Synthesis of carbasugars from aldonolactones. Part II.[1] Preparation of polyhydroxy/aminocyclopentanes functionalised at all five ring carbons[2]

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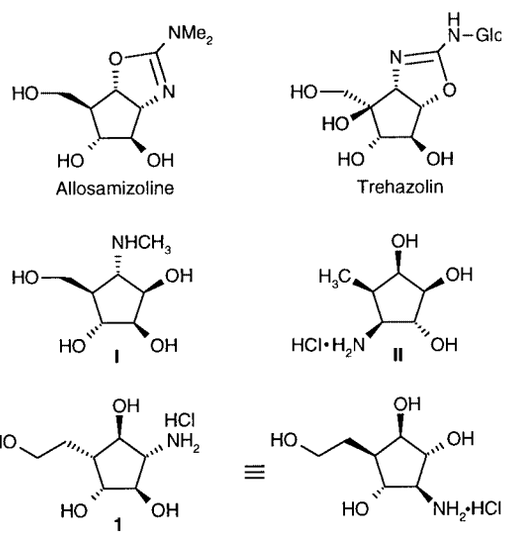
Starting from (1*R*,5*R*,8*R*)-8-acetoxy-2-oxabicyclo[3.3.0]oct-6-en-3-one **4** the syntheses of 5-deoxy-4a(*R*)-hydroxy-4a-carba-α-D-*ribo*-hexofuranose **17**, 5-deoxy-4a(*R*)-hydroxy-4a-carba-α-D-*lyxo*-hexofuranose **21**, 5-deoxy-4a(*R*)-hydroxy-4a-carba-α-D-*xylo*-hexofuranose **23** and 4a(*R*)-hydroxy-2-amino-2,5-dideoxy-4a(*R*)-hydroxy-4a-carba-α-D-*arabino*-hexofuranose **1** have been achieved. The methodology included OsO_4-catalysed dihydroxylation as well as regioselective epoxide opening followed by calcium borohydride reduction of the lactone moiety.

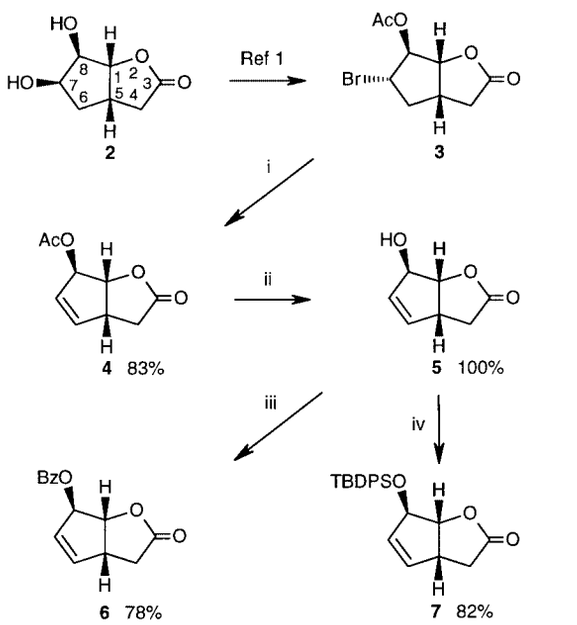
Introduction

There is a considerable interest in the synthesis of highly functionalised cyclopentanes bearing polyhydroxy as well as amino substituents. One area where this class of compounds is of great interest is as carbohydrate mimics. These polyhydroxycyclopentanes or carbasugars[3] can mimic furanoses as well as pyranoses and the lack of the acetal function makes them resistant to hydrolytic enzymes.

In particular, polyhydroxylated aminocyclopentanes have been pursued by a number of groups, both for the synthesis of carbocyclic nucleosides[4] such as aristeromycin,[5] carbovir[6] and the fully substituted epinor-BCA,[7] as well as for the preparation of glycosidase inhibitors[8] like mannostatin A.[9]



A number of polyhydroxylated aminocyclopentanes bearing a methyl or hydroxymethyl group have been shown to be potent glycosidase inhibitors. Allosamizoline[10] is the aminocyclopentitol moiety of the chitinase inhibitor allosamidin, trehazolin[11] is a trehalase inhibitor, and the two aminocyclopentanes **I**[12] and **II**[13] are potent α-mannosidase and α-L-fucosidase inhibitors, respectively. It has been postulated that the activity of these compounds as glycosidase inhibitors arises from their ability to act as transition-state analogues.[13]



Scheme 1 *Reagents and conditions*: (i) DBU, THF, reflux, 16 h; (ii) HCl–MeOH, rt, 40 h; (iii) BzCl, pyridine, rt, 1.5 h; (iv) TBDPSCl, imidazole, DCM, rt, 3.5 h.

We recently developed a short and efficient synthesis of bicyclic *cis*-fused cyclopentane lactones like **2**[14] (Scheme 1) starting from bromodeoxyaldonolactones, which in themselves are very useful synthons for a number of applications.[15] These bicyclic lactones have been converted into carbahexo- and pentofuranoses functionalised at four of the five carbons in the ring.[1,14] We here report the functionalisation of the C-6 methylene group in **2**, thereby giving access to cyclopentane derivatives bearing functional groups at all five ring carbons. In particular we have synthesised the novel polyhydroxyaminocyclopentane **1**, which can be viewed as an analogue of the above mentioned compounds. Furthermore the synthesis of three novel polyhydroxycyclopentanes is also reported.

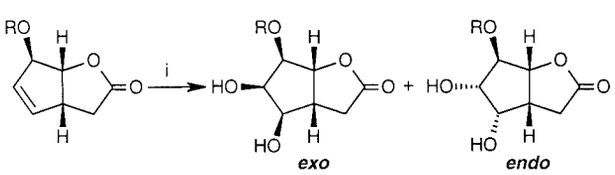
Results and discussion

Having prepared a series of carbasugars[1] we turned our attention to finding methods for functionalising the remaining

carbon atom in the cyclopentane ring. Previously, we have described the preparation of the *trans*-bromo acetate **3** from the *cis*-diol **2** in good yield.[1] Elimination of HBr from **3** would introduce an allylic alcohol functionality, which in turn can easily be further functionalised at both the double bond and in the allylic position. The use of DBU as the base cleanly gave the allylic acetate **4** in 83% yield (Scheme 1), while weaker bases like Et_3N and *t*-BuOK gave unsatisfactory results. Deprotection then gave the allylic alcohol **5** in quantitative yield.

For hydroxylation of the double bond we first investigated the OsO_4-catalysed dihydroxylation. Standard OsO_4-catalysed dihydroxylation conditions call for mixtures of acetone–water or *tert*-butyl alcohol–water to be used as the solvent. However, when **4** or **5** was dihydroxylated under these conditions, we observed the formation of a third product besides the expected *endo* and *exo* products. This compound, which complicates separation by flash chromatography, arises from opening of the lactone function in the *endo* product, followed by lactone formation with the C-6 hydroxy group. The use of dry solvents circumvented this problem with the necessary water for the dihydroxylation supplied from *N*-methylmorpholine *N*-oxide (NMO) monohydrate.

Catalytic dihydroxylation of the allylic alcohol **5** using the OsO_4–NMO system gave a 3:1 ratio of *exo* to *endo* products (Scheme 2 – entry a). This selectivity was reversed to 1:3 in



Entry	Compound	R	Ratio
a	**5**	H	3 : 1
b	**4**	Ac	1 : 3
c	**6**	Bz	1 : 6
d	**7**	TBDPS	>1 : 13

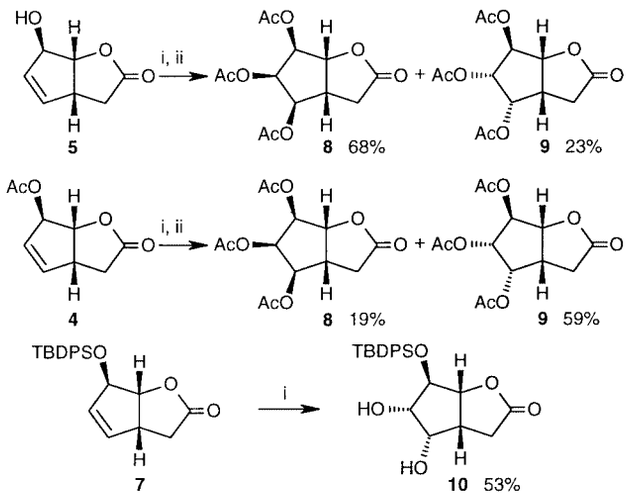
Scheme 2 *Reagents and conditions*: (i) OsO_4, NMO, acetone, rt, 16 h.

favour of the *endo* product with the allylic acetate **4** (entry b), so we decided to investigate the influence of the size of the protecting group in this dihydroxylation. The benzoate **6** (78%) and *tert*-butyldiphenylsilyl (TBDPS) ether **7** (82%) (Scheme 1) were synthesised and dihydroxylated to give 1:6 and greater than 1:13 *exo* to *endo* ratios, respectively (Scheme 2 – entry c and d). Thus, the selectivity of the dihydroxylation can be controlled to a large degree by the size of the group in the allylic position.

