ELSEVIER

Carbohydrate Research 268 (1995) 73–84

CARBOHYDRATE RESEARCH

Synthesis of specifically deoxygenated analogues of the methyl α-glycoside of the intracatenary monosaccharide repeating unit of the O-polysaccharide of *Vibrio cholerae* O:1 ☆

Makoto Gotoh [1], Pavol Kováč *

NIDDK, National Institutes of Health, LMC, Section on Carbohydrates, Bldg. 8, Room B1A24 Bethesda, MD 20892-0815, USA

Received 10 June 1994; accepted 16 September 1994

Abstract

Treatment of methyl α-D-perosaminide (**1**) with γ-butyrolactone gave the 2′-deoxy analogue of methyl 4,6-dideoxy-4-(3-deoxy-L-*glycero*-tetronamido)-α-D-mannopyranoside (**13**), the methyl α-glycoside of the intracatenary monosaccharide repeating unit of the O-polysaccharide of *Vibrio cholerae* O:1. The analogous 4′-deoxy derivative was obtained by hydrogenolysis of a 4′-chlorodeoxy precursor, obtained by chlorination of methyl 2,3-di-*O*-benzyl-4-(2-*O*-benzyl-3-deoxy-L-*glycero*-tetronamido)-4,6-dideoxy-α-D-mannopyranoside with methanesulfonyl chloride in DMF. To obtain the 3-deoxy analogue of **13**, methyl 4-amino-2-*O*-benzyl-4,6-dideoxy-3-*O*-*p*-methoxybenzyl-α-D-mannopyranoside was converted into methyl 2-*O*-benzyl-4,6-dideoxy-4-(2,4-di-*O*-benzyl-3-deoxy-L-*glycero*-tetronamido)-α-D-mannopyranoside, which was deoxygenated via the corresponding 3-*O*-(imidazol-1-ylthiocarbonyl) derivative. Subsequent catalytic debenzylation gave the deoxy compound (**24**). In an alternative synthesis, which is also generally useful for the preparation of 4-*N*-acyl-3-deoxy derivatives of **1**, methyl 4-azido-4,6-dideoxy-α-D-mannopyranoside was converted through a series of transformations into methyl 4-amino-2-*O*-benzyl-3,4,6-tri-

☆ Synthesis of ligands related to the *Vibrio cholerae* O-specific antigen. Part 4. For Part 3 see Ref. [1].

* Corresponding author. NIDDK, National Institutes of Health, LMC, Section on carbohydrates, Bldg. 8, Room B1A24, Bethesda, MD 20892-0815, USA

[1] On leave from Pharmaceutical Research Center, Nihon Nohyaku Co. Ltd., 326-2 Oyamada-cho, Kawachinagano-shi, Osaka 586, Japan.

SSDI 0008-6215(94)00319-X

deoxy-α-D-mannopyranoside. Subsequent reaction with 2-*O*-benzyl-3-deoxy-L-*glycero*-tetronolactone, followed by hydrogenolysis of the formed tetronamido derivative, gave **24**.

Keywords: Deoxygenated analogues; Methyl α-glycoside; Monosaccharide repeating unit; O-Polysaccharide; *Vibrio cholerae* O:1

1. Introduction

This laboratory has studied the binding of carbohydrate antigens to immunoglobulins for many years [2]. We are interested, *inter alia*, in evaluating the role of hydrogen bonding in the binding process. Data germane to these phenomena can be obtained by measuring the binding of antibodies to a series of ligands related to the polymeric O-antigen, some of which have been deoxygenated or fluorinated at a specific position. We can draw important conclusions from these studies because we can rationally interpret changes in binding resulting from the specific replacement, with fluorine or hydrogen, of hydroxyl groups in ligands that bind to proteins [2]. We are currently evaluating in such a way the binding of the O-specific antigenic polysaccharide (OPS) of *Vibrio cholerae* O:1 to its homologous antibodies. These studies require a large number of ligands related to the OPS.

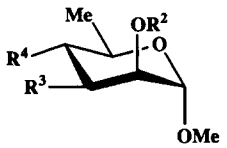
Vibrio cholerae O:1 occurs as two main serologically distinct forms, Ogawa and Inaba. The third, Hikojima, is a rare, unstable intermediate serotype [3]. The O-antigens of seroforms Ogawa and Inaba contain the same intracatenary monosaccharide repeating unit, namely 4-amino-4,6-dideoxy-D-mannose (D-perosamine) which is *N*-acylated with 3-deoxy-L-*glycero*-tetronic acid. The synthesis of the methyl α-glycoside (**13**) of this intracatenary monosaccharide repeating unit of the OPS, as well as of the corresponding α-(1 → 2)-linked disaccharide [1], have already been described. Here, we report on the synthesis of analogues of **13**, deoxygenated specifically at each of positions [2] 3, 2′, and 4′.

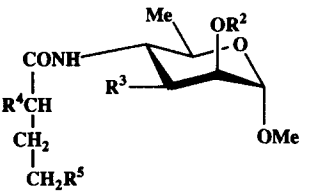
2. Results and discussion

The method for 3-deoxy-L-*glycero*-tetronylation of methyl perosaminide (**1**) with 3-deoxy-L-*glycero*-tetronolactone (**28**) was originally developed by Kenne et al. [5]. Compound **14**, the 2′-deoxy analogue of **13**, was prepared in a similar way, using the γ-lactone of 4-hydroxybutyric acid (**26**) for *N*-acylation. The inexpensive, commercially available lactone **26** was used in excess, serving as both solvent and reagent. The

[2] In the description of the NMR data, and occasionally elsewhere in the text, atoms associated with the 3-deoxy-L-*glycero*-tetronamido group are denoted with a prime.

crystalline product **14** was obtained in a yield of 88%, and it was further characterized through the crystalline per-*O*-acetyl derivative **15**.

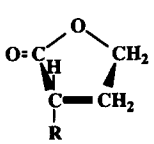


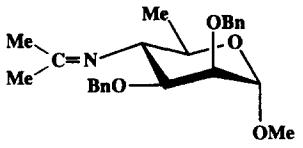


	R^2	R^3	R^4		R^2	R^3	R^4	R^5
1	H	OH	NH_2	**13**	H	OH	OH	OH
2	H	OH	N_3	**14**	H	OH	H	OH
3	Bn	OBn	N_3	**15**	Ac	OAc	H	OAc
4	Bn	OBn	NH_2	**16**	Bn	OBn	OBn	OH
5	Bn	OH	N_3	**17**	Bn	OBn	OBn	Cl
6	Bn	OMBn	N_3	**18**	H	OH	OH	H
7	Bn	OMBn	NH_2	**19**	Bn	OMBn	OBn	OH
8	Bn	OH	NH_2	**20**	Bn	OMBn	OBn	OBn
9	Bn	OH	NHAc	**21**	Bn	OH	OBn	OBn
10	Bn	OItc	NHAc	**22**	Bn	OItc	OBn	OBn
11	Bn	H	NHAc	**23**	Bn	H	OBn	OBn
12	Bn	H	NH_2	**24**	H	H	OH	OH
				25	Bn	H	OBn	OH

