, 72.1, 72.6, 72.8, 73.6, 74.5 (8 × t, C-6^{II}, 7 × PhCH_2), 74.4, 74.8, 77.0, 80.2 (4 × d), 99.0 (d, C-1^I), 124.0, 127.4, 127.5, 127.6, 127.6, 127.7, 127.7, 127.8, 127.9, 128.1, 128.3, 128.3, 128.4, 128.4, 128.4, 128.5, 128.5 (17 × d, C-5a^{II}, Ar-CH), 131.1, 131.2, 132.8 (3 × d, Ar-CH), 133.6 (s, C-5^{II}), 138.2, 138.4, 138.4, 138.5, 138.5, 138.7, 138.8 (7 × s, Ar-C), 148.0, 150.2 (2 × s, Ar-C); m/z (ESI^+) 1189 (M+Na^+, 100%); HRMS (ESI^+) calcd for $C_{69}H_{70}O_{13}N_2SNa$ (M+Na^+) 1189.4491; found 1189.4517.

*Signals nearly invisible, can be perceived as minor 'bumps' only. Many signals in the ^{1}H NMR spectrum appear very broad. Signals are not observed for some carbons in the ^{13}C NMR spectrum.

4.10. Methyl 6-*N*-[2,3,4,6-tetra-*O*-benzyl-5a-carba-α-D-*lyxo*-hex-5(5a)-enopyranosylamino]-2,3,4-tri-*O*-benzyl-6-deoxy-α-D-mannopyranoside 16

Sulfonamide **15** (40 mg) was dissolved in DMF (1 mL), and thiophenol (15 μL, 0.15 mmol) was added. Potassium carbonate (34 mg, 0.24 mmol) was added, and the resulting mixture was heated to 50 °C. After 1 h 15 min, TLC (toluene–EtOAc, 4:1) indicated the complete consumption of the starting material (R_f 0.7) and the formation of a major product (R_f 0.1). The reaction mixture was allowed to cool to rt and then concentrated in vacuo. The crude product was purified by flash column chromatography (toluene–EtOAc, 8:1→5:1→2:1, 1% NEt_3) to yield the pseudodisaccharide amine **16** (29 mg, 51% over two steps) as a colourless oil; $[\alpha]_D^{22}$ + 27.6 (c 1.0, $CHCl_3$); δ_H (500 MHz, $CDCl_3$) 2.69 (1H, dd, $J_{5,6}$ 8.1 Hz, $J_{6,6'}$ 12.0 Hz, H-6^I), 2.86 (1H, dd, $J_{5,6'}$ 2.1 Hz, $J_{6,6'}$ 11.9 Hz, H-6′^{I}), 3.17 (3H, s, OCH_3), 3.58–3.71 (5H, m, H-2^I, H-4^I, H-5^I, H-1^{II}, H-2^{II}), 3.74–3.80 (2H, m, H-3^I, H-6^{II}), 3.84 (1H, dd, $J_{2,3}$ 1.8 Hz, $J_{3,4}$ 3.5 Hz, H-3^{II}), 4.03 (1H, d, $J_{3,4}$ 3.5 Hz, H-4^{II}), 4.10 (1H, d, $J_{6,6'}$ 12.1 Hz, H-6′^{II}), 4.24 (1H, d, J 11.8 Hz, PhC*H*H′), 4.38–4.58 (11H, m, H-1^I, PhC*H*H′, PhCH*H*′, 4 × PhCH_2), 4.62, 4.68 (2H, 2 × d, J 12.3 Hz, PhCH_2), 4.80 (1H, d, J 11.8 Hz, PhCH*H*′), 5.73 (1H, s, H-5a^{II}), 7.12–7.29 (35H, m, Ar-H); δ_C (125 MHz, $CDCl_3$) 47.2 (t, C-6^I), 54.9 (q, OCH_3), 54.9 (d, C-1^{II}), 71.0 (t, C-6^{II}), 71.5, 71.8, 72.3, 73.0, 73.7, 75.1 (6 × t, PhCH_2), 71.3, 74.9*, 75.0, 75.2, 76.8, 77.2 (6 × d, C-2^I, C-4^I, C-5^I, C-2^{II}, C-3^{II}, C-4^{II}), 80.4 (d, C-3^I), 99.1 (d, C-1^I), 127.6, 127.6, 127.7, 127.7, 127.7, 127.8, 127.8, 127.9, 128.0, 128.1, 128.4, 128.4, 128.5 (13 × d, Ar-CH), 129.3* (d, C-5a^{II}), 134.2* (s, C-5^{II}), 138.5, 138.5, 138.6, 138.6, 138.7, 138.8 (6 × s, Ar-C); m/z (ESI^+) 1004 (M+Na^+, 27), 982 (M+H^+, 100%); HRMS (ESI^+) calcd for $C_{63}H_{68}O_9N$ 982.4889 (M+H^+); found 982.4856; calcd for $C_{63}H_{67}O_9NNa$ 1004.4714 (M+Na^+); found 1004.4639.

