Chain Extension of Carbohydrates VI[1]. Synthesis of the Two C-6 Epimers of the 6-Acetylamino-4,6-dideoxyheptopyranosiduronic Acid Present in Amipurimycin by Means of Stereocontrolled Ethynylation of Methyl 2,3-Di-*O*-benzyl-4-deoxy-α-D-*xylo*-hexodialdo-1,5-pyranoside

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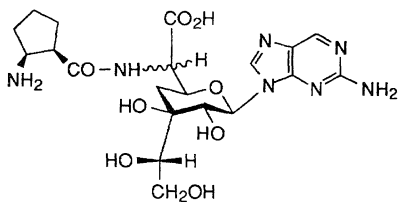
The two C-6 epimers of 6-acetylamino-4,6-dideoxy-heptopyranosiduronic acid present in amipurimycin were prepared by selective reactions from methyl 2,3-di-*O*-benzyl-4,6,7,8-tetradeoxy-α-L-*ido*-7-ynopyranoside (**4**) in which the ethynyl group was employed as a precursor of the carboxylic acid function. The masked amino group was introduced at C-6 by reaction of **4** with zinc azide in the presence of triphenylphosphine and diisopropyl azodicarboxylate. The resulting methyl 6-azido-2,3-di-*O*-benzyl-4,6,7,8-tetradeoxy-α-D-*gluco*-oct-7-ynopyranoside (**5**) was transformed into benzyl[6-(acetylamino)-2,3-di-*O*-benzyl-4,6-dideoxy-α-D-*gluco*-heptopyranosid]uronate (**7**) by two different sequences of reactions: (1) oxidative cleavage of the triple bond, benzylation, reduction of the azido group, *N*-acetylation or (2) reduction of the azido group, *N*-acetylation, oxidative cleavage of the triple bond and treatment with phenyldiazomethane. The second sequence of reactions was found to be more efficient (33% overall yield versus 13%). The configuration at C-6 was unambiguously confirmed by X-ray diffraction with a single crystal of **7**. Final hydrogenolysis of benzyl groups afforded methyl 6-(acetylamino)-4,6-dideoxy-α-D-*gluco*-heptopyranosiduronic acid (**9**). A Mitsunobu reaction on acetylenic alcohol **4** followed by saponification afforded the C-6 epimer **11**. The same sequences of reactions was applied to **11** and methyl 6-(acetylamino)-4,6-dideoxy-α-L-*ido*-heptopyranosiduronic acid (**16**) was obtained.

The unusual naturally occurring α-aminocarboxylic acids are mainly produced by various microorganisms and have revealed to interfere with biochemical pathways of other organisms. These derivatives were used as patterns for the design of compounds targeted to the control of plant growth and diseases.[2]

Among such derivatives, amipurimycin was first isolated and characterized as a 2-aminopurine nucleoside by a Japanese group in 1976.[3] Although amipurimycin showed a strong curative effect against rice blast disease together with a potent activity against *Pyricularia Oryzae*,[4] its structure was elucidated several years later[5] and is depicted in Chart 1. However the absolute configuration of amipurimycin as well as the stereochemistry at C-6′ position remain unclear.

The structural complexity of this molecule, as well as the goal of studying structure–activity relationships, prompted us to an exploration of total synthesis of amipurimycin.



1 Amipurimycin

Chart 1.

We report herein the syntheses of the D-*gluco* and L-*ido* isomers of the 6-amino-4,6-dideoxyhepturonic acid present in amipurimycin. The stereocontrolled ethynylation of hexodialdo-1,5-pyranose derivatives[6] was recently shown to be a valuable tool for the construction of 6-amino-6-deoxyhepturonic acids of predictable configuration at C-6.[1]

This methodology was employed on methyl 2,3-di-*O*-benzyl-4-deoxy-α-D-*xylo*-hexodialdo-1,5-pyranoside **2** for the elongation of the chain at C-6 and the azido group was used as masked amino group. The carboxylic acid function could then be generated by oxidative cleavage of the triple bond

