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TETRAHEDRON

A Novel Access to Derivatives of 3-Azido-3-deoxy-4a-carba-α-DL-ribofuranose, Potential Intermediates for the Synthesis of Carbachryscandin and Carbapuromycin

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Abstract: 1,4-Anhydro-3-O-benzyl-2,5-dideoxy-4a-carba-DL-*erythro*-hex-1-enitol-uronic acid (**5**) was transformed by chain degradation under suitable protection and reaction with *m*-CPBA into 5-O-acetyl-1,2-anhydro-4a-carba-α-DL-xylofuranose (**37**). Replacement of the triflate by azide gave 5-O-acetyl-1,2-anhydro-3-azido-3-deoxy-4a-carba-α-DL-ribofuranose (**39**), a versatile intermediate for the preparation of 3-azido- and 3-amino-4a-carbanucleosides. Similarly *via* 5-deoxy-4a-carba-α-DL-*xylo*-hexofuranurono-6,3-lactone (**2**) 5-O-acetyl-3-azido-3-deoxy-1,2-isopropylidene-4a-carba-α-DL-ribofuranose (**19**) was prepared which can serve for the same purpose.

Keywords: azides; carbohydrates; nitroso compounds; nucleosides.

INTRODUCTION

Puromycin, 6-dimethylamino-9-[3′-deoxy-3′-(4-methoxy-L-β-phenylalanylamino)-β-D-ribofuranosyl]-9*H*-purine, was isolated by *Porter* [1] from the fermentation broth of *Streptomyces alboniger* and the first total synthesis was performed by *Baker* [2] in 1955. Chryscandin, 1-(6-amino-9*H*-purine-9-yl)-3-deoxy-3-(4-methoxy-L-β-phenylalanylamino)-β-D-ribofuranuronic acid, was isolated in 1984 by *Yamashita* [3] from the fermentation broth of *Chrysosporum pannorum*, and the structure was determined in the same laboratory [4,5]. Since these days numerous derivatives were characterised [6]. Puromycin and carbapuromycin possess a biological broad-band activity against Gram-positive and Gram-negative bacteria

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[7,8,9] and are cytotoxic to mouse leukemia cells [10]. Chryscandin also shows antibacterial activity, but it has no activity against Gram-negative bacteria and filamentous fungi.

The total synthesis of carbapuromycin was published by *Vince* [11,12,13], starting from 3-azabicyclo[2.2.1]hept-5-en-2-one, whilst a similar synthesis for carbachryscandin was not performed yet. The synthesis of the carbasugar part was achieved *via* epoxide opening with NaN_3, or from the corresponding oxime [14].

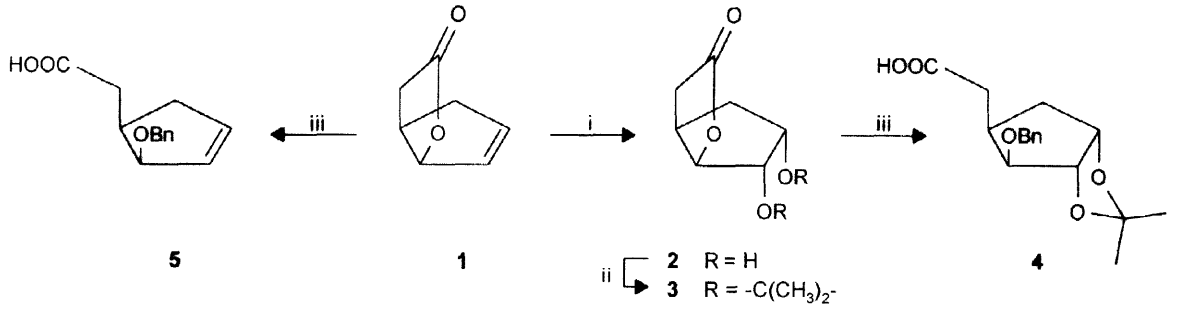
In continuation of our work on syntheses of carbanucleosides [15,16] and carbasugars [17,18,19] here are reported pathways to 3-azido-3-deoxy-4a-carba-α-DL-ribofuranoses **19**, **21**, **32** and **39**. The aim is to explore novel preparative strategies for this class of 3-azido-4a-carbasugars. Thus the synthetic access can be chosen depending on the starting material or the desired protection pattern and derivatisation of the product. In particular these intermediates allow the direct introduction of the nucleoside base at C-1 [20,21,22,23] whereas in the syntheses described [12,13,14] the purine ring had to be built up.

Starting from easily accessible acid **4** [24] chain degradation necessary was achieved either *via* a variant of the *Hunsdiecker* reaction [25,26,27] or by *Curtius* degradation. Alternatively, unsaturated acid **5** was transformed into amine **24** and further on the corresponding N-nitroso amides **26** and **34** were rearranged into benzoate **27** or acetate **35**. Derivatisation of the double bond was done stereoselectively after chain degradation. To estimate the influence of the side chain on the S_N2 reaction benzoate or acetate was used, where acetate always gave better yields. The steric effect of the isopropylidene group favoured the concurring elimination, whereas an epoxide showed no steric influence on the substitution.

RESULTS AND DISCUSSION

The known [28,29] lactone **1** was synthesised starting from bicyclo[2.2.1]hept-5-en-2-one in 71% yield. *cis*-Dihydroxylation with OsO_4/N-methylmorpholine-N-oxide (NMNO) and formation of the acetonide afforded compound **3**. Lactones **1** or **3** were opened by treatment with KOH in boiling 1,4-dioxane. Protection of the intermediate hydroxy acids was performed with benzyl bromide [24] to afford carboxylic acids **4** and **5**.

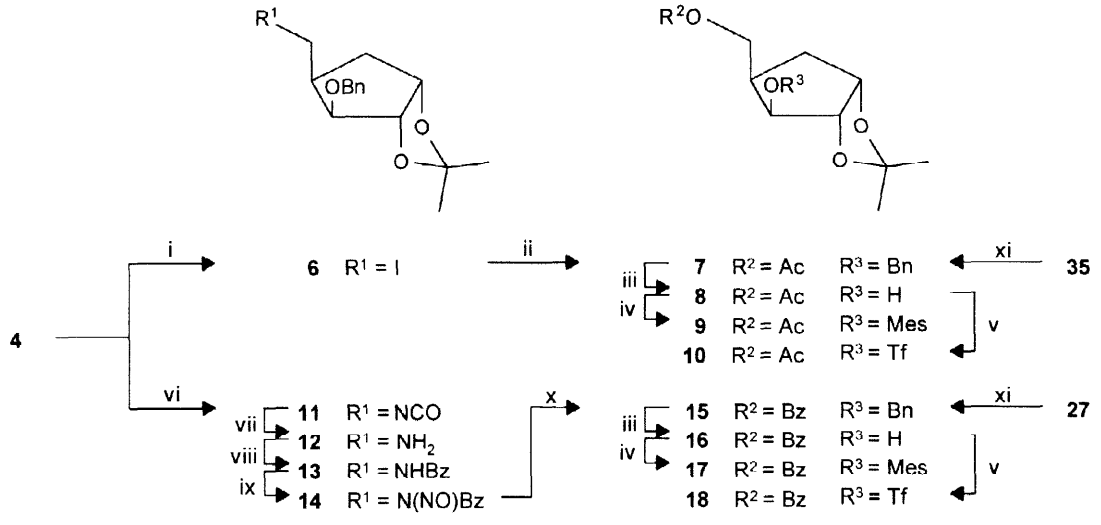
For the synthesis of iodide **6** a variant of the *Hunsdiecker* reaction was performed, as described by *Ötvös* [25,26]. Carboxylic acid **4** was treated with iodine and iodosobenzene diacetate (IBDA) in cyclohexane by irradiation with photo lamps to yield 62% of iodide **6** and 12% of the corresponding eliminated product **6a** (not drawn). Substitution of the iodine by acetate with CsOAc in DMF and cleavage of the benzyl ether with Pd-C (10%)/H_2 in ethanol afforded alcohol **8** in 33% overall yield, calculated from lactone **1**.



Scheme 1 Reagents and conditions: i OsO_4/NMNO/acetone/r.t.; ii acetone/HCl conc.; iii KOH/BnBr/1,4-dioxane/reflux. All compounds are racemic, only one enantiomer is drawn.

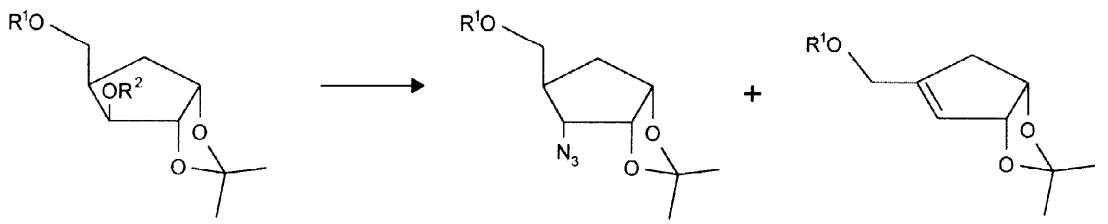
For alternative chain degradation isocyanate **11** was synthesised by reaction of carboxylic acid **4** with ethyl chloroformate to give an intermediate mixed anhydride. By treatment with saturated aqueous NaN_3 the acid azide was formed which was rearranged into isocyanate **11** by refluxing in anhydrous toluene. Hydrolysis with KOH in THF/H_2O yielded 54% of amine **12**, calculated from lactone **1**.

For further synthetic manipulations the replacement of the side chain amino group by an oxygen functionality or a halide, which could be treated further on with suitable nucleophiles, was desirable. For this purpose several methods are described in the literature [30,31] but only one gave excellent yields and allowed simple up-scaling.



