Carbohydrate Research, 244 (1993) 69–84
Elsevier Science Publishers B.V., Amsterdam

Synthesis of allyl *O*-[sodium (α-D-*glycero*-D-*talo*-2-octulopyranosyl)onate]-(2 → 6)-2-acetamido-2-deoxy-β-D-glucopyranoside, a core constituent of the lipopolysaccharide from *Acinetobacter calcoaceticus* NCTC 10305

Josef Gass [a], Martina Strobl [a], Andreas Loibner [a], Paul Kosma [a]* and Ulrich Zähringer [b]

[a] *Institut für Chemie der Universität für Bodenkultur, A-1180 Wien (Austria)*
[b] *Forschungsinstitut Borstel, D-2061 Borstel (Germany)*

(Received March 12th, 1991; accepted August 24th, 1991)

ABSTRACT

Reaction of methyl 2,6-anhydro-2,3-dideoxy-D-*manno*-2-octenoate **1** with 3-chloroperoxybenzoic acid gave the 2,3-anhydro derivative **2**, which was converted into the per-*O*-acetylated anomeric methyl glycosides of D-*glycero*-D-*galacto*-2-octulopyranosylonic acid in good yield. Subsequent inversion of the configuration at C-3 and deprotection afforded sodium (methyl β-D-*glycero*-D-*talo*-2-octulopyranosid)onate. Alternatively, **2** was transformed into methyl (α-D-*glycero*-D-*talo*-2-octulopyranosyl bromide)onate derivatives. Reaction with methanol or allyl 2-acetamido-2-deoxy-3,4-*O*-(1,1,3,3-tetraisopropyldisiloxan-1,3-diyl)-β-D-glycopyranoside, promoted by silver triflate, gave good yields of the corresponding orthoester derivatives. Me_3Si triflate-catalyzed orthoester rearrangement and removal of the protecting groups afforded sodium *O*-(methyl α-D-*glycero*-D-*talo*-2-octulopyranosid)onate and the disacchanide, allyl *O*-[sodium (α-D-*glycero*-D-*talo*-2-octulopyranosyl)onate]-(2 → 6)-2-acetamido-2-deoxy-β-D-glucopyranoside in high yield.

INTRODUCTION

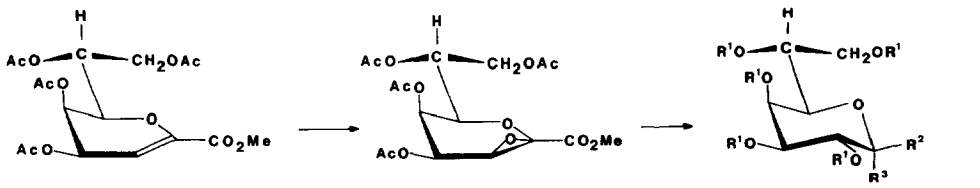
Recently, a novel octulosonic acid[1] has been isolated from acid-degraded lipopolysaccharide (LPS) of *Acinetobacter calcoaceticus* NCTC 10305, a member of the *Neisseriaceae*. This octulosonic acid has been shown to interlink the core oligosaccharide and lipid A in a highly acid-stable linkage, thus replacing 3-deoxy-D-*manno*-2-octulosonic acid (Kdo), a common constituent of enterobacterial LPS[2]. Paulsen et al.[3] reported the synthesis of D-*glycero*-D-*galacto*-2-octulosonic acid, which, however, does not correspond to the configuration of the natural isomer[4]. For an extended structural study of this novel octulosonic acid, we report herein

* Corresponding author.

the syntheses of the anomeric methyl glycosides of D-*glycero*-D-*talo*-2-octulosonic acid and the disaccharide allyl *O*-[sodium (α-D-*glycero*-D-*talo*-2-octulopyranosyl)onate]-(2 → 6)-2-acetamido-2-deoxy-β-D-glucopyranoside, which corresponds to the inner-core region of *Acinetobacter calcoaceticus* NCTC 10305 lipopolysaccharide[5], and is suitable for a subsequent conversion into a multivalent hapten by copolymerization with acrylamide[6].

RESULTS AND DISCUSSION

Reaction of methyl 2,6-anhydro-2,3-dideoxy-D-*manno*-2-octenoate[7] (**1**) with 3-chloroperbenzoic acid in CH_2Cl_2 gave the unstable 2,3-anhydro derivative **2** in 80% yield. The formation of the oxirane ring was inferred from the ^1H NMR signal attributable to H-3 (δ 3.49, $J_{3,4} \approx 1.3$ Hz) and from the ^{13}C NMR signal of C-3 (δ 54.65), which are similar to those reported for 1,2-anhydro-β-D-mannopyranose derivatives[8–10]. The use of similar anhydro derivatives as glycosyl donors has previously been reported for the synthesis of β-D-linked oligosaccharides[11] and α-glycosides of neuraminic acid[12]. Treatment of **2** with MeOH in the presence of Dowex 50-WX8 (H^+) cation-exchange resin at 0°C gave a 9:1 mixture of the β- and α-linked glycosides **3** and **4** in 70% yield, which were separated after acetylation (Ac_2O–pyridine) of the mixture. The axial orientation of H-3 was easily deduced from the large value of the coupling constant, $J_{3,4}$ (10.8 Hz for **3**, 10.6 Hz for **4**). The anomeric configuration was assigned on the basis of the ^{13}C NMR chemical shift value of C-6; the signal of C-6 in the β isomer **3** occurs at a field lower (δ 70.9) than that of the corresponding signal of **4** (δ 67.9), similar to reported values for per-*O*-acetylated Kdo derivatives[13]. Zemplén *O*-deacetylation of **3** gave a quantitative yield of the methyl ester derivative **5**, which was converted into the 4,5:7,8-di-*O*-isopropylidene derivative **6** in 94% yield by treatment with 2,2-dimethoxypropane and 4-toluenesulfonic acid in *N*,*N*-dimethylformamide. Oxidation of OH-3 was accomplished by Me_2SO–Ac_2O[14], whereas the RuO_4-catalyzed reaction was ineffective. Stereoselective reduction of the keto group pro-