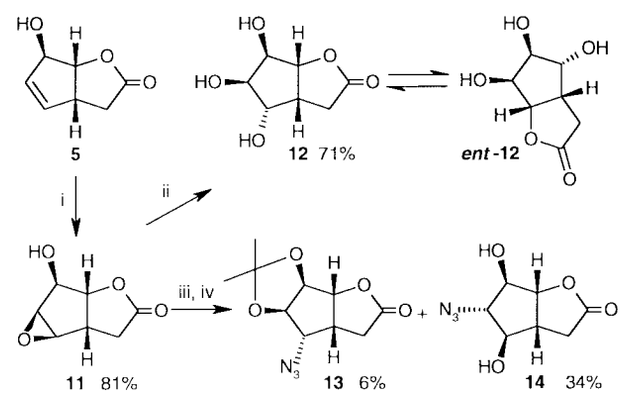
For practical applications the catalytic dihydroxylation of compounds **4**, **5** and **7** was found to be the most synthetically useful (Scheme 3). From the allylic alcohol **5** the *exo* and *endo* products (**8** and **9**) were isolated in 68 and 23% yield respectively, whereas the allylic acetate **4** gave 19 and 59% yields of the two products, respectively. Finally, dihydroxylation of TBDPS ether **7** gave the *endo* product **10** (53%) as the only product isolated.

We next investigated the epoxidation of the C-6/C-7 double bond in **5**, as the nucleophilic ring opening of epoxides usually leads to formation of *trans*-products. Epoxidation using MCPBA proceeded in very low yield and was non-selective, whereas the vanadium catalysed epoxidation[16] using *tert*-butyl hydroxyperoxide (TBHP) and vanadyl acetylacetonate [VO(acac)$_2$] exclusively gave the epoxide **11** in 81% yield (Scheme 4).

Opening of the epoxide **11** under aqueous acidic conditions gave regioselective opening at C-6 resulting in a 50:1 mixture of epimers from which the major product could be isolated by recrystallisation in 71% yield. The isolated product did not show an optical rotation, which is due to the compound being a *meso* compound in non-lactonised form. Apparently the



Scheme 3 *Reagents and conditions*: (i) OsO_4, NMO, acetone, rt, 16 h; (ii) Ac_2O, pyridine, rt, 16 h.



Scheme 4 *Reagents and conditions*: (i) TBHP, VO(acac)$_2$, DCM, reflux, 4 h; (ii) $HClO_4$, H_2O, rt, 40 h; (iii) NaN_3, NH_4Cl, DMF, 55 °C, 40 h; (iv) acetone, $MgSO_4$, H_2SO_4, rt, 40 h.

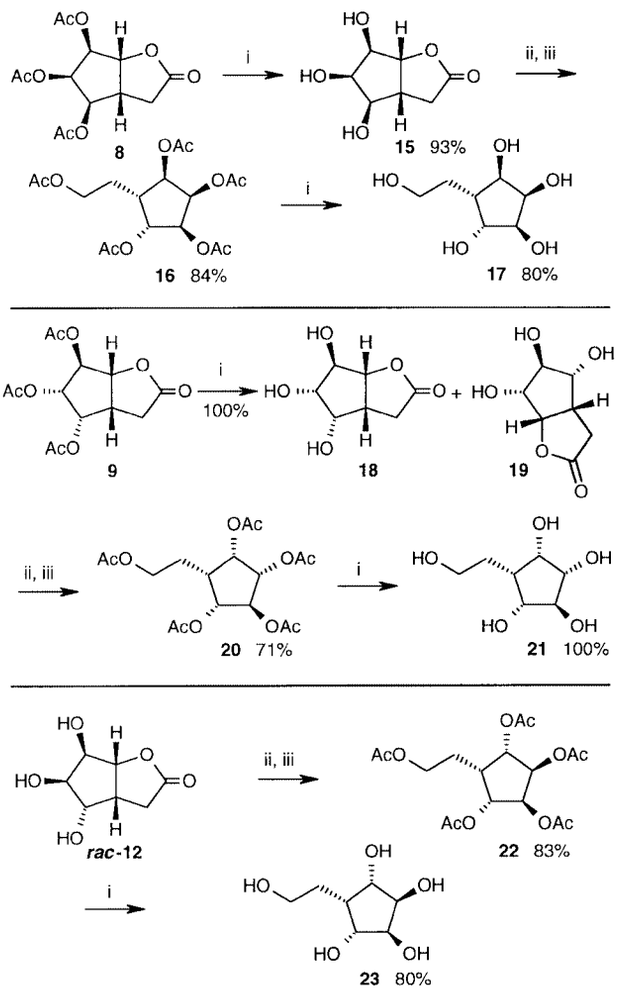
formed product **12** rapidly equilibrates under the reaction conditions giving a racemic mixture of **12** and *ent*-**12** as the isolated product.

The epoxide **11** was also used as a precurser for preparation of the amino hydroxy motif, and opening of the epoxide with various nitrogen nucleophiles was investigated. Treatment of the epoxide **11** with liquid ammonia proceeded very slowly, resulting in only 10% conversion after 12 days at 120 °C, and the reaction was not deemed synthetically useful. For comparison full conversion was obtained after 5 days at 90 °C when the epoxide was located in the 7,8-position.[1] Previously, we also had good results in opening of epoxides using acetonitrile and boron trifluoride–diethyl ether in a Ritter-type reaction to give *trans*-amino alcohols.[1] Treatment of **11** under these conditions gave however, a complex and inseparable mixture of different amino alcohols. When sodium azide was used as the nucleophile a 6:1 mixture of two regioisomeric azides was obtained, inseparable by flash chromatography. Derivatisation of the minor isomer as the acetonide allowed their separation by flash chromatography giving the protected C-6 azide **13** (6%) and the C-7 azide **14** (34% after recrystallisation) (Scheme 4). Compared with the aforementioned 7,8-epoxide,[1] the epoxide **11** reacts more slowly and less stereoselectively, which can only be attributed to the lack of a neighbouring lactone moiety.

The lactone moieties of the bicyclic systems were now reduced in order to obtain carbahexofuranoses. Simple sodium borohydride reduction is not possible due to the lack of an electron-withdrawing substituent at C-4 and although lithium aluminium hydride and borane are standard reagents for such conversions, we prefer the use of calcium borohydride. This

reagent, which can easily be prepared *in situ* from calcium chloride and sodium borohydride[1,17] and is commercially available, nicely spans the gap between sodium borohydride and lithium aluminium hydride. It is capable of working in protic solvents like ethanol or methanol and still retains the activity to reduce non-activated lactones.

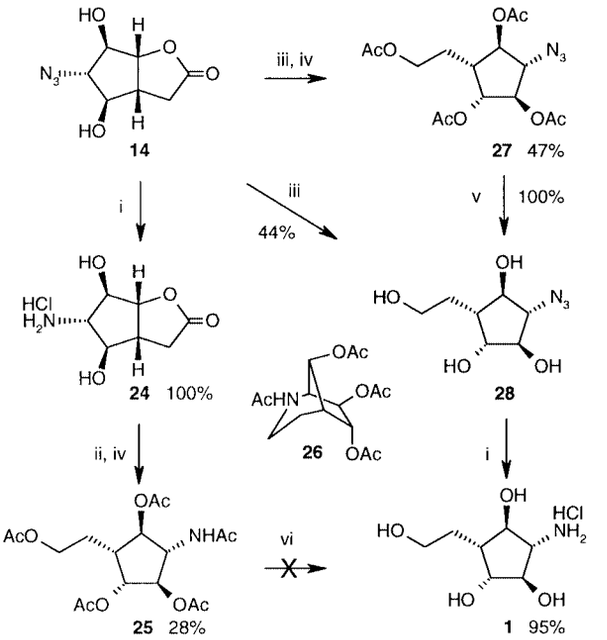
Compound **8** was deacetylated to give the triol **15** (93%) followed by calcium borohydride reduction and acetylation (to ease purification) to give the pentaacetate **16** in 84% yield. Deprotection gave 5-deoxy-4a(*R*)-hydroxy-4a-carba-α-D-*ribo*-hexofuranose **17** in 80% yield (Scheme 5).



Scheme 5 *Reagents and conditions*: (i) HCl–MeOH, rt, 40 h; (ii) $CaCl_2$, $NaBH_4$, EtOH, −20 °C to rt, 16 h; (iii) Ac_2O, $HClO_4$, rt, 1.5 h.

When compound **9** was deacetylated a 3:1 mixture of two trihydroxy lactones tentatively assigned as **18** and **19** was obtained in quantitative yield. Recrystallisation gave pure **18** (46%) which, as expected, equilibrated back to a 3:1 mixture of **18** and **19** upon dissolution in water. Likewise a 3:1 mixture of **18** and **19** was obtained from compound **10** (59%) after deprotection (not shown). The mixture of **18** and **19** was reduced and acetylated to give **20** (71%), which after deprotection gave 5-deoxy-4a(*R*)-hydroxy-4a-carba-α-D-*lyxo*-hexofuranose **21** (100%). In a similar manner 5-deoxy-4a(*R*)-hydroxy-4a-carba-α-D-*xylo*-hexofuranose **23** was obtained from racemic compound **12** following reduction–acetylation to the pentaacetate **22** (83%) and deprotection (80%).