Scheme 2 Reagents and conditions: i IBDA/I_2/hv/cyclohexane/reflux; ii CsOAc/DMF/r.t.; iii Pd-C (10%)/H_2/ethanol; iv MesCl/pyr/CH_2Cl_2/0 °C; v Tf_2O/pyr/CH_2Cl_2/0 °C; vi a) ClC(O)OEt/ Et_3N/acetone/0 °C, b) NaN_3/H_2O/acetone, c) toluene/reflux; vii KOH/THF/H_2O; viii BzCl/Et_3N/ CH_2Cl_2/r.t.; ix a) N_2O_4/CCl_4/0 °C, b) NaOAc; x petrol ether/reflux; xi a) OsO_4/NMNO/acetone/r.t., b) acetone/HCl/r.t.. All compounds are racemic, only one enantiomer is drawn.

Investigations by *White* [32,33,34] showed that the transformation of benzamides or acetamides into the corresponding benzoates or acetates was best done with N_2O_4 in sodium acetate buffer. For this purpose benzamide **13** was synthesised by the reaction of amine **12** with benzoyl chloride in the presence of triethylamine. Reaction of **13** with N_2O_4, obtained by reaction of $NaNO_2$ with sulphuric acid, afforded the thermally unstable N-nitroso amide **14** which was immediately rearranged to benzoate **15** in boiling petrol ether [35]. Hydrogenolysis of the benzyl ether afforded alcohol **16** in 19% overall yield starting from lactone **1**. As an alternative acetate **7** or benzoate **15** were synthesised from olefin **27** or **35**, respectively, by *cis*-dihydroxylation and subsequent acetalisation, but the overall yields are lower due to the lower yields for the syntheses of olefins **27** and **35** (Scheme 4) as described on the next page.



9 R^1 = Ac R^2 = Mes
10 R^1 = Ac R^2 = Tf
17 R^1 = Bz R^2 = Mes
18 R^1 = Bz R^2 = Tf

19 R^1 = Ac

21 R^1 = Bz

20 R^1 = Ac

22 R^1 = Bz

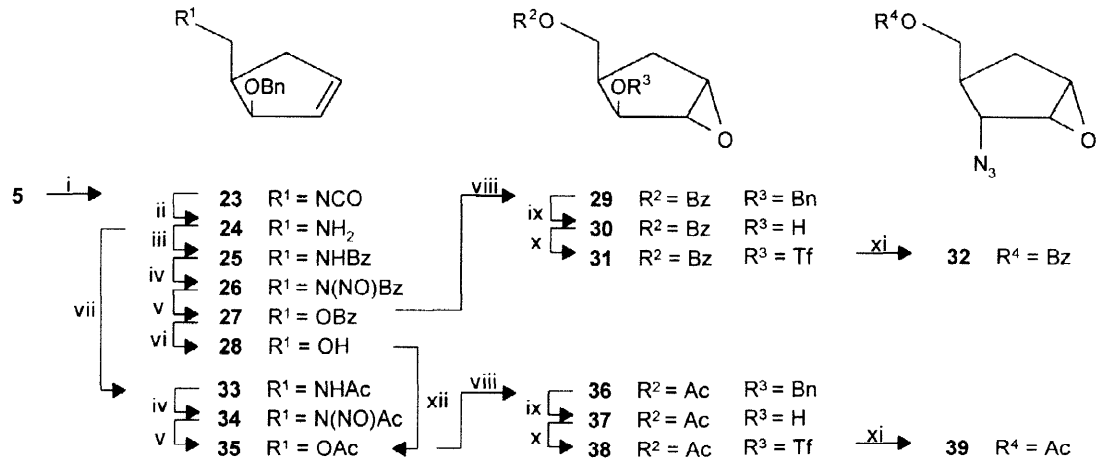
Scheme 3 Reagents and conditions: see table 1. All compounds are racemic, only one enantiomer is drawn.

For the introduction of the azide group alcohols **8** and **16** were transformed into mesylates **9** and **17** or into triflates **10** and **18**, respectively. Unfortunately, the S_N2 reaction was always accompanied by elimination, dependent on the reagent, the reaction temperature and the solvent used. Table 1 gives an overview of isolated yields achieved with starting materials **9**, **10**, **17** and **18** by treating with NaN_3 in various solvents. To sum up triflate **18** gave lower yields than triflate **10** and mesylates **9** and **17** only eliminated products **20** and **22**, respectively.

Table 1 Experiments to introduce the azide group by S_N2-displacements besides an isopropylidene moiety.

Substrate	Reagent	Reaction time (h)	Azide; yield (%)	Olefin; yield (%)
9	NaN_3, DMF	24	**19**; 0	**20**; 95
17	NaN_3, DMF	24	**21**; 0	**22**; 94
10	NaN_3, DMF	24	**19**; 45	**20**; 50
18	NaN_3, DMF	0.5	**21**; 32	**22**; 63
18	NaN_3, EtOH	72	**21**; 30	**22**; 65
18	NaN_3, acetone	6	**21**; 30	**22**; 67

For the synthetic pathway *via* olefins **27** or **35** (see Scheme 2 and below) preparation of benzoate **27** was performed in a similar way as described for **15**. Starting from carboxylic acid **5** isocyanate **23** was obtained again by *Curtius* degradation. Hydrolysis of the isocyanate with $KOH/H_2O/THF$ afforded amine **24**, which was transformed into benzamide **25** or acetamide **33**, versatile intermediates for the preparation of the corresponding N-nitroso amides **26** and **34**, by treatment with N_2O_4. Thermal rearrangement afforded benzoate **27** or acetate **35**. The reaction of acylamide **33** was found to give better yields of **35** than reaction of isocyanate **23** with N_2O_4 in acidic media ($HOAc/Ac_2O/CH_2Cl_2$) [24].



Scheme 4 Reagents and conditions: i a) $ClC(O)OEt/Et_3N$/acetone/0 °C, b) NaN_3/H_2O/acetone, c) toluene/reflux; ii $KOH/THF/H_2O$; iii $BzCl/Et_3N/CH_2Cl_2$/r.t.; iv a) N_2O_4/CCl_4/0 °C, b) NaOAc; v petrol ether/reflux; vi NaOMe/ MeOH/r.t.; vii $Ac_2O/Et_3N/CH_2Cl_2$/0 °C; viii *m*-CPBA/ethyl acetate/reflux; ix Pd-C (10%)/H_2/ethanol; x $Tf_2O/Pyr/CH_2Cl_2$/0 °C; xi NaN_3/DMF/r.t.; xii $Ac_2O/Pyr/CH_2Cl_2$/r.t. All compounds are racemic, only one enantiomer is drawn.

Acetate **35** can also be synthesised from alcohol **28**, because chain degradation *via* the N-nitroso amide **26** afforded better yields. Benzoate **27** and acetate **35** were epoxidised with *m*-CPBA and hydrogenated with Pd-C (10%) to give the corresponding 1,2-anhydro-4a-carba-α-DL-xylofuranoses **30** and **37**. Then triflates **31** and **38** were treated with NaN_3 in DMF. Benzoate **31** and acetate **38** were found to give azides **32** and **39** in yields of 58% and 70%, respectively. In this case not the elimination was the main competing reaction but to a slight extent the attack on the epoxide.

Table 2 Experiments to introduce the azide groups by S_N2-displacements besides an epoxide.

Substrate	Reagent	Reaction time (h)	Azide; yield (%)
31	NaN_3, DMF	24	**32**; 58
38	NaN_3, DMF	24	**39**; 70

CONCLUSION

An optimised medium scale procedure for the synthesis of intermediates **8**, **16**, **30**, and **37** was described using either a modified *Hunsdiecker* reaction or a *Curtius* degradation followed by subsequent transformation of an acylamide into the corresponding protected ribofuranoses **30** and **37**, potent intermediates in the synthesis of carbasugars [17,18,19,24,28,29] and carbanucleosides [20,21,22,23]. To estimate the influence of the protective groups for the hydroxyl functionality at position 5, benzoate and acetate was used in 1,2-anhydro-α-DL-xylofuranoses and for 1,2-O-isopropylidene-4a-carba-α-DL-xylofuranoses. For the introduction of the azide moiety at C-3 to give final products **32** or **39** the more bulky benzoate used as protective group at C-5 was found to give lower yields in each case.

EXPERIMENTAL

Melting points were obtained on a Büchi-Tottoli apparatus and were uncorrected. Column chromatography was performed on silica gel 60, 230-400 mesh (Merck, Darmstadt), and TLC on aluminium sheets coated with silica gel 60 F_{254} (Merck, Darmstadt). ^{1}H NMR and ^{13}C NMR spectra were recorded on a Bruker MSL 300 instrument (300.13 MHz) or on a Varian Gemini 200 (199.97 MHz). TMS was used as internal standard, δ-values are given in ppm and $CDCl_3$ as solvent unless otherwise indicated. IR spectra were determined as film on NaCl on a Bomem Michelson 100 FT-spectrophotometer. MS spectra were recorded on a Kratos Profile spectrometer. Solvents were dried by standard procedures. THF was absoluted with potassium under reflux and always used freshly distilled. The elemental analyses were performed at the Institute of Organic Chemistry, University of Graz.

5-Deoxy-4a-carba-α-DL-*xylo*-hexofuranurono-6,3-lactone (2)

48.6 g (392 mmol) of lactone **1**, dissolved in 500 mL of acetone, was treated with 90.0 g (770 mmol) of N-methylmorpholine-N-oxide monohydrate (NMNO) and a catalytic amount of OsO_4. After complete turnover (about 1 day) 1 g of $Na_2S_2O_5$ was added to reduce and precipitate the catalyst and the solvent was removed *in vacuo*. The residue was diluted with 100 mL of cold acetone, the precipitate (excess of NMNO) was filtered through a glass filter funnel and washed with cold acetone. Coevaporation with toluene (3 x 200 mL) to remove the formed N-methylmorpholine and bulb-to-bulb distillation yielded 48.3 g (78%) of diol **2**.