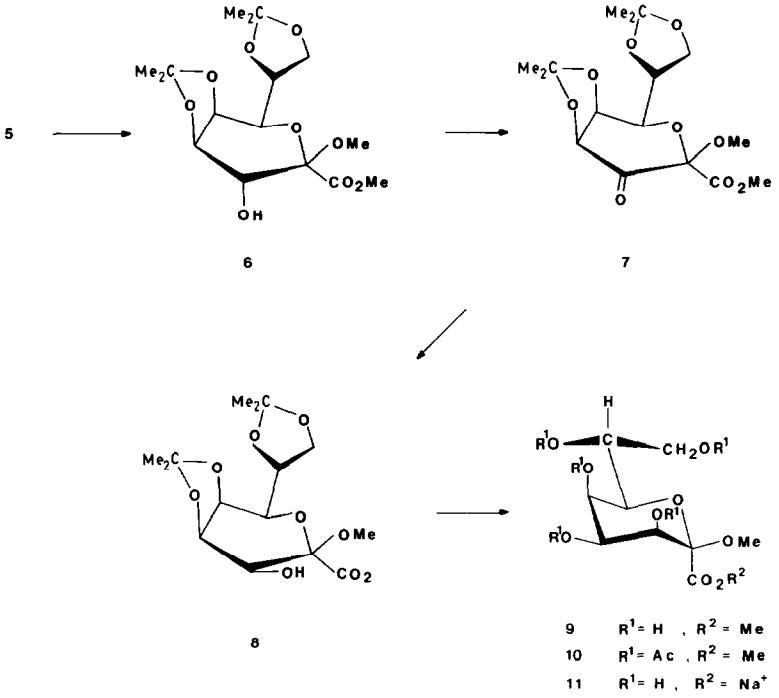
1 2

3 R^1 = Ac, R^2 = OMe, R^3 = CO_2Me

4 R^1 = Ac, R^2 = CO_2Me, R^3 = OMe

5 R^1 = H, R^2 = OMe, R^3 = CO_2Me

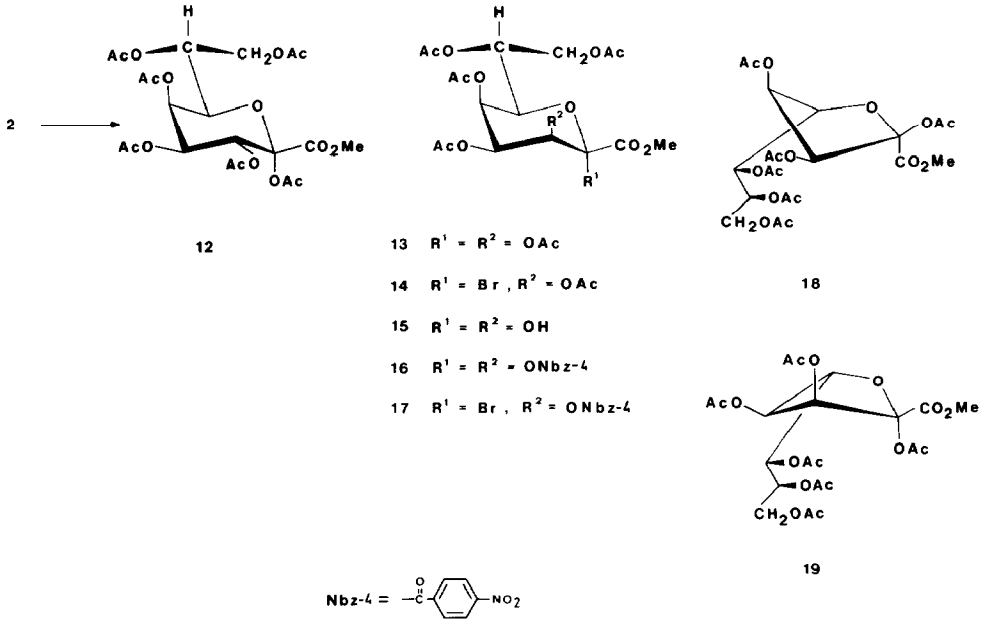
Scheme 1.



Scheme 2.

ceeded smoothly with BH_3–NH_3 complex[15] at 0°C to give a 94% yield of the D-*glycero*-D-*talo* derivative **8**. The inversion of configuration at C-3 was proven by quantitative removal of the isopropylidene groups and subsequent *O*-acetylation of **9** to give the per-*O*-acetylated β-glycoside **10** in 97% yield. The ^1H NMR spectrum of **10** showed a doublet of doublets at δ 6.24, coupled to H-4 ($J_{3,4} \approx 3.4$ Hz) and H-5 ($^4J_{3,5} \approx 0.6$ Hz). Zemplén *O*-deacetylation and hydrolysis of the methyl ester groups in aqueous NaOH afforded sodium (methyl β-D-*glycero*-D-*talo*-2-octylopyranosid)onate (**11**) in quantitative yield.

For the synthesis of the α-linked D-*glycero*-D-*talo*-2-octulopyranosidonate derivatives **25** and **30**, the oxirane derivative **2** was hydrolyzed on silica gel and the products were acetylated to give the D-*glycero*-D-*galacto* derivative[3] **12** in 12% yield and a syrup, from which the per-*O*-acetylated methyl ester derivative **13** was isolated by crystallization in 46% yield. The equatorial position of H-3 in compound **13** was readily deduced from the values of the coupling constant in the ^1H NMR spectrum ($J_{3,4} \approx 4.0$, $^4J_{3,5} \approx 1.0$ Hz). The mother liquor was separated by liquid chromatography to give additional **13** and the per-*O*-acetylated furanose derivatives **18** and **19** in the ratio of 2:3:6. Reaction of **13** with $TiBr_4$ in CH_2Cl_2 gave the bromide derivative **14** in 96% yield. Alternatively, the 2,3-di-*O*-nitrobenzoyl derivative **16** was prepared in 36% yield by silica gel-promoted hydrolysis of the oxirane derivative **2**, followed by *O*-nitrobenzoylation (4-nitrobenzoyl chlo-

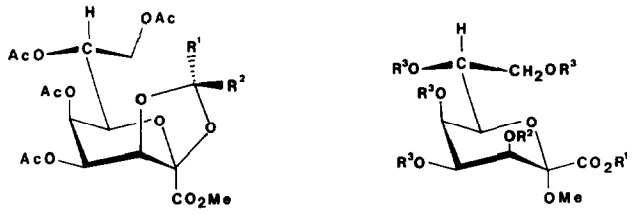


Scheme 3.

ride–pyridine), similar to the preparation of **13**. Compound **16** was also obtained upon nitrobenzoylation of the 2,3-dihydroxy derivative **15** (70% yield), which in turn was prepared by regioselective *O*-deacetylation of the bromide derivative **14** with MeOH–Ag triflate in 40% yield. Treatment of **16** with $TiBr_4$ afforded **17** in quantitative yield.

Reaction of MeOH with **14** in acetonitrile in the presence of $Hg(CN)_2$ gave a 89% yield of the *exo*-orthoester derivative **21**, which was also obtained by use of Ag triflate–*N,N,N',N'*-tetramethylurea in CH_2Cl_2. The formation of the orthoester was deduced from the ^{13}C NMR chemical shift values at δ 127.3 for the quaternary carbon atom, 77.5 for C-3, and 26.8 for the *endo*-CH_3-group, respectively. Catalysis of the reaction by Me_3Si triflate in CH_2Cl_2 and 4A molecular sieves gave a mixture of *endo*- and *exo*-orthoester derivatives **20** (20%) and **21** (32%), and the methyl ketoside **23** (12%), which were separated by column chromatography on silica gel. Promotion of the reaction by Ag triflate and 4A molecular sieves furnished **23** in a similar yield (13%). The assignment of the *exo*- and *endo*-configuration[16] was based on the ^1H NMR chemical shift values of the CH_3-groups ($\delta_{exo\text{-}CH_3}$ 1.60 for **20**, $\delta_{endo\text{-}CH_3}$ 1.80 for **21**).