Catalytic hydrogenation of the azide **14** gave the amino lactone **24** as a hygroscopic oil in quantitative yield (Scheme 6). We have previously with success used $Ca(BH_4)_2$ for the reduction of amino lactones similar to **14**,[1] but in this case we could not avoid lactam formation under the reaction conditions and the subsequent reduction of the amide functionality. Reduction of



Scheme 6 *Reagents and conditions*: (i) Pd/C, H_2, EtOH or MeOH, HCl, rt, 16 h; (ii) $CaCl_2$, $NaBH_4$, EtOH, −20 °C to rt, 16 h; (iii) $Ca(BH_4)_2$·2THF, THF, −20 °C, 16 h; (iv) Ac_2O, pyridine, rt, 16 h; (v) HCl–MeOH, rt, 40 h; (vi) 4 M HCl, reflux, 4 h.

24 followed by acetylation and chromatography gave a 12:1 mixture of the aminocyclopentane **25** and the corresponding bicyclic amine **26**† and recrystallisation provided pure **25** in low yield (28%). To add insult to injury, it turned out that deacetylation of **25** proved to be more difficult than expected. In order to ensure complete deprotection rather harsh conditions (1 M HCl; reflux; 4 h) had to be employed and this led to isomerisation of the product. Milder reaction conditions (1 M HCl; 70 °C; 16 h, or NaOMe–MeOH; rt; 2 h) did not give N-deacetylation as the literature might suggest.[18]

A different approach was thus needed and we decided to return to the azide **14**. If reduction of the lactone moiety could be achieved without concomitant reduction of the azide group, lactam formation should be avoided. As an added bonus this would not give N-acetylation if acetylation were needed for purification purposes. Our first attempt at reduction of the lactone moiety using $Ca(BH_4)_2$·2THF complex in ethanol–THF gave formation of the desired azide **28** as well as the fully reduced aminocyclopentane **1**. When using THF as the only solvent, the reduction followed by acetylation proceeded to give the protected azidocyclopentane **27** as the only product in 47% yield. This was then deacetylated to give the azide **28** (100%), which could also be obtained directly from compound **14** (44%). Finally, catalytic hydrogenation of **28** gave 2-amino-2,5-dideoxy-4a(*R*)-hydroxy-4a-carba-α-D-*arabino*-hexofuranose **1** isolated as the hydrochloride in 95% yield.

In summary, four fully substituted hydroxy/aminocyclopentane derivatives have been synthesised from the easily available allylic acetate **3**. The compounds, which can be viewed as sugar mimics, are 5-deoxy-4a(*R*)-hydroxy-4a-carba-α-D-*ribo*-hexofuranose **17**, 5-deoxy-4a(*R*)-hydroxy-4a-carba-α-D-*lyxo*-hexofuranose **21**, 5-deoxy-4a(*R*)-hydroxy-4a-carba-α-D-*xylo*-hexofuranose **23** together with 2-amino-2,5-dideoxy-4a(*R*)-hydroxy-4a-carba-α-D-*arabino*-hexofuranose **1**. The compounds presented here are both interesting in their own right as possible glycosidase inhibitors but can also be used as building blocks for synthesis of mimics of more complex natural products such as nucleoside or saccharide analogues.

† Although we did not isolate this by-product, it is expected to have the shown structure **26**. For additional information see ref. 1.

Experimental

THF was distilled from sodium/benzophenone, and dichloromethane from calcium hydride under nitrogen. Acetone was dried over $MgSO_4$. Mps were measured on a Heidolph oil bath apparatus and are uncorrected. Specific rotations were measured on a Perkin-Elmer 241 polarimeter and the concentrations are given in g 100 ml^{-1}. $[a]_D$-Values are given in units of 10^{-1} deg cm^2 g^{-1}. NMR spectra were recorded on Bruker AM 500 and AC 250 spectrometers. Chemical shifts (δ) were measured in ppm and coupling constants (J) in Hz. For NMR spectra in deuterated solvents, the solvent peak was used as reference [$CDCl_3$: δ 7.27 for ^1H, δ_C 76.93 for ^{13}C; D_2O: δ 4.63 for ^1H, dioxane (δ_C 66.5) as internal reference for ^{13}C; benzene-d_6: δ 7.16 for ^1H, MeOH-d_4: δ 3.31 for ^1H, δ_C 49.0 for ^{13}C]. When necessary, NMR data were assigned using HH- and CH-correlated spectra. Elemental analyses were performed by the Institute of Physical Chemistry, University of Vienna and the Department of Chemistry, University of Copenhagen. HRMS (FAB) was performed by the Department of Chemistry, University of Copenhagen. 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% $Ce(SO_4)\cdot 4H_2O$ in 10% H_2SO_4 followed by charring. Flash chromatography was performed with silica gel 60 (Grace AB Amicon, 35–70 μm). Concentrations were performed on a rotary evaporator at a temperature below 40 °C. $Ca(BH_4)_2\cdot 2THF$ was purchased from Fluka Chemie AG.

(1*R*,5*R*,8*R*)-8-Acetoxy-2-oxabicyclo[3.3.0]oct-6-en-3-one 4

To a solution of bromo acetate **3**[1] (4.77 g, 18.1 mmol) in dry THF (40 ml) was added DBU (4.0 ml, 27.3 mmol) and the mixture was heated to reflux for 16 h. The reaction mixture was cooled to rt and concentrated to give a residue, which was dissolved in water (25 ml) and extracted with dichloromethane (5 × 40 ml). The combined organic phases were washed with 1 M HCl (2 × 25 ml) followed by re-extraction of the aqueous phases with dichloromethane (25 ml). The combined organic phases were washed with brine (25 ml), dried ($MgSO_4$) and concentrated to give a crude product (2.93 g, 88%), which was purified by flash chromatography (EtOAc–hexane 1 : 1) to give the title compound **4** as colourless crystals (2.74 g, 83%), mp 45–46 °C. Recrystallisation (Et_2O) gave mp 49–50 °C; $[a]_D$ −285.0 (*c* 1.00, $CHCl_3$) (Found: C, 59.15; H, 5.5. Calc. for $C_9H_{10}O_4$: C, 59.3; H, 5.5%); δ_H(500 MHz; benzene-d_6) 1.58 (3 H, s, CH_3CO), 1.66 (1 H, dd, $J_{4',5}$ 2.0, $J_{4,4'}$ 18.5, H′-4), 1.85 (1 H, dd, $J_{4,5}$ 10.5, $J_{4,4'}$ 18.5, H-4), 2.64 (1 H, m, H-5), 4.37 (1 H, dd, $J_{1,8}$ 0.5, $J_{1,5}$ 6.0, H-1), 5.08 (1 H, dd, J 2.0, $J_{6,7}$ 5.5, H-6 or -7), 5.53 (1 H, ddt, J 0.5, J 2.0, $J_{6,7}$ 5.5, H-7 or -6), 5.58 (1 H, ddd, $J_{1,8}$ 0.5, J 1.5, J 2.0, H-8); δ_C(62.5 MHz; $CDCl_3$) 20.7 (CH_3CO), 32.1 (C-4), 43.6 (C-5), 81.9 (C-8), 85.2 (C-1), 128.8 and 138.8 (C-6 + -7), 169.8 (CH_3CO), 175.1 (C-3).

(1*R*,5*R*,8*R*)-8-Hydroxy-2-oxabicyclo[3.3.0]oct-6-en-3-one 5

A solution of compound **4** (530 mg, 2.91 mmol) in acidic methanol (10 ml; 1% v/v acetyl chloride in methanol) was stirred at rt for 40 h. Concentration gave the title compound **5** as colourless crystals (407 mg, quant.), mp 63–65 °C. Recrystallisation (EtOAc–hexane) gave mp 67–68 °C; $[a]_D$ −170.9 (*c* 1.00, $CHCl_3$) (Found: C, 59.9; H, 5.8. Calc. for $C_7H_8O_3$: C, 60.0; H, 5.75%); δ_H(500 MHz; benzene-d_6) 1.66 (1 H, br s, OH), 1.71 (1 H, dd, $J_{4',5}$ 2.0, $J_{4,4'}$ 18.0, H′-4), 1.89 (1 H, dd, $J_{4,5}$ 10.0, $J_{4,4'}$ 18.0, H-4), 2.75 (1 H, m, H-5), 4.33 (1 H, d, $J_{1,5}$ 6.0, H-1), 4.45 (1 H, br s, H-8), 5.07 (1 H, dd, J 2.0, $J_{6,7}$ 5.5, H-6 or -7), 5.42 (1 H, dt, J 2.0, $J_{6,7}$ 5.5, H-7 or -6); δ_C(62.5 MHz; $CDCl_3$) 32.3 (C-4), 43.3 (C-5), 79.7 (C-8), 88.4 (C-1), 131.8 and 136.4 (C-6 + -7), 176.5 (C-3).