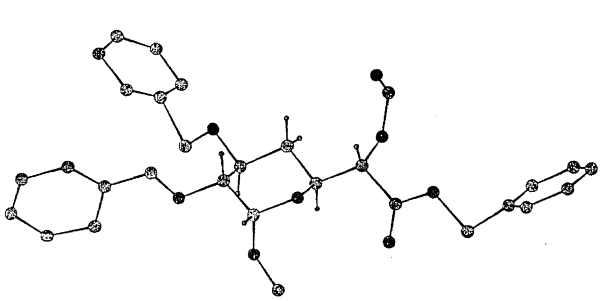
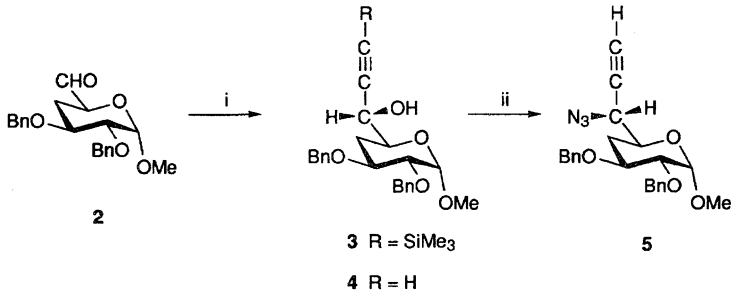
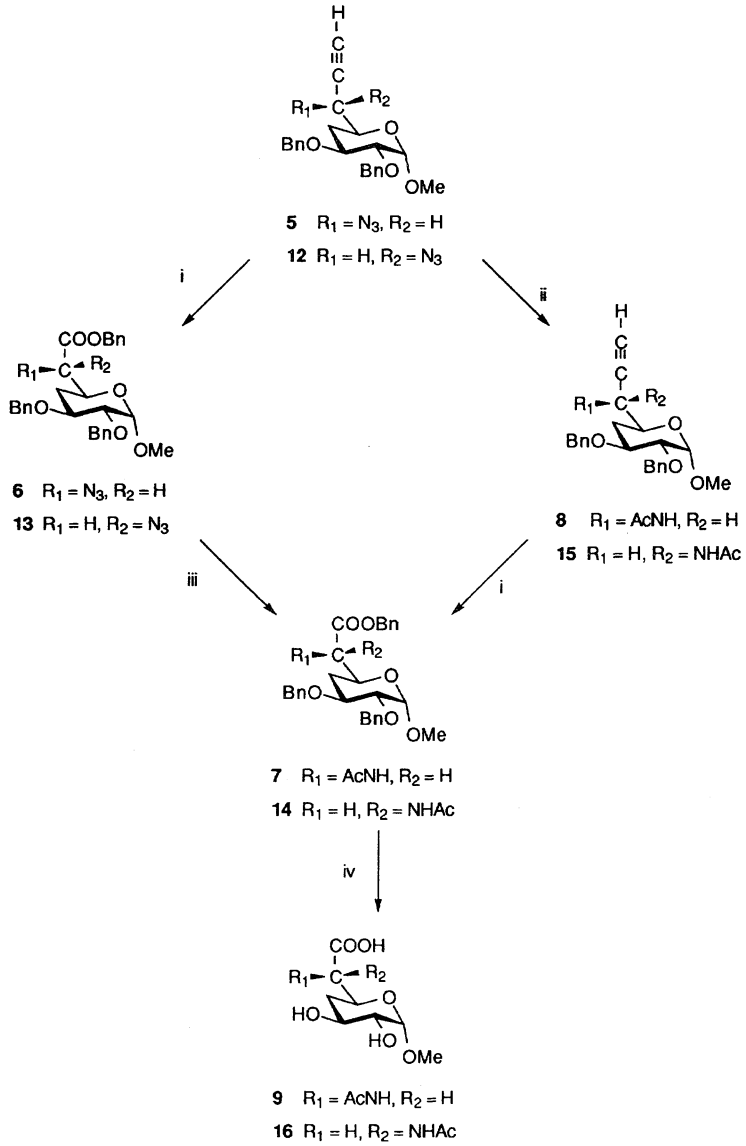


Fig. 1. Ortep representation of compound **7**.



Scheme 1. Reagents and conditions: (i)[8]; (ii) DIAD, $[Zn(N_3)_2(py)_2]$, PPh_3, PhMe (66%).

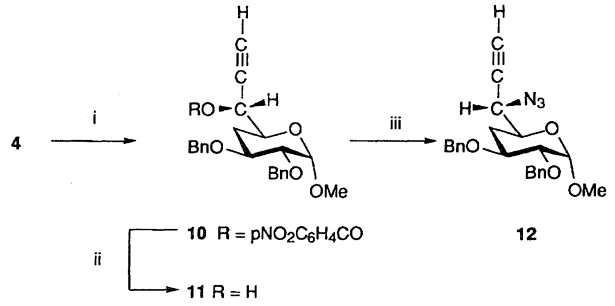


Scheme 2. Reagents and conditions: (i) OsO_4, $NaIO_4$, THF–H_2O then $PhCHN_2$; (ii) $HS(CH_2)SH$, Et_3N, MeOH then Ac_2O, pyridine (63%); (iii) CH_3COSH (65%); (iv) 10% Pd/C, MeOH (100%).

prior to the reduction of the azido group. Alternatively cleavage of the acetylenic bond could be performed after creation and protection of the amino group.

