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Note

Preparation of building blocks for carba-oligosaccharides related to cell-surface glycans *

Seiichiro Ogawa, Takeshi Tonegawa, Kenji Nishi, and Junichi Yokoyama

Department of Applied Chemistry, Faculty of Science and Technology, Keio University, Hiyoshi, Kohoku-ku, Yokohama, 223 (Japan)

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The appropriately protected derivative **10** of 5a-carba-β-D-mannopyranosylamine (**1**) and the precursor **19** of 2-acetamido-5a-carba-2-deoxy-β-D-glucopyranosylamine (**2**) have/been synthesized.

Carba-sugar analogues[2] of naturally occurring oligosaccharides of biological interest have been utilized as model compounds for conformational analysis of true oligosaccharides or as substrates analogues for study of enzymic actions.

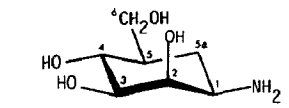
The carba-mannopyranosylamine **1** is regarded as the carba-sugar building block for construction of the α-(1→3) and α-(1→6) linked branch point β-mannopyranose residue of *N*-linked glycoproteins[3], and would itself link to the C-4 position of 2-acetamido-2-deoxy-D-glucopyranose by way of an imino bond.

The latter compound **2** corresponds to the 2-acetamido-2-deoxy-β-D-glucopyranose residue linked to the asparagine residue by way of a β-*N*-glycosyl linkage, and is readily convertible into the protected 5a-carba-β-D-glucopyranosylamine derivative, before or after the OH-4 group being glycosylated, for example, by 2-acetamido-2-deoxy-β-D-glucopyranose. Furthermore, it may be possible to deblock the C-6 position, at which an α-L-fucopyranosyl residue could be introduced.

(1*R*,3*R*,6*R*,10*R*)-10-Hydroxy-3-phenyl-2,4-dioxabicyclo[4.4.0]dec-8-ene (**3**) was prepared from (1*S*,2*R*,3*R*)-2,3-diacetoxy-4-cyclohexene-1-carboxylic acid[5], in 60% overall yield, by reduction with lithium aluminium hydride, and successive benzylidenation with α,α-dimethoxytoluene and *p*-toluenesulfonic acid in *N*,*N*-dimethylformamide. Benzylation of **3** with benzyl bromide and sodium hydride in *N*,*N*-dimethylformamide afforded the benzyl ether **4** quantitatively. First, compound **4** was reduced with sodium cyanoborohydride[5] in tetrahydrofuran and the product

Correspondence to: Professor S. Ogawa, Department of Applied Chemistry, Faculty of Science and Technology, Keio University, Hiyoshi, Kohoku-ku, Yokohama, 223, Japan.

* Pseudo-sugars, Part XXVII. Part XXVI, see ref. 1. This paper also constitutes Part I of The Series Synthesis of Carba-oligosaccharides Related to Cell-surface Glycans.



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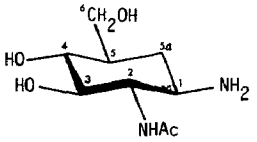

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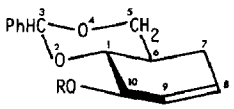
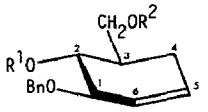


3 R = H
4 R = Bn

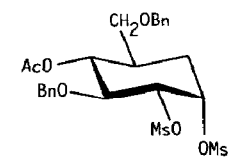


	R^1	R^2
5	Ac	Bn
6	Bn	Ac

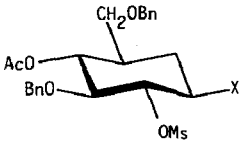
Scheme 1

was acetylated to give mainly the "2-acetate" **5** (62%), together with the "7-acetate" **6** (7%). Oxidation of **5** with osmium tetraoxide in the presence of 4-methylmorpholine *N*-oxide in 1:1 acetone–water proceeded through selective rearside attack to give a single α-diol, which was isolated as the dimesylate **7** (90%). Selective displacement of the axial 1-methylsulfonyloxyl function of **7** by an azide ion was effected by treatment with excess of sodium azide in *N*,*N*-dimethylformamide at 80°, affording the crystalline azide **8** (96%), the ^{1}H-NMR spectrum of which revealed two signals coupled to each other: a doublet of doublets of doublets (δ 3.52, J 4.8, 9.5, 13.2 Hz) and a triplet (δ 4.45, J 9.5 Hz), attributable to the signals of the H-1,2 atoms, respectively. Hydrogenolysis of the azido group of **8** in the presence of Raney nickel in EtOAc–EtOH containing acetic anhydride produced the *N*-acetyl derivative **9** (91%). Treatment of **9** with excess of sodium acetate in aq 90% 2-methoxyethanol at reflux temperature resulted in an inversion of the configuration of C-2 via anchimeric assistance of the acetamido group to afford, after conventional acetylation, the crystalline 5a-carba-β-D-mannopyranosylamine derivative **10** in 97% yield. In the ^{1}H-NMR spectrum of **10**, the H-2 signal appeared as a triplet (δ 5.61, J 2.7 Hz), indicative of the axial orientation of the 2-acetoxyl group.