MBn = *p*-methoxybenzyl
Itc = imidazol-1-ylthiocarbonyl

To prepare the 4′-deoxy derivative **18**, the azide **2** [1,6,7] was benzylated, applying the simple and efficient method for the alkylation of carbohydrates developed by Fügedi [8]. This afforded the di-*O*-benzyl derivative **3** in virtually theoretical yield. Compound **3** was previously obtained [9] as a byproduct of partial benzylation of **2**. The conversion of **3** to the benzylated amine **4** was effected with hydrogen sulfide [10,11]. Coupling of **4** with the 2-*O*-benzylated lactone **29**, obtained through **27** [1], then gave the fully protected, except HO-4′, perosaminide derivative **16** in 88% yield. To minimize the number of synthetic steps required from this stage to the desired deoxy derivative **18**, we converted **16** to the chloro derivative **17** (95%) in one step [12]. The presence and the position of the chlorine atom at C-4′ in the product **17** were evident from the upfield ^{13}C NMR chemical shift observed for the signal of C-4′ (40.69 ppm), which was assigned by heteronuclear correlation spectroscopy, supported by the attached proton test. Compound **17** was hydrogenolyzed in the presence of a palladium-on-charcoal catalyst. This effected simultaneous cleavage of the benzyl protecting groups and the chlorine atom, resulting in the formation of the target derivative **18**, which was obtained crystalline.





	R	30
26	H	
27	OAc	
28	OH	
29	OBn	

The starting material for the synthesis of the 3-deoxy-α-D-perosaminide derivative **24** was the known [9] 2-*O*-benzylated azido compound **5**, which was first *p*-methoxybenzylated at O-3. The resulting, fully protected substance **6** was converted to amine **7**, which was sequentially *N*-tetronylated with lactone **29** (→ **19**, 90%) and benzylated at the primary position O-4′. In view of the labor-intensive nature of the substrate **19**, the phase-transfer method of benzylation [13] was applied in the latter step, as a more powerful benzylation method could lead to the corresponding *N*-acyl-*N*-benzyl derivative [14]. This afforded the fully protected, crystalline derivative **20** in 95% yield. The hydroxyl group at O-3 was regenerated by treatment of **20** with ceric ammonium nitrate (CAN) to give **21**, the subsequent treatment of which with *N,N′*-thiocarbonyldiimidazole in refluxing tetrahydrofuran [15] gave the activated compound **22** in virtually theoretical yield. Deoxygenation at position 3 was effected by treatment of the latter with tributyltin hydride, to give the benzylated intermediate **23**. Subsequent hydrogenolysis gave the crystalline, deoxygenated ligand **24**.

In addition to the OPS of *Vibrio cholerae* O:1, *N*-acyl derivatives of perosamine occur also as constituents of other OPSs [9,16,17]. Therefore, in view of a potential interest in *N*-acyl derivatives of methyl perosaminide deoxygenated at position 3, we have designed a synthesis of methyl 4-amino-2-*O*-benzyl-3,4,6-trideoxy-α-D-mannopyranoside (**12**), which can be realized via a sequence of simple synthetic operations. Substance **12** can be used as a starting material for the preparation of virtually any *N*-acyl derivative of methyl 3-deoxy-α-D-perosaminide. The synthesis of **12** started with the versatile intermediate **5**, which was successively treated with hydrogen sulfide (→ **8**) and acetic anhydride. The formed acetamido derivative **9** was then deoxygenated, via the thiocarbonyl derivative **10** to give, after *N*-deacetylation, the target amine **12**, in a 43% overall yield (based on **5**). When this amine was treated with **29**, the *N*-tetronyl derivative **25** was obtained in 83% yield, and catalytic hydrogenolysis then produced **24**, indistinguishable from the independently synthesized material.

3. Experimental

General methods.—Thin-layer chromatography (TLC) was performed with *A*, 3:1 CH_2Cl_2–MeOH; *B*, 2:1 toluene–EtOAc; *C*, 6:1 hexane–EtOAc; *D*, 25:1 CH_2Cl_2–MeOH; *E*, 1:1 hexane–EtOAc; *F*, 10:1 CH_2Cl_2–MeOH; *G*, EtOAc (neat), and *H*, 1:4

hexane–EtOAc. Detection was effected with iodine vapors, by charring with 5% H_2SO_4 in EtOH, or with UV light, as applicable. Preparative chromatography was performed by gradient elution from columns of Silica Gel 60 (particle size 0.04–0.063 mm) using, at the onset of development, a solvent mixture slightly less polar than that used for TLC. Unless stated otherwise, optical rotations were measured at 25°C for solutions in $CHCl_3$, using a Perkin–Elmer Model 241 MC polarimeter. NMR spectra were obtained at 300 MHz for ^1H, and 75 MHz for ^{13}C. The measurements were done at ambient temperature, using a Varian XL 300 or a Varian Gemini spectrometer. The solvent used is listed for each measurement. For measurements in organic solvents, ^1H NMR chemical shifts are reported in ppm downfield of the signal of Me_4Si, while those determined in D_2O were measured from the signal of DHO (δ 4.78). The ^{13}C NMR chemical shifts were measured from the signal of $CDCl_3$ (δ 77.0), benzene (δ 128.0), or MeOH (δ 49.0 for measurements in D_2O). Assignments of NMR signals were made by first-order analysis of the spectra and by comparison with spectra of related substances. When feasible, the assignments were supported by homonuclear decoupling experiments or homonuclear and heteronuclear 2-dimensional correlation spectroscopy, using commercial software supplied with the spectrometers. Chemical ionization mass spectra (CIMS) were measured using ammonia as the reactive gas. γ-Butyrolactone was purchased from Aldrich Chemical Company, and used as supplied. Solutions in organic solvents were dried with anhydrous sodium sulfate, and concentrated at or below 40°C/2 kPa.

