Synthesis of New Cyclitol Derivatives

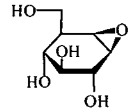
P. Letellier, R. Ralainairina, D. Beaupère, R. Uzan*

Laboratoire de Chimie organique, Groupe de Chimie des Glucides, Université de Picardie Jules Verne, 33 rue Saint Leu, F-80000 Amiens, France

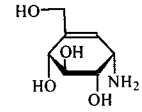
Received 17 October 1996; revised 17 December 1996

The synthesis of new aminocyclitols from the corresponding epoxides is reported.

In recent years, an increasing interest in the synthesis of glycosidase inhibitors has been observed due to their biological properties. Glycosidase inhibitors can be classified in two distinct classes: reversible inhibitors (glycals, glyconolactones, glycosylamines, aminocyclitols, etc),[1] and irreversible inhibitors (conduritol epoxides, 5,6-anhydro-1-deoxynojirimycine).[2] Among the naturally occurring glycosidase inhibitors,[3] cyclitol epoxides and aminocyclitols have been extensively studied due to their antibiotic properties.[4] They have been synthesized from carbohydrate derivatives,[5] *endo*-adducts of furan and acrylic acid or by chemoenzymatic conversion of aromatic derivatives.[6] As part of our investigation on the synthesis of new potential enzyme inhibitors,[7] we have recently prepared some new thiirane analogs.[8] We also reported in a preliminary communication the synthesis of analogs of naturally occurring aminocyclitols.[9] We now describe these previous results in further detail.



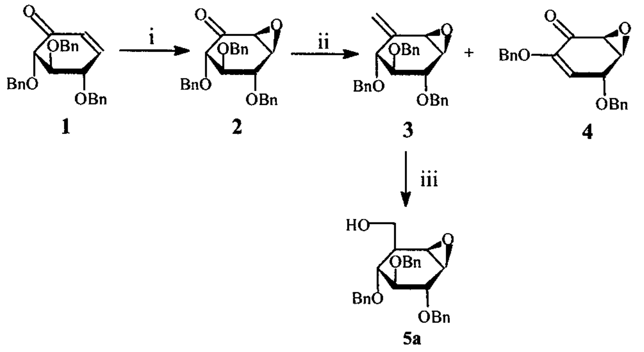
Cyclophellitol



Valienamine

Our aim was to synthesize an aziridine analog of cyclophellitol, allylic amine analogs of valienamine and *pseudo*-disaccharides having either a conduritol epoxide or cyclophellitol moiety, starting from methyl-α-D-glucopyranoside. All these products have a *pseudo*-sugar structure in order to delay their metabolism.

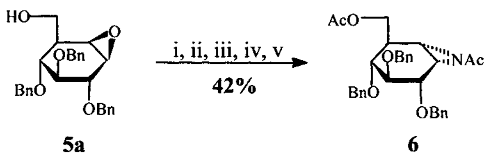
We first decided to convert the enone **1**, prepared using a four-step procedure,[9,10] into the epoxymethylene derivative **3**. The stereoselective epoxidation of **1** was performed using *tert*-butyl hydroperoxide in dichloromethane, affording **2** in 72% yield after 1 hour at room temperature (Scheme 1). The orientation of the epoxide was determined by ^{1}H NMR. The H-2 appears at $\delta = 3.55$ as a doublet ($J_{1,2} = 3.7$ Hz, and $J_{2,3} = 0$ Hz). The value of $J_{2,3}$ can be explained by the presence of the carbonyl group in the α position of the epoxide **2** which distorts the chair conformation. The H-2 is then in a pseudo axial position, forming a dihedral angle of ~90° with H-3. The conversion of **2** into the corresponding epoxymethylene **3** is then achieved by reacting **2** with 1.5 equivalents of triphenylphosphonium methylide in THF at 0°C under an anhydrous atmosphere. The epoxymethylene **3** is obtained in 62% yield with 21% of the byproduct **4**. The structure of **4** was assigned by ^{13}C NMR, the carbonyl and the epoxide still being present ($\delta_{C=O} = 195$, $\delta_{C\text{-}5} = 54.26$, $\delta_{C\text{-}4} = 55.66$). The double bond is characterised by the chemical shifts of C-1 ($\delta = 148.60$) and C-2 ($\delta = 110.24$).



i) tBuO$_2$H, CH$_2$Cl$_2$, Triton B ; ii) Ph$_3$PCH$_3$Br, nBuLi, THF ;
iii) NaBH$_4$, Et$_2$O-BF$_3$, H$_2$O$_2$, NaOH

Scheme 1

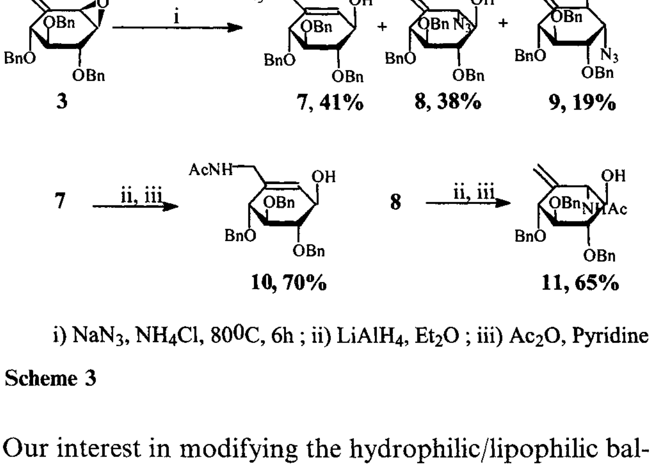
The hydroboration of **3** was performed by reacting **3** in THF with bubbling diborane generated in situ. The intermediate organoborane is then converted into the epoxy alcohol **5a** in a 55% yield by treatment with H_2O_2 in an alkaline medium (Scheme 1). The coupling constant of 7.4 Hz for $J_{5,6}$ involves a C-5, C-6 *anti*-methine configuration. We also noticed that the hydroboration of **3** was accompanied by a partial reduction of the epoxide, due to the large excess of diborane. Our first attempt to react **5a** with NaN_3 was unsuccessful, therefore the primary hydroxyl was first acetylated and the nucleophilic ring opening of the intermediate acetate **5b** by NaN_3 (3.5 equiv) in the presence of ammonium chloride (3.5 equiv) yielded a mixture of two azido isomers resulting from the nucleophilic attack at C-2 (70%) and C-1 (20%). In a preliminary experiment, only the product of *trans* diaxial opening was mesylated with mesyl chloride in pyridine in the presence of a catalytic amount of DMAP. The mesylate has the same R_f as the starting material, a ^{13}C NMR was performed after 12 hours which showed the spectrum of a single product. A new signal at $\delta = 41.64$ and a shift of the signal of the C-5 from $\delta = 66.75$ to 72.29 was in accordance with the presence of a mesyl group. The mesylate was then reduced with $LiAlH_4$ (0.7 equiv) at room temperature to afford, after conventional acetylation, the aziridine **6** in 62% overall yield. Then we performed the same sequence of reactions on the mixture of azides. The aziridine **6** was obtained in an overall yield of 43% starting from **5a** (Scheme 2). In the ^{1}H NMR spectrum of **6**, the signal of H-1 is a doublet ($J_{1,2} = 5.5$ Hz) and the signal of H-2 is a doublet of doublets ($J_{2,3} = 3.4$ Hz). These results confirmed the inversion of configuration of C-1 and C-2.



i) Ac_2O, Pyridine ; ii) NaN_3, NH_4Cl, 16h reflux;
iii) MsCl, Pyridine ; iv) $LiAlH_4$, Et_2O ; v) Ac_2O, Pyridine