Results and Discussion

When **2**[7] was treated with a fourfold excess of the Grignard reagent of (trimethylsilyl)acetylene in diethyl ether in the presence of a large excess of magnesium bromide at low temperature, only **3** was formed and isolated in good yield.[8] The experimental conditions for the addition are of prime importance to ensure this stereospecificity.[6] Quantitative desilylation by tetrabutylammonium fluoride afforded the ace-



Scheme 3. Reagents and conditions: (i) p-$NO_2C_6H_4$-COOH, DEAD, PPh_3, THF (96%); (ii) K_2CO_3, MeOH (99%); (iii) DIAD, $[Zn(N_3)_2(py)_2]$, PPh_3, PhMe (90%).

tylenic alcohol **4** in 80% overall yield. Due to mechanistic considerations the stereochemical outcome of the reaction was expected to afford the L-*ido* isomer. However although it was supported by analogous results[6] this forecast remained to be proved. This was unambiguously carried out by means of X-ray crystallographic studies on a crystalline intermediate later in the synthesis.

Azidation of **4** was performed under Mitsunobu conditions in the presence of diazidobis(pyridine)zinc[9] and **5** was obtained in 66% yield (Scheme 1). As indicated in the ^{1}H NMR spectrum (signal at $\delta = 2.60$ ppm for H-8) the acetylene moiety was still present.

For the transformation of **5** into the protected aminoacid **9** two different routes were explored (Scheme 2). First the oxidative cleavage of the triple bond was realized by means of the osmium tetraoxide–sodium periodate combination; the carboxylic acid was not isolated but rather directly reacted with phenyldiazomethane[10] to afford the benzyl ester **6**. The benzyl ester was chosen for simultaneous final deprotection of all hydroxyl groups at the end of the synthesis. Surprisingly, although we have previously obtained satisfactory results when using an analogous sequence in the miharamycin series,[1] the yield observed for **6** could not exceed 20%. Further transformation of the azido group into the acetylamino functionality was readily achieved by reaction with thioacetic acid,[11] but the overall yield in the acetamidobenzyl ester **7** from compound **5** was only 13%. In order to obtain better results we considered the transformation of the azido residue before oxidative cleavage of the triple bond. The reaction of the acetylenic azide **5** with propane-1,3-dithiol in the presence of triethylamine[12] followed by conventional acetylation afforded the acetylenic acetamide **8** in 63% yield. Then the oxidative cleavage of the triple bond was conducted as above and led to compound **7** in 53% yield. This last result seemed to point out the incompatibility of the azido group with the conditions necessary to the cleavage of the triple bond. However this route allowed us to obtain an overall yield of more than 33% for the preparation of the crystalline derivative **7** from the acetylenic azide **5**. At this stage, a crystallographic study was conducted on a single crystal of **7** and has established the configuration at C-6 to be *S* as shown in Fig. 1. Debenzylation of **7** to **9**, was quantitative.

To prepare the epimeric amino acid **16** the same sequence of reactions could be carried out from the L-*ido*-acetylenic azide **12**. The later was prepared from alcohol **4** by inversion of configuration at C-6 followed by introduction of the azido group on the epimeric acetylenic alcohol **11** (Scheme 3). A Mitsunobu reaction[13] on **4** with p-nitrobenzoic acid was followed by saponification to afford **11** in high yield. The replacement of the hydroxyl group by an azido group was done as above and gave **12** in 85% overall yield from **4**.

The reaction pathway depicted in Scheme 2 was used to prepare the acetylamino acid **16**. Once more it was more efficient to realize the transformation of the azido group before performing the oxidative cleavage of the triple bond. Indeed the 6-azido dideoxy benzyl ester **13** was obtained in only 25% yield from **12**, whereas by the other route the cleavage of the triple bond of **15** afforded **14** in 75% yield. Further debenzylation gave **16** in 93% yield.

At this stage the comparison of the ^{1}H NMR spectra of the epimeric amino acids **9** and **16** showed that only the signal of H-5 was significantly altered. The chemical shift of this proton was 4.1 ppm for the D-*gluco* isomer **9** whereas the corresponding signal for **16** appeared at 4.4 ppm. The $J_{5,6}$ coupling constant was 6.1 Hz for compound **9** versus 1.9 Hz for the L-*ido* epimer **16**.

