Synthesis of carba sugars from aldonolactones. Part IV. Stereospecific synthesis of carbaheptopyranoses by radical-induced carbocyclisation of 2,3-unsaturated octonolactones

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Received (in Cambridge, UK) 19th January 2001, Accepted 26th January 2001
First published as an Advance Article on the web 8th March 2001

Three new carbaheptopyranoses, 6-deoxy-5a-carba-β-L-*gulo*- (**8**), 5a-carba-D-*glycero*-β-D-*ido*- (**22**) and 5a-carba-L-*glycero*-α-L-*galacto*-heptopyranose (**25**), have been prepared from 8-bromo-8-deoxy-2,3-unsaturated octono-1,4-lactones with L-*galacto*-, D-*gluco*- and D-*manno*-configuration, respectively. The key step was a regio- and stereoselective 6-*exo*-trig radical-induced carbocyclisation of the unsaturated octonolactones to give bicyclic cyclohexane-lactone derivatives. Reduction of the lactone moiety using $Ca(BH_4)_2$ gave the said carbaheptopyranoses. The 8-bromo-8-deoxy-2,3-unsaturated octonolactones were prepared from the inexpensive, commercially available D-*glycero*-D-*gulo*-heptonolactone and L-tartaric acid.

Introduction

Highly oxygenated cyclopentanes and cyclohexanes are often referred to as pseudosugars[1] or carba sugars,[2,3] due to their close resemblance to sugars. This family of carbohydrate mimics currently attracts interest among chemists as well as biochemists due to the interesting biological activities which they exhibit.[4] Thus, in accordance with their sugar-like structures, it was proposed as early as 1968[1b] that carba sugars could be accepted by enzymes or biological systems in place of ordinary sugars and therefore behave as glycosidase inhibitors, due to their stability towards acid as well as enzymatic hydrolysis. Since this hypothesis was proposed, it has been established that several carba sugars have shown promising applications in the field of glycosidase inhibition.[3,5] Interestingly, they have also found use as non-nutritive artificial sweeteners.[6] Consequently, the preparation of carba sugars is of interest and since the discovery of the first carba sugar in 1966[1a] a number of methods have been developed for the synthesis of both carbafuranoses and carbapyranoses.[7] Among the methods, carbocyclisation, based on free-radical addition to an unsaturated radical acceptor, has been a valuable synthetic approach[8] since the neutral reaction conditions are compatible with a range of functional groups.

Whereas the free-radical cyclisation of acyclic carbohydrate derivatives based on hex-5-enyl radicals has been widely used to prepare polyhydroxylated cyclopentanes (carbafuranoses),[9] only a few reports on the construction of polyhydroxylated cyclohexane rings (carbapyranoses) by radical cyclisation of hept-6-enyl radicals have appeared.[8,10] The 6-*exo*-trig cyclisation of the hept-6-enyl radical is about 40-times slower than the 5-*exo*-trig cyclisation of the hexenyl radical and thus competing reactions, such as reduction of the initial radical, become important.[8] However, by choosing the radical acceptor properly, *i.e.* tuning the substrates electronically, leading to proper conformations in the transition state,[10a,11] the 6-*exo*-trig cyclisation has successfully been used to prepare cyclic hexitols in a diastereomeric ratio varying from 50 : 50 to 100 : 0.[11] Also 6-*endo*-trig cyclisations have been reported when using alkenes as radical acceptors,[10c] while 6-*exo*-dig cyclisation to give unsaturated cyclohexenes has been achieved by carbocyclisation onto an alkyne.[10b]

Recently, we have described the synthesis of carba-analogues of hexo- and pento-furanoses by 5-*exo*-trig radical cyclisations of ω-bromo-ω-deoxy-α,β-unsaturated heptonolactones.[12] The radical cyclisation occurred regio- and stereoselectively, generating one[12c,d] or two chiral centers.[12a,b,d] The stereoselectivity was governed by the formation of a bicyclic cyclopentane-lactone compound. Since the methods described for 6-*exo*-trig cyclisations yielded diastereomers, we now wanted to extend the synthetic use of the radical-induced carbocyclisations of ω-bromo-ω-deoxy-α,β-unsaturated aldonolactones for the preparation of cyclohexane rings, *i.e.* to synthesise optically pure carbapyranoses. The starting materials for the carbocyclisations should thus be 2,3-unsaturated 1,4-octonolactones, activated at the primary position for generation of a radical.

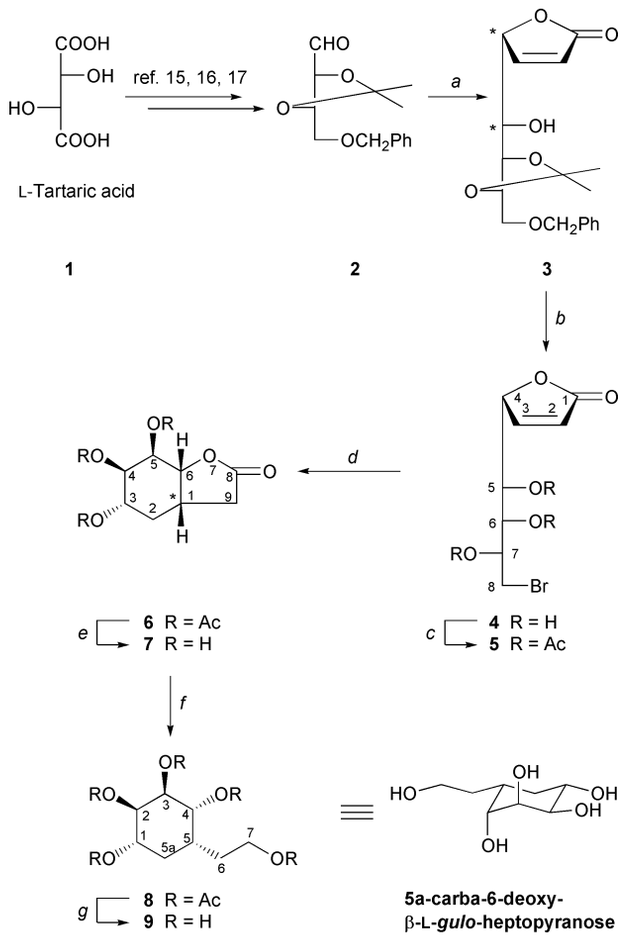
The unsaturation in the substrates can either be prepared by reductive elimination from acetylated 2-bromo-2-deoxyaldonolactones[12c,12d,13] or by elimination of acetic acid from acetylated aldonolactones.[12a,12b] Alternatively, condensation of an α-hydroxy aldehyde with 2-(trimethylsiloxy)furan (TMSOF) following the method described by Casiraghi and Rassu gives likewise access to 2,3-unsaturated aldonolactones.[14]

In this work we have used the commercially available, inexpensive compounds L-tartaric acid and D-*glycero*-D-*gulo*-heptonolactone as the starting materials for the preparation of the unsaturated octonolactones and thus for new carbaheptopyranoses.

Results and discussion

L-Tartaric acid **1** was transformed into the protected L-threose derivative **2** by modified literature procedures, which involve isopropylidation and esterification,[15] reduction,[15] followed by monobenzylation[16] and finally a Swern oxidation[17] (Scheme 1). The aldehyde **2** was fairly stable and easy to handle, but required re-distillation before use due to formation of tri- or tetramers.[17] Four-carbon elongation of **2** with TMSOF in the presence of BF_3–diethyl ether cleanly generated the 8-*O*-benzyl-6,7-*O*-isopropylidene-2,3-unsaturated octonolactone **3** in 70%

 DOI: 10.1039/b100708o



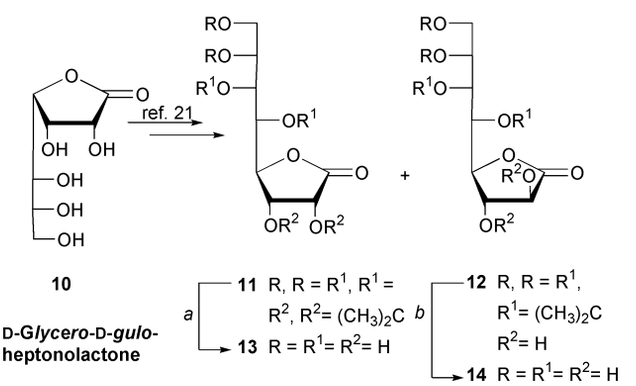
Scheme 1 *Reagents and conditions*: (*a*) TMSOF, BF_3–Et_2O, CH_2Cl_2, −78 °C, 5 h (70%); (*b*) i HBr in AcOH, rt, 30 min; ii MeOH, rt, overnight; (*c*) Ac_2O, H^+, rt, 1.5 h (51% from **3**); (*d*) Bu_3SnH, AIBN, EtOAc, reflux, 4 h (82%); (*e*) HCl MeOH, rt, overnight (89%); (*f*) $Ca(BH_4)_2$, ETOH, −10 °C, 2 h, then at rt overnight; (*g*) Ac_2O, H^+, rt 1.5 h (71% from **7**).

crystalline yield using a slightly modified literature procedure.[18] The compound could be characterised without protecting the newly formed C-5 hydroxy group as a silyl ether as described.[18] For activation at C-8 the benzyl group should be removed, but several attempts were made without success. Either no debenzylation took place ($SnCl_4$, 1,4-dioxane; $FeCl_3$, CH_2Cl_2) or no selective reduction could be obtained, *i.e.* the double bond was hydrogenated as well (20% $Pd(OH)_2$/C, cyclohexene, EtOH; 10% Pd/C, cyclohexene, EtOH; 10% Pd/C, MeOH; 5% Pd/C, $HCOONH_4$, acetone). Finally, treatment of **3** with hydrogen bromide in acetic acid for 30 min followed by deacetylation with methanol gave in one step 8-bromo-2,3,8-trideoxy-L-*galacto*-oct-2-enono-1,4-lactone **4**, since both debenzylation, deisopropylidation and introduction of bromine at C-8 had taken place. Acetylation, under acidic conditions, of the α,β-unsaturated bromo octonolactone **4** gave the crystalline tri-*O*-acetate **5** (51% yield based on **3**).