Orthoester rearrangement of **21** using $HgBr_2$ in nitromethane[17], $SnCl_4$ in CH_2Cl_2 (ref. 18), or BF_3–diethyletherate[19] resulted in hydrolysis, whereas treatment with Me_3Si triflate[20] afforded a low yield of the glycoside **23** (26%). Better results were obtained in the orthoester rearrangement of the nitrobenzylidene derivative **22**, which gave the corresponding glycoside **24** in 40% yield. Zemplén



20 R^1 = OMe, R^2 = Me

21 R^1 = Me, R^2 = OMe

22 R^1 = $C_6H_4NO_2(4)$, R^2 = OMe

23 R^1 = Me, R^2 = R^3 = Ac

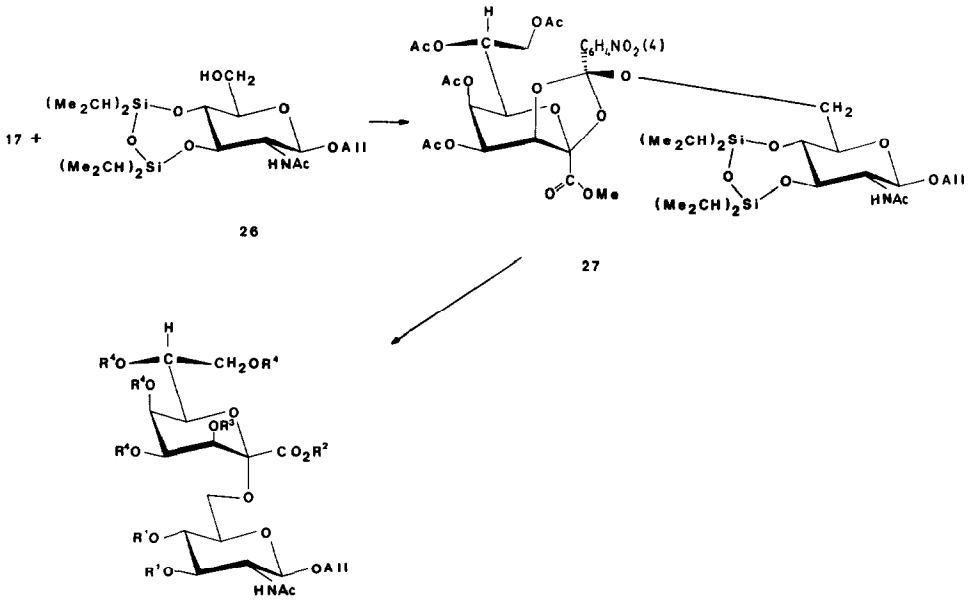
24 R^1 = Me, R^2 = Nbz-4, R^3 = Ac

25 R^1 = Na^+, R^2 = R^3 = H

Scheme 4.

O-deacylation and hydrolysis of the methyl ester group gave sodium *O*-(methyl α-D-*glycero*-D-*talo*-2-octylopyranosid)onate (**25**) in quantitative yield.

For the synthesis of the disaccharide **30**, the previously described[21] glycosyl acceptor **26** was coupled with the bromide derivative **17** in acetonitrile in the presence of Ag triflate and 4A molecular sieves to give the corresponding *exo*-orthoester disaccharide derivative **27** in 63% yield. Me_3Si triflate-catalyzed rear-



26

27

28 R^1 = $-Si(CHMe_2)_2OSi(CHMe_2)_2-$, R^2 = Me, R^3 = Nbz-4, R^4 = Ac

29 R^1 = R^3 = R^4 = Ac, R^2 = Me

30 R^1 = R^3 = R^4 = H, R^2 = Na^+

Scheme 5.

TABLE I

Assignments [a] of ^{13}C NMR chemical shifts (δ) for compounds **11**, **25**, and **30**

Carbon atom	**11**	**25**	**30**
1			100.98
2			56.27
3			74.86
4			70.89
5			74.86
6			62.70
1′	173.18	174.49	174.04
2′	102.21	103.24	102.45
3′	73.04	72.15	72.45
4′	68.38	67.24	67.28
5′	68.58	69.02	68.96
6′	74.51	72.46	72.45
7′	69.79	70.25	70.29
8′	64.80	63.90	64.11
OCH_3	52.69	51.52	
-CH=			134.16
CH_2=			118.98
OCH_2			71.38
CH_3			22.94
-NHC=O			175.42

[a] Based on ^1H,^{13}C-COSY experiments.

rangement gave the disaccharide derivative **28** in 70% yield. The ^1H NMR signal attributable to H-3′ in compound **28** was shifted downfield (δ 5.77) in comparison to the orthoester derivative **27** (δ 4.86). Removal of the protecting groups with Bu_4NF (ref 22), Zemplén *O*-deacylation, and reacetylation (Ac_2O–pyridine) gave the crystalline per-*O*-acetylated disaccharide derivative **29** in 76% yield. Zemplén *O*-deacylation and deesterification in aqueous NaOH afforded allyl *O*-[sodium (α-D-*glycero*-D-*talo*-2-octulopyranosyl)onate]-(2 → 6)-2-acetamido-2-deoxy-β-D-glucopyranoside (**30**) in 98% yield. The ^{13}C NMR spectra (Table I) of the anomeric methyl ketosides **11** and **25** exhibit chemical shift differences of the respective C-4 and C-6 signals similar to the corresponding methyl ketosides of Kdo[23], thus confirming the assignments of the anomeric configuration. The ^{13}C NMR data of **30** compare favorably with published[21] values of the related disaccharide structure, α-Kdo*p*-(2 → 6)-β-D-GlcNAc; the previous empirical assignment of C-4 and C-7′, however, needs to be ascertained by ^1H–^{13}C-heteronuclear correlation experiments.

