Highly Functionalised Cyclopentanes by Radical Cyclisation of Unsaturated Bromolactones III. Preparation of Carbaaldohexofuranoses. Determination of the Relative Configuration at C-4/C-5 of 2,3-Unsaturated Heptono-1,4-lactones by Means of ^{1}H NMR Spectroscopy

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Received 7 May 1998

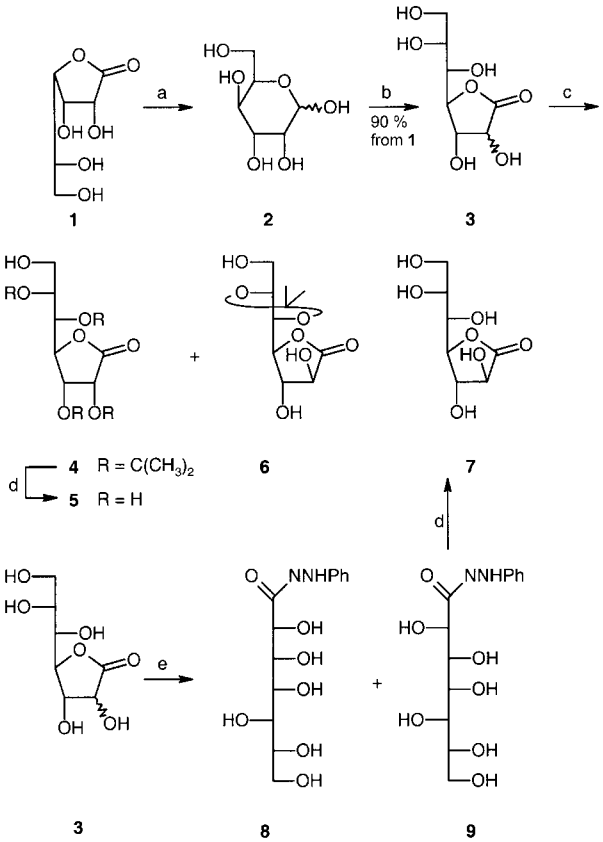
Abstract: Two new carbaaldohexofuranoses, carba-β-D-glucofuranose and carba-α-L-mannofuranose, have been prepared using 5,6-*O*-isopropylidene-D-*glycero*-L-*galacto*-heptono-1,4-lactone **(6)** as the starting material. The key step was a highly stereoselective intramolecular 5-*exo*-trig radical cyclisation of C-2 substituted 2,3-unsaturated 7-bromo-7-deoxyheptono-1,4-lactones promoted by tributyltin hydride. Assignment of the configuration of the unsaturated lactones was based upon NMR data of related compounds. The starting material, compound **6**, was obtained by chain elongation of D-gulose, and a facile method for separation of the epimers from the chain elongation has been developed. Thus 5,6-*O*-isopropylidene-D-*glycero*-L-*galacto*-heptono-1,4-lactone **(6)** and D-*glycero*-L-*talo*-heptono-1,4-lactone **(5)** were isolated crystalline in ca. 30% and 10% yield, respectively.

Key words: carbasugars, radical cyclisation, bromoaldonolactones, 2,3-unsaturated 1,4-aldonolactones, heptonolactones

Polyoxygenated cyclopentanes[1] have attracted attention as structural elements of carbocyclic nucleosides[2] and glycosidase inhibitors[3] and as carbocyclic analogues of carbohydrates,[4,5] often referred to as carbasugars. The carbocyclic analogues are resistant to hydrolysis due to the lack of an acetal moiety, making them interesting compounds from a biological point of view.

We have recently reported the preparation of the first carbaaldohexofuranoses starting from 7-bromo-7-deoxyheptono-1,4-lactones.[6] The bromolactones were converted into C-2 substituted 2,3-unsaturated 7-bromo-7-deoxyheptono-1,4-lactones, which upon treatment with tributyltin hydride underwent a highly stereoselective intramolecular 5-*exo*-trig radical cyclisation[7] to give cyclopentane derivatives. These, in turn, could be converted to carbaaldohexofuranoses and carbapentofuranoses. This synthesis of carbasugars is short and high yielding, and the carbasugars are obtained optically pure, as the starting compounds are obtained from the chiral pool. However, access to other isomers of carbahexofuranoses by this strategy is limited by the availability of bromodeoxyheptono-1,4-lactones.[8,9] Our next aim was, therefore, the preparation of new isomers of bromodeoxyheptono-1,4-lactones and their subsequent conversion to new carbahexofuranoses. Retrosynthesis showed that chain elongation of D-gulose to give the epimers D-*glycero*-L-*galacto*-heptono-1,4-lactone and D-*glycero*-L-*talo*-heptono-1,4-lactone would finally lead to new carbahexofuranoses.

D-Gulono-1,4-lactone **(1)** was reduced with sodium borohydride to give D-gulose **(2)**, which after treatment with aqueous sodium cyanide gave a mixture of D-*glycero*-L-*galacto*- and D-*glycero*-L-*talo*-heptonic acid **3** (Scheme 1). The separation of these isomers has already been reported by other groups. As early as 1920, La Forge[10] described the purification of D-*glycero*-L-*galacto*-heptonic acid via crystallisation of the barium salt. Isbell[11] obtained both D-*glycero*-L-*galacto*-heptonic acid and D-*glycero*-L-*talo*-heptonic acid in low yields by repeated crystallisation of the lead salts. Hudson et al.[12] separated the isomers by fractional crystallisation of the corresponding phenylhydrazides, obtaining D-*glycero*-L-*galacto*- and D-*glycero*-L-*talo*-heptonic phenylhydrazide in 36% and 34% yield, respectively. Recently Fleet and co-workers[13] obtained the protected derivatives 3,4:6,7-di-*O*-isopropylidene-D-*glycero*-L-*galac*-



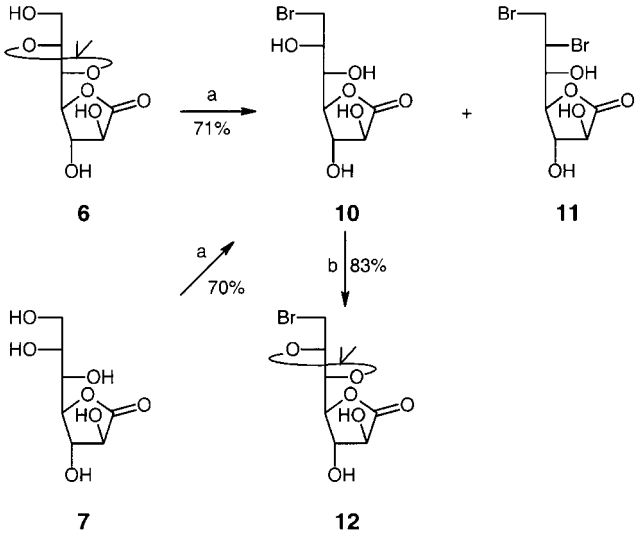
(a) $NaBH_4$, H^+; (b) NaCN; (c) acetone, H^+; (d) H_3O^+; (e) $PhNHNH_2$.

Scheme 1

to-heptono-1,5-lactone and 2,3:6,7-di-*O*-isopropylidene-D-*glycero*-L-*talo*-heptono-1,5-lactone in 11% and 16% yield, respectively, by cyanohydrin chain elongation of 2,3:5,6-di-*O*-isopropylidene-D-gulofuranose followed by chromatographic separation of the isomers.

Hudson's procedure[12] for the separation of isomers seemed the most rewarding, and, thus, the heptonic acids were converted to the corresponding phenylhydrazides, but repeated attempts to separate the isomers by fractional crystallisation were unsuccessful since only 2–4% D-*glycero*-L-*galacto*-heptonic phenylhydrazide **(9)** was obtained. Hudson's procedure describing the reaction of aldonic acids and phenylhydrazine to give the hydrazides was, therefore, modified slightly, since it seemed more efficient to prepare hydrazides from a lactone rather than from an acid. The two isomeric heptonic acids were lactonised by concentration from acidic solution prior to reaction with phenylhydrazine. Crystallisation gave in this case 27% D-*glycero*-L-*galacto*-heptonic phenylhydrazide **(9)**, which by acidic hydrolysis gave D-*glycero*-L-*galacto*-heptono-1,4-lactone **(7)** (Scheme 1). Crystallisation of the second isomer, D-*glycero*-L-*talo*-heptonic phenylhydrazide **(8)**, could not be reproduced. Yields in the modified Hudson procedure were modest and only one isomer was isolated, and a search for a better separation strategy was therefore undertaken. Isopropylidenation of the mixture of epimeric heptono-1,4-lactones **3** was expected to give mono- and diprotected lactones which presumably could be separated by a simple extraction procedure. This strategy was inspired by the work of Fleet et al.[14] on acetonides of octonolactones in which the separation of acetals of the epimeric octonolactones relied on chromatographic methods. In our case, **3** was refluxed in acidic acetone to give isopropylidene-protected heptonolactones which were partitioned between the aqueous and organic phases. From the aqueous phase 5,6-*O*-isopropylidene-D-*glycero*-L-*galacto*-heptono-1,4-lactone **(6)** was obtained in 36% yield from **1** which could be used directly for further synthesis. After chromatography **6** was obtained crystalline in 30% yield. Crude di-*O*-isopropylidene-protected D-*glycero*-L-*talo*-heptono-1,4-lactone **4** was found in the organic phase. In order to remove some lipophilic byproducts the organic phase was extracted with aqueous sodium hydroxide and the alkaline water phase was acidified. Deionisation with acidic ion exchange resin gave crystalline D-*glycero*-L-*talo*-heptono-1,4-lactone **(5)** in 10% yield from **1**.