Scheme 2

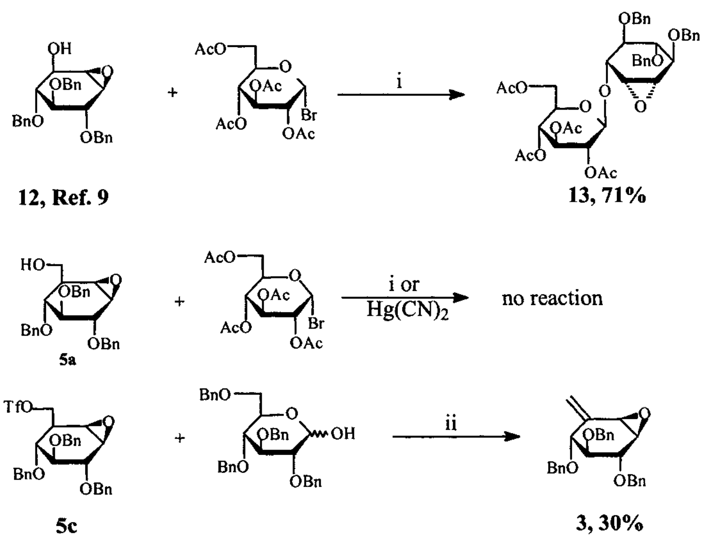
The second objective of our project was the synthesis of allylic aminocyclitol analogs of valienamine. Indeed, aminocyclitols are known to be less active glycosidase reversible inhibitors than glycosylamines because of the replacement of the carbonyl oxygen by a methylene group. Cyclohexyl systems would be less adapted to the half-chair conformation required to interact with the active site of the enzyme than glycosidic analogs. The cyclohexene double bond, which induces a half-chair conformation of valienamine makes it an exception. The epoxymethylene **3** was treated with sodium azide/ammonium chloride (3.5/3.5 equiv) in 10 % aqueous 2-methoxyethanol at 80 °C to afford a mixture of three azido derivatives, **7**,**8** and **9** in 41, 38, and 19 % yield, respectively. The reaction time is shorter than for the azidation of the acetate **5b** (*vide supra*, cf. Scheme 2) due to the ethylenic bond which activates the reaction. The formation of **7** by a 1,4 attack of N_3^- is not the only explanation. Indeed when **8** was heated at 50 °C in THF, an equilibrium between **7** and **8** was observed. The same equilibrium was observed when **7** was reacted under the same conditions. Therefore the formation of **7** can also result from a 6 center intramolecular rearrangement. Reduction of the azido derivative **7** by $LiAlH_4$ (0.7 equiv) at room temperature followed by *N*-acetylation led to **10** in 70 % yield. Similar treatment transformed **8** into **11** in 65 % yield (Scheme 3).



i) NaN_3, NH_4Cl, 80oC, 6h ; ii) $LiAlH_4$, Et_2O ; iii) Ac_2O, Pyridine

Scheme 3

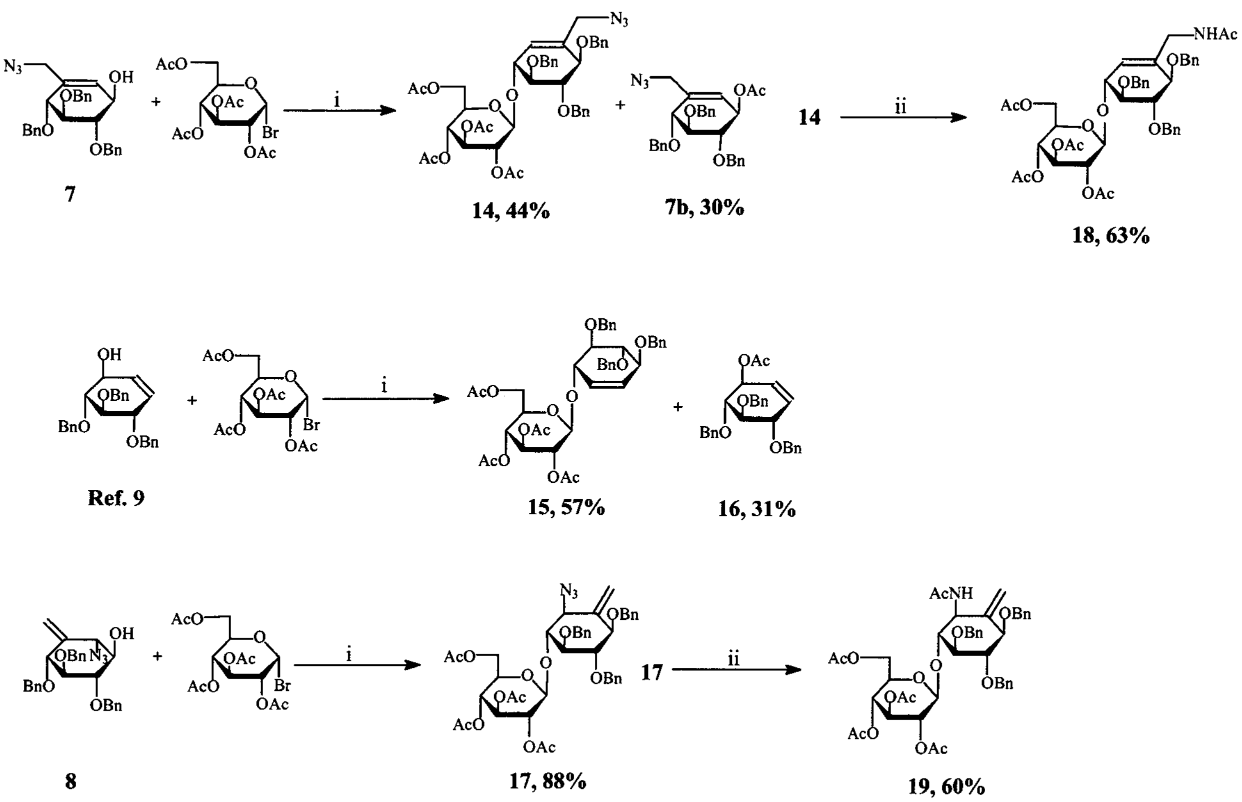
Our interest in modifying the hydrophilic/lipophilic balance of the naturally occurring conduritol epoxide and cyclophellitol, as well as one of 3*S*(3,5/4,6)-1-acetamidomethyl-4,5,6,-tri-*O*-benzyl-1-ene-cyclohexane-3,4,5,6-tetrol (**10**) and 2*R*(2,4,6/3,5)-2-acetamido-4,5,6-tri-*O*-benzyl-1-methylenecyclohexane-3,4,5,6,-tetrol (**11**), led us to attempt the coupling reactions to a glycosyl residue. Best results for the coupling reactions with 2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranosyl bromide were obtained by using 3 equivalents of glucosyl bromide, 3 equivalents of 1,1,3,3-tetramethylurea (TMU) and 3 equivalents of silver trifluoromethanesulfonate in dichloromethane at −30 °C. The condensation of the 1*R*(1,2,4,6/3,5)-1,2-anhydro-3,4,5-tri-*O*-benzylcyclohexane-1,2,3,4,5,6-hexol (**12**)[8,11] under the previously described conditions afforded the expected pseudodisaccharide **13** in 71 % yield. On the other hand the condensation of **5a** under the same conditions or using $Hg(CN)_2$ was unsuccessful in our hands. Therefore, we attempted to react the triflate derivative **5c** with 2,3,4,6-tetra-*O*-benzyl-D-glucopyranose (TBG) in the presence of NaH. No reaction was observed at room temperature in CH_2Cl_2. The reaction was then performed under reflux and with 10 % hexamethylphosphoric triamide (HMPT). After 2 hours a new product was obtained in 30 % yield which was identified as **3**. The unexpected behaviour of **5c** in not undergoing condensation with TBG was attributed to the acidity of the H-6 due to the presence of the epoxide ring, leading to the elimination product **3** (Scheme 4).



i) AgOTf, TMU, CH_2Cl_2 ; ii) NaH, CH_2Cl_2, 10% HMPT, reflux

Scheme 4

The glycosylation of **7** led stereoselectively to the β anomer ($J_{1',2'}$ = 7.8 Hz) of **14** in 44 % yield accompanied with 30 % of **7b** resulting from a transesterification of the allylic hydroxy group with the 2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranosyl bromide. Our attempt to optimize the yield by modifying the relative ratio between the reagents was unsuccessful. To confirm that the transesterification was due to the presence of an allylic hydroxy group, we reacted 3*R*(3,5/4,6)-3,4,5-tri-*O*-benzyl-1-ene-cyclohexane-3,4,5,6-tetrol[11] with the 2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranosyl bromide under the same conditions. The *pseudo*-disaccharide **15** was obtained in 57 % yield as the β anomer ($J_{1',2'}$ = 7.8 Hz) together with the 3*R*(3,5/4,6)-6-*O*-acetyl-3,4,5-tri-*O*-benzyl-1-ene-cyclohexane-3,4,5,6-tetrol (**16**). The condensation of **8** was performed under the same conditions leading to the *pseudo*-disaccharide **17** in 88 % yield. The anomeric hy-



i) AgOTf, TMU, CH_2Cl_2 ; ii) $LiAlH_4$, Et_2O, then Ac_2O, Pyridine

Scheme 5

drogen signal in the ^{1}H NMR spectrum of **17** being masked, the anomeric configuration of this product was deduced indirectly. As for the *pseudo*-monosaccharide **8**, a 6 center rearrangement involving an allylic azido group migration was observed. In that case the rearrangement occurred at room temperature (1 month) to afford **14** as a single product. This result allowed us to confirm the β configuration of **17**. No rearrangement of **14** to **17** was observed. The reduction of **14** and **17** by 4 equivalents of $LiAlH_4$, followed by *O*- and *N*-acetylation gave respectively **18** (63 %) and **19** (60 %) (Scheme 5).

