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Highly Functionalised Cyclopentanes by Radical Cyclisation of Unsaturated Bromolactones. I Preparation of 5-Deoxycarbahexofuranoses[#]

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Abstract: Three carbasugars: 5-Deoxycarba-α-L-*xylo*-hexofuranose, 5-deoxycarba-α-L-*lyxo*-hexofuranose and 5-deoxycarba-β-D-*lyxo*-hexofuranose have been prepared starting from readily available 2,7-dibromo-2,7-dideoxy-D-*glycero*-D-*ido*-heptono-1,4-lactone and 2,7-dibromo-2,7-dideoxy-D-*glycero*-L-*gluco*-heptono-1,4-lactone. 2,3-Unsaturated 7-bromo-7-deoxy-heptono-1,4-lactones were prepared by reductive elimination of the starting compounds. The key step was a highly regio- and stereoselective 5-*exo*-trig radical cyclisation of the unsaturated bromolactones to give bicyclic cyclopentane derivatives. The lactone moiety of these compounds were reduced using $H_3B \cdot S(CH_3)_2$ to give the above-mentioned carbahexofuranoses. © 1997 Elsevier Science Ltd.

INTRODUCTION

Highly functionalised cyclopentanes appear as structural elements in biologically interesting compounds such as carbocyclic nucleosides[1] and certain glycosidase inhibitors.[2] These oxygenated cyclopentanes may be seen as carbohydrate mimics in which the ring oxygen of a furanose derivative has been replaced by a methylene group. Consequently, the preparation of carbocyclic sugar analogues, also known as carbasugars, is of interest, and non-derivatised carbafuranoses have thus been prepared by a number of research groups.[3,4] The two main approaches to the preparation of carbafuranoses have been either synthesis using carbohydrates as starting materials to give optically pure compounds[3,5] or a total synthesis approach starting from racemic compounds such as norbornene[4a, 4b] or achiral compounds as cyclopentadiene.[4c, 4d]

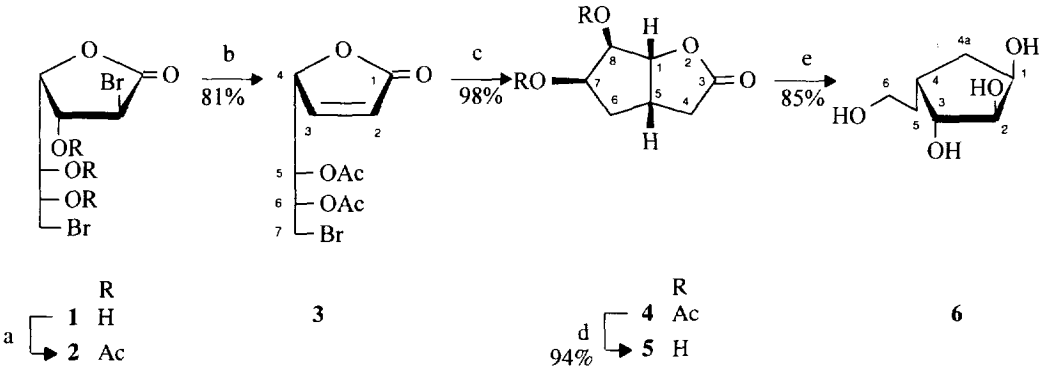
Bromodeoxyaldonolactones have previously been used as chiral synthons for the preparation of a variety of carbohydrate analogues and derivatives[6] and in the present paper we describe the use of bromo-deoxyheptonolactones for the preparation of a number of 5-deoxycarbahexofuranoses.[7] We have envisaged an intramolecular radical cyclisation for the preparation of carbocycles from unsaturated bromolactones as these compounds possess both a radical precursor, the bromo atom, as well as a radical trap, the double bond. Since the most favoured radical cyclisations are 5-*exo*-trig cyclisations[8] 7-bromo-7-deoxy-2,3-

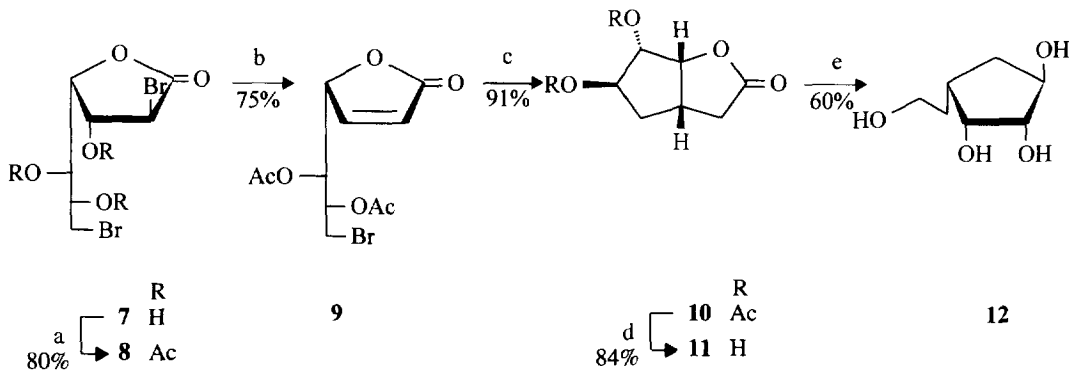
[#] Dedicated to Professor Hans Paulsen on the occasion of his 75th birthday

unsaturated 1,4-heptonolactones should be the starting material of choice, and hence preparation of these compounds was commenced.

RESULTS AND DISCUSSION

The readily available dibromoheptonolactone **1**[9] was acetylated under acidic conditions to give 3,5,6-tri-*O*-acetyl-2,7-dibromo-2,7-dideoxy-D-*glycero*-D-*ido*-heptono-1,4-lactone (**2**). A regioselective reductive *trans*-β-bromo-acetoxy elimination induced by $NaHSO_3$ was carried out using the method described by Vekemans *et al.*[10] This gave 5,6-di-*O*-acetyl-7-bromo-2,3,7-trideoxy-D-*arabino*-hept-2-enono-1,4-lactone (**3**) in good yield. The unsaturated bromolactone **3** was treated with Bu_3SnH and AIBN in refluxing ethyl acetate to give the fused cyclopentane derivative **4** in 98% yield (numbering of the carbon atoms in **3**, **4** and **6** is in accordance with the respective structures, *i.e.* C-1 in **4** and **6** does not originate from C-1 in **3**).





a: Ac_2O, H^+; b: $Na_2S_2O_5$, Na_2SO_3, H_2O, MeOH; c: Bu_3SnH, AIBN, EtOAc, reflux; d: MeOH, HCl, e: $H_3B \cdot S(CH_3)_2$, THF, reflux