^{1}H NMR ($CDCl_3$, 200 MHz) δ 1.68 (ddd, J = 13.7, 6.3, 5.4 Hz, 1H), 2.17 (dd, J = 13.7, 5.3 Hz, 1H), 2.31 (dd, J = 18.6, 3.4 Hz, 1H), 2.82 (dd, J = 18.6, 10.4 Hz, 1H), 3.17 (m, 1H),

3.30-3.60 (bm, 2H), 4.14 (dd, J = 4.0, 2.7 Hz, 1H), 4.25 (dd, J = 7.8, 5.1 Hz, 1H), 4.78 (dd, J = 7.8, 2.7 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 34.48, 35.53, 37.67, 72.67, 77.87, 89.14, 178.50 ; IR (NaCl) ν 3383, 2946, 1761, 1416, 1348, 1181, 1111, 1026, 923 cm^{-1}. Anal. calcd. for $C_7H_{10}O_4$ (158.15): C, 53.16; H, 6.37. Found: C, 53.26; H, 6.30.

5-Deoxy-1,2-O-isopropylidene-4a-carba-α-DL-*xylo*-hexofuranurono-6,3-lactone (3)

48.0 g (304 mmol) of diol **2** was dissolved in 500 mL of acetone and 5 mL of HCl conc. was added. After complete turnover (about 1 h) saturated aqueous $NaHCO_3$ was added until pH 7, and the solvent was removed *in vacuo*. Extraction with CH_2Cl_2, drying over Na_2SO_4, and flash chromatography (hexane/ethyl acetate 9/1 v/v) yielded 57.1 g (95%) of lactone **3** as colourless crystals.

mp 82-83 °C; ^{1}H NMR and ^{13}C NMR were in accordance with the literature [18]; IR (NaCl) ν 2985, 2928, 1779, 1367, 1264, 1205, 1155, 1064, 1034, 1012, 870, 844 cm^{-1}. Anal. calcd. for $C_{10}H_{14}O_4$ (198.22): C, 60.59; H, 7.12. Found: C, 60.53; H, 7.18.

3-O-Benzyl-5-deoxy-1,2-O-isopropylidene-4a-carba-α-DL-*xylo*-hexofuranuronic acid (4)

A mixture of 56.0 g (283 mmol) of lactone **3** and 79.3 g (1.41 mol) of powdered KOH in 1 L of 1,4-dioxane was refluxed for 1 h. 100 mL (840 mmol) of benzyl bromide was added in 5 portions (caution: strongly exothermic). The reaction mixture was refluxed over night. Water (300 mL) was added and the reaction mixture was extracted with diethyl ether (4 x 100 mL) to remove benzyl alcohol and dibenzyl ether. The aqueous layer was acidified with HCl conc. (pH 1) and extracted with diethyl ether (5 x 100 mL). The combined organic extracts were dried (Na_2SO_4) and evaporated *in vacuo* to yield 86.6 g (100%) of carboxylic acid **4** as an oil.

^{1}H NMR ($CDCl_3$) δ 1.30 (s, 3H), 1.44 (s, 3H), 1.70 (dt, J = 13.0, 4.8 Hz, 1H), 1.93 (dt, J = 13.0, 5.5 Hz, 1H), 2.43-2.66 (m, 3H), 3.82 (d, J = 3.7 Hz, 1H), 4.42 (d, J = 11.6 Hz, 1H), 4.56 (t, J = 5.5 Hz, 1H), 4.63 (d, J = 11.6 Hz, 1H), 4.72 (m, 1H), 7.23-7.43 (m, 5H), 10.3-10.6 (bs, 1H); ^{13}C NMR ($CDCl_3$) δ 23.86, 26.18, 32.67, 36.16, 36.42, 71.47, 79.74, 82.69, 83.70, 110.02, 127.74, 127.78, 128.43, 138.07, 178.85; MS m/z (rel int %) 306 ($M^{+\cdot}$, 2), 291 (16), 183 (60), 157 (8), 142 (39), 123 (11), 111 (19), 91 (100), 84 (9), 59 (4), 43 (6); IR (NaCl) ν 2947, 1782, 1710, 1377, 1285, 1208, 1154, 1051, 843, 742 cm^{-1}. Anal. calcd. for $C_{17}H_{22}O_5$ (306.36): C, 66.65; H, 7.24. Found: C, 66.42; H, 7.09.

1,4-Anhydro-3-O-benzyl-2,5-dideoxy-4a-carba-DL-*erythro*-hex-1-enitol-uronic acid (5)

A mixture of 25.0 g (202 mmol) of lactone **1** and 56.2 g (1 mol) of powdered KOH in 1 L of 1,4-dioxane was treated in the same manner as described for acid **4** with 71 mL (600 mmol) of benzyl bromide to yield 45.8 g (98%) of crude carboxylic acid **5** as an oil.

^{1}H NMR ($CDCl_3$) δ 2.18-2.26 (m, 1H), 2.49-2.58 (m, 2H), 2.77 (m, 2H), 4.50-4.60 (AB, J = 11.7 Hz, 2H), 4.58 (m, 1H), 5.97 (m, 1H), 6.05 (m, 1H), 7.25-7.37 (m, 5H); ^{13}C NMR and DEPT ($CDCl_3$) δ 34.34 (t), 37.38 (t), 37.87 (d), 71.64 (t), 83.48 (d), 127.68 (d), 127.79 (d), 128.48 (d), 130.64 (d), 135.50 (d), 138.80 (s), 179.80 (s); IR (NaCl) ν 3046, 2927, 1710, 1453, 1410, 1282, 1217, 1060, 930, 738, 698 cm^{-1}.

3-O-Benzyl-5-deoxy-5-iodo-1,2-O-isopropylidene-4a-carba-α-DL-xylofuranose (6) and **3-O-Benzyl-5-deoxy-1,2-isopropylidene-4a-carba-β-DL-*threo*-pent-4-enofuranose (6a)**

A solution of 15.0 g (48.9 mmol) of acid **4**, 8.90 g (35.1 mmol) of I_2, and 11.3 g (35.0 mmol) of iodosobenzene diacetate (IBDA) in 700 mL of cyclohexane was refluxed and irradiated with two 150 W photolamps for 1 h. After addition of a second crop of I_2 (8.90 g, 35.1 mmol) and of IBDA (11.3 g, 35.0 mmol) refluxing and irradiation was continued for an additional hour. The reaction mixture was extracted with aqueous 1 N $Na_2S_2O_3$ and saturated aqueous $NaHCO_3$ solution (30 mL each), dried (Na_2SO_4), and evaporated to dryness. Purification of the residue on a silica gel column (cyclohexane/ethyl acetate 9/1 v/v) yielded 11.7 g (62%) of **6** and 1.53g (12%) of the eliminated product **6a** as colourless oils.

Spectroscopic data of **6**: ^{1}H NMR ($CDCl_3$) δ 1.34 (s, 3H), 1.67 (s, 3H), 1.72 (dt, J = 12.9, 5.1 Hz, 1H), 2.03 (dd, J = 12.9, 6.2 Hz, 1H), 2.68 (m, 1H), 3.26 (dd, J = 9.3, 6.2 Hz, 1H), 3.35 (t, J = 9.3 Hz, 1H), 3.99 (d, J = 4.2 Hz, 1H), 4.56 (d, J = 11.4 Hz, 1H), 4.61 (d, J = 5.8 Hz, 1H), 4.71 (d, J = 11.4 Hz, 1H), 4.81 (t, J = 5.3 Hz, 1H), 7.38 (m, 5H); ^{13}C NMR and DEPT ($CDCl_3$) δ 3.68 (t), 23.96 (q), 26.29 (q), 36.73 (t), 44.27 (d), 72.03 (t), 80.39 (d), 82.37 (d), 84.26 (d), 110.00 (s), 127.82, (d), 128.45 (d), 137.54 (s); MS m/z (rel int %) 388 ($M^{+\cdot}$, 3), 373 (14), 261 (4), 203 (11), 155 (4), 111 (9), 91 (100), 81 (8), 59 (13), 43 (35); IR (NaCl) ν 2981, 2926, 1454, 1357, 1264, 1208, 1058, 865, 740, 697, 516 cm^{-1}. Anal. calcd. for $C_{16}H_{21}IO_3$ (388.24): C, 49.50; H, 5.45. Found: C, 49.61; H, 5.39.

Spectroscopic data of **6a**: ^{1}H NMR ($CDCl_3$) δ 1.35 (s, 3H), 1.45 (s, 3H), 2.45 (d, J = 16.0 Hz, 1H), 2.70-2.79 (m, 1H), 4.06 (s, 1H), 4.46 (d, J = 11.8 Hz, 1H), 4.60 (m, 2H), 4.80 (t, J = 5.9 Hz, 1H), 5.28 (m, 2H), 7.29-7.41 (m, 5H); ^{13}C NMR and DEPT ($CDCl_3$) δ 24.71 (q), 26.74 (q), 37.80 (t), 69.99 (t), 79.24 (d), 84.87 (d), 85.27 (d), 110.36 (s), 114.03 (d), 127.67 (d), 127.90 (d), 128.48 (d), 138.26 (s), 147.03 (d); IR (NaCl) ν 2984, 2926, 1453, 1374, 1265, 1210, 1071, 1047, 904, 866, 738, 697 cm^{-1}. Anal. calcd. for $C_{16}H_{20}O_3$ (260.33): C, 73.82; H, 7.74. Found: C, 73.89; H, 7.61.

5-O-Acetyl-3-O-benzyl-1,2-O-isopropylidene-4a-carba-α-DL-xylofuranose (7)

To a solution of 11.5 g (29.6 mmol) of iodide **6** in 300 mL of DMF was added 14.2 g (74.1 mmol) of cesium acetate, and stirred at room temperature until complete turnover (about

3 days). 300 mL of CH_2Cl_2 was added, and the reaction mixture was extracted twice with water, dried (Na_2SO_4), and evaporated to dryness *in vacuo*. Flash chromatography (hexane/ethyl acetate 5/1 v/v) yielded 7.80 g (82%) of acetate **7** as colourless oil.