In vitro assays were carried out on products **6**, **10** and **11**. At a 4 mmol concentration, all products exhibited an inhibition activity against chitine synthetase between 45 and 89 %. However, these tests also demonstrated the need to improve the hydrosolubility of these products. Indeed at 4 mmol, DMSO (8 %) was added to obtain a total solubility.

Melting points were determined with a Büchi apparatus and are uncorrected. Optical rotations were recorded at r.t. in $CHCl_3$ with a Perkin-Elmer 241 polarimeter using a 1 dm cell. ^{1}H NMR spectra were recorded in $CDCl_3$-TMS at 300.13 MHz (Bruker AM300). Chromatography was performed on Merck silica gel (230–400 mesh) and precoated Merck silica gel plates (60 F-254) were used for TLC.

1*R*(1,2,4/3,5)-1,2-Anhydro-3,4,5-tri-*O*-benzyl-6-enecyclohexane-1,2,3,4,5-pentol (2):

To a solution of **1**[9] (3 g, 7.1 mmol) in CH_2Cl_2 (30 mL) was added *tert*-butyl hydroperoxide (*t*-BuO_2H, 10 mL, 70 % in CH_2Cl_2, 7.3 mmol) and Triton B (1.65 mL, 9.5 mmol). After stirring for 1 h at r.t. under Ar, the solution was neutralized to pH 7 by washing with aq 0.1 N HCl. The organic layer was dried (Na_2SO_4) and evaporated under vacuum. The crude product was chromatographed on silica gel (hexane/EtOAc, 9 : 1) to give **2** (2.21 g, 72 %) as a white solid which was recrystallized from hexane/EtOAc; $[\alpha]_D$ +45.0 (c = 1.43, $CHCl_3$); mp 72–74 °C.

Anal calcd for $C_{27}H_{26}O_5$ C 75.33; H 6.09; found C 75.49; H 6.14.

^{1}H NMR ($CDCl_3$/TMS): δ = 3.45 (d, 1 H, $J_{1,2}$ = 3.7 Hz, H-1), 3.55 (d, 1 H, $J_{1,2}$ = 3.7 Hz, H-2), 3.90 (dd, 1 H, $J_{3,4}$ = 6.5 Hz, $J_{4,5}$ = 10 Hz, H-4), 3.20 (d, 1 H, $J_{3,4}$ = 6.5 Hz, H-3), 4.45 (d, 1 H, $J_{4,5}$ = 10 Hz, H-5), 4.50–4.95 (m, 6 H, 3 × CH_2Ph), 7.20–7.40 (m, 15 H, 3 × C_6H_5).

^{13}C NMR ($CDCl_3$/TMS): δ = 56.38 (C-1), 57.54 (C-2), 78.03 (C-3), 80.90 (C-5), 85.65 (C-4), 202.84 (C-6), 73.72, 73.59, 75.41 (3 × CH_2Ph), 127.49–128.58 (CH_{arom}), 137.15, 137.35, 137.85 (C_{arom}).

1*S*(1,2,4/3,5)-1,2-Anhydro-3,4,5-tri-*O*-benzyl-6-methylenecyclohexane-1,2,3,4,5-pentol (3):

To a solution of methyltriphenylphosphonium bromide (3.12 g, 8.7 mmol) in THF (20 mL) under Ar was added dropwise BuLi (5.44 mL, 1.6 M in hexane 8.7 mmol). After the solution became red, **2** (2.5 g, 5.8 mmol) in THF (20 mL) was added at 0 °C. After stirring for 15 min at r.t. under Ar, the solution was poured into H_2O (50 mL) and extracted with hexane (3 × 50 mL). The organic layer was dried (Na_2SO_4) and solvents were removed under reduced pressure. The crude product was chromatographed on silica gel (hexane/EtOAc, 9 : 1) to give **3** (1.54 g, 62 %) after recrystallization from EtOH as a white solid; $[\alpha]_D$ +16.9 (c = 1, $CHCl_3$); mp 89–90 °C).

Anal calcd for $C_{28}H_{28}O_4$ C 78.48; H 6.59; found C 78.39; H 6.66.

^{1}H NMR ($CDCl_3$/TMS): δ = 3.40 (d, 1 H, $J_{1,2}$ = 3.5 Hz, H-1), 3.65

(dd, 1 H, $J_{3,4} = 7.5$ Hz, $J_{4,5} = 10.3$ Hz, H-4), 3.70 (d, 1 H, $J_{1,2} = 3.5$ Hz, H-2), 4.05 (d, 1 H, $J_{3,4} = 7.5$ Hz, H-3), 4.55 (d, 1 H, $J_{4,5} = 10.3$ Hz, H-5), 4.60–5.00 (m, 6 H, $3 \times CH_2Ph$), 5.40 (s, 1 H, H-7), 5.70 (s, 1 H, H-7'), 7.30–7.50 (m, 15 H, $3 \times C_6H_5$).

^{13}C NMR ($CDCl_3$/TMS): $\delta = 55.85$ (C-1), 57.70 (C-2), 79.77 (C-3), 77.25 (C-5), 85.00 (C-4), 114.40 (C-7), 141.65 (C-6), 73.20, 74.15, 75.35 ($3 \times CH_2Ph$), 127.40–128.50 (CH_{arom}), 137.75, 138.28, 138.70 (C_{arom}).

1*R*(1,2,4,6/3,5)-1,2-Anhydro-3,4,5-tri-*O*-benzyl-6-hydroxymethylcyclohexane-1,2,3,4,5-pentol (5a):

Two 3-necked flasks were linked by a glass tube. B_2H_6 was prepared in the first flask by addition of a suspension of $NaBH_4$ (1.1 g, 29 mmol) in diglyme (30 mL) to a solution of $Et_2O{\cdot}BF_3$ (7.6 mL, 61 mmol) in diglyme (6.6 mL). The B_2H_6 thus formed was bubbled into the second flask containing a solution of **3** (2 g, 4.67 mmol) in THF (20 mL) by means of N_2 as carrier gas. The hydroboration occurred at r.t. and the addition of B_2H_6 was stopped as soon as the starting material had disappeared. The excess of hydride was destroyed by addition of a mixture of H_2O/THF (1:1 v/v, 10 mL) at 0 °C. Then aq 2 N NaOH (15 mL) was added, followed by 30 % H_2O_2 (7.5 mL, 6.6 mmol) and the solution was allowed to warm to r.t. After stirring for 30 min, the solvents were removed under reduced pressure. The residue was poured into H_2O (50 mL) and extracted with Et_2O (4×30 mL). The organic layer was dried (Na_2SO_4) and solvents were removed under reduced pressure. The crude product was chromatographed on silica gel (hexane/EtOAc, 9:1) to give **5a** (1.13 g, 55 %) as a white solid; $[\alpha]_D$ +4.0 (*c* = 1, $CHCl_3$); mp 44.6–47.5 °C.

Anal calcd for $C_{28}H_{30}O_5$ C 75.31; H 6.77; found C 75.49; H 6.69.