EXPERIMENTAL

General methods.—Melting points were determined with a Kofler hot-stage melting-point apparatus and are uncorrected. Optical rotations were measured with a Perkin–Elmer 243 B polarimeter. ^1H NMR spectra were recorded with

Bruker WM-250, AC 300F or AM 360L instruments and Me_4Si as the internal standard; coupling constants are first order. ^{13}C NMR spectra were recorded at 75.47 or 90.6 MHz for solutions in D_2O at 24°C; the instruments were operated in the FT mode with complete proton-decoupling; chemical shifts (δ) are given from the signal of internal acetonitrile (δ 1.70). TLC was performed on Merck precoated plates (5 × 10 cm, layer thickness 0.25 mm, Silica Gel $60F_{254}$); spots were detected by spraying with an anisaldehyde–H_2SO_4 reagent[24]. Column chromatography was performed on Merck Lichroprep columns (size *A*, 24 × 1, *B*, 31 × 2.5; and *C*, 44 × 3.7 cm; silica gel 40–63 μm) under pressure (0.2 MPa). HPLC chromatography was performed on a Du Pont instrument (model 870). Elemental analyses were performed by Mag. J. Theiner, Mikroanalytisches Laboratorium am Institut für Physikalische Chemie, Universität Wien.

*Methyl 4,5,7,8-tetra-*O*-acetyl-2,3-anhydro-*D-glycero-D-talo-*2-octulopyranosonate* (**2**).—A solution of **1** (213 mg, 0.53 mmol) and 3-chloroperoxybenzoic acid (276 mg, 1.6 mmol) in CH_2Cl_2 (50 mL) was stirred for 48 h at reflux temperature. The solution was washed with sated aq $NaHCO_3$ solution, water, and 5% aq $FeSO_4$ solution. The organic layer was dried ($MgSO_4$) and evaporated. The product was purified by chromatography (*B*, 1:1 toluene–EtOAc) giving **2** as a colorless syrup; yield, 178 mg (80%); $[\alpha]_D^{20}$ + 37° (*c* 0.9, $CHCl_3$); ^1H NMR (250 MHz, $CDCl_3$): δ 5.27 (ddd, 1 H, $J_{4,5}$ 4.5, $^4J_{4,6}$ 1.0 Hz, H-4), 5.22 (dd, 1 H, $J_{5,6} < 1.0$ Hz, H-5), 5.20 (ddd, 1 H, $J_{7,6}$ 10.0, $J_{7,8a}$ 2.5, $J_{7,8b}$ 4.0 Hz, H-7), 4.56 (dd 1 H, $J_{8a,8b}$ −12.5 Hz, H-8a), 4.21 (dd, 1 H, H-8b), 4.06 (dd, 1 H, H-6), 3.87 (s, 3 H, CO_2CH_3), 3.49 (d, 1 H, $J_{3,4}$ 1.3 Hz, H-3), 2.11 (s, 3 H), 2.09 (s, 3 H), 2.07 (s, 3 H), and 2.03 (s, 3 H, 4 CH_3CO); ^{13}C NMR (75.47 MHz, $CDCl_3$): 170.6, 170.5, 170.2, 169.6, 169.1 (CO), 94.8 (C-2), 68.4 (C-6), 67.4 (C-7), 66.3 (C-5), 61.8 (C-8), 59.8 (C-4), 54.6 (C-3), 53.4 (CO_2CH_3), 20.7, 20.6, 20.5, and 20.4 (4 CH_3CO). Anal. Calcd for $C_{17}H_{22}O_{12}$: C, 48.81; H, 5.30. Found: C, 48.42; H, 5.36.

*Methyl (methyl 3,4,5,7,8-penta-*O*-acetyl-β-*D-glycero-D-galacto-*2-octulopyranosid)onate* (**3**) *and methyl (methyl 3,4,5,7,8-penta-*O*-acetyl-α-*D-glycero-D-galacto-*2-octulopyranosid)onate* (**4**).—Dowex 50 (H^+) cation-exchange resin (570 mg) was added to a freshly prepared solution of **2** (337 mg, 0.8 mmol) in MeOH (7 mL). The mixture was stirred for 3 h at room temperature and filtered, and the filtrate was taken to dryness. The residue was dissolved in pyridine (10 mL) and Ac_2O (1 mL) was added at 0°C. The solution was stirred overnight at room temperature and evaporated three times with addition of toluene. Purification of the residue by chromatography (*B*, 3:2 toluene–EtOAc) afforded **3** as colorless prisms; yield, 243 mg (61%); mp 133–136°C (dec, EtOAc–hexane); $[\alpha]_D^{20}$ +83° (*c* 1.6, $CHCl_3$); ^1H NMR (360 MHz, C_6D_6): δ 6.04 (d, 1 H, $J_{3,4}$ 10.8 Hz, H-3), 5.93 (dd, 1 H, $J_{4,5}$ 3.0 Hz, H-4), 5.86 (dd, 1 H, $J_{5,6}$ 1.5 Hz, H-5), 5.44 (ddd, 1 H, $J_{7,6}$ 9.8, $J_{7,8a}$ 2.4, $J_{7,8b}$ 4.6 Hz, H-7), 4.94 (dd, 1 H, H-6), 4.42 (dd, 1 H, $J_{8a,8b}$ −12.3 Hz, H-8a), 4.35 (dd, 1 H, H-8b), 3.42 (s, 3 H, CO_2CH_3), 3.30 (s, 3 H, OCH_3), 1.75 (s, 3 H), 1.71 (s, 9 H), and 1.63 (s, 3 H, 5 CH_3CO); ^{13}C NMR (75.47 MHz, $CDCl_3$): δ 171.3, 170.5, 170.2, 169.9, 169.8, 167.6 (CO), 99.4 (C-2), 70.9 (C-6), 69.6 (C-3), 67.8 (C-7), 66.8, 66.0

(C-4, 5), 62.3 (C-8), 52.7 (CO_2CH_3), 51.1 (OCH_3), and 20.8–20.3 (5 CH_3CO). Anal. Calcd for $C_{20}H_{28}O_{14}$: C, 48.78; H, 5.73. Found: C, 48.81; H, 5.70.

Further elution of the column gave **4** as colorless prisms, mp 190–195°C (dec, EtOAc–hexane); yield, 32 mg (8%); $[\alpha]_D^{20}$ +88° (*c* 0.7, $CHCl_3$); ^{1}H NMR (360 MHz, C_6D_6): δ 5.95 (d, 1 H, $J_{3,4}$ 10.6 Hz, H-3), 5.84 (dd, 1 H, $J_{4,5}$ 3.3 Hz, H-4), 5.79 (dd, 1 H, $J_{5,6}$ 1.5 Hz, H-6), 5.55 (ddd, 1 H, $J_{7,6}$ 10.1, $J_{7,8a}$ 2.2, $J_{7,8b}$ 4.8 Hz, H-7), 4.61 (dd, 1 H, $J_{8a,8b}$ −12.4 Hz, H-8a), 4.03 (dd, 1 H, H-8b), 3.88 (dd, 1 H, H-6), 3.40 (s, 3 H, CO_2CH_3), 3.18 (s, 3 H, OCH_3), 1.74 (s, 3 H), 1.73 (s, 3 H), 1.70 (s, 3 H), 1.68 (s, 3 H), and 1.58 (s, 3 H, 5 CH_3CO); ^{13}C NMR (75.47 MHz, $CDCl_3$): δ 170.4, 170.0, 169.9, 169.6 (CO), 98.6 (C-2), 67.9, 67.8, 67.3 (C-3,4,6,7), 66.5 (C-5), 61.9 (C-8), 53.2 (CO_2CH_3), 51.4 (OCH_3), and 20.6 (br s, CH_3CO). Anal. Calcd for $C_{20}H_{28}O_{14}$: C, 48.78; H, 5.73. Found: C, 48.81; H, 5.67.