^{1}H NMR ($CDCl_3$) δ 1.31 (s, 3H), 1.44 (s, 3H), 1.74 (dt, J= 13.3, 5.1 Hz, 1H), 1.89 (dd, J= 13.3, 6.4 Hz, 1H), 1.98 (s, 3H), 2.54 (m, 1H), 3.80 (d, J= 4.3 Hz, 1H), 4.20 (dd, J= 10.7, 6.5 Hz, 1H), 4.22 (dd, J= 10.7, 8.5 Hz, 1H), 4.44 (d, J= 12.0 Hz, 1H), 4.56 (d, J= 5.7 Hz, 1H), 4.65 (d, J= 12.0 Hz, 1H), 4.75 (t, J= 5.3 Hz, 1H), 7.25-7.36 (m, 5H); ^{13}C NMR and DEPT ($CDCl_3$) δ 21.05 (q), 24.03 (q), 26.35 (q), 33.88 (t), 39.91 (d), 63.07 (t), 71.64 (t), 79.92 (d), 82.73 (d), 83.06 (d), 110.23 (s), 127.88 (d), 128.58 (d), 138.31 (s), 171.02 (s); MS m/z (rel int %) 320 ($M^{+\cdot}$, 1), 305 (8), 260 (2), 245 (5), 171 (1), 156 (6), 111 (36), 91 (100), 83 (7), 65 (5), 43 (27); IR (NaCl) ν 2928, 1739, 1454, 1371, 1242, 1209, 1158, 1048, 742, 699 cm^{-1}. Anal. calcd. for $C_{18}H_{24}O_5$ (320.38): C, 67.48; H, 7.55. Found: C, 67.61; H, 7.49.

5-O-Acetyl-1,2-O-isopropylidene-4a-carba-α-DL-xylofuranose (8)

5.5 g (17.2 mmol) of **7** was diluted with 25 mL of ethanol and about 80 mg of palladium on carbon (10%) was added. The reaction mixture was hydrogenated for 16 h at 55 bar in an autoclave. The catalyst was removed by filtration over a pad of Celite® 454 (Merck) and washed with ethanol. Evaporation of the solvent under reduced pressure and flash chromatography (ethyl acetate/hexane 1/2 v/v) yielded 3.48 g (88%) of alcohol **8** as colourless crystals.

mp 68-69 °C; ^{1}H NMR ($CDCl_3$) δ 1.23 (s, 3H), 1.38 (s, 3H), 1.59-1.76 (m, 2H), 2.03 (s, 3H), 2.36-2.43 (m, 1H), 3.13 (bs, 1H), 3.89 (d, J= 3.1 Hz, 1H), 3.97 (dd, J= 11.3, 5.1 Hz, 1H), 4.32 (dd, J= 11.1, 9.9 Hz, 1H), 4.38 (d, J= 5.6 Hz, 1H), 4.68 (t, J= 5.1 Hz, 1H); ^{13}C NMR and DEPT ($CDCl_3$) δ 20.99 (q), 23.86 (q), 26.21 (q), 32.76 (t), 40.88 (d), 62.84 (t), 74.96 (d), 79.38 (d), 86.07 (d), 109.94 (s), 172.19 (s); MS m/z (rel int %) 230 ($M^{+\cdot}$, 1), 215 (100), 173 (3), 155 (22), 141 (7), 113 (26), 95 (51), 83 (27), 67 (16), 59 (20), 43 (93); IR (NaCl) ν 3450, 2944, 1726, 1374, 1255, 1208, 1155, 1116, 1033, 863, 826 cm^{-1}. Anal. calcd. for $C_{11}H_{18}O_5$ (230.26): C, 57.38; H, 7.88. Found: C, 57.21; H, 7.96.

5-O-Acetyl-1,2-O-isopropylidene-3-O-methylsulphonyl-4a-carba-α-DL-xylofuranose (9)

To a cold (0 °C) solution of 1.0 g (4.34 mmol) of alcohol **8** and 0.73 mL (5.2 mmol) of dry triethylamine in 50 mL of dry CH_2Cl_2, was added drop by drop a solution of 0.37 mL (4.8 mmol) of methanesulphonyl chloride in 2 mL of dry CH_2Cl_2. After complete turnover the reaction mixture was extracted with 1 N HCl and saturated aqueous $NaHCO_3$ solution and dried over Na_2SO_4. Evaporation to dryness yielded in quantity 1.33 g of compound **9** as a colourless oil.

^{1}H NMR ($CDCl_3$) δ 1.23 (s, 3H), 1.38 (s, 3H), 1.62 (dt, J = 13.5, 5.0 Hz, 1H), 1.90 (dd, J = 13.5, 6.3 Hz, 1H), 2.00 (s, 3H), 2.68 (m, 1H), 2.98 (s, 3H), 4.06 (dd, J = 11.1, 9.3 Hz, 1H), 4.13 (dd, J = 11.1, 6.0 Hz, 1H), 4.64 (d, J = 5.6 Hz, 1H), 4.73 (dd, J = 5.6, 5.0 Hz, 1H), 4.84 (d, J = 4.0 Hz, 1H); ^{13}C NMR and DEPT ($CDCl_3$) δ 20.82 (q), 23.83 (q), 26.03 (q), 33.21 (t), 38.09 (q), 39.26 (d), 61.52 (t), 79.11 (d), 84.19 (d), 84.40 (d), 110.85 (s), 170.64 (s); MS m/z (rel int %) 308 ($M^{+\cdot}$, not detected), 293 ($M^{+\cdot}$-CH_3, 48), 191 (8), 173 (5), 111 (40), 95 (39), 83 (16), 67 (9), 59 (12), 42 (100). Anal. calcd. for $C_{12}H_{20}O_7S$ (308.35): C, 46.74; H, 6.54. Found: C, 46.86; H, 6.38.

5-O-Acetyl-1,2-O-isopropylidene-3-O-trifluoromethylsulphonyl-4a-carba-α-DL-xylofuranose (10)

To a cold (0 °C) solution of 200 mg (0.87 mmol) of alcohol **8** and 84 µl (1.04 mmol) of dry pyridine in 10 mL of dry CH_2Cl_2, was added drop by drop a solution of 161 µl (0.96 mmol) of trifluoromethanesulphonic anhydride in 1 mL of dry CH_2Cl_2. After complete turnover the reaction mixture was extracted with cold 0.1 N HCl and cold (0 °C) saturated aqueous $NaHCO_3$ solution and dried thoroughly over Na_2SO_4. Evaporation under reduced pressure at low bath temperature (5-10 °C) to dryness yielded crude **10** as yellow oil, which was reacted immediately to azide **19**.

3-O-Benzyl-5-deoxy-5-isocyanato-1,2-O-isopropylidene-4a-carba-α-DL-*xylo*-hexofuranose (11)

To a stirred solution of 61.3 g (200 mmol) of carboxylic acid **4** and 39.0 mL (280 mmol) of triethylamine in 500 mL of acetone was added at -30 °C 29.6 mL (310 mmol) of ethyl chloroformate drop by drop. The reaction mixture was allowed to warm to -5 °C and was stirred for additional 15 minutes. 26.0 g (400 mmol) of NaN_3 dissolved in 50 mL of water was added and stirring was continued for additional 30 min. The reaction mixture was poured into ice/water (250 mL) and extracted with toluene (3 x 150 mL). The combined organic layers were dried (Na_2SO_4), concentrated under reduced pressure to approximately a volume of 500 mL, dropped into a flask with boiling toluene (100 mL), and refluxed. After the liberation of nitrogen has ceased, the solution was evaporated *in vacuo*. Bulb-to-bulb distillation yielded 54.0 g (89%) of isocyanate **11** as a colourless oil.

^{1}H NMR ($CDCl_3$, 200 MHz) δ 1.30 (s, 3H), 1.45 (s, 3H), 1.68 (dt, J = 13.3, 5.0Hz, 1H), 1.90 (dd, J = 13.3, 6.5Hz, 1H), 2.44-2.58 (m, 1H), 3.35 (dd, J = 12.8, 6.3 Hz, 1H), 3.52 (dd, J = 12.8, 6.5 Hz, 1H), 3.83 (d, J = 4.4 Hz, 1H), 4.47 (d, J = 11.7 Hz, 1H), 4.57 (d, J = 5.7 Hz, 1H), 4.68 (d, J = 11.7 Hz, 1H), 4.75 (t, J = 5.3 Hz, 1H), 7.26-7.36 (m, 5H); ^{13}C NMR and DEPT ($CDCl_3$, 200 MHz) δ 23.83 (q), 26.17 (q), 34.13 (t), 41.59 (t), 42.10 (d), 71.50 (t), 79.76

(d), 82.63 (d), 110.11 (s), 127.74 (d), 128.03 (d), 128.35 (d), 137.89 (s). Anal. calcd. for $C_{17}H_{21}NO_4$ (303.36): C, 67.31; H, 6.98; N, 4.62. Found: C, 67.36; H, 7.06; N, 4.58.

5-Amino-3-O-benzyl-5-deoxy-1,2-O-isopropylidene-4a-carba-α-DL-xylofuranose (12)

53.0 g (175 mmol) of isocyanate **11** was dissolved in a cold (0 °C) mixture of 300 mL of tetrahydrofuran and 300 mL of water. To the vigorously stirred solution was added a cold (0 °C) solution of 29.4 g (520 mmol) of KOH in 50 mL of water within 5 min and vigorously stirring was continued until complete turnover. The reaction mixture was evaporated *in vacuo* to remove tetrahydrofuran, acidified to pH 9-10 with 5 N HCl, extracted with CH_2Cl_2, dried over Na_2SO_4, and concentrated *in vacuo*. Flash chromatography (petrol ether/ethyl acetate 9/1 v/v) yielded 39.9 g (82%) of amine **12** as a colourless oil.