*Methyl 4,6-dideoxy-4-(4-hydroxybutyramido)-α-*D*-mannopyranoside* (**14**).—A solution of the amine **1** [4] (180 mg, 1 mmol) and γ-butyrolactone (**26**, 2 mL, 18.5 mmol) was heated for 48 h at 100°C. TLC (solvent *A*) showed that the reaction was complete and that one major and one minor product were formed. Concentration and chromatography gave **14** (233 mg, 88%); mp 115–117°C (from acetone); $[\alpha]_D$ +59.2° (*c* 0.8, H_2O). Diagnostically significant signals in the ^1H NMR spectrum (acetone-d_6) were at δ 7.05 (bs, 1 H, NH), 4.60 (bs, 1 H, H-1), 4.00–3.80 (m, partially overlapped, H-4), 3.78–3.50 (m, partially overlapped, H-4′a,b,5), 3.30 (s, 3 H, OCH_3), 2.35–2.25 (m, 2 H, H-2′a,b), 1.90–1.75 (m, 2 H, H-3′a,b), and 1.15 (d, 3 H, $J_{5,6}$ 6.2 Hz, H-6); ^{13}C NMR (acetone-d_6): δ 174.63 (CO), 101.86 (C-1), 70.80, 70.34 (C-2,3), 67.94 (C-5), 61.97 (C-4′), 54.68, 54.07 (OCH_3, C-4), 33.97 (C-2′), 29.49 (C-3′), and 18.42 (C-6); ^1H NMR (D_2O): δ 4.72 (d, 1 H, $J_{1,2}$ 1.8 Hz, H-1), 3.91 (dd, 1 H, $J_{2,3}$ 2.8 Hz, H-2), 3.87–3.71 (m, 3 H, H-3,4,5), 3.62–3.58 (m, 2 H, H-4′a,b), 3.38 (s, 3 H, OCH_3), 2.36–2.31 (m, 2 H, H-2′a,b), 1.88–1.78 (m, 2 H, H-3′a,b), and 1.19 (d, 3 H, $J_{5,6}$ 6.0 Hz, H-6); ^{13}C NMR (D_2O): δ 176.95 (CO), 100.99 (C-1), 69.20 (C-2), 68.41 (C-3), 67.50 (C-5), 61.00 (C-4′), 54.88 (OCH_3), 52.96 (C-4) 32.72 (C-2′), 27.92 (C-3′), and 16.96 (C-6); CIMS: *m/z* 264 ($[M + 1]^+$) and 281 ($[M + 18]^+$). Anal. Calcd for $C_{11}H_{21}NO_6$: C, 50.18; H, 8.04; N, 5.32. Found: C, 50.24; H, 8.08; N, 5.29.

*Methyl 4-(4-acetoxybutyramido)-2,3-di-*O*-acetyl-4,6-dideoxy-α-*D*-mannopyranoside* (**15**).—Compound **14** (100 mg) was treated overnight at room temperature with 1:1 pyridine–Ac_2O (2 mL). TLC (solvent *B*) showed that the reaction was complete and that one product was formed. Concentration and chromatography gave **15**; mp 76–78°C (from ether–hexane); $[\alpha]_D$ +72° (*c* 0.9, CHCl3); ^1H NMR ($CDCl_3$): δ 5.45 (d, 1 H, $J_{4,NH}$ 9.6 Hz, NH), 5.22, dd, 1 H, $J_{2,3}$ 3.2, $J_{3,4}$ 11.0 Hz, H-3), 5.14 (dd, 1 H, $J_{1,2}$ 2.0, Hz H-2), 4.66 (d, 1 H, H-1), 4.29–4.19 (m, 1 H, H-4), 4.12–4.05 (m, 2 H, 4′a,b),

3.70–3.65 (m, 1 H, H-5), 3.38 (s, 3 H, OCH_3), 2.24–2.10 (m, 5 H, H-2'a,b, $OCOCH_3$), 2.08–1.90 (m, 8 H, H-3'a,b, 2 $COCH_3$), and 1.28 (d, 3 H, $J_{5,6}$ 6.5 Hz, H-6); ^{13}C NMR ($CDCl_3$): δ 172.03, 171.06, 170.97, 170.16 (4 CO), 98.27 (C-1), 69.01 (C-2), 68.74 (C-3), 67.99 (C-5), 63.29 (C-4'), 54.92 (OCH_3), 51.11 (C-4), 32.75 (C-2'), 24.48 (C-3'), 20.82, 20.75, 20.67 ($COCH_3$), and 17.71 (C-6). Anal. Calcd for $C_{17}H_{27}NO_9$: C, 52.44: H, 6.99; N, 3.60. Found: C, 52.51; H, 6.99; N, 3.61.

*Methyl 4-azido-2,3-di-*O*-benzyl-4,6-dideoxy-α-*D*-mannopyranoside* (**3**).—Powdered KOH (5.5 g, 98 mmol) followed by benzyl bromide (3.3 mL, 28 mmol) was added to a solution of the azide **2** [1,6,7] (1.9 g, 9.35 mmol) in Me_2SO (10 mL). The suspension was stirred at room temperature for 2 h, when TLC (solvent *B*) showed that the reaction was complete. The mixture was filtered into a separatory funnel containing aq NaCl, the solids were washed with CH_2Cl_2, and after conventional processing the crude product was chromatographed (solvent *C*) to give **3** (3.5 g, 97%). The ^1H NMR data ($CDCl_3$) agreed with those reported [9], but a better resolved spectrum was obtained using C_6D_6 as the solvent: δ 4.63 (d, 1 H, $J_{1,2}$ 2.2 Hz, H-1), 4.49 (dd, 2 H, ^2J 12.2 Hz, CH_2Ph), 4.38 (dd, 2 H, ^2J 12.7 Hz, CH_2Ph), 3.83 (dd, partially overlapped, 1 H, $J_{2,3}$ 3.0, $J_{3,4}$ 10.1 Hz, H-3), 3.78 (dd, partially overlapped, 1 H, $J_{4,5}$ 10.0 Hz, H-4), 4.67 (t, 1 H, H-2), 3.49 (m, 1 H, H-5), 2.97 (s, 3 H, OCH_3), and 1.25 (d, 3 H, $J_{5,6}$ 6.0 Hz, H-6); ^{13}C NMR (C_6D_6): d 99.43 (C-1), 79.12 (C-3), 74.26 (C-2), 73.19, 71.88 (2 CH_2Ph), 67.62 (C-5), 64.96 (C-4), 54.54 (OMe), and 18.85 (C-6).

*Methyl 4-amino-2,3-di-*O*-benzyl-4,6-dideoxy-α-*D*-mannopyranoside* (**4**).—Hydrogen sulfide was passed for 30 min through a solution of the foregoing di-*O*-benzyl derivative **3** (3.55 g) in 7:3 pyridine–Et_3N (100 mL), and the solution was kept overnight at room temperature. TLC (solvent *D*) showed that the reaction was complete and that one product was formed. After concentration the residue was chromatographed to give **4** as an oil (3.2 g, 97%); $[\alpha]_D$ −18.7 (*c* 0.8, $CHCl_3$); ^1H NMR (C_6D_6): δ 4.80 (d, 1 H, $J_{1,2}$ 1.7 Hz, H-1), 4.53 (s, 2 H, CH_2Ph), 4.42, 4.21 (2 d, 1 H each, ^2J 11.7 Hz, CH_2Ph), 3.76 (dd, 1 H, $J_{2,3}$ 2.9 Hz, H-2), 3.60 (dd, partially overlapped, $J_{3,4}$ 10.0 Hz, H-3), 3.58 (m, partially overlapped, H-5), 3.25 (t, 1 H, *J* 9.8 Hz, H-4), 3.13 (s, 3 H, OCH_3), 1.30 (d, 3 H, $J_{5,6}$ 6.2 Hz, H-6), and 1.09 (bs, 2 H, NH_2); ^{13}C NMR (C_6D_6): δ 99.63 (C-1), 80.80 (C-3), 73.87 (C-2), 72.71, 71.10 (2 CH_2Ph), 70.36 (C-5), 54.17 (2 C, C-4, OCH_3), and 18.29 (C-6). Anal. Calcd for $C_{21}H_{27}NO_4$: C, 70.56: H, 7.61; N, 3.91. Found: C, 70.45; H, 7.62; N, 3.87.