Radical cyclisation of the unsaturated bromo lactone **5** was carried out in EtOAc at reflux temperature by adding Bu_3SnH and AIBN (α,α′-azoisobutyronitrile) in EtOAc with a syringe pump in the course of 2 h. Only one product was obtained according to the ^{1}H NMR spectrum of the crude product. Purification by column chromatography gave the *cis*-fused cyclohexane-lactone derivative **6** in 82% yield, which by deacetylation gave the crystalline triol **7**. The configuration of the new stereogenic center could not unambiguously be verified by the coupling constant between H-1 and H-6, $J_{1,6}$, which was found to be 5.5 Hz in compound **6** and 3.5 Hz in the deacetylated compound **7**. The carbocyclisation leading to *cis*-fused rings was finally confirmed by NMR spectroscopic analysis of the carba sugar derived from **7**, as outlined below. The lactone moiety of the bicyclic compound **7** was readily reduced to the corresponding alcohol using $Ca(BH_4)_2$[19,20], in ethanol to give the carbocyclic analogue of 6-deoxy-β-L-*gulo*-heptopyranose, compound **8**, characterised as the penta-*O*-acetate **9** (71% based on **7**) (Scheme 1).

The structure of **9** was found to be 1,2,3,4,7-penta-*O*-acetyl-6-deoxy-5a-carba-β-L-*gulo*-heptopyranose based on analysis of ^{1}H NMR and COSY spectra. First, the $^1C_4$-conformation (Scheme 1) was determined by the large coupling constant between the two axial protons H-5a (δ 1.55) and H-1 (δ 5.50) ($J_{1,5aa}$ = 11 Hz). The coupling constant between the axial H-5a and H-5, $J_{5,5aa}$ = 12 Hz, confirmed the configuration at the new stereogenic center C-5. The conformation was further supported by the signal from H-4 at δ 5.22, having two small coupling constants (4.0 and 3.0 Hz), showing an equatorial position of this proton. If the radical cyclisation had occurred to give a *trans*-fused bicyclic system, the configuration at C-1 in **6** and **7** would have been opposite and thus also the configuration at C-5 in the carba sugar. This would most probably have changed the conformation of the carba sugar from $^1C_4$ to $^4C_1$ conformation, placing H-4 in an axial and H-1 in an equatorial position. This was not in agreement with the analysis of the ^{1}H NMR spectrum of **9**. Thus, formation of the cyclohexane ring by radical induced carbocyclisation occurred stereospecifically to give a *cis*-fused bicyclic cyclohexane-lactone system.

The second synthesis started from the commercially available D-*glycero*-D-*gulo*-heptonolactone **10**. The heptonolactone was reduced to the heptose, subjected to a Kiliani ascension and, without purification, converted into the tri- and diacetonides **11** and **12**, respectively, by improving literature methods.[21] The di- and triacetonide could be separated by extraction because of their differences in polarity, a method which we have used previously with success (Scheme 2).[12a] Hereby two octonolactones were obtained, having the OH-2 and OH-3 groups either *cis* (**11**) or *trans* (**12**) oriented, which could give access to a 2,3-unsaturated lactone or a 2-substituted 2,3-unsaturated lactone, respectively.

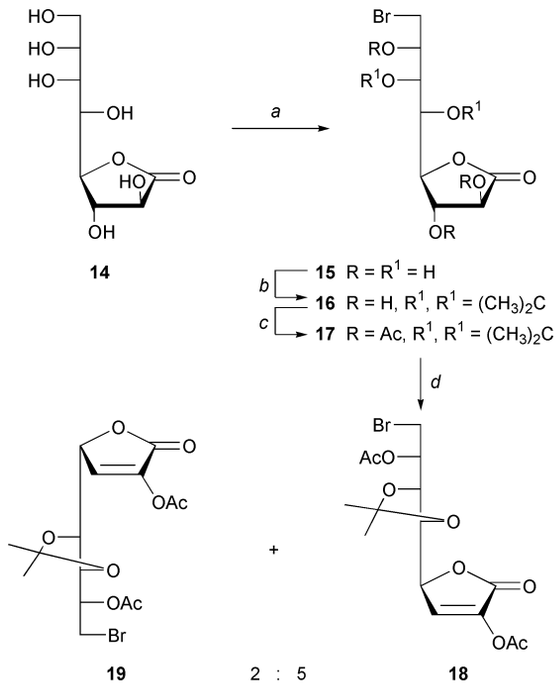


Scheme 2 *Reagents and conditions*: (*a*) TFA, water, rt, 1.5 h (84%); (*b*) TFA, water, rt, 22 h (84%).

The 2,3-*cis*-configured protected lactone **11** was treated with hydrogen bromide in acetic acid, aiming to introduce bromine directely at C-8 and C-2,[22] but no promising results were obtained. Deprotection of the diacetonide **11** gave **13**[21] but several attempts to convert the lactone **13** into a 2,8-dibromo-2,8-dideoxy lactone, failed, possibly due to polyhalogenation. These results were obtained both using hydrogen bromide in acetic acid as well as thionyl dibromide in *N*,*N*-dimethylformamide.[23] Apparently, the four-carbon side chain of the octonolactone behaves as a polyol, which can be polybrominated under the conditions used, as also described for reactions of pentitols and hexitols with acetyl bromide.[24] Likewise, we have previously isolated a 6,7-dibromoheptonolactone

(24%) by reaction of a heptonolactone with hydrogen bromide in acetic acid.[12a] No further attempts were made to convert **13** into a 8-bromo-8-deoxy-2,3-unsaturated 1,4-octonolactone.

For conversion of the diisopropylidene lactone **12** into a substrate for the carbocyclisation, deprotection gave the octonolactone **14**,[21] which by treatment with hydrogen bromide in acetic acid for 30 min followed by deacetylation with methanol yielded the lactone **15**, monobrominated at C-8 (Scheme



Scheme 3 *Reagents and conditions*: (*a*) i HBr in AcOH, rt, 30 min, ii MeOH, rt, overnight; (*b*) CH_3COCH_3, H^+, reflux, 2 days (50% from **14**); (*c*) Ac_2O, pyridine, rt, 1.5 h (87%); (*d*) Et_3N, CH_2Cl_2, rt, 2.5 h (76%).

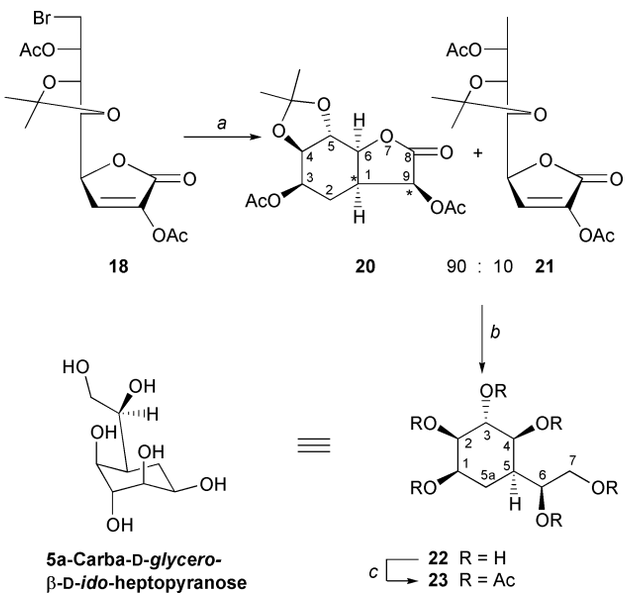
3). In this case no polybromination was observed. Treatment of the crude bromo lactone **15** with acidic acetone gave the 5,6-*O*-isopropylidene-protected bromo lactone **16**, isolated in 50% crystalline overall yield from **14**. The structure of **16** was assigned to be a 5,6- and not a 6,7-isopropylidene-protected lactone. This was based on acetylation of **16** in pyridine to give the acetate **17**, isolated in 87% yield. The ^{1}H NMR spectrum of **17** showed a downfield shift of the H-7 proton, from 3.9 ppm in **16** to 5.0 ppm in **17**, thus confirming the presence of a free hydroxy group at C-7 in **16**.

It is important to protect the C-5 of a 2,3-unsaturated 1,4-lactone as an ether before acetylation in pyridine, since the influence of a base on a fully acetylated 1,4-lactone would most likely lead to polyunsaturated systems. This is a result of β-eliminations, first of the C-3 acetyl group to generate the 2,3-unsaturated lactone, followed by elimination of the *O*-acetyl leaving group at C-5.[25]

Treatment of **17** with triethylamine led to only one β-elimination to give the unsaturated lactone **18** and no further eliminations were observed. The reaction was, however, accompanied by an epimerisation at the allylic position, C-4,[12a] giving the unsaturated lactone **19** as well, in the ratio **18** : **19** ≈ 5 : 2 according to a ^{13}C NMR spectrum. The two isomeric 2,3-unsaturated octonolactones could be separated by flash chromatography to give crystalline **18** and syrupy **19**. The assignment of the configuration at C-4 of the unsaturated lactones was based on the coupling constants $J_{4,5}$. By analysis of a range of 2,3-unsaturated heptonolactones, we have previously found that $J_{4,5}$ was in the range of 1–2.5 Hz for lactones with 4,5-*threo*-configuration, while the corresponding coupling constant was in the range of 6–9.5 Hz for the unsaturated lactones having 4,5-*erythro*-configuration.[12a] The ^{1}H NMR spectrum of **18** showed $J_{4,5}$ = 2.5 Hz (δ 5.06, H-4), confirming the 4,5-*threo*-configuration, while the spectrum for **19** showed $J_{4,5}$ = 7.0 Hz (δ 4.96, H-4), in agreement with the 4,5-*erythro*-configuration. For comparison the coupling constant $J_{4,5}$ for the unsaturated octonolactones **3** and **5** (Scheme 1) was found to be 3.0 and 2.0 Hz, respectively, in agreement with the 4,5-*threo*-configuration. Our method for determination of the relative configurations between C-4 and C-5 in 2,3-unsaturated heptono-1,4-lactones[12a] could thus also be extended to octonolactones.

Thus, two substrates for radical-induced carbocyclisation had been synthesised (Scheme 3).