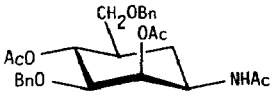
Epoxidation of **3** with *m*-chloroperoxybenzoic acid in dichloromethane with phosphate buffer solution, followed by conventional *O*-benzylation with benzyl chloride, produced the β-epoxide **11** in 88% yield, together with the α-epoxide **12** (9.3%). The selectivity may be explained by the *cis*-directing effect of the 10-hydroxyl group[6,7]. The structure of **11** was confirmed by the following transformation. Cleavage of the epoxide ring of **11** with excess of sodium azide in *N*,*N*-dimethylformamide at 110° proceeded in a diaxial fashion to give the azides **13** (82%) and **16** (7.3%). The azide **13** was converted into the mesylate **14**, the ^{1}H-NMR



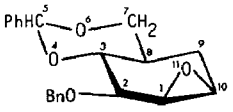
7



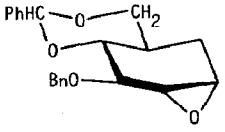
8 X = N_3
9 X = NHAc



10



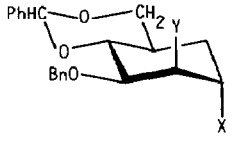
11



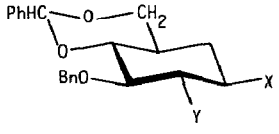
12

Scheme 2

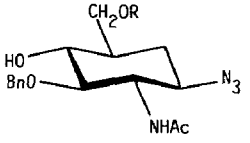
spectrum of which indicated a quartet (δ 4.13, J 3 Hz) due to CHN_3, supporting the proposed structure of **13**. Reduction of **14** with lithium aluminum hydride in tetrahydrofuran, followed by conventional acetylation, afforded the *N*-acetyl aziridine. Without purification, it was successively treated with sodium azide in *N*,*N*-dimethylformamide at 100° to give rise to the crystalline azides **15** (12%) and **17** (59%). The ^{1}H-NMR spectrum of **17** showed a triplet of doublets (δ 3.7, J 4.5, 11.5, 11.5 Hz) due to CHN_3, indicative of the structure assigned. *O*-Debenzylidenation of **17** with aqueous 70% acetic acid at 65° gave the diol **18** (90%), which



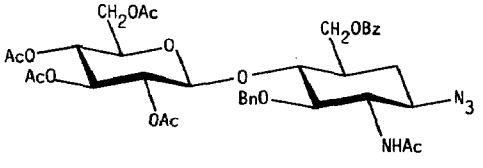
	X	Y
13	N_3	OH
14	N_3	OMs
15	NHAc	N_3



	X	Y
16	OH	N_3
17	N_3	NHAc



18 R = H
19 R = Bz



20

Scheme 3

was selectively benzoylated with benzoyl chloride in pyridine at −15° to give the crystalline "6-benzoate" **19** (84%).

Reaction of **19** with 2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranosyl bromide in the presence of silver triflate and tetramethylurea in 1,2-dichloroethane at reflux temperature readily afforded the blocked carba-disaccharide **20** in 80% yield. The structure was assigned on the basis of the ^{1}H-NMR spectrum.

EXPERIMENTAL

General methods.–Melting points were determined with a Mel–Temp capillary melting-point apparatus and are uncorrected. Optical rotations were measured with a Jasco DIP-370 polarimeter. ^{1}H-NMR spectra were recorded for solutions in $CDCl_3$ (internal Me_4Si) with a Jeol JNM FX90A (90 MHz) or JNM GSX-270 (270 MHz) instruments. TLC was performed on Silica Gel 60 GF (E. Merck, Darmstadt) with detection by charring with H_2SO_4. Column chromatography was conducted on Wakogel C-300 (300 mesh). Organic solutions were dried over anhydrous Na_2SO_4 and evaporated at $< 50°$ under diminished pressure.

(*1*R,*3*R,*6*R,*10*S)-*10-Hydroxy-3-phenyl-2,4-dioxabicyclo[4.4.0]dec-8-ene* (**3**).—To a solution of (1*S*,2*R*,3*R*)-2,3-diacetoxy-4-cyclohexene-1-carboxylic acid[5] (2.50 g, 10.3 mmol) in tetrahydrofuran (30 mL) was added $LiAlH_4$ (1.18 g, 31 mmol), and the mixture was stirred for 2 h at room temperature. Water (5 mL) and aq 15% NaOH (1 mL) were added in turn at 0°, and the mixture was diluted with 1:1 acetone–H_2O (40 mL) and filtered through a Celite bed. The filtrate was neutralized with aq M HCl and then evaporated to dryness. The throughly dried residue was dissolved in DMF (20 mL) and stirred with α,α-dimethoxytoluene (2.32 mL, 15.5 mmol) and *p*-toluenesulfonic acid (180 mg, 1.03 mmol) for 2 h at 60° under diminished pressure (aspirator). The mixture was then neutralized with $NaHCO_3$ and evaporated. The residue was dissolved in EtOAc (200 mL), washed with brine, dried, and evaporated. The product was chromatographed on a column of silica gel (20 g) with 1:8 butanone–PhMe as eluent to give **3** (1.45 g, 60%) as crystals; mp 124.5–126° (from EtOH); $[\alpha]_D^{26}$ − 8.4° (*c* 1.2, $CHCl_3$); ^{1}H-NMR (90 MHz, $CDCl_3$): δ 7.65–7.15 (m, 5 H, Ph), 5.75–5.50 (m, 3 H, H-3,3,9) 4.50–4.25 (m, 1 H, H-10), 4.25 (dd, 1 H, $J_{5eq,6}$ 4.9, $J_{5,5}$ 11 Hz, H-5*eq*), 3.65 (dd, 1 H, *J* 8, *J* 9.5 Hz, H-1), 3.64 (t, 1 H, $J_{5ax,6}$ 11 Hz, H-5*ax*), 2.62 (bd, 1 H, $J_{10,OH}$ 3.2 Hz, OH), and 2.40–1.62 (m, 3 H, H-6,7a,7b).