Bromodeoxyaldonolactones can be prepared from aldonolactones by treatment with HBr in HOAc as described previously.[9,15] When D-*glycero*-L-*galacto*-heptono-1,4-lactone **(7)** was stirred with HBr in HOAc for 20 minutes 7-bromo-7-deoxy-D-*glycero*-L-*galacto*-heptono-1,4-lactone **(10)** was isolated in 70% yield together with 4% of a dibromoheptonolactone, tentatively assigned as 6,7-dibromo-6,7-dideoxy-L-*glycero*-L-*galacto*-heptono-1,4-lactone **(11)** (Scheme 2). Assignment of the configuration at C-6 of the latter was based on the experience[9,15] that substitution with bromide of the intermediate acetoxonium ion occurs with inversion of configuration. The bromolactone **10** could also be prepared by treatment of 5,6-*O*-isopropylidene-D-*glycero*-L-*galacto*-heptono-1,4-lactone **(6)** with HBr in HOAc for 40 minutes. In this case, the yield of the monobrominated lactone **10** was 71%, while the dibrominated lactone **11** was obtained in 24% yield.

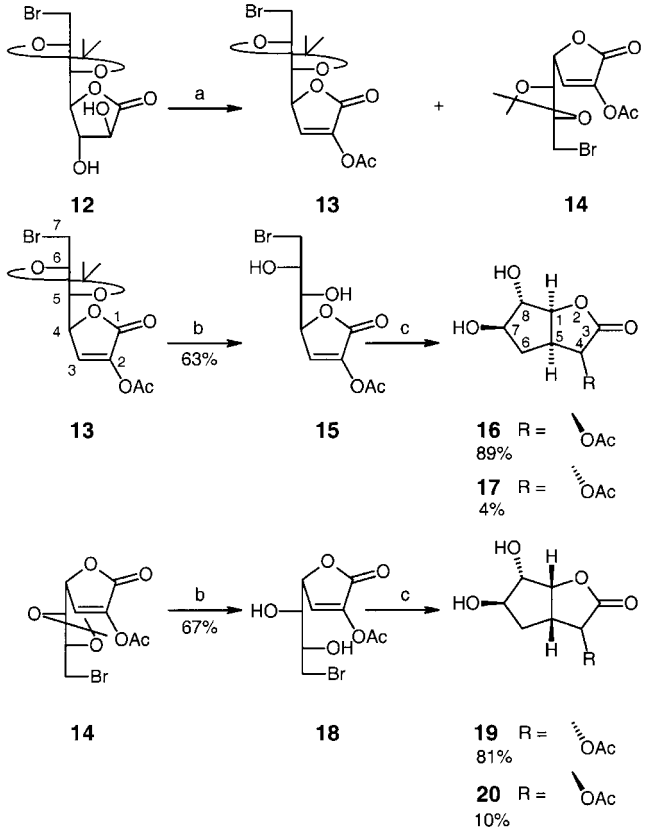


(a) HBr, HOAc (b) acetone, H^+

Scheme 2

2-Substituted 2,3-unsaturated 7-bromo-7-deoxyheptono-1,4-lactones were the starting materials for intramolecular radical cyclisations as in previous related work.[6] For the introduction of the double bond β-elimination of acetic acid was considered. Compound **10** was protected at the exocyclic hydroxy groups with an isopropylidene group to afford compound **12**, and the hydroxy groups at C-2 and C-3 were acetylated using acetic anhydride and triethylamine (Scheme 3). β-Elimination of acetic acid and isomerisation at C-4 occurred in the same step to give a mixture of the unsaturated lactones having D-*xylo*- (**13**) and D-*lyxo*-configuration (**14**), which were isolated by chromatography in 31% and 21% yield, respectively. Previous experience has shown that the base induced isomerisation at C-4 is difficult to avoid.[6,16] The assignment of the configuration at C-4 of the unsaturated heptonolactones will be discussed below. Attempts to cyclise **13** and **14** by reaction with tributyltin hydride gave only the 7-deoxy analogues of the starting material. The radical cyclisations were hindered by the *trans*-oriented isopropylidene groups, so the isopropylidene groups were removed using aqueous trifluoroacetic acid to give the corresponding lactones **15** and **18**. When the unsaturated lactone **15** was reacted with tributyltin hydride cyclisation took place to give **16** (89%) and **17** (4%), which were separated by flash chromatography. ^{1}H NMR spectroscopy showed **16** and **17** to be C-4 epimers, and the configurations at C-4 were determined by the coupling constants between H-4 and H-5; the larger coupling constant, $J_{4,5}$ = 10 Hz (**16**), indicating *cis*-oriented protons, and the smaller coupling constant, $J_{4,5}$ = 4.5 Hz (**17**), indicating *trans*-oriented pro-

tons. Similarly, the reaction of **18** with tributyltin hydride gave a major cyclisation product **19** (81%), and the C-4 epimer **20** (10%) as a minor product. The assignment of configuration was again based on coupling constants between H-4 and H-5, $J_{4,5}$ = 9.5 Hz (**19**) indicating *cis*-oriented protons and $J_{4,5}$ = 6.5 Hz (**20**) indicating *trans*-oriented protons. The high stereoselectivity in the ring-closure reactions can be explained by steric shielding of the enolate radical by the cyclopentane ring.[6,17a]

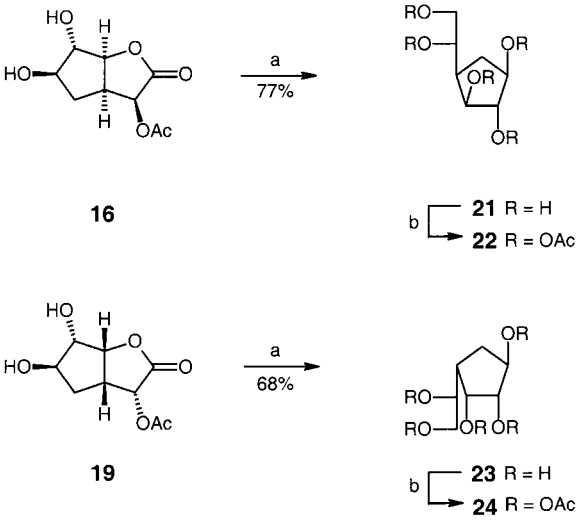


(a) Ac_2O, Et_3N (b) CF_3COOH, H_2O (c) Bu_3SnH, AIBN

Scheme 3

The yields in the flash chromatographic separation of **13** and **14** were low because the compounds were close running and repeated chromatographic separations were necessary. It was found that the total yield of **16** and **19** was raised if **13** and **14** were not separated, but used directly in the hydrolysis step followed by flash chromatographic separation of **16** and **19** after the cyclisation step. In this way **16** was isolated in 24% yield and **19** in 22% yield based on the starting material **12**.

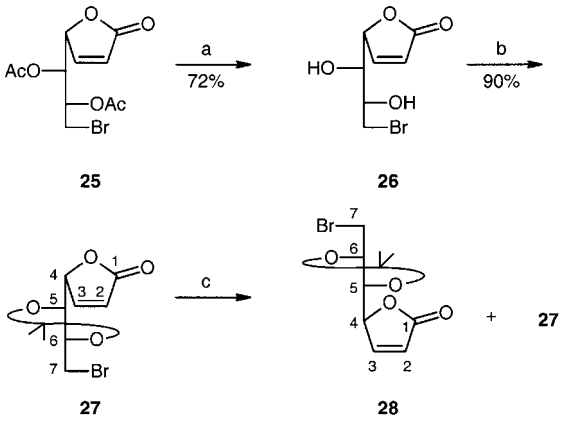
The bicyclic compounds **16** and **19** were both converted to carbaaldohexofuranoses by reduction of the lactone moiety and the acetoxy group (Scheme 4). Thus reduction of **16** using borane–dimethyl sulfide complex gave carba-β-D-glucofuranose **(21)** and similar reduction of **19** gave carba-α-L-mannofuranose **(23)**. It should be noted that the borane–dimethyl sulfide reductions of **16** and **19** were considerably slower than reduction of similar compounds without an oxy-substituent at C-4 in the bicyclic system.[17a] The carbahexofuranoses **21** and **23** were acetylated for characterisation to give **22** and **24** respectively. Thus, two new carbaaldohexofuranoses have been prepared, new types of compounds which we have recently described.[6]



(a) BH_3•SMe_2; (b) Ac_2O, H^+.