(1*R*,5*R*,8*R*)-8-Benzoyloxy-2-oxabicyclo[3.3.0]oct-6-en-3-one 6

To a solution of compound **5** (396 mg, 2.83 mmol) in pyridine (5 ml) at 0 °C was added benzoyl chloride (0.45 ml, 3.87 mmol) and the mixture was stirred at rt for 1.5 h. Water (0.5 ml) was added and the mixture was stirred for 0.5 h, followed by further addition of water (40 ml) and extraction with dichloromethane (4 × 25 ml). The combined organic phases were washed successively with water (20 ml), 1 M HCl (20 ml) and sat. aq. $NaHCO_3$ (20 ml), dried ($MgSO_4$) and concentrated to give a crude crystalline product (659 mg, 95%), which was recrystallised from EtOAc–hexane to give the title compound **6** as colourless crystals (541 mg, 78%), mp 121–124 °C. Further recrystallisation (EtOAc–hexane) gave mp 125–126 °C; $[a]_D$ −321.6 (*c* 1.00, $CHCl_3$) (Found: C, 68.9; H, 5.0. Calc. for $C_{14}H_{12}O_4$: C, 68.85; H, 4.95%); δ_H(500 MHz; benzene-d_6) 1.68 (1 H, dd, $J_{4',5}$ 2.5, $J_{4,4'}$ 18.0, H′-4), 1.88 (1 H, dd, $J_{4,5}$ 10.5, $J_{4,4'}$ 18.0, H-4), 2.70 (1 H, m, H-5), 4.45 (1 H, br d, $J_{1,5}$ 6.0, H-1), 5.12 (1 H, dd, J 2.0, $J_{6,7}$ 5.5, H-6 or -7), 5.55 (1 H, dt, J 2.5, $J_{6,7}$ 5.5, H-7 or -6), 5.81 (1 H, d, J 2.5, H-8), 7.01–7.05 (2 H, m, ArH), 7.10 (1 H, m, ArH), 8.03–8.05 (2 H, m, ArH); δ_C(62.5 MHz; $CDCl_3$) 32.2 (C-4), 43.7 (C-5), 82.6 and 85.4 (C-1 + -8), 128.3 (Ar-CH), 128.9 (C-6 or -7), 129.4 (Ar-CH), 129.5 (Ar-C), 133.2 (Ar-CH), 139.0 (C-7 or -6), 165.5 (ArCO), 175.2 (C-3).

(1*R*,5*R*,8*R*)-8-(*tert*-Butyldiphenylsilyloxy)-2-oxabicyclo[3.3.0]-oct-6-en-3-one 7

To a solution of compound **5** (225 mg, 1.61 mmol) in dichloromethane (10 ml) were added imidazole (134 mg, 1.97 mmol) and *tert*-butyl(chloro)diphenylsilane (0.49 ml, 1.92 mmol) and the solution was stirred at rt for 3.5 h. The reaction mixture was diluted with dichloromethane (40 ml) and washed with 1 M HCl (2 × 10 ml) followed by re-extraction of the aqueous phases with dichloromethane (20 ml). The combined organic phases were washed with sat. aq. $NaHCO_3$ (20 ml), dried ($MgSO_4$) and concentrated to give a crude product (quant.). Purification by flash chromatography (EtOAc–hexane 25 : 75) gave the title compound **7** as a colourless oil (500 mg, 82%), $[a]_D$ −104.0 (*c* 1.05, $CHCl_3$); δ_H(500 MHz; benzene-d_6) 1.14 [9 H, s, $C(CH_3)_3$], 1.64 (1 H, dd, $J_{4',5}$ 2.5, $J_{4,4'}$ 18.0, H′-4), 1.85 (1 H, dd, $J_{4,5}$ 10.0, $J_{4,4'}$ 18.0, H-4), 2.77 (1 H, m, H-5), 4.51 (1 H, br d, $J_{1,5}$ 6.0, H-1), 4.89 (1 H, br s, H-8), 5.01 (1 H, dd, J 2.0, $J_{6,7}$ 5.5, H-6 or -7), 5.33 (1 H, dt, J 2.5, $J_{6,7}$ 5.5, H-7 or -6), 7.18–7.25 (6 H, m, ArH), 7.68–7.75 (4 H, m, ArH); δ_C(62.5 MHz; $CDCl_3$) 18.8 [$C(CH_3)_3$], 26.5 [$C(CH_3)_3$], 32.0 (C-4), 43.1 (C-5), 81.5 (C-8), 88.1 (C-1), 127.4, 127.5, 129.5 and 129.6 (Ar-CH), 132.0 (C-6 or -7), 132.8 and 133.2 (Ar-C), 135.2 (Ar-CH), 135.4 (C-7 or -6), 175.3 (C-3).

(1*R*,5*R*,6*R*,7*R*,8*S*)-6,7,8-Triacetoxy-2-oxabicyclo[3.3.0]octan-3-one 8 and (1*R*,5*R*,6*S*,7*S*,8*S*)-6,7,8-triacetoxy-2-oxabicyclo-[3.3.0]octan-3-one 9

From compound 5. To a solution of compound **5** (99 mg, 2.78 mmol) in dry acetone (10 ml) was added NMO monohydrate (194 mg, 1.40 mmol) together with a catalytic amount of OsO_4 and the mixture was stirred at rt for 16 h. Na_2SO_3 (127 mg) was added and the mixture was stirred for 0.5 h and then concentrated and co-concentrated with toluene to give a residue, which was dissolved in pyridine (5 ml) and cooled to 0 °C. Acetic anhydride (2.0 ml, 21.1 mmol) was then added and the reaction mixture was stirred at rt for 16 h. Ice–water (10 ml) was added and the mixture was stirred for 0.5 h, followed by extraction with dichloromethane (3 × 25 ml). The combined organic phases were washed with 1 M HCl (2 × 20 ml) followed by re-extraction of the aqueous phases with dichloromethane (10 ml). The combined organic phases were dried ($MgSO_4$) and concentrated to give a crude 3 : 1 mixture of the two diastereomeric products. Separation by flash chromatography (EtOAc–hexane 55 : 45) gave compound **8** (145 mg, 68%) mp 82–90 °C, followed by compound **9** (48 mg, 23%) mp 112–118 °C.

Compound **8**: Recrystallisation (EtOAc–hexane) gave mp 90–93 °C; $[a]_D$ −64.9 (*c* 1.00, $CHCl_3$) (Found: C, 51.7; H, 5.2.

Calc. for $C_{13}H_{16}O_8$: C, 52.0; H, 5.4%); δ_H(500 MHz; $CDCl_3$) 2.07 (3 H, s, CH_3CO), 2.09 (3 H, s, CH_3CO), 2.11 (3 H, s, CH_3CO), 2.68 (1 H, dd, $J_{4',5}$ 4.0, $J_{4,4'}$ 19.0, H′-4), 2.87 (1 H, dd, $J_{4,5}$ 11.0, $J_{4,4'}$ 19.0, H-4), 3.16 (1 H, m, H-5), 5.00 (1 H, dd, $J_{1,8}$ 4.5, $J_{1,5}$ 9.5, H-1), 5.06 (1 H, dd, $J_{6,7}$ 4.0, $J_{5,6}$ 7.0, H-6), 5.24 (1 H, dd, $J_{7,8}$ 4.0, $J_{1,8}$ 4.5, H-8), 5.56 (1 H, t, $J_{6,7} = J_{7,8}$ 4.0, H-7); δ_C(62.5 MHz; $CDCl_3$) 20.3 and 20.4 (3 × $COCH_3$), 32.4 (C-4), 40.2 (C-5), 71.9 (C-7), 75.4 (C-8), 75.8 (C-6), 83.1 (C-1), 169.2, 169.4 and 169.8 (3 × $COCH_3$), 175.2 (C-3).

Compound **9**: Recrystallisation (EtOAc–hexane) gave mp 121–122.5 °C; $[a]_D$ −17.6 (*c* 1.00, $CHCl_3$) (Found: C, 52.2; H, 5.2%); δ_H(500 MHz; $CDCl_3$) 2.05 (3 H, s, CH_3CO), 2.11 (3 H, s, CH_3CO), 2.12 (3 H, s, CH_3CO), 2.60–2.62 (2 H, m, H_2-4), 3.33 (1 H, m, H-5), 4.80 (1 H, dd, $J_{1,8}$ 1.5, $J_{1,5}$ 8.0, H-1), 5.29 (1 H, dd, $J_{6,7}$ 4.0, $J_{7,8}$ 5.5, H-7), 5.32 (1 H, dd, $J_{1,8}$ 1.5, $J_{7,8}$ 5.5, H-8), 5.56 (1 H, dd, $J_{6,7}$ 4.0, $J_{5,6}$ 6.5, H-6); δ_C(62.5 MHz; $CDCl_3$) 19.8 and 20.1 (3 $COCH_3$), 28.1 (C-4), 37.0 (C-5), 71.7 (C-6), 74.4 (C-7), 77.6 (C-8), 83.8 (C-1), 168.9, 169.0 and 169.1 (3 × $COCH_3$), 175.2 (C-3).

From compound 4. Compound **4** (96 mg, 0.537 mmol) was dihydroxylated followed by acetylation according to the above procedure to give a 1:3 mixture of the two diastereomeric compounds. Separation by flash chromatography (EtOAc–hexane 55:45) gave compound **8** (30 mg, 19%), mp 81–88 °C, followed by compound **9** (93 mg, 59%), mp 120–121 °C. ^{1}H and ^{13}C NMR data as described above.