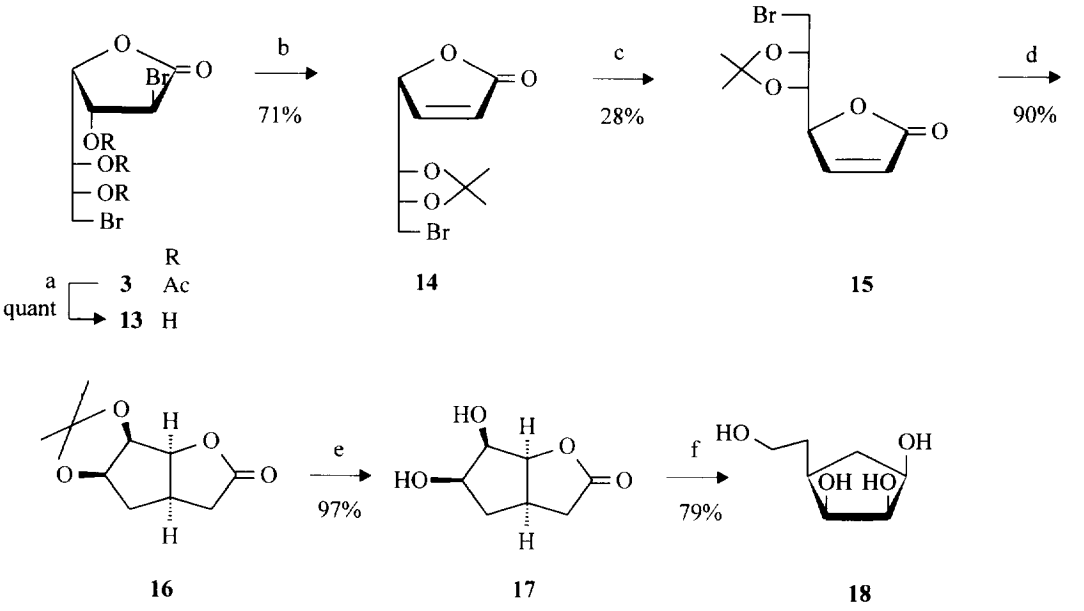
Scheme 1

Initially the radical cyclisation was carried out in toluene but as the solubility of **3** in refluxing toluene was rather low, ethyl acetate was eventually chosen as solvent for the radical reactions to facilitate large scale reactions. The solvent change had no effect on the outcome of the radical cyclisation. ^{1}H NMR of the crude cyclisation product revealed no other compounds. This showed that the cyclisation occured with a high degree of regio and stereoselectivity.

Similarly to the reaction sequence described above, the C-5 epimer of **1**, 2,7-dibromo-2,7-dideoxy-D-*glycero*-L-*gluco*-heptono-1,4-lactone (**7**), was converted into the carbasugar **12**. Thus, **7**, prepared by a slightly modified literature procedure[11] (see Experimental), was acetylated under acidic conditions to give 3,5,6-tri-*O*-acetyl-2,7-dibromo-2,7-dideoxy-D-*glycero*-L-*gluco*-heptono-1,4-lactone (**8**). Reductive elimination of **8** using $NaHSO_3$ gave the 2,3-unsaturated heptonolactone **9** (75% yield) which by cyclisation using Bu_3SnH and AIBN, gave the cyclopentane derivative **10** (91% yield after chromatography). ^{1}H-NMR of the crude product revealed no by-products. This observation again showed the high degree of regio- and stereoselectivity of the radical cyclisation of 2,3-unsaturated 7-bromo-heptonolactones.

The bicyclic compounds **4** and **10** were readily converted into carbasugars by reduction of the lactone moiety to the corresponding alcohol using $H_3B \cdot S(CH_3)_2$ as the reducing agent. Prior to reduction, the acetyl groups were removed by treatment with acidic methanol in order to minimise the consumption of the reducing agent. Thus **4** was converted to **5** (94% yield) which was treated with $H_3B \cdot S(CH_3)_2$ in refluxing tetrahydrofuran to give the carbocyclic analogue of 5-deoxy-α-L-*xylo*-hexofuranose (**6**) in 85% yield. Similarly, lactone **10** was deacetylated under acidic conditions to give **11**, followed by reduction of the lactone moiety to give crystalline 5-deoxycarba-α-L-*lyxo*-hexofuranose (**12**) (Scheme 1).

4-Substituted 2,3-unsaturated-1,4-lactones are most likely to undergo base catalysed epimerisation at C-4. Therefore, base catalysed epimerisation of the readily available unsaturated lactone **3** was investigated to obtain yet another isomer of the 2,3-unsaturated bromoheptonolactones. Since treatment of **3** with base would most likely lead to β-elimination of the C-5 acetoxy substituent and of the bromosubstituent to give a conjugated polyunsaturated lactone,[12] **3** was deacetylated in acidic methanol to give **13**, followed by conversion to the isopropylidene protected heptonolactone **14** (Scheme 2). When **14** was exposed to triethylamine in dichloromethane an equilibrium between the C-4 epimers was reached and 28% of 7-bromo-2,3,7-trideoxy-5,6-*O*-isopropylidene-D-*ribo*-hept-2-enono-1,4-lactone (**15**) and 42% of recovered starting material **14** were isolated after chromatography. **15** Was treated with Bu_3SnH and AIBN in refluxing ethyl acetate to give the cyclisation product **16** in 90% yield. No other compounds were detectable by ^{1}H-NMR of the crude product. Yet another carbasugar could be prepared from **16** in analogy to the preparation of the carbasugars **6** and **12**. The isopropylidene protecting group was removed using aqueous HCl prior to reduction in order to avoid reduction of the acetal to an ether.[13] Reduction of **17** using $H_3B \cdot S(CH_3)_2$ gave 5-deoxycarba-β-D-*lyxo*-hexofuranose (**18**) in 79% yield (Scheme 2).



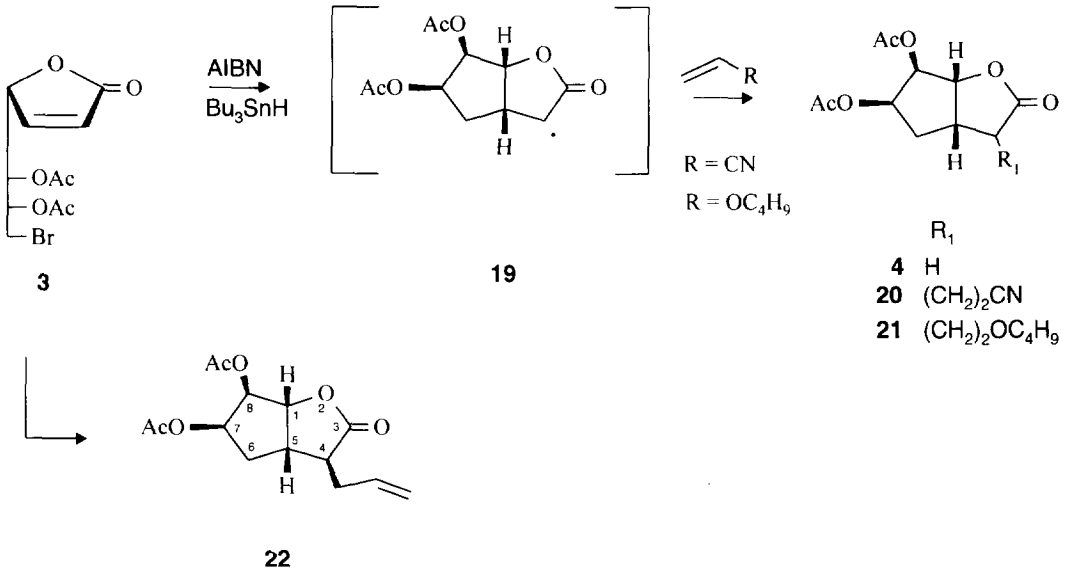
a: MeOH, HCl; b: acetone, campher sulfonic acid; c: Et_3N, CH_2Cl_2; d: Bu_3SnH, AIBN, EtOAc, reflux; e: 1M HCl; f: $H_3B \cdot S(CH_3)_2$, THF, reflux.