Anal. Calcd for $C_{14}H_{16}O_3 \cdot 0.25H_2O$: C, 71.02; H, 7.02. Found: C, 71.33; H, 6.93.

(*1*R,*3*R,*6*R,*10*S)-*10-Benzyloxy-3-phenyl-2,4-dioxabicyclo[4.4.0]dec-8-ene* (**4**).—To a solution of **3** (1.45 g, 6.23 mmol) in DMF (20 mL) was added NaH (0.50 g, 60%, 12.5 mmol), and the mixture was stirred for 0.5 h at room temperature. Then benzyl bromide (1.48 mL, 12.5 mmol) was added and the mixture was stirred for 2 h at room temperature. After addition of MeOH, the mixture was evaporated and the residue was dissolved in EtOAc (100 mL) and washed with H_2O, dried, and

evaporated. The product was chromatographed on a column of silica gel (30 g) with EtOAc–hexane as eluent to give **4** (2.03 g, ~ 100%) as needles; mp 68–69° (from EtOH); $[\alpha]_D^{26}$ – 32° (*c* 1.1, $CHCl_3$); ^{1}H-NMR (90 MHz, $CDCl_3$): δ 7.70–7.10 (m, 10 H, 2 Ph), 5.90–5.50 (m, 3 H, H-3,8,9), 4.88 and 4.70 (ABq, 2 H, *J* 12 Hz, CH_2Ph), 4.35–4.25 (m, 1 H, H-10), 4.18 (dd, 1 H, $J_{5eq,6}$ 4.7, $J_{5,5}$ 11 Hz, H-5*eq*), 3.88 (dd, 1 H, *J* 7.6, *J* 10.2 Hz, H-1), 3.65 (t, 1 H, $J_{5ax,6}$ 11 Hz, H-5*ax*), and 2.40–1.45 (m, 3 H, H-6,7a,7b).

Anal. Calcd for $C_{21}H_{22}O_3$: C, 78.23; H, 6.88. Found: C, 78.21; H, 7.18.

1L-(1,3/2)-2-O-Acetyl-1-O-benzyl-3-benzyloxymethyl- (**5**) and *1L-(1,3/2)-3-acetoxymethyl-1,2-di-O-benzyl-5-cyclohexene-1,2,-diol* (**6**).—To a solution of **4** (670 mg, 2.1 mmol) in tetrahydrofuran (THF) (25 mL) was added $NaCNBH_3$ (2.6 g, 42 mmol) and 4A molecular sieves (400 mg), and the mixture was stirred at room temperature by addition of HCl–ether until evolution of gas ceased. The mixture was then partitioned between $CHCl_3$ (100 mL) and H_2O (50 mL), and the organic layer was washed with satd aq $NaHCO_3$ and H_2O, dried, and evaporated. The residue was treated with Ac_2O (10 mL) and pyridine (10 mL) overnight at room temperature, and the mixture was evaporated and the residue was extracted with $CHCl_3$. The extract was washed with H_2O, dried, and evaporated. The products were chromatographed on a column of silica gel (25 g) with 1:8 EtOAc–hexane as eluent to give, first, **5** (472 mg, 62%) as an amorphous solid; $[\alpha]_D^{27}$ – 34° (*c* 1.1, $CHCl_3$); ^{1}H-NMR (270 MHz, $CDCl_3$): δ 7.35–7.23 (m, 10 H, 2 Ph), 5.82–5.77 (m, 1 H, H-5), 5.71–5.65 (m, 1 H, H-6), 5.20 (dd, 1 H, $J_{1,2}$ 7.3, $J_{2,3}$ 10.3 Hz, H-2), 4.64 and 4.54 (2 d, each 1 H, *J* 11.7 Hz, CH_2Ph), 4.48–4.41 (2 d, each 1 H, *J* 12.1 Hz, CH_2Ph), 4.12 (ddd, 1 H, $J_{1,5}$ 2.2, $J_{1,6}$ 5.1 Hz, H-1), 3.50 (dd, 1 H, $J_{3,7a}$ 4.6 $J_{7,7}$ 9.2 Hz, H-7a), 3.39 (dd, 1 H, $J_{3,7b}$ 6.2 Hz, H-7b), 2.37–2.29 (m, 2 H, H-4e), 2.26–2.04 (m, 2 H, H-3,4a), and 1.99 (s, 3 H, Ac).

Anal. Calcd for $C_{23}H_{26}O_4$: C, 75.38; H, 7.15. Found: C, 75.56; H, 7.08.

The second fraction gave **6** (55 mg, 7.2%), isolated as a syrup; $[\alpha]_D^{25}$ + 3.8° (*c* 1.3, $CHCl_3$); ^{1}H-NMR (270 MHz, $CDCl_3$): δ 7.37–7.25 (m, 10 H, 2 Ph), 5.78–5.69 (m, 2 H, H-5,6), 4.91, 4.72, 4.66, and 4.62 (4 d, each 1 H, *J* 12.5 Hz, 2 CH_2Ph), 4.23 (d, 2 H, $J_{3,7}$ 3.7 Hz, H-7,7), 4.19 (bd, 1 H, $J_{1,2}$ 7.3 Hz, H-1), 3.62 (dd, 1 H, $J_{2,3}$ 10.3 Hz, H-2), 2.25–2.07 (m, 3 H, H-3,4,4), and 2.00 (s, 3 H, Ac).