When an acetone-containing solvent mixture was used for column chromatography, the material eluted consisted of an ~1:1 mixture of **4** and **30**, as indicated by NMR spectroscopy. Compound **30** could be converted into **4** by heating a solution of the mixture in aq 50% MeOH at 70°C for 1 h.

*Methyl 2,3-di-*O*-benzyl-4-(2-*O*-benzyl-3-deoxy-*L*-glycero-tetronamido)-4,6-dideoxy-α-*D*-mannopyranoside* (**16**).—A solution of **4** (1.74 g, 4.9 mmol) and the lactone **29** [1] (1.4 g, 7.3 mmol) in pyridine (2 mL) was heated at 110°C until all the starting amine was consumed (~3 days). TLC (solvent *E*) showed that essentially one product was formed. After concentration, chromatography gave **16** (2.35 g, 88%); mp 115–117°C (from EtOAc–hexane); $[\alpha]_D$ −10.7° (*c* 0.8); ^1H NMR ($CDCl_3$): δ 6.46 (d, 1 H, $J_{4,NH}$ 8.8 Hz, NH), 4.75–4.35 (m, 7 H, 3 CH_2Ph, H-1), 4.71 (H-1, overlapped with the CH_2Ph signal), 4.11–4.01 (m, 1 H, H-4), 4.00 (t, 1 H, *J* 6.2 Hz, H-2'), 3.87 (dd, 1 H,

$J_{2,3}$ 2.1, $J_{3,4}$ 10.5 Hz, H-3), 3.81 (bt, 1 H, H-2), 3.78–3.71 (m, 1 H, H-5), 3.70–3.60 (m, 2 H, H-4'a,b), 3.33 (s, 3 H, OCH_3), 2.41 (t, 1 H, $J_{4',OH}$ OH), 2.00–1.90 (m, 2 H, H-3'a,b), and 1.23 (d, 3 H, $J_{5,6}$ 6.3 Hz, H-6); ^{13}C NMR ($CDCl_3$): δ 99.20 (C-1), 78.73 (C-2'), 76.12 (C-3), 72.80 (2 C, C-2, CH_2Ph), 72.64, 71.02 (2 CH_2Ph), 67.49 (C-5), 59.38 (C-4'), 54.89 (OCH_3), 52.78 (C-4), 35.40 (C-3'), and 18.24 (C-6); CIMS: m/z 550 ($[M + 1]^+$) and 567 ($[M + 18]^+$). Anal. Calcd for $C_{32}H_{39}NO_7$: C, 69.92; H, 7.15. Found: C, 70.04; H, 7.22.

*Methyl 2,3-di-*O*-benzyl-4-[(2*S*)-2-benzyloxy-4-chlorobutyramido]-4,6-dideoxy-α-*D*-mannopyranoside* (**17**).—Mesyl chloride (0.4 mL, 5 mmol) was added, dropwise at room temperature, to a solution of **16** (0.28 g, 0.5 mmol) in DMF (5 mL). The mixture was heated at 65°C (bath) with stirring for 1 h, when TLC (solvent *F*) showed that the reaction was complete, and that one product was formed. After concentration, the residue was partitioned between CH_2Cl_2 and aq $NaHCO_3$, and the organic phase was dried and concentrated. Chromatography gave **17** (0.27 g, 95%); mp 144–146°C (from EtOAc–hexane); $[\alpha]_D$ −9.5° (*c* 1.3); ^1H NMR ($CDCl_3$): δ 6.36 (d, 1 H, $J_{4,NH}$ 8.7 Hz, NH), 4.75–4.66 (m, 3 H, H-1, CH_2Ph), 4.56–4.33 (m, 4 H, 2 CH_2Ph), 4.10–4.00 (m, 2 H, H-4,2'), 3.87–3.78 (m, 2 H, H-2,3), 3.75–3.65 (m, 1 H, H-5), 3.58–3.54 (m, 2 H, H-4'a,b), 3.33 (s, 3 H, OCH_3), 2.26–2.14, 2.06–1.94 (2 m, 2 H, H-3'a,b), and 1.21 (d, 3 H, $J_{5,6}$ 6.2 Hz, H-6); ^{13}C NMR ($CDCl_3$): δ 99.30 (C-1), 76.32 (C-3), 73.30, 72.71, 71.10 (3CH_2Ph), 72.97 (C-2), 67.60 (C-5), 54.89 (OCH_3), 52.73 (C-4), 40.69 (C-4'), 35.94 (C-3'), and 18.24 (C-6); CIMS: m/z. 568 ($[M + 1]^+$) and 585 ($[M + 18]^+$). Anal. Calcd for $C_{32}H_{38}ClNO_6$: C, 67.65; H, 6.74. Found: C, 67.66; H, 6.79.

*Methyl 4,6-dideoxy-4-[(2*S*)-2-hydroxybutyramido]-α-*D*-mannopyranoside* (**18**).—A mixture of **17** (0.2 g), Et_3N (0.7 mL) and 10% Pd–C catalyst (0.15 g) in EtOH (5 mL) was stirred under H_2 for 16 h at room temperature. One product was formed, as shown by TLC (solvent *G*). After conventional processing and chromatography, crystallization from $CHCl_3$ gave the product (**18**, 0.066 g, 71%); mp 135–137°C; $[\alpha]_D$ +42° (*c* 1, H_2O); ^1H NMR (D_2O): δ 4.76 (d, 1 H, $J_{1,2}$ 1.7 Hz, H-1), 4.15 (dd, 1 H, $J_{2',3'a}$ 4.6, $J_{2',3'b}$ 7.1 Hz, H-2'), 3.97–3.80 (m, 4 H, H-2,3,4,5), 3.42 (s, 3 H, OCH_3), 1.91–1.60 (m, 2 H, H-3'a,b), 1.22 (d, 3 H, $J_{5,6}$ 5.6 Hz, H-6), and 0.96 (t, 3 H, *J* 7.5 Hz, H-4'); ^{13}C NMR (D_2O): δ 101.11 (C-1), 72.89 (C-2'), 69.38 (C-2), 68.06 (C-3), 67.39 (C-5), 54.84 (OCH_3), 52.93 (C-4), 26.95 (C-3'), 16.90 (C-6), and 8.51 (C-4'); CIMS: m/z 264 ($[M + 1]^+$) and 281 ($[M + 18]^+$). Anal. Calcd for $C_{11}H_{21}NO_6$: C, 50.18; H, 8.04. Found: C, 50.27; H, 8.09.

