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Synthesis of Methyl 5-azido-5-deoxy-2,3-*O*-isopropylidenecarba-α-D-*allo*-hexafuranuronate, the Sugar Part of Carbapolyoxins and Carbanikkomycins

H. Kapeller and H. Griengl*

Institute of Organic Chemistry, Technical University Graz, Stremayrgasse 16, A - 8010 Graz, Austria.

Abstract: The sugar part of carbapolyoxins and carbanikkomycins, methyl 5-azido-5-deoxy-2,3-*O*-isopropylidenecarba-α-D-*allo*-hexafuranuronate (**16**), was synthesised starting from enantiomerically enriched norborn-5-en-2-yl acetate (**2**). For the introduction of the hydroxy groups and the azido functionality the rigidity of the norbornene skeleton provided the regioselective attack of the reagents. For the key step in this synthesis, the *Baeyer-Villiger* oxidation of ketone **6**, a method was developed, which might either be used for the synthesis of Ohno's lactone **10** or the isomeric lactone **9.**

INTRODUCTION

The nikkomycins[1] and polyoxins[2] are a group of nucleoside antibiotics isolated from the fermentation broth of *Streptomyces tendae* and *S. cacaoi ssp. asoensis*. These compounds are potent chitin synthetase inhibitors and exhibit fungicidal, insecticidal and acaricidal activities.[3] The sugar part was shown to be a substituted 5-amino-5-deoxy-β-D-*allo*-hexafuranuronate (**1**), whilst the amino functionality is substituted with natural or unnatural aminoacids and position C-1 is substituted with various heterocyclic bases.

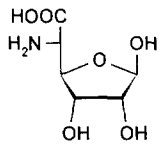

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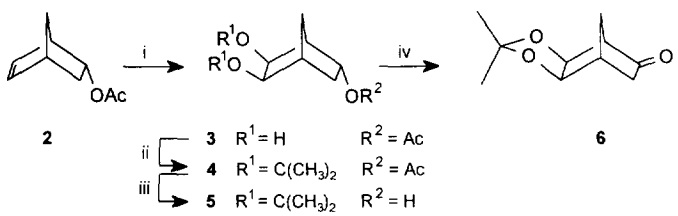
Fig 1. Structure of the sugar part of nikkomycins and polyoxins

RESULTS AND DISCUSSION

In continuation of our work on the synthesis of carbasugars[4] and of carbocyclic nucleosides, e.g. the partial synthesis of a carbocyclic nikkomycin analogue,[5] an enantio- and stereoselective approach to the sugar part of carbapolyoxins and carbanikkomycins will be presented here.

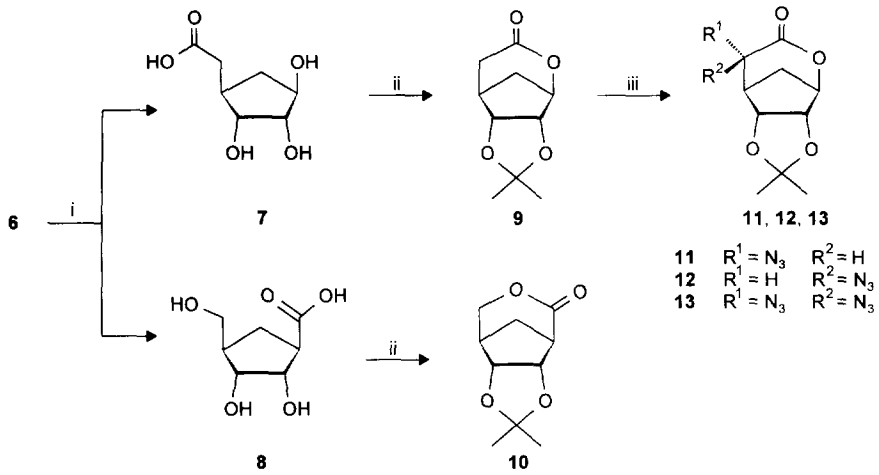
The enantiomerically enriched starting material for the synthesis of the sugar part of carbapolyoxins and carbanikkomycins, norborn-5-en-2-yl acetate (**2**), was easily obtained from racemic norborn-5-en-2-one.[6] The rigidity of the bicyclic skeleton[7] of acetate **2** allowed the stereoselective *exo cis*-dihydroxylation of the double bond with OsO_4/NMNO, followed by acetalisation of diol **3** and the isolation of the tricyclic intermediate **4** in 94% yield. Cleavage of the acetate was performed with MeOH/MeONa and *Swern*[8] oxidation led to the known[6,7,9] tricyclic ketone **6** in 83% yield.