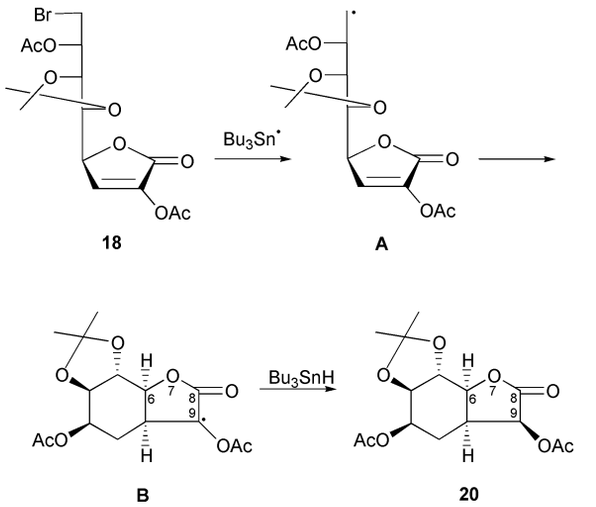
Radical cyclisation of **18** was carried out using Bu_3SnH and AIBN in refluxing EtOAc to give the crystalline bicyclic compound **20** as the only cyclisation product (73% yield) (Scheme 4). The 8-deoxy compound **21** was isolated in minor amounts



Scheme 4 *Reagents and conditions*: (*a*) Bu_3SnH, AIBN, EtOAc, reflux, 4 h (73% of **20** and 9% of **21**); (*b*) $Ca(BH_4)_2$, ETOH, −10 °C, 2 h, then at rt overnight (80%); (*c*) Ac_2O, H^+, rt, 1.5 h (77%).

(9%, crystalline). The formation of the latter was probably due to the slower ring-closing reaction of the primary formed radical on a substrate having a *trans*-isopropylidene group. The intramolecular ring closure was again stereoselective and in this case *two* new stereogenic centers were formed. Again, the *cis*-fused ring closure could not be verified unambiguously based on the coupling constant between H-1 and H-6 ($J_{1,6}$ = 6.5 Hz), but the coupling constant between H-1 and H-9 was in agreement with a *cis*-orientation of these protons ($J_{1,9}$ = 8.5 Hz).[12a,12b] It has to be emphasised that the *cis*-fused cyclopentane-lactone compounds obtained in our previous studies exhibited $J_{1,6}$ 4.5–7.5 and $J_{1,9}$ 7.5–10 Hz, both for *cis*-oriented protons. An X-ray structure confirmed the assignments.[12d]

Reduction of the lactone moiety in **20** was carried out as described for compound **7** above to give the hexahydroxy (ethylcyclohexane) **22** which was characterised as the hexaacetate **23** (62% crystalline yield from **20**) (Scheme 4). The structure was confirmed by ^{1}H NMR spectroscopy. The conformation of **23** was determined to be $^4C_1$ based on the large coupling constant between the axial H-5a (δ 1.99, H-5a) and H-1 (δ 5.29, H-1) $J_{1,5aa}$ = 13 Hz, showing an axial H-1 proton. Furthermore the value $J_{5,5aa}$ = 13 Hz confirmed the presence of an axial H-5 proton (δ 2.38, H-5), confirming the configuration of the newly created chiral center, and thus a *cis*-fusion of the bicyclic compound **20**. The H-1, H-6 and H-9 protons in **20** are consequently all *cis*-oriented. According to the proposed mechanism[12d] (Scheme 5) the initially formed radical **A** from **18** adds

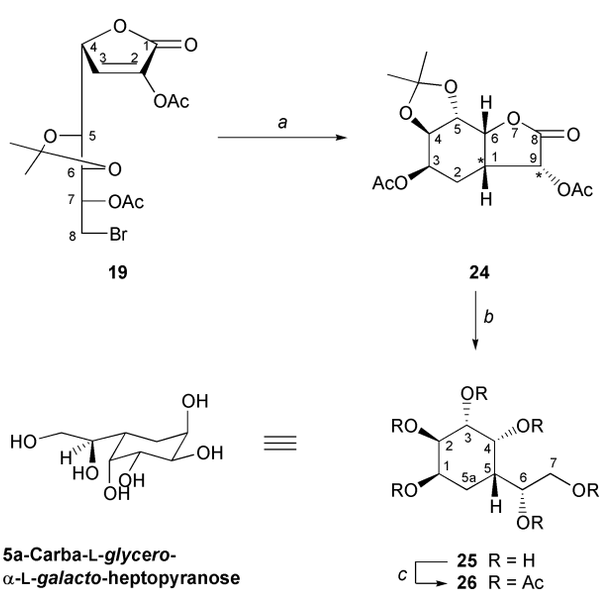


Scheme 5 Proposed mechanism for the radical cyclisation of **18** giving the cyclohexane-lactone **20**.

to the double bond, generating a radical at C-9 (**B**) which is trapped by Bu_3SnH from the less hindered *exo*-side of the roof-shaped bicyclic intermediate to give **20**.

The structure of **23** was thus 1,2,3,4,6,7-hexa-*O*-acetyl-5a-carba-D-*glycero*-β-D-*ido*-heptopyranose, and thus a new carbaheptose, 5a-carba-D-*glycero*-β-D-*ido*-heptopyranose **22**, has been synthesised.

Radical cyclisation of **19** was performed in analogy to the cyclisation of **18** to give the bicyclic compound **24** isolated in 73% crystalline yield (Scheme 6). No other products were formed according to a ^{1}H NMR spectrum of the crude product. Again the stereochemistry of the two stereogenic centers could not be unambigously determined from the coupling constants ($J_{1,6}$ = 3.0 Hz, $J_{1,9}$ = 6.5 Hz). However, reduction with $Ca(BH_4)_2$ afforded 5a-carba-L-*glycero*-α-L-*galacto*-heptopyranose **25** that was characterised as the acetate **26**. The $^1C_4$ conformation was determined by the equatorially oriented H-1 (δ 5.61, $J_{1,5aa}$ = 2.5 Hz, $J_{1,5ae}$ = 2.0 Hz) and the configuration at C-5 by the large coupling constant between H-5 and the axial H-5a ($J_{5,5aa}$ = 13.5 Hz) (Scheme 6).



Scheme 6 *Reagents and conditions*: (*a*) Bu_3SnH, AIBN, EtOAc, reflux, 4 h (73%); (*b*) $Ca(BH_4)_2$, ETOH, −10 °C, 2 h, then at rt overnight (96%); (*c*) Ac_2O, H^+, rt 1.5 h (83%).

In summary, we have developed a route for the preparation of 3 different carbaheptopyranoses starting from readily available 2,3-unsaturated 8-bromo-8-deoxyoctonolactones. The key step was a regio- and stereoselective 6-*exo*-trig radical cyclisation, which gave optically active *cis*-fused cyclohexane-lactone derivatives. The configuration of the stereogenic center was thus controlled by the configuration of the side chain at C-4 of the unsaturated bromo lactone. For the 2-substituted 2,3-unsaturated lactones the hydrogen transfer at C-2 was controlled by steric effects from the newly formed *cis*-fused bicyclic system, protecting the *endo*-side of the molecule. The relative configuration at C-4/C-5 of 2,3-unsaturated octono-1,4-lactones has been determined by ^{1}H NMR spectroscopy.

Experimental

Mps are uncorrected. Optical rotations were determined on a Perkin-Elmer 241 polarimeter. $[\alpha]_D$-Values are given in units of 10^{-1} deg cm^2 g^{-1}. NMR spectra were recorded on Bruker AC-250 and AM-500 instruments. Chemical shifts were measured in δ (ppm) and coupling constants J are in Hz. 1,4-Dioxane (δ_C = 67.4) or acetone (δ_C = 29.8) were used as internal standard for ^{13}C NMR spectra in D_2O, and HDO (δ = 4.60) for ^{1}H NMR spectra. For spectra in $CDCl_3$ the solvent signal was used as internal standard (δ_C = 76.93) in ^{13}C NMR spectra and TMS (δ = 0.00) for ^{1}H NMR spectra. For spectra obtained in benzene-d_6 (δ = 7.16) and acetone-d_6 (δ = 2.05) the solvent signal was used as internal standard in ^{1}H NMR. TLC was performed on Merck 60 F_{254} precoated silica plates and spots were detected by spraying with a solution of 1.5% $(NH_4)_6Mo_7O_{24}\cdot 4H_2O$, 1% $Ce^{IV}SO_4$ and 10% H_2SO_4 followed by charring. Flash chromatography was performed with silica gel 60 Å, particle sizes 60–75 μm from Merck. Concentrations were performed on a rotary evaporator at a temperature below 40 °C. All solvents were distilled before use. Microanalyses were performed by Mikroanalytisches Laboratorium am Institut für Physikalische Chemie der Universität Wien, Austria. The radical cyclisations with Bu_3SnH were carried out using a syringe pump Harvard Apparatus 11.

4-*O*-Benzyl-2,3-*O*-isopropylidene-L-threose 2

Compound **2** was prepared by slight modification of the literature procedure.[15–17] A mixture of L-tartaric acid **1** (50.0 g, 333 mmol), 2,2-dimethoxypropane (80.5 g, 95 mL, 861 mmol), toluene-*p*-sulfonic acid monohydrate (PTSA) (0.212 g) in MeOH (20 mL) was refluxed under nitrogen until a dark red homogeneous solution was obtained (1 h). Additional 2,2-dimethoxypropane (50 mL) and cyclohexane (225 mL) were added. The mixture was refluxed and the acetone–cyclohexane and MeOH–cyclohexane azeotropes were slowly removed over a period of two days (approximately 300 mL of distillate was removed until the temperature at the solvent head was ≈79 °C). After cooling of the mixture to rt, anhydrous K_2CO_3 (0.5 g, 3.6 mmol) was added and the mixture was stirred until the reddish colour had abated. Volatile material was evaporated off and the residue was fractionally distilled at 96–102 °C/1.3 mmHg (lit., [15] 94–101 °C/0.5 mmHg) to afford dimethyl 2,3-*O*-isopropylidene-L-tartrate[15] as a pale yellow syrup (49.9 g, 69%); δ_C ($CDCl_3$; 50.3 MHz) 169.9 (C-1, -4), 113.6 (ketal), 76.7 (C-2, -3), 52.6 (2 × CH_3), 26.1 (2 × CH_3).