This compound did not give satisfactory analytical data because of its volatility.

4-O-Acetyl-3,6-di-O-benzyl-5a-carba-1,2-di-O-(methylsulfonyl)-α-D-glucopyranose (**7**).—To a solution of **5** (367 mg, 1.00 mmol) in 1:1 acetone–H_2O (8 mL) was added 4-methylmorpholine *N*-oxide (234 mg, 2.0 mmol) and 0.05 M osmium tetraoxide–*tert*-butanol (1.0 mL, 0.05 mmol), and the mixture was stirred for 2 h at room temperature in the dark. Then, $NaHSO_3$ (21 mg, 0.20 mmol) was added to the mixture, which was stirred for 1 h and diluted with EtOAc (100 mL). The organic layer was washed with H_2O, dried, and evaporated. The residue was dissolved in pyridine (8 mL) and treated with $MeSO_2Cl$ (0.31 mL, 4.0 mmol) for 14 h at room temperature. The mixture was diluted with EtOAc (100 mL) and washed with H_2O, dried, and evaporated. The product was chromatographed on a column

of silica gel (28 g) with 1:12 butanone–PhMe as eluent to give **7** (499 mg, 90%) as a syrup; $[\alpha]_D^{23}$ + 59° (*c* 1.1, $CHCl_3$); ^{1}H-NMR (270 MHz, $CDCl_3$): δ 7.36–7.23 (m, 10 H, 2 Ph), 5.18 (dd, 1 H, $J_{3,4}$ 9.5, $J_{4,5}$ 10.6 Hz, H-4), 5.10 (q, 1 H, $J_{1,2} = J_{1,5a.ax} = J_{1,5a.eq}$ = 2.9 Hz, H-1), 4.71 and 4.65 (2 d, each 1 H, *J* 11.2 Hz, CH_2Ph), 4.43 (dd, 1 H, $J_{2,3}$ 9.5 Hz, H-2), 4.41 (s, 2 H, CH_2Ph), 3.91 (t, 1 H, H-3), 3.36 (d, 2 H, $J_{5,6}$) 3.7 Hz, H-6,6), 3.15 and 2.82 (2 s, each 3 H, 2 SO_2Me), 2.33 and 2.23 (m, 2 H, H-5, 5a.*eq*), 1.91 (s, 3 H, Ac), and 1.82 (ddd, 1 H, $J_{1,5a.ax}$ 1.8, $J_{5,5a.ax}$ 13.9, $J_{5a,5a}$ 15.8 Hz, H-5a.*ax*).

Anal. Calcd for $C_{25}H_{32}O_{10}S_2$: C, 53.94; H, 5.79. Found: C, 53.79; H, 5.65.

*4-O-Acetyl-1-azido-3,6-di-O-benzyl-5a-carba-1-deoxy-2-O-(methylsulfonyl)-β-*D*-glucopyranose* (**8**).—A mixture of **7** (84 mg, 0.15 mmol), sodium azide (40 mg, 0.69 mmol), and *N*,*N*-dimethylformamide (DMF) (4 mL) was stirred for 3 days at 80°, and, after cooling, diluted with EtOAc (80 mL) and washed with H_2O, dried, and evaporated. The residue was chromatographed on a column of silica gel (3 g) with 1:20 EtOAc–PhMe as eluent to given **8** (73 mg, 96%) as crystals; mp 118–119° (from EtOH); $[\alpha]_D^{27}$ – 9° (*c* 1.4, $CHCl_3$); ^{1}H-NMR (270 MHz, $CDCl_3$): δ 7.38–7.24 (m, 10 H, 2 Ph), 5.01 (dd, 1 H, $J_{3,4}$ 9.5, $J_{4,5}$ 10.6 Hz, H-4), 4.80 and 4.63 (2 d, each 1 H, *J* 11 Hz, CH_2Ph), 4.45 (t, 1 H, $J_{1,2} = J_{2,3}$ = 9.5 Hz, H-2), 4.43 (s, 2 H, CH_2Ph), 3.57 (t, 1 H, H-3), 3.52 (ddd, 1 H, $J_{1,5a.ax}$ 13.2, $J_{1,5a.eq}$ 4.8 Hz, H-1), 3.41 (dd, 1 H, $J_{5,6a}$ 4, $J_{6,6}$ 9.2 Hz, H-6a), 3.29 (dd, 1 H, $J_{5,6b}$ 6.6 Hz, H-6b), 2.99 (s, 1 H, SO_2Me), 2.30 (dt, 1 H, $J_{5,5a.eq}$ 4.8 Hz, $J_{5a,5a}$ 13.2 Hz, H-5a.*eq*), 1.99–1.88 (m, 1 H, H-5), 1.85 (s, 3 H, Ac), and 1.48 (q, $J_{5,5a.ax}$ 13.2 Hz, H-5a.*ax*).

Anal. Calcd for $C_{24}H_{29}N_3O_7S$: C, 57.24; H, 5.80; N, 8.34. Found: C, 57.54; H, 5.81; N, 8.13.