Scheme 2

The carbasugars reported here have previously been prepared[4a] either as the identical compound (**18**), as the enantiomer (**12**) or as a racemic mixture (**6**). These syntheses either start from racemic or resolved norbornenone and the carbafuranoses were obtained as non-crystalline compounds. We have now obtained **6** and **12** as crystalline compounds. The specific optical rotation of 5-deoxycarba-α-L-*lyxo*-hexofuranose (**12**) is - 36° (*c* 3.3 MeOH), whereas the specific optical rotation of the enantiomer was reported to be +14.7° (*c* 3.2 MeOH). The difference in optical rotation of the enantiomers can partly be explained by the optical purity of the starting materials: our approach uses optically pure D-galactose whereas (+)-norborn-5-en-2-one with an *e.e* of 86% was earlier reported as the starting material.[4a] Furthermore, the difference in optical rotation might also be explained by the crystalline state of **12**, since carbafuranoses are hygroscopic compounds which are not easily dried in the non-crystalline state.

The radical cyclisations discussed above generated one stereogenic centre with high regio- and stereo selectivity. Radical cyclisations leading to fused five membered rings give the thermodynamically more stable *cis*-fused rings.[8c] Thus the stereochemistry at the new stereogenic centre is dictated by the configuration at C-4 of the unsaturated lactone. The *cis*-orientation of the cyclisation product **4** could be verified by the coupling constant of 7 Hz for H-1 and H-5, which indicates a small dihedral angle between the

protons. Similarly, *cis*-configuration of the cyclisation products **10** and **17** was supported by coupling constants of 7 Hz for H-1 and H-5.



Scheme 3

An investigation regarding the formation of two stereogenic centers during the radical cyclisation step was commenced. During the radical cyclisation of **3** the intermediate radical α to the carbonyl group is trapped by Bu_3SnH to give **4**. The enolate radical **19** (Scheme 3) may however, also be trapped by an alkene thus generating another carbon-carbon bond and a second stereogenic center. Acrylonitrile and butylvinyl ether were investigated as radical trapping agents. Thus Bu_3SnH and AIBN were slowly added to a mixture of **3** and varying amounts of acrylonitrile or butylvinyl ether, and the outcome was judged by ^{13}C-NMR. Optimal conditions were found to be one equivalent of **3** and 12 equivalents of acrylonitrile which gave a 1:1 mixture of **4** and **20**. Using butylvinyl ether as the trapping agent optimal conditions were one equivalent of **3** and 100 equivalents of the trapping agent. This gave a 1:2 mixture of **4** and **21**. The configuration of the new stereogenic center in **20** and **21** was not determined. These experiments showed that the competion between trapping the radical **19** either with tributyltin hydride or an alkene could not be controlled in a satisfactory manner. The competition problem was, however, overcome by using allyltributyl stannane in place of tributyltin hydride. When allyltributyl stannane was added to a refluxing solution of **3** in ethyl acetate, the intermediate radical **19** was trapped by addition to the allyl stannane, and subsequent β-fragmentation gave the allylated product **22** in 78% isolated yield. Only one product could be detected by ^1H NMR of the crude product, indicating that the trapping of the radical intermediate **19** occurred stereoselectively. The

configuration at C-4 was determined by the coupling constant of 4.5 Hz between H-4 and H-5, indicating *trans*-oriented protons. When the *cis*-fused five membered rings are formed, the resulting bicyclic system takes up a cup shape. The shielding from the cyclopentane ring directs the attack on the prochiral enolate radical **19** to occur from the convex (*exo*) side. Thus the trapping agent, allyltributyl stannane, is added *anti* to the cyclopentane with high stereoselectivity. A comparison with the work of Hanessian *et al.*[14] illustrates the importance of the bicyclic system for the stereoselectivity, since 2-bromo-2-deoxy-D-xylono-1,4-lactone or 2-bromo-2-deoxy-D-arabinono-1,4-lactone, when treated with allytributyl stannane, gave epimeric mixtures of C-2 allylated lactones.[14]

In summary, we have developed an efficient route for the preparation of 5-deoxycarbahexofuranoses starting from 2,3-unsaturated 7-bromoheptonolactones. The key step is a highly regio- and stereoselective 5-*exo*-trig radical cyclisation to give optically active fused cyclopentane derivatives. The configuration of the first stereogenic centre is controlled by the configuration of the side chain of the unsaturated bromolactone. It was shown that a second stereogenic centre α to the carbonyl group could be formed with high stereoselectivity due to steric effects in cis-fused bicyclic systems. Further progress in highly selective formation of two stereogenic centers in the cyclisation step will be reported in due course.

EXPERIMENTAL

Melting points are uncorrected. Optical rotations were determined on a Perkin Elmerr 241 polarimeter. NMR spectra were recorded on Bruker AC-250 and AM-500 instruments. Evaporations were carried out below 40°C *in vacuo*. Tributyltin hydride was prepared from bis(tributyltin) oxide and polymethylhydrosiloxane,[15] and the hydride reagent was added to the reaction mixture via a syringe pump, Harvard Apparatus 11. Reactions using $H_3B \cdot S(CH_3)_2$ and Bu_3SnH were run under a nitrogen atmosphere. Microanalysis were performed by Leo Microanalytical Laboratory, Denmark, and the Research Institute for Pharmacy and Biochemistry, Prague, Czech Republic.

*3,5,6-Tri-*O*-acetyl-2,7-dibromo-2,7-dideoxy-D-glycero-D-ido-heptono-1,4-lactone* (**2**). 2,7-Dibromo-2,7-dideoxy-D-*glycero*-D-*ido*-heptono-1,4-lactone[9] (**1**) (5.10 g, 15.3 mmol) was suspended in acetic anhydride (18 ml), 1 drop of perchloric acid was added, and the reaction mixture was stirred for 1 h. H_2O (35 ml) was added, and the water phase was extracted with CH_2Cl_2 (3 x 50 ml). The combined organic phases were washed with H_2O (4 x 50 ml), neutralised ($NaHCO_3$, solid) and dried ($MgSO_4$), filtered and concentrated to give 3,5,6-tri-*O*-acetyl-2,7-dibromo-2,7-dideoxy-D-*glycero*-D-*ido*-heptono-1,4-lactone (**2**) as a syrup (quant). The product could be used directly for further synthesis, but crystallisation was possible from ether/hexane; mp. 86 - 87 °C, $[\alpha]_D^{20}$ -38° (*c* 1.0 , $CHCl_3$). *Anal.* Found: C 33.96; H 3.53; Br 34.54. Calc. for $C_{13}H_{16}Br_2O_8$ (460.07): C 33.94; H 3.51; Br 34.74, ^{1}H NMR ($CDCl_3$, 500 MHz): δ 5.55 (dd, H-3, $J_{3,4}$ 5.5Hz), 5.52 (dd, H-

5, $J_{5,6}$ 5Hz), 5.12 (m, H-6, $J_{6,7'}$ 4.5Hz, $J_{6,7}$ 6.5Hz), 5.09 (dd, H-4, $J_{4,5}$ 5Hz), 4.34 (d, H-2, $J_{2,3}$ 4.5Hz), 3.67 (dd, H-7', $J_{7,7'}$ 11.5Hz), 3.41 (dd, H-7), 2.11, 2.17, 2.19 (3 OAc). ^{13}C NMR ($CDCl_3$): δ 175.1, 168.5 , 169.8 (C-1, 3 OAc), 76.9 , 74.7 , 70.3 , 68.0 (C-3, C-4, C-5, C-6), 38.7 (C-2) , 28.9 (C-7), 20.2, 20.0, 19.8 (3 OAc).