The 2,3-*O*-isopropylidene-L-tartrate (49.9 g, 201.2 mmol) was dissolved in EtOH (300 mL), the solution was cooled to −20 °C, and $NaBH_4$ (15.2 g, 402.4 mmol) was added slowly under continuous stirring. The mixture was allowed to come to rt overnight and stirred for 4 days. After neutralisation with ion-exchange resin (Amberlite IR-120, H^+) the resin was filtered off, and the filtrate was concentrated to a syrup, which was co-evaporated with MeOH (3 × 100 mL) and distilled at 103–107 °C/1.0 mmHg (lit.,[15] 94–106 °C/0.4 mmHg; lit.,[26] 96–96.5 °C/0.5 mmHg) to afford 2,3-*O*-isopropylidene-L-threitol[15,26] (19.7 g, 61%) as a yellow syrup; δ_C ($CDCl_3$; 50.3 MHz) 109.2 (ketal), 78.7 (C-2, -3), 62.1 (C-1, -4), (2 × CH_3).

NaH (55–60% in mineral oil; 4.4 g, ≈92.6 mmol) was washed with hexane and suspended in DMF (30 mL) in an argon atmosphere and the mixture was cooled to −20 °C. A solution of 2,3-*O*-isopropylidene-L-threitol (15.0 g, 92.6 mmol) in DMF (90 mL) was added over 15 min followed by addition of benzyl bromide (15.8 g, 92.6 mmol) in DMF (30 mL) in the course of 5 min. After stirring for 12 h the mixture was concentrated to a residue, which was dissolved in CH_2Cl_2 (80 mL) and washed with water (50 mL). The aqueous phase was extracted with CH_2Cl_2 (2 × 50 mL) and the combined organic phases were washed with water (30 mL), dried ($MgSO_4$), filtered through activated charcoal, and the solvent was evaporated. The product was purified by flash chromatography (EtOAc–hexane, 1 : 3) to afford 1-*O*-benzyl-2,3-*O*-isopropylidene-L-threitol[16] (18.7 g, 80%); δ_C ($CDCl_3$; 50.3 MHz) 137.2, 127.8, 127.1 (Ph), 108.7 (ketal), 78.9, 76.0 (C-2, -3), 73.0, 69.9 (C-1, *C*H_2Ph), 61.8 (C-4), 26.4 (2 × CH_3).

A solution of $(COCl)_2$ (8.22 g, 5.6 mL, 64.8 mmol) in CH_2Cl_2 (100 mL) was cooled to −78 °C, DMSO (9.26 g, 10.9 mL, 118.7 mmol) in CH_2Cl_2 (25 mL) was added, and the mixture was stirred for 5 min, after which time 1-*O*-benzyl-2,3-*O*-isopropylidene-L-threitol (13.6 g, 54.0 mmol) in CH_2Cl_2 (50 mL) was added. After stirring of the mixture for 2 h at −78 °C, Et_3N (27.3 g, 37.5 mL, 267.0 mmol) was added and the temperature was increased to 0 °C during 1 h. The mixture was poured into cold phosphate buffer (pH 7, 1.5 L), and extracted with Et_2O (2 × 200 mL). The organic layer was washed with water (400 mL) and concentrated. The residue was diluted with Et_2O (150 mL), washed with water (3 × 200 mL) and dried (Na_2SO_4). Distillation at reduced pressure at 107–111 °C/0.3 mmHg (lit.,[17] 121 °C/0.4 mmHg) gave **2** as a colourless syrup (7.4 g, 55%); δ_C ($CDCl_3$; 50.3 MHz) 200.5 (C-1), 137.5, 128.3, 127.6, 127.5 (Ph), 111.5 (ketal), 81.9 (C-2), 76.0 (C-3), 73.4 (*C*H_2Ph), 69.7 (C-4), 26.7, 26.0 (2 × CH_3).

8-*O*-Benzyl-2,3-dideoxy-6,7-*O*-isopropylidene-L-*galacto*-oct-2-enono-1,4-lactone 3

Compound **3** was prepared by a slight modification of the literature procedure.[14] The threose **2** (7.35 g, 29.4 mmol) and TMSOF[14,27] (5.05 g, 32.3 mmol) were dissolved in dry CH_2Cl_2 (130 mL) under nitrogen and the mixture was cooled to −78 °C. BF_3–diethyl ether (3.62 mL, 29.4 mmol) was added with stirring, which was continued for 5 h, after which time saturated aq. $NaHCO_3$ (70 mL) was added and the mixture was allowed to come to rt. The mixture was extracted with CH_2Cl_2 (3 × 50 mL), dried ($MgSO_4$), and the mixture was evaporated to give a crude oil which was purified by flash chromatography (EtOAc–hexane, 4 : 3; R_f 0.32) to give colourless crystals (6.9 g, 70%), mp 91–92 °C. Recrystallisation from EtOAc–hexane gave **3**, mp 93–94 °C; $[a]_D^{20}$ +33.4 (*c* 1.0 $CHCl_3$) (Found: C, 64.55; H, 6.58. Calc. for $C_{18}H_{22}O_6$: C, 64.66; H, 6.63%); δ_H ($CDCl_3$; 500 MHz) 1.38 (s, 3H, CH_3), 1.40 (s, 3H, CH_3), 3.54 (dd, $J_{8,8'}$ = 9.0, $J_{7,8}$ = 7.5, 1H, H-8), 3.72 (dd, $J_{5,6}$ = 8.5, $J_{4,5}$ = 3.0, 1H, H-5) 3.78 (dd, $J_{8,8'}$ = 9.0, $J_{7,8'}$ = 4.5, 1H, H′-8), 3.98 (dd, $J_{5,6}$ = 8.5, $J_{6,7}$ = 7.5, 1H, H-6), 4.09 (ddd, $J_{7,8}$ = 7.5, $J_{6,7}$ = 7.5, $J_{7,8'}$ = 4.5, 1H, H-7), 4.59, 4.57 (2 d, J = 17.0, 2H, CH_2Ph), 5.25 (ddd, $J_{4,5}$ = 3.0, $J_{2,4}$ = 2.0, $J_{3,4}$ = 1.5, 1H, H-4), 6.15 (dd, $J_{2,3}$ = 6.0, $J_{2,4}$ = 2.0, 1H, H-2), 7.35 (m, 5H, Ph), 7.47 (dd, $J_{2,3}$ = 6.0, $J_{3,4}$ = 1.5, 1H, H-3); δ_C ($CDCl_3$; 50.3 MHz) 173.5 (C-1), 153.6 (C-3), 136.5, 128.5, 128.2, 128.0 (Ph), 122.4 (C-2), 109.9 (ketal), 83.3 (C-4), 79.4, 78.5 (C-6, -7); 73.9 (CH_2Ph), 72.4 (C-5), 70.1 (C-8), 26.7 (2 × CH_3).

8-Bromo-2,3,8-trideoxy-L-*galacto*-oct-2-enono-1,4-lactone 4 and 5,6,7-tri-*O*-acetyl-8-bromo-2,3,8-trideoxy-L-*galacto*-oct-2-enono-1,4-lactone 5

The lactone **3** (4.00 g, 11.9 mmol) was dissolved in 32.6% HBr in AcOH (20 mL) and the solution was stirred for 30 min. Then MeOH (100 mL) was added and the mixture was left overnight, concentrated and co-concentrated with MeOH (3 × 50 mL) and with water (3 × 50 mL). The residue was dissolved in water (50 mL), extracted with Et_2O (4 × 50 mL), and the extracts concentrated and co-concentrated with toluene (4 × 100 mL) to give crude **4** (3.96 g); δ_C (D_2O; 50.3 MHz) 175.6 (C-1), 156.3 (C-3), 120.1 (C-2), 82.7 (C-4), 68.6, 68.0, 67.7 (C-5, -6, -7), 32.5 (C-8).

Crude, acidic **4** was dissolved in Ac_2O (50 mL) and left for 1.5 h. Then ice–water (80 mL) was slowly added and the mixture was concentrated. The residue was suspended in water and extracted with CH_2Cl_2 (4 × 30 mL). The combined organic phases were washed with water (until pH ≈ 7), dried ($MgSO_4$), filtered through activated charcoal, and concentrated to give **5** as colourless crystals (2.4 g, 51% from **3**), mp 170–173 °C. Recrystallisation from EtOAc gave **5** as colourless crystals, mp 174–175 °C; $[a]_D^{20}$ +42.3 (*c* 1.0, $CHCl_3$) (Found: C, 43.00; H, 4.30; Br, 20.23. Calc. for $C_{14}H_{17}BrO_8$: C, 42.77; H, 4.36; Br, 20.32%); δ_H ($CDCl_3$; 500 MHz) 1.95 (s, 3H, CH_3), 2.10 (s, 3H, CH_3), 2.15 (s, 3H, CH_3), 3.29 (dd, $J_{8,8'}$ = 11.0, $J_{7,8}$ = 8.0, 1H, H-8), 3.44 (dd, $J_{8,8'}$ = 11.0, $J_{7,8'}$= 5.5, 1H, H′-8), 5.12 (ddd, $J_{4,5}$ = 2.0, $J_{2,4}$ = 2.0, $J_{3,4}$ = 1.5, 1H, H-4), 5.19 (dd, $J_{5,6}$ = 9.5, $J_{6,7}$ = 2.0, 1H, H-6), 5.39 (ddd, $J_{7,8}$ = 8.0, $J_{7,8'}$ = 5.5, $J_{6,7}$ = 2.0, 1H, H-7), 5.67 (dd, $J_{5,6}$ = 9.5, $J_{4,5}$ = 2.0, 1H, H-5), 6.12 (dd, $J_{2,3}$ = 5.5, $J_{2,4}$ = 2.0, 1H, H-2), 7.32 (dd, $J_{2,3}$ = 5.5, $J_{3,4}$ = 1.5, 1H, H-3); δ_C ($CDCl_3$; 50.3 MHz) 171.6 (C-1), 169.7 (3 × CO), 151.8 (C-3), 122.9 (C-2), 80.1 (C-4), 69.8, 69.7, 67.1 (C-5, -6, -7), 29.3 (C-8), 20.5 (3 × CH_3).