^1H NMR ($CDCl_3$/TMS): $\delta = 2.85$ (m, 1 H, H-6), 3.22 (d, 1 H, $J_{1,2} = 3.5$ Hz, H-2), 3.35 (m, 1 H, H-1), 3.78 (dd, 1 H, $J_{4,5} = 10.9$ Hz, $J_{5,6} = 7.4$ Hz, H-5), 3.82 (dd, 1 H, $J_{3,4} = 6.1$ Hz, $J_{4,5} = 10.9$ Hz, H-4), 3.85 (t, 1 H, $J_{7,7'} = J_{7,6} = 11.3$ Hz, H-7), 3.96 (d, 1 H, $J_{3,4} = 6.1$ Hz, H-3), 4.00 (dd, 1 H, $J_{7,7'} = 11.3$ Hz, $J_{7',6} = 7.4$ Hz, H-7'), 4.60–4.90 (m, 6 H, $3 \times CH_2Ph$), 7.20–7.30 (m, 15 H, $3 \times C_6H_5$).

^{13}C NMR ($CDCl_3$/TMS): $\delta = 36.80$ (C-6), 53.63 (C-2), 55.56 (C-1), 61.11 (C-7), 79.47 (C-3), 77.16 (C-5), 80.17 (C-4), 73.04, 73.70, 74.91 ($3 \times CH_2Ph$), 126.63–128.76 (CH_{arom}), 136.74, 137.06, 137.66 (C_{arom}).

1*S*(1,2,3,5/4,6)-3,4,5-Tri-*O*-benzyl-1,2-epimine-*N*-acetyl-6-hydroxymethyl-7-*O*-acetylcyclohexane-3,4,5-triol (6):

To a solution of **5b** (2 g, 4.5 mmol) prepared by conventional acetylation of **5a** in 10 % aq 2-methoxyethanol (100 mL) was added NaN_3 (1.04 g, 17 mmol) and NH_4Cl (840 mg, 10.1 mmol). After stirring for 16 h at 80 °C, the solvents were removed. The residue was dissolved in $CHCl_3$ (50 mL) and washed with H_2O (50 mL). The organic layer was dried (Na_2SO_4), concentrated, and dissolved in pyridine (120 mL). 4-Dimethylaminopyridine (DMAP, 8 mg) and then methanesulfonyl chloride (MsCl, 2 mL, 26 mmol) were added at 0 °C to the solution. After stirring overnight at r.t. under argon, the solvent was removed under reduced pressure. The crude product was filtered on silica gel (20 g) (hexane/EtOAc, 7:3) to give a colorless syrup which was dissolved in anhyd Et_2O (20 mL) and was added dropwise to a suspension of $LiAlH_4$ (100 mg, 2.6 mmol) in anhyd Et_2O (20 mL). After stirring for 1 h, EtOAc (20 mL) and MeOH (10 mL) were added. After the solvents were removed under reduced pressure, the residue was acetylated by the conventional method. The solvents were removed under reduced pressure and the crude product was chromatographed on silica gel (hexane/EtOAc, 9:1) to give **6** (1.03 g, 43 %) as a colorless syrup; $[\alpha]_D$ −3.0 (*c* = 0.4, $CHCl_3$).

Anal calcd for $C_{32}H_{35}NO_6$ C 72.57; H 6.66; N 2.64; found C 72.69; H 6.69; N 2.89.

^1H NMR ($CDCl_3$/TMS): $\delta = 2.00$ (s, 3 H, CH_3CO), 2.10 (s, 3 H, CH_3CNO), 2.70 (d, 1 H, $J_{1,2} = 5.5$ Hz, H-1), 2.75 (dd, 1 H, $J_{1,2} = 5.5$ Hz, $J_{2,3} = 3.4$ Hz, H-2), 2.89 (ddd, $J_{5,6} = 7.9$ Hz, $J_{6,7} = 10.2$ Hz, $J_{6,7'} = 3.7$ Hz, 1 H, H-6), 3.43 (dd, 1 H, $J_{3,4} = 6.0$ Hz, $J_{4,5} = 10.3$ Hz, H-4), 3.58 (dd, 1 H, $J_{4,5} = 10.3$ Hz, $J_{5,6} = 7.9$ Hz, H-5), 3.75 (dd, 1 H, $J_{2,3} = 3.4$ Hz, $J_{3,4} = 6.0$ Hz, H-3), 4.25 (t, 1 H, $J_{7,7'} = J_{7,6} = 10.2$ Hz, H-7), 4.55 (dd, 1 H, $J_{7,7'} = 10.2$ Hz, $J_{7,6} = 3.7$ Hz, H-7'), 4.70–5.20 (m, 6 H, $3 \times CH_2Ph$), 7.20–7.40 (m, 15 H, $3 \times C_6H_5$).

^{13}C NMR ($CDCl_3$/TMS): $\delta = 35.14$ (C-2), 36.89 (C-6), 37.53 (C-1), 62.58 (C-7), 78.63 (C-3), 78.25 (C-5), 79.06 (C-4), 20.99 (CH_3CO), 23.32 (CH_3CNO), 72.85, 73.12, 75.70 ($3 \times CH_2Ph$), 127.66–128.39 (CH_{arom}), 137.99, 138.22, 138.55 (C_{arom}), 171.07 (CH_3CO), 183.12 (CH_3CNO).

Azidation of 1*S*(1,2,4/3,5)-1,2-Anhydro-3,4,5-tri-*O*-benzyl-6-methylenecyclohexane-1,2,3,4,5-pentol (3):

To a solution of **3** (1 g, 2.3 mmol) in 2-methoxyethanol/H_2O (90:10 v/v, 20 mL) was added NaN_3 (0.52 g, 8.5 mmol) and NH_4Cl (0.42 g, 8.05 mmol). After stirring for 6 h at 80 °C, the solvents were removed under reduced pressure. The crude product was dissolved in $CHCl_3$ (50 mL) and washed with H_2O (2×25 mL). The organic layer was dried (Na_2SO_4) and concentrated under reduced pressure. The crude product was chromatographed on silica gel (hexane/EtOAc, 9:1) to give a mixture of **8**, **9** and **7** in the order of elution.

1R(1,3,5/2,4)-1-Azido-3,4,5-tri-O-benzyl-6-methylenecyclohexane-2,3,4,5-tetrol (**8**): (410 mg, 38 %); syrup; $[\alpha]_D$ −44.6 (*c* = 0.6, $CHCl_3$).

Anal calcd for $C_{28}H_{29}N_3O_4$ C 71.32; H 6.20; N 8.91; found C 71.61; H 6.52; N 8.80.

^1H NMR ($CDCl_3$/TMS): $\delta = 3.40$ (t, 1 H, $J_{1,2} = J_{2,3} = 9.7$ Hz, H-2), 3.40 (dd, 1 H, $J_{3,4} = 8.6$ Hz, $J_{4,5} = 8.9$ Hz, H-4), 3.45 (dd, 1 H, $J_{2,3} = 9.7$ Hz, $J_{3,4} = 8.6$ Hz, H-3), 3.82 (d, 1 H, $J_{1,2} = 9.7$ Hz, H-1), 3.90 (d, 1 H, $J_{4,5} = 8.9$ Hz, H-5), 4.60–5.05 (m, 6 H, $3 \times CH_2Ph$), 5.30 (s, 1 H, H-7), 5.50 (s, 1 H, H-7'), 7.30–7.50 (m, 15 H, $3 \times C_6H_5$).

^{13}C NMR ($CDCl_3$/TMS): $\delta = 64.04$ (C-1), 76.06 (C-2), 81.35 (C-5), 83.17 (C-3), 84.42 (C-4), 110.24 (C-7), 138.92 (C-6), 73.45, 75.62 ($3 \times CH_2Ph$), 127.83–128.61 (CH_{arom}), 137.88, 138.42 (C_{arom}).

1S(1,2,4/3,6)-1-Azido-2,3,4-tri-O-benzyl-5-methylenecyclohexane-2,3,4,6-tetrol (**9**): (205 mg, 19 %); syrup; $[\alpha]_D$ −54.2 (*c* = 0.7, $CHCl_3$).

Anal calcd for $C_{28}H_{29}N_3O_4$ C 71.32; H 6.20; N 8.91; found C 71.48; H 6.32; N 8.75.