Scheme 4

The β-elimination step described above was accompanied by isomerisation at C-4 to give two 2-acetoxy-2,3-unsaturated heptono-1,4-lactones **13** and **14**. In order to elucidate the configuration at C-4 of **13** and **14,** two configurationally related unsaturated heptonolactones were prepared from the known 2,3-unsaturated heptonolactone (**25**)[17a] (Scheme 5). Compound **25** was deacetylated by reaction with acidic methanol to give **26** and the exocyclic hydroxy groups were protected with an isopropylidene group to give 7-bromo-7-deoxy-5,6-di-*O*-isopropylidene-D-*lyxo*-hept-2-enono-1,4-lactone **(27)** (Scheme 5). Treatment of **27** with triethylamine in dichloromethane caused epimerisation at C-4 to give 7-bromo-2,3,7-trideoxy-5,6-di-*O*-isopropylidene-D-*xylo*-hept-2-enono-1,4-lactone **(28)**. The configuration at C-4 of the related compounds **13** and **14** was established by compar-



(a) HCl, MeOH (b) acetone, H^+ (c) Et_3N, CH_2Cl_2

Scheme 5

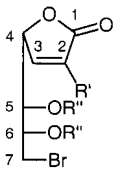
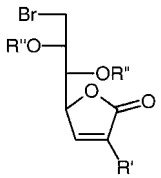
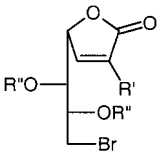
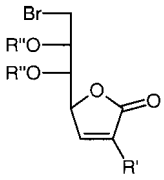
ison with the coupling constants between H-4 and H-5 in **27** ($J_{4,5}$ = 8.0 Hz) and **28** ($J_{4,5}$ = 2.0 Hz). Compound **13** ($J_{4,5}$ = 2.0 Hz) was thereby established to be 2-*O*-acetyl-7-bromo-3,7-dideoxy-5,6-*O*-isopropylidene-D-*xylo*-hept-2-enono-1,4-lactone, and compound **14** ($J_{4,5}$ = 7.0 Hz) was established to be 2-*O*-acetyl-7-bromo-3,7-dideoxy-5,6-*O*-isopropylidene-D-*lyxo*-hept-2-enono-1,4-lactone.

In the course of our program of preparing carbasugars via radical cyclisations of unsaturated lactones we have prepared a series of 2,3-unsaturated heptono-1,4-lactones, and occasionally assignment of the configuration at C-4 has demanded more detailed studies as exemplified above. Structure determination by comparison with NMR data of 2,3-unsaturated aldono-1,4-lactones known from the literature did not always allow a definite assignment.[18,19] Furthermore, the empirical rule set up by Casiraghi et al.[19] stating that 2,3-unsaturated γ-lactones having the 'tail' group 'up' in the conventional Haworth's depiction display levorotation, while those bearing this group 'down' show dextrorotations has in our case not been useful, as the compounds in question have displayed optical rotations of the same sign,[6] e.g. compound **15** and **18**. For this reason we have confirmed the structures via chemical proofs.[6] We have, however, observed some general trends in the NMR spectra of 2,3-unsaturated heptono-1,4-lactones which may be helpful in the structure determination of related compounds (Table 1). The coupling constant between H-4 and H-5 indicates whether the configuration is 4,5-*erythro* or 4,5-*threo*. Thus $J_{4,5}$ of the 4,5-*threo* configurated hept-2-enono-1,4-lactones was generally found in the range of 1–2.5 Hz, with the exception of compound **15** ($J_{4,5}$ = 5.5 Hz), whereas $J_{4,5}$ of 4,5-*erythro* configurated hept-2-enono-1,4-lactones was larger, between 6 and 9.5 Hz. The chemical shift of H-4 was generally found at higher field for 4,5-*erythro* configurated hept-2-enono-1,4-lactones as compared to the corresponding 4,5-*threo* configurated hept-2-enono-1,4-lactones.

Further evidence for the assignment of the relative configuration at C-4/C-5 of the 2,3-unsaturated-1,4-lactones was obtained from chemical shifts of the bicyclic lactones, which were formed by radical cyclisation of the unsaturated heptonolactones. The ^{13}C chemical shift of C-1 in the bicyclic lactones indicates whether the relative configuration at C-1/C-8 (corresponding to C-4/C-5 in the unsaturated lactones) is *erythro* or *threo* (Table 2). In the 1,8-*erythro*-configurated compounds C-1 is more shielded and therefore an absorption at higher field was observed as compared to the corresponding 1,8-*threo*-configurated compounds. Thus, for the 1,8-*erythro*-configurated bicyclic lactones C-1 was observed at ca. δ = 80–82 ($CDCl_3$) and δ = 84–85 (D_2O) while C-1 of the 1,8-*threo*-configurated bicyclic lactones was observed at ca. δ = 84–87 ($CDCl_3$) and δ = 88–89 (D_2O). These observations are supported by a previous ^{13}C NMR study of *cis*/*trans* substituted cyclopentanols.[20,21]

In summary, we have reported a new strategy for the separation of isomers from cyanohydrin chain elongation of D-gulose which relies on extraction. This is an easy and reproducible method in contrast to the classical crystallisations of various derivatives of D-*glycero*-L-*galacto*-heptonic acid and D-*glycero*-L-*talo*-heptonic acid. D-*glycero*-L-*galacto*-Heptono-1,4-lactone was used as the starting material for the preparation of two new carbahexofuranoses, carba-β-D-glucofuranose and carba-α-L-mannofuranose, via an intramolecular 5-*exo*-trig radical cyclisation of 2,3-unsaturated 7-bromo-7-deoxyheptono-1,4-lactones. The relative configuration at C-4/C-5 of the 2,3-unsaturated heptono-1,4-lactones was determined by comparison with ^1H NMR data of related compounds.

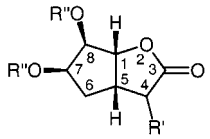
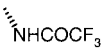
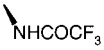
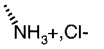
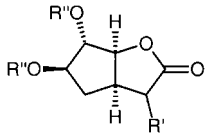
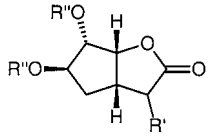
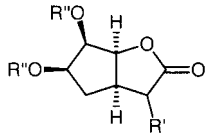
Table 1 ^1H NMR Data for Determination of the Relative Configuration of C-4 and C-5 in 2,3-Unsaturated Aldonolactones

Compound	R'	R"	$J_{4,5}$ (Hz)	H-4 δ	Ref
	H	Ac	1.5	5.30	17
	OAc	$C(CH_3)_2$	1.2	5.36	6
	H	$C(CH_3)_2$	2.5	5.38	17
	N_3	Ac	2.5	5.24	6
	$NHCOCF_3$	Ac	2.5	5.49	6
4,5-*threo*					
	OAc	$C(CH_3)_2$	2.0	5.17	[a] (**13**)
	OAc	H	5.5	5.20	[a] (**15**)
	H	$C(CH_3)_2$	2.0	5.25	[a] (**28**)
4,5-*threo*					
	H	Ac	6.0	5.15	17
	OAc	$C(CH_3)_2$	7.0	5.02	[a] (**14**)
	OAc	H	7.0	5.09	[a] (**18**)
	H	$C(CH_3)_2$	8.0	5.01	[a] (**27**)
4,5-*erythro*					
	OAc	$C(CH_3)_2$	9.0	5.03	6
	H	$C(CH_3)_2$	9.5	5.05	17
4,5-*erythro*					

[a] This work.

Mps are uncorrected. Optical rotations were determined on a Perkin–Elmer 241 polarimeter. NMR were recorded on Bruker AC-250 and AM-500 instruments. For spectra in D_2O, either dioxane (δ = 67.4), acetone (δ = 29.8) or MeCN (δ = 1.3) were used as the internal reference for ^{13}C NMR, and the solvent peak (δ = 4.63) for ^1H NMR. For spectra in $CDCl_3$ δ = 76.9 was used as internal reference for ^{13}C NMR and $CHCl_3$ (δ = 7.27) for ^1H NMR. Column chromatography was performed on silica gel 60, Merck (mesh 230–400, particle size 0.040–0.63 mm) using the flash technique. D-Gulono-1,4-lactone was prepared from D-xylose.[22] Bu_3SnH was prepared from bis(tributyltin)oxide and polymethylhydrosiloxane.[23] Reactions involving Bu_3SnH or $BH_3•SMe_2$ were performed under N_2. All concentrations were performed in vacuo. Anhydrous solvents

Table 2 ^{13}C Chemical Shifts for Determination of the Relative Configuration at C-1 and C-8 in *cis*-Fused 2-Oxabicyclo[3.3.0]oct-3-ones

Compound	R'	R"	C-1 δ	Ref
 1,8-*threo*	H	Ac	84.9[b]	17
		$C(CH_3)_2$	85.5[b]	6
		Ac	84.3[b]	6
		Ac	83.9[b]	6
		Ac	83.0[b]	17
		H	88.3[c]	6
	H	H	89.2[c]	17
 1,8-*threo*		H	86.7[b]	[a](**16**)
 1,8-*erythro*	H	Ac	79.8[b]	17
	H	H	84.1[c]	17
		H	80.5[b]	[a](**19**)
 1,8-*erythro*	H	$C(CH_3)_2$	82.2[b]	17
	H	H	84.5[c]	17
		$C(CH_3)_2$	79.8[b]	6

[a] This work. [b] $CDCl_3$. [c] D_2O.

were obtained by storing over molecular sieves. Microanalysis were carried out by Research Institute for Pharmacy and Biochemistry, Prague, Czech Republic and Microanalytical Laboratory, Institute for Physical Chemistry, University of Vienna, Austria. MS were obtained on a VG TRIO-2 instrument by chemical ionisation mass spectrometry with NH_3 as reagent gas.