(1*S*,3*S*,4*R*,5*R*,6*R*)-3,4,5-Triacetoxy-7-oxabicyclo[4.3.0]nonan-8-one 6

The bromo lactone **5** (1.56 g, 4.0 mmol) was dissolved in dry EtOAc (25 mL) and the solution was heated to reflux temperature. A solution of Bu_3SnH (1.58 ml, 6.0 mmol) and AIBN (0.098 g, 0.6 mmol) in EtOAc (5 mL) was added in the course of 2 h *via* a syringe pump. The mixture was stirred for another 2 h at reflux temperature after which time the mixture was evaporated. The residue was suspended in CH_3CN (15 mL) and washed with hexane (3 × 30 mL). Evaporation of the solvent gave a syrup, which was purified by flash chromatography (EtOAc–hexane 2 : 1; R_f 0.32). This gave **6** as a colourless syrup (0.97 g, 82%); δ_H ($CDCl_3$; TMS; 500 MHz) 1.63 (dt, $J_{2,2'}$ = 14.0, $J_{2',3}$ = 14.0, $J_{1,2'}$ = 9.0, 1H, H′-2), 2.05 (s, 3H, CH_3), 2.07 (s, 3H, CH_3), 2.11 (s, 3H, CH_3), 2.22 (ddd, $J_{2,2'}$ = 14.0, $J_{1,2}$ = 6.0, $J_{2,3}$ = 4.5, 1H, H-2), 2.45 (dd, $J_{9,9'}$ = 17.5, $J_{1,9'}$ = 4.5, 1H, H′-9), 2.69 (dd, $J_{9,9'}$ = 17.5, $J_{1,9}$ = 7.5, 1H, H-9), 2.87 (m, 1H, H-1), 4.51 (t, $J_{5,6}$ = 5.5, $J_{1,6}$ = 5.5, 1H, H-6), 5.15 (ddd, $J_{2',3}$ = 14.0, $J_{3,4}$ = 8.0, $J_{2,3}$ = 4.5, 1H, H-3), 5.24 (dd, $J_{3,4}$ = 8.0, $J_{4,5}$ = 3.0, 1H, H-4), 5.52 (dd, $J_{5,6}$ = 5.5, $J_{4,5}$ = 3.0, 1H, H-5); δ_C ($CDCl_3$; 50.3 MHz) 174.6 (C-8), 169.8, 169.3, 169.1 (3 × CO), 78.1 (C-6), 69.2, 68.5, 67.9 (C-3, -4, -5), 35.5 (C-9), 32.3 (C-2), 29.0 (C-1), 20.9, 20.5, 20.5 (3 × CH_3).

(1*S*,3*S*,4*R*,5*R*,6*R*)-3,4,5-Trihydroxy-7-oxabicyclo[4.3.0] nonan-8-one 7

Compound 6 (0.550 g, 1.6 mmol) was dissolved in dry MeOH containing 1% HCl (25.5 mL, 7.0 mmol) and kept for 19 h followed by concentration. The syrupy residue was purified by flash chromatography (EtOAc–hexane 9 : 1; R_f 0.27) to afford **7** (0.293 g, 89%) as colourless crystals, mp 124–128 °C. Recrystallisation from acetone–Et_2O gave the title compound, mp 128–129 °C; $[a]_D^{20}$ −18.4 (*c* 1.0, MeOH) (Found: C, 50.99; H, 6.42. Calc. for $C_8H_{12}O_5$: C, 51.06; H, 6.43%); δ_H (D_2O–acetone; 500 MHz) 1.13 (dt, $J_{2,2'}$ = 14.0, $J_{2',3}$ = 10.0, $J_{1,2'}$ = 10.0, 1H, H′-2), 1.89 (ddd, $J_{2,2'}$ = 14.0, $J_{1,2}$ = 4.5, $J_{2,3}$ = 4.5, 1H, H-2); 2.27 (dd, $J_{9,9'}$ = 20.0, $J_{1,9'}$ = 5.5, 1H, H′-9), 2.65 (m, 1H, H-1), 2.68 (dd, $J_{9,9'}$ = 20.0, $J_{1,9}$ = 7.0, 1H, H-9), 3.64 (dd, $J_{3,4}$ = 8.5, $J_{4,5}$ = 3.5, 1H, H-4), 3.69 (ddd, $J_{2',3}$ = 10.0, $J_{3,4}$ = 8.5, $J_{2,3}$ = 4.5, 1H, H-3), 4.09 (t, $J_{5,6}$ = 3.5, $J_{4,5}$ = 3.5, 1H, H-5), 4.43 (t, $J_{5,6}$ = 3.5, $J_{1,6}$ = 3.5, 1H, H-6); δ_C (D_2O–acetone; 50.3 MHz) 174.3 (C-8),

83.7 (C-6), 73.1, 69.5, 67.8 (C-3, -4, -5), 37.2 (C-9), 32.9 (C-2), 32.8 (C-1).

6-Deoxy-5a-carba-β-L-*gulo*-heptopyranose 8 and 1,2,3,4,7-penta-*O*-acetyl-6-deoxy-5a-carba-β-L-*gulo*-heptopyranose 9

Finely powdered $CaCl_2$ (0.865 g, 7.8 mmol) and $NaBH_4$ (0.648 g, 17.1mmol) were suspended in EtOH (20 mL) and the mixture was stirred at −20 °C for 4 h to ensure the formation of $Ca(BH_4)_2$. Compound **7** (0.293 g, 1.6 mmol) was added and the solution was stirred for 2 h at −10 °C and then overnight at rt. 4 M Aq. HCl (8 mL) was added and the mixture was stirred for 30 min followed by concentration and co-concentrated with MeOH (2 × 30 mL). The crystalline residue was dissolved in water (30 mL) and then poured onto a column of ion-exchange resin (Amberlite IR-120 H^+, 120 mL). The column was washed with water (600 mL) to neutral pH. The eluent was concentrated to give the crude pentahydroxy compound **8** in quantitative yield; δ_C (D_2O–1,4-dioxane; 50.3 MHz) 73.9, 73.3, 72.6, 70.0 (C-1, -2, -3, -4), 60.1 (C-7), 33.6, 32.9 (C-6, -5a), 31.4 (C-5).

Acetylation of crude **8** was performed in Ac_2O (10 mL) and $HClO_4$ (60% aq.; 2 drops) for 1.5 h similarly to the procedure for **5,** gave a syrup which was purified by flash chromatography (EtOAc–hexane 4 : 3; R_f 0.38) to give **9** as a colourless syrup (0.443 g, 71% from **7**) (Found: C, 53.49; H, 6.28. Calc. for $C_{18}H_{26}O_{10}$: C, 53.73; H, 6.51%); δ_H (benzene-d_6; 500 MHz) 1.25 (ddt, $J_{6,6'}$ = 13.5, $J_{5,6'}$ = 6.5, $J_{6',7}$ = 6.5, $J_{6',7'}$ = 6.5, 1H, H′-6), 1.47 (ddt, $J_{6,6'}$ = 13.5, $J_{5,6}$ = 6.5, $J_{6,7}$ = 6.5, $J_{6,7'}$ = 6.5, 1H, H-6), 1.55 (dd, $J_{5aa,5ae}$ = 12.0, $J_{5aa,5}$ = 12.0, $J_{1,5aa}$ = 11.0, 1H, H^a-5a), 1.59 (s, 3H, CH_3), 1.63 (s, 3H, CH_3), 1.71 (s, 3H, CH_3), 1.75 (s, 3H, CH_3), 1.81 (s, 3H, CH_3), 1.97 (dt, $J_{5ae,5aa}$ = 12.0, $J_{5ae,5}$ = 4.5, $J_{1,5ae}$ = 4.5, 1H, H^e-5a), 2.05 (m, 1H, H-5), 3.89 (dt, $J_{7',7}$ = 11.5, $J_{6,7'}$ = 6.5, $J_{6',7'}$ = 6.5, 1H, H′-7), 4.03 (dt, $J_{7,7'}$ = 11.5, $J_{6,7}$ = 6.5, $J_{6',7}$ = 6.5, 1H, H-7), 5.22 (dd, $J_{3,4}$ = 4.0, $J_{4,5}$ = 3.0, 1H, H-4), 5.50 (ddd, $J_{1,5aa}$ = 11.0, $J_{1,2}$ = 11.0, $J_{1,5ae}$ = 4.5, 1H, H-1), 5.53 (dd, $J_{1,2}$ = 11.0, $J_{2,3}$ = 3.0, 1H, H-2), 5.81 (dd, $J_{3,4}$ = 4.0, $J_{2,3}$ = 3.0, 1H, H-3); δ_C ($CDCl_3$, 50.3 MHz) 170.3, 169.8, 169.5, 169.0, 168.7 (5 × C=O), 69.9, 69.7, 68.7, 68.0 (C-1, -2, -3, -4), 61.3 (C-7), 30.6 (C-5), 30.1, 29.1 (C-5a, -6), 20.4, 20.3, 20.2, 20.2, 20.2 (5 × CH_3).

2,3 : 5,6 : 7,8-Tri-*O*-isopropylidene-D-*erythro*-L-*talo*-octono-1,4-lactone 11 and 5,6;7,8-di-*O*-isopropylidene-D-*erythro*-L-*galacto*-octono-1,4-lactone 12

Compounds **11** and **12** were prepared by a slight modification of the literature procedure.[21] D-*glycero*-D-*gulo*-Heptono-1,4-lactone **10** (50.0 g, 240.2 mmol) was dissolved in water (450 mL) and ion-exchange resin (Amberlite IR-120 H^+, 150 mL) was added. The mixture was cooled in an ice-bath and $NaBH_4$ (10.9 g, 288.2 mmol) was added slowly, with pH kept in range pH 3–5. Stirring was maintained for 30 min, when more ion-exchange resin (Amberlite IR-120 H^+, 160 mL) was added and the mixture was stirred for another 30 min. The ion-exchange resin was filtered off and the filtrate concentrated. The residue was co-concentrated with MeOH (5 × 100 mL) to give D-*glycero*-D-*gulo*-heptose as colourless crystals (47.9 g, 94.9%), mp 184–186 °C (lit.,[21] 189–190 °C); δ_C (D_2O–1,4-dioxane; 50.3 MHz) 93.9 (C-1), 72.1, 71.0, 68.9, 68.7, 68.2 (C-2, -3, -5, -6, -7), 62.8 (C-8).