^1H NMR ($CDCl_3$/TMS) $\delta = 3.45$ (t, 1 H, $J_{2,3} = 8.2$ Hz, $J_{3,4} = 8.7$ Hz, H-3), 3.65 (dd, 1 H $J_{1,2} = 2.6$ Hz, $J_{1,6} = 3.7$ Hz, H-1), 3.80 (dd, 1 H, $J_{1,2} = 3.5$ Hz, $J_{2,3} = 8.2$ Hz, H-2), 4.20 (d, 1 H, $J_{3,4} = 8.7$ Hz, H-4), 4.40 (d, 1 H, $J_{1,6} = 3.7$ Hz, H-6), 4.65–5.00 (m, 6 H, $3 \times CH_2Ph$), 5.50 (s, 2 H, H-7 and H-7'), 7.30–7.50 (m, 15 H, $3 \times C_6H_5$).

^{13}C NMR ($CDCl_3$/TMS): $\delta = 73.09$ (C-1), 81.49 (C-4), 83.17 (C-6), 83.62 (C-2), 84.23 (C-3), 115.22 (C-7), 139.15 (C-5), 73.76, 75.06, 75.35 ($3 \times CH_2Ph$), 127.40–128.54 (CH_{arom}), 137.93, 138.46 (C_{arom}).

1S(1,3/2,4)-6-Azidomethyl-1,2,3-tri-O-benzyl-5-enecyclohexane-1,2,3,4-tetrol (**7**): (440 mg, 41 %); white solid; $[\alpha]_D$ −48.6 (*c* = 1.5, $CHCl_3$), mp 75–77 °C.

Anal calcd for $C_{28}H_{29}N_3O_4$ C 71.32; H 6.20; N 8.91; found C 71.42; H 6.35; N 8.77.

^1H NMR ($CDCl_3$/TMS): $\delta = 3.45$ (dd, 1 H, $J_{2,3} = 9.8$ Hz, $J_{3,4} = 7.5$ Hz, H-3), 3.65 (d, 1 H, $J_{7,7'} = 12$ Hz, H-7), 3.70 (t, 1 H, $J_{1,2} = 10.3$ Hz, $J_{2,3} = 9.8$ Hz, H-2), 3.75 (d, 1 H, $J_{7,7'} = 12$ Hz, H-7'), 4.30 (d, 1 H, $J_{1,2} = 10.3$ Hz, H-1), 4.35 (d, 1 H, $J_{3,4} = 7.5$ Hz, H-4), 4.50–4.90 (m, 6 H, $3 \times CH_2Ph$), 7.20–7.40 (m, 15 H, $3 \times C_6H_5$).

^{13}C NMR ($CDCl_3$/TMS): $\delta = 52.57$ (C-7), 69.16 (C-4), 80.86 (C-1), 83.38 (C-3), 83.77 (C-2), 128.81 (C-5), 133.67 (C-6), 75.07, 75.64 ($3 \times CH_2Ph$), 127.70–128.40 (CH_{arom}), 137.80, 137.90, 138.10 (C_{arom}).

1*S*(1,3/2,4)-6-Acetamidomethyl-1,2,3-tri-*O*-benzyl-5-enecyclohexane-1,2,3,4-tetrol (10); Typical Procedure:

To a suspension of $LiAlH_4$ (100 mg, 2.6 mmol) in Et_2O (20 mL) at 0 °C under Ar, was added a solution of **7** (1.5 g, 3.18 mmol) in Et_2O (10 mL). The suspension was allowed to warm to r.t. and stirred for 2 h. The excess of hydride was destroyed with MeOH (5 mL).

The solvents were removed under reduced pressure, and the crude product was dissolved in MeOH (20 mL), and Ac_2O (2 mL) and Et_3N (2 mL) were added. After 15 min, the solvents were removed under reduced pressure, and the crude mixture was chromatographed on silica gel (EtOH/EtOAc, 6:4) to give **10** as a white solid after recrystallization from EtOH (1.08 g, 70 %); $[\alpha]_D$ −46.0 ($c = 0.5$, $CHCl_3$); mp 169–170 °C.

Anal calcd for $C_{30}H_{33}NO_5$ C 73.90; H 6.82; N 2.87; found C 73.75; H 6.92; N 2.80.

^{1}H NMR ($CDCl_3$/TMS): $\delta = 1.75$ (s, 3 H, CH_3CO), 2.55 (s, 1 H, OH), 3.50 (dd, 1 H, $J_{2,3} = 9.5$ Hz, $J_{3,4} = 6.4$ Hz, H-3), 3.65 (dd, 1 H, $J_{7,7'} = 14.5$ Hz, $J_{7,NH} = 3.6$ Hz, H-7), 3.75 (dd, 1 H, $J_{1,2} = 6.8$ Hz, $J_{2,3} = 9.5$ Hz, H-2), 3.90 (dd, 1 H, $J_{7,7'} = 14.5$ Hz, $J_{7',NH} = 6.9$ Hz, H-7′), 4.15 (d, 1 H, $J_{1,2} = 6.8$ Hz, H-1), 4.25 (d, 1 H, $J_{3,4} = 6.4$ Hz, H-4), 4.55–4.90 (m, 6 H, 3 × CH_2Ph), 5.55 (s, 1 H, H-5), 5.65 (m, 1 H, N*H*Ac), 7.20–7.40 (m, 15 H, 3 × C_6H_5).

^{13}C NMR ($CDCl_3$/TMS): $\delta = 40.59$ (C-7), 70.38 (C-4), 79.28 (C-1), 82.41 (C-2), 82.98 (C-3), 127.00 (C-5), 133.96 (C-6), 22.21 (CH_3CNO), 73.25, 74.05 (3 × CH_2Ph), 123.02–124.08 (CH_{arom}), 137.41, 137.93 (C_{arom}), 168.93 (CH_3CNO).

1S(1,3,5/2,4)-1-Acetamido-3,4,5-tri-O-benzyl-6-methylenecyclohexane-2,3,4,5-tetrol **(11)**:

The previous procedure applied to **8** afforded **11** as a white solid after recrystallization from EtOH (1.00 g, 65 %); $[\alpha]_D$ −42.8 ($c = 0.4$, $CHCl_3$); mp 199–201 °C.

Anal calcd for $C_{30}H_{33}NO_5$ C 73.90; H 6.82; N 2.87; found C 73.82; H 6.95; N 2.74.

^{1}H NMR ($CDCl_3$/TMS): $\delta = 2.00$ (s, 3 H, CH_3CO), 3.36 (t, 1 H, $J_{1,2} = J_{2,3} = 8.3$ Hz, H-2), 3.51 (t, 1 H, $J_{3,4} = J_{4,5} = 8.3$ Hz, H-4), 3.60 (dd, 1 H, $J_{2,3} = J_{3,4} = 8.3$ Hz, H-3), 4.05 (d, 1 H, $J_{4,5} = 8.3$ Hz, H-5), 4.42 (t, 1 H, $J_{1,2} = J_{1,NH} = 8.3$ Hz, H-1), 4.5–5 (s, 1 H, OH), 4.55–5.00 (m, 6 H, 3 × CH_2Ph), 5.15 (s, 1 H, H-7), 5.35 (s, 1 H, H-7′), 6.32 (d, 1 H, $J_{1,NH} = 8.3$ Hz, N*H*Ac), 7.25–7.35 (m, 15 H, 3 × C_6H_5).

^{13}C NMR ($CDCl_3$/TMS): $\delta = 52.95$ (C-1), 73.50 (C-2), 80.72 (C-5), 81.85 (C-3), 82.64 (C-4), 108.98 (C-7), 139.63 (C-6), 22.26 (CH_3CNO), 72.10, 74.23 (3 × CH_2Ph), 126.70–127.51 (CH_{arom}), 137.04, 137.98 (C_{arom}), 169.61 (CH_3CNO).

Glycosylation of 7, 8 and 12; General Procedure:

To a suspension of AgOTf (3 equiv) in CH_2Cl_2 (20 mL) at −30 °C under Ar in darkness, was added a solution of the appropriate alcohol (1 equiv), tetra-*O*-acetyl-α-D-glucopyranosyl bromide (3 equiv) and TMU (3 equiv) in CH_2Cl_2 (10 mL). The suspension was allowed to warm to r.t. and stirred for 30 min (unless specified), filtered and washed with an aq solution of $NaHCO_3$. The organic layer was dried (Na_2SO_4) and concentrated under reduced pressure. The crude mixture was chromatographed on silica gel (hexane/EtOAc, 8:2, unless specified).