Scheme 1. i) OsO_4/NMNO/acetone; ii) acetone/conc. HCl; iii) a) MeONa/MeOH, b) gaseous CO_2; iv) a) $(ClCO)_2$/DMSO/CH_2Cl_2/-80°C, b) Et_3N.

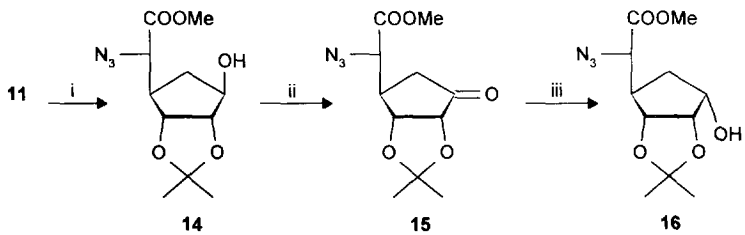
The key step in the synthesis was the *Baeyer-Villiger* oxidation of the tricyclic intermediate **6**. It was known, that norbornenone and norbornanone would give the expected oxygen insertion between the brigdehead atom and the carbonyl moiety, but for electron deficient systems, e.g. the 5,6-*cis*-dihydroxylated tricyclus **6**, the oxidation with peracids, e.g. *m*-chloroperbenzoic acid (*m*-CPBA), should give a mixture of Ohno's lactone[10] **10** and the expected lactone **9**. It was found, that the yield of isolated products depended on the pH value and the reaction temperature necessary for quantitative turnover.[11] A suspension of ketone **6** and *m*-CPBA in distilled water was vigorously stirred and warmed to 80° C within 3-4 hours. In neutral or alkaline medium (addition of 2 equivalents of $NaHCO_3$) the percentage of lactone **10** as compared to lactone **9** shifted to 70% in favour of Ohno's lactone **10**. In acidic medium with slow warming (and continuous dissolution of the reagent) the percentage of lactone **9** could be risen to 81%. By heating the reaction mixture *m*-CPBA was dissolved and reacted, and as a consequence the pH value was decreased to about pH 3. As a result the acetal moiety was cleaved and the products were a mixture of acids **7** and **8**, well dissolved in water, whilst the resulting *m*-chlorobenzoic acid was insoluble in cold water, and therefore easily to separate.

The mixture of acids **7** and **8** was treated after acetalisation with Et_3N and ethyl chloroformate to afford lactones **9** and **10**. Separation could be done by fractional crystallisation from cyclohexane/ethyl acetate, but for the introduction of the azide moiety the mixture of both lactones was used.



Scheme 2. i) *m*-CPBA/H_2O/80° C; ii) a) acetone/conc. HCl, b) Et_3N/ClC(O)OEt; iii) a) KHMDS/2,4,6-triisopropylbenzenesulphonyl azide, b) HOAc.

The introduction of the azide functionality was performed as described by *Evans*.[12] The corresponding enolate was generated with potassium bis(trimethylsilyl)amide (KHMDS), and the reagent of choice was found to be 2,4,6-triisopropylbenzenesulphonyl azide. With *p*-toluenesulphonyl azide or methanesulphonyl azide the isolated yields were lower because the bulkiness of the reagent was too week for the predominant regioselective attack from the *exo*-side of the tricyclic enolate. With 2,4,6-triisopropylbenzenesulphonyl azide only traces of the *endo*-azide **12** were formed.



Scheme 3. i a) MeONa/MeOH/0° C, b) gaseous CO_2; ii) PCC/ethyl acetate/80° C; iii) $NaBH_4$/MeOH.