Experimental

Melting point were measured with a Thomas–Hoover apparatus and are uncorrected. IR spectra were recorded with a Unicam spectrometer. ^{1}H NMR spectra were recorded on Bruker AM 200 or AM 250 spectrometers. Optical rotations were measured on a Perkin–Elmer 141 polarimeter in a 10 cm cell at 22 °C. Analytical TLC was performed on Merck aluminium precoated plates of silica gel 60 F-254 which detection by UV and by spraying with 6 equiv aq H_2SO_4 and heating about 2 min at 300 °C. Evaporation of solvents was carried out under reduced pressure at 40 °C. Merck silica gel 60 (300—400) and anhydrous solvents were employed for flash chromatography. Elemental analyses were performed at the Service de microanalyse of Pierre et Marie Curie University.

Methyl 6-Azido-2,3-di-*O*-benzyl-4,6,7,8-tetradeoxy-α-D-*gluco*-oct-7-ynopyranoside (5). Under an argon atmosphere alcohol **4**[8] (647 mg, 1.69 mmol) was dissolved in anhydrous toluene (5 mL). At room temperature PPh_3 (892 mg, 3.4 mmol), $[Zn(N_3)_2(py)_2]$ (400 mg, 1.3 mmol) and diisopropyl azodicarboxylate (DIAD, 0.69 mL, 3.4 mmol) were added. After stirring the mixture for 15 min at room temperature, the solvent was evaporated. Flash chromatography (hexane–EtOAc 8 : 1) gave **5** as a colorless syrup (453 mg, 66%): $[\alpha]_D^{20}$ +12° (*c* 1, $CHCl_3$); ^{1}H NMR (200 MHz, $CDCl_3$) $\delta = 1.6$ (ddd, 1H, H-4a), 2.15 (ddd, 1H, H-4b), 2.6 (d, 1H, H-8), 3.4 (s, 3H, OMe), 3.5 (dd, 1H, H-2), 3.9 (ddd, 1H, H-5), 3.95 (ddd, 1H, H-3), 4.05 (dd, 1H, H-6), 4.7 (d, 1H, H-1), 4.6—4.9 (m, 4H, CH_2Ph), 7.2—7.4 (m, 10H, Harom.); $J_{1,2} = 3.6$; $J_{2,3} = 9.4$; $J_{3,4a} = 11.1$; $J_{3,4b} = 5.1$; $J_{4a,4b} = 12.7$; $J_{4a,5} = 12.1$; $J_{4b,5} = 2.1$; $J_{5,6} = 2.3$; $J_{6,8} = 2.3$ Hz. Found: C, 67.65; H, 7.25; N, 10.40%. Calcd for $C_{23}H_{25}N_3O_4$: C, 67.79; H, 6.18; N, 10.31%.

Benzyl (Methyl 6-Azido-2,3-di-*O*-benzyl-4,6-dideoxy-α-D-*gluco*-heptopyranosid)uronate (6). To a solution of azide **5** (132 mg, 0.32 mmol) in THF (5 mL), water (3 mL), $NaIO_4$ (373 mg, 1.75 mmol) and an aqueous solution of OsO_4 (4%, 230 μL, 37 μmol) were successively added. The mixture was stirred at 45 °C. After 6 h further $NaIO_4$ (187 mg, 0.88 mmol) and aqueous solution of OsO_4 (4%, 230 μL, 37 μmol) were added and the mixture was stirred at

room temperature for 16 h. A 10% aqueous of $NaHSO_3$ (10 mL) and CH_2Cl_2 (10 mL) were added. The mixture was stirred at room temperature for 15 min and after decantation, the aqueous layer was extracted with CH_2Cl_2 (2×10 mL). The organic phase was dried ($MgSO_4$) and evaporated to give a black syrup. The crude product was dissolved in CH_2Cl_2 and a solution of phenyldiazomethane[10] in CH_2Cl_2 was added until completion of esterification. Excess of $PhCHN_2$ was destroyed with formic acid and the solvent was evaporated. After coevaporation with toluene, the crude residue was purified by flash chromatography. Elution with hexane/EtOAc 9 : 1 afforded **6** as a syrup (32 mg, 19%): $[\alpha]_D^{20}$ +18.6° (*c* 1, $CHCl_3$); ^{1}H NMR (200 MHz, $CDCl_3$) δ = 1.6 (ddd, 1H, H-4a), 2.1 (ddd, 1H, H-4b), 3.3 (s, 3H, OMe), 3.4 (ddd, 1H, H-2), 3.9 (m, 2H, H-3 and H-6), 4.1 (ddd, 1H, H-5), 4.6—4.2 (2d, 2H, H-1 and CH_2Ph), 4.65, 4.7, 4.85, and 5.3 (5d, 5H, CH_2Ph), 7.25—7.45 (m, 15H, Harom.); $J_{1,2}$ = 3.6; $J_{2,3}$ = 9.4; $J_{3,4a}$ = 11.2; $J_{3,4b}$ = 5.1; $J_{4a,4b}$ = 12.8; $J_{4a,5}$ = 12; $J_{4b,5}$ = 2.3; $J_{5,6}$ = 5.9; J_{AB} = 12.1—12.3 Hz.