(1*R*,5*R*,6*S*,7*S*,8*R*)-8-(*tert*-Butyldiphenylsilyloxy)-6,7-dihydroxy-2-oxabicyclo[3.3.0]octan-3-one 10

Compound **7** (486 mg, 1.28 mmol) was dihydroxylated according to the procedure for the preparation of compounds **8** and **9**. After concentration the residue was dissolved in 1 M HCl saturated with NaCl (10 ml) and extracted with dichloromethane (4 × 25 ml). The combined organic phases were washed successively with sat. aq. $NaHCO_3$ (25 ml) and brine (25 ml), dried ($MgSO_4$) and concentrated to give a crude 13:1 mixture of the two diastereomeric products. Separation by flash chromatography (EtOAc–hexane 6:4) gave the title compound **10** as colourless crystals (280 mg, 53%), mp 132–133 °C. Recrystallisation (toluene) gave mp 136–137 °C; $[a]_D$ −20.1 (*c* 0.37, $CHCl_3$); δ_H(500 MHz; benzene-d_6–$CDCl_3$ 1:1) 1.12 [9 H, s, $C(CH_3)_3$], 1.86 (1 H, dd, $J_{4,5}$ 11.0, $J_{4,4'}$ 18.0, H′-4), 2.24 (1 H, m, H-5), 2.52 (1 H, dd, $J_{4',5}$ 3.0, $J_{4,4'}$ 18.0, H′-4), 3.66 (1 H, t, $J_{6,7} = J_{7,8}$ 4.0, H-7), 3.84 (1 H, dd, $J_{6,7}$ 4.0, $J_{5,6}$ 6.5, H-6), 4.29 (1 H, dd, $J_{1,8}$ 1.5, $J_{7,8}$ 4.0, H-8), 4.33 (1 H, dd, $J_{1,8}$ 1.5, $J_{1,5}$ 8.0, H-1), 7.21–7.26 (6 H, m, ArH), 7.67–7.70 (4 H, m, ArH); δ_C(62.5 MHz; $CDCl_3$) 19.0 [$C(CH_3)_3$], 26.7 ($C(CH_3)_3$), 29.7 (C-4), 38.4 (C-5), 72.3 (C-6), 78.4 (C-7), 80.2 (C-8), 88.4 (C-1), 127.7 and 129.9 (Ar-CH), 132.7 and 132.9 (Ar-C), 135.5 (Ar-CH), 178.1 (C-3).

(1*R*,5*R*,6*R*,7*R*,8*S*)-6,7-Epoxy-8-hydroxy-2-oxabicyclo[3.3.0]-octan-3-one 11

To a solution of compound **5** (1.19 g, 8.48 mmol) in dry dichloromethane (30 ml) were added $VO(acac)_2$ (30 mg, cat.) and TBHP[19] (4.1 M in toluene; 2.4 ml, 9.84 mmol) and the mixture was heated to reflux for 4 h. The reaction mixture was cooled to rt and concentrated to give a crude crystalline product, which was quickly recrystallised from ethanol to give the title compound **11** as slightly yellow crystals (1.07 g, 81%), mp 110–113 °C. Further recrystallisation (EtOH) gave mp 114–115 °C; $[a]_D$ −24.2 (*c* 1.00, MeOH) (Found: C, 53.7; H, 5.2. Calc. for $C_7H_8O_4$: C, 53.85; H, 5.2%); δ_H(500 MHz; $CDCl_3$) 2.30 (1 H, d, $J_{8,OH}$ 8.5, OH), 2.41 (1 H, dd, $J_{4',5}$ 7.0, $J_{4,4'}$ 18.5, H′-4), 2.75 (1 H, dd, $J_{4,5}$ 11.0, $J_{4,4'}$ 18.5, H-4), 3.33 (1 H, dt, $J_{1,5} = J_{4',5}$ 7.0, $J_{4,5}$ 11.0, H-5), 3.61 (1 H, d, $J_{6,7}$ 2.5, H-6 or -7), 3.76 (1 H, t, $J_{6,7} = J_{7,8}$ 2.5, H-7 or -6), 4.36 (1 H, br d, $J_{8,OH}$ 8.5, H-8), 4.55 (1 H, dd, $J_{1,8}$ 2.0, $J_{1,5}$ 7.0, H-1); δ_C(62.5 MHz; $CDCl_3$) 29.7 (C-4), 39.5 (C-5), 59.7 and 60.2 (C-6 + -7), 77.6 (C-8), 88.9 (C-1), 175.2 (C-3).

(*rac*)-6,7,8-Trihydroxy-2-oxabicyclo[3.3.0]octan-3-one 12

To a solution of compound **11** (131 mg, 0.839 mmol) in water (10 ml) was added perchloric acid (60%; 6 drops) and the mixture was stirred at rt for 40 h. The reaction mixture was neutralised with ion-exchange resin (Amberlite IRA-67, OH^-, 5 ml), filtered, and the resin was washed with water. The combined water phases were concentrated to give a 50:1 mixture of the title compound **12** and the 6,7-diepi-isomer (148 mg, 99%), mp 102–106 °C. Recrystallisation (EtOH) gave pure title compound **12** as colourless crystals (104 mg, 71%); mp 107–109 °C; $[a]_D$ 0.0 (*c* 1.00, MeOH) (Found: C, 48.0; H, 5.7. Calc. for $C_7H_{10}O_5$: C, 48.3; H, 5.8%); δ_H(500 MHz; D_2O) 2.64 (2 H, m, H_2-4), 3.19 (1 H, m, H-5), 3.95 (1 H, dd, $J_{7,8}$ 4.5, $J_{6,7}$ 6.0, H-7), 4.11 (1 H, dd, 1H, $J_{1,8}$ 2.5, $J_{7,8}$ 4.5, H-8), 4.12 (1 H, dd, $J_{6,7}$ 6.0, $J_{5,6}$ 7.5, H-6), 4.76 (1 H, dd, $J_{1,8}$ 2.5, $J_{1,5}$ 8.0, H-1); δ_C(62.5 MHz; D_2O) 28.1 (C-4), 38.2 (C-5), 73.9, 74.6 and 75.8 (C-6, -7 + -8), 88.1 (C-1), 181.3 (C-3).

(1*R*,5*R*,6*S*,7*R*,8*S*)-6-Azido-7,8-isopropylidenedioxy-2-oxabicyclo[3.3.0]octan-3-one 13 and (1*R*,5*R*,6*R*,7*S*,8*R*)-7-azido-6,8-dihydroxy-2-oxabicyclo[3.3.0]octan-3-one 14

To a solution of compound **11** (401 mg, 2.57 mmol) in DMF (10 ml) were added NaN_3 (497 mg, 7.64 mmol) and NH_4Cl (391 mg, 7.31 mmol) and the mixture was stirred at 55 °C for 40 h. After cooling to rt the reaction mixture was concentrated and the residue was dissolved in water (25 ml) and extracted with EtOAc (6 × 40 ml). The combined organic phases were washed with brine (20 ml), dried ($MgSO_4$) and concentrated to give a 6:1 mixture of the two isomeric azides (360 mg, 70%). The mixture was dissolved in dry acetone (40 ml), treated with $MgSO_4$ (25.0 g) and H_2SO_4 (96%; 1 drop) and the solution was stirred at rt for 40 h. The reaction mixture was neutralised with solid $NaHCO_3$, filtered and concentrated to give a 6:1 mixture of unprotected and protected azides (310 mg). Separation by flash chromatography (EtOAc–hexane 75:25) gave compound **13** (37 mg, 6.0%) followed by compound **14** (235 mg, 46%, 1% unprotected **13** as seen from ^{13}C NMR), which was recrystallised (EtOAc) to give pure compound **14** (176 mg, 34%).

Compound **13**: mp 81–82 °C; $[a]_D$ −128.0 (*c* 1.26, $CHCl_3$) (Found: C, 50.4; H, 5.5; N, 17.3. Calc. for $C_{10}H_{13}N_3O_4$: C, 50.2; H, 5.5; N, 17.6%); δ_H(500 MHz; $CDCl_3$) 2.19 [3 H, s, $(CH_3)_2C$], 2.30 [3 H, s, $(CH_3)_2C$], 3.47–3.49 (2 H, m, H_2-4), 4.16 (1 H, m, H-5), 5.08 (1 H, d, $J_{5,6}$ 6.0, H-6), 5.52 (1 H, d, $J_{1,5}$ 6.0, H-1), 5.63 (1 H, d, $J_{7,8}$ 5.0, H-7 or -8), 5.69 (1 H, d, $J_{7,8}$ 5.0, H-8 or -7); δ_C(62.5 MHz; $CDCl_3$) 24.3 and 26.4 [2 × $(CH_3)_2C$], 30.3 (C-4), 40.9 (C-5), 67.1 (C-6), 83.1 and 84.1 (C-7 + -8), 88.9 (C-1), 111.7 [$(CH_3)_2C$], 175.2 (C-3).