For the formation of the geminal diazide **13** the amount of KHMDS was the decisive parameter. Under anhydrous conditions and with one equivalent of KHMDS only 3-5% of diazide **13** and 66% of the *exo*-azide were formed.

Lactone **11** was opened in MeOH with traces of a freshly prepared solution of sodium in MeOH. Strong alkaline conditions might cause racemisation at C-5. The oxidation of alcohol **14** was performed with PCC in refluxing ethyl acetate to yield ketone **15** in 85% yield. Reduction of **15** was performed with $NaBH_4$ in absolute MeOH to give carbasugar **16,** readily substituted and protected for syntheses of various polyoxins and nikkomycins. Reduction of the azide moiety[13] would give the aminoacid for subsequent syntheses of dipeptides. Derivatisation of the alcohol moiety with, e.g. triflates or mesylates, provides a highly reactive intermediate for the syntheses of carbanucleosides.[14]

EXPERIMENTAL

Melting points were obtained on a Büchi-Tottoli apparatus and are 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). Optical rotations were determined on a Jasco DIP 370 polarimeter. GC analysis was performed on a DANI 8500 gas chromatograph, column DB 1701. ^1H NMR and ^{13}C NMR spectra were recorded on a Bruker MSL 300 instrument (TMS as internal standard, δ-values are given in ppm, $CDCl_3$ as solvent). IR spectra were determined as films on NaCl or KBr on a Bomem Michelson 100 FT-spectrophotometer. MS spectra were recorded on a Kratos Profile. The elemental analyses were performed at the Institute of Organic Chemistry, Karl-Franzens University Graz. The enantiomeric excess of norbornenyl acetate **2** was determined by derivatisation with menthyl chloroformate and separation of the diastereomeric mixture by GC-analysis as 86.3% and assumed to be constant over all steps.

(1*R*,2*R*,3*S*,4*S*,5*R*)-2,3-Dihydroxybicyclo[2.2.1]hept-5-yl acetate (3)

12.5 g (82 mmol) of enantiomerically enriched norbornenyl acetate **2** (86.3% e.e.) were dissolved in 200 ml of acetone and treated with a catalytic amount (about 30 mg) of OsO_4 and 14.8 g (110 mmol) of *N*-methylmorpholine-*N*-oxide monohydrate (NMNO). The reaction mixture was stirred at room temperature until complete turnover (1-2 days). 2 g of $Na_2S_2O_3$ were added to reduce and precipitate OsO_4 and the solvent

was removed *in vacuo*. Coevaporation with toluene (3 x 100 ml) yielded 16.4 g (107%) of crude diol **3** as viscous oil. Further purification was not necessary for the following *trans*-acetalysation step. An analytic sample was purified by bulb to bulb distillation.

$[\alpha]_D^{20}$ = -8.15° (c 1.71, CH_2Cl_2); ^1H NMR ($CDCl_3$) δ 0.85 (dt, *J* = 13.8, 3.5 Hz, 1H), 1.20 (d, *J* = 11.1 Hz, 1H), 1.80 (dt, *J* = 11.1, 1.5 Hz, 1H), 1.99 (s, 3H), 2.01 (ddd, *J* = 13.8, 5.2, 10.4 Hz, 1H), 2.10-2.14 (m, 1H), 2.38 (d, *J* = 3.5 Hz, 1H), 3.70 (bs, 1H), 3.76 (d, *J* = 5.5 Hz, 1H), 3.85 (bs, 1H), 4.17 (d, *J* = 5.5 Hz, 1H), 4.87 (dt, *J* = 10.4, 4.1 Hz, 1H); ^{13}C NMR and DEPT ($CDCl_3$) δ 21.12 (q), 30.97 (t), 32.75 (t), 43.39 (d), 47.16 (d), 68.37 (d), 73.14 (d), 74.04 (d), 171.23 (s); IR (NaCl) ν 3381, 2963, 1727, 1374, 1251, 1147, 1039, 967, 942 cm^{-1}; Anal. Calcd for $C_9H_{14}O_4$ (186.21): C, 58.05; H, 7.58. Found: C, 57.61; H, 7.64.