D-*glycero*-L-*galacto*-Heptono-1,4-lactone and D-*glycero*-L-*talo*-Heptono-1,4-lactone (3)

D-Gulono-1,4-lactone **(1)** (30 g, 168 mmol) was dissolved in water (300 mL) and ion exchange resin (IR 120 H^+, 120 mL) was added. The flask was cooled in an ice bath and $NaBH_4$ (7.85 g, 207 mmol) was added slowly with stirring keeping pH 3–5. Stirring was maintained for 0.5 h after which time ion exchange resin (IR 120 H^+, 150 mL) was added and the mixture was stirred for another 0.5 h. The ion exchange resin was filtered off and the filtrate concentrated. The residue was concentrated from MeOH (5 × 100 mL) to give D-gulose **(2)** as a syrup (ca. 30 g); $[\alpha]_D^{20}$ –18.3 (*c* = 1.1, H_2O) [Lit.[24] $[\alpha]_D^{20}$ –20.4 (H_2O)].

^{13}C NMR (D_2O/dioxane, 62.9 MHz): δ = 61.8 (C-6), 69.9, 70.2, 72.1, 74.6 (C-2, C-3, C-4, C-5), 94.7 (C-1).

The crude D-gulose **(2)** was stirred with basic ion exchange resin (IRA-67, 100 mL). Filtration and concentration gave **2** (29.9 g, 166 mmol) which was dissolved in water (300 mL), and NaCN (9 g, 183 mmol, 1 equiv) was added to the solution. The mixture was left at r.t. overnight. Ion exchange resin (IR 120 H^+, 150 mL) was added and stirred for 0.5 h. The aqueous solution was poured onto a column of ion exchange resin (IR 120 H^+, 200 mL) which was washed with water until pH 6–7. The solvent was evaporated and the residue was concentrated from toluene to give a mixture of the two C-2 epimeric heptonolactones **3** as a syrup (31 g, 90%).

^{13}C NMR (D_2O/dioxane, 62.9 MHz): δ = 62.0, 62.1, (2 × C-7), 68.3, 68.7, 69.9, 70.0, 71.5, 72.9, 73.3 (C-2, C-3, C-5, C-6), 80.1, 86.2, (2 × C-4), 175.6, 178, (2 × C-1).

D-*glycero*-L-*talo*-Heptono-1,4-lactone (5) and 5,6-*O*-Isopropylidene-D-*glycero*-L-*galacto*-heptono-1,4-lactone (6)

A mixture of the two epimeric heptono-1,4-lactones **3** (31 g, 149 mmol) was dissolved in anhyd acetone (300 mL) and TsOH (3 g) was added. The reaction flask was equipped with a Soxhlet apparatus containing molecular sieves (3 Å) and the solution was refluxed for 22 h. The mixture was neutralised with ion exchange resin (IR 67 OH^- washed in acetone), filtered and concentrated to give a syrup. The residue was suspended in water (150 mL) and washed with CH_2Cl_2 (3 × 150 mL) and the combined organic phases were extracted with water (50 mL).

Preparation of ***5*** *from the Organic Phase*: The combined organic phases were extracted with 2 N NaOH (3 × 75 mL) and the combined basic aqueous phases were acidified with ion exchange resin (IR 120, H^+) until pH 1, and stirring maintained for 1 h. The ion exchange resin was filtered off and washed with water until neutral. The filtrate was stirred with activated charcoal, filtered and concentrated to give the title compound as a syrup (5.39 g, 17%), which crystallised upon standing. Recrystallisation from EtOH gave compound **5** (3.2 g, 10%); mp 139–141 °C (Lit.[11] mp 145 °C); $[\alpha]_D^{20}$ +25.4 (*c* = 4, H_2O) [Lit.[11] $[\alpha]_D^{20}$ +25.5].

^{13}C NMR (D_2O/dioxane, 62.9 MHz): δ = 63.1 (C-7), 69.4, 70.9, 71.1, 72.7, (C-2, C-3, C-5, C-6), 87.4 (C-4), 179.2 (C-1).

Preparation of 6 from the Aqueous Phase

The combined aqueous phases were concentrated to give compound **6** as a syrup (13.3 g, 36% from **1**) which was pure enough for further synthesis as seen from its ^{13}C NMR spectrum. Purification by flash chromatography (EtOAc) gave pure **6** (11.1 g, 30% from **1**) which crystallised upon standing at –18 °C. Recrystallisation from EtOAc/hexane gave a
colourless crystalline compound; mp 98–100 °C; $[\alpha]_D^{20}$ +59 (*c* = 1.0, EtOH).

^1H NMR (CD_3OD, 500 MHz): δ = 1.37, 1.41, (2 × CH_3), 3.72 (d, 2H, H-7, H-7'), 4.14 (m, 3H, H-4, H-5, H-6), 4.25 (dd, 1H, $J_{3,4}$ = 7 Hz, H-3), 4.36 (d, 1H, $J_{2,3}$ = 7.5 Hz, H-2).

^{13}C NMR (CD_3OD, 62.9 MHz): δ = 26.9, 27.5, (2 × CH_3), 62.7 (C-7), 75.4, 75.5, 77.0, 78.2, 79.7 (C-2, C-3, C-4, C-5, C-6), 111 (acetal C), 176 (C-1).

CI-MS: *m/z* = 266 ($M + NH_4^+$), 249 ($M + H^+$).

Anal. $C_{10}H_{16}O_7$ (248.23): calcd C, 48.39; H, 6.50. Found C, 48.58; H, 6.27.

D-*glycero*-L-*galacto*-Heptonic Acid Phenylhydrazide (9)

A mixture of the two epimeric heptono-1,4-lactones **3** (33.5 g, 161 mmol) was dissolved in 50% EtOH (250 mL) and phenylhydrazine (19 mL, 193 mmol) was added. After refluxing for 3.5 h the mixture was cooled to r.t. and EtOH was evaporated. The aqueous phase

was washed with CH_2Cl_2 (4 × 100 mL) and concentrated. The residue was dissolved in warm 80% EtOH (30 mL) and the solution was left at r.t. overnight during which time a precipitate formed. The precipitate was suspended in 80% EtOH (20 mL), filtered and washed with 80% EtOH to give the title compound **9** (13.70 g, 27%) as slightly coloured crystals, mp 174–179°C. Recrystallisation from 80% EtOH raised the melting point; mp 190–192°C (Lit.[12] mp 193–194°C); $[\alpha]_D^{20}$ –12.0 (*c* = 1.0, H_2O) [Lit.[12] $[\alpha]_D^{20}$ –11.2 (*c* = 1.0, H_2O)].

^{13}C NMR (D_2O/acetone, 62.9 MHz): δ = 62.0 (C-7), 68.9, 69.3, 70.4, 70.6, 72.8, (C-2, C-3, C-4, C-5, C-6), 113.1, 120.7, 129.0, 146.8 (phenyl), 175 (C-1).

D-*glycero*-L-*galacto*-Heptono-1,4-lactone (7)

Phenylhydrazide **9** (10.0 g, 31.6 mmol) was dissolved in warm water (100 mL), ion exchange resin (IR 120 H^+, 300 mL) was added and the mixture refluxed for 5 h. Filtration and evaporation gave compound **7** as a coloured foam (7.0 g, quant). The crude product was used without further purification.

^{13}C NMR (D_2O, 62.9 MHz): δ = 62.1 (C-7), 68.7, 71.4, 72.9, 73.3 (C-2, C-3, C-5, C-6), 80.0 (C-4), 175.5 (C-1).