Benzyl [Methyl 6-(Acetylamino)-2,3-di-*O*-benzyl-4,6-dideoxy-α-D-*gluco*-heptopyranosid]uronate (7). A: Compound **6** (30 mg, 58 μmol) was dissolved in CH_3COSH (150 μL) under an argon atmosphere and stirred at room temperature for 40 h. The solvent was evaporated, coevaporated with toluene and the residue purified by flash chromatography (toluene/acetone 10 : 1) to afford **7** (20 mg, 64.5%).

B: Treatment of **8** (179 mg, 0.42 mmol) by OsO_4 and $NaIO_4$ (179 mg, 0.42 mmol) by OsO_4 and $NaIO_4$ followed by esterification with phenyldiazomethane as described for **5** afforded **7** (170 mg, 53.5%): Mp 113 °C; $[\alpha]_D^{20}$ +42.6° (*c* 1.0, $CHCl_3$); ^{1}H NMR (200 MHz, $CDCl_3$) δ = 1.6 (ddd, 1H, H-4a), 2.0 (s, 3H, $COCH_3$), 2.1 (ddd, 1H, H-4b), 3.3 (s+dd, 4H, OMe and H-2), 3.85 (ddd, 1H, H-3), 3.95 (ddd, 1H, H-5), 4.6—4.62 (2d, 2H, H-1 and CH_2Ph), 4.65, 4.7, 4.8, and 5.25 (5d, 5H, CH_2Ph), 4.67 (dd, 1H, H-6), 7.2—7.4 (m, 15H, Harom.); $J_{1,2}$ = 3.5; $J_{2,3}$ = 9.5; $J_{3,4a}$ = 11.1; $J_{3,4b}$ = 5.0; $J_{4a,4b}$ = 12.9; $J_{4a,5}$ = 12.3; $J_{4b,5}$ = 2.3; $J_{5,6}$ = 3.9; $J_{6,NH}$ = 8.3; $J_{A,B}$ = 11.3—12.2 Hz. Found: C, 69.67; H, 6.51; N, 2.61%. Calcd for $C_{31}H_{35}NO_7$: C, 69.77; H, 6.61; N, 2.63%.

Methyl 6-(Acetylamino)-2,3-di-*O*-benzyl-4,6,7,8-tetradeoxy-α-D-*gluco*-oct-7-ynopyranoside (8). To a solution of azide **5** (372 mg, 0.91 mmol) in MeOH (4.6 mL), propane-1,3-dithiol (0.46 mL, 496 mg, 4.56 mmol) and triethylamine (0.63 mL, 458 mg, 4.53 mmol) were added under an argon atmosphere. After stirring for 4 h at 45 °C the reaction mixture was concentrated in vacuo and coevaporated with toluene. The residue was acetylated with acetic anhydride (1 mL) in pyridine (2 mL). The resulting product was purified by flash chromatography (elution with hexane/EtOAc 2 : 1 then 1.25 : 1) to yield **8** (242 mg, 63%): mp 134 °C (toluene–hexane); $[\alpha]_D^{20}$ +31° (*c* 1, $CHCl_3$); ^{1}H NMR (200 MHz, $CDCl_3$) δ = 1.72 (ddd, 1H, H-4a), 2.0 (s, 3H, $COCH_3$), 2.1 (ddd, 1H, H-4b), 2.3 (d, 1H, H-8), 3.35 (s, 3H, OMe), 3.5 (dd, 1H, H-2), 3.8 (ddd, 1H, H-5), 3.95 (ddd, 1H, H-3), 4.7 (d, 1H, OCH_2Ph), 4.75 (2d, 2H, H-1 and OCH_2Ph), 4.85 (2d, 2H, H-6 and OCH_2Ph), 6.0 (d, 1H, NH), 7.3—7.4 (m, 10H, Harom.); $J_{1,2}$ = 3.5; $J_{2,3}$ = 9.4; $J_{3,4a}$ = 11.1; $J_{3,4b}$ = 5.1; $J_{4a,4b}$ = 12.8; $J_{4a,5}$ = 12.1; $J_{4b,5}$ = 2.1; $J_{5,6}$ = 3.3; $J_{6,8}$ = 2.4; $J_{A,B}$ = 11.6—12.2 Hz. Found: C, 70.82; H, 6.92; N, 3.30%. Calcd for $C_{25}H_{29}NO_5$: C, 70.90; H, 6.90; N, 3.431%.