*Low intensity signals.

4.11. Methyl 6-*N*-[2,3,4,6-tetra-*O*-benzyl-5a-carba-β-D-*lyxo*-hex-5(5a)-enopyranosyl]-6-amino-2,3,4-tri-*O*-benzyl-6-deoxy-6-*N*-(2-nitrobenzenesulfonyl)-α-D-mannopyranoside 17

Alcohol **10** (30 mg, 0.056 mmol) and sulfonamide **14** (46 mg, 0.071 mmol) were dissolved in toluene (2 mL) under Ar. Triphenylphosphine (60 mg, 0.23 mmol) was added, and the resulting yellowish solution was cooled to 0 °C. Next, DIAD (48 μL, 0.25 mmol) was added, and the reaction mixture was left to warm slowly to rt. After 5.5 h, TLC (toluene–EtOAc, 4:1) indicated the formation of two products (R_f's 0.7 and 0.6) and the presence of some alcohol (R_f 0.2) and sulfonamide (R_f 0.5) starting materials. The reaction mixture was concentrated in vacuo and the crude residue purified twice by column chromatography (toluene→toluene–EtOAc, 30:1→15:1 →10:1), to yield an elimination product (17 mg, 59%) as a colourless oil; data for the major component: δ_H (400 MHz, $CDCl_3$) 3.95–4.01 (2H, m, H-2, H-3), 4.39, 4.53 (2H, 2 × d, J 12.2 Hz, PhCH_2), 4.44 (1H, m, H-4), 4.64–4.75 (4H, m, 2 × PhCH_2), 4.89, 4.95 (2H, 2 × d, J 12.6 Hz, PhCH_2), 5.72 (1H, ddd, J 1.3 Hz, J 2.6 Hz, $J_{1,5a}$ 10.2 Hz, H-1), 6.09 (1H, s, H-6), 6.65 (1H, dat, J_{at} 1.0 Hz, $J_{1,5a}$ 10.2 Hz, H-5a), 7.15–7.17 (2H, m, Ar-H), 7.24–7.48 (18H, m, Ar-H).

And pseudodisaccharide **17** (13 mg, 20%) as a colourless oil; δ_H (500 MHz, $CDCl_3$) 2.97 (3H, s, OCH_3), 3.24 (1H, at, J 9.0 Hz, H-4^I), 3.59–3.71 (4H, m, H-2^I, H-3^I, H-5^I, H-6^I), 3.90 (1H, d, $J_{3,4}$ 8.6 Hz, H-3^{II}), 3.93 (1H, d, $J_{6,6'}$ 12.6 Hz, H-6^{II}), 4.09–4.12 (2H, m, H-6′^{I}, PhC*H*H′), 4.28 (1H, d, J 10.7 Hz, PhC*H*H′), 4.33 (1H, d, J 11.6 Hz, PhC*H*H′), 4.39 (1H, s, H-2^{II}), 4.47–4.60 (8H, m, H-1^I, H-4^{II}, H-6′^{II}, PhCH*H*′, 2 × PhCH_2), 4.67 (1H, d, J 11.6 Hz, PhC*H*H′), 4.72–4.78 (3H, m, PhC*H*H′, 2 × PhCH*H*′), 4.83 (1H, s, H-1^{II}), 4.86 (1H, d, J 10.8 Hz, PhCH*H*′), 4.97 (1H, d, J 10.8 Hz, PhCH*H*′), 6.15 (1H, s, H-5a^{II}), 7.05–7.60 (36H, m, Ar-H), 7.61–7.66 (2H, m, Ar-H), 7.98 (1H, d, J 8.0 Hz, Ar-H); δ_C (125 MHz, $CDCl_3$) 49.8 (t, C-6^I), 54.7 (q, OCH_3), 58.6 (d, C-1^{II}), 70.1, 74.3, 80.1 (3 × d, C-2^I, C-3^I, C-5^I), 77.0* (d, C-4^{II}), 77.5* (d, C-4^I), 80.0 (d, C-2^{II}), 83.9 (d, C-3^{II}), 98.8 (d, C-1^I), 123.9 (d, Ar-CH), 125.4 (d, C-5a^{II}), 127.4, 127.5, 127.6, 127.7, 127.8, 127.8, 128.0, 128.2, 128.4, 128.4, 128.5, 128.5 (12 × d, Ar-CH), 131.8, 132.2, 133.6 (3 × d, Ar-CH), 134.7 (s, C-5^{II}), 138.0, 138.2, 138.4, 138.5, 138.7, 138.8, 138.9, 138.9, 148.1 (9 × s, 9 × Ar-C); m/z (ESI^+) 1189 (M+Na^+, 100%); HRMS (ESI^+) calcd for $C_{69}H_{70}O_{13}N_2SNa$ (M+Na^+) 1189.4491; found 1189.4458.