7-Bromo-7-deoxy-D-*glycero*-L-*galacto*-heptono-1,4-lactone (10)

Procedure A: From **7**: Heptonolactone **7** (7.0 g, 31.6 mmol) was dissolved in glacial HOAc (7 mL) at ca. 80°C. The solution was cooled to r.t. and then 37% HBr in HOAc (45 mL) was added. The mixture was stirred vigorously for 20 min to obtain a homogeneous solution. MeOH (70 mL) was added and the mixture was left at r.t. overnight. The solvent was evaporated and the residue was concentrated from water (3 × 50 mL) and toluene (50 mL). The syrup was purified by flash chromatography (EtOAc) to give the title compound **10** as colourless crystals (6.01 g, 70%), mp 119–122°C; R_f 0.30 (EtOAc). Repeated crystallisations from EtOAc gave mp 125–126°C; $[\alpha]_D^{20}$ +52 (*c* = 0.4, MeOH).

A dibromoheptonolactone, tentatively assigned as 6,7-dibromo-6,7-dideoxy-L-*glycero*-L-*galacto*-heptono-1,4-lactone **(11)**, was isolated as a solid (0.4 g, 4%); R_f 0.65 (EtOAc).

Procedure B: From 6

Protected heptonolactone **6** (0.50 g, 2.0 mmol) was suspended in 37% HBr in HOAc (4 mL) and the suspension was stirred vigorously for 40 min. MeOH (10 mL) was added and the solution was left at r.t. overnight. The solvents were evaporated and the residue was concentrated from water (3 × 30 mL) and toluene (30 mL). Flash chromatography (EtOAc) gave **10** (0.39 g, 71%) and **11** (0.16 g, 24%).

Compound 10

^{1}H NMR (D_2O, 500 MHz): δ = 3.46 (dd, 1H, $J_{6,7}$ = 6 Hz, H-7), 3.57 (dd, 1H, $J_{6,7'}$ = 4, $J_{7,7'}$ = 11 Hz, H-7'), 3.88 (dd, 1H, $J_{5,6}$ = 5 Hz, H-5), 3.92 (m, 1H, H-6), 4.25 (dd, 1H, $J_{3,4}$ = 9 Hz, H-3), 4.31 (dd, 1H, $J_{4,5}$ = 3.5 Hz, H-4), 4.50 (d, 1H, $J_{2,3}$ = 9 Hz, H-2).

^{13}C NMR (D_2O/dioxane, 62.9 MHz): δ = 35.2 (C-7), 70.8, 71.2, 74.0, 74.3, (C-2, C-3, C-5, C-6), 80.8 (C-4), 176.6 (C-1).

CI-MS: *m/z* = 288 (^{79}Br, M + NH_4^+), 290 (^{81}Br, M + NH_4^+).

Anal. $C_7H_{11}BrO_6$ (271.06): calcd C, 31.02; H, 4.09; Br, 29.48. Found C, 31.22; H, 4.05; Br, 29.59.

Compound 11

^{1}H NMR (CD_3COCD_3, 500 MHz): δ = 4.07 (m, 2H, H-5, H-7), 4.18 (dd, 1H, $J_{7,7'}$ = 11.5 Hz, H-7), 4.39 (ddd, 1H, $J_{5,6}$ = 2.5, $J_{6,7'}$ = 5 Hz, H-6), 4.41 (dd, 1H, H-3), 4.49 (d, 1H, $J_{2,3}$ = 8.5 Hz, H-2), 4.62 (dd, 1H, $J_{3,4}$ = 8, $J_{4,5}$ = 1.5 Hz, H-4).

^{13}C NMR (CD_3COCD_3, 62.9 MHz): δ = 38.5 (C-7), 53.2 (C-6), 70.5, 74.3, 75.2 (C-2, C-3, C-5), 80.0 (C-4), 174.5 (C-1).

7-Bromo-7-deoxy-5,6-*O*-isopropylidene-D-*glycero*-L-*galacto*-heptono-1,4-lactone (12)

Camphorsulfonic acid (0.65 g, 2.8 mmol) was added to a solution of **10** (11.40 g, 42.1 mmol) in anhyd acetone (250 mL). The flask was equipped with a Soxhlet apparatus containing molecular sieves (3Å) and the mixture was refluxed for 21 h. The solution was then neutralised with excess $NaHCO_3$ (5 g), filtered and concentrated. The residue was dissolved in water (25 mL), extracted with EtOAc (4 × 25 mL) and the organic phases dried (Na_2SO_4) and concentrated. The crude product was purified by flash chromatography (EtOAc/hexane 1:1) to give **12** as a syrup (10.92 g, 83%); $[\alpha]_D^{20}$ +50.5 (*c* = 0.3, EtOH).

^{1}H NMR ($CDCl_3$, 500 MHz): δ = 1.42, 1.47 (2 × CH_3), 3.21 (bd, OH), 3.50 (dd, 1H, $J_{6,7'}$ = 7 Hz, H-7), 3.59 (dd, 1H, $J_{6,7'}$ = 4.5, $J_{7,7'}$ = 10.5 Hz, H-7'), 3.63 (bd, OH), 4.48 (bd, 1H, H-2), 4.21 (dd, 1H, $J_{5,6}$ = 7.6 Hz, H-5), 4.37 (dd, 1H, $J_{3,4}$ = 7.5, $J_{4,5}$ = 2.5 Hz, H-4), 4.40 (ddd, 1H, H-6), 4.52 (bdd, 1H, $J_{2,3}$ = 7 Hz, H-3).

^{13}C NMR ($CDCl_3$, 62.9 MHz): δ = 27.2, 26.6 (2 × CH_3), 31.7 (C-7), 74.1, 74.6, 75.1, 77.6, 78.9 (C-2, C-3, C-4, C-5, C-6), 110.9 (acetal C), 174.5 (C-1).

CI-MS: *m/z* = 328, 330 (^{79}Br, ^{81}Br, M + NH_4^+), 311, 313 (^{79}Br, ^{81}Br, M + H^+)

Anal. $C_{10}H_{15}BrO_6$ (311.13): calcd C, 38.60; H, 4.86. Found C, 38.73; H, 4.94.

2-*O*-Acetyl-7-bromo-3,7-dideoxy-5,6-*O*-isopropylidene-D-*xylo*-hept-2-enono-1,4-lactone (13) and 2-*O*-Acetyl-7-bromo-3,7-dideoxy-5,6-*O*-isopropylidene-D-*lyxo*-hept-2-enono-1,4-lactone (14)

Bromolactone **12** (1.00 g, 3.2 mmol) was dissolved in Ac_2O (2.43 mL, 25.7 mmol) and Et_3N (1.79 mL, 12.8 mmol) and left at r.t. for 0.5 h after which the solvents were evaporated. The residue was dissolved in CH_2Cl_2 (20 mL), washed with water (4 × 20 mL), dried ($MgSO_4$) and concentrated. The two isomers were separated by repeated flash chromatography (EtOAc/CH_2Cl_2 1:100) to give 2-*O*-acetyl-7-bromo-3,7-dideoxy-5,6-*O*-isopropylidene-D-*lyxo*-hept-2-enono-1,4-lactone **(14)** (0.23 g, 21%); R_f 0.48 (CH_2Cl_2/EtOAc 40:1); $[\alpha]_D^{20}$ +39 (*c* = 1.2, $CHCl_3$) and 2-*O*-acetyl-7-bromo-3,7-dideoxy-5,6-*O*-isopropylidene-D-*xylo*-hept-2-enono-1,4-lactone **(13)** (0.33 g, 31%); R_f 0.42 (CH_2Cl_2/EtOAc 40:1); $[\alpha]_D^{20}$ –1.2 (*c* = 2 $CHCl_3$) as colourless syrups.

Compound 13

^{1}H NMR ($CDCl_3$, 500 MHz): δ = 1.30, 1.35, (2s, 6H, 2 × CH_3), 2.24 (s, OAc), 3.39 (dd, 1H, H-7), 3.52 (dd, 1H, $J_{7,7'}$ = 10.5 Hz, H-7'), 4.09 (dd, 1H, $J_{5,6}$ = 7 Hz, H-5), 4.36 (ddd,1H, $J_{6,7'}$ = 4.5, $J_{6,7}$ = 7.5 Hz, H-6), 5.17 (dd, 1H, $J_{4,5}$ = 2.0 Hz, H-4), 6.99 (d, 1H, $J_{3,4}$ = 2 Hz, H-3).

^{13}C NMR ($CDCl_3$, 62.9 MHz): δ = 20.8 (OAc), 26.3, 27.2, (2 × CH_3), 31.7 (C-7), 75.3, 77.2, 78.9 (C-4, C-5, C-6), 111.2 (acetal C), 129.9 (C-3), 138.1 (C-2), 166.8, 166.6 (C-1, OAc).

Anal. $C_{12}H_{15}BrO_6$ (335.15): calcd C, 43.01; H, 4.51; Br, 23.84. Found C, 42.97; H, 4.46; Br, 23.76.