Methyl 6-(Acetylamino)-4,6-dideoxy-α-D-*gluco*-heptopyranosiduronic Acid (9). To a solution of **7** (75 mg, 0.14 mmol) in MeOH (3 mL) was added 10% Pd/C (10 mg). The mixture was stirred under hydrogen (1 atm) for 20 h. After filtration and evaporation of the solvent **9** was obtained as a syrup (25 mg, 68%): $[\alpha]_D^{20}$ +123° (*c* 1, MeOH); ^{1}H NMR (250 MHz, D_2O) δ = 1.55 (ddd, 1H, H-4a), 2.05 (s+m, 4H, H-4b and $COCH_3$), 3.35 (s, 3H, OMe), 3.45 (dd, 1H, H-2), 3.9 (ddd, 1H, H-3), 4.1 (ddd, 1H, H-5), 4.5 (d, 1H, H-6), 4.8 (d, 1H, H-1); $J_{1,2}$ = 3.7; $J_{2,3}$ = 9.8; $J_{3,4a}$ = 11.4; $J_{3,4b}$ = 5.0; $J_{4a,4b}$ = 12.6; $J_{4a,5}$ = 11.9; $J_{4b,5}$ = 1.8; $J_{5,6}$ = 6.1 Hz. Found: C, 45.60; H, 6.61; N, 5.29%. Calcd for $C_{10}H_{17}NO_7$: C, 45.63; H, 6.51; N, 5.32%.

Methyl 2,3-Di-*O*-benzyl-6-*O*-(4-nitrobenzoyl)-4,7,8-trideoxy-α-D-*gluco*-oct-7-ynopyranoside (10). To a solution of **4** (359 mg, 0.94 mmol) and Ph_3P (493 mg, 1.88 mmol) in anhydrous THF were successively added *p*-nitrobenzoic acid (314 mg, 1.88 mmol) and diethyl azodicarboxylate (0.3 mL, 1.88 mmol) under stirring at r.t. After completion of the reaction (5 h at r.t.) the solvent was evaporated and the residue purified by flash chromatography. Elution with EtOAc/hexane 1 : 5 afforded **10** as a syrup (481 mg, 96%): $[\alpha]_D^{20}$ +18.6° (*c* 1.2, $CHCl_3$); ^{1}H NMR (200 MHz, $CDCl_3$) δ = 1.80 (ddd, 1H, H-4a), 2.3 (ddd, 1H, H-4b), 2.55 (d, 1H, H-8), 3.4 (s, 3H, OMe), 3.5 (dd, 1H, H-2), 4.0 (ddd, 1H, H-3), 4.1 (ddd, 1H, H-5), 4.65 (d, 1H, H-1), 4.7—4.9 (m, 4H, CH_2Ph), 5.7 (d, 1H, H-6), 7.1—7.45 (m, 10H, Harom.), 8.3 (m, 4H, $NO_2C_6H_4$); $J_{1,2}$ = 3.5; $J_{2,3}$ = 9.4; $J_{3,4a}$ = 11.1; $J_{3,4b}$ = 5.1; $J_{4a,4b}$ = 12.7; $J_{4a,5}$ = 12.1; $J_{4b,5}$ = 2.1; $J_{5,6}$ = 3.1; $J_{6,8}$ = 2.1 Hz.

Methyl 2,3-Di-*O*-benzyl-4,7,8-trideoxy-α-D-*gluco*-oct-7-ynopyranoside (11). To a solution to **10** (815 mg, 1.53 mmol) in MeOH (10 mL), K_2CO_3 (7.5 mg, 54 μmol) was added and the mixture was stirred for 20 min at r.t. After evaporation of the solvent the product was purified by flash chromatography. Elution with EtOAc/hexane 1 : 5, then 1 : 2, afforded **11** (583 mg, 99%): $[\alpha]_D^{20}$ +22° (*c* 0.55, $CHCl_3$); ^{1}H NMR (200 MHz, $CDCl_3$) δ = 1.7 (ddd, 1H, H-4a), 2.2 (ddd, 1H, H-4b), 2.3 (d, 1H, OH), 2.5 (d, 1H, H-8), 3.4 (s, 3H, OMe), 3.5 (dd, 1H, H-2), 3.9 (ddd, 1H, H-5), 3.95 (ddd, 1H, H-3), 4.4 (ddd, 1H, H-6), 4.7 (d, 1H, H-1), 4.65—4.9 (m, 4H, CH_2Ph), 7.2—7.45 (m, 10H, Harom.); $J_{1,2}$ = 3.6; $J_{2,3}$ = 9.4; $J_{3,4a}$ = 11.2; $J_{3,4b}$ = 5.1; $J_{4a,4b}$ = 12.8; $J_{4a,5}$ = 12.1; $J_{4b,5}$ = 2.3; $J_{5,6}$ = 3.8; $J_{6,8}$ = 2.3; $J_{6,OH}$ = 7 Hz. Found: C, 71.94; H, 6.95%. Calcd for $C_{23}H_{26}O_5$: C, 72.23; H, 6.85%.