*Methyl 2-*O*-benzyl-4-(2-*O*-benzyl-3-deoxy-*L*-glycero-tetronamido)-4,6-dideoxy-3-*O*-p-methoxybenzyl-α-*D*-mannopyranoside* (**19**).—Potassium hydroxide (1.35 g) and then *p*-methoxybenzyl chloride (1.2 mL) were added to a solution of 2-*O*-benzyl derivative **5** [9] (2 g, 6.8 mmol) in Me_2SO (20 mL). The mixture was stirred at room temperature for 3 h, when TLC (solvent *C*) showed that the reaction was complete. After processing as described above for the preparation of **3**, chromatography gave methyl 4-azido-2-*O*-benzyl-4,6-dideoxy-3-*O*-*p*-methoxybenzyl-α-*D*-mannopyranoside (**6**, 2.59 g, 92%); ^1H NMR ($CDCl_3$): δ 4.74–4.64 (m, 3 H, CH_2Ph, H-1), 4.65 (d, 1 H, $J_{1,2}$ 1.2 Hz, H-1), 4.52 (s, 2 H, CH_2Ph), 3.80 (s, 3 H, CH_3OPh), 3.72–3.70 (m, 1.5 H, H-2 overlapped with a portion of the H-3 signal), 3.70 (dd, partially overlapped, 0.5 H, $J_{2,3}$ 3.0 Hz, H-3), 3.57 (bt, 1 H, $J_{3,4}$ ~ 9.8 Hz, H-4), 3.50–3.40 (m, 1 H, H-5), 3.29 (s, 3 H, OCH_3), and 1.33

(d, 3 H, $J_{5,6}$ 6.1 Hz, H-6); ^{13}C NMR ($CDCl_3$): δ 99.17 (C-1), 78.03 (C-3), 73.19 (C-2), 72.78, 71.55 (2 CH_2Ph), 67.06 (C-5), 64.24 (C-4), 55.19 (CH_3OPh), 54.77 (OCH_3), and 18.42 (C-6); CIMS: m/z 431 ($[M + 18]^+$).

The foregoing azide **6** (2.59 g, 6.3 mmol) was treated with H_2S as described for the preparation of **4**, then chromatographed (solvent *F*) to give amorphous methyl 4-amino-2-*O*-benzyl-4,6-dideoxy-3-*O*-*p*-methoxybenzyl-α-D-mannopyranoside (**7**, 2.3 g, 95%); ^{1}H NMR ($CDCl_3$): δ 4.77–4.27 (m, 5 H, 2 CH_2Ph, H-1), 4.73 (d, partially overlapped, $J_{1,2}$ ~ 1.7 Hz, H-1), 3.80 (s, 3 H, CH_3OPh), 3.74 (dd, 1 H, $J_{2,3}$ 2.9 Hz, H-2), 3.54–3.45 (m, 2 H, H-3,5), 3.32 (s, 3 H. OCH_3), 3.01 (t, 1 H, *J* 9.8 Hz, H-4), and 1.28 (d, 3 H, *J* 6.4 Hz, H-6); ^{13}C NMR ($CDCl_3$): δ 99.22 (C-1), 79.43 (C-3), 72.63 (C-2), 72.56, 70.85 (2 CH_2Ph), 69.69 (C-5), 55.27 (OCH_3Ph), 54.60 (OCH_3), 53.58 (C-4), and 18.15 (C-6); CIMS: m/z 388 ($[M + 1]^+$).

A mixture of **7** (1.33 g, 3.4 mmol) and lactone **29** (0.82 g, 4.3 mmol) was heated at 110–115°C until almost all the amine was consumed (~ 2 days). One major product was formed (TLC, solvent *G*) which, after chromatography, was shown to be **19** (1.78 g, 90%); mp 98–99°C (from EtOAc–hexane); $[\alpha]_D$ −4° (*c* 0.9); ^{1}H NMR ($CDCl_3$): δ 6.43 (d, 1 H, $J_{4,NH}$ 9.0 Hz, NH), 4.76–4.28 (m, 7 H incl s, 1 H, at 4.70, H-1, 3 CH_2Ph), 4.08–3.98 (m, 2 H, H-2′,4), 3.85 (dd, 1 H, $J_{2,3}$ 2.9, $J_{3,4}$ 10.6 Hz, H-3), 3.78–3.64 (m, 7 H incl s, 3 H, at 3.76, CH_3OPh, H-2,5,4′a,b), 3.33 (s, 3 H, OCH_3), 2.50 (t, 1 H, $J_{4',OH}$ 6.1 Hz, OH), 1.98–1.92 (m, 2 H, H-3′), and 1.22 (d, 3 H, $J_{5,6}$ 6.2 Hz, H-6); ^{13}C NMR ($CDCl_3$): δ 99.25 (C-1), 78.87 (C-2′), 75.77 (C-3), 72.86 (2 C, C-2, CH_2Ph), 72.69, 70.74 (2CH_2Ph), 67.55 (C-5), 59.51 (C-4′), 55.28 (CH_3OPh), 54.95 (OCH_3), 52.86 (C-4), 35.47 (C-3′), and 18.35 (C-6); CIMS: m/z 588 ($[M + 1]^+$) and 597 ($[M + 18]^+$). Anal. Calcd for $C_{33}H_{41}NO_8$: C, 68.38; H, 7.13; N, 2.42. Found: C, 68.15; H, 7.27; N, 2.21.

*Methyl 2-*O*-benzyl-4,6-dideoxy-4-(2,4-di-*O*-benzyl-3-deoxy-*L*-glycero-tetronamido)-3-*O*-p-methoxybenzyl-α-D-mannopyranoside* (**20**).—A solution of NaOH (20%, 30 mL) was added to a solution of compound **19** (1.5 g, 2.6 mmol), benzyl bromide (2 mL, 16.8 mmol), and Bu_4NBr (0.2 g, 0.6 mmol) in CH_2Cl_2, and the mixture was stirred at room temperature until almost all starting material was consumed (~ 2 days). One product was formed, as shown by TLC (solvent *E*). The phases were separated, the aqueous phase was washed with CH_2Cl_2, and the organic phases were combined, washed with water, dried, and concentrated. Chromatography gave **20** (1.65 g, 95%); mp 89–90°C (from EtOAc–hexane); $[\alpha]_D$ −7° (*c* 0.8); ^{1}H NMR ($CDCl_3$): δ 6.38 (d, 1 H, $J_{4,NH}$ 8.8 Hz, NH), 4.75–4.30 (m, 9 H incl s, 1 H, at 4.67, H-1, 4 CH_2Ph), 4.04–3.94 (m, 2 H, H-2′,4), 3.86 (dd, 1 H, $J_{2,3}$ 2.9, $J_{3,4}$ 10.5 Hz, H-3), 3.77–3.69 (m, 5 H incl s, 3 H, at 3.73, CH_3OPh, H-2,5), 3.64–3.49 (m, 2 H, H-4′a,b), 3.32 (s, 3 H, OCH_3), 2.22–2.10, 1.92–1.80 (2 m, 2 H, H-3′a,b), and 1.20 (d, 3 H, H-6); ^{13}C NMR ($CDCl_3$): δ 99.38 (C-1), 77.68 (C-2′), 75.85 (C-3), 73.06 (C-2), 72.96, 72.70, 70.84 (C, 2 C, C, 4CH_2Ph), 67.48 (C-5), 66.05 (C-4′), 55.16 (CH_3OPh), 54.83 (OCH_3), 52.84 (C-4), 33.23 (C-3′), and 18.15 (C-6); CIMS: m/z 670 ($[M + 1]^+$) and 687 ($[M + 18]^+$). Anal. Calcd for $C_{40}H_{47}NO_8$: C, 71.73; H, 7.07; N, 2.09. Found: C, 71.64; H, 7.25; N, 2.02.