Compound **14**: mp 107–108 °C; $[a]_D$ −33.7 to −11.9 (5 min to 5 days) (*c* 1.01 MeOH) (Found: C, 42.4; H, 4.65; N, 21.0. Calc. for $C_7H_9N_3O_4$: C, 42.2; H, 4.55; N, 21.1%); δ_H(500 MHz; MeOH-d_4) 2.50 (1 H, dd, $J_{4',5}$ 2.0, $J_{4,4'}$ 17.5, H′-4), 2.78 (1 H, m, H-5), 2.83 (1 H, dd, $J_{4,5}$ 10.5, $J_{4,4'}$ 17.5, H-4), 3.52 (1 H, t, $J_{6,7} = J_{7,8}$ 9.0, H-7), 3.66 (1 H, t, $J_{5,6} = J_{6,7}$ 9.0, H-6), 3.84 (1 H, dd, $J_{1,8}$ 4.0, $J_{7,8}$ 9.0, H-8), 4.67 (1 H, dd, $J_{1,8}$ 4.0, $J_{1,5}$ 8.5, H-1); δ_C(62.5 MHz; MeOH-d_4) 33.7 (C-4), 42.9 (C-5), 72.4 (C-7), 78.7 (C-6), 79.2 (C-8), 87.7 (C-1), 190.0 (C-3).

(1*R*,5*R*,6*R*,7*R*,8*R*)-6,7,8-Trihydroxy-2-oxabicyclo[3.3.0]octan-3-one 15

Compound **8** (140 mg, 0.47 mmol) was deacetylated according to the procedure for **5**. Concentration gave the title compound **15** as colourless crystals (75 mg, 93%), mp 116–117 °C. Recrystallisation (EtOH) gave mp 117–118 °C; $[a]_D$ −30.8 (*c* 0.38, MeOH) (Found: C, 48.45; H, 5.9. Calc. for $C_7H_{10}O_5$: C, 48.3; H, 5.8%); δ_H(500 MHz; D_2O) 2.50 (1 H, dd, $J_{4',5}$ 3.5, $J_{4,4'}$

19.0, H′-4), 2.86 (1 H, dd, $J_{4,5}$ 11.0, $J_{4,4'}$ 19.0, H-4), 2.94 (1 H, m, H-5), 3.93 (1 H, dd, $J_{6,7}$ 4.0, $J_{5,6}$ 7.5, H-6), 3.98 (1 H, t, $J_{6,7}$ = $J_{7,8}$ 4.0, H-7), 4.05 (1 H, dd, $J_{7,8}$ 4.0, $J_{1,8}$ 4.5, H-8), 4.83 (1 H, dd, $J_{1,8}$ 4.5, $J_{1,5}$ 9.0, H-1); δ_C(62.5 MHz; D_2O) 32.7 (C-4), 41.7 (C-5), 74.0, 76.2 and 76.4 (C-6, -7 + -8), 89.4 (C-1), 181.0 (C-3).

4a(*R*)-Acetoxy-1,2,3,6-tetra-*O*-acetyl-5-deoxy-4a-carba-α-D-*ribo*-hexofuranose 16

Finely powdered calcium chloride (1.09 g, 9.82 mmol) and sodium borohydride (720 mg, 19.0 mmol) were suspended in ethanol (30 ml) and the mixture was stirred at −20 °C for 6 h to ensure the formation of $Ca(BH_4)_2$. A solution of compound **15** (252 mg, 0.63 mmol) in ethanol (10 ml) was added and the reaction mixture was stirred at rt for 16 h. The reaction mixture was carefully quenched with 4 M HCl (10 ml) and stirred for 0.5 h, followed by concentration and coevaporation twice with methanol. The crystalline residue was dissolved in water (50 ml) and then loaded onto a column of ion-exchange resin (Amberlite IR-120, H^+, 125 ml). The column was eluted with water (250 ml) to neutral pH, after which the aqueous phases were concentrated to give the crude pentahydroxy compound. This was dissolved in acetic anhydride (10 ml), perchloric acid was added (60%, 1 drop) and the mixture was stirred for 1.5 h. Concentration gave an oil, which was dissolved in dichloromethane (40 ml) and washed successively with water (20 ml) and sat. aq. $NaHCO_3$ (2 × 20 ml). The aqueous phases were re-extracted with dichloromethane (10 ml) and the combined organic phases were washed with brine (20 ml), dried ($MgSO_4$) and concentrated to give a crude product (615 mg, quant.). Purification by flash chromatography (EtOAc–hexane 45 : 55) gave the title compound **16** as a colourless oil (470 mg, 84%), $[\alpha]_D$ +17.8 (*c* 0.84, $CHCl_3$) (Found: C, 52.3; H, 5.9. Calc. for $C_{17}H_{24}O_{10}$: C, 52.6; H, 6.2%); δ_H(500 MHz; $CDCl_3$) 1.71 (1 H, dq, $J_{4,5'} = J_{5',6} = J_{5',6'}$ 6.5, $J_{5,5'}$ 14.0, H′-5), 1.84 (1 H, ddt, $J_{5,6}$ = $J_{5,6'}$ 6.5, $J_{4,5}$ 7.0, $J_{5,5'}$ 14.0, H-5), 2.04 (3 H, s, CH_3CO), 2.05 (3 H, s, CH_3CO), 2.07 (3 H, s, CH_3CO), 2.08 (3 H, s, CH_3CO), 2.11 (3 H, s, CH_3CO), 2.63 (1 H, m, H-4), 4.03 (1 H, dt, $J_{5,6'}$ = $J_{5',6'}$ 6.5, $J_{6,6'}$ 11.0, H′-6), 4.10 (1 H, dt, $J_{5,6} = J_{5',6}$ 6.5, $J_{6,6'}$ 11.0, H-6), 5.08 (1 H, dd, *J* 4.5, *J* 9.0, H-3 or -4a), 5.16 (1 H, t, *J* 4.5, H-1 or -2), 5.38 (1 H, dd, *J* 4.0, *J* 8.0, H-4a or -3), 5.51 (1 H, t, *J* 5.0, H-2 or -1); δ_C(62.5 MHz; $CDCl_3$) 19.8, 19.9, 19.9, 20.1 and 20.2 (5 $CO\mathit{C}H_3$), 25.4 (C-5), 40.1 (C-4), 61.8 (C-6), 69.3, 73.6, 74.3 and 76.9 (C-1, -2, -3 + -4a), 168.8, 168.8, 169.2, 169.3 and 170.1 (5 × $\mathit{C}OCH_3$).

5-Deoxy-4a(*R*)-hydroxy-4a-carba-α-D-*ribo*-hexofuranose 17

Compound **16** (223 mg, 0.57 mmol) was deacetylated according to the procedure for **5**. The solution was then neutralised with ion-exchange resin (Amberlite IRA-67, OH^-, 5 ml), filtered and the resin was washed with methanol. The combined methanol phases were concentrated to give the title compound **17** as a colourless oil (82 mg, 80%), $[\alpha]_D$ +26.7 (*c* 2.4, H_2O) (Found: C, 47.2; H, 7.6. Calc. for $C_7H_{12}O_5$: C, 47.2; H, 7.9%); δ_H(500 MHz; D_2O) 1.53 (1 H, ddt, *J* 7.0, *J* 8.0, $J_{5,5'}$ 14.0, H′-5), 1.70 (1 H, ddt, *J* 7.0, *J* 8.0, $J_{5,5'}$ 14.0, H-5), 2.03 (1 H, m, H-4), 3.56–3.60 (2 H, m, H_2-6), 3.71 (1 H, dd, *J* 4.5, *J* 9.0, H-3 or -4a), 3.78 (1 H, t, *J* 5.0, H-1 or -2), 3.91 (1 H, dd, *J* 4.5, *J* 5.0, H-2 or -1), 4.01 (1 H, dd, *J* 5.0, *J* 8.5, H-4a or -3); δ_C(62.5 MHz; D_2O) 29.7 (C-5), 43.1 (C-4), 60.5 (C-6), 71.6, 75.0, 75.3 and 77.4 (C-1, -2, -3 + -4a).

(1*R*,5*R*,6*S*,7*S*,8*R*)-6,7,8-Trihydroxy-2-oxabicyclo[3.3.0]octan-3-one 18 and (1*S*,5*S*,6*R*,7*S*,8*R*)-6,7,8-trihydroxy-2-oxabicyclo-[3.3.0]octan-3-one 19

From compound 9. Compound **9** (86 mg, 0.286 mmol) was deacetylated according to the procedure for **17**. Concentration gave a 3 : 1 mixture of the title compounds **18** and **19** as an oil (50 mg, quant.). Crystallisation (EtOH) gave pure compound **18** as colourless crystals (23 mg, 46%), mp 144–147 °C.

Compound **18**: Further recrystallisation (EtOH) gave mp 146–149 °C; $[\alpha]_D$ −41.0 to −17.2 (5 min to 4 days) (*c* 0.57, MeOH) (Found: C, 48.2; H, 5.6. Calc. for $C_7H_{10}O_5$: C, 48.3; H, 5.8%); δ_H(500 MHz; D_2O) 2.61–2.64 (2 H, m, H_2-4), 3.02 (1 H, m, H-5), 3.84 (1 H, dd, $J_{6,7}$ 4.0, $J_{7,8}$ 8.0, H-7), 4.01 (1 H, dd, $J_{6,7}$ 4.0, $J_{5,6}$ 5.5, H-6), 4.08 (1 H, dd, $J_{1,8}$ 3.0, $J_{7,8}$ 8.0, H-8), 4.70 (1 H, dd, $J_{1,8}$ 3.0, $J_{1,5}$ 8.0, H-1); δ_C(62.5 MHz; D_2O) 28.7 (C-4), 37.9 (C-5), 71.9, 77.1 and 79.3 (C-6, -7 + -8), 88.9 (C-1), 181.5 (C-3).