Methyl 6-Azido-2,3-di-*O*-benzyl-4,6,7,8-tetradeoxy-α-L-*ido*-oct-7-ynopyranoside (12). Treatment of **11** (108 mg, 0.28 mmol) with $[Zn(N_3)_2(py)_2]$ under the conditions for **4** and flash chromatography afforded **12** as a syrup (103 mg, 90%): $[\alpha]_D^{20}$ + 68.5° (*c* 1 $CHCl_3$); ^{1}H NMR (200 MHz, $CDCl_3$) δ = 1.6 (ddd, 1H, H-4a), 2.2 (ddd, 1H, H-4b), 2.6 (d, 1H, H-8), 3.4 (s, 3H, OMe), 3.5 (dd, 1H, H-2), 3.8 (ddd, 1H, H-5), 3.95 (ddd, 1H, H-3), 4.1 (dd, 1H, H-6), 4.2—4.9 (m, 4H, CH_2Ph), 7.25—7.45 (m, 10H, Harom.); $J_{1,2}$ = 3.5; $J_{2,3}$ = 9.3; $J_{3,4a}$ = 11.2; $J_{3,4b}$ = 5.1; $J_{4a,4b}$ = 12.7; $J_{4a,5}$ = 11.9; $J_{4b,5}$ = 2.2; $J_{5,6}$ = 5.9; $J_{6,8}$ = 2.3 Hz. Found: C, 67.62; H, 6.28; N, 10.42%. Calcd for $C_{23}H_{25}N_3O_4$: C, 67.79; H, 6.18; N, 10.31%.

Benzyl(Methyl 6-Azido-2,3-di-*O*-benzyl-4,6-dideoxy-α-L-*ido*-heptopyranosid)uronate (13). Treatment of **12** (100 mg, 0.24 mmol) with OsO_4 in the presence of $NaIO_4$ under the conditions described for **5** followed by esterification with $PhCHN_2$ and flash chromatography (EtOAc/hexane 1 : 7) afforded **13** (32 mg, 26%): $[\alpha]_D^{20}$ +51° (*c* 1, $CHCl_3$); ^{1}H NMR (200 MHz, $CDCl_3$) δ = 1.8 (ddd, 1H, H-4a), 2.0 (ddd, 1H, H-4b), 3.2 (s, 3H, OMe), 3.45 (dd, 1H, H-2), 3.75 (d, 1H, H-6), 3.9 (ddd, 1H, H-3), 4.3 (ddd, 1H, H-5), 4.6 (d, 1H, H-1), 4.65 (m, 2H, CH_2Ph), 4.75 and 4.82 (ABq, 2H, CH_2, Ph), 5.2 and 5.3 (ABq, 2H, CH_2Ph), 7.25—7.45 (m, 15H, Harom.); $J_{1,2}$ = 3.5; $J_{2,3}$ = 9.4; $J_{3,4a}$ = 11.0; $J_{3,4b}$ = 5.2; $J_{4a,4b}$ = 18.8; $J_{4a,5}$ = 11.8; $J_{4b,5}$ = 2.6; $J_{5,6}$ = 3.4; $J_{A,B}$ = 11.7—12.1 Hz.

Benzyl [Methyl 6-(Acetylamino)-2,3-di-*O*-benzyl-4,6-dideoxy-α-L-*ido*-heptopyranosid]uronate (14). A: Compound **13** (13 mg, 25 μmol) was treated with CH_3COSH (65 μL) at 45 °C for 16 h. After evaporation and coevaporation with toluene the residue was purified by preparative T.L.C. (toluene/acetone 10 : 1) to yield

14 (7 mg, 53%).