*Methyl (methyl 4,5:7,8-di-*O*-isopropylidene-β-*D*-glycero-*D*-galacto-2-octulopyranosid)onate* (**6**).—A solution of **3** (169 mg, 0.34 mmol) in MeOH (15 mL) was stirred with 0.1 M methanolic NaOMe (0.5 mL) for 90 min at room temperature. The solution was de-ionized by addition of Dowex 50-WX8 (H^+) cation-exchange resin, filtered, and evaporated to give **5** (97 mg, 100%). A solution of the residue in dry DMF (3 mL) was treated with 2,2-dimethoxypropane (0.5 mL, 4.1 mmol) and 4-toluenesulfonic acid (10 mg) for 15 h at room temperature. Solvents were removed in vacuo and the residue was purified by chromatography (*B*, 1:1 toluene–EtOAc) to yield **6** (116 mg, 94%) as colorless needles; mp 163–164°C (EtOAc–pentane); $[\alpha]_D^{20}$ −5° (*c* 1.1, $CHCl_3$); ^{1}H NMR (360 MHz, $CDCl_3$): δ4.46–4.40 (m, 2 H, H-4, 5), 4.33 (ddd, 1 H, $J_{7,6}$ 8.1, $J_{7,8a}$ 4.0, $J_{7,8b}$ 6.1 Hz, H-7), 4.27 (dd, 1 H, $J_{8a,8b}$ 8.7 Hz, H-8a), 4.13 (dd, 1 H, H-8b), 4.07 (dd, $J_{3,4}$ 3.6 Hz, H-3), 3.95 (dd, $J_{6,5}$ 1.0 Hz, H-6), 3.84 (s, 3 H, CO_2CH_3), 3.35 (s, 3 H, OCH_3), 2.58 (d, 1 H, $J_{3,OH}$ 5.9 Hz, OH), 1.63 (s, 3 H), 1.51 (s, 3 H), 1.43 (s, 3 H), and 1.38 [s, 3 H, 2 $C(CH_3)_2$]. Anal. Calcd for $C_{16}H_{26}O_9$: C, 53.03; H, 7.23. Found: C, 53.23; H, 7.17.

*Methyl (methyl 4,5:7,8-di-*O*-isopropylidene-β-*D*-manno-2,3-octadiulopyranosid)onate* (**7**).—A solution of **6** (60 mg, 0.16 mmol) in 2:1 Me_2SO–Ac_2O (3 mL) was stirred for 60 h at room temperature. Solvents were removed by lyophilization and the residue was subjected to chromatography (*A*, 1:1 toluene–EtOAc) to give **7** as a syrup; yield, 42 mg (70%); $[\alpha]_D^{20}$ +43°C (*c* 1.4, $CHCl_3$); ^{1}H NMR (360 MHz, C_6D_6): δ 4.50 (ddd, 1 H, $J_{7,6}$ 8.0, $J_{7,8a}$ 4.9, $J_{7,8b}$ 6.3 Hz, H-7), 4.39 (dd, 1 H, $J_{5,6}$ 1.6, $J_{5,4}$ 5.6 Hz, H-5), 4.34 (d, 1 H, H-4), 4.28 (dd, 1 H, $J_{8a,8b}$ −8.8 Hz, H-8a), 4.04 (dd, 1 H, H-8b), 4.01 (dd, 1 H, H-6), 3.43 (s, 3 H, CO_2CH_3), 3.13 (s, 3 H, OCH_3), 1.43 (s, 6 H), 1.24 (s, 3 H) and 1.21 [s, 3 H, 2 $C(CH_3)_2$]. Anal. Calcd for $C_{16}H_{24}O_9$: C, 53.33; H, 6.71. Found: C, 53.42; H, 6.66.

*Methyl (methyl 4,5:7,8-di-O-isopropylidene-β-*D*-glycero-*D*-talo-2-octulopyranosid)onate* (**8**).—A solution of **7** (32 mg, 0.09 mmol) in MeOH (2 mL) was stirred with BH_3–NH_3 (3 mg, commercially available from Aldrich) for 30 min at 0°C. The residue obtained upon evaporation was purified by chromatography (*A*, 1:1 toluene–EtOAc) which afforded **8** as an amorphous solid; yield, 30 mg (94%); $[\alpha]_D^{20}$ +15° (*c* 0.8, $CHCl_3$); ^{1}H NMR (360 MHz, C_6D_6): δ 4.39 (ddd, 1 H, $J_{7,6}$ 8.3, $J_{7,8a}$

5.3, $J_{7,8b}$ 6.3 Hz, H-7), 4.30 (dd, 1 H, $J_{5,4}$ 8.8, $J_{5,6}$ 1.6 Hz, H-5), 4.23 (dd, 1 H, $J_{8a,8b}$ −8.4 Hz, H-8a), 4.09 (dd, 1 H, $J_{4,3}$ 4.2 Hz, H-4), 4.07 (dd, 1 H, H-8b), 3.76 (dd, 1 H, $J_{3,OH}$ 12.2 Hz, H-3), 3.63 (dd, 1 H, H-6), 3.41 (s, 3 H, CO_2CH_3), 3.31 (s, 3 H, OCH_3), 3.02 (d, 1 H, OH), 1.47 (s, 3 H), 1.43 (s, 3 H), 1.27 (s, 3 H) and 1.14 [s, 3 H, 2 $C(CH_3)_2$]. Anal. Calcd for $C_{16}H_{26}O_9$: C, 53.03; H, 7.23. Found: C, 53.05; H, 7.25.