Compound 14

^{1}H NMR ($CDCl_3$, 500 MHz): δ = 1.44, 1.47 (2s, 6H, 2 × CH_3), 2.32 (2s, OAc), 3.50 (dd, 1H, H-7), 3.63 (dd, 1H, $J_{7,7'}$ = 11 Hz, H-7'), 3.85 (dd, 1H, $J_{5,6}$ = 7 Hz, H-5), 4.29 (ddd, 1H, $J_{6,7}$ = 5, $J_{6,7'}$ = 4.5 Hz, H-6), 5.02 (dd, 1H, $J_{4,5}$ = 7.0 Hz, H-4), 7.38 (d, 1H, $J_{3,4}$ = 2.0 Hz, H-3).

^{13}C NMR ($CDCl_3$, 62.9 MHz): δ = 20.7 (OAc), 27.0, 27.2 (2 × CH_3), 32.2 (C-7), 78.2, 78.8, 79.5, (C-4, C-5, C-6), 111.3 (acetal), 131.3 (C-3), 138.4 (C-2), 165.8, 166.7 (C-1, OAc).

Anal. $C_{12}H_{15}BrO_6$ (335.15): calcd C, 43.01; H, 4.51; Br, 23.84. Found C, 43.23; H, 4.47; Br, 24.02.

2-*O*-Acetyl-7-bromo-3,7-dideoxy-D-*xylo*-hept-2-enono-1,4-lactone (15)

Protected lactone **13** (0.27 g, 0.8 mmol) was dissolved in 80% TFA (1.3 mL) and left at r.t. for 0.5 h. Water (3 mL) was added and the aqueous phase was extracted with CH_2Cl_2 (10 × 5 mL). The combined organic phases were neutralised with excess $NaHCO_3$, filtered, dried ($MgSO_4$), stirred with activated charcoal, filtered and concentrated to give **15**, a slightly coloured crystalline solid (0.15 g, 63%) which could be recrystallised from EtOAc/Et_2O; mp 131–133 °C; $[\alpha]_D^{20}$ +0.8 (*c* = 0.5, EtOH).

^{1}H NMR ($CDCl_3$, 500 MHz): δ = 2.34 (s, 3H, OAc), 2.68 (m, 2 × OH), 3.54 (dd, 1H, $J_{7,7'}$ = 10.5 Hz, H-7), 3.57 (dd, 1H, H-7'), 3.97 (m, 1H, $J_{6,7}$ = 6.5, $J_{6,7'}$ = 5.5 Hz, H-6), 4.01 (m, 1H, H-5), 5.20 (dd, 1H, $J_{4,5}$ = 5.5 Hz, H-4), 7.31 (d, 1H, $J_{3,4}$ = 1.5 Hz, H-3).

^{13}C NMR (CD_3OD, 62.9 MHz): δ = 20.5 (OAc), 34.4 (C-7), 72.9, 73.5 (C-5, C-6), 82.1 (C-4), 134.0 (C-3), 139.4 (C-2), 168.5, 168.6 (C-1, OAc).

MS: *m/z* = 295, 297 (^{79}Br, ^{81}Br M + H^+), 312, 314 (^{79}Br, ^{81}Br M + NH_4^+).

Anal. $C_9H_{11}BrO_6$ (295.09): calcd C, 36.63; H, 3.76. Found C, 36.66; H, 3.75.

(1*S*,4*S*,5*R*,7*R*,8*S*)-4-*O*-Acetyl-7,8-dihydroxy-2-oxabicyclo-[3.3.0]octan-3-one (16)

Unsaturated lactone **15** (0.10 g, 0.34 mmol) was dissolved in anhyd EtOAc (2 mL) and heated to reflux. A solution of Bu_3SnH (0.18 mL, 0.67 mmol) and AIBN (5 mg, 0.03 mmol) in EtOAc (2 mL) was added over the course of 1 h. The solvent was evaporated and the residue was suspended in MeCN (10 mL) and washed with hexane (4 × 10 mL). The MeCN was concentrated to give a residue which was purified by flash chromatography (CH_2Cl_2/acetone 2:1). The title compound **16** was isolated as a syrup (65 mg, 89%); R_f 0.34 (CH_2Cl_2/acetone 2:1); $[\alpha]_D^{20}$ +78 (*c* = 0.7, $CHCl_3$). The C-4 isomer of the title compound, (1*S*,4*R*,5*R*,7*R*,8*S*))-4-*O*-acetyl-7,8-dihydroxy-2-oxabicyclo[3.3.0]octan-3-one **(17)**, was isolated as a syrup (3 mg, 4%); R_f 0.45 (CH_2Cl_2/acetone 2:1).

Compound 16

^{1}H NMR ($CDCl_3$, 500 MHz): δ = 1.87 (ddd, 1H, $J_{6,7}$ = 5 Hz, H-6), 2.10 (ddd, 1H, $J_{6,6'}$ = 14.5, $J_{6',7}$ = 5 Hz, H-6'), 2.22 (s, 3H, OAc), 3.40 (dddd, 1H, $J_{5,6'}$ = 9, $J_{5,6}$ = 5 Hz, H-5), 4.17 (m, 1H, H-7), 4.24 (m, 1H, H-8), 4.79 (dd, 1H, $J_{1,8}$ = 1, $J_{1,5}$ = 7 Hz, H-1), 5.54 (d, 1H, $J_{4,5}$ = 10 Hz, H-4).

^{13}C NMR ($CDCl_3$, 125.8 MHz): δ = 20.3 (OAc), 30.9 (C-6), 37.8 (C-5), 69.4 (C-4), 76.9 (C-7), 80.9 (C-8), 86.7 (C-1), 169.9, 173.3, (C-1, OAc).

CI-MS: *m/z* = 234 (M + NH_4^+), 217 (M + H^+).

Anal. $C_9H_{12}O_6$ (216.19): calcd C, 50.00; H, 5.59. Found C, 50.22; H, 5.36.

Compound 17

^{1}H NMR ($CDCl_3$, 500 MHz): δ = 2.16 (m, 1H, H-6), 2.38 (m, 1H, H-6'), 2.96 (m, 1H, H-5), 4.09 (m, 2H, H-7, H-8), 4.86 (dd, 1H, $J_{1,8}$ = 1, $J_{1,5}$ = 9 Hz, H-1), 5.16 (d, 1H, $J_{4,5}$ = 4.5 Hz, H-4).

^{13}C NMR ($CDCl_3$, 125.8 MHz): δ = 20.4 (OAc), 36.5 (C-6), 43.3 (C-5), 67.0, 75.9, 81.5, (C-4, C-7, C-8), 87.7 (C-1).

2-*O*-Acetyl-7-bromo-3,7-dideoxy-D-*lyxo*-hept-2-enono-1,4-lactone (18)

Protected lactone **14** (0.20 g, 0.6 mmol) was dissolved in 80% TFA (1 mL) and treated as described above for compound **13** to give **18** as a crystalline compound (0.12 g, 67%); mp 113–115 °C; $[\alpha]_D^{20}$ +48 (*c* = 0.7, EtOH).

^{1}H NMR ($CDCl_3$, 500 MHz): δ = 2.32 (s, 3H, OAc), 2.78, 2.85, (2 × OH), 3.55 (m, 2H, 2 × H-7), 3.83 (m, 1H, H-5), 4.14 (m, 1H, H-6), 5.09 (dd, 1H, $J_{4,5}$ = 7.0 Hz, H-4), 7.48 (d, 1H, $J_{3,4}$ = 2 Hz, H-3).

^{13}C NMR (CD_3OD, 62.9 MHz): δ = 20.5 (OAc), 33.7 (C-7), 72.2, 72.6 (C-5, C-6), 81.1 (C-4), 135.6 (C-3), 139.3 (C-2), 168.6, 177.5 (C-1, OAc).

CI-MS: *m/z* = 295, 297 (^{79}Br, ^{81}Br M + H^+), 312, 314 (^{79}Br, ^{81}Br M + NH_4^+).

Anal. $C_9H_{11}BrO_6$ (295.09): calcd C, 36.63; H, 3.76; Br, 27.08. Found C, 37.08; H, 3.60; Br, 26.51.

(1*R*,4*R*,5*S*,7*R*,8*S*)-4-*O*-Acetyl-7,8-dihydroxy-2-oxabicyclo-[3.3.0]octan-3-one (19)

Unsaturated lactone **18** (85 mg, 0.29 mmol) was dissolved in EtOAc (2 mL) and heated to reflux. A solution of Bu_3SnH (0.12 mL, 0.43 mmol) and AIBN (4 mg, 0.02 mmol) in EtOAc (1 mL) was added over 1 h. The solvent was evaporated and the residue was dissolved in MeCN (10 mL), washed with hexane (4 × 10 mL) and concentrated. The product mixture was separated by flash chromatography (CH_2Cl_2/acetone 2:1). The title compound **19** was isolated as slightly coloured crystals (50 mg, 81%); R_f 0.23 (CH_2Cl_2/acetone 2:1); mp 121–123 °C (EtOAc); $[\alpha]_D^{20}$ –136 (*c* = 0.5, EtOH). The C-4 isomer of the title compound, (1*R*,4*S*,5*S*,7*R*,8*S*)-4-*O*-acetyl-7,8-dihydroxy-2-oxabicyclo[3.3.0]octan-3-one **(20)**, was isolated as a crystalline compound (6 mg, 10%); R_f 0.42 (CH_2Cl_2/acetone 2:1).