N-*Acetyl-4-O-acetyl-3,6-di-O-benzyl-5a-carba-2-O-(methylsulfonyl)-β-*D*-glucopyranosylamine* (**9**).—A solution of **8** (319 mg, 0.63 mmol) in 2:1 EtOAc–EtOH (6 mL) containing Ac_2O (0.08 mL) was hydrogenated in the presence of Raney nickel (0.5 mL) for 2 days at room temperature under atmospheric pressure. The catalyst was removed by filtration and the filtrate was evaporated. The residue was chromatographed on a column of silica gel (15 g) with 1:2 butanone–PhMe as eluent to give **9** (299 mg, 91%) as crystals; mp 126–127.5° (from EtOH); $[\alpha]_D^{25}$ + 7.6° (*c* 1.2, $CHCl_3$); ^{1}H-NMR (270 MHz, $CDCl_3$): δ 7.36–7.23 (m, 10 H, 2 Ph), 6.09 (d, 1 H, $J_{1,NH}$ 7.7 Hz, NH), 5.12 (dd, 1 H, $J_{3,4}$ 9.5, $J_{4,5}$ 11 Hz, H-4), 4.71 and 4.66 (2 d, each 1 H, *J* 11.2 Hz, CH_2Ph), 4.43 and 4.38 (2 d, each 1 H, *J* 11.7 Hz, CH_2Ph), 4.31 (dd, 1 H, $J_{1,2}$ 10.6, $J_{2,3}$ 9.5 Hz, H-2), 4.18–4.06 (m, 1 H, H-1), 3.65 (t, 1 H, H-3), 3.37 (dd, 1 H, $J_{5,6a}$ 4, $J_{6,6}$ 9.3 Hz, H-6a), 3.31 (dd, 1 H, $J_{5,6b}$ 4.8 Hz, H-6b), 2.78 (s, 3 H, SO_2Me), 2.26 (dt, 1 H, $J_{1,5a.eq} = J_{5,5a.eq}$ 4, $J_{5a,5a}$ 13.9 Hz, H-5a.*eq*), 1.99 and 1.89 (2 s, each 3 H, 2 Ac), 1.98–1.84 (m, 1 H, H-5), and 1.33 (q, 1 H, $J_{1,5a.ax} = J_{5,5a.ax}$ 13.9 Hz, H-5a.*ax*).

Anal. Calcd for $C_{26}H_{33}NO_8S$: C, 60.10, H, 6.40; N, 2.70. Found: C, 60.27, H, 6.52; N, 2.62.

N-*Acetyl-2,4-di-O-acetyl-3,6-di-O-benzyl-5a-carba-β-*D*-mannopyranosylamine* (**10**).—A mixture of **9** (263 mg, 0.51 mmol), anhyd NaOAc (125 mg, 1.52 mmol),

and aq 90% 2-methoxyethanol (5 mL) was refluxed for 23 h, and then evaporated to dryness. The residue was acetylated in the usual manner and the product was chromatographed on a column of silica gel (10 g) with 1:2 butanone–PhMe as eluent to give **10** (237 mg, 97%) as crystals; mp 169–171° (from EtOH), $[\alpha]_D^{27}$ – 6° (*c* 1.5, $CHCl_3$); ^{1}H-NMR (270 MHz, $CDCl_3$): δ 7.36–7.23 (m, 10 H, 2 Ph), 5.61 (t, 1 H, $J_{1,2} = J_{2,3}$ 2.7 Hz, H-2), 5.50 (d, 1 H, $J_{1,NH}$ 8.4 Hz, NH), 5.11 (t, 1 H, $J_{3,4} = J_{4,5} = 10.3$ Hz, H-4), 4.65, 4.46, 4.41 and 4.36 (4 d, each 1 H, *J* 12.1 Hz, 2 CH_2Ph), 4.19–4.09 (m, 1 H, H-1), 3.46 (dd, 1 H, $J_{2,3}$ 2.7, $J_{3,4}$ 10.3 Hz, H-3), 3.40 (dd, 1 H, $J_{5,6a}$ 3.8, $J_{6,6}$ Hz, H-6a), 3.30 (dd, 1 H, $J_{5,6b}$ 6.2 Hz, H-6b), 2.17, 1.95 and 1.93 (3 s, each 3 H, 3 Ac).

Anal. Calcd for $C_{27}H_{33}NO_7$; C, 67.06; H, 6.88; N, 2.90. Found: C, 67.02; H, 6.58; N, 2.95.

(*1*R,*2*R,*3*R,*5*R,*8*R,*10*R)- (**11**) and (*1*S,*2*R,*3*R,*5*R,*8*R,*10*S)-*2-Benzyloxy-5-phenyl-4,6,11-trioxatricyclo[8.1.0^{3,8}]undecane* (**12**).—To a solution of **3** (1.84 g, 7.9 mmol) in CH_2Cl_2 (23 mL) was added aq M sodium phosphoric acid (8 mL), M sodium phosphinic acid (8 mL), and *m*-chloroperoxybenzoic acid (1.95 g, 7.9 mmol), and this was stirred for 2 h at room temperature. The mixture was then diluted with CH_2Cl_2 (120 mL) and washed successively with H_2O, 20% aq $Na_2S_2O_3$, and H_2O, dried, and evaporated, giving a mixture (2.25 g) of the epoxides. Without separation, the mixture was treated with NaH (630 mg, 15.8 mmol) in DMF (14 mL) for 1 h at room temperature, and, with benzyl chloride (1.82 mL, 15.8 mmol) for a further 1 h. After addition of MeOH, the mixture was evaporated and the residue was dissolved in EtOAc (120 mL), and the solution was washed with H_2O thoroughly, dried, and evaporated. The products were chromatographed on a column of silica gel (60 g) with 1:30 EtOAc–hexane as eluent to give, first, **12** (250 mg, 9.3%) as crystals; mp 86–87° (from EtOH–hexane); $[\alpha]_D^{22}$ – 26° (*c* 1.2, $CHCl_3$); ^{1}H-NMR (90 MHz, $CDCl_3$): δ 7.60–7.20 (m, 10 H, 2 Ph), 5.54 (s, 1 H, C*H*Ph), 4.90 and 4.75 (ABq, 2 H, *J* 11.2 Hz, CH_2Ph), 4.16 (dd, 1 H, $J_{7eq,8}$ 4.7, $J_{7,7}$ 11 Hz, H-7*eq*), 3.86 (d, 1 H, $J_{2,3}$ 8.2 Hz, H-2), 3.60 (dd, 1 H, $J_{3,8}$ 10.4 Hz, H-3), 3.55 (t, 1 H, $J_{7ax,8}$ 11 Hz, H-7*ax*), 3.30–3.15 (m, 2 H, H-10), 2.19–1.68 (m, 2 H, H-8, 9*eq*), and 1.49 (ddd, 1 H, *J* 1.8, *J* 2.5, $J_{9,9}$ 11.5 Hz, H-9*ax*).