*Methyl (methyl-3,4,5,7,8-penta-*O*-acetyl-β-*D*-glycero-*D*-talo-2-octulopyranosid)onate* (**10**).—A solution of **8** (22 mg, 0.06 mmol) in CH_2Cl_2 (3 mL) was cooled to −20°C, and 90% aq CF_3CO_2H (0.3 mL) was added, the solution was stirred for 30 min, and the acid neutralized by adding Dowex 1-X8 (HCO_3^-) anion-exchange resin. The resin was removed by filtration and the filtrate was taken to dryness. The residue was dissolved in pyridine (5 mL), and 4-dimethylaminopyridine (5 mg) and Ac_2O (0.2 mL) were added. The solution was stirred for 30 h at room temperature and the solvent evaporated. Purification of the residue by chromatography (*A*, 1:1 toluene–EtOAc) gave **10** as a syrup; yield, 28.9 mg (96%); $[\alpha]_D^{20}$ +55° (*c* 0.7, $CHCl_3$); ^{1}H NMR (360 MHz, C_6D_6): δ 6.24 (d, 1 H, $J_{3,4}$ 3.4 Hz, H-3), 5.64 (ddd, 1 H, $J_{7,6}$ 9.8, $J_{7,8a}$ 4.6, $J_{7,8b}$ 2.1 Hz, H-7), 5.48 (dd, 1 H, $J_{5,6}$ 1.8 Hz, H-5), 5.10 (dd, 1 H, $J_{4,5}$ 3.6 Hz, H-4), 4.64 (dd, 1 H, $J_{8a,8b}$ −12.6 Hz, H-8a), 4.38 (dd, 1 H, H-8b), 4.21 (dd, 1 H, H-6), 3.22 (s, 3 H, CO_2CH_3), 3.19 (s, 3 H, OCH_3), 1.94 (s, 3 H), 1.87 (s, 3 H), 1.83 (s, 3 H), 1.70 (s, 3 H), and 1.65 (s, 3 H, 5 CH_3CO); ^{13}C NMR (90.6 MHz, C_6D_6): δ 170.2, 169.7, 169.6, 169.1, 166.6 (CO), 99.2 (C-2), 71.0 (C-6), 68.3 (C-7), 67.4 (C-4), 67.4 (C-3), 64.0 (C-5), 62.4 (C-8), 52.2 (CO_2CHOCH_3), and 20.7–20.0 (CH_3CO). Anal. Calcd for $C_{20}H_{28}O_{14}$: C, 48.78; H, 5.73. Found: C, 48.85; H, 5.70.

*Sodium (methyl β-*D*-glycero-*D*-talo-2-octulopyranosid)onate* (**11**).—A solution of **10** (15.3 mg, 0.03 mmol) in MeOH (7 mL) was stirred with 0.1 M methanolic NaOMe (0.15 mL) for 90 min at room temperature. The solution was de-ionized by addition of Dowex 50-WX8 (H^+) resin, filtered, and evaporated. A solution of the residue in water (5 mL) was stirred with 0.2 M NaOH (1.5 mL) for 2.5 h at room temperature. The pH of the solution was adjusted to 8.2 by addition of Dowex 50-WX8 (H^+) resin. The mixture was filtered, the filtrate lyophilized, and the residue was purified on Bio-Gel P-2 (2.6 × 100 cm, water) giving **11** as an amorphous solid; yield, 9.0 mg, (100%); $[\alpha]_D^{20}$ +34° (*c* 0.9; H_2O); ^{1}H NMR (360 MHz, D_2O): δ 4.22 (d, 1 H, $J_{3,4}$ 3.0 Hz, H-3), 3.92 (dd, 1 H, $J_{5,6}$ 1.2, $J_{5,4}$ 3.2 Hz, H-5), 3.91 (ddd, 1 H, $J_{7,6}$ 9.0, $J_{7,8a}$ 4.8, $J_{7,8b}$ 2.4 Hz, H-7), 3.81 (dd, 1 H, $J_{8a,8b}$ −12.2 Hz, H-8a), 3.74 (dd, 1 H, H-8b), 3.66 (dd, 1 H, H-6), 3.59 (dd, 1 H, H-4), and 3.27 (s, 3 H, OCH_3). Anal. Calcd for $C_9H_{15}NaO_9 \cdot H_2O$: C, 37.07; H, 5.56. Found: C, 37.37; H, 5.64.

*Methyl 2,3,4,5,7,8-hexa-*O*-acetyl-α-*D*-glycero-*D*-galacto-2-octulopyranosonate* (**12**), *methyl 2,3,4,5,7,8-hexa-*O*-acetyl-α-*D*-glycero-*D*-talo-2-octulopyranosonate* (**13**), *methyl 2,3,4,6,7,8-hexa-*O*-acetyl-β-*D*-glycero-*D*-talo-2-octulofuranosonate* (**18**), and *methyl 2,3,4,6,7,8-hexa-*O*-acetyl-α-*D*-glycero-*D*-talo-2-octulofuranosonate* (**19**).—A solution of **1** (540 mg, 1.3 mmol) and 3-chloroperoxybenzoic acid (470 mg, 2.7

mmol) in CH_2Cl_2 (50 mL) was stirred under reflux for 48 h. Silica gel (Merck Kieselgel 60, ø40–60 μm, 4 g) and EtOAc (80 mL) were added and the suspension was stirred for 30 h at 40 °C. The mixture was filtered and the filtrate was taken to dryness. The residue was dissolved in dry pyridine (10 mL), 4-dimethylaminopyridine (15 mg) and Ac_2O (0.6 mL) were added at 0°C. The solution was stirred for 15 h at room temperature and evaporated. A solution of the residue in EtOAc (100 mL) was washed with satd aq $NaHCO_3$ and dried ($NaSO_4$). Evaporation of the solvent afforded a syrup, which upon chromatography gave the less polar compound **12** (*C*, 2:1 toluene–EtOAc) as colorless needles; yield, 85 mg (12%); mp 169–170°C (EtOAc–hexane), lit.[3] 169°C; $[\alpha]_D^{20}$ +111° (*c*, 1.2, $CHCl_3$), lit.[3] +110°; ^{1}H NMR (250 MHz, $CDCl_3$): δ 5.51 (dd, 1 H, $J_{5,6}$ 1.5, $J_{5,4}$ 3.0 Hz, H-5), 5.40 (m, 2 H, H-3, 4), 5.25 (ddd, 1 H, $J_{7,6}$ 10.0, $J_{7,8a}$ 2.5, $J_{7,8b}$ 3.5 Hz, H-7), 4.45 (dd, 1 H, $J_{8a,8b}$ −12.5 Hz, H-8a), 4.16 (dd, 1 H, H-6), 4.09 (dd, 1 H, H-8b), 3.77 (s, 3 H, CO_2CH_3), 2.21 (s, 3 H), 2.14 (s, 3 H), 2.08 (s, 3 H), 2.05 (s, 3 H), 1.99 (s, 3 H), and 1.98 (s, 3 H, 6 CH_3CO).