B: Compound **15** (240 mg, 0.56 mmol) was treated with OsO_4 in the presence of $NaIO_4$ as described for **5** followed by esterification with phenyldiazomethane. Purification by flash chromatography (EtOAc/toluene 1 : 2) afforded **14** (226 mg, 75%): $[\alpha]_D^{20}+16°$ (*c* 1, $CHCl_3$); ^{1}H NMR (200 MHz, $CDCl_3$) $\delta=1.5$ (ddd, 1H, H-4a), 2.05 (s, 3H, $COCH_3$), 2.1 (ddd, 1H, H-4b), 3.05 (s, 3H, OMe), 3.35 (dd, 1H, H-2), 3.9 (ddd, 1H, H-3), 4.3 (ddd, 1H, H-5), 4.5 (d, 1H, H-1), 4.65 (m, 2H, CH_2Ph), 4.7 (d, 1H, CH_2Ph), 4.8 (dd, 1H, H-6), 4.85 (d, 1H, CH_2Ph), 5.1 (d, 1H, CH_2Ph), 5.2 (d, 1H, CH_2Ph), 6.1 (d, 1H, NH), 7.2—7.4 (m, 15H, Harom.); $J_{1,2}=3.5$; $J_{2,3}=9.4$; $J_{3,4a}=11.1$; $J_{3,4b}=5.2$; $J_{4a,4b}=12.8$; $J_{4a,5}=12.1$; $J_{4b,5}=2.5$; $J_{5,6}=2.0$; $J_{6,NH}=9.3$; $J_{A,B}=12.1$—12.3 Hz. Found: C, 69.72; H, 6.66; N, 2.72 %. Calcd for $C_{31}H_{35}NO_7$: C, 69.77; H, 6.61; N, 2.63 %.

Methyl 6-(Acetylamino)-2,3-di-*O*-benzyl-4,6,7,8-tetradeoxy-α-L-*ido*-oct-7-ynopyranoside (15). Treatment of **12** (342 mg, 0.84 mmol) with propane-1,3-dithiol and triethylamine followed by acetylation under the conditions described for **5** afforded **15** (705 mg, 81%): Mp 145 °C; $[\alpha]_D^{20}+41°$ (*c* 0.65, $CHCl_3$); ^{1}H NMR (250 MHz, $CDCl_3$) $\delta=1.5$ (ddd, 1H, H-4a), 2.0 (s, 3H, $COCH_3$), 2.05 (ddd, 1H, H-4b), 2.25 (d, 1H, H-8), 3.4 (s, 3H, OMe), 3.45 (dd, 1H, H-2), 3.85 (ddd, 1H, H-5), 3.95 (ddd, 1H, H-3), 4.6 (d, 1H, CH_2Ph), 4.75 (d, 1H, CH_2Ph), 4.85 (d, 1H, CH_2Ph), 4.9 (ddd, 1H, H-6), 5.8 (d, 1H, NH), 7.3—7.4 (m, 10H, Harom.); $J_{1,2}=3.5$; $J_{2,3}=9.3$; $J_{3,4a}=11.1$; $J_{3,4b}=5.2$; $J_{4a,4b}=12.8$; $J_{4a,5}=12.4$; $J_{4b,5}=2.2$; $J_{5,6}=2.8$; $J_{6,8}=2.4$; $J_{6,NH}=9.1$; $J_{AB}=11.5$—12.4 Hz. Found: C, 70.74; H, 6.97; N, 3.41%. Calcd for $C_{25}H_{29}NO_5$: C, 70.90; H, 6.90; N, 3.31%.

Methyl 6-(Acetylamino)-4,6-dideoxy-α-L-*ido*-heptopyranosiduronic Acid (16). Treatment of **14** (116 mg, 0.22 mmol) under the conditions described for **7** afforded **16** (54 mg, 93%): $[\alpha]_D^{20}+42.5°$ (*c* 1, MeOH); ^{1}H NMR (200 MHz, D_2O) $\delta=1.5$ (ddd, 1H, H-4a), 2.0 (ddd, 1H, H-4b), 2.2 (s, 3H, $COCH_3$), 3.3 (s, 3H, OMe), 3.35 (dd, 1H, H-2), 3.9 (ddd, 1H, H-3), 4.4 (ddd, 1H, H-5), 4.6 (d, 1H, H-6), 4.8 (d, 1H, H-1); $J_{1,2}=3.5$; $J_{2,3}=9.7$; $J_{3,4a}=11.0$; $J_{3,4b}=5.1$; $J_{4a,4b}=12.9$; $J_{4a,5}=12.1$; $J_{4b,5}=2.0$; $J_{5,6}=1.9$ Hz. Found: C, 45.65; H, 6.49; N, 5.33 %. Calcd for $C_{10}H_{17}NO_7$: C, 45.63; H, 6.51; N, 5.32%.

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