*Methyl 3,4,6-trideoxy-4-(3-deoxy-*L*-glycero-tetronamido)-α-D-mannopyranoside* (**24**). —(*a*) From **20**. Ceric ammonium nitrate (3.2 g, 5.8 mmol) was added to a solution of **20** (1.66 g, 2.5 mmol) in aq 90% MeCN (60 mL), and the solution was stirred at room

temperature for 1 h. TLC (solvent *E*) showed that the reaction was complete and that one slower moving product was formed. After concentration to remove MeCN, satd aq $NaHCO_3$ (100 mL) was added to the residue, the mixture was filtered through a Celite pad, the solids were washed with CH_2Cl_2, and the material in the combined filtrates was partitioned between CH_2Cl_2 and water. The organic phase was dried and concentrated, and the residue was chromatographed to give methyl 2-*O*-benzyl-4,6-dideoxy-4-(2,4-di-*O*-benzyl-3-deoxy-L-*glycero*-tetronamido)-α-D-mannopyranoside (**21**, 1.3 g, 96%); ^1H NMR ($CDCl_3$): δ 6.38 (d, 1 H, $J_{4,NH}$ 9.3 Hz, NH), 4.74–4.42 (m, 7 H incl s, 1 H, at 4.71, H-1, 3 CH_2Ph), 4.08 (dd, 1 H, $J_{2',3'a}$ 4.5, $J_{2',3'b}$ 7.5 Hz, H-2'), 4.00–3.90 (m, 1 H, H-4), 3.70–3.60 (m, 4 H, H-2,3,4'a,b), 3.58–3.48 (m, 1 H, H-5), 3.32 (s, 3 H, OCH_3), 2.51 (d, 1 H, $J_{3,OH}$ 9.3 Hz, OH), 2.23–2.12, 2.07–1.96 (2 m, 2 H, 3'a,b), and 1.20 (d, 3 H, $J_{5,6}$ 6.2 Hz, H-6); ^{13}C NMR ($CDCl_3$): δ 98.31 (C-1), 77.42 (C-2'), 77.00 (C-2), 73.07, 72.82, 72.67 (3 CH_2Ph), 70.02 (C-3), 67.00 (C-5), 65.70 (C-4'), 54.90 (OCH_3), 53.95 (C-4), 32.94 (C-3'), and 18.09 (C-6); CIMS: *m/z* 550 ($[M + 1]^+$) and 567 ($[M + 18]^+$).

N,N'-Thiocarbonyldiimidazole (1 g, 5.6 mmol) was added to a solution of **21** (1.3 g, 2.4 mmol) in THF (20 mL), and the mixture was heated under reflux until TLC (solvent *E*) showed that the reaction was complete (~ 4 h). After concentration, chromatography gave methyl 2-*O*-benzyl-4,6-dideoxy-4-(2,4-di-*O*-benzyl-3-deoxy-L-*glycero*-tetronamido)-3-*O*-(imidazol-1-ylthiocarbonyl)-α-D-mannopyranoside (**22**) in virtually theoretical yield; ^1H NMR ($CDCl_3$): δ 6.46 (d, 1 H, $J_{4,NH}$ 10.3 Hz, NH), 5.62 (dd, 1 H, $J_{2,3}$ 3.4, $J_{3,4}$ 10.9 Hz, H-3), 4.76 (d, 1 H, $J_{1,2}$ 1.8 Hz, H-1), 4.70–4.20 (m, 7 H, 3 CH_2Ph, H-4), 4.07 (dd, 1 H, H-2), 4.03 (dd, 1 H, $J_{2',3'a}$ 4.3, $J_{2',3'b}$ 8.3 Hz, H-2'), 3.75–3.62 (m, 1 H, H-5), 3.45–3.28 (m, 5 H, incl s, 3 H, at 3.40, OCH_3, H-4'a,b), 1.95–1.83, 1.63–1.52 (2 m, 2 H, H-3'a,b), and 1.26 (d, 3 H, $J_{5,6}$ 6.4 Hz, H-6); ^{13}C NMR ($CDCl_3$): δ 98.73 (C-1), 80.26 (C-3), 77.12 (C-2'), 72.88 (3 C, C-2, 2 CH_2Ph), 72.54 (CH_2Ph), 67.14 (C-5), 65.39 (C-4'), 55.04 (OCH_3), 50.05 (C-4), 32.73 (C-3'), and 17.79 (C-6); CIMS: *m/z* 660 ($[M + 1]^+$).

A solution of **22** (1.4 g) in toluene (20 mL) was treated under reflux with Bu_3SnH (1.5 mL, 5.7 mmol). After 3 h, TLC (solvent *E*) showed that the reaction was almost complete, and that one major product was formed. The mixture was concentrated and the residue was chromatographed to give methyl 2-*O*-benzyl-3,4,6-trideoxy-4-(2,4-di-*O*-benzyl-3-deoxy-L-*glycero*-tetronamido)-α-D-mannopyranoside (**23**, 0.88 g, 78%), which was sufficiently pure for the next step; ^1H NMR ($CDCl_3$): δ 6.30 (d, 1 H, $J_{4,NH}$ 9.5 Hz, NH), 4.65–4.40 (m, 7 H incl s, 1 H, at 4.59, H-1, 3 CH_2Ph), 4.11–3.97 (m, 2 H, H-4,2'), 3.67–3.45 (m, 4 H, H-2,5,4'a,b), 3.35 (s, 3 H, OCH_3), 2.25–2.13 (m, 1 H, H-3'a), 2.05–1.88 (m, 2 H, H-3a,3'b), 1.65–1.53 (m, 1 H, H-3b), and 1.18 (d, 3 H, $J_{5,6}$ 6.3 Hz, H-6); ^{13}C NMR ($CDCl_3$): δ 98.30 (C-1), 77.40 (C-2'), 73.16 (C-2), 73.07, 72.76, 70.71 (3 CH_2Ph), 68.11 (C-5), 65.86 (C-4'), 54.65 (OCH_3), 46.13 (C-4), 33.00 (C-3'). 29.82 (C-3), and 18.20 (C-6); CIMS: *m/z* 534 ($[M + 1]^+$).