Further elution of the column afforded a syrup which crystallized upon addition of Et_2O–hexane; yield, 320 mg (46%) of **13**; mp 143–144°C, colorless needles, $[\alpha]_D^{20}$ +79.5° (*c* 0.5, $CHCl_3$); ^{1}H NMR (250 MHz, $CDCl_3$): δ 5.45 (dd, 1 H, $J_{3,4}$ 4.0, $J_{3,5}$ 1.0 Hz, H-3), 5.41 (t, 1 H, $J_{4,5}$ 4.0 Hz, H-4), 5.38 (m, 1 H, H-5), 5.36 (ddd, 1 H, $J_{7,6}$ 9.0, $J_{7,8a}$ 2.5, $J_{7,8b}$ 3.5 Hz, H-7), 4.54 (dd, 1 H, $J_{8a,8b}$ −12.5 Hz, H-8a), 4.22 (dd, 1 H, $J_{6,5}$ 1.5 Hz, H-6), 4.17 (dd, 1 H, H-8b), 3.77 (s, 3 H, CO_2CH_3), 2.19 (s, 3 H), 2.10 (s, 3 H), 2.08 (s, 3 H), 2.05 (s, 3 H) and 2.00 (s, 6 H, 6 CH_3CO). Anal. Calcd for $C_{21}H_{28}O_{15}$: C, 48.51; H, 5.42. Found: C, 48.51; H, 5.36.

The mother liquor was evaporated to give a syrup (195 mg, 28%). An aliquot (60 mg) was subjected to preparative liquid chromatography on silica gel (0.7 × 25 cm, Nucleosil 50, 5 μm, 11 MPa) using 5:1 toluene–acetone as eluant, which gave a pure fraction of **18** (4.8 mg), a mixture of **18** and **19** (14.5 mg), **19** (16.9 mg), and **13** (8.1 mg).

Compound **18**. ^{1}H NMR (360 MHz, C_6D_6): δ 6.30 (d, 1 H, $J_{3,4}$ 6.0 Hz, H-3), 5.72 (dd, 1 H, $J_{6,7}$ 5.7, $J_{6,5}$ 2.5 Hz, H-6), 5.69 (dd, 1 H, $J_{4,5}$ 5.7 Hz, H-4), 5.57 (ddd, 1 H, $J_{7,8a}$ 2.5, $J_{7,8b}$ 5.5 Hz, H-7), 4.80 (d, 1 H, H-5), 4.55 (dd, 1 H, $J_{8a,8b}$ −12.6 Hz, H-8a), 4.25 (dd, 1 H, H-8b), 3.44 (s, 3 H, CO_2CH_3), 1.81 (s, 3 H), 1.69 (s, 3 H), 1.67 (s, 3 H), 1.65 (s, 3 H), 1.64 (s, 3 H), and 1.62 (s, 3 H, 6 CH_3CO); ^{13}C NMR (90.6 MHz, C_6D_6): δ 170.0, 169,7, 169.5 (2 ×), 169.4, 167.0 (CO), 102.7 (C-2), 81.0 (C-5), 73.2 (C-3), 70.4, 70.0, 69.3 (C-7,4,6), 62.0 (C-8), 52.3 (CO_2CH_3), 51.2 (OCH_3), 20.3, 20.2 (2 ×), 20.0, and 19.9 (CH_3CO).

Compound **19**. $[\alpha]_D^{20}$ +46° (*c* 0.7, $CHCl_3$); ^{1}H NMR (360 MHz, C_6D_6): δ 6.00 (d, 1 H, $J_{3,4}$ 4.8 Hz, H-3), 5.75 (dd, 1 H, $J_{4,5}$ 8.1 Hz, H-4), 5.67 (dd, 1 H, $J_{6,7}$ 4.8 Hz, H-6), 5.46 (ddd, 1 H, $J_{7,8a}$ 3.1, $J_{7,8b}$ 3.0 Hz, H-7), 4.86 (dd, 1 H, $J_{5,6}$ 4.9 Hz, H-5), 4.48 (dd, 1 H, $J_{8a,8b}$ −12.4 Hz, H-8a), 4.25 (dd, 1 H, H-8b), 3.40 (s, 3 H, CO_2CH_3), 1.68 (s, 3 H), 1.66 (s, 6 H), 1.65 (s, 3 H), 1.61 (s, 3 H), and 1.60 (s, 3 H, 6 CH_3CO); ^{13}C NMR (90.6 MHz, C_6D_6): δ 170–165 (6 CO), 106.4 (C-2), 79.7 (C-5), 75.8 (C-3), 70.9 (C-7), 70.1 (C-4), 69.0 (C-6), 61.7 (C-8), 51.9 (CO_2CH_3), 51.5 (OCH_3), 20.4,

20.3, 20.2, 19.9 and 19.9 (CH_3CO). Anal. Calcd for $C_{21}H_{28}O_{15}$: C, 48.51; H, 5.42. Found: C, 48.49; H, 5.43.

Methyl 3,4,5,7,8-penta-O-acetyl-α-D-glycero-D-talo-2-octulopyranosyl bromide)-onate (**14**).—A solution of **13** (230 mg, 0.44 mmol) in CH_2Cl_2 (40 mL) was stirred with $TiBr_4$ (540 mg, 1.48 mmol) under reflux for 20 h. The solution was diluted with $CHCl_3$ (50 mL), washed with satd aq $NaHCO_3$, dried ($MgSO_4$), and evaporated; yield, 230 mg (96%), slightly yellow syrup; $[\alpha]_D^{20}$ +109° (*c* 0.9, $CHCl_3$); ^1H NMR (250 MHz, $CDCl_3$): δ 5.80 (dd, 1 H, $J_{3,4}$ 3.6, $^4J_{3,5}$ 1.0 Hz, H-3), 5.73 (t, 1 H, $J_{5,4}$ 3.7 Hz, H-4), 5.46 (ddd, 1 H, $J_{5,6}$ 1.7 Hz, H-5), 5.40 (ddd, 1 H, $J_{7,8a}$ 2.2, $J_{7,8b}$ 3.9, $J_{7,6}$ 9.8 Hz, H-7), 4.52 (dd, 1 H, H-6), 4.47 (dd, 1 H, $J_{8a,8b}$ −12.5 Hz, H-8a), 4.25 (dd, 1 H, H-8b), 3.87 (s, 3 H, CO_2CH_3), 2.09 (s, 3 H), 2.07 (s, 3 H), 2.05 (s, 3 H), 2.03 (s, 3 H), and 1.98 (s, 3 H, 5 CH_3CO).