(1*R*,2*R*,6*S*,7*S*,8*R*)-4,4-Dimethyl-3,5-dioxatricyclo[5.2.1.$0^{2,6}$]dec-8-yl acetate (4)

16.4 g of the crude diol **3** were dissolved in 200 ml of acetone, treated with conc. HCl until pH 1, and stirred at room temperature until complete turnover (1-3 h). Saturated aqueous $NaHCO_3$ was added to neutralise HCl and the solvent was evaporated *in vacuo*. The resulting oil was extracted with H_2O/CH_2Cl_2, the organic layer was dried (Na_2SO_4), and concentrated under reduced pressure. Flash chromatography (petrol ether/ethyl acetate 9/1 v/v) yielded 18.6 g (94%, calculated from olefin **2**) of compound **4** as a colourless oil.

$[\alpha]_D^{20}$ = -4.50° (c 2.43, CH_2Cl_2); ^1H NMR ($CDCl_3$) δ 0.80 (dt, *J* = 14.0, 3.6 Hz, 1H), 1.15 (d, *J* = 10.8 Hz, 1H), 1.30 (s, 3H), 1.43 (s, 3H), 1.69-1.74 (m, 1H), 2.00 (s, 3H), 2.06 (ddd, *J* = 14.0, 10.3, 5.3 Hz, 1H), 2.45 (d, *J* = 5.3 Hz, 1H), 2.53 (d, *J* = 4.2 Hz, 1H), 4.11 (d, *J* = 5.4 Hz, 1H), 4.46 (d, *J* = 5.4 Hz, 1H), 4.56 (dt, *J* = 10.3, 4.2 Hz, 1H); ^{13}C NMR and DEPT ($CDCl_3$) δ 21.04 (q), 24.37 (q), 25.74 (q), 30.74 (t), 31.78 (t), 40.65 (d), 44.37 (d), 72.49 (d), 76.86 (d), 81.75 (d), 108.93 (s), 170.68 (s); IR (KBr) ν 2970, 1737, 1373, 1242, 1205, 1052, 1028, 889, 860 cm^{-1}; Anal. Calcd for $C_{12}H_{18}O_4$ (226.27): C, 63.70; H, 8.02. Found: C, 63.09; H, 8.06.

(1*R*,2*R*,6*S*,7*S*,8*R*)-4,4-Dimethyl-3,5-dioxatricyclo[5.2.1.$0^{2,6}$]decan-8-ol (5)

17.0 g (75 mmol) of acetate **4** were dissolved in 200 ml of dry MeOH and treated with a freshly prepared solution of 0.1 g sodium in 10 ml of dry MeOH at room temperature. After complete turnover the reaction mixture was neutralised with CO_2 and evaporated *in vacuo*. The resulting oil was extracted with H_2O/CH_2Cl_2, the organic layer was dried (Na_2SO_4), and concentrated under reduced pressure. Flash chromatography (petrol ether/ethyl acetate 4/1 v/v) and bulb to bulb distillation yielded 13.4 g (97%) of alcohol **5** as a colourless oil.

$[\alpha]_D^{20}$ = +5.73° (c 1.57, CH_2Cl_2); ^1H NMR ($CDCl_3$) δ 0.73 (dt, *J* = 13.5, 3.4 Hz, 1H), 1.10 (d, *J* = 10.6Hz, 1H), 1.30 (s, 3H), 1.43 (s, 3H), 1.64-1.68 (m, 1H), 1.97 (ddd, *J* = 13.5, 5.3, 10.1 Hz, 1H), 2.15-2.25 (bs, 1H),