*5,6-Di-*O*-acetyl-7-bromo-2,3,7-trideoxy-*D*-arabino-hept-2-enono-1,4-lactone (**3**).* 3,5,6-Tri-*O*-acetyl-2,7-dibromo-2,7-dideoxy-D-*glycero*-D-*ido*-heptono-1,4-lactone (**2**) (syrup,15.3 mmol) was dissolved in MeOH:H_2O (9:1, 35 ml) and $Na_2S_2O_5$ (1.46 g , 7.76 mmol) followed by Na_2SO_3 (3.96 g , 31.4 mmol) were added slowly. The suspension was stirred for 3.5 h at room temperature, followed by addition of HCl (1 N , 50 ml). The water phase was extracted with CH_2Cl_2 (4 x 50 ml), and the combined organic phases were dried ($MgSO_4$), filtered and evaporated to give a solid residue. Crystallisation from EtOAc gave 5,6-di-*O*-acetyl-7-bromo-2,3,7-trideoxy-D-*arabino*-hept-2-enono-1,4-lactone (**3**) as colourless crystals (3.95 g, 81 %), mp. 151 - 152°C, $[\alpha]_D^{20}$ +94° (*c* 1, $CHCl_3$). *Anal.* Found: C 41.33; H,4.11; Br 24.90. Calc. for $C_{11}H_{13}BrO_6$ (321.12): C 41.14; H 4.08; Br 24.88. ^{1}H-NMR ($CDCl_3$, 500 MHz): δ 7.40 (dd, H-2, $J_{2,3}$ 5.5Hz, $J_{2,4}$ 1.5Hz), 6.15 (dd, H-3, $J_{3,4}$ 2Hz), 5.44 (dd, H-5, $J_{4,5}$ 1.5Hz, $J_{5,6}$ 8Hz), 5.33 (ddd, H-6, $J_{6,7'}$ 3Hz, $J_{6,7}$ 4.5Hz), 5.30 (ddd, H-4), 3.86 (dd, H-7', $J_{7,7'}$ 11.5Hz), 3.52 (dd, H-7), 2.18, 2.06 (2 x OAc). ^{13}C-NMR ($CDCl_3$, 62.9 MHz) δ 172, 169 (C-1, 2 OAc), 152.2 (C-2), 122.3 (C-3), 80.3 (C-4), 69.9 , 68.9 (C-5, C-6), 30.9 (C-7) 20.5 , 20.1 (2 x OAc)

*1(R),5(S)-7(R),8(R)-Di-*O*-acetyl-2-oxabicyclo[3.3.0]oct-3-one (**4**).* 5,6-Di-*O*-acetyl-7-bromo-2,3,7-trideoxy-D-*arabino*-hept-2-enono-1,4-lactone (**3**) (3.21 g, 10 mmol) was dissolved in dry EtOAc (19 ml) and heated to reflux. Bu_3SnH (2.96 ml, 11 mmol) and AIBN (0.16 g, 1 mmol) dissolved in dry EtOAc (10 ml) were added over 1 h, the solution was refluxed for a further 0.5 h followed by concentration of the solvent, the residue was dissolved in CH_3CN (20 ml) and extracted with hexane (4 x 50 ml). Evaporation of the acetonitrile gave 1(*R*),5(*S*)-7(*R*),8(*R*)-di-*O*-acetyl-2-oxabicyclo[3.3.0]oct-3-one (**4**) (2.52 g, quant.) as a slightly coloured syrup. ^{1}H-NMR ($CDCl_3$, 500 MHz): δ 5.38 (dd, H-7, $J_{7,6}$ 9.5Hz), 5.27 (t, H-8, $J_{8,7}$ 4 Hz), 4.88 (dd, H-1, $J_{5,1}$ 8Hz, $J_{1,8}$ 3.5 Hz), 3.20 (m, H-5), 2.86 (dd, H-4', $J_{4',5}$ 10.5Hz), 2.38 (dd, H-4, $J_{4,4'}$ 18.5Hz, $J_{4,5}$ 3.5Hz), 2.30 (ddd, H-6, $J_{6,5}$ 5Hz, $J_{6,6'}$ Hz), 2.08, 2.10 (2 x CH_3), 1.88 (ddd, H-6'). ^{13}C NMR ($CDCl_3$, 6 2.9 MHz): δ 176 (C-3), 169.2 , 169.3 (2x OAc), 84.91 (C-1), 77.0 (C-8), 72.3 (C-7), 35.2 (C-6), 34.7 (C-4), 33.59 (C-5), 20.4 , 20.3 (2 x OAc).

*1(R),5(S)-7(R),8(R)-Dihydroxy-2-oxabicyclo[3.3.0]oct-3-one (**5**).* 1(*R*),5(*S*)-7(*R*),8(*R*)-Di-*O*-acetyl-2-oxabicyclo[3.3.0]oct-3-one (**4**) (2.52 g, 10 mmol) was dissolved in HCl/MeOH (30 ml, 1% AcCl in MeOH), and kept at room temperature for 72 h. Evaporation gave the product 1(*R*),5(*S*)-7(*R*),8(*R*)-dihydroxy-2-oxabicyclo[3.3.0]oct-3-one (**5**) (1,49 g, 94%) as colourless crystals, mp. 72 - 77°C. Crystallisation from EtOAc an analytical sample; mp. 82 - 84 °C. $[\alpha]_D^{20}$ -69.5° (*c* 1.0 , MeOH). *Anal.* Found: C 53.11, H 6.28. Calc. for $C_7H_{10}O_4$ (158.15): C 53.16; H 6.37. ^{1}H-NMR (D_2O, 500 MHz): δ 4.70 (dd, H-1, $J_{5,1}$ 8Hz, $J_{1,8}$ 4Hz), 4.06 (dd, H-7, $J_{7,6}$ 5.5Hz, $J_{7,6'}$ 5.5Hz), 3.98 (t, H-8, $J_{8,7}$ 4Hz), 3.04 (m, H-5), 2.78 (dd, H-4, $J_{4,4'}$,

19Hz, $J_{4,5}$ 11Hz), 2.27 (dd, H-4', $J_{4',5}$ 4Hz), 1.62 (dt, H-6, $J_{5,6}$ 5.5Hz, $J_{6,6'}$ 14 Hz), 1.97 (m, H-6', $J_{5,6'}$ 9Hz). ^{13}C NMR (D_2O, acetone, 62.9 MHz): δ 181 (C-3), 89.2 (C-1), 76.8 (C-8), 71.7 (C-7) 36.0, 34.7, 33.1 (C-4 , C-5 , C-6)

*5-Deoxycarba-α-L-xylo-hexofuranose (**6**).* 1(*R*),5(*S*)-7(*R*),8(*R*)-Dihydroxy-2-oxabicyclo[3.3.0]oct-3-one (**5**) (0.40 g, 2.5 mmol) was dissolved in dry THF (5 ml). $H_3B \cdot S(Me)_2$ (0.6 ml, 6 mmol, 10 M in hexane) was added at room temperature. The solution was refluxed for 45 min, during which a white gelantinous precipitate was formed. The suspension was cooled and H_2O (10 ml) was added. Stirring for 0.5 h followed by evaporation of the solvent and evaporation from MeOH (4 x 20 ml) gave a crystalline product (0.42 g); mp. 60 - 66 °C. Recrystallisation from acetone and recrystallisation of the product from the mother liquor gave **6** (0.35 g, 85%), mp. 74 - 76 °C. Repeated crystallisations of an aliquot from acetone gave crystals with mp. 76 - 77 °C, $[\alpha]_D^{20}$ -14° (*c* 1.0 MeOH). *Anal.* Found: C 51.81; H 8.70. Calc. for $C_7H_{14}O_4$ (162.19): C 51.84; H 8.70. ^{1}H-NMR (D_2O, acetone, 500 MHz): δ 4.08 (ddd, H-1, $J_{1,2}$ 4Hz), 3.94 (dd, H-3, $J_{3,4}$ 6.5Hz), 3.77 (dd, H-2, $J_{2,3}$ 4.5Hz), 3.50 (m, 2 x H-6, $J_{6,6'}$ 11Hz), 2.22 (m, H-4), 1.65 (m, 2 x H-4a, H-5), 1.31 (m, H-5) ^{13}C-NMR (D_2O, acetone, 62.9 MHz): δ 78.0 , 76.5, 70.4 (C-1, C-2, C-3), 60.0 (C-6), 34.6, 34.3, 31.3 (C-4, C-4a, C-5).