Compound **19**: δ_C(62.5 MHz; D_2O) 27.8 (C-4), 36.6 (C-5), 71.4, 73.1 and 77.1 (C-6, -7 + -8), 82.6 (C-1), 181.1 (C-3).

From compound 10. To a solution of compound **10** (404 mg, 1.07 mmol) in THF (20 ml) was added TBAF (2 ml; 1 M in THF) and the mixture was stirred at rt for 40 h. The reaction mixture was treated with water (10 ml) and washed with EtOAc (3 × 25 ml). The aqueous phase was then loaded onto a column of ion-exchange resin (Amberlite IR-120, H^+, 20 ml) and eluted with water (50 ml) to neutral pH. The aqueous phase was concentrated to give a crude product, which was purified by flash chromatography (EtOAc–methanol 8 : 2) to give the title products **18** and **19** as a crystalline 3 : 1 mixture (110 mg, 59%), mp 116–145 °C. ^{13}C NMR data as described above.

4a(*R*)-Acetoxy-1,2,3,6-tetra-*O*-acetyl-5-deoxy-4a-carba-β-D-*lyxo*-hexofuranose 20

Reduction and acetylation of compounds **18** and **19** (3 : 1 mixture; 119 mg, 0.683 mmol) was done according to the procedure for **16**. Purification by flash chromatography (EtOAc–hexane 45 : 55) gave the title compound **20** as a colourless oil (188 mg, 71%); $[\alpha]_D$ + 24.4 (*c* 0.93, $CHCl_3$) (Found: C, 52.3; H, 6.0. Calc. for $C_{17}H_{24}O_{10}$: C, 52.6; H, 6.2%); δ_H(500 MHz; $CDCl_3$) 1.71 (1 H, dq, $J_{4,5'} = J_{5',6} = J_{5',6'}$ 5.0, $J_{5,5'}$ 11.5, H′-5), 1.76 (1 H, ddt, $J_{5,6} = J_{5,6'}$ 5.0, $J_{4,5}$ 6.5, $J_{5,5'}$ 11.5, H-5), 2.01 (3 H, s, CH_3CO), 2.02 (3 H, s, CH_3CO), 2.06 (3 H, s, CH_3CO), 2.11 (3 H, s, CH_3CO), 2.13 (3 H, s, CH_3CO), 2.54 (1 H, m, H-4), 4.01 (2 H, m, H_2-6), 5.18 (1 H, dd, *J* 4.0, *J* 8.0, H-3 or -4a), 5.27 (1 H, dd, *J* 3.0, *J* 8.0, H-1 or -2), 5.38 (1 H, dd, *J* 3.0, *J* 8.0, H-4a or -3), 5.44 (1 H, t, *J* 4.0, *J* 4.0, H-2 or -1); δ_C(62.5 MHz; $CDCl_3$) 20.3, 20.4, 20.5 and 20.5 (5 × $CO\mathit{C}H_3$), 22.4 (C-5), 38.7 (C-4), 62.0 (C-6), 72.7, 75.0, 75.2 and 80.8 (C-1, -2, -3 + -4a), 169.8, 169.9, 170.0 and 170.6 (5 × $\mathit{C}OCH_3$).

5-Deoxy-4a(*R*)-hydroxy-4a-carba-α-D-*lyxo*-hexofuranose 21

Compound **20** (109 mg, 0.28 mmol) was deacetylated according to the procedure for **17**. Concentration gave the title compound **21** as colourless crystals (50 mg, quant.), mp 126–128 °C. Recrystallisation (MeOH) gave mp 131–134 °C; $[\alpha]_D$ + 29.0 (*c* 0.30, H_2O) (Found: C, 47.0; H, 7.7. Calc. for $C_7H_{12}O_5$: C, 47.2; H, 7.9%); δ_H(500 MHz; MeOH-d_4) 1.83 (2 H, m, H_2-5), 2.11 (1 H, m, H-4), 3.68 (2 H, ddt, *J* 6.5, *J* 10.5, $J_{6,6'}$ 13.5, H_2-6), 3.72 (1 H, dd, *J* 4.0, *J* 6.0, H-1 or -2), 3.81 (1 H, dd, *J* 2.5, *J* 6.5, H-3 or -4a), 3.93 (1 H, t, *J* 4.0, H-4a or -3), 3.97 (1 H, dd, *J* 2.5, *J* 6.0, H-2 or -1); δ_C(62.5 MHz; MeOH-d_4) 27.3 (C-5), 42.0 (C-4), 61.6 (C-6), 75.8, 79.8, 78.8 and 88.4 (C-1, -2, -3 + -4a).

4a(*R*)-Acetoxy-1,2,3,6-tetra-*O*-acetyl-5-deoxy-4a-carba-α-D-*xylo*-hexofuranose 22

Reduction and acetylation of compound **12** (239 mg, 1.37 mmol) was done according to the procedure for **16**. Purification by flash chromatography (EtOAc–hexane 45 : 55) gave the title compound **22** as colourless crystals (440 mg, 83%), mp 86–87 °C. Recrystallisation (toluene) gave mp 88.5–90 °C; $[\alpha]_D$ 0.0 (*c* 1.00, $CHCl_3$) (Found: C, 52.6; H, 6.15. Calc. for $C_{17}H_{24}O_{10}$: C, 52.6; H, 6.2%); δ_H(500 MHz; benzene-d_6) 1.62 (6 H, s, CH_3CO), 1.65 (3 H, s, CH_3CO), 1.66 (2 H, q, *J* 7.0, H_2-5), 1.66 (6 H, s, CH_3CO), 2.59 (1 H, quintet, *J* 7.0, H-4), 3.92 (2 H, t, *J* 7.0, H_2-6), 5.50 (2 H, ddd, *J* 0.5, *J* 2.0, *J* 7.0, H-3 + -4a), 5.64 (2 H, dd, *J* 0.5, *J* 2.0, H-1 + -2); δ_C(62.5 MHz; $CDCl_3$) 20.1,

20.4 and 20.4 (5 × CO*C*H$_3$), 22.3 (C-5), 38.8 (C-4), 62.2 (C-6), 75.0 and 75.5 (C-1, -2, -3 + -4a), 169.0, 169.5 and 170.4 (5 × *C*OCH$_3$).

5-Deoxy-4a(*R*)-hydroxy-4a-carba-α-D-*xylo*-hexofuranose 23

Compound **22** (120 mg, 0.31 mmol) was deacetylated according to the procedure for **17**. Concentration gave the title compound **23** as a colourless oil (44 mg, 80%); $[\alpha]_D$ 0.0 (*c* 0.84, MeOH) (Found: C, 47.0; H, 8.1. Calc. for $C_7H_{12}O_5$: C, 47.2; H, 7.9%); δ_H(500 MHz; MeOH-d$_4$) 1.76 (2 H, dt, *J* 6.5, *J* 7.0, H$_2$-5), 2.35 (1 H, tt, *J* 6.0, *J* 7.5, H-4), 3.67 (2 H, t, *J* 6.5, H$_2$-6), 3.94 (2 H, dd, *J* 2.0, *J* 6.0, H-3 + -4a), 4.00 (2 H, d, *J* 2.0, H-1 + -2); δ_C(62.5 MHz; MeOH-d$_4$) 27.7 (C-5), 42.3 (C-4), 62.2 (C-6), 79.0 and 79.3 (C-1, -2, -3 + -4a).

(1*R*,5*R*,6*R*,7*S*,8*R*)-7-Amino-6,8-dihydroxy-2-oxabicyclo[3.3.0]-octan-3-one hydrochloride 24

To a solution of compound **14** (142 mg, 0.713 mmol) in acidic ethanol (ethanol 5 ml + 12 M HCl 0.5 ml) was added Pd/C (30 mg) and the mixture was stirred at rt in a hydrogen atmosphere for 16 h. Filtration through a pad of Celite and concentration gave the title compound **24** as a colourless, hygroscopic foam (149 mg, quant.); $[\alpha]_D$ −31.8 (*c* 1.0, MeOH); δ_H(500 MHz; MeOH-d$_4$) 2.59 (1 H, m, H′-4), 2.80–2.96 (2 H, m, H-4 + -5), 3.23 (1 H, dd, $J_{7,8}$ 9.5, $J_{6,7}$ 10.0, H-7), 3.87 (1 H, dd, $J_{5,6}$ 7.5, $J_{6,7}$ 10.0, H-6), 4.58 (1 H, dd, $J_{1,8}$ 4.0, $J_{7,8}$ 9.5, H-8), 4.73 (1 H, dd, $J_{1,8}$ 4.0, $J_{1,5}$ 6.0, H-1); δ_C(62.5 MHz; MeOH-d$_4$) 35.8 (C-4), 45.8 (C-5), 64.7 (C-7), 78.5 and 79.5 (C-6 + -8), 90.0 (C-1), 180.7 (C-3).