6-O-(2′,3′,4′,6′-Tetra-O-acetyl-β-D-glucopyranosyl)-1R(1,2,4,6/3,5)-1,2-anhydro-3,4,5-tri-O-benzylcyclohexane-1,2,3,4,5,6-hexol **(13)**:

The foregoing procedure applied to **12** (500 mg, 1.16 mmol) afforded after 2.5 h at r.t. **13** as a white solid in 71 % yield (620 mg); $[\alpha]_D$ +76.6 ($c = 1$, $CHCl_3$); mp 121–124 °C.

Anal calcd for $C_{41}H_{46}O_{14}$ C 64.56; H 6.08; found C 64.71; H 6.32.

^{1}H NMR ($CDCl_3$/TMS): $\delta = 3.19$ (d, 1 H, H-1), 3.42 (d, 1 H, $J_{1,2} = 3.7$ Hz, H-2), 3.47 (t, 1 H, $J_{4,5} = 10.2$ Hz, H-5), 3.58 (t, H, $J_{3,4} = 7.9$ Hz, H-4), 3.65 (m, 1 H, $J_{4',5'} = 6.3$ Hz, H-5′), 3.85 (d, 1 H, H-3), 4.08 (d, 1 H, $J_{1,6} = 8$ Hz, H-6), 4.16 (d, 2 H, $J_{5',6'} = J_{5',6''} = 3.5$ Hz, H-6′ and H-6″), 4.95 (d, 1 H, $J_{1',2'} = 7.8$ Hz, H-1′), 5.03 (t, 1 H, $J_{2',3'} = 9.1$ Hz, H-2′), 5.15 (t, 1 H, $J_{3',4'} = 9.1$ Hz, H-3′), 1.80, 1.90, 2.00, 2.10 (4 s, 12 H, 4 × CH_3CO), 4.60 4.80 (m, 6 H, 3 × CH_2Ph), 7.20 to 7.40 (m, 15 H, 3 × C_6H_5).

^{13}C NMR ($CDCl_3$/TMS): $\delta = 52.71$ (C-1), 55.46 (C-2), 60.93 (C-6′), 67.51 (C-4′), 70.69 (C-2′), 70.95 (C-5′), 72.22 (C-3′), 77.46 (C-5), 78.19 (C-3), 78.49 (C-6), 82.49 (C-4), 100.31 (C-1′), 19.55 (4 × CH_3CO), 72.22, 74.40, 76.64 (3 × CH_2Ph), 126.50–127.50 (CH_{arom}), 136.52, 137.19, 137.44 (C_{arom}), 168,02, 168.91, 169.24, 169.51 (4 × CH_3CO).

4-O-(2′,3′,4′,6′-Tetra-O-acetyl-β-D-glucopyranosyl)-1S(1,3/2,4)-6-azidomethyl-1,2,3-tri-O-benzyl-5-enecyclohexane-1,2,3,4-tetrol **(14)**:

The foregoing procedure applied to **7** afforded its acetate **7b** and the coupling product **14**.

7b: colorless syrup (65 mg, 30 %); $[\alpha]_D$ −74.6 ($c = 0.85$, $CHCl_3$).

Anal calcd for $C_{30}H_{31}N_3O_5$ C 70.16; H 6.08; N 8.18; found C 70.31; H 6.22; N 8.03.

^{1}H NMR ($CDCl_3$/TMS): $\delta = 1.95$ (s, 3 H, CH_3CO), 3.75–3.90 (m, 4 H, H-2, H-3, H-7, H-7′), 4.18 (d, 1 H, $J_{1,2} = 7.4$ Hz, H-1), 4.55–4.95 (m, 6 H, 3 × CH_2Ph), 5.45 (d, 1 H, $J_{3,4} = 10$ Hz, H-4), 5.50 (s, 1 H, H-5), 7.30–7.50 (m, 15 H, 3 × C_6H_5).

^{13}C NMR ($CDCl_3$/TMS): $\delta = 51.38$ (C-7), 72.62 (C-4), 78.21 (C-1), 80.52 (C-3), 83.05 (C-2), 124.07 (C-5), 134.92 (C-6), 20.04 (CH_3CO), 74.04, 74.27, 74.56 (3 × CH_2Ph), 126.60–127.70 (CH_{arom}), 136.21, 137.29 (C_{arom}).

14: white solid (149 mg, 44 %) after recrystallization from EtOH; $[\alpha]_D$ +46.5 ($c = 1$, $CHCl_3$); mp 117–119 °C.

Anal calcd for $C_{42}H_{47}N_3O_{13}$ C 62.91; H 5.91; N 5.24; found C 63.08; H 6.12; N 5.08.

^{1}H NMR ($CDCl_3$/TMS): $\delta = 2.00$ (s, 12 H, CH_3CO), 3.65 (m, 1 H, H-5′), 3.70 (t, 1 H, $J_{2,3} = 8.6$ Hz, $J_{3,4} = 6.3$ Hz, H-3), 3.70–3.85 (m, 5 H, H-2, H-3, H-5′, H-7, H-7′), 4.03 (dd, 1 H, $J_{6',6''} = 12.4$ Hz, $J_{5',6''} = 2.2$ Hz, H-6″), 4.20 (d, 1 H, $J_{1,2} = 7.0$ Hz, H-1), 4.25 (dd, 1 H, $J_{6',6''} = 12.4$ Hz, $J_{5',6'} = 4.2$ Hz, H-6′), 4.60–5.10 (m, 6 H, 3 × CH_2Ph), 4.75 (d, 1 H, $J_{1',2'} = 7.8$ Hz, H-1′), 5.01 (t, 1 H, $J_{1',2'} = 7.8$ Hz, $J_{2',3'} = 8.8$ Hz, H-2′), 5.13 (t, 1 H, $J_{3',4'} = J_{4',5'} = 9.5$ Hz, H-4′), 5.20 (t, 1 H, $J_{2',3'} = 8.8$ Hz, $J_{3',4'} = 9.5$ Hz, H-3′), 7.20–7.35 (m, 15 H, 3 × C_6H_5).

^{13}C NMR ($CDCl_3$/TMS): $\delta = 51.38$ (C-7), 60.81 (C-6′), 67.20 (C-4′), 70.70 (C-2′), 71.01 (C-5′), 71.92 (C-3′), 78.09 (C-1), 78.78 (C-4), 81.34 (C-3), 82.73 (C-2), 99.57 (C-1′), 123.38 (C-5), 134.56 (C-6), 19.60 (4 × CH_3CO), 74.11, 74.38 (3 × CH_2Ph), 126.63–127.47 (CH_{arom}), 136.98, 137.40, 137.68 (C_{arom}), 168.33, 169.21, 169.59 (4 × CH_3CO).

6-O-(2′,3′,4′,6′-Tetra-O-acetyl-β-D-glucopyranosyl)-3R(3,5/4,6)-3,4,5-tri-O-benzyl-1-enecyclohexane-3,4,5,6-tetrol **(15)** *and Acetate* **16**:

The foregoing procedure applied to 3*R*(3,5/4,6)-3,4,5-tri-*O*-benzyl-1-enecyclohexane-3,4,5,6-tetrol[9] (300 mg, 0.72 mmol) after silica gel chromatography (hexane/EtOAc, 85:15) afforded the acetate **16** and the coupling product **15**.

16: colorless syrup (102 mg, 31 %); $[\alpha]_D$ +101.8 ($c = 0.99$, $CHCl_3$).

Anal calcd for $C_{29}H_{30}O_5$ C 75.96; H 6.59; found C 76.15; H 6.52.

^{1}H NMR ($CDCl_3$/TMS): $\delta = 1.95$ (s, 3 H, CH_3CO), 3.77 (t, 1 H, $J_{4,5} = J_{5,6} = 10.3$ Hz, H-5), 3.85 (t, 1 H, $J_{3,4} = 7.5$ Hz, $J_{4,5} = 10.3$ Hz, H-4), 4.27 (dd, 1 H, $J_{1,3} = 1.8$ Hz, $J_{3,4} = 7.5$ Hz, H-3), 4.70–4.95 (m, 6 H, 3 × CH_2Ph), 5.60 (m, 2 H, H-2, H-6), 5.80 (dd, 1 H, $J_{1,2} = 10.5$ Hz, $J_{1,3} = 1.8$ Hz, H-1), 7.25–7.40 (m, 15 H, 3 × C_6H_5).