*2,7-dibromo-2,7-dideoxy-D-*glycero-*L-*gluco-*heptono-1,4-lactone (7).* D-Galactose (60.0 g, 333 mmol) was suspended in water (150 ml) and cooled in an ice bath. Sodium cyanide (24.0 g, 490 mmol) was added followed by glacial acetic acid (36.5 ml, 626 mmol) until pH 6 - 7 was reached and the solution was stored at 5°C for seven days. Ion exchange resin (IR 120 H^+, 150 ml) was added and the mixture was stirred for 1 h after which time it was poured on a column of ion exchange resin (IR 120 H^+ , 300 ml). Elution with water until pH 4 -5 was reached, followed by evaporation of the solvent gave a residue which was evaporated with MeOH (4 x 100 ml). The residue was dissolved in HCl/MeOH (100 ml MeOH + 4 ml AcCl) by heating and kept at 5°C for 4 days. Filtration gave methyl D-*glycero*-L-*manno*-heptonate (21.3 g, 27%) as colourless crystals; mp. 151 - 154 °C, $[\alpha]_D^{20}$ -9° (*c* 1, H_2O). ^{13}C NMR (D_2O, MeOH, 62.9 MHz): 175.4 (C-1), 71.4, 70.4, 70.3, 69.2, 68.4 (C-2, C-3, C-4, C-5, C-6), 63.4 (C-7) 52.7 (OCH_3). [If a mixture of products precipitated at this stage instead of the pure methyl ester, as recognized by ^{13}C NMR of the material, the combined crystals and mother liquor were evaporated from MeOH (3 x 100 ml) and the procedure of dissolving in HCl/MeOH followed by precipitation was repeated]. Methyl D-*glycero*-L-*manno*-heptonate (15.0 g, 62.50 mmol, powdered) was suspended in HBr/HOAc (105 ml) and stirred vigorously for 1 h. MeOH (140 ml) was added and the solution was left at room temperature overnight. The solvent was evaporated and the residue was evaporated from H_2O (2 x 100 ml). The syrup was dissolved in water (50 ml) and washed with CH_2Cl_2 (2 x 50 ml) and extracted with Et_2O (10 x 25 ml). The ether phases were dried (Na_2SO_4), filtered and evaporated to give the title compound **7** as slightly coloured crystals (11.80 g, 56% from the

methyl ester), mp. 115 - 118 °C [lit.[11] 121 - 123 °C]. ^{13}C NMR (D_2O,dioxane, 62.9 MHz): δ 175.5 (C-1), 81.4 (C-4), 74.0, 71.4, 67.7 (C-3, C-5, C-6), 41.9 (C-2), 34.1 (C-7), in accordance with literature data.[11]

3,5,6-Tri-O-*acetyl-2,7-dibromo-2,7-dideoxy-*D-glycero-*L*-gluco-*heptono-1,4-lactone* ***(8)***. 2,7-Dibromo-2,7-dideoxy-D-*glycero*-L-*gluco*-heptono-1,4-lactone (**7**) (11.30 g, 33.8 mmol) was suspended in acetic anhydride (40 ml, 420 mmol), 5 drops of perchloric acid were added and the solution was stirred for 1 h followed by addition of H_2O (100 ml). The water phase was extracted with CH_2Cl_2 (3 x 50 ml), the combined organic phases were washed with H_2O (8 x 70 ml), dried (Na_2SO_4) and stirred for 5 min. with solid $NaHCO_3$, filtered and evaporated to give a syrup which crystallised upon trituration with Et_2O (25 ml). Filtration gave the title compound **8** (12.47 g, 80%); mp. 128 - 133°C. Repeated crystallisations from EtOAc/ether, mp. 135 - 136 °C, $[\alpha]_D^{20}$ -38° (*c* 1, $CHCl_3$). *Anal.* Found: C 33.94; H 3.47; Br 34.56. Calc. for $C_{13}H_{16}Br_2O_8$ (460.07): C 33.94; H 3.51; Br 34.74. ^{1}H-NMR ($CDCl_3$, 500 MHz): δ 5.60 (H-5, dd, $J_{4,5}$ 9.5 Hz, $J_{5,6}$ 2.5Hz), 5.47 (H-3, d, $J_{3,4}$ 3.5Hz), 5.37 (H-6, ddd, $J_{6,7}$ 6.5Hz, $J_{6,7'}$ 6.5Hz), 4.94 (H-4, dd), 4.12 (H-2, s), 3.46 (H-7, H-7', dd, $J_{7,7'}$ 15Hz), 2.19, 2.12, 2.10 (3 x OAc). ^{13}C-NMR ($CDCl_3$, 62.9 MHz): δ 169 (4 s, C-1, 3 x OAc), 76.8 (C-4) 37.7 (C-2), 73.2 , 70.8 , 66.9 (C-3, C-5, C-6), 28.3 (C-7), 20.3, 20.2, 20.1 (3 x OAc).

5,6-Di-O-*acetyl-7-bromo-2,3,7-trideoxy-*D-lyxo-*hept-2-enono-1,4-lactone* ***(9)***. 3,5,6-Tri-*O*-acetyl-2,7-dibromo-2,7-dideoxy-D-*glycero*-L-*gluco*-heptono-1,4-lactone (**8**) (3.62 g, 10.8 mmol), was suspended in MeOH/H_2O (9:1, 30 ml). $Na_2S_2O_5$ (0.75 g, 3.9 mmol) and Na_2SO_3 (1.98 g, 15.7 mmol) were added and the suspension was stirred for 3 h. Aq HCl (1 M, 25 ml) was added and the water phase was extracted with CH_2Cl_2 (3 x 25 ml). The combined organic phases were washed with H_2O (3 x 25 ml), dried ($MgSO_4$) and neutralised (solid $NaHCO_3$), filtered and then evaporated to give a crystalline solid (2.55 g) mp. 82 - 93 °C. Recrystallisation from EtOAc/hexane gave 5,6-di-*O*-acetyl-7-bromo-2,3,7-trideoxy-D-*lyxo*-hept-2-enono-1,4-lactone (**9**) as colourless crystals (1.90 g, 75%), mp. 100-102 °C. Repeated crystallisations from EtOAc/hexane gave **9**; mp. 103 - 104 °C, $[\alpha]_D^{20}$ +75° (*c* 1.$CHCl_3$). *Anal.* Found: C 41.22; H 4.07; Br 24.74. Calc. for $C_{11}H_{13}BrO_6$ (321.12): C 41.14; H 4.08; Br 24.88. ^{1}H-NMR ($CDCl_3$, 500 MHz): δ 7.44 (dd, H-2, $J_{2,3}$ 6Hz, $J_{2,4}$ 1,5Hz), 6.23 (dd, H-3, $J_{3,4}$ 2,5Hz), 5.15 (ddd, H-4, $J_{4,5}$ 6Hz), 5.34 (m, 2 H, H-5, H-6), 3.46 (H-7', dd, $J_{6,7'}$ 5.5Hz), 3.42 (dd, H-7, $J_{6,7}$ 6.5Hz, $J_{7,7'}$ 10.5Hz), 2.17, 2.15 (2 x CH_3). ^{13}C-NMR ($CDCl_3$, 62.9 MHz): δ 172, 169 (C-1, 2 x OAc), 152.3 (C-2), 122.7 (C-3), 80.0 (C-4), 76.6 (C-5, C-6), 27.8 (C-7), 20.4, 20.2 (2 x OAc).