*Chemical shifts estimated from HSQC spectrum due to overlap with $CDCl_3$ peaks.

Acknowledgement

We are grateful to Vetenskapsrådet (the Swedish research council) for support.

References

1. (a) Lichtenthaler, F. W.; Mondel, S. *Pure Appl. Chem.* **1997**, *69*, 1853–1866; (b) Lichtenthaler, F. W. *Carbohydr. Res.* **1998**, *313*, 69–89; (c) *Carbohydrates as Organic Raw Materials*; Lichtenthaler, F. W., Ed.; VCH: Weinheim, 1991.
2. Cumpstey, I.; Gehrke, S.; Erfan, S.; Cribiu, R. *Carbohydr. Res.* **2008**, *343*, 1675–1692.
3. Cumpstey, I. *Carbohydr. Res.* **2010**, *345*, 1056–1060.
4. Ramstadius, C.; Hekmat, O.; Eriksson, L.; Stålbrand, H.; Cumpstey, I. *Tetrahedron: Asymmetry* **2009**, *20*, 795–807.
5. Mitchell, M. L.; Tian, F.; Lee, L. V.; Wong, C.-H. *Angew. Chem., Int. Ed.* **2002**, *41*, 3041–3044.
6. Shing, T. K. M.; Cheng, H. M. *Org. Lett.* **2008**, *10*, 4137–4139.
7. Shing, T. K. M.; Kwong, C. S. K.; Cheung, A. W. C.; Kok, S. H.-L.; Yu, Z.; Li, J.; Cheng, C. H. K. *J. Am. Chem. Soc.* **2004**, *126*, 15990–15992.
8. Shing, T. K. M.; Li, T. Y.; Kok, S. H.-L. *J. Org. Chem.* **1999**, *64*, 1941–1946.
9. Arjona, O.; Gomez, A. M.; Lopez, J. C.; Plumet, J. *Chem. Rev.* **2007**, *107*, 1919–2036.
10. Madsen, R. *Eur. J. Org. Chem.* **2007**, 399–415.
11. (a) Ogawa, S.; Kanto, M.; Suzuki, Y. *Mini-Rev. Med. Chem.* **2007**, *7*, 679–691; (b) Ogawa, S. *Trends Glycosci. Glyc.* **2004**, *16*, 33–53.
12. Cumpstey, I. *Carbohydr. Res.* **2009**, *344*, 2285–2310.
13. Raaijmakers, H. W. C.; Arnouts, E. G.; Zwanenburg, B.; Chittenden, G. J. F. *Recl. Trav. Chim. Pays-Bas* **1993**, *112*, 511–514.
14. Raaijmakers, H. W. C.; Arnouts, E. G.; Zwanenburg, B.; Chittenden, G. J. F. *Carbohydr. Res.* **1994**, *257*, 293–297.
15. Sung'hwa, F.; Strik, A.; Regeling, H.; Zwanenburg, B.; Chittenden, G. J. F. *Carbohydr. Res.* **2006**, *341*, 846–854.
16. Lichtenthaler, F. W.; Klotz, J.; Flath, F.-J. *Liebigs Ann.* **1995**, 2069–2080.
17. Fraser-Reid, B.; Wu, Z.; Udodong, U. E.; Ottosson, H. *J. Org. Chem.* **1990**, *55*, 6068–6070.
18. Kok, S. H.-L.; Shing, T. K. M. *Tetrahedron Lett.* **2000**, *41*, 6865–6868.
19. Fukuyama, T.; Jow, C.-K.; Cheung, M. *Tetrahedron Lett.* **1995**, *36*, 6373–6374.
20. Cumpstey, I.; Ramstadius, C.; Borbas, K.E.; Alonzi, D.S.; Butters, T.D., manuscript in preparation.
21. Akhtar, T.; Cumpstey, I. *Tetrahedron Lett.* **2007**, *48*, 8673–8677.
22. Yang, J.; Xu, H.; Zhang, Y.; Bai, L.; Deng, Z.; Mahmud, T. *Org. Biomol. Chem.* **2011**, *9*, 438–449.