^{1}H NMR ($CDCl_3$, 200 MHz) δ 1.25 (s, 3H), 1.37 (s, 3H), 1.42 (bs, 2H), 1.66 (ddd, J = 13.2, 4.7, 1.0 Hz, 1H), 1.80 (dd, J = 13.3, 6.5 Hz, 1H), 2.13-2.27 (m, 1H), 2.70 (dd, J = 12.5, 5.9 Hz, 1H), 2.83 (dd, J = 12.5, 8.4 Hz, 1H), 3.72 (d, J = 4.3 Hz, 1H), 4.36 (dd, J = 12.1, 1.4 Hz, 1H), 4.48 (dd, J = 5.7, 1.2 Hz, 1H), 4.62 (dd, J = 12.1, 1.4 Hz, 1H), 4.69 (m, 1H), 7.26 (m, 5H); ^{13}C NMR and DEPT ($CDCl_3$, 200 MHz) δ 23.85 (q), 26.14 (q), 34.26 (t), 40.57 (t), 43.72 (d), 71.01 (t), 79.84 (d), 82.64 (d), 82.74 (d), 109.77 (s), 127.68 (d), 127.77 (d), 128.46 (d), 138.18 (s); IR (NaCl) ν 2981, 2926, 1454, 1357, 1263, 1208, 1054, 740, 699 cm^{-1}. Anal. calcd. for $C_{16}H_{23}NO_3$ (277.36): C, 69.29; H, 8.36; N, 5.05. Found: C, 69.37; H, 8.30; N, 5.09.

5-Benzoylamino-3-O-benzyl-5-deoxy-1,2-O-isopropylidene-4a-carba-α-DL-xylofuranose (13)

To a cooled (0 °C) solution of 38.0 g (137 mmol) of amine **12** in 300 mL of dry CH_2Cl_2 and 26.7 mL (192 mol) of dry triethylamine was added slowly 19.1 mL (164 mmol) of benzoyl chloride dissolved in 50 mL of dry CH_2Cl_2. After complete turnover 50 mL of methanol was added and stirred for 30 min to react the excess of benzoyl chloride. The reaction mixture was washed with 1 N HCl and saturated aqueous $NaHCO_3$, dried (Na_2SO_4), and evaporated *in vacuo*. Flash chromatography (ethyl acetate/petrol ether 1/4 v/v) yielded 48.7 g (93%) of compound **13** as colourless crystals.

mp 128-131 °C; ^{1}H NMR ($CDCl_3$) δ 1.32 (s, 3H), 1.44 (s, 3H), 1.87 (m, 2H), 2.55 (m, 1H), 3.58 (dt, J = 13.8, 4.3 Hz, 1H), 3.80 (dd, J = 13.8, 6.9 Hz, 1H), 3.89 (d, J = 8.8 Hz, 1H), 4.43 (d, J = 11.5 Hz, 1H), 4.60 (d, J = 5.8 Hz, 1H), 4.74 (d, J = 11.5 Hz, 1H), 4.78 (m, 1H), 6.60 (m, 1H), 7.22-7.42 (m, 10H); ^{13}C NMR and DEPT ($CDCl_3$) δ 23.98 (q), 26.29 (q), 33.54 (t), 38.48 (t), 39.84 (d), 71.50 (t), 79.92 (d), 82.70 (d), 85.12 (d), 110.19 (s), 126.89 (d), 128.33 (d), 128.42 (d), 128.85 (d), 131.14 (d), 134.63 (s), 137.87 (s), 167.15 (s); MS m/z (rel int %) 381 ($M^{+\cdot}$, not detected), 366 ($M^{+\cdot}$-CH_3, 4), 275 (9), 260 (24), 232 (12), 200 (12), 162 (5), 122 (19),

105 (100), 91 (72), 77 (22), 51 (5); IR (NaCl) ν 3330, 2927, 1644, 1536, 1499, 1374, 1287, 1209, 1156, 1125, 1056, 897, 865, 703 cm^{-1}. Anal. calcd. for $C_{23}H_{27}NO_4$ (381.47): C, 72.42; H, 7.13; N, 3.67. Found: C, 72.40; H, 7.22; N, 3.56.

5-O-Benzoyl-3-O-benzyl-1,2-O-isopropylidene-4a-carba-α-DL-xylofuranose (15)

CAUTION: This reaction has to be carried out in a well working hood and appropriate safety clothing has to be worn!

Preparation of N_2O_4: To a flask with 200 mL of preheated (about 150 °C) and well stirred conc. sulphuric acid were added **cautiously** 100 g of $NaNO_2$ in small portions *via* a Normag® powder addition funnel and 50 mL of conc. sulphuric acid within about 1 h. The produced mixture of NO_2 and NO was carried away by a good N_2 stream, washed with glacial acetic acid, dried in a cooled (0 °C) funnel filled with *Raschig* rings, and condensed in a four-neck flask, cooled with liquid N_2. The amount of N_2O_4 (and N_2O_3), produced by this method will be sufficient to react about 130 mmol of amides, in this case of benzamide **13**.

The produced N_2O_4 was dissolved with 100 mL of carbon tetrachloride (the solution was dark green), the cooling bath with liquid N_2 was removed, and an ice bath was used further on. 38.1 g (100 mmol) of benzamide **13**, dissolved in 80 mL of carbon tetrachloride was added slowly - the colour changes to bright green. After 5 min 82 g (1 mol) of NaOAc was added *via* a Normag® powder addition funnel. Through the bright yellow solution was bubbled N_2 for 30 min, and the reaction was then poured into 200 mL of ice-water. Extraction with CH_2Cl_2 (3 x 100 mL), washing of the organic layer with saturated aqueous $NaHCO_3$ solution, drying over Na_2SO_4, and evaporation *in vacuo* yielded the N-nitroso benzamide **14** as yellow oil. **14** was dissolved in 50 mL of CCl_4 and dropped into a flask with 5 L of boiling petrol ether (bp 80 °C) and refluxed for 12 h. Flash chromatography (hexane/ethyl acetate 19/1 v/v) yielded 31.0 g (81%) of benzoate **15** as colourless crystals.

mp 128-131 °C; ^1H NMR ($CDCl_3$) δ 1.34 (s, 3H), 1.48 (s, 3H), 1.84 (dt, J = 13.3, 5.0 Hz, 1H), 1.99 (dd, J = 13.3, 6.4 Hz, 1H), 2.71 (m, 1H), 3.93 (d, J = 4.2 Hz, 1H), 4.44-4.51 (m, 3H), 4.62 (d, J = 5.7 Hz, 1H), 4.69 (d, J = 11.9 Hz, 1H), 4.81 (t, J = 5.3 Hz, 1H), 7.20-7.58 (m, 8H), 7.98 (m, 2H); ^{13}C NMR and DEPT ($CDCl_3$) δ 24.07 (q), 26.38 (q), 33.94 (t), 40.12 (d), 63.55 (t), 71.73 (t), 79.98 (d), 82.79 (d), 83.14 (d), 110.29 (s), 127.88 (d), 128.49 (d), 128.60 (d), 129.84 (d), 129.98 (d), 130.67 (d), 132.99 (d), 138.24 (s), 166.61 (s); MS m/z (rel int %) 382 ($M^{+\cdot}$, 1), 367 (8), 260 (7), 245 (19), 218 (5), 122 (5), 111 (35), 105 (53), 91 (100), 77 (16), 43 (5); IR (NaCl) ν 2944, 1718, 1452, 1376, 1313, 1273, 1208, 1177, 1158, 1110, 1058, 1027, 711 cm^{-1}. Anal. calcd. for $C_{23}H_{26}O_5$ (382.46): C, 72.23; H, 6.85. Found: C, 72.28; H, 6.92.

5-O-Benzoyl-1,2-O-isopropylidene-4a-carba-α-DL-xylofuranose (16)

30.0 g (78.4 mmol) of **15** was diluted with 100 mL of ethanol and about 100 mg of palladium on carbon (10%) was added. The reaction mixture was hydrogenated for 4 days at 50 bar and 70 °C in an autoclave. The catalyst was removed by filtration over a pad of Celite® 454 (Merck) and washed with ethanol. Evaporation *in vacuo* and flash chromatography (ethyl acetate/hexane 1/2 v/v) yielded 10.3 g (45%) of alcohol **16** as a colourless oil.

^{1}H NMR ($CDCl_3$) δ 1.29 (s, 3H), 1.44 (s, 3H), 1.78-1.88 (m, 2H), 2.57-2.64 (m, 1H), 3.20 (d, J = 3.4 Hz, 1H), 4.01 (t, J = 6.6 Hz, 1H), 4.24 (dd, J = 11.4, 4.8 Hz, 1H), 4.48 (d, J = 5.6 Hz, 1H), 4.68 (dd, J = 11.3, 10.3 Hz, 1H), 4.74 (m, 1H), 7.47 (m, 2H), 7.57 (m, 1H), 8.04 (m, 2H); ^{13}C NMR and DEPT ($CDCl_3$) δ 23.98 (q), 26.35 (q), 32.90 (t), 41.40 (d), 63.35 (t), 75.13 (d), 79.49 (d), 86.16 (d), 110.08 (s), 128.66 (d), 130.01 (d), 133.48 (d), 167.82 (s); MS m/z (rel int %) 292 (M^+, 1), 277 (74), 217 (9), 170 (5), 141 (8), 123 (24), 112 (43), 105 (100), 95 (40), 83 (38), 77 (53), 59 (22), 43 (38); IR (NaCl) ν 3474, 2930, 1709, 1453, 1376, 1275, 1207, 1176, 1154, 1118, 1027, 861, 713 cm^{-1}. Anal. calcd. for $C_{16}H_{20}O_5$ (292.33): C, 65.74; H, 6.90. Found: C, 65.67; H, 6.98.