2-Acetamido-4a(*R*)-acetoxy-1,3,6-tri-*O*-acetyl-2,5-dideoxy-4a-carba-α-D-*arabino*-hexofuranose 25

Reduction of compound **24** (66 mg, 0.316 mmol) was done according to the procedure for **16**. The crystalline residue was dissolved in water (50 ml) and loaded onto a column of ion-exchange resin (Amberlite IR-120, H^+, 100 ml). The column was eluted with water (200 ml) to neutral pH followed by 12.5% aq. NH_3 (200 ml) and the alkaline phases were concentrated to give the crude aminohydroxy compound. This was then acetylated according to the procedure for compound **16** and concentrated to give a crude product (106 mg, 86%). Purification by flash chromatography (EtOAc) gave a 12 : 1 mixture of the title compound **25** and the bicyclic amine **26** (60 mg, 49%). Recrystallisation (toluene–ethanol) gave the pure title compound **25** as colourless crystals (35 mg, 28%), mp 95–96 °C; $[\alpha]_D$ +27.2 (*c* 3.50, $CHCl_3$) (Found: C, 52.4; H, 6.2; N, 3.6. Calc. for $C_{17}H_{25}NO_9$: C, 52.7; H, 6.5; N, 3.6%); δ_H(500 MHz; $CDCl_3$) 1.71 (1 H, dq, $J_{4,5'} = J_{5',6} = J_{5',6'}$ 6.5, $J_{5,5'}$ 14.5, H′-5), 1.81 (1 H, ddt, $J_{5,6} = J_{5,6'}$ 6.5, $J_{4,5}$ 8.5, $J_{5,5'}$ 14.5, H-5), 1.95 (3 H, s, CH_3CO), 2.04 (3 H, s, CH_3CO), 2.09 (3 H, s, CH_3CO), 2.10 (3 H, s, CH_3CO), 2.12 (3 H, s, CH_3CO), 2.47 (1 H, m, H-4), 4.02–4.11 (2 H, m, H$_2$-6), 4.28 (1 H, dt, $J_{1,2}$ 6.0, $J_{2,3} = J_{2,N}$ 8.0, H-2), 4.95 (1 H, dd, $J_{1,4a}$ 2.5, $J_{4,4a}$ 6.5, H-4a), 5.07 (1 H, dd, $J_{2,3}$ 8.0, $J_{3,4}$ 10.5, H-3), 5.19 (1 H, dd, $J_{1,4a}$ 2.5, $J_{1,2}$ 6.0, H-1), 5.87 (1 H, br d, $J_{1,N}$ 8.0, NH); δ_C(62.5 MHz; $CDCl_3$) 20.7, 20.8, 20.8, 20.8 and 23.7 (5 × CO*C*H$_3$), 25.3 (C-5), 41.4 (C-4), 59.5 (C-2), 62.1 (C-6), 74.6, 78.1 and 79.5 (C-1, -3 + -4a), 169.4, 169.8, 170.4, 170.8 and 171.2 (5 × *C*OCH$_3$).

4a(*R*)-Acetoxy-1,3,6-tri-*O*-acetyl-2-azido-2,5-dideoxy-4a-carba-α-D-*arabino*-hexofuranose 27

A solution of $Ca(BH_4)_2$·2THF (267 mg, 1.24 mmol) in dry THF (20 ml) under argon was cooled to −20 °C and stirred for 5 min. Compound **14** (51 mg, 0.256 mmol) was then added and the reaction mixture was stirred at −20 °C for 16 h. The reaction mixture was then worked-up and acetylated according to the procedure for **25**. Purification by flash chromatography (EtOAc–hexane 45 : 55) gave the title compound **27** as a colourless oil (44 mg, 47%), $[\alpha]_D$ +37.6 (*c* 1.6, $CHCl_3$) (Found: C, 48.5; H, 5.7; N, 11.1. Calc. for $C_{15}H_{21}N_3O_8$: C, 48.5; H, 5.7; N, 11.3%); δ_H(500 MHz; $CDCl_3$) 1.69 (1 H, dq, $J_{4,5'} = J_{5',6} = J_{5',6'}$ 6.5, $J_{5,5'}$ 14.5, H′-5), 1.81 (1 H, ddt, $J_{5,6} = J_{5,6'}$ 6.5, $J_{4,5}$ 8.5, $J_{5,5'}$ 14.5, H-5), 2.01 (3 H, s, CH_3CO), 2.10 (3 H, s, CH_3CO), 2.11 (6 H, s, 2 × CH_3CO), 2.38 (1 H, m, H-4), 3.71 (1 H, ddd, $J_{2,4}$ 1.0, $J_{1,2}$ 4.0, $J_{2,3}$ 6.5, H-2), 3.97–4.07 (2 H, m, H$_2$-6), 4.85 (1 H, dd, $J_{1,4a}$ 2.0, $J_{4,4a}$ 6.0, H-4a), 5.11 (1 H, dd, $J_{2,3}$ 6.5, $J_{4,3}$ 10.0, H-3), 5.14 (1 H, dd, $J_{1,4a}$ 2.0, $J_{1,2}$ 4.0, H-1); δ_C(62.5 MHz; $CDCl_3$) 20.5, 20.6, 20.7 and 20.7 (4 × CO*C*H$_3$), 24.9 (C-5), 42.3 (C-4), 62.1 (C-6), 69.5 (C-2), 74.7, 78.8 and 79.5 (C-1, -3 + -4a), 169.3, 169.5, 170.0 and 170.7 (4 × *C*OCH$_3$).

2-Azido-2,5-dideoxy-4a(*R*)-hydroxy-4a-carba-α-D-*arabino*-hexofuranose 28

From compound 14. Reduction of compound **14** (51 mg, 0.256 mmol) was done according to the procedure for **27**. The reaction mixture was then carefully quenched with 1 M HCl (5 ml) and stirred for 1 h followed by concentration and coevaporation twice with methanol to give a crude product (quant.). Purification by flash chromatography (7.5% methanol in EtOAc) gave the title compound **28** as a colourless, hygroscopic oil (23 mg, 44%), $[\alpha]_D$ +44.4 (*c* 0.89, MeOH); δ_H(500 MHz; MeOH-d$_4$) 1.50 (1 H, dq, $J_{4,5'} = J_{5',6} = J_{5',6'}$ 6.5, $J_{5,5'}$ 14.0, H′-5), 1.81 (1 H, ddt, $J_{5,6} = J_{5,6'}$ 6.5, $J_{4,5}$ 8.0, $J_{5,5'}$ 14.0, H-5), 1.89 (1 H, m, H-4), 3.33 (1 H, dd, $J_{1,2}$ 7.5, $J_{2,3}$ 8.5, H-2), 3.46–3.54 (2 H, m, H$_2$-6), 3.55 (1 H, dd, $J_{2,3}$ 8.5, $J_{4,3}$ 9.5, H-3), 3.59 (1 H, dd, $J_{1,4a}$ 4.5, $J_{1,2}$ 7.5, H-1), 3.85 (1 H, dd, $J_{1,4a}$ 4.5, $J_{4a,4}$ 8.0, H-4a); δ_C(62.5 MHz; MeOH-d$_4$): 28.8 (C-5), 43.1 (C-4), 60.0 (C-6), 71.3, 74.2, 77.0 and 79.7 (C-1, -2, -3 + -4a).

From compound 27. Compound **27** (44 mg, 0.118 mmol) was deacetylated according to the procedure for **17**. Concentration gave the title compound **28** as a colourless, hygroscopic oil (24 mg, quant.). ^{1}H NMR and ^{13}C NMR data as described above.

2-Amino-2,5-dideoxy-4a(*R*)-hydroxy-4a-carba-α-D-*arabino*-hexofuranose hydrochloride 1

Compound **28** (20 mg, 0.098 mmol) was hydrogenated according to the procedure for **24** (acidic methanol was used instead of acidic ethanol). Concentration gave the title compound **1** as a colourless, hygroscopic foam (20 mg, 95%); $[\alpha]_D$ +30.9 (*c* 0.94, MeOH) (Found: *M* + H, 178.1083. $C_7H_{15}NO_4$ requires *M* + H, 178.1079); δ_H(250 MHz; MeOH-d$_4$) 1.70–1.94 (2 H, m, H$_2$-5), 2.07 (1 H, m, H-4), 3.05 (1 H, dd, $J_{1,2}$ 6.0, $J_{2,3}$ 8.0, H-2), 3.61–3.75 (2 H, m, H$_2$-6), 3.80 (1 H, dd, $J_{2,3}$ 8.0, $J_{4,3}$ 10.0, H-3), 3.84 (1 H, dd, $J_{1,4a}$ 2.5, $J_{1,2}$ 6.0, H-1), 3.94 (1 H, dd, $J_{1,4a}$ 2.5, $J_{4a,4}$ 6.5, H-4a); δ_C(62.5 MHz; MeOH-d$_4$) 30.4 (C-5), 47.3 (C-4), 61.7 (C-6), 64.8 (C-2), 77.2, 77.7 and 80.2 (C-1, -3 + -4a).

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