2.20 (d, J = 5.3 Hz, 1H), 2.35 (d, J = 4.1 Hz, 1H), 4.13 (d, J = 5.5 Hz, 1H), 4.22 (dt, J = 10.1, 4.1 Hz, 1H), 4.63 (d, J = 5.5 Hz, 1H); ^{13}C NMR and DEPT ($CDCl_3$) δ 24.17 (q), 25.56 (q), 31.08 (t), 33.70 (t), 40.93 (d), 46.36 (d), 69.80 (d), 76.62 (d), 81.65 (d), 108.41 (s); HRMS: $M^{+\cdot}$ not found, $M^{+\cdot}$ - CH_3: Calcd: 169.08647, Found: 169.08349; IR (KBr) ν 3419, 2961, 1376, 1271, 1206, 1160, 1048, 1022, 885, 855 cm^{-1}; Anal. Calcd for $C_{10}H_{16}O_3$ (184.23): C, 65.19; H, 8.75. Found: C, 64.75; H, 8.86.

(1*R*,2*R*,6*S*,7*R*)-4,4-Dimethyl-3,5-dioxatricyclo[5.2.1.0^{2,6}]decan-8-one (6)

6.6 ml (93 mmol) of dry dimethyl sulphoxide were dissolved in 300 ml of dry CH_2Cl_2 and cooled to -80° C internal temperature. 7.6 ml (87 mmol) of oxalyl chloride were dissolved in 100 ml of CH_2Cl_2 and added within 1 h with good mechanical stirring and under dry nitrogen. After half an hour 12.8 g (70 mmol) of alcohol **5** were added within 10 min and stirred at -80° C for 15 min. After cooling to -110° C 26.5 ml (190 mmol) of dry Et_3N were added to the well stirred solution. Caution: The internal temperature rises dramatically (to about -10° C) and 26 g of Et_3N·HCl precipitate!

100 ml of water were added and the organic layer extracted with 1 N HCl and saturated aqueous $NaHCO_3$, dried (Na_2SO_4), and concentrated under reduced pressure. Flash chromatography (petrol ether/ethyl acetate 4/1 v/v) and recrystallisation from petrol ether yielded 11.0 g (86%) of ketone **6**.

$[\alpha]_D^{20}$ = +102.75° (c 1.46, CH_2Cl_2); mp 96-7°C; ^{1}H NMR and ^{13}C NMR were in accordance with the literature;[9] MS m/z (rel int %) 182 ($M^{+\cdot}$, 0.5), 167 (100), 153 (6), 125 (47), 107 (60), 95 (42), 82 (7), 79 (48), 67 (28), 59 (24), 55 (47), 43 (55), 39 (31); IR (KBr) ν 2989, 2929, 1750, 1460, 1375, 1271, 1208, 1162, 1057, 869, 807 cm^{-1}; Anal. Calcd for $C_{10}H_{14}O_3$ (182.22): C, 65.92; H, 7.74. Found: C, 65.98; H, 7.54.

5-Deoxy-2,3-*O*-isopropylidenecarba-β-D-*ribo*-hexafuranurono-1,6-lactone (9)

10.0 g (55 mmol) of ketone **6** were dissolved in 2.5 l of water and 22.1 g (70 mmol) of *m*-chloroperbenzoic acid (55%) were added in one portion. The reaction mixture was warmed to 80° C, and stirring was continued until complete turnover (3-4 h). The reaction mixture was concentrated under reduced pressure to a volume of about 250 ml, the precipitated excess of *m*-CPBA and produced *m*-chlorobenzoic acid was filtered off, and washed with cold water. The solution was concentrated to a volume of 100 ml, cooled to 0° C and the precipitate was filtered off again. The aqueous solution was evaporation to dryness to yield a mixture of acid **7** and acid **8** as viscous oil.

300 ml of acetone and 1 ml of conc. HCl were added and stirred at 50° C until acetalisation was complete. To the solution 22.6 ml (163 mmol) of Et_3N and after 10 min 6.65 ml (70.6 mmol) of ethyl

chloroformate were added and stirring was continued for 12 h. The reaction mixture was concentrated to 50 ml, diluted with 300 ml of ethyl acetate and 100 ml of petrol ether, washed with 1 N HCl and saturated aqueous $NaHCO_3$, dried (Na_2SO_4), and evaporated to dryness. Flash chromatography yielded 9.7 g (90%) of a mixture of lactones **9** and **10**. The ratio of **9** to **10** was 81% to 19% (determined by gaschromatographic separation) in favour of lactone **9**. Separation could be done by fractional crystallisation from cyclohexane/ethyl acetate, but for the following transformation the mixture of both lactones was used.