5-O-Benzoyl-1,2-O-isopropylidene-3-O-methylsulphonyl-4a-carba-α-DL-xylofuranose (17)

To a cold (0 °C) solution of 1.0 g (3.42 mmol) of alcohol **16** and 0.57 mL (4.1 mmol) of dry triethylamine in 50 mL of dry CH_2Cl_2, was added drop by drop a solution of 0.31 mL (4.0 mmol) of methanesulphonyl chloride in 2 mL of dry CH_2Cl_2. After complete turnover the reaction mixture was extracted with 1 N HCl and saturated aqueous $NaHCO_3$ solution and dried over Na_2SO_4. Evaporation to dryness yielded 1.25 g (99%) of compound **17** as colourless crystals.

mp 98-100 °C; ^{1}H NMR ($CDCl_3$) δ 1.25 (s, 3H), 1.41 (s, 3H), 1.73 (dt, J = 13.5, 4.8 Hz, 1H), 2.00 (dd, J = 13.5, 6.1 Hz, 1H), 2.87 (m, 1H), 2.95 (s, 3H), 4.32 (t, J = 10.7 Hz, 1H), 4.44 (dd, J = 11.1, 5.8 Hz, 1H), 4.70 (d, J = 5.5 Hz, 1H), 4.77 (t, J = 5.1 Hz, 1H), 4.98 (d, J = 3.9 Hz, 1H), 7.40 (t, J = 7.5 Hz, 2H), 7.52 (t, J = 7.2 Hz, 1H), 8.00 (d, J = 7.5 Hz, 2H); ^{13}C NMR and DEPT ($CDCl_3$) δ 23.89 (q), 26.11 (q), 33.35 (t), 38.25 (q), 39.50 (d), 62.14 (t), 79.16 (d), 84.45 (d), 84.53 (d), 110.95 (s), 128.60 (d), 129.75 (d), 129.98 (d), 133.31 (d), 166.30 (s). Anal. calcd. for $C_{17}H_{22}O_7S$ (370.42): C, 55.12; H, 5.99. Found: C, 55.26; H, 5.93.

5-O-Benzoyl-3-O-trifluoromethylsulphonyl-4a-carba-α-DL-xylofuranose (18)

200 mg (0.68 mmol) of alcohol **16** and 77 µl (0.95 mmol) of dry pyridine in 50 mL of dry CH_2Cl_2 were treated with 116 µl (0.82 mmol) of trifluoromethanesulphonic anhydride as described for **10** to afford triflate **18**, which was reacted immediately to azide **21**.

5-O-Acetyl-3-azido-3-deoxy-1,2-isopropylidene-4a-carba-α-DL-ribofuranose (19) and **5-O-Acetyl-3-deoxy-1,2-O-isopropylidene-4a-carba-α-DL-*glycero*-pent-3-enofuranose (20)**

0.31 g (0.87 mmol) of crude triflate **10** was dissolved in 20 mL of DMF. 1.13 g (17.4 mmol) of NaN_3 was added and stirred at 60 °C for 2 days. The solvent was removed under reduced pressure and the residue extracted with H_2O/CH_2Cl_2. The combined organic extracts were dried over Na_2SO_4, and the solvent was evaporated *in vacuo*. Flash chromatography (hexane/ethyl acetate 4/1 v/v) yielded 100 mg (45%) of azide **19** and 95 mg (50%) of the eliminated product **20**.

Spectroscopic data of **19**: ^{1}H NMR ($CDCl_3$) δ 1.34 (s, 3H), 1.37-1.48 (m, 1H), 1.51 (s, 3H), 1.99 (dd, J = 14.1, 6.0 Hz, 1H), 2.09 (s, 3H), 2.59 (m, 1H), 2.98 (m, 1H), 4.19-4.22 (ABX, J_{AB} = 11.4 Hz, J_{AX} = 5.2 Hz, 2H), 4.63 (m, 2H); ^{13}C NMR and DEPT ($CDCl_3$) δ 21.02 (q), 24.19 (q), 25.90 (q), 32.86 (t), 38.26 (d), 64.04 (t), 64.11 (d), 78.11 (d), 80.57 (d), 110.85 (s), 171.02 (s). Anal. calcd. for $C_{11}H_{17}N_3O_4$ (255.27): C, 51.76; H, 6.71; N, 16.46. Found: C, 51.81; H, 6.79; N, 16.32.

Spectroscopic data of **20**: ^{1}H NMR ($CDCl_3$) δ 1.29 (s, 3H), 1.36 (s, 3H), 2.04 (s, 3H), 2.42 (d, J = 17.6 Hz, 1H), 2.54 (dd, J = 17.6, 5.9 Hz, 1H), 4.57 (s, 2H), 4.75 (t, J = 5.9 Hz, 1H), 5.05 (d, J = 5.8 Hz, 1H), 5.65 (s, 1H); ^{13}C NMR and DEPT ($CDCl_3$) δ 20.83 (q), 25.79 (q), 27.61 (q), 39.16 (t), 62.61 (t), 78.18 (d), 85.19 (d), 110.04 (s), 126.99 (d), 141.19 (s), 170.57 (s). Anal. calcd. for $C_{11}H_{16}O_4$ (212.25): C, 62.25; H, 7.60. Found: C, 62.36; H, 7.69.

3-Azido-5-O-benzoyl-3-deoxy-1,2-O-isopropylidene-4a-carba-α-DL-ribofuranose (21) and **5-O-Benzoyl-3-deoxy-1,2-O-isopropylidene-4a-carba-α-DL-*glycero*-pent-3-enofuranose (22)**

0.29 g (0.68 mmol) of crude triflate **18** was dissolved in 20 mL of DMF, 20 mL of ethanol/H_2O 4/1, or 20 mL of acetone, respectively. 0.76 g (10.3 mmol) of NaN_3 was added and stirred at 60 °C until complete turnover (see table 1). The solvent was removed under reduced pressure and the residue extracted with H_2O/CH_2Cl_2. The combined organic extracts were dried over Na_2SO_4, and the solvent was evaporated *in vacuo*. Flash chromatography (hexane/ethyl acetate 6/1 v/v) yielded 65-69 mg (30-32%) of azide **21** and 118-126 mg (63-67%) of the eliminated product **22** (see table 1).

Spectroscopic data of **21**: ^{1}H NMR ($CDCl_3$) δ 1.35 (s, 3H), 1.48-1.58 (m, 1H), 1.53 (s, 3H), 2.09 (dd, J = 14.1, 5.9 Hz, 1H), 2.69-2.80 (m, 1H), 3.06 (dd, J = 11.3, 4.7 Hz, 1H), 4.44-4.51 (ABX, J_{AB} = 11.5 Hz, J_{AX} = 5.1 Hz, 2H), 4.63-4.69 (m, 2H), 7.45 (m, 2H), 7.58 (m, 1H), 8.04 (m, 2H); ^{13}C NMR and DEPT ($CDCl_3$) δ 24.10 (q), 25.83 (q), 32.82 (t), 38.25 (d), 63.96 (d), 64.39 (t), 78.05 (d), 80.54 (d), 110.77 (s), 128.65 (d), 129.81 (d), 130.10 (s), 133.35 (d), 166.57

(s). Anal. calcd. for $C_{16}H_{19}N_3O_4$ (317.34): C, 60.56; H, 6.03; N, 13.24. Found: C, 60.46; H, 6.12; N, 13.02.

Spectroscopic data of **22**: ^{1}H NMR ($CDCl_3$) δ 1.35 (s, 3H), 1.44 (s, 3H), 2.56 (d, J = 19.2 Hz, 1H), 2.68 (dd, J = 19.2, 5.5 Hz 1H), 4.83 (t, J = 5.8 Hz, 1H), 4.89 (bs, 2H), 5.14 (d, J = 5.8 Hz, 1H), 5.82 (s, 1H), 7.45 (m, 2H), 7.58 (m, 1H), 8.06 (m, 2H); ^{13}C NMR and DEPT ($CDCl_3$) δ 25.97 (q), 27.79 (q), 39.44 (t), 63.21 (t), 78.37 (d), 85.39 (d), 110.26 (s), 127.20 (d), 128.59 (d), 129.92 (d), 130.30 (d), 133.40 (d), 141.44 (s), 166.32 (s); IR (NaCl) ν 2985, 2930, 2103, 1722, 1373, 1273, 1208, 1109, 1050, 866, 713 cm^{-1}. Anal. calcd. for $C_{16}H_{18}O_4$ (274.32): C, 70.06; H, 6.61. Found: C, 70.14; H, 6.69.

1,4-Anhydro-3-O-benzyl-2,5-dideoxy-5-isocyanato-4a-carba-DL-*erythro*-pent-1-enit (23)

46.5 g (200 mmol) of carboxylic acid **5** was reacted as described for isocyanate **11** to yield after bulb-to-bulb distillation 41.7 g (91%) of isocyanate **23** as a colourless oil.

^{1}H NMR ($CDCl_3$) δ 2.29 (m, 1H), 2.24-2.34 (m, 1H), 2.45-2.66 (m, 1H), 3.39 (dd, J = 13.0, 7.0 Hz, 1H), 3.67 (dd, J = 13.0, 7.6 Hz, 1H), 4.57 (m, 1H), 4.59-4.66 (AB, J = 11.6 Hz, 2H), 6.02-6.10 (m, 2H), 7.32-7.43 (m, 5H); ^{13}C NMR and DEPT ($CDCl_3$) δ 35.25 (t), 42.82 (t), 43.21 (d), 71.47 (t), 82.63 (d), 122.85 (s), 127.61 (d), 127.69 (d), 128.20 (d), 130.67 (d), 135.10 (d), 138.73 (s); MS m/z (rel int %) 229 ($M^{+\cdot}$, 1), 201 (1), 173 (1), 138 (13), 123 (38), 107 (82), 91 (100), 79 (49), 65 (31), 56 (19), 51 (10), 39 (20); IR (NaCl) 3050, 2898, 2271, 1733, 1542, 1452, 1360, 1235, 1120, 1060, 1119, 866, 736, 698 cm^{-1}. Anal. calcd. for $C_{14}H_{15}NO_2$ (229.28): C, 73.34; H, 6.59; N, 6.11. Found: C, 73.43; H, 6.67; N, 5.97.