A solution of the foregoing compound **23** (0.7 g) in EtOH was treated with H_2, as described above, and the product **24** (0.3 g, 87%), obtained in virtually theoretical yield after elution from a column of silica gel (solvent *F*), was crystallized from EtOAc; mp 142–143°C; $[\alpha]_D$ +65.5° (*c*, 0.8, water); ^1H NMR (D_2O): δ 4.60 (d, 1 H, $J_{1,2}$ 1.5 Hz, H-1), 4.26 (dd, 1 H, $J_{2',3'a}$ 3.9, $J_{2',3'b}$ 8.6 Hz, H-2'), 3.99–3.81 (m, 3 H, H-2,4,5),

3.76–3.71 (m, 2 H, H-4'a,b), 3.43 (s, 3 H, OCH_3), 2.08–1.97 (m, 1 H, H-3'a), 1.94–1.88 (m, 2 H, H-3a,b), 1.87–1.77 (m, 1 H, H-3'b) and 1.19 (d, 3 H, $J_{5,6}$ 6.0 Hz, H-6); ^{13}C NMR ($CDCl_3$): δ 99.82 (C-1), 68.93 (C-2'), 67.88, 66.18 (C-2,5), 57.90 (C-4'), 54.97 (OCH_3), 46.27 (C-4), 36.01 (C-3'), 31.32 (C-3), and 17.13 (C-6); CIMS: m/z 264 ($[M + 1]^+$) and 281 ($[M + 18]^+$). Anal. Calcd for $C_{11}H_{21}NO_6$: C, 50.18; H, 8.04; N, 5.32. Found: C, 50.06; H, 8.33; N, 5.15.

(*b*) From **5**. Compound **5** (1.76 g) was treated with hydrogen sulfide as described for the preparation of **4**. The crude product was chromatographed (solvent *D*) to give amorphous methyl 4-amino-2-*O*-benzyl-4,6-dideoxy-α-D-mannopyranoside (**8**, 1.21 g, 75%); ^1H NMR ($CDCl_3$): δ 4.75, 4.56 (2 d, 1 H each, ^2J 11.7 Hz, CH_2Ph), 4.75 (d, 1 H, $J_{1,2}$ 1.5 Hz, H-1), 3.67 (dd, 1 H, $J_{2,3}$ 3.7 Hz, H-2), 3.55 (dd, 1 H, $J_{3,4}$ 10.0 Hz, H-3), 3.50–3.45 (m, 1 H, H-5), 3.34 (s, 3 H, OCH_3), 2.69 (t, J 9.7 Hz, H-4), and 1.29 (d 3 H, $J_{5,6}$ 6.2 Hz, H-6); ^{13}C NMR ($CDCl_3$): δ 98.23 (C-1), 77.28 (C-2), 73.00 (CH_2Ph), 71.46 (C-3), 69.17 (C-5), 56.18 (C-4), 54.76 (OCH_3), and 17.93 (C-6); CIMS: m/z 268 ($[M + 1]^+$) and 285 ($[M + 18]^+$).

A solution of the foregoing amine **8** (1.2 g) in MeOH (25 mL) was treated for 1 h at room temperature with Ac_2O (2 mL). After concentration and chromatography (solvent *E*) the isolated methyl 4-acetamido-2-*O*-benzyl-4,6-dideoxy-α-D-mannopyranoside (**9**) (1.25 g, 90%); showed mp 133–134°C (CH_2Cl_2–hexane); $[\alpha]_D$ +23.6° (*c* 0.8); ^1H NMR ($CDCl_3$): δ 5.30 (d, 1 H, $J_{4,NH}$ 9.5 Hz, NH), 4.74, 4.59 (2 d, 1 H each, ^2J 11.7 Hz, CH_2Ph), 4.73 (bs, 1 H, H-1), 4.04–3.93 (m, 1 H, H-4), 3.70–3.65 (m, 2 H, H-2,3), 3.62–3.52 (m, 1 H, H-5), 3.33 (s, 3 H, OCH_3), 2.02 (s, 3 H, $NHCOCH_3$), and 1.26 (d, 3 H, $J_{5,6}$ 6.2 Hz, H-6); ^{13}C NMR ($CDCl_3$): δ 98.16 (C-1), 77.28 (C-2), 73.05 (CH_2Ph), 69.88 (C-3), 67.39 (C-5), 54.85 (OCH_3), 54.33 (C-4), 23.41 ($NHCOCH_3$), and 17.87 (C-6); CIMS: m/z 310 ($[M + 1]^+$) and 327 ($[M + 18]^+$). Anal. Calcd for $C_{16}H_{23}NO_5$: C, 62.11; H, 7.49; N, 4.43. Found: C, 61.73; H, 7.58; N, 4.52.

Compound **9** (0.45 g) was treated with *N*,*N*'-thiocarbonyldiimidazole, as described for the preparation of **22**. After processing as described above, chromatography (solvent *G*) gave the amorphous methyl 4-acetamido-2-*O*-benzyl-4,6-dideoxy-3-*O*-(imidazol-1-ylthiocarbonyl)-α-D-mannopyranoside (**10**, 0.58 g, 95%); ^1H NMR ($CDCl_3$): δ 5.62 (dd, 1 H, $J_{2,3}$ 3.2, $J_{3,4}$ 10.9 H, H-3), 5.52 (d, 1 H, $J_{4,NH}$ 9.8 Hz, NH), 4.78 (d, 1 H, $J_{1,2}$ 1.8 Hz, H-1), 4.67, 4.46 (2 d, 1 H each, ^2J 12.2 Hz, CH_2Ph), 4.67–4.57 (m, 1 H, H-4), 4.09 (dd, 1 H, $J_{2,3}$ 3.2 Hz, H-2), 3.81–3.71 (m, 1 H, H-5), 3.40 (s, 3 H, OCH_3), 1.90 (s, 3 H, $NHCOCH_3$), and 1.33 (d, 3 H, $J_{5,6}$ 6.3 Hz, H-6); ^{13}C NMR ($CDCl_3$): δ 98.72 (C-1), 80.43 (C-3), 72.98 (2 C, C-2, CH_2Ph), 67.61 (C-5), 55.12 (OCH_3), 50.75 (C-4), 23.39 ($NHCOCH_3$), and 17.86 (C-6); CIMS: m/z 420 ($[M + 1]^+$).