$[\alpha]_D^{20}$ = -14.70° (c 1.65 , CH_2Cl_2); mp 103-5°C; ^{1}H NMR ($CDCl_3$) δ 1.27 (s, 3H), 1.40 (s, 3H), 1.80 (d, *J* = 13.3 Hz, 1H), 2.08-2.15 (m, 1H), 2.45-2.52 (m, 2H), 2.71-2.80 (m, 1H), 4.51 (m, 1H), 4.58 (m, 1H), 4.62 (m, 1H); ^{13}C NMR and DEPT ($CDCl_3$) δ 23.98 (q), 25.77 (q), 29.35 (t), 36.14 (t), 36.72 (d), 80.95 (t), 82.76 (d), 83.45 (d), 110.98 (s), 168.03 (s); IR (KBr) ν 2988, 1738, 1376, 1331, 1198, 1175, 1062, 926, 894, 855, 836 cm^{-1}; Anal. Calcd for $C_{10}H_{14}O_4$ (198.22): C, 60.59; H, 7.12. Found: C, 60.29; H, 7.25.

5-Azido-5-deoxy-2,3-*O*-isopropylidenecarba-β-D-*allo*-hexafuranurono-1,6-lactone (11) and **5,5-Diazido-5-deoxy-2,3-O-isopropylidenecarba-β-D-*ribo*-hexafuranurono-1,6-lactone (13)**

Under dry nitrogen 6.0 g of the mixture of lactones **9** and **10** (81% of lactone **9** = 24.2 mmol) were dissolved in 250 ml of dry THF, and cooled to -80° C internal temperature. 58 ml of potassium bis(trimethylsilyl)amide (KHMDS) solution (0.5 M in toluene = 29 mmol, supplier: Aldrich) were added and the reaction mixture was allowed to warm to room temperature within 50 min. The reaction was cooled again to -80° C and 8.24 g (26.6 mmol) of 2,4,6-triisopropylbenzenesulphonyl azide were added in one portion. After 10 min 13.8 ml (315 mmol) of acetic acid were added and stirring was continued at room temperature for 1 h. 315 ml of 1 M K_2HPO_4/KH_2PO_4 buffer solution (pH 7.00) were added and stirred for 15 min. The organic layer was separated, extracted with saturated aqueous $NaHCO_3$, dried (Na_2SO_4), and concentrated *in vacuo*. Flash chromatography yielded 4.6 g (79%) of azide **11** as colourless oil and 0.34 g (5.8%) of diazide **13** as colourless crystals.

Spectroscopic data of compound **11**: $[\alpha]_D^{20}$ = -140.25° (c 0.5, CH_2Cl_2); ^{1}H NMR ($CDCl_3$) δ 1.30 (s, 3H), 1.43 (s, 3H), 2.02 (m, 2H), 2.48 (m, 1H), 4.05 (m, 1H), 4.55 (d, *J* = 5.3 Hz, 1H), 4.61 (d, *J* = 5.3 Hz, 1H), 4.66 (m, 1H); ^{13}C NMR and DEPT ($CDCl_3$) δ 24.07 (q), 25.82 (q), 26.38 (t), 43.18 (d), 61.47 (d), 80.79 (d), 81.72 (d), 82.27 (d), 111.93 (s), 166.06 (s); MS m/z (rel int %) 239 ($M^{+\cdot}$, <0.1), 224 ($M^{+\cdot}$-CH_3, 91), 194 (4), 97 (7), 81 (25), 69 (13), 59 (23), 43 (100); IR (KBr) ν 2987, 2935, 2111, 1736, 1447, 1377, 1266, 1209, 1077, 1051, 919, 868, 737 cm^{-1}; Anal. Calcd for $C_{10}H_{13}N_3O_4$ (239.23): C, 50.21; H, 5.48; N, 17.56. Found: C, 50.22; H 5.50; N, 17.48.