Anal. Calcd for $C_{21}H_{22}O_4$: C, 74.54; H, 6.55. Found: C, 74.27; H, 6.73.

The second fraction gave **11** (2.37 g, 88%), isolated as crystals; mp 78–79° (from EtOH); $[\alpha]_D^{22}$ – 6.8° (*c* 0.9, $CHCl_3$); ^{1}H-NMR: δ 7.60–7.20 (m, 10 H, 2 Ph), 5.53 (s, 1 H, C*H*Ph), 4.98 and 4.73 (ABq, 2 H, *J* 13 Hz, CH_2Ph), 4.12 (dd, $J_{7eq,8}$ 4.4, $J_{7,7}$ 11 Hz, H-7*eq*), 4.00–3.85 (m, 2 H, H-2,3), 3.52 (dd, 1 H, $J_{7ax,8}$ 10.4 Hz, H-7*ax*), 3.38–3.20 (m, 2 H, H-1,10), and 2.15–1.45 (m, 3 H, H-8,9*ax*,9*eq*).

Anal. Found: C, 74.38; H, 6.64.

*1-Azido-3-*O*-benzyl-4,6-*O*-benzylidene-5a-carba-1-deoxy-α-*D*-mannopyranose* (**13**) *and 2-azido-3-*O*-benzyl-4,6-*O*-benzylidene-5a-carba-2-deoxy-β-*D*-glucopyranose* (**16**).—A mixture of **11** (2.35 g, 6.94 mmol), NaN_3 (1.35 g, 20.8 mmol), and DMF (36 mL) was stirred for 2 days at 110°, and evaporated and then coevaporated with PhMe to dryness. The residue was dissolved in EtOAc (100 mL), washed thor-

oughly with H_2O, dried, and evaporated. The products were chromatographed on a column of silica gel (70 g) with 1:20 butanone–PhMe as eluent to give, first, **13** (2.14 g, 82%) as a syrup; $[\alpha]_D^{22}$ + 39° (*c* 1.2, $CHCl_3$); ^{1}H-NMR (90 MHz, $CDCl_3$): δ 1.40–1.85 (m, 2 H, H-5a,5a), 2.13 (m, 1 H, H-5), 2.80 (s, 1 H, OH), 3.63 (t, 1 H, $J_{5,6ax} = J_{6,6}$ = 11 Hz, H-6*ax*), 3.53–4.12 (m, 4 H, H-1,2,3,4), 4.13 (dd, 1 H, $J_{5,6eq}$ 4.2 Hz, H-6*eq*), 4.66 and 4.89 (ABq, 2 H, *J* 11.4 Hz, CH_2Ph), 5.60 (s, 1 H, C*H*Ph), and 7.26–7.60 (m, 10 H, 2 Ph).

Anal. Calcd for $C_{21}H_{23}N_3O_4$: C, 66.13; H, 6.08; N, 11.02. Found: C, 66.37; H, 6.02; N, 10.91.

The second fraction gave **16** (194 mg, 7.3%) isolated as crystals; mp 100–101° (from EtOAc–hexane); $[\alpha]_D^{22}$ – 145° (*c* 0.85, $CHCl_3$); ^{1}H-NMR (90 MHz, $CDCl_3$): δ 1.06 (q, 1 H, $J_{1,5a.ax} = J_{5,5a.ax} = J_{5a,5a}$ = 9 Hz, H-5a.*ax*), 1.50–2.05 (m, 2 H, H-5,5a.*eq*), 2.48 (br s, 1 H, OH), 3.15–3.80 (m, 5 H, H-1,2,3,4,6*ax*), 4.17 (dd, 1 H, $J_{5,6eq}$ 4.2, $J_{6,6}$ 11 Hz, H-6*eq*), 4.76 and 4.79 (ABq, 2 H, *J* 10.5 Hz, CH_2Ph), 5.56 (s, 1 H, C*H*Ph), and 7.20–7.60 (m, 10 H, 2 Ph).

Anal. Found: C, 66.40; H, 6.29; N, 10.85.