Compound **10** (0.58 g) was treated with Bu_3Sn as described for the preparation of **23**. After processing as described above, chromatography (solvent *H*) gave methyl 4-acetamido-2-*O*-benzyl-3,4,6-trideoxy-α-D-mannopyranoside (**11**, 0.3 g, 74%); ^1H NMR ($CDCl_3$): δ 5.37 (d, 1 H, $J_{4,NH}$ 9.0 Hz, NH), 4.63, 4.55 (2 d, 1 H each, ^2J 12.2 Hz, CH_2Ph), 4.60 (bs, 1 H, H-1), 4.16–4.03 (m, 1 H, H-4), 3.63–3.53 (m, 1 H, H-5), 3.51–3.48 (m, 1 H, H-2), 3.36 (s, 3 H, OCH_3), 2.13–2.09, 1.71–1.61 (2 m, 1 H each, H-3a,b), 1.97 (s, 3 H, $NHCOCH_3$), and 1.24 (d, 3 H, $J_{5,6}$ 6.3 Hz, H-6); ^{13}C NMR ($CDCl_3$): δ 98.28 (C-1), 73.25 (C-2), 70.72 (CH_2Ph), 68.47 (C-5), 54.66 (OCH_3),

46.63 (C-4), 30.06 (C-3), 23.49 ($NHCOCH_3$), and 18.16 (C-6); CIMS: m/z 294 ($[M + 1]^+$) and 311 ($[M + 18]^+$).

A mixture of **11** (0.3 g) and hydrazine hydrate (5 mL) was stirred under reflux for 3 days, when TLC (solvent *F*) showed that the *N*-deacetylation was complete. After concentration the crude product was chromatographed to give syrupy methyl 4-amino-2-*O*-benzyl-3,4,6-trideoxy-α-D-mannopyranoside (**12**, 0.24 g, 92%); ^1H NMR ($CDCl_3$): δ 4.60 (s, 1 H, H-1), 4.58 (s, 2 H, CH_2Ph), 3.53–3.49 (m, 1 H, H-2), 3.48–3.39 (m, 1 H, H-5), 3.35 (s, 3 H, OCH_3), 2.86–2.76 (m, 1 H, H-4), 2.06–1.96, 1.62–1.50 (2 m, 1 H each, H-3a,b), and 1.25 (d, 3 H, $J_{5,6}$ 6.4 Hz, H-6); ^{13}C NMR ($CDCl_3$): δ 98.11 (C-1), 74.11 (C-2), 70.85 (C-5), 70.69 (CH_2Ph), 54.29 (OCH_3), 48.41 (C-4), 32.60 (C-3), and 17.83 (C-6); CIMS: m/z 252 ($[M + 1]^+$) and 269 ($[M + 18]^+$).

Compound **12** (0.02 g, 0.045 mmol) was treated with the benzylated lactone **29** (0.02 g, 0.1 mmol), as described for the preparation of **19**. TLC (solvent *G*) showed that almost all the starting amine was consumed, and that one faster, largely predominating product was formed. The crude product was chromatographed to give amorphous methyl 2-*O*-benzyl-4-(2-*O*-benzyl-3-deoxy-L-*glycero*-tetronamido)-3,4,6-trideoxy-α-D-manno-pyranoside (**25**, 0.025g, 83%); $[\alpha]_D$ +24° (*c* 1); ^1H NMR ($CDCl_3$): δ 4.42 (d, 1 H, $J_{4,NH}$ 9.5 Hz, NH), 4.66–4.53 (m, 5 H, 2 CH_2Ph, H-1), 4.61 (bs, 1 H, H-1), 4.13–4.01 (m, 2 H, H-4,2′), 3.77–3.71 (m, 2 H, H-4′a,b), 3.61–3.54 (m, 1 H, H-5), 3.51–3.48 (m, 1 H, H-2), 3.37 (s, 3 H, OCH_3), 2.59 (bs, 1 H, OH), 2.10–1.96 (m, 3 H, H-3′a,b, H-3a) 1.72–1.61 (m, 1 H, H-3b), and 1.20 (d, 3 H, $J_{5,6}$ 6.4 Hz, H-6); ^{13}C NMR ($CDCl_3$): δ 172.39 (CO), 98.30 (C-1), 78.60 (C-2′), 73.14 (C-2), 72.99, 70.81 (2 CH_2Ph), 67.98 (C-5), 59.55 (C-4′), 54.72 (OCH_3), 46.37 (C-4), 35.35 (C-3′), 29.86 (C-3), and 18.22 (C-6); CIMS: m/z 444 ($[M + 1]^+$) and 461 ($[M + 18]^+$). Anal. Calcd for $C_{25}H_{33}NO_6$: C, 67.69; H, 7.50; N, 3.16. Found: C, 67.54; H, 7.67; N, 3.15.

Treatment of a small amount of the protected derivative **25** with hydrogen, as described above, gave material indistinguishable from compound **24** synthesized by method *a*.

References

[1] M. Gotoh and P. Kováč, *J. Carbohydr. Chem.*, 13 (1994) 1193–1213.
[2] C.P.J. Glaudemans, *Chem. Rev.*, 91 (1991) 25–35.
[3] P.A. Manning, in I.M. Roitt (Ed.), *Encyclopedia of Immunity*, Vol. 3, Academic Press, New York, 1992, pp 1554–1556.
[4] M. Gotoh, C.L. Barnes, and P. Kováč, *Carbohydr. Res.*, 260 (1994) 203–218.
[5] L. Kenne, P. Unger, and T. Wehler, *J. Chem. Soc., Perkin Trans. 1*, (1988) 1183–1196.
[6] M.J. Eis and B. Ganem, *Carbohydr. Res.*, 176 (1988) 316–323.
[7] D.R. Bundle, M. Gerken, and T. Peters, *Carbohydr. Res.*, 174 (1988) 239–251.
[8] P. Fügedi and P. Nanási, *J. Carbohydr. Nucleosides, Nucleotides*, 8 (1981) 547–555.
[9] T. Peters and D.R. Bundle, *Can. J. Chem.*, 67 (1989) 497–502.
[10] T. Adachi, Y. Yamada, I. Inoue, and M. Saneyoshi, *Synthesis*, 62 (1977) 45–46.
[11] R.U. Lemieux, S.Z. Abbas, M.H. Burzynska, and R.M. Ratcliffe, *Can. J. Chem.*, 60 (1982) 63–67.
[12] M.E. Evans, L. Long, and F.P. Parrish, *J. Org. Chem.*, 33 (1968) 1074–1076.
[13] P.J. Garegg, T. Iversen, and S. Oscarson, *Carbohydr. Res.*, 50 (1976) C12–C14.

[14] P. Kováč, in K. Blau and J.M. Halket (Eds.), *Handbook of Derivatives for Chromatography*, Wiley, Chichester, 1993, pp 109–129.
[15] L.A. Mulard, P. Kováč and C.P.J. Glaudemans, *Carbohydr. Res.*, 251 (1994) 213–232.
[16] M. Caroff, D.R. Bundle, and M.B. Perry, *Eur. J. Biochem.*, 139 (1984) 195–200.
[17] T. Peters and D.R. Bundle, *Can. J. Chem.*, 67 (1989) 491–496.