Spectroscopic data of compound **13**: decomposition at 135° C; ^{1}H NMR ($CDCl_3$) δ 1.32 (s, 3H), 1.44 (s, 3H), 2.20 (m, 2H), 2.55 (m, 1H), 4.61 (d, J = 5.4 Hz, 1H), 4.68 (m, 1H), 4.84 (d, J = 5.4 Hz, 1H); ^{13}C NMR and DEPT ($CDCl_3$) δ 24.13 (q), 25.86 (q), 28.00 (t), 47.38 (d), 78.77 (d), 79.52 (s), 81.68 (d), 82.53 (d), 111.99 (s), 163.38 (s); IR (KBr) ν 2971, 2132, 2084, 1737, 1375, 1250, 1211, 1169, 1050, 1028, 948, 896 cm^{-1}; Anal. Calcd for $C_{10}H_{12}N_6O_4$ (280.24): C, 42.86; H, 4.32; N, 29.99. Found: C, 43.14; H, 4.24; N, 30.13.

Methyl 5-azido-5-deoxy-2,3-*O*-isopropylidenecarba-β-D-*allo*-hexafuranuronate (14)

4.0 g (16.7 mmol) of lactone **11** were dissolved in 50 ml of dry MeOH. 0.1 ml of a freshly prepared solution of 0.1 g sodium in 10 ml of dry MeOH was added and the reaction mixture was stirred for 3-4 h at room temperature. CO_2 was bubbled through the slightly yellow solution for 1 min and the solvent was evaporated *in vacuo* at 20° C bath temperature. The resulting oil was diluted with 50 ml of CH_2Cl_2, washed once with H_2O, dried over Na_2SO_4 and concentrated to dryness. Column chromatography (petrol ether/ethyl acetate 6/1 v/v) yielded 4.0 g (88%) of ester **14** as colourless oil.

$[\alpha]_D^{20}$ = -43.71° (c 0.40, CH_2Cl_2); ^{1}H NMR ($CDCl_3$) δ 1.18-1.25 (m, 1H and s, 3H), 1.39 (s, 3H), 1.53 (dt, J = 14.2, 4.0 Hz, 1H), 2.22 (ddd, J = 14.2, 5.3, 8.0 Hz, 1H), 2.41-2.49 (m, 1H), 3.00 (bs, 1H), 3.78 (s, 3H), 3.94 (d, J = 9.6 Hz, 1H), 4.16 (m, 1H), 4.39 (d, J = 6.0 Hz, 1H), 4.63 (dd, J = 6.0, 2.0 Hz, 1H); ^{13}C NMR and DEPT ($CDCl_3$) δ 24.61 (q), 26.91 (q), 34.84 (t), 46.83 (d), 52.90 (q), 64.10 (d), 76.75 (d), 82.43 (d), 86.95 (d), 111.53 (s), 170.51 (s); MS m/z (rel int %) ($M^{+\cdot}$ not detected), 256 ($M^{+\cdot}$ - CH_3, 100), 224 (9), 213 (5), 186 (10), 153 (5), 126 (23), 108 (18), 99 (31), 82 (15), 59 (40), 43 (39); IR (KBr) ν 3436, 2986, 2936, 2107, 1740, 1440, 1376, 1211, 1055, 1013, 865 cm^{-1}; Anal. Calcd for $C_{11}H_{17}N_3O_5$ (271.27): C, 48.70; H, 6.32; N, 15.49. Found: C, 48.20; H, 6.28: N, 15.67.

Methyl 5-azido-5-deoxy-2,3-*O*-isopropylidenecarba-D-*allaro*-1,4-lactone (15)

4.0 g (14.7 mmol) of alcohol **14** were dissolved in 150 ml of ethyl acetate, 6.35 g (29.5 mmol) of pyridinium chlorochromate (PCC) were added and the reaction mixture was refluxed until complete turnover (5-8 h). 50 ml of diethyl ether were added and filtered over a pad of silica gel (about 10 g). Exhaustive washing of the pad of silica gel with diethyl ether, evaporation of the combined organic extracts to dryness, and flash chromatography (petrol ether/ethyl acetate 9/1 v/v) yielded 3.25 g (82%) of ketone **15** as a colourless oil, which crystallised slowly on standing.