1(R),5(S)-7(R),8(S)-Di-O-*acetyl-2-oxabicyclo[3.3.0]oct-3-one* ***(10)***. 5,6-Di-*O*-acetyl-7-bromo-2,3,7-trideoxy-D-*lyxo*-hept-2-enono-1,4-lactone (**9**) (4.00 g, 12.5 mmol) was dissolved in dry EtOAc (40 ml) at reflux. Bu_3SnH (3.95 ml, 15 mmol) and AIBN (0.20 g, 1.2 mmol) dissolved in dry EtOAc (16 ml) were added during 1 h. Reflux was maintained for another 0.5 h after which time the solvent was evaporated. The residue was dissolved in CH_3CN (50 ml) and washed with hexane (4 x 50 ml), and the acetonitrile was evaporated. This gave a syrup which was crystallised from Et_2O to give 1(*R*),5(*S*)-7(*R*),8(*S*)-di-*O*-acetyl-2-

oxabicyclo[3.3.0]oct-3-one (**10**) as slightly coloured crystals (2.29 g, 75 %); mp. 59 - 63 °C. Crystallisation of the mother liqour from ether/hexane gave a second crop of **10** (0.47g, 16%). Purification of an aliquot by flash chromatography (EtOAc/hexane 1:1), followed by crystallisation from EtOAc/Et_2O gave a sample of colourless crystals; mp. 65 - 66 °C, $[\alpha]_D^{20}$ -169° (*c* 1, $CHCl_3$). *Anal.* Found: C 54.53; H 5.85. Calc. for $C_{11}H_{14}O_6$ (242.23): C 54.54; H 5.83. ^{1}H-NMR ($CDCl_3$, 500 MHz): δ 5.22 (dd, H-8, $J_{1,8}$ 5.0Hz, $J_{8,7}$ 6.5Hz), 5.06 (m, 2 H, H-1 , H-7), 3.09 (m, H-5, $J_{5,1}$ 7.0Hz), 2.88 (dd, H-4, $J_{4,5}$ 10Hz), 2.38 (dd, H-4', $J_{4',5}$ 3.8Hz, $J_{4,4'}$ 18.5Hz), 2.11 (ddd, H-6, $J_{6,7}$ 7Hz, $J_{5,6}$ 4.5Hz), 2.01 (ddd, H-6', $J_{7,6'}$ 7Hz, $J_{6,6'}$ 14.5Hz, $_{6',5}$ 9.5Hz), 2.06 , 2.08 (2 x OAc). ^{13}C-NMR ($CDCl_3$, 62.9 MHz): δ 176, 169 (C-3, 2 x OAc), 79.70 (s, C-1), 75.8 (C-8), 74.6 (C-7), 35.6 (C-4), 34.3 (C-6), 33.2 (C-5), 20.5, 20.3 (2 x OAc).

*1(R),5(S)-7(R),8(S)-Dihydroxy-2-oxabicyclo[3.3.0]oct-3-one (**11**).* 1(*R*),5(*S*)-7(*R*),8(*S*)-Di-*O*-acetyl-2-oxabicyclo[3.3.0]oct-3-one (**10**) (2.28 g, 9.4 mmol) was dissolved in HCl/MeOH (22 ml, 1% (v/v) AcCl in MeOH) and left at room temperature for 72 h, after which time the solution was evaporated. The crude product was purified by flash chromatography (EtOAc) to give **11** as colourless crystals (1.25 g, 84%); mp. 75 - 80 °C. Repeated crystallisations from acetone/EtOAc gave a mp. 80 - 82 °C, $[\alpha]_D^{20}$ -57° (*c* 0.76 EtOH). MS: m/z 176 ($M + NH_4^+$), 159 ($M + H^+$). *Anal.* Found: C 53.18; H 6.36. Calc. for $C_7H_{10}O_4$ (158.15): C 53.16; H 6.37. ^{1}H-NMR (D_2O, 500 Mhz): δ 4.84 (dd, H-1, $J_{1,5}$ 6.5Hz, $J_{1,8}$ 5Hz), 4.00 (dd, H-7, $J_{7,8}$ 8.5Hz), 3.83 (dd, H-8), 2.97 (m, H-5), 2.89 (H-4', $J_{4,4'}$ 18.5Hz, $J_{4',5}$ 11Hz), 2.31 (dd, H-4, $J_{4,5}$ 2.5Hz), 1.77 (m, 2 H,H-6, H-6') ^{13}C-NMR (D_2O, acetone, 62.9 MHz): δ 181 (C-3), 84.1 (C-5), 76.7, 73.1 (C-7, C-8), 35.9, 35.1, 31.3 (C-4, C-5, C-6)

*5-Deoxycarba-α-L-*lyxo-*hexofuranose (**12**).* 1(*R*),5(*S*)-7(*R*),8(*S*)-Dihydroxy-2-oxabicyclo[3.3.0]oct-3-one (**11**) (0.92 g, 5.8 mmol) was dissolved in dry THF (25 ml), and $H_3B{\cdot}S(CH_3)_2$ (1.2 ml, 12 mmol) was added at room temperature. After reflux for 1 h, H_2O (20 ml) was added. The solvent was evaporated, and the residue was evaporated from MeOH (2 x 20 ml) to give a syrup (0.85 g). Flash chromatography (acetone) gave **12** (0.56g, 60%) which was crystallised from EtOH:acetone to give colourless crystals; mp. 68 - 71 °C. Repeated crystallisations from EtOH:acetone gave a melting point of 70 - 72 °C; $[\alpha]_D^{20}$ -36° (*c* 3.3 MeOH) [lit.[4a] for the enantiomer $[\alpha]_D^{20}$ +14.7° (*c* 3.2 MeOH)] . MS: m/z 180 ($M + NH_4^+$), 163 ($M + H^+$). *Anal.* Found: C 51.93; H 8.67. Calc. for $C_7H_{14}O_4$ (162.19): C 51.84; H 8.70. ^{1}H-NMR (D_2O, 500 MHz): δ 4.05 (m, H-1, $J_{1,2}$ 4.5Hz), 3.87 (dd, H-3), 3.79 (dd, H-2, $J_{2,3}$ 7Hz), 3.51 (m, 2H, 2 x H-6), 2.13 (m, H-4), 1.76 (ddd, H-4a', $J_{4a',4a}$ 10Hz), 1.63 (m, H-5', $J_{5,5'}$ 13Hz), 1.58 (m, H-4a), 1.43 (m, H-5) ^{13}C-NMR (D_2O, acetone, 62.9 MHz): δ 80.3, 75.3, 73.9 (C-1, C-2, C-3); 59.5 (C-6); 34.7, 34.3, 31.3 (C-4, C-4a, C-5).