The crude heptose (47.6 g, 226.5 mmol) was dissolved in water (225 mL), NaCN (12.2 g, 249.1 mmol) was added, and the mixture was stirred for 17 h. Ion-exchange resin (Amberlite IR-120 H^+, 220 mL) was added and stirring was maintained for 30 min. The aqueous solution was poured onto a column of ion exchange resin (Amberlite IR-120 H^+, 330 mL), which was washed with water until pH ≈ 7. The eluent was concentrated and co-concentrated with toluene (5 × 100 mL) to give a mixture of the two lactones **11** and **12** as colourless crystals (50.8 g, 94.2%);[21] δ_C (D_2O–1,4-dioxane; 50.3 MHz) 175.9 (C-1), 87.4, 81.5 (2 × C-4), 73.5, 73.4, 72.9, 71.1, 70.6, 70.2, 69.9, 69.0, 68.5 (2 × C-2, -3, -5, -6, -7), 63.7, 61.8 (2 × C-8). The mixture of **11** and **12** (50.6 g, 212.6 mmol) was dissolved in dry acetone (600 mL), and PTSA (3.29 g) was added. The reaction flask was equipped with a Soxhlet condenser containing molecular sieves (3 Å) and the mixture was heated at reflux for 2 days. The solution was neutralised with ion exchange resin (Amberlite IRA-67, OH^-), filtered, and evaporated to give a crude residue, to which water (300 mL) and CH_2Cl_2 (500 mL) were added. *The organic phase* was extracted with water (2 × 100 mL), dried ($MgSO_4$), and filtered through activated charcoal. The filtrate was concentrated and trituration with ethanol–water to give 2,3 : 5,6 : 7,8-tri-*O*-isopropylidene-D-*erythro*-L-*talo*-octono-1,4-lactone **11** as colourless crystals (11.1 g, 15%), mp 125–126 °C (lit.,[21] 126–127 °C); δ_C (acetone-d_6; 50.3 MHz) 173.8 (C-1), 112.5, 110.3, 109.5 (3 × ketal), 79.7, 79.2, 78.6, 76.8, 76.5, 74.7 (C-2, -3, -4, -5, -6, -7), 67.3 (C-8), 26.5, 26.2, 25.5, 24.4, 24,6 (6 × CH_3).

The combined water phases were concentrated to give 5,6 : 7,8-di-*O*-isopropylidene-D-*erythro*-L-*galacto*-octono-1,4-lactone **12** as a pale yellow oil (41.1 g, 61%); δ_C (acetone-d_6; 50.3 MHz) 173.6 (C-1), 109.6, 109.4 (2 × ketal); 78.2, 77.4, 76.9, 76.3, (C-4, -5, -6, -7), 74.2, 74.0 (C-2, -3); 67.0 (C-8), 26.6, 26.0, 25.9, 24.5 (4 × CH_3).

D-*erythro*-L-*talo*-Octono-1,4-lactone 13

Compound **13** was prepared by a slight modification of the literature procedure.[21] The triacetonide **11** (9.3g, 26.0 mmol) was dissolved in a mixture of water (25 mL) and trifluoroacetic acid (TFA) (25 mL) and the solution was stirred for 1.5 h. The mixture was concentrated, dissolved in water (50 mL) and washed with EtOAc (3 × 50 mL). The water phase was concentrated to give pale yellow crystals, mp 178–183 °C. Recrystallisation from aq. CH_3OH gave colourless crystals (5.2 g, 84%), mp 184–185 °C (lit.,[21] 190–191 °C); δ_C (D_2O–1,4-dioxane; 50.3 MHz) 179.1 (C-1), 88.4 (C-4), 71.8, 71.7 (C-2, -3), 70.8, 70.0 (C-6, -7); 69.4 (C-5), 63.5 (C-8).

D-*erythro*-L-*galacto*-Octono-1,4-lactone 14

The diacetonide **12** (41.1g, 129.2 mmol) was deprotected as described above for **11** to give a syrup, which could be crystallised from aq. EtOH to afford title compound **14** (25.9 g, 84%), mp 146–147 °C (lit.,[21] 147–148 °C); δ_C (D_2O–1,4-dioxane; 50.3 MHz) 175.9 (C-1), 81.5 (C-4), 73.6 (C-2, -3), 71.1 (C-6, -7), 69.0 (C-5), 62.6 (C-8).

8-Bromo-8-deoxy-D-*erythro*-L-*galacto*-octono-1,4-lactone 15 and 8-bromo-8-deoxy-5,6-*O*-isopropylidene-D-*erythro*-L-*galacto*-octono-1,4-lactone 16

The lactone **14** (5.01 g, 21.0 mmol) was treated with 32.6% HBr in AcOH (30 mL) according to the procedure for **4** and the mixture was stirred for 30 min. This gave **15** as a crude syrup; δ_C (D_2O–MeOH; 50.3 MHz) 171.3 (C-1), 80.1 (C-4), 72.5, 72.5, 70.5, 68.4, 67.2 (C-2, -3, -5, -6, -7), 35.7 (C-8).

The crude, acidic mixture was dissolved in dry acetone (600 mL) in a flask equipped with a Soxhlet condenser containing molecular sieves (3 Å). The solution was refluxed for 2 days after which time it was neutralised with ion-exchange resin (Amberlite IRA-67, OH^-), filtered, and evaporated. The residue was dissolved in CH_2Cl_2 (50 mL) and extracted with H_2O (8 × 75 mL). The water phase was concentrated and extracted with EtOAc (3 × 50 mL). The organic phase was dried ($MgSO_4$), filtered, and concentrated to give **16** as pale yellow crystals (3.6 g, 50% from **14**), mp 169–172 °C. Recrystallisations from EtOAc–pentane gave colourless crystals, mp 173–174 °C; $[a]_D^{20}$ +69.8 (*c* 1, MeOH) (Found: C, 38.91; H, 4.91; Br, 23.59. Calc. for $C_{11}H_{17}BrO_7$: C, 38.73; H, 5.02; Br, 23.42%); δ_H (acetone-d_6; 500 MHz) 1.34 (s, 3H, CH_3), 1.37 (s, 3H, CH_3), 3.59 (dd, $J_{8,8'}$ = 10.5, $J_{7,8}$ = 6.0, 1H, H-8), 3.73 (dd, $J_{8,8'}$ = 10.5,

$J_{7,8'}$ = 2.5, 1H, H′-8), 3.88 (ddt, $J_{6,7}$ = 8.5, $J_{7,8}$ = 6.0, $J_{OH\text{-}7,7}$ = 6.0, $J_{7,8'}$ = 2.5, 1H, H-7), 4.07 (dd, $J_{3,4}$ = 8.5, $J_{4,5}$ = 7.5, 1H, H-4), 4.27 (dd, $J_{6,7}$ = 8.5, $J_{5,6}$ = 2.0, 1H, H-6), 4.32 (dd, $J_{4,5}$ = 7.5, $J_{5,6}$ = 2.0, 1H, H-5), 4.33 (dt, $J_{2,3}$ = 8.5, $J_{3,4}$ = 8.5, $J_{OH\text{-}3,3}$ = 6.0, 1H, H-3), 4.43 (dd, $J_{2,3}$ = 8.5, $J_{OH\text{-}2,2}$ = 5.5, 1H, H-2), 4.82 (d, $J_{OH\text{-}7,7}$ = 6.0, 1H, OH-7), 5.11 (d, $J_{OH\text{-}3,3}$ = 6.0, 1H, OH-3), 5.16 (d, $J_{OH\text{-}2,2}$ = 5.5, 1H, OH-2); δ_C (acetone-d_6; 50.3 MHz) 174.1 (C-1), 110.6 (ketal), 79.6, 78.7, 77.5, 75.2, 75.1, 73.8 (C-2, -3, -4, -5, -6, -7), 38.4 (C-8), 27.5, 26.8 (2 × CH_3).

2,3,7-Tri-*O*-acetyl-8-bromo-8-deoxy-5,6-*O*-isopropylidene-D-*erythro*-L-*galacto*-octono-1,4-lactone 17

The bromo lactone **16** (3.40 g, 10.0 mmol) was dissolved in a mixture of pyridine (15 mL) and Ac_2O (7.5 mL) and the solution was stirred for 1.5 h, after which time it was concentrated, dissolved in CH_2Cl_2 (20 mL), and washed with water (6 × 30 mL). The organic layer was dried (Na_2SO_4), filtered through activated charcoal, and evaporated. The residue was purified by flash chromatography (pentane–EtOAc 2 : 1; R_f 0.32) to give a colourless oil (4.0 g, 87%); δ_H ($CDCl_3$; TMS; 500 MHz) 1.41 (s, 3H, CH_3), 1.42 (s, 3H, CH_3), 2.13 (s, 3H, CH_3), 2.19 (s, 3H, CH_3) 3.60 (dd, $J_{8a,8b}$ = 11.5, $J_{7,8a}$ = 5.0, 1H, H^a-8), 3.76 (dd, $J_{8a,8b}$ = 11.5, $J_{8b,7}$ = 3.5, 1H, H^b-8), 4.21 (dd, $J_{5,6}$ = 7.5, $J_{4,5}$ = 2.0, 1H, H-5), 4.32 (t, $J_{5,6}$ = 7.5, $J_{6,7}$ = 8.0, 1H, H-6), 4.36 (dd, $J_{3,4}$ = 6.0, $J_{4,5}$ = 2.0, 1H, H-4), 5.01 (ddd, $J_{6,7}$ = 8.0, $J_{7,8a}$ = 5.0, $J_{7,8b}$ = 3.5, 1H, H-7), 5.49 (t, $J_{3,4}$ = 6.0, $J_{2,3}$ = 6.0, 1H, H-3), 5.68 (d, $J_{2,3}$ = 6.0, 1H, H-2); δ_C ($CDCl_3$, 50.3 MHz) 169.7, 169.5, 169.4 (3 × CO), 168.5 (C-1), 111.5 (ketal), 78.1, 77.5, 74.7, 73.6, 72.8, 71.6 (C-2, -3, -4, -5, -6, -7), 31.6 (C-8), 27.1, 26.2 (2 × CH_3), 20.5, 20.4, 20.2 (3 × CH_3).