$[\alpha]_D^{20}$ = -169.36° (c 0.50, CH_2Cl_2); ^{1}H NMR ($CDCl_3$) δ 1.32 (s, 3H), 1.42 (s, 3H), 2.18 (d, J = 17.8 Hz, 1H), 2.86 (dd, J = 17.8, 9.7 Hz, 1H), 2.93-2.98 (m, 1H), 3.89 (s, 3H), 4.24 (d, J = 3.2 Hz, 1H), 4.33 (d,

J = 5.5 Hz, 1H), 4.52 (d, J = 5.5 Hz, 1H); ^{13}C NMR and DEPT ($CDCl_3$) δ 24.74 (q), 26.81 (q), 38.07 (t), 39.33 (d), 53.35 (q), 64.69 (d), 78.89 (d), 79.08 (d), 112.08 (s), 169.37 (s), 211.28 (s); MS m/z (rel int %) 269 ($M^{+\cdot}$, 0.1), 254 (3), 212 (3), 184 (11), 156 (4), 141 (4), 127 (24), 100 (47), 96 (25), 85 (20), 69 (58), 59 (100), 43 (62); IR (KBr) ν 2963, 2117, 1749, 1379, 1214, 1155, 1051, 1019, 984, 859 cm^{-1}; Anal. Calcd for $C_{11}H_{15}N_3O_5$ (269.26): C, 49.07; H, 5.61; N, 15.61. Found: C, 48.65; H, 5.60; N, 15.82.

Methyl 5-azido-5-deoxy-2,3-*O*-isopropylidenecarba-α-D-*allo*-hexafuranuronate (16)

3.0 g (11.1 mmol) of ketone **15** were dissolved in 60 ml of dry MeOH and 0.17 g (4.45 mmol) of $NaBH_4$ were added. The reaction mixture was stirred at room temperature until complete turnover (about 24 h). 10 ml of 0.5 N HCl were added and stirring was continued for 15 min. 100 ml of CH_2Cl_2 and about 5 g of NaCl were added, the organic layer was separated, washed with saturated aqueous $NaHCO_3$, dried (Na_2SO_4), and concentrated *in vacuo*. Flash chromatography (petrol ether/ethyl acetate 7/1 v/v) yielded 2.8 g (93%) of the inverted alcohol **16** as a colourless oil.

$[\alpha]_D^{20}$ = -51.58° (c 1.80, CH_2Cl_2); ^{1}H NMR ($CDCl_3$) δ 1.34 (s, 3H), 1.51 (s, 3H), 1.74 (dt, J = 13.5, 6.8 Hz, 1H), 1.99 (dt, J = 13.5, 5.9 Hz, 1H), 2.54 (bs, 1H), 2.66 (m, 1H), 3.82 (s, 3H), 3,86 (d, J = 6.4 Hz, 1H), 4.18 (m, 1H), 4.50 (m, 2H); ^{13}C NMR and DEPT ($CDCl_3$) δ 24.70 (q), 26.37 (q), 36.20 (t), 44.43 (d), 52.90 (q), 63.98 (d), 70.68 (d), 80.16 (d), 81.83 (d), 113.09 (s), 169.99 (s); MS m/z (rel int %) 271 ($M^{+\cdot}$ not detected), 256 ($M^{+\cdot}$ - CH_3, 71), 213 (4), 186 (5), 170 (7), 153 (9), 126 (15), 108 (15), 99 (42), 84 (61), 71 (17), 59 (83), 49 (39), 43 (100), 28 (67); IR (KBr) ν 2949, 2109, 1743, 1439, 1377, 1265, 1209, 1074, 868 cm^{-1}; Anal. Calcd for $C_{11}H_{17}N_3O_5$ (271.27): C, 48.70; H, 6.32; N, 15.49. Found: C, 48.45; H, 6.29; N, 15.52.

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