*1-Acetamido-2-azido-3-*O*-benzyl-4,6-*O*-benzylidene-5a-carba-1,2-dideoxy-α-*D*-mannopyranose* (**15**) *and 2-acetamido-1-azido-3-*O*-benzyl-4,6-*O*-benzylidene-5a-carba-1,2-dideoxy-β-*D*-glucopyranose* (**17**).—To a solution of **13** (2.14 g, 5.61 mmol) in dry pyridine (40 mL) was added $MeSO_2Cl$ (0.72 mL, 11.2 mmol) at 0°, and the mixture was stirred for 3 h at room temperature. After addition of MeOH (5 mL), the mixture was evaporated and the residue was chromatographed on a column of silica gel (50 g) with 1:10 EtOAc–hexane as eluent to give a crude mesylate **14** (2.56 g, 99%) as a syrup, $[\alpha]_D^{22}$ + 9.5° (*c* 0.6, $CHCl_3$); ^{1}H-NMR (270 MHz, $CDCl_3$): δ 2.20 (m, 1 H, H-5), 3.01 (s, 3 H, SO_2Me), 3.69 (t, 1 H, $J_{5,6ax} = J_{6,6}$ = 11 Hz, H-6*ax*), 3.90 (dd, 1 H, $J_{2,3}$ 2.8, $J_{3,4}$ 9 Hz, H-3), 3.96 (t, 1 H, $J_{4,5}$ 9 Hz, H-4), 4.13 (q, 1 H, $J_{1,2} = J_{1,5a.ax} = J_{1,5a.eq}$ = 3 Hz, H-1), 4.17 (dd, 1 H, $J_{5,6eq}$ 4.4 Hz, H-6eq), 4.71 and 4.90 (ABq, 2 H, *J* 11.6 Hz, CH_2Ph), 4.89 (dd, 1 H, $J_{1,2}$ 3, $J_{2,3}$ 2.8 Hz, H-2), 5.65 (s, 1 H, C*H*Ph), and 7.28–7.55 (m, 10 H, 2 Ph).

To a stirred suspension of $LiAlH_4$ (1.05 g, 28 mmol) in tetrahydrofuran (25 mL) was added dropwise a solution of crude **14** (2.54 g, 5.53 mmol) in THF (25 mL) at 0°, and then the mixture was stirred for 2 h at room temperature. After addition of MeOH (10 mL) and 15% aq NaOH (5 mL), the mixture was evaporated to dryness. The residue was treated with Ac_2O (25 mL) and pyridine (25 mL) for 2 h at room temperature, and the mixture was evaporated and then azeotroped with PhMe several times. A mixture of the residue and NaN_3 (0.88 g, 17 mmol) in DMF (35 mL) was stirred overnight at 100° and then evaporated. The residue was dissolved in EtOAc (100 mL), and the solution was washed with H_2O thoroughly, dried, and evaporated. The residual products were chromatographed on a column of silica gel (50 g) with 1:8 butanone–PhMe as eluent to give, first, **17** (1.39 g, 59%) as crystals; mp 230–231° (from EtOH); $[\alpha]_D^{19}$ + 10° (*c* 2.3, $CHCl_3$); ^{1}H-NMR (270 MHz, $CDCl_3$): δ 1.07 (q, 1 H, $J_{1,5a.ax} = J_{5,5a.ax} = J_{5a,5a}$ = 11.5 Hz, H-5a.*ax*), 1.80 (dt, 1 H, $J_{1,5a.eq} = J_{5,5a.eq}$ = 4.5 Hz, H-5a.*eq*), 1.91 (s, 3 H, Ac), 3.52 (dt, 1 H, $J_{1,2} = J_{2,3}$ = 11.5,

$J_{2,NH}$ 1.9 Hz, H-2), 3.59 (t, 1 H, $J_{5,6ax} = J_{6,6} = 11$ Hz, H-6), 3.61 (dd, 1 H, $J_{3,4}$ 9.5 Hz, H-3), 3.79 (td, 1 H, H-1), 3.87 (t, 1 H, $J_{4,5}$ 9.5 Hz, H-4), 4.17 (dd, 1 H, $J_{5,6eq}$ 4.4 Hz, H-6*eq*), 4.62 and 4.91 (ABq, 2 H, *J* 11.7 Hz, CH_2Ph), 5.58 (m, 2 H, PhCH), and 7.28–7.55 (m, 10 H, 2 Ph).

Anal. Calcd for $C_{23}H_{26}N_4O_4$: C, 65.39; H, 6.20; N, 13.26. Found: C, 65.22; H, 6.16; N, 13.14.

The second fraction gave **15** (284 mg, 12%) isolated as crystals; mp 208–209° (from EtOAc–hexane); $[\alpha]_D^{23} - 22°$ (*c* 0.9, $CHCl_3$); ^{1}H-NMR (270 MHz, $CDCl_3$): δ 1.60 (m, 1 H, H-5a.*ax*), 1.95 (s, 3 H, Ac), 3.68 (t, 1 H, $J_{5,6ax} = J_{6,6} = 11$ Hz, H-6*ax*), 3.75 (dd, 1 H, $J_{2,3}$ 2.9, $J_{3,4}$ 9.5 Hz, H-3), 4.07 (t, 1 H, $J_{4,5}$ 9.5 Hz, H-4), 4.14 (dd, 1 H, $J_{5,6eq}$ 4.4 Hz, H-6*eq*), 4.14–4.25 (m, 2 H, H-1,2), 4.73 and 4.88 (ABq, 2 H, *J* 12.3 Hz, CH_2Ph), 5.54 (br. d, 1 H, $J_{1,NH}$ 6.6 Hz, NH), 5.66 (s, 1 H, C*H*Ph), and 7.28–7.55 (m, 10 H, 2 Ph).

Anal. Found: C, 65.04; H, 6.08; N, 13.18.