2,7-Di-*O*-acetyl-8-bromo-3,8-dideoxy-5,6-*O*-isopropylidene-D-*gluco*-oct-2-enono-1,4-lactone 18 and 2,7-di-*O*-acetyl-8-bromo-3,8-dideoxy-5,6-*O*-isopropylidene-D-*manno*-oct-2-enono-1,4-lactone 19

The bromo lactone **17** (3.8 g, 8.1 mmol) and Et_3N (1.25 mL, 9.0 mmol) were dissolved in CH_2Cl_2 (30 mL) and the solution was stirred for 2.5 h. The mixture was concentrated, dissolved in CH_2Cl_2 (30 mL) and washed with water (7 × 50 mL). The organic phase was dried (Na_2SO_4), filtered, and evaporated. The residue, containing **18** and **19** in the ratio 5 : 2 according to a ^{13}C NMR spectrum, was triturated with EtOAc (5 mL) whereby **18** (0.937 g) was isolated as colourless crystals, mp 151–152 °C. The mother liquor was purified by flash chromatography (pentane–EtOAc 2 : 1; **19**: R_f 0.40, **18**: 0.36). This afforded a further amount of crystalline **18** (total yield 1.78 g, 54%) and the C-4 epimer **19** as a colourless syrup (0.72 g, 22%).

Compound 18. Mp 152–153 °C, recrystallisations from EtOAc–Et_2O gave mp 153–154 °C; $[\alpha]_D^{20}$ +28.0 (*c* 1.0, $CHCl_3$) (Found: C, 43.96; H, 4.55; Br, 19.70. Calc. for $C_{15}H_{19}BrO_8$: C, 44.24; H, 4.70; Br, 19.62%); δ_H (CD_3Cl; TMS; 500 MHz) 1.38 (s, 3H, CH_3) 1.39 (s, 3H, CH_3), 2.16 (s, 3H, CH_3), 2.33 (s, 3H, CH_3), 3.59 (dd, $J_{8,8'}$ = 11.5, $J_{7,8'}$ = 5.5, 1H, H′-8), 3.75 (dd, $J_{8,8'}$ = 11.5, $J_{7,8}$ = 3.0, 1H, H-8), 4.20 (dd, $J_{5,6}$ = 7.0, $J_{4,5}$ = 2.5, 1H, H-5), 4.30 (dd, $J_{6,7}$ = 7.5, $J_{5,6}$ = 7.0, 1H, H-6), 5.05 (ddd, $J_{6,7}$ = 7.5, $J_{7,8'}$ = 5.5, $J_{7,8}$ = 3.0, 1H, H-7), 5.06 (dd, $J_{4,5}$ = 2.5, $J_{3,4}$ = 2.0, 1H, H-4), 7.25 (d, $J_{3,4}$ = 2.0, 1H, H-3); δ_C ($CDCl_3$; 50.3 MHz) 169.8 (C-1), 166.8, 166.1 (2 × CO), 138.3 (C-2), 129.8 (C-3), 111.2 (ketal), 77.9, 77.4, 75.4, 72.9 (C-4, -5, -6, -7), 31.5 (C-8), 27.0, 26.1 (2 × CH_3), 20.7, 20.7 (2 × CH_3).

Compound 19. δ_H ($CDCl_3$; TMS; 500 MHz) 1.40 (s, 3H, CH_3), 1.41 (s, 3H, CH_3), 2.18 (s, 3H, CH_3), 2.33 (s, 3H, CH_3), 3.60 (dd, $J_{8,8'}$ = 11.5, $J_{7,8'}$ = 5.5, 1H, H′-8), 3.71 (dd, $J_{8,8'}$ = 11.5, $J_{7,8}$ = 3.5, 1H, H-8), 3.94 (dd, $J_{5,6}$ = 5.5, $J_{4,5}$ = 7.0, 1H, H-5), 4.25 (dd, $J_{6,7}$ = 8.0, $J_{5,6}$ = 5.5, 1H, H-6), 4.96 (dd, $J_{4,5}$ = 7.0, $J_{3,4}$ = 2.5, 1H, H-4), 5.09 (ddd, $J_{6,7}$ = 8.0, $J_{7,8'}$ = 5.5, $J_{7,8}$ = 3.5, 1H, H-7), 7.38 (d, $J_{3,4}$ = 2.5, 1H, H-3); δ_C ($CDCl_3$; 50.3 MHz) 170.2 (C-1), 166.7, 165.9 (2 × CO), 138.3 (C-2), 131.1 (C-3), 111.2 (ketal), 79.5, 78.8, 78.3 (C-4, -5, -6), 72.0 (C-7), 31.7 (C-8), 27.0, 26.9 (2 × CH_3), 20.7, 20.7 (2 × CH_3).

(1*S*,3*R*,4*R*,5*R*,6*S*,9*S*)-3,9-Diacetoxy-4,5-isopropylidenedioxy-7-oxabicyclo[4.3.0]nonan-8-one 20 and 2,7-di-*O*-acetyl-3,8-dideoxy-5,6-*O*-isopropylidene-D-*gluco*-oct-2-enono-1,4-lactone 21

The bromo lactone **18** (1.75 g, 4.3 mmol) was dissolved in dry EtOAc (30 mL) and the solution was heated at reflux temperature. A solution of Bu_3SnH (1.71 mL, 6.4mmol) and AIBN (0.071 g, 0.43 mmol) in EtOAc (10 mL) was added over 2 h *via* a syringe pump. The mixture was stirred for another 2 h at reflux and then concentrated. The residue was suspended in CH_3CN (30 mL), which was then washed with hexane (3 × 20 mL). Evaporation of the CH_3CN gave a syrup that contained two products (1 : 8) according to a ^{13}C NMR spectrum. Purification by flash chromatography (EtOAc–pentane 1 : 2; **21**: R_f 0.33; **20**: R_f 0.22) gave the minor product **21** as colourless crystals (0.151 g, 9%) and the major product **20** as a syrup, which by trituration with Et_2O–hexane gave colourless crystals (1.05 g, 73%).

Compound 20. Mp 139–140 °C; $[\alpha]_D^{20}$ +50.4 (*c* 1.0, $CHCl_3$) (Found: C, 54.71; H, 6.01. Calc. for $C_{15}H_{20}O_8$: C, 54.88; H, 6.14%); δ_H ($CDCl_3$; TMS; 500 MHz) 1.41 (s, 3H, CH_3), 1.45 (s, 3H, CH_3), 1.61 (ddd, $J_{2,2'}$ = 15.0, $J_{1,2}$ = 13.5, $J_{2,3}$ = 6.0, 1H, H-2), 2.08 (s, 3H, CH_3), 2.14 (ddd, $J_{2,2'}$ = 15.0, $J_{2',3}$ = 8.5, $J_{1,2'}$ = 5.0, 1H, H′-2), 2.18 (s, 3H, CH_3), 3.08 (dddd, $J_{1,2}$ = 13.5, $J_{1,9}$ = 8.5, $J_{1,6}$ = 6.5, $J_{1,2'}$ = 5.0, 1H, H-1), 3.65 (dd, $J_{4,5}$ = 11.0, $J_{3,4}$ = 5.0, 1H, H-4), 4.14 (dd, $J_{4,5}$ = 11.0, $J_{5,6}$ = 6.5, 1H, H-5), 4.75 (t, $J_{5,6}$ = 6.5, $J_{1,6}$ = 6.5, 1H, H-6), 5.40 (ddd, $J_{2',3}$ = 8.5, $J_{2,3}$ = 6.0, $J_{3,4}$ = 5.0, 1H, H-3), 5.57 (d, $J_{1,9}$ = 8.5, 1H, H-9); δ_C ($CDCl_3$; 50.3 MHz) 171.0 (C-8), 170.0, 169.4 (2 × CO), 113.2 (ketal), 77.9 (C-6), 76.4, 73.7 (C-4, -5), 68.6 (C-9), 63.6 (C-3), 34.4 (C-1), 26.9 (C-2), 26.3, 25.2 (2 × CH_3), 20.7, 20.3 (2 × CH_3).

Compound 21. Mp 121–123 °C, recrystallisation from Et_2O–hexane gave mp 122–123 °C; $[\alpha]_D^{20}$ +25.8 (*c* 1.0, $CHCl_3$); δ_H ($CDCl_3$; TMS; 500 MHz) 1.34 (d, $J_{7,8}$ = 6.5, 3H, H-8), 1.38 (s, 3H, CH_3), 1.39 (s, 3H, CH_3), 2.09 (s, 3H, CH_3), 2.32 (s, 3H, CH_3), 4.08 (dd, $J_{5,6}$ = 7.5, $J_{4,5}$ = 2.0, 1H, H-5), 4.16 (dd, $J_{5,6}$ = 7.5, $J_{6,7}$ = 6.5, 1H, H-6), 4.99 (quintet, $J_{6,7}$ = 6.5, $J_{7,8}$ = 6.5, 1H, H-7), 5.06 (t, $J_{3,4}$ = $J_{4,5}$ = 2.0, 1H, H-4), 7.28 (d, $J_{3,4}$ = 2.0, 1H, H-3); δ_C ($CDCl_3$; 50.3 MHz) 170.9 (2 × CO), 168.9 (C-1), 138.2 (C-2), 130.0 (C-3), 110.8, 108.9 (2 × ketal), 78.2, 77.6, 76.4 (C-4, -5, -6), 70.8 (C-7), 27.0, 26.1 (2 × CH_3), 20.9, 20.8 (2 × CH_3), 16.3 (C-8).

5a-Carba-D-*glycero*-β-D-*ido*-heptopyranose 22 and 1,2,3,4,6,7-hexa-*O*-acetyl-5a-carba-D-*glycero*-β-D-*ido*-heptopyranose 23

A solution of $Ca(BH_4)_2$ in EtOH (10 mL) was prepared from finely powdered $CaCl_2$ (0.576 g, 5.2 mmol) and $NaBH_4$ (0.410 g, 10.8 mmol) as described for **9**. Compound **20** (0.302 g, 0.9 mmol) was added and the solution was stirred for 2 h at −10 °C and then overnight at rt. 4 M Aq. HCl (4 mL) was then added, and the mixture was stirred for 30 min and then concentrated and co-concentrated with MeOH (2 × 25 mL). The crystalline residue was dissolved in water (10 mL) and the solution was poured onto a column of ion-exchange resin (Amberlite IR-120 H^+, 100 mL). The column was washed with water (500 mL) to neutral pH. The aqueous eluent was concentrated to give the crude hexahydroxy compound **22** as a syrup (0.173 g, 80%); δ_C (D_2O–acetone; 50.3 MHz) 71.9, 71.3, 70.3, 68.8, 67.0 (C-1, -2, -3, -4, -6), 63.3 (C-7), 36.9 (C-5), 24.4 (C-5a).