Compound 19

^{1}H NMR (CD_3OD, 500 MHz): δ = 1.56 (ddd, 1H, $J_{5,6}$ = 10.5, $J_{6,7}$ = 8.5 Hz, H-6), 2.08 (ddd, 1H, $J_{6,6'}$ = 14, $J_{6',7}$ = 7.5, $J_{5,6'}$ = 4 Hz, H-6'), 2.17 (s, 3H, OAc), 3.28 (m,1H, H-5), 3.86 (dd, 1H, H-8), 3.95 (dd, 1H, $J_{7,8}$ = 7.5 Hz, H-7), 4.84 (dd, 1H, $J_{1,5}$ = 6.5, $J_{1,8}$ = 4.5 Hz, H-1), 5.65 (d, 1H, $J_{4,5}$ = 9.5 Hz, H-4).

^{13}C NMR ($CDCl_3$, 125.8 MHz): δ = 20.3 (OAc), 27.5 (C-6), 35.8 (C-5), 68.6 (C-4), 75.0 (C-7), 78.9 (C-8), 80.5 (C-1).

CI-MS: *m/z* = 234 (M + NH_4^+), 217 (M + H^+).

Anal. $C_9H_{12}O_6$ (216.19): calcd C 50.00; H, 5.59. Found C, 50.21; H, 5.44.

Compound 20

^{1}H NMR (CD_3OD, 500 MHz): δ = 2.03 (ddd, 1H, $J_{6,7}$ = 2 Hz, H-6), 2.12 (s, 3H, OAc), 2.22 (ddd, 1H, $J_{6,6'}$ = 14.5, $J_{6',7}$ = 5 Hz, H-6'), 2.94 (dddd, 1H, $J_{5,6}$ = 10, $J_{5,6'}$ = 5 Hz, H-5), 3.96 (dd, 1H, H-8), 4.10 (ddd, 1H, $J_{7,8}$ = 2.5 Hz, H-7), 5.05 (dd, 1H, $J_{1,5}$ = 9.5, $J_{1,8}$ = 4 Hz, H-1), 5.11 (d, 1H, $J_{4,5}$ = 6.5 Hz, H-4).

^{13}C NMR ($CDCl_3$, 125.8 MHz): δ = 36.6 (C-6), 41.3 (C-5), 75.4, 75.9, 76.9, (C-4, C-7, C-8), 82.3 (C-1).

(1*S*,4*S*,5*R*,7*R*,8*S*)-4-*O*-Acetyl-7,8-dihydroxy-2-oxabicyclo-[3.3.0]octan-3-one (16) and (1*R*,4*R*,5*S*,7*R*,8*S*)-4-*O*-Acetyl-7,8-dihydroxy-2-oxabicyclo[3.3.0]octan-3-one (19)

The syntheses of **16** and **19** could be performed on a mixture of products in analogy with the synthesis of each isomer. Bromolactone **12** (3.68 g, 11.8 mmol) was treated with Ac_2O (8.9 mL, 94.7 mmol) and Et_3N (6.6 mL, 47.3 mmol) as described above to give a mixture of unsaturated lactones **13** and **14** (4.02 g,) as a coloured syrup. The isopropylidene groups were hydrolysed using 80% TFA (15 mL) to give a mixture of **15** and **18** (2.20 g) as a slightly coloured crystalline residue. A quantity of this residue (1.85 g, ca. 6.3 mmol) was treated with Bu_3SnH (4.3 mL, 15.6 mmol) and AIBN in the usual manner to give after workup a mixture of **16** and **19** (1.78 g, syrup). The isomers were separated by repeated flash chromatography (CH_2Cl_2/acetone 5:2) to give **16** (0.51 g, 24%), and **19** (0.47 g, 22%). NMR spectra were identical with those described above.

Carba-β-D-glucofuranose (21)
Compound **16** (0.195 g, 0.9 mmol) was dissolved in anhyd THF (5 mL), BH_3•SMe_2 (0.9 mL, 9.0 mmol) was added at r.t. and the solution was refluxed for 6 h. The reaction was quenched by addition of water (10 mL), the solvents were evaporated and the residue was concentrated from MeOH (3 × 30 mL). The crude product was purified by flash chromatography (acetone/MeOH 9:1). The isolated product was dissolved in water filtered through activated charcoal to give **21** as a colourless syrup (0.11g, 77%); $[\alpha]_D^{20}$ –39 (*c* = 0.4, MeOH).

^{1}H NMR (D_2O, 500 MHz): δ = 1.38 (ddd, 1H, *J* = 8.5 Hz, H-4a), 1.98 (ddd, 1H, $J_{4a',4a}$ = 12, *J* = 7, *J* = 6 Hz, H-4a'), 2.06 (m, 1H, H-4), 3.41 (dd, 1H, $J_{5,6}$ = 6.5 Hz, H-6), 3.60 (dd, 1H, $J_{5,6'}$ = 3, $J_{6,6'}$ = 12 Hz, H-6'), 3.74 (m, 2 H, H-2, H-5), 3.88 (m, 1H, $J_{1,2}$ = 2.5 Hz, H-1), 3.96 (dd, 1H, $J_{2,3}$ = 6, $J_{3,4}$ = 2.5 Hz, H-3).

^{13}C NMR (CD_3OD, 62.9 MHz): δ = 33.9 (C-4a), 42.3 (C-4), 72.5, 77.6, 77.8, 85.1, (C-1, C-2, C-3, C-5), 65.3 (C-6).

CI-MS: *m/z* = 196 ($M + NH_4^+$), 179 ($M + H^+$). $C_7H_{14}O_5$ (178.19).

1,2,3,5,6-Penta-*O*-acetyl-carba-β-D-glucofuranose (22)
Carba-β-D-glucofuranose **(21)** (0.082 g, 0.46 mmol) was dissolved in Ac_2O (1.1 mL, 1.2 mmol) and $HClO_4$ (1 drop) was added. The solution was left for 3 h after which water (2 mL) was added. The solution was extracted with CH_2Cl_2 (3 × 5 mL), the combined organic phases were washed with water (3 × 5 mL) and aq $NaHCO_3$ (10 mL), dried ($MgSO_4$), filtered and concentrated. The residue was purified by flash chromatography (EtOAc/hexane 2:3) to give the title compound as a syrup (0.159 g. 89%); $[\alpha]_D^{20}$ –23 (*c* = 1.2, $CHCl_3$).

^{1}H NMR ($CDCl_3$, 500 MHz): δ = 1.72 (dtr, 1H, *J* = 8.5, *J* = 13 Hz, H-4a), 2.01, 2.06, 2.07, 2.08, 2.09 (5s, 5 × 3H, 5 × CH_3), 2.39 (ddd, 1H, *J* = 6, *J* = 7, *J* = 13 Hz, H4a'), 2.57 (m, 1H, H-4), 3.93 (dd, 1H, $J_{5,6'}$ = 5, $J_{6,6'}$ = 12 Hz, H-6'), 4.40 (dd, 1H, $J_{5,6}$ = 2.5 Hz, H-6), 5.01 (d, 1H, *J* = 3 Hz), 5.09 (dtr, 1H, *J* = 3, *J* = 8.5 Hz), 5.15 (m, 1H), 5.18 (m, 1H).

^{13}C NMR ($CDCl_3$, 125.7 MHz): δ = 20.63, 20.67, 20.72, 20.75 (5 × CH_3), 32.2 (C-4), 41.0 (C-4a), 63.9 (C-6), 69.2, 75.0, 77.6, 81.6 (C-1, C-2, C-3, C-5), 169.2, 169.4, 170.0, 170.1, 170.5 (5 × OAc).

Anal. $C_{17}H_{24}O_{10}$ (388.37): calcd C, 52.57; H, 6.23. Found C, 52.35; H, 6.05.

Carba-α-L-mannofuranose (23)
Compound **19** (0.20 g, 0.92 mmol) was dissolved in anhyd THF (5 mL). BH_3•SMe_2 (0.92 mL, 9.2 mmol) was added at r.t. and the solution was refluxed overnight during which time a colourless precipitate was formed. Workup was conducted as described for the preparation of **21** to give the title compound **23** as a colourless syrup (0.10 g, 68%); $[\alpha]_D^{20}$ –24 (*c* = 0.98, MeOH).

^{1}H NMR (D_2O, 500 MHz): δ = 1.46 (dd, 1H, *J* = 4.5, *J* = 10 Hz, H-4a), 1.83 (ddd, 1H, $J_{4a',4a}$ = 14, *J* = 10 Hz, H-4a'), 2.12 (ddd, 1H, H-4), 3.36 (dd, 1H, $J_{5,6}$ = 6.5 Hz, H-6), 3.60 (ddd, 1H, $J_{4,5}$ = 10 Hz, H-5), 3.79 (dd, 1H, $J_{1,2}$ = 7.5 Hz, H-2), 4.04 (dd, 1H, $J_{2,3}$ = 4, $J_{3,4}$ = 3.5 Hz, H-3), 4.08 (ddd, 1H, H-1).