1,4-Anhydro-5-amino-3-O-benzyl-2,5-dideoxy-4a-carba-DL-*erythro*-pent-1-enit (24)

41.3 g (180 mmol) of isocyanate **23** was dissolved in 50 mL of tetrahydrofuran and 50 mL of water and reacted with 30.3 g (540 mmol) of KOH as described for amine **12**. Flash chromatography (hexane/ethyl acetate 2/1 v/v) yielded 31.5 g (86%) of amine **24** as colourless oil.

^{1}H NMR ($CDCl_3$) δ 1.49 (bs, 2H), 2.18 (m, 1H), 2.31 (m, 2H), 2.79 (dd, J = 12.6, 5.5 Hz, 1H), 3.00 (dd, J = 12.6, 7.6 Hz, 1H), 4.62 (AB, J = 11.9 Hz, 2H), 4.54 (m, 1H), 5.97 (m, 1H), 6.03 (m, 1H), 7.22-7.33 (m, 5H); ^{13}C NMR and DEPT ($CDCl_3$) δ 35.35 (t), 42.00 (t), 44.82 (d), 70.98 (t), 83.35 (d), 127.30 (d), 128.22 (d), 130.39 (d), 135.61 (d), 138.90 (s); MS m/z (rel int %) 204 (MH^+, 2), 138 (5), 108 (11), 95 (65), 91 (100), 80 (13), 66 (57), 51 (6), 31 (35); IR (NaCl) ν 3046, 2895, 1569, 1470, 1341, 1308, 1068, 735, 698, 607 cm^{-1}. Anal. calcd. for $C_{13}H_{17}NO$ (203.28): C, 76.81; H, 8.43; N, 6.89. Found: C, 76.93; H, 8.31; N, 6.80.

1,4-Anhydro-5-N-benzoylamino-3-O-benzyl-2,5-dideoxy-4a-carba-DL-*erythro*-pent-1-enit (25)

15.0 g (73.8 mmol) of amine **24** 13.4 mL (95.9 mmol) of dry triethylamine in 50 mL of CH_2Cl_2 were reacted with 10.3 mL (88.6 mmol) of benzoyl chloride as described for **13**. Flash chromatography (ethyl acetate/petrol ether 1/3 v/v) yielded 20.7g (91%) of benzamide **25** as colourless oil.

^{1}H NMR ($CDCl_3$) δ 2.31 (m, 1H), 2.42 (dd, J= 17.0, 7.9 Hz, 1H), 2.66 (m, 1H), 3.65 (dt, J= 13.7, 4.6 Hz, H-5), 3.81 (dt, J= 13.7, 7.0 Hz, 1H), 4.50 (d, J= 11.1 Hz, 1H), 4.63 (m, 1H), 4.67 (d, J= 11.1 Hz, 1H), 6.03 (m, 1H), 6.07 (m, 1H), 7.15 (bs, 1H), 7.23-7.53 (m, 10H); ^{13}C NMR and DEPT ($CDCl_3$) δ 34.87 (t), 39.68 (t), 40.94 (d), 71.64 (t), 85.20 (d), 126.89 (d), 127.99 (d), 128.06 (d), 128.42 (d), 128.68 (d), 129.67 (d), 131.10 (d), 134.90 (s), 136.40 (d), 138.54 (s), 167.23 (s); MS m/z (rel int %) 308 ($MH^{+\cdot}$, 1), 216 (4), 199 (26), 134 (16), 122 (12), 105 (100), 91 (33), 77 (58), 66 (10), 51 (14), 39 (10); IR (NaCl) ν 3340, 3051, 2894, 1644, 1530, 1487, 1295, 1227, 1120, 1059, 698, 668 cm^{-1}. Anal. calcd. for $C_{20}H_{21}NO_2$ (307.39): C, 78.15; H, 6.89; N, 4.56. Found: C, 78.28; H, 6.78; N, 4.66.

1,4-Anhydro-5-O-benzoyl-3-O-benzyl-2-deoxy-4a-carba-DL-*erythro*-pent-1-enit (27)

20.0 g (65.1 mmol) of benzamide **25** was reacted as described for the synthesis of **15** to yield after flash chromatography (hexane/ethyl acetate 19/1 v/v) 16.5 g (82%) of benzoate **27** as colourless oil.

^{1}H NMR ($CDCl_3$) δ 2.46 (m, 2H), 2.79 (dt, J= 7.3, 14.6 Hz, 1H), 4.50 (dd, J= 10.8, 7.6 Hz, 1H), 4.63 (m, 3H), 4.74 (dd, J= 10.8, 7.6 Hz, 1H), 6.05 (m, 1H), 6.09 (m, 1H), 7.27-7.61 (m, 8H), 8.11 (m, 2H); ^{13}C NMR and DEPT ($CDCl_3$) δ 34.93 (t), 41.17 (d), 64.75 (t), 71.7 (t), 82.96 (d), 127.58 (d), 127.64 (d), 128.45 (d), 129.71 (d), 130.81 (s), 131.00 (d), 132.89 (d), 135.20 (d), 138.96 (s), 166.72 (s); MS m/z (rel int %) 308 ($M^{+\cdot}$, 1), 279 (1), 202 (2), 156 (6), 142 (2), 122 (12), 105 (81), 91 (74), 80 (100), 66 (13), 51 (21), 39 (13); IR (NaCl) ν 2927, 1717, 1451, 1274, 1110, 711 cm^{-1}. Anal. calcd. for $C_{20}H_{20}O_3$ (308.38): C, 77.90; H, 6.54. Found: C, 78.06; H, 6.69.

1,4-Anhydro-3-O-benzyl-2-deoxy-4a-carba-DL-*erythro*-pent-1-enit (28)

5.0 g (16.2 mmol) of benzoate **27** or 4.0 g (16.2 mmol) of acetate **35**, respectively, was reacted with a freshly prepared solution of 0.1 g of sodium in 100 mL of dry methanol at room temperature. After complete turnover, gaseous CO_2 was bubbled through the reaction mixture. The solvent was removed *in vacuo*. Flash chromatography (petrol ether/ethyl acetate 3/1 v/v) yielded 3.2 g (97%) of alcohol **28** as a colourless oil.

^{1}H NMR ($CDCl_3$) δ 2.38-2.42 (m, 2H), 2.52-2.63 (m, 1H), 2.60-3.00 (bm, 1H), 3.77 (dd, J = 11.3, 6.8 Hz, 1H), 3.85 (dd, J = 11.3, 4.1 Hz, 1H), 4.54 (d, J = 11.8 Hz, 1H), 4.67 (d, J = 11.8 Hz, 1H), 4.69 (m, 1H), 5.94-5.98 (m, 1H), 6.06-6.10 (m, 1H), 7.29-7.39 (m, 5H); ^{13}C NMR and DEPT ($CDCl_3$) δ 37.08 (t), 42.91 (d), 63.07 (t), 71.84 (t), 85.75 (d), 127.78 (d), 127.94 (d), 128.71 (d), 129.77 (d), 136.47 (d), 138.67 (s); MS m/z (rel int %) 204 ($M^{+\cdot}$, 0.1), 188 (1), 107 (52), 91 (100), 80 (41), 67 (28), 51 (11), 39 (13); IR (NaCl) ν 3407, 2923, 2854, 1731, 1453, 1357, 1117, 1056, 1028, 735, 699 cm^{-1}. Anal. calcd. for $C_{13}H_{16}O_2$ (204.27): C, 76.44; H, 7.90. Found: C, 76.34; H, 8.04.

1,2-Anhydro-5-O-benzoyl-3-O-benzyl-4a-carba-α-DL-xylofuranose (29)

A mixture of 16.0 g (51.9 mmol) of olefin **27** and 11.6 g (67.4 mmol) of *m*-chloroperbenzoic acid (*m*-CPBA) in 200 mL of ethyl acetate was refluxed until complete turnover. The reaction mixture was washed with saturated aqueous $NaHCO_3$ solution (150 mL). The aqueous layer was reextracted with CH_2Cl_2 (3 x 100 mL). The combined organic extracts were dried over Na_2SO_4, and evaporated under reduced pressure. The residue was purified on silica gel (toluene/ethyl acetate 19/1 v/v) to yield 10.0 g (60%) of epoxide **29** as a colourless oil.

^{1}H NMR ($CDCl_3$) δ 1.64 (dd, J = 13.6, 10.7 Hz, 1H), 2.18 (dd, J = 13.6, 7.4 Hz, 1H), 2.40 (m, 1H), 3.56 (m, 2H), 4.16 (d, J = 5.4 Hz, 1H), 4.44 (dd, J = 10.7, 6.3 Hz, 1H), 4.52 (t, J = 10.7 Hz, 1H), 4.60-4.69 (AB, J = 11.7 Hz, 2H), 7.24-7.60 (m, 8H), 8.05 (m, 2H); ^{13}C NMR and DEPT ($CDCl_3$) δ 29.31 (t), 38.03 (d), 56.40 (2 x d), 63.33 (d), 73.16 (t), 78.00 (d), 127.99 (d), 128.48 (d), 128.57 (d), 129.65 (s), 130.44 (d), 138.09 (s), 166.34 (s); MS m/z (rel int %) 324 ($M^{+\cdot}$, 1), 218 (7), 202 (38), 145 (2), 122 (9), 105 (65), 91 (100), 77 (48), 65 (12), 51 (16), 39 (13); IR (NaCl) ν 3037, 2948, 1716, 1451, 1275, 1110, 1064, 1025, 840, 709 cm^{-1}. Anal. calcd. for $C_{20}H_{20}O_4$ (324.38): C, 74.06; H, 6.21. Found: C, 73.91; H, 6.14.