Crude hexol **22** was acetylated with Ac_2O (7 mL) and $HClO_4$ (60% aq.; 2 drops) for 1.5 h in the usual way to give colourless crystals. Purification by flash chromatography (EtOAc–pentane 1 : 1; R_f 0.40) gave **23** as colourless crystals

(0.241 g, 77%), mp 155–156 °C; $[a]_D^{20}$ −8.3 (*c* 1.0, $CHCl_3$) (Found: C, 52.18; H, 5.92. Calc. for $C_{20}H_{28}O_{12}$: C, 52.17; H, 6.13%); δ_H (benzene-d_6; 500 MHz) 1.41 (s, 3H, CH_3), 1.60 (dt, $J_{5ae,5aa}$ = 13.0, $J_{5ae,5}$ = 4.0, $J_{1,5ae}$ = 4.0, 1H, H^e-5a), 1.62 (s, 3H, CH_3), 1.67 (s, 3H, CH_3), 1.73 (s, 3H, CH_3), 1.77 (s, 3H, CH_3), 1.78 (s, 3H, CH_3), 1.99 (q, $J_{5aa,5ae}$ = 13.0, $J_{5aa,5}$ = 13.0, $J_{1,5aa}$ = 13.0, 1H, H^a-5a), 2.38 (ddt, $J_{5,5aa}$ = 13.0, $J_{5,6}$ = 10.0, $J_{5,5ae}$ = 4.0, $J_{4,5}$ = 4.0, 1H, H-5), 3.78 (dd, $J_{7',7}$ = 12.5, $J_{6,7'}$ = 6.0, 1H, H′-7), 4.44 (dd, $J_{7,7'}$ = 12.5, $J_{6,7}$ = 2.5, 1H, H-7), 5.27 (ddd, $J_{5,6}$ = 10.0, $J_{6,7'}$ = 6.0, $J_{6,7}$ = 2.5, 1H, H-6), 5.29 (dt, $J_{1,5aa}$ = 13.0, $J_{1,2}$ = 4.0, $J_{1,5ae}$ = 4.0, 1H, H-1), 5.35 (t, $J_{4,5}$ = 4.0, $J_{3,4}$ = 3.0, 1H, H-4), 5.39 (t, $J_{3,4}$ = 3.0, $J_{2,3}$ = 3.0, 1H, H-3), 5.60 (t, $J_{1,2}$ = 4.0, $J_{2,3}$ = 3.0, 1H, H-2); δ_C ($CDCl_3$; 50.3 MHz) 170.5, 170.0, 169.9, 169.3, 169.2, 168.1 (6 × C=O), 69.4, 67.8, 67.8, 66.8, 65.5 (C-1, -2, -3, -4, -6), 62.9 (C-7), 35.4 (C-5), 28.7 (C-5a), 20.7, 20.6, 20.6, 20.5, 20.5, 20.4 (6 × CH_3).

(1*R*,3*R*,4*R*,5*R*,6*R*,9*R*)-3,9-Diacetoxy-4,5-isopropylidenedioxy-7-oxabicyclo[4.3.0]nonan-8-one 24

The unsaturated bromo lactone **19** (0.552 g, 1.4 mmol) was dissolved in dry EtOAc (10 mL) and the solution was heated at reflux and treated with Bu_3SnH (0.54 mL, 2.0 mmol) and AIBN (0.022 g, 0.14 mmol) in EtOAc (5 mL) as described for **18**. The crude product was suspended in CH_3CN (10 mL) and washed with hexane (3 × 6 mL). Evaporation of the mixture gave a syrup, which was purified by flash chromatography (EtOAc–pentane 1 : 2, R_f 0.27) to give a colourless syrup. Trituration with Et_2O–hexane gave colourless crystals (0.321 g, 73%), mp 116–117 °C; $[a]_D^{20}$ −122.7 (*c* 1.0, EtOAc) (Found: C, 55.03; H, 6.00. Calc. for $C_{15}H_{20}O_8$: C, 54.88; H, 6.14%); δ_H ($CDCl_3$; TMS; 500 MHz) 1.43 (s, 3H, CH_3), 1.46 (s, 3H, CH_3), 1.56 (ddd, $J_{2,2'}$ = 16.0, $J_{1,2'}$ = 11.0, $J_{2',3}$ = 3.0, 1H, H′-2), 1.99 (ddd, $J_{2,2'}$ = 16.0, $J_{1,2}$ = 6.5, $J_{2,3}$ = 3.0, 1H, H-2), 2.09 (s, 3H, CH_3), 2.18 (s, 3H, CH_3), 3.01 (ddt, $J_{1,2'}$ = 11.0, $J_{1,9}$ = 6.5, $J_{1,2}$ = 6.5, $J_{1,6}$ = 3.0, 1H, H-1), 3.85 (dd, $J_{4,5}$ = 10.5, $J_{3,4}$ = 2.5, 1H, H-4), 4.11 (dd, $J_{4,5}$ = 10.5, $J_{5,6}$ = 3.0, 1H, H-5), 4.93 (t, $J_{5,6}$ = 3.0, $J_{1,6}$ = 3.0, 1H, H-6), 5.51 (dt, $J_{2,3}$ = 3.0, $J_{2',3}$ = 3.0, $J_{3,4}$ = 2.5, 1H, H-3), 5.63 (d, $J_{1,9}$ = 6.5, 1H, H-9); δ_C ($CDCl_3$; 50.3 MHz) 171.3 (C-8), 170.0, 169.4 (2 × CO), 110.8 (ketal), 73.3 (C-6), 72.3, 72.3 (C-4, -5), 71.6 (C-9), 66.3 (C-3), 35.9 (C-1), 26.4, 26.4 (2 × CH_3), 25.3 (C-2), 20.8, 20.3 (2 × CH_3).

5a-Carba-L-*glycero*-α-L-*galacto*-heptopyranose 25 and 1,2,3,4,6,7-hexa-*O*-acetyl-5a-carba-L-*glycero*-α-L-*galacto*-heptopyranose 26

Reduction of **24** (0.303 g, 0.9 mmol) was performed using finely powdered $CaCl_2$ (0.576 g, 5.2 mmol) and $NaBH_4$ (0.410 g, 10.8 mmol) in EtOH (10 mL) as described above for **20** to give syrupy hexol **25** (0.185 g, 96%); δ_C (acetone-d_6; 50.3 MHz) 76.0, 75.3, 74.8, 73.5, 72.8 (C-1, -2, -3, -4, -6), 67.6 (C-7), 39.7 (C-5), 31.6 (C-5a).

Acetylation using acetic anhydride (7 mL) and perchloric acid (60% aq.; 2 drops) in the usual way gave a syrup which was purified by flash chromatography (EtOAc–pentane 1 : 1; R_f 0.39). This gave crystalline **26** (0.262 g, 83%), mp 97–98 °C. Recrystallisation from Et_2O–hexane gave colourless crystals, mp 97–98 °C; $[a]_D^{20}$ −61.5 (*c* 1.0, $CHCl_3$) (Found: C, 52.32; H, 6.22. Calc. for $C_{20}H_{28}O_{12}$: C, 52.17; H, 6.13%); δ_H (benzene-d_6; 500 MHz) 1.34 (ddd, $J_{5aa,5ae}$ = 14.5, $J_{5aa,5}$ = 13.5, $J_{1,5aa}$ = 2.5, 1H, H^a-5a), 1.39 (dt, $J_{5ae,5aa}$ = 14.5, $J_{5ae,5}$ = 4.5, $J_{1,5ae}$ = 2.0, 1H, H^e-5a), 1.63 (s, 3H, CH_3), 1.64 (s, 3H, CH_3), 1.77 (s, 9H, 3 × CH_3), 1.78 (s, 3H, CH_3), 2.28 (m, $J_{5,5aa}$ = 13.5, $J_{5,6}$ = 10.5, $J_{5,5ae}$ = 4.5, $J_{4,5}$ = 2.5, 1H, H-5), 3.68 (dd, $J_{7',7}$ = 12.5, $J_{6,7'}$ = 5.5, 1H, H′-7), 4.18 (dd, $J_{7,7'}$ = 12.5, $J_{6,7}$ = 2.0, 1H, H-7), 4.93 (ddd, $J_{5,6}$ = 10.5, $J_{6,7'}$ = 5.5, $J_{6,7}$ = 2.0, 1H, H-6), 5.42 (dd, $J_{2,3}$ = 11.0, $J_{1,2}$ = 3.5, 1H, H-2), 5.52 (dd, $J_{2,3}$ = 11.0, $J_{3,4}$ = 3.0, 1H, H-3), 5.61 (dt, $J_{1,2}$ = 3.5, $J_{1,5aa}$ = 2.5, $J_{1,5ae}$ = 2.0, 1H, H-1), 5.85 (dd, $J_{4,5}$ = 2.5, $J_{3,4}$ = 3.0, 1H, H-4); δ_C ($CDCl_3$; 50.3 MHz) 170.1, 170.1, 169.9, 169.9, 169.8, 169.4 (6 × C=O), 69.1, 69.1, 68.9, 67.7, 67.1 (C-1, -2, -3, -4, -6), 62.8 (C-7), 33.7 (C-5), 26.1 (C-5a), 20.6, 20.4, 20.4, 20.3, 20.3, 20.2 (6 × CH_3).

Acknowledgements

The Danish National Research Council and The Danish Technical Research Council are gratefully acknowledged for financial support (KEMI-programmet).

In memoriam of Professor Göran Magnusson. A good colleague, Professor Göran Magnusson, has deceased at a time when he was on the top of his career. Our common interest in synthetic carbohydrate chemistry and the proximity of our universities promoted a close personal contact. He was always willing to participate in scientific matters in the surrounding area and ready to take part in constructive discussions on how to improve the development in the chemical sphere of our common interests.

Göran Magnusson very impressively changed from being engaged in synthetic aspects of natural products and monosaccarides to the development of methods for the preparation of biologically important oligosaccharide derivatives. The biological aspects were a leading theme for the synthetic targets, and he was highly involved in the development of inhibitors of different pathogens. With his very thorough work, he placed himself as a leading scientist within the field. Due to his engagement and personal friendliness he always had a group of engaged and productive young researchers around him.

We will miss him as a scientist and as a good friend and colleague.

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