^{13}C NMR (D_2O/MeCN, 62.9 MHz): δ = 32.0 (C-4a), 40.9 (C-4), 64.5 (C-6), 71.7, 73.4, 75.9, 80.9, (C-1, C-2, C-3, C-5).

CI-MS: *m/z* = 196 ($M + NH_4^+$), 179 ($M + H^+$). $C_7H_{14}O_5$ (178.19).

1,2,3,5,6-Penta-*O*-acetyl-carba-α-L-mannofuranose (24)
Compound **23** (0.030 g, 0.17 mmol) was dissolved in Ac_2O (0.4 mL, 4.2 mmol) and $HClO_4$ (1 drop) was added. The reaction, workup and purification were done as described for the preparation of compound **22**. The title compound **24** was obtained as colourless crystals (0.052 mg, 80%), which were recrystallised from Et_2O; mp 121–122 °C; $[\alpha]_D^{20}$ –59 (*c* = 0.5, $CHCl_3$).

^{1}H NMR ($CDCl_3$, 500 MHz): δ = 1.73 (ddd, 1H, *J* = 3.5, *J* = 9.5, *J* = 14 Hz, H-4a'), 2.0, 2.02, 2.06, 2.07, 2.08 (5s, 15 H, 5 × CH_3), 2.28 (ddd, 1H, *J* = 9.5, *J* = 10, *J* = 14 Hz, H-4a), 2.66 (dq, 1H, *J* = 3.5, *J* = 10 Hz, H-4), 3.94 (dd, 1H, *J* = 5.5, *J* = 12.5 Hz, H-6'), 4.33 (dd, 1H, *J* = 2.5, *J* = 12.5 Hz, H-6), 5.09 (ddd, 1H, *J* = 2.5, *J* = 5.5, *J* = 8 Hz), 5.22 (dd, 1H, *J* = 3.5, *J* = 7.5 Hz), 5.27 (m, 1H), 5.46 (tr, 1H, *J* = 3.5 Hz).

^{13}C NMR ($CDCl_3$, 125.7 MHz): δ = 20.4, 20.5, 20.6, 20.61, 20.8 (5 × CH_3), 30.6 (C-4a), 38.8 (C-4), 63.4 (C-6), 69.6, 71.9, 75.4, 77.0 (C-1, C-2, C-3, C-5), 169.8, 169.9, 170.0, 170.4, 170.5 (5 × OAc).

Anal. $C_{17}H_{24}O_{10}$ (388.37): calcd C, 52.57; H, 6.23. Found C, 52.84; H, 6.13.

7-Bromo-2,3,7-trideoxy-D-*lyxo*-hept-2-enono-1,4-lactone (26)
Acetylated lactone **25**[6] (3.0 g, 9.3 mmol) was suspended in HCl/MeOH (30 mL, 1% AcCl in MeOH) and stirring was maintained for 72 h. The solvent was evaporated and the crude product was crystallised from Et_2O affording **26** as colourless crystals (1.57 g, 72%); mp 109–111 °C; $[\alpha]_D^{20}$ + 133 (*c* = 1.6, EtOH).

^{1}H NMR (D_2O, 500 MHz): δ = 3.43 (dd, 1H, $J_{6,7}$ = 7.5 Hz, H-7), 3.49 (dd, 1H, $J_{6,7'}$ = 5.5, $J_{7,7'}$ = 11 Hz, H-7'), 3.96 (m, 2H, H-5, H-6), 5.23 (ddd, 1H, $J_{4,5}$ = 5.5 Hz, H-4), 6.18 (dd, 1H, $J_{3,4}$ = 1.5 Hz, H-3), 7.81 (dd, 1H, $J_{2,3}$ = 5.5, $J_{2,4}$ = 1 Hz, H-2).

^{13}C NMR (D_2O/acetone, 62.9 MHz): δ = 35.8 (C-7), 73.1, 73.5 (C-5, C-6), 87.1 (C-4), 123.8 (C-3), 160.0 (C-2), 178.5 (C-1).

Anal. $C_7H_9BrO_4$ (237.05): calcd C, 35.45; H, 3.83; Br, 33.71. Found C, 35.50; H, 3.75; Br, 33.19.

7-Bromo-2,3,7-trideoxy-5,6-*O*-isopropylidene-D-*lyxo*-hept-2-enono-1,4-lactone (27)
Camphorsulfonic acid (68 mg, 0.3 mmol) was added to a solution of lactone **26** (1.40 g, 5.9 mmol) in anhyd acetone (20 mL) and 2,2-dimethoxypropane (10 mL). The solution was left at r.t. for 35 h after which excess solid $NaHCO_3$ was added and stirred until neutral. The suspension was filtered, the filtrate was concentrated and the syrup was suspended in Et_2O, filtered, concentrated and purified by flash chromatography (EtOAc/hexane 1:2) to give **27** as a colourless oil (1.46 g, 90%); $[\alpha]_D^{20}$ +124 (*c* = 1.0, $CHCl_3$)

^{1}H NMR ($CDCl_3$, 500 MHz): δ = 1.46, 1.48 (2s, 6H, 2 × CH_3), 3.52 (dd, 1H, H-7), 3.67 (dd, 1H, $J_{7,7'}$ = 11.5 Hz, H-7'), 3.76 (dd, 1H, $J_{5,6}$ = 6.5 Hz, H-5), 4.32 (ddd, 1H, $J_{6,7}$ = 5.5, $J_{6,7'}$ = 4 Hz, H-6), 5.01 (ddd, 1H, $J_{4,5}$ = 8 Hz, H-4), 6.24 (dd, 1H, $J_{3,4}$ = 2 Hz, H-3), 7.64 (dd, 1H, $J_{2,3}$ = 5.5, $J_{2,4}$ = 1.5 Hz, H-2).

^{13}C NMR ($CDCl_3$, 62.9 MHz): δ = 26.6, 26.8 (2 × CH_3), 32.1 (C-7), 77.9, 78.8, 82.4 (C-4, C-5, C-6), 110.6 (acetal), 122.0 (C-3), 154.0 (C-2), 171.5 (C-1).

Anal. $C_{10}H_{13}BrO_4$ (277.11): calcd C, 43.34; H, 4.73; Br, 28.83. Found C, 43.21; H, 4.47; Br, 28.90.

7-Bromo-2,3,7-trideoxy-5,6-*O*-isopropylidene-D-*xylo*-hept-2-enono-1,4-lactone (28)
7-Bromo-2,3,7-trideoxy-5,6-*O*-isopropylidene-D-*lyxo*-hept-2-enono-1,4-lactone **(27)** (0.32 g, 1.2 mmol) was dissolved in CH_2Cl_2 (3 mL) and Et_3N (0.18 mL, 1.3 mmol). The solvent was evaporated after 1 h and the products were separated by flash chromatography (EtOAc/hexane 1:3). Starting material **27** was recovered (0.10 g, 31%); R_f 0.36 (EtOAc/hexane 1:2). The compound **28** was obtained as a solid (0.10 g, 31%); R_f 0.29 (EtOAc/hexane 1:2); mp 89–90 °C(Et_2O); $[\alpha]_D^{20}$ –70.3 (*c* = 0.5, $CHCl_3$).

^{1}H NMR ($CDCl_3$, 500 MHz): δ = 1.38, 1.42, (2s, 6H, 2 × CH_3), 3.47 (dd, 1H, H-7), 3.59 (dd, 1H, $J_{7,7'}$ = 10.5 Hz, H-7'), 4.17 (dd, 1H, $J_{5,6}$

= 7.5 Hz, H-5), 4.45 (ddd, 1H, $J_{6,7'}$ = 4.5, $J_{6,7}$ = 7.5 Hz, H-6), 5.25 (ddd, 1H, $J_{4,5}$ = 2 Hz, H-4), 6.21 (dd, 1H, $J_{3,4}$ = 2 Hz, H-3), 7.47 (dd, 1H, $J_{2,3}$ = 5.5, $J_{2,4}$ = 1.5 Hz, H-2).

^{13}C NMR ($CDCl_3$, 62.9 MHz): δ = 26.3, 27.2, (2 × CH_3), 31.7 (C-7), 75.5, 78.6, 81.1 (C-4, C-5, C-6), 111.0 (acetal C), 122.6 (C-3), 152.6 (C-2), 172.3 (C-1).

Anal. $C_{10}H_{13}BrO_4$ (277.11): calcd C, 43.34; H, 4.73; Br, 28.83. Found C, 43.81; H, 4.65; Br, 31.64.

Acknowledgement

We thank Jytte Grove-Rasmussen for technical assistance, Mr. Henrik Kragh for preparation of the two heptonolactones **5** and **6**. We also thank Dr. Jørgen Øgaard Madsen for recording the mass spectra.

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