*7-Bromo-2,3,7-trideoxy-D-*arabino-*hept-2-enono-1,4-lactone (**13**).* 5,6-Di-*O*-acetyl-7-bromo-2,3,7-trideoxy-D-*arabino*-hept-2-enono-1,4 -lactone (**3**) (1.88 g, 5.86 mmol) was suspended in HCl/MeOH (1 ml AcCl in 50 ml MeOH) and stirred at room temperature for 3 days. The solvent was evaporated to give **13** as a

crystalline compound (1.40 g, quant). Recrystallisation from EtOAc/hexane gave mp. 125-127 °C, $[\alpha]_D^{20}$ + 71.4° (*c* 0.7, EtOAc). *Anal.* Found: C 35.29; H, 3.86. Calc. for $C_7H_9BrO_4$ (237.07): C 35.46; H 3.83. ^{1}H-NMR (D_2O, acetone, 500 MHz): δ 7.59 (dd, H-3, $J_{2,3}$ = 6.0 Hz, $J_{3,4}$ = 1.2 Hz), 6.11 (dd, H-2, $J_{2,4}$ = 2.0 Hz), 6.42 (ddd, H-4), 3.84 (dd, H-5, $J_{4,5}$ = 1.8 Hz, $J_{5,6}$ = 9.0 Hz), 3.78 (ddd, H-6, $J_{6,7}$ = 2.8 Hz, $J_{6,7'}$ = 4.5 Hz), 3.62 (dd, H-7, $J_{7,7'}$ = 11.0 Hz), 3.55 (dd, H-7'). ^{13}C NMR (D_2O, acetone, 62.9 MHz): 177 (C-1), 156.8 (C-3), 121.0 (C-2), 83.5 (C-4), 69.5, 69.0 (C-5, C-6), 36.7 (C-7).

*7-Bromo-3,7-dideoxy-5,6-*O*-isopropylidene-*D*-*arabino*-hept-2-enono-1,4-lactone (**14**).* 7-Bromo-2,3,7-trideoxy-D-*arabino*-hept-2-enono-1,4-lactone (**13**) (5.86 g, 24.6 mmol) was suspended in dry acetone (90 ml). 2,2-Dimethoxypropane (45 ml) and camphorsulphonic acid (0.22 g, 1 mmol) were added and the reaction mixture was left at room temperature for 40 h after which it was stirred with $NaHCO_3$ (4 g) until neutral. The suspension was filtered and the filtrate was evaporated. The residue was dissolved in CH_2Cl_2 (50 ml) and washed with H_2O (4 x 30 ml). Drying (Na_2SO_4) and evaporation of the solvent gave a crystalline product which was recrystallised from Et_2O/hexane to give **14** (4.80 g, 71%) as colourless crystals; mp. 76 - 78 °C. Repeated crystallisations from Et_2O/hexane gave a product with mp. 76 - 78°, $[\alpha]_D^{20}$ -21.5° (*c* 1.0 $CHCl_3$) *Anal.* Found: C 43.28; H 4.71; Br 28.84. Calc. for $C_{10}H_{13}BrO_4$ (277.11): C 43.34; H 4.73; Br 28.83. ^{1}H-NMR ($CDCl_3$, 500 MHz): δ 7.41 (dd, H-3, $J_{2,3}$ 9Hz, $J_{3,4}$ 2.5Hz), 6.22 (dd, H-2, $J_{2,4}$ 3.5Hz), 5.38 (ddd, H-4, $J_{4,5}$ 2.5Hz), 4.66 (m, H-6), 4.43 (dd, H-5, $J_{5,6}$ 10.5Hz), 3.74 (m, 2H, H-7, H-7'), 1.34, 1.40 (2 CH_3). ^{13}C-NMR ($CDCl_3$, 62.9 MHz): δ 173 (C-1), 153.0 (C-3), 122.6 (C-2), 110.1 (acetal C), 80.2, 76.5, 75.1 (C-4, C-5, C-6), 28.4 (C-7), 26.1, 24.9 (2 x CH_3).

*7-Bromo-3,7-dideoxy-5,6-*O*-isopropylidene-*D*-ribo-hept-2-enono-1,4-lactone (**15**).* 7-Bromo-3,7-dideoxy-5,6-*O*-isopropylidene-D-*arabino*-hept-2-enono-1,4-lactone (**14**) (5.0 g, 18.1 mmol) was dissolved in CH_2Cl_2 (50 ml) and Et_3N (0.25 ml, 1.8 mmol) and left at room temperature for 16 h. The solvent was evaporated and the residue was purified by flash chromatography using EtOAc/Hexane 1:4 as the eluent. This gave **15**, (1.4 g, 28%) as a syrup, as well as recovered **14** (2.1 g, 42%). ^{1}H-NMR ($CDCl_3$, 500 MHz): δ 7.67 (dd, H-3, $J_{2,3}$ 5.7Hz, $J_{3,4}$ 1.5Hz), 6.23 (dd, H-2, $J_{2,4}$ 2Hz), 5.05 (ddd, H-4, $J_{4,5}$ 9.5Hz), 4.58 (ddd, H-6, $J_{6,7'}$ 3.5Hz, $J_{6,7}$ 8.5Hz), 3.86 (dd, H-5, $J_{5,6}$ 5.5Hz), 3.80 (dd, H-7', $J_{7,7'}$ 11Hz), 3.59 (dd, H-7, $J_{6,7}$ 8.7Hz) 1.54, 1.40 (2 CH_3). ^{13}C-NMR ($CDCl_3$, 62.9 MHz): δ 172.0 (C-1), 155.6 (C-3), 122.2 (C-2),109.9 (acetal C), 79.4, 78.0, 77.7 (C-4, C-5, C-6), 29.1 (C-7), 27.5, 25.0 (2 x CH_3).

*1(S),5(R)-7(R),8(R)-*O*-Isopropylidene-2-oxabicyclo[3.3.0]oct-3-one (**16**).* 7-Bromo-3,7-dideoxy-5,6-*O*-isopropylidene-D-*ribo*-hept-2-enono-1,4-lactone (**15**) (2.20 g, 7.9 mmol) was dissolved in dry EtOAc (22 ml) and boiled at reflux temperature. A solution of Bu_3SnH (5.25 ml, 19.8 mmol, 2.5 eq.) and AIBN (0.21 g, 1.3 mmol) in dry EtOAc (20 ml) was added to the refluxing solution over 3 h, and the reaction mixture was refluxed overnight. The solvent was evaporated and the residue was dissolved in CH_3CN (30 ml) and washed

with hexane (5 x 40 ml). The acetonitrile was evaporated. This gave **16** as slightly coloured crystals (1.42 g, 90%); mp. 70 - 72 °C. Recrystallisation from Et_2O:hexane gave colourless crystals 0.98 g (62%), mp. 74 - 76 °C. Further purification of the compound was done by flash chromatography (EtOAc/hexane 3:2) followed by recrystallisation; mp 76 - 78 °C, $[\alpha]_D^{20}$ -42° (*c* 1.0, $CHCl_3$). *Anal.* Found: C 60.64; H 7.11. Calc. for $C_{10}H_{14}O_4$ (198.22): C 60.59; H 7.12. ^{1}H-NMR ($CDCl_3$, 500 MHz): δ 4.81 (dd, H-1, $J_{1,5}$ 7.5Hz, $J_{1,8}$ 6Hz), 4.77 (ddd, H-7, $J_{6',7}$ 1.5Hz, $J_{7,8}$ 6Hz), 4.61 (dd, H-8), 3.00 (m, H-5), 2.66 (m, 2H, H-4, H-4'), 2.10 (m, H-6'), 1.96 (ddd, H-6, $J_{6,6'}$ 15.5Hz, $J_{5,6}$ 8.5Hz, $J_{6,7}$ 5.5Hz), 1.51 , 1.33 (2 CH_3). ^{13}C-NMR ($CDCl_3$, 62.9 MHz): δ 177 (C-3), 111.5 (acetal C), 82.2 (C-1), 81.6 (C-7), 78.9 (C-8), 38.6 (C-5), 34.2 (c-4), 31.8 (C-6), 25.6, 23.4 (2 CH_3)