^{13}C NMR ($CDCl_3$/TMS): $\delta = 73.43$ (C-6), 78.85 (C-3), 80.69 (C-5), 82.53 (C-4), 125.25 (C-2), 128.19 (C-1), 20.01 (CH_3CO), 71.99, 74.21, 76.58 (3 × CH_2Ph), 126.60–127.40 (CH_{arom}), 137.32, 137.63 (C_{arom}).

15: colorless syrup (312 mg, 57 %); $[\alpha]_D$ +38.3 ($c = 2.4$, $CHCl_3$).

Anal calcd for $C_{41}H_{46}O_{13}$ C 65.94; H 6.12; found C 65.81; H 6.31.

^{1}H NMR ($CDCl_3$/TMS): $\delta = 1.80$–2.00 (4 s, 12 H, CH_3CO), 3.60–3.75 (m, 3 H, H-4, H-5, H-5′), 4.10 (dd, 1 H, $J_{6',6''} = 12.5$ Hz, $J_{5',6'} = 3.9$ Hz, H-6′), 4.18 (dd, 1 H, $J_{3,4} = 8$ Hz, $J_{1,3} = 2.5$ Hz, H-3), 4.20 (dd, 1 H, $J_{6',6''} = 12.5$ Hz, $J_{5,6''} = 5.2$ Hz, H-6″), 4.40 (dd, 1 H, $J_{5,6} = 10.2$ Hz, $J_{2,6} = 1.8$ Hz, H-6), 4.60–4.90 (m, 6 H, 3 × CH_2Ph), 4.85 (d, 1 H, $J_{1',2'} = 7.8$ Hz, H-1′), 5.05 (t, 1 H, $J_{1',2'} = 7.8$ Hz, $J_{2',3'} = 9.5$ Hz, H-2′), 5.10 (t, 1 H, $J_{3',4'} = J_{4',5'} = 9.5$ Hz, H-3′), 5.20 (t, 1 H, $J_{2',3'} = J_{3',4'} = 9.5$ Hz, H-3′), 5.72 (2 dd, 2 H, $J_{1,2} = 11.6$ Hz, $J_{1,3} = 2.5$ Hz, H-1, $J_{1,2} = 11.6$ Hz, $J_{2,6} = 1.8$ Hz, H-2), 7.20–7.40 (m, 15 H, 3 × C_6H_5).

^{13}C NMR ($CDCl_3$/TMS): $\delta = 61.02$ (C-6′), 67.59 (C-4′), 70.66 (C-5′), 70.79 (C-2′), 72.09 (C-3′), 78.09 (C-3), 79.49 (C-6), 82.61 (C-4, C-5), 100.23 (C-1′), 19.51, 19.63 (4 × *C*H_3CO), 71.39, 74.49 (3 × CH_2Ph), 126.55–127.49 (C-1, C-2, CH_{arom}), 137.17, 137.31, 137.59 (C_{arom}), 168.08, 168.31, 169.12, 169.44 (4 × CH_3*C*O).

2-O-(2′,3′,4′,6′-Tetra-O-acetyl-β-D-glucopyranosyl)-1R(1,3,5/2,4)-1-azido-3,4,5-tri-O-benzyl-6-methylenecyclohexane-2,3,4,5-tetrol **(17)**:

The foregoing procedure applied to **8** (200 mg, 0.42 mmol) afforded **17** as a white solid (280 mg, 88 %); $[\alpha]_D$ −22.5 ($c = 0.4$, $CHCl_3$); mp 130–131 °C.

Anal calcd for $C_{42}H_{47}N_3O_{13}$ C 62.91; H 5.91; N 5.24; found C 62.80; H 6.03; N 5.02.

^{1}H NMR ($CDCl_3$/TMS): $\delta = 1.85–2.10$ (m, 12 H, CH_3CO); 3.30 (t, 1 H, $J_{1,2} = J_{2,3} = 9.0$ Hz, H-2), 3.50 (m, 2 H, H-4, H-5′), 3.55 (t, 1 H, $J_{2,3} = J_{3,4} = 9.0$ Hz, H-3), 3.80 (m, 3 H, H-1, H-5, H-6″), 4.10 (dd, 1 H, $J_{6',6''} = 12.3$ Hz, $J_{6',5'} = 3.9$ Hz, H-6′), 4.60–5.10 (m, 6 H, 3 × C*H*$_2$Ph), 4.95–5.25 (m, 4 H, H-1′, H-2′, H-3′, H-4′), 5.35 (s, 1 H, H-7), 5.45 (s, 1 H, H-7′), 5.13 (t, 1 H, $J_{3',4'} = J_{4',5'} = 9.5$ Hz, H-4′), 5.20 (t, 1 H, $J_{2',3'} = 8.8$ Hz, $J_{3',4'} = 9.5$ Hz, H-3′), 7.20–7.40 (m, 15 H, 3 × C_6H_5).

^{13}C NMR ($CDCl_3$/TMS): $\delta = 60.73$ (C-6′), 64.51 (C-1), 67.18 (C-4′), 70.94 (C-5′), 71.26 (C-2′), 72.19 (C-3′), 79.75 (C-5), 81.13 (C-4), 81.26 (C-3), 83.32 (C-2), 99.73 (C-1′), 109.56 (C-7), 138.15 (C-6), 19.59, 19.81 (4 × *C*H_3CO), 72.48, 74.42, 76.71 (3 × *C*H_2Ph), 126.25–127.49 (CH_{arom}), 136.86, 137.42, 137.89 (C_{arom}), 168.32, 168.54, 169.25, 169.55 (4 × CH_3*C*O).

4-*O*-(2′,3′,4′,6′-Tetra-*O*-acetyl-*β*-D-glucopyranosyl)-1*S*(1,3/2,4)-6-acetamidomethyl-1,2,3-tri-*O*-benzyl-5-enecyclohexane-1,2,3,4-tetrol (18):

To a suspension of $LiAlH_4$ (40 mg, 1.04 mmol) in Et_2O (20 mL) at 0 °C under argon, was added a solution of **14** (200 mg, 0.25 mmol) in Et_2O (10 mL). The suspension was allowed to warm to r.t. and stirred for 2 h. The excess of hydride was destroyed with MeOH (5 mL). The solvents were removed under reduced pressure, and the crude was acetylated overnight in pyridine (20 mL) and Ac_2O (2 mL). The solvents were removed under reduced pressure, and the crude mixture was chromatographed on silica gel (hexane/EtOAc, 3:7) to give **18** as a colorless syrup (130 mg, 65 %); $[\alpha]_D$ −21.7 ($c = 0.8$, $CHCl_3$).

Anal calcd for $C_{44}H_{51}NO_{14}$ C 64.62; H 6.28; N 1.71; found C 64.73; H 6.41; N 1.97.

^{1}H NMR ($CDCl_3$/TMS): $\delta = 1.90–2.10$ (m, 15 H, CH_3CO); 3.55–3.75 (m, 4 H, H-2, H-3, H-5′, H-7′), 3.90 (dd, 1 H, $J_{7,7'} = 14.5$ Hz, $J_{7,NH} = 6.9$ Hz, H-7), 4.00 (dd, 1 H, $J_{6',6''} = 12.3$ Hz, $J_{5',6''} = 1.9$ Hz, H-6″), 4.15 (d, 1 H, $J_{1,2} = 5.4$ Hz, H-1), 4.20 (dd, 1 H, $J_{5',6'} = 3.8$ Hz, $J_{6',6''} = 12.3$ Hz, H-6′), 4.43 (d, 1 H, $J_{3,4} = 6.6$ Hz, H-4), 4.60–5.00 (m, 6 H, 3 × C*H*$_2$Ph), 4.68 (d, 1 H, $J_{1',2'} = 7.8$ Hz, H-1′), 4.95 (t, 1 H, $J_{1',2'} = 7.8$ Hz, $J_{2',3'} = 9.6$ Hz, H-2′), 5.10 (t, 1 H, $J_{3',4'} = J_{4',5'} = 9.6$ Hz, H-4′), 5.15 (t, 1 H, $J_{2',3'} = J_{3',4'} = 9.6$ Hz, H-3′), 5.50 (m, 1 H, N*H*Ac), 5.51 (s, 1 H, H-5), 7.20–7.40 (m, 15 H, 3 × C_6H_5).