1,2-Anhydro-5-O-benzoyl-4a-carba-α-DL-xylofuranose (30)

9.5 g (29.3 mmol) of **29** was diluted with 50 mL of ethanol and about 80 mg of palladium on carbon (10%) was added. The reaction mixture was hydrogenated for 4 days at 60 bar in an autoclave. The catalyst was removed by filtration over a pad of Celite® 454 (Merck) and washed with ethanol. Evaporation of the solvent under reduced pressure and flash chromatography (ethyl acetate/hexane 1/3 v/v) yielded 5.80 g (84%) of alcohol **30** as colourless crystals.

mp 53-56 °C; ^{1}H NMR ($CDCl_3$, 200 MHz) δ 1.52-1.63 (m, 1H), 2.05-2.23 (m, 1H), 3.34 (d, J = 4.0 Hz, 1H), 3.54 (bs, 2H), 4.16-4.26 (m, 2H), 4.68 (dd, J = 11.2, 10.1 Hz, 1H), 7.45-7.61 (m, 3H), 8.00 (m, 2H); ^{13}C NMR and DEPT ($CDCl_3$, 200 MHz) δ 28.22 (t), 39.21 (d), 55.66 (d), 57.93 (d), 62.83 (t), 69.99 (d), 128.53 (d), 129.71 (d), 129.78 (d), 133.43 (d), 167.65 (s);

MS m/z (rel int %) 234 ($M^{+\cdot}$, 2), 205 (1), 162 (1), 122 (25), 122 (65), 105 (100), 94 (16), 83 (31), 77 (43), 66 (19), 51 (13). Anal. calcd. for $C_{13}H_{14}O_4$ (234.25): C, 66.66; H, 6.02. Found: C, 66.72; H, 5.91.

1,2-Anhydro-5-O-benzoyl-3-O-trifluoromethylsulphonyl-4a-carba-α-DL-xylofuranose (31)

500 mg (2.13 mmol) of alcohol **30** and 190 μL (2.23 mmol) of dry pyridine in 25 mL of dry CH_2Cl_2 were reacted with 360 μL (2.14 mmol) of trifluoromethanesulphonic anhydride as described for **10** to afford crude **31**, which was reacted immediately to azide **32**.

1,2-Anhydro-3-azido-5-O-benzoyl-3-deoxy-4a-carba-α-DL-ribofuranose (32)

782 mg (2.13 mmol) of crude **31** was dissolved in 15 mL of dry DMF, 1.39 g (21.3 mmol) of NaN_3 was added and stirred at room temperature for about 24 h. After complete turnover the reaction mixture was extracted with 0.5 N HCl, saturated aqueous $NaHCO_3$ solution, dried over Na_2SO_4, and evaporated *in vacuo*. Flash chromatography (hexane/ethyl acetate 9/1 v/v) yielded 0.32 g (58%) of azide **39** as colourless oil.

^{1}H NMR ($CDCl_3$, 200 MHz) δ 1.74 (ddd, J = 13.8, 9.6, 1.1 Hz, 1H), 2.26 (m, 1H), 2.38 (dd, J = 13.8, 7.6 Hz, 1H), 3.54 (m, 1H), 3.62 (d, J = 8.1 Hz, 1H), 3.69 (dd, J = 2.8, 1.6 Hz, 1H), 4.41 (d, J = 5.1 Hz, 1H), 7.46 (m, 2H), 7.59 (m, 1H), 8.03 (m, 2H); ^{13}C NMR and DEPT ($CDCl_3$) δ 29.74 (t), 30.95 (d), 54.08 (d), 57,48 (d), 64.02 (2 x C, d and t), 128.42 (d), 128.53 (d), 129.64 (d), 133.28 (d), 166.69 (s). Anal. calcd. for $C_{13}H_{13}N_3O_3$ (259.26): C, 60.23; H, 5.05; N, 16.21. Found: C, 60.31; H, 4.91; N, 15.98.

5-Acetylamino-1,4-anhydro-3-O-benzyl-2,5-dideoxy-4a-carba-DL-*erythro*-pent-1-enit (33)

15.0 g (73.8 mmol) of amine **24**, 13.4 mL (95.9 mmol) of dry triethylamine in 50 mL of CH_2Cl_2 were reacted with 8.4 mL (88.5 mmol) of acetic anhydride as described for **13** to yield after flash chromatography (ethyl acetate/petrol ether 1/4 v/v) 17.0g (94%) of acetamide **25** as colourless oil.

^{1}H NMR ($CDCl_3$) δ 1.78 (s, 3H), 2.11-2.20 (m, 1H), 2.27-2.36 (m, 1H), 2.42-2.49 (m, 1H), 3.35-3.49 (m, 1H), 4.42 (d, J = 11.7 Hz, 1H), 4.48 (m, 1H), 4.56 (d, J = 11.7 Hz, 1H), 5.88-5.92 (m, 1H), 5.95-5.99 (m, 1H), 6.35 (bm, 1H), 7.21-7.32 (m, 5H); ^{13}C NMR and DEPT ($CDCl_3$) δ 23.15 (q), 34.96 (t), 39.16 (t), 40.78 (d), 71.25 (t), 84.06 (d), 127.54 (d), 127.67 (d), 128.45 (d), 129.84 (d), 135.76 (d), 138.63 (s), 169.99 (s); MS m/z (rel int %) 246 ($MH^{+\cdot}$, 3), 216 (1), 154 (9), 137 (56), 106 (17), 95 (49), 91 (100), 78 (39), 73 (41), 66 (39), 60 (37), 51 (15), 43 (48); IR (NaCl) ν 3294, 3067, 2900, 1649, 1550, 1445, 1363, 1289, 1065, 736, 699,

603 cm^{-1}. Anal. calcd. for $C_{15}H_{19}ON_2$ (245.32): C, 73.44; H, 7.81; N, 5.71. Found: C, 73.49; H, 7.73; N, 5.68.

5-O-Acetyl-1,4-anhydro-3-O-benzyl-2-deoxy-4a-carba-DL-*erythro*-pent-1-enit (35)

17.0 g (69.3 mmol) of acetamide **33** was reacted in the same manner as described for **15** to yield after flash chromatography 12.7 g (74%) of acetate **35** as colourless oil.

^{1}H NMR and ^{13}C NMR data in accordance with literature [27]; Anal. calcd. for $C_{15}H_{18}O_3$ (246.31): C, 73.15; H, 7.37. Found: C, 73.24; H, 7.41.

5-O-Acetyl-1,2-anhydro-3-O-benzyl-4a-carba-α-DL-xylofuranose (36)

12.0 g (48.7 mmol) of acetate **35** was reacted with 10.9 g (63.3 mmol) of *m*-CPBA as described for **28** to yield 10.1 g (79%) of epoxide **36** as a colourless oil.

^{1}H NMR and ^{13}C NMR data in accordance with literature [24]; Anal. calcd. for $C_{15}H_{18}O_4$ (262.30): C, 68.69; H, 6.92. Found: C, 68.35; H, 6.84.

5-O-Acetyl-1,2-anhydro-4a-carba-α-DL-xylofuranose (37)

10.0 g (38.1 mmol) of benzyl ether **36** was hydrogenated as described for **30** to yield after flash chromatography (petrol ether/ethyl acetate 3/1 v/v) 5.55 g (85%) of alcohol **37** as white crystals.

mp 55-56 °C; ^{1}H NMR ($CDCl_3$, 200 MHz) δ 1.46 (ddd, J = 15.6, 12.8, 0.9 Hz, 1H), 1.96-2.10 (m, 2H), 2.05 (s, 3H), 3.20 (m, 1H), 3.47 (d, J = 2.5 Hz, 1H), 3.50 (s, 1H), 3.96 (dd, J = 11.4, 4.2 Hz, 1H), 4.16 (t, J = 4. Hz, 1H), 4.34 (dd, J = 11.4, 9.5 Hz, 1H); ^{13}C NMR and DEPT ($CDCl_3$) δ 21.00 (q), 28.22 (t), 38.82 (d), 55.74 (d), 57.91 (d), 62.43 (t), 69.98 (d), 172.28 (s). Anal. calcd. for $C_8H_{12}O_4$ (172.18): C, 55.81; H, 7.02. Found: C, 55.85; H, 6.91.

5-O-Acetyl-1,2-anhydro-3-O-trifluoromethylsulphonyl-4a-carba-α-DL-xylofuranose (38)

500 mg (2.90 mmol) of alcohol **37** and 260 μL (3.19 mmol) of dry pyridine in 25 mL of dry CH_2Cl_2 were reacted with 490 μL (2.90 mmol) of trifluoromethanesulphonic anhydride as described for **10** to afford crude **38**, which was reacted immediately to azide **39**.

5-O-Acetyl-1,2-anhydro-3-azido-3-deoxy-4a-carba-α-DL-ribofuranose (39)

880 mg (2.90 mmol) of crude **38** was reacted with 1.90 g (29 mmol) of NaN_3 in 20 mL of dry DMF as described for azide **32**. Flash chromatography (hexane/ethyl acetate 6/1 v/v) yielded 0.40 g (70%) of azide **39** as colourless oil.

^{1}H NMR ($CDCl_3$) δ 1.62 (dd, J = 14.0, 9.3 Hz, 1H), 2.08 (s, 3H), 2.07-2.18 (m, 1H), 2.29 (dd, J = 14.0, 7.8 Hz, 1H), 3.51 (s, 1H), 3.55 (d, J = 8.2 Hz, 1H), 3.64 (m, 1H), 4.12-4.16

(ABX, J_{AB} = 11.3 Hz, J_{AX} = 5.5 Hz, 2H); ^{13}C NMR and DEPT ($CDCl_3$) δ 21.01 (q), 29.93 (t), 37.21 (d), 54.23 (d), 57.65 (t), 63.97 (d), 64.58 (d), 170.81 (s). Anal. calcd. for $C_8H_{11}N_3O_3$ (197.19): C, 48.73; H, 5.62; N, 21.31. Found: C, 48.71; H, 5.51; N, 21.36.

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