1(S),5(R),7(R),8(R)-2-Oxabicyclo[3.3.0]oct-3-one (17). 1(*S*),5(*R*)-7(*R*),8(*R*)-*O*-Isopropylidene-2-oxabicyclo[3.3.0]oct-3-one (**16**) (0.86 g, 4.3 mmol) was dissolved in aq. HCl (1 M, 8.6 ml) and stirred for 0.5 h at room temperature. The solvent was evaporated and the residue was dissolved in water (10 ml). The solution was neutralised with ion exchange resin (IR 67 OH^-, 10 ml). Filtration and concentration gave **17** as a syrup (0.67 g, 97%), $[\alpha]_D^{20}$ +44° (*c* 0.54, EtOH). ^{1}H-NMR (D_2O, 500 MHz):δ 4.86 (dd, H-1, $J_{1,5}$ 7Hz, $J_{1,8}$ 5Hz), 4.07 (ddd, H-7, $J_{7,8}$ 3.5Hz), 3.92 (dd, H-8), 2.97 (m, H-5), 2.91 (dd, H-4', $J_{4',5}$ 11.5Hz), 2.35 (dd, H-4, $J_{4,4'}$ 18Hz, $J_{4,5}$ 1.5Hz), 1.98 (ddd, H-6', $J_{6,6'}$ 15Hz, $J_{5,6'}$ 9Hz, $J_{6',7}$ 4.5Hz), 1.60 (ddd, H-6, $J_{5,6}$ 2Hz, $J_{6,7}$ 2.5Hz). ^{13}C-NMR (D_2O, acetone, 62.9 MHz): δ 181.9 (C-3), 84.5 (C-1), 73.8, 72.3 (C-7, C-8), 37.0, 36.0, 33.5 (C-4, C-5, C-6)

5-Deoxycarba-β-D-lyxo-hexofuranose (18). 1(*S*),5(*R*),7(*R*),8(*R*)-2-Oxabicyclo[3.3.0]oct-3-one (**17**) (0.55 g, 3.5 mmol) was dissolved in dry THF under an argon atmopsphere. $H_3B \cdot S(CH_3)_2$ (10 M, 1.04 ml, 10.4 mmol) was added at room temperature and the solution was refluxed for 1 h, during which a white solid precipitated. The reaction was quenched with H_2O (10 ml) and the solvent was evaporated. The residue was evaporated from H_2O (2 x 50 ml), acidic MeOH (30 ml + 2 dr. of conc. HCl), and MeOH (4 x 30 ml). The syrup was dissolved in H_2O (10 ml) and neutralised with IR 420 resin (5 ml), filtered and evaporated to give **18** as a colourless syrup; 0.45 g (79%), $[\alpha]_D^{20}$ -15.0° (*c* 0.3 MeOH) [lit.[4a] $[\alpha]_D^{20}$ -17.6° (*c* 0.3 CH_3OH)]. MS: m/z 180 ($M + NH_4^+$), 163 ($M + H^+$). Calc for $C_7H_{14}O_4$: 162.19. ^{1}H-NMR (D_2O, 500 MHz,): δ 4.02 (ddd, H-1, $J_{1,2}$ 6Hz, $J_{1,4a'}$ 8Hz, $J_{1,4a}$ 10.5Hz), 3.89 (dd, H-3, $J_{3,4}$ 4Hz), 3.79 (dd, H-2, $J_{2,3}$ 4.5Hz), 3.54 (m, 2H, H-6, H-6'), 2.20 (ddd, H-4a', $J_{4a,4a'}$ 14Hz, $J_{4a',4}$ 8Hz), 1.82 (m, H-4), 1.73 (dddd, H-5', $J_{5,5'}$ 13Hz, $J_{4,5'}$ 7Hz, $J_{5',6}$ 7Hz, $J_{5',6'}$ 7Hz), 1.51 (dddd, H- 5, $J_{4,5}$ 8Hz, $J_{5,6}$ 7Hz, $J_{5,6'}$ 7Hz), 1.31 (ddd, H-4a, $J_{4a,4}$ 4.5Hz). ^{13}C-NMR (D_2O, dioxane, 62.9 Mhz): δ 74.8, 74.7, 71.5 (C-1, C-2, C-3), 61.1 (C-6), 37.5, 35.5, 32.8 (C-4, C-4a, C-5)

1(R),5(S)-4(S)-Allyl-7(R),8(R)-di-O-acetyl-2-oxabicyclo[3.3.0]oct-3-one (**22**). 5,6-Di-*O*-acetyl-7-bromo-2,3,7-trideoxy-D-*arabino*-hept-2-enono-1,4-lactone (**3**) (1.00 g, 3.1 mmol) was dissolved in dry EtOAc (10 ml) and heated at reflux. Allyltributyl stannane[16] (1.95 ml, 6.3 mmol) and AIBN (0.08g, 0.5

mmol) both dissolved in dry EtOAc (10.5 ml) were added during 5 h, and the reaction mixture was refluxed for additional 19 h, after which the solution was evaporated. The residue was dissolved in CH_3CN (50 ml) and washed with hexane (4 x 30 ml), and the acetonitrile was evaporated to give the crude product (1.00 g, quant) as a slightly coloured oil. The crude product was purified by flash chromatography (EtOAc/hexane, 1:2), to give 1(*R*),5(*S*)-4(*S*)-allyl-7(*R*),8(*R*)-di-*O*-acetyl-2-oxabicyclo[3.3.0]oct-3-one **22** (0.68 g, 78%) as a colourless oil. $[\alpha]_D^{20}$ -86° (*c* 1, $CHCl_3$). *Anal.* Found: C 59.33; H 6.49. Calc. for $C_{14}H_{18}O_6$ (282.29): C 59.57; H 6.43. ^{1}H-NMR ($CDCl_3$, 500 MHz): δ 5.76 (H-2', $J_{2',3'}$ 10.5Hz, $J_{2',3''}$ 17Hz), 5.36 (H-7, $J_{7,8}$ 4.5Hz), 5.21 (H-8), 5.18 (2H, H-3', H-3'', $J_{3',3''}$ 1Hz), 4.81 (H-1, $J_{1,5}$ 8.5Hz, $J_{1,8}$ 4.5Hz), 2.88 (H-5, $J_{5,6}$ 9Hz, $J_{5,6'}$ 5.5Hz), 2.58 (H-1', $J_{1',1''}$ 14.5Hz, $J_{1',4}$ 4.5Hz, $J_{1',2'}$ 7Hz), 2.50 (H-4, $J_{4,5}$ 4.5Hz), 2.35 (H-1'', $J_{1'',2'}$ 1Hz, $J_{1'',4}$ 8.5Hz), 2.28 (H-6, $J_{6,6'}$ 14Hz, $J_{6,7}$ 4.5Hz), 2.05, 2.08 (6H, 2 OAc), 1.89 (H-6', $J_{6',7}$ 5.5). ^{13}C NMR ($CDCl_3$, 125.8 MHz): δ 170, 169.5 (C-3, 2 OAc), 133.2 (C-2'), 118.0 (C-3'), 83.0 (C-1), 76.6, 72.1 (C-7, C-8), 46.1, 38.3, 35.0, 34.3 (C1', C-4, C-5, C-6), 20.1, 19.9 (2 OAc)

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