^{13}C NMR ($CDCl_3$/TMS): $\delta = 40.64$ (C-7), 60.81 (C-6′), 67.23 (C-4′), 70.72 (C-5′), 70.98 (C-2′), 71.92 (C-3′), 78.74 (C-1, C-4), 81.41 (C-3), 82.91 (C-2), 98.64 (C-1′), 123.35 (C-5), 135.84 (C-6), 19.58 (4 × *C*H_3CO), 22.17 (*C*H_3CNO), 73.68, 74.03, 74.30 (3 × *C*H_2Ph), 126.68–127.73 (CH_{arom}), 137.00, 137.39, 137.68 (C_{arom}), 168.49, 169.19 (4 × CH_3*C*O, CH_3*C*NO).

2-*O*-(2′,3′,4′,6′-Tetra-*O*-acetyl-*β*-D-glucopyranosyl)-1*S*(1,3,5/2,4)-1-acetamido-3,4,5-tri-*O*-benzyl-6-methylenecyclohexane-2,3,4,5-tetrol (19):

The same procedure applied to **17** (100 mg, 0.125 mmol) gave **19** as a white solid (61 mg, 60 %); $[\alpha]_D$ −35.6 ($c = 0.5$, $CHCl_3$); mp = 165–168 °C.

Anal calcd for $C_{44}H_{51}NO_{14}$ C 64.62; H 6.28; N 1.71; found C 64.48; H 6.31; N 2.02.

^{1}H NMR ($CDCl_3$/TMS): $\delta = 1.90–2.10$ (m, 15 H, CH_3CO); 3.55 (t, 1 H, $J_{3,4} = J_{4,5} = 7.8$ Hz, H-4), 3.60 (t, 1 H, $J_{2,3} = 7.6$ Hz, $J_{3,4} = 7.8$ Hz, H-3), 3.65 (m, 1 H, H-5′), 3.70 (t, 1 H, $J_{1,2} = 7.5$ Hz, $J_{2,3} = 7.6$ Hz, H-2), 4.05 (d, 1 H, $J_{4,5} = 7.8$ Hz, H-5), 4.10 (dd, 1 H, $J_{6',6''} = 12.5$ Hz, $J_{5',6'} = 2.2$ Hz, H-6′), 4.15 (dd, 1 H, $J_{5',6''} = 3.9$ Hz, $J_{6',6''} = 12.5$ Hz, H-6″), 4.50 (t, 1 H, $J_{1,2} = 7.5$ Hz, $J_{1,NH} = 8.3$ Hz, H-1), 4.55–4.90 (m, 6 H, 3 × C*H*$_2$Ph), 4.95 (m, 2 H, H-1′, H-2′), 5.00 (t, 1 H, $J_{3',4'} = J_{4',5'} = 9.4$ Hz, H-4′), 5.10 (s, 1 H, H-7), 5.15 (t, 1 H, $J_{2',3'} = J_{3',4'} = 9.4$ Hz, H-3′), 5.30 (s, 1 H, H-7′), 6.18 (d, 1 H, $J_{1,NH} = 8.3$ Hz, N*H*Ac), 5.51 (s, 1 H, H-5), 7.20–7.30 (m, 15 H, 3 × C_6H_5).

^{13}C NMR ($CDCl_3$/TMS): $\delta = 52.88$ (C-1), 61.01 (C-6′), 67.51 (C-4′), 70.74 (C-2′, C-5′), 72.04 (C-3′), 79.68 (C-2), 79.99 (C-3), 80.78 (C-5), 81.54 (C-4), 98.57 (C-1′), 111.91 (C-7), 138.75 (C-6), 19.51 (4 × *C*H_3CO), 22.22 (*C*H_3CNO), 71.13, 73.52 (3 × *C*H_2Ph), 126.40–127.70 (CH_{arom}), 136.75, 137.60 (C_{arom}), 168.31, 168.51, 169.14, 169.53 (4 × CH_3*C*O, CH_3*C*NO).

The authors wish to thank the Centre de Valorisation des Glucides (Amiens, France) for the financial support.

(1) Lehmann,, J.; Schröter, E. *Carbohydr. Res.* **1972**, *23*, 359.
Ezaki, S. *J. Biochem.* (Tokio) **1940**, *32*, 104.
Lai, H.Y.L.; Axelrod, B.; *Biochem. Biophys. Res. Commun.* **1973**, *54*, 463.
Horii, S.; Isawa, T.; Mizuka, E. *J. Antibiot.* **1971**, *24*, 59.
Kameda, Y.; Asawa, N.; Yoshikawa, M.; Takaishi, M.; Yamaguchi, T.; Matsu, K. *J. Antibiot.* **1984**, *37*, 1301.

(2) Herrchen, M.; Legler, G. *Eur. J. Biochem.* **1984**, *138*, 527.
Tong, M.K.; Ganem, B. *J. Am. Chem. Soc.* **1988**, *110*, 312.
Hozel, W.; Banz, W. *Eur. J. Biochem.* **1975**, *57*, 607.

(3) Legler, G. *Adv. Carbohydr. Chem. and Biochem.* **1990**, *48*, 319, and references cited therein.
Atsumi, S.; Iinuma, H.; Nosaka, C.; Umezawa, K. *J. Antibiotics* **1990**, *43*, 1579.
Withers, S.G.; Umezawa, K. *Biochem. Biophys. Res. Commun.* **1991**, *177*, 532.

(4) Horii, S.; Fukase, H. *Carbohydr. Res.* **1985**, *140*, 185.
Ogawa, S.; Shibata, Y.; Nose, T.; Suami, T. *Bull. Chem. Soc. Jpn.* **1985**, *58*, 3387.
Junge, B.; Boshagen, H.; Stoltefub, J.; Muller, L. *Enzymes Inhibitors, Ed Verlag Chem.* **1980**, 123.
Truscheit, E.; Frommer, W.; Junge, B.; Muller, L. *Angew. Chem.* **1981**, *93*, 738; *Angew. Chem. Int. Ed. Engl.* **1981**, *20*, 744.

(5) Fukase, H.; Horii, S. *J. Org. Chem.* **1992**, *57*, 3642 and 3651.
Madi-Puskas, M.; Pelivas, I.; Bognar, R. *J. Carbohydr. Chem.* **1985**, *4*, 323.
Meszanos, P.; Pinter, I.; Messmer, A.; Toth, G.; Gero, S.D. *Carbohydr. Res.* **1990**, *197*, 302.
Corbett, F.; Dean, D.K.; Robinson, S.R. *Tetrahedron Lett.* **1993**, *34*, 1525.

(6) Ogawa, S. *Stud. Nat. Prod. Chem.* **1993**, *13*, 187.
Suami, T.; Ogawa, S. *Adv. Carbohydr. Chem. Biochem.* **1990**, *48*, 21.
Hudlicky, T.; Entwistle, D.A.; Pitzer, K.K.; Thorpe, A.J. *Chem. Rev.* **1996**, *96*, 1195.

(7) Beaupère, D.; Stasik, B.; Uzan, R.; Demailly, G. *Carbohydr. Res.* **1989**, *191*, 163.
Benazza, M.; Uzan, R.; Beaupère, D.; Demailly, G. *Tetrahedron Lett.* **1992**, *33*, 3129.
Mbongo, A.; Fréchou, C.; Beaupère, D.; Uzan, R.; Demailly, G. *Carbohydr. Res.* **1993**, *246*, 361.

(8) Letellier, P.; El Meslouki, A.; Beaupère, D.; Uzan, R. *Synthesis* **1996**, 1435.

(9) Letellier, P.; Ralainairina, R.; Beaupère, D.; Uzan, R. *Tetrahedron Lett.* **1994**, *35*, 4555.

(10) Ferrier, R.J.; Middleton, S. *Chem. Rev.* **1993**, *93*, 2779.

(11) Jaramillo, J.; Fernández de la Pradilla, R.; Martin-Lomas, M. *Carbohydr. Res.* **1991**, *209*, 296.