*2-Acetamido-1-azido-3-*O*-benzyl-5a-carba-1,2-dideoxy-β-*D*-glucopyranose* (**18**).—A mixture of **17** (332 mg, 0.786 mmol) and 70% aq AcOH (10 mL) was stirred for 2 h at 65°, and then evaporated. The residue was chromatographed on a column of silica gel (11 g) with 1:10 EtOH–PhMe as eluent to give the diol **18** (237 mg, 90%) as a syrup; $[\alpha]_D^{19} + 52°$ (*c* 1.4, $CHCl_3$); ^{1}H-NMR (90 MHz, $CHCl_3$): δ 1.96 (s, 3 H, Ac), 3.35–3.85 (m, 6 H, H-1,2,3,4,6,6′), 4.71 (s, 2 H, CH_2Ph), 5.62 (br d, 1 H, $J_{2,NH}$ 8.3 Hz, NH), and 7.20–7.40 (m, 5 H, Ph).

Anal. Calcd for $C_{16}H_{22}N_4O_4$: C, 57.17; H, 6.63; N, 16.76. Found: C, 57.18; H, 6.34; N, 16.54.

*2-Acetamido-1-azido-6-*O*-benzoyl-3-*O*-benzyl-5a-carba-1,2-dideoxy-β-*D*-glucopyranose* (**19**).—To a solution of **18** (52 mg, 0.16 mmol) in pyridine (1.5 mL) was added BzCl (20 μL, 0.17 mmol), and the mixture was stirred for 40 min at −15°. After treatment with a small amount of MeOH, the mixture was azeotroped with PhMe and the residue was chromatographed on a column of silica gel (2.4 g) with 1:30 EtOH–PhMe as eluent to give the benzoate **19** (58 mg, 84%) as crystals; mp 213.5–214.5° (from EtOH–hexane); $[\alpha]_D^{19} + 9°$ (*c* 1.3, $CHCl_3$); ^{1}H-NMR (90 MHz, $CDCl_3$): δ 1.41 (q, 1 H, $J_{1,5a.ax} = J_{5,5a.ax} = J_{5a,5a} = 12$ Hz, H-5a.*ax*), 1.94 (s, 3 H, Ac), 2.84 (d, 1 H, $J_{4,OH}$ 3 Hz, OH), 3.25–4.00 (m, 4 H, H-1,2,3,4), 4.37 (dd, 1 H, $J_{5,6}$ 2.7, $J_{6,6}$ 11.5 Hz, H-6), 4.62 (dd, 1 H, $J_{5,6}$ 4.1 Hz, H-6′), 4.73 (s, 2 H, CH_2Ph), 5.51 (br d, 1 H, $J_{2,NH}$ 7.9 Hz, NH), and 7.28–8.20 (m, 10 H, 2 Ph).

Anal. Calcd for $C_{23}H_{26}N_4O_5 \cdot 0.25H_2O$: C, 62.36; H, 6.03; N, 12.64. Found: C, 62.30; H, 5.91; N, 12.62.

*2-Acetamido-1-azido-6-*O*-benzoyl-3-*O*-benzyl-5a-carba-1,2-dideoxy-4-*O*-(2,3,4,6-tetra-*O*-acetyl-β-*D*-glucopyranosyl)-β-*D*-glucopyranose* (**20**).—To a solution of **19** (56 mg, 0.13 mmol) in 1,2-dichloroethane (5 mL) was added in turn tetramethylurea (45 μL), silver triflate (49 mg, 0.19 mmol), and 2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranosyl bromide (168 mg, 0.14 mmol), and the mixture was stirred for 24 h at reflux temperature. After neutralization with Et_3N, insoluble material was removed by filtration and the filtrate was evaporated. Chromatography of the

residue on silica gel (10 g) with 3:2 EtOAc–hexane as eluent gave the condensate **20** (77 mg, 80%) as crystals; mp 171–172° (from EtOH); $[\alpha]_D^{19} - 3.5°$ (*c* 0.74, $CHCl_3$); ^{1}H-NMR (270 MHz, $CDCl_3$): δ 1.51 (q, 1 H, $J_{1,5a.ax} = J_{5,5a.ax} = J_{5a,5a} = 11.8$ Hz, H-5a.*ax*), 1.85, 1.96, 1.98, 1.99, and 2.09 (5 s, each 3 H, 5 Ac), 1.95–2.15 (m, 2 H, H-5,5a.*eq*), 3.47 (ddd, 1 H, $J_{4',5'}$ 9.2, $J_{5',6'a}$ 2.2, $J_{5',6'b}$ 4.2 Hz, H-5′), 3.66–3.72 (m, 3 H, H-1,2,3), 3.86 (m, 1 H, H-4), 3.90 (dd, 1 H, $J_{6',6'}$ 12.5 Hz, H-6′a), 4.18 (dd, 1 H, H-6′b), 4.36 (dd, 1 H, $J_{6,6}$ 11, $J_{5,6a}$ 5.3 Hz, H-6a), 4.54 (dd, 1 H, $J_{5,6b}$ 4 Hz, H-6b), 4.60 and 4.89 (ABq, 2 H, *J* 12.5 Hz, CH_2Ph), 4.62 (d, 1 H, $J_{1',2'}$ 7.7 Hz, H-1′), 5.04 (dd, 1 H, $J_{2',3'}$ 9.2 Hz, H-2′), 5.06 (t, 1 H, $J_{3',4'} = J_{4',5'} = 9.2$ Hz, H-4′), 5.14 (t, 1 H, H-3′), 5.54 (br s, 1 H, NH), and 7.28–8.10 (m, 10 H, 2 Ph).

Anal. Calc. for $C_{37}H_{44}N_4O_{14}$: C, 57.80; H, 5.77; N, 7.29. Found: C, 57.56; H, 5.64; N, 7.25.

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