Methyl 4,5,7,8-tetra-O-acetyl-α-D-glycero-D-talo-2-octulopyranosonate (**15**).—A solution of **14** (1.5 g, 2.7 mmol) in CH_2Cl_2 (50 mL) was stirred with MeOH (8 mL) and Ag triflate (0.8 g) for 5 h at room temperature. The solution was washed with 5% aq. $Na_2S_2O_3$, satd aq $NaHCO_3$, and dried (Na_2SO_4). Chromatography of the residue obtained upon evaporation (*B*, 1:5 toluene–EtOAc) gave **15** as a syrup; yield, 478 mg (40%); $[\alpha]_D^{20}$ +37° (*c* 0.4, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$): δ 5.45 (ddd, 1 H, $J_{5,6}$ 2.8, $J_{5,4}$ 3.3, $^4J_{5,3}$ 1.2 Hz, H-5), 5.32 (t, 1 H, $J_{4,3}$ 3.7 Hz, H-4), 5.28 (ddd, 1 H, $J_{7,8a}$ 3.1, $J_{7,8b}$ 4.2, $J_{7,6}$ 9.9 Hz, H-7), 4.84 (br s, 1 H, OH-2), 4.41 (dd, 1 H, $J_{8a,8b}$ −12.0 Hz, H-8a), 4.39 (dd, 1 H, H-6), 4.33 (dd, 1 H, H-8b), 4.03 (ddd, 1 H, $J_{3,OH}$ 12.0 Hz, H-3), 3.85 (s, 3 H, CO_2CH_3), 2.80 (d, 1 H, OH-3), 2.12 (s, 3 H), 2.08 (s, 3 H), 2.07 (s, 3 H), and 2.00 (s, 3 H, 4 CH_3CO). Anal. Calcd for $C_{17}H_{24}O_{13}$: C, 46.79; H, 5.54. Found C, 47.24, H, 5.43.

Methyl 4,5,7,8-tetra-O-acetyl-2,3-di-O-(4-nitrobenzoyl)-α-D-glycero-D-talo-2-octulopyranosonate (**16**).—4-Nitrobenzoyl chloride (106 mg, 3.8 mmol) was added to a solution of **15** (330 mg, 0.76 mmol) in pyridine (10 mL). The solution was stirred for 60 h at room temperature and evaporated. The residue was dissolved in CH_2Cl_2 (50 mL), washed with satd aq $NaHCO_3$, dried ($NaSO_4$), and evaporated. The residue was purified by chromatography (*B*, 1:1 toluene–EtOAc) which gave 380 mg (70%) of **16**, slightly yellow crystals; mp 206°C (EtOAc–hexane); $[\alpha]_D^{20}$ +51° (*c* 0.75, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$): δ 8.41–8.26 (m, 8 H, arom. H), 5.92 (dd, 1 H, $J_{3,4}$ 3.8, $^4J_{3,5}$ 0.9 Hz, H-3), 5.66 (t, 1 H, $J_{4,5}$ 3.7 Hz, H-4), 5.53 (ddd, 1 H, $J_{5,6}$ 1.6 Hz, H-5), 5.47 (dt, 1 H, $J_{7,8a}$ 2.3, $J_{7,8b}$ 3.2, $J_{7,6}$ 9.9 Hz, H-7), 4.54 (dd, 1 H, $J_{8a,8b}$ −12.4 Hz, H-8a), 4.33 (dd, 1 H, H-6), 4.23 (dd, 1 H, H-8b), 3.68 (s, 3 H, CO_2CH_3), 2.01 (s, 3 H), 1.98 (s, 3 H), 1.97 (s, 3 H) and 1.66 (s, 3 H, 4 CH_3CO). Anal. Calcd for $C_{31}H_{30}N_2O_{19}$: C, 50.69; H, 4.12; N, 3.81. Found: C, 50.80; H, 4.18; N, 3.79.

Alternatively, **16** was prepared from **1** (202 mg, 0.5 mmol) similar to the preparation of **13**. The resulting syrup was dissolved in dry pyridine (10 mL) and stirred with 4-nitrobenzoyl chloride (1.4 g) for 48 h at room temperature. Workup as described above gave 135 mg (36%) of **16**.

Methyl [4,5,7,8-tetra-O-acetyl-3-O-(4-nitrobenzoyl)-α-D-glycero-D-talo-2-octulopy-

ranosyl bromide]onate (**17**).—A solution of **16** (180 mg, 0.25 mmol) and $TiBr_4$ (270 mg, 0.74 mmol) in CH_2Cl_2 (50 mL) was stirred at reflux temperature for 48 h. The solution was diluted with $CHCl_3$ (100 mL), washed with ice-cold satd aq $NaHCO_3$, dried ($MgSO_4$), and evaporated to give a yellow syrup; yield, 160 mg (quant), $[\alpha]_D^{20}$ +45° (*c* 0.4, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$): δ 8.33–8.24 (m, 4 H, arom. H), 6.07 (dd, 1 H, $J_{3,4}$ 3.6, $^4J_{3,5}$ 0.9 Hz, H-3), 5.86 (t, 1 H, $J_{4,5}$ 3.7 Hz, H-4), 5.54 (ddd, 1 H, $J_{5,6}$ 1.7 Hz, H-5), 5.50 (ddd, 1 H, $J_{7,6}$ 9.8, $J_{7,8a}$ 2.1, $J_{7,8b}$ 4.0 Hz, H-7), 4.61 (dd, 1 H, H-6), 4.52 (dd, 1 H, $J_{8a,8b}$ −12.5 Hz, H-8a), 4.31 (dd, 1 H, H-8b), 3.74 (s, 3 H, CO_2CH_3), 2.12 (s, 3 H), 2.04 (s, 3 H), 1.95 (s, 3 H), and 1.92 (s, 3 H, 4 CH_3CO). Anal. Calcd for $C_{24}H_{26}BrNO_{15}$: C, 44.46; H, 4.04; N, 2.16. Found: C, 44.87; H, 4.06; N, 2.13.

*Methyl 4,5,7,8-tetra-*O*-acetyl-2,3-*O*-[(1-*endo*-methoxy)ethylidene]-β-*D*-glycero-*D*-talo-2-octulopyranosonate* (**20**), *methyl 4,5,7,8-tetra-*O*-acetyl-2,3-*O*-[1-*exo*-methoxy)ethylidene]-β-*D*-glycero-*D*-talo-2-octulopyranosonate* (**21**), and *methyl (methyl 3,4,5,7,8-penta-*O*-acetyl-α-*D*-glycero-*D*-talo-2-octulopyranosid)onate* (**23**). — A suspension of **14** (119 mg, 0.22 mmol), MeOH (0.2 mL), 4A molecular sieves (500 mg), and Me_3Si triflate (60 μL) in dry CH_2Cl_2 (5 mL) was stirred for 48 h at room temperature. The mixture was diluted with CH_2Cl_2 (50 mL) and filtered over Celite. The filtrate was washed with satd aq $NaHCO_3$, dried (Na_2SO_4), and evaporated. The residue was purified on a column of silica gel, (*B*, 2:1 toluene–EtOAc), which afforded **20** as the faster moving component; yield, 21.5 mg (20%); ^1H NMR (300 MHz, $CDCl_3$): δ 5.36 (ddd, 1 H, $J_{6,5}$ 1.1 Hz, H-5), 5.29 (t, 1 H, $J_{4,3}$, $J_{4,5}$ 4.0 Hz, H-4), 5.14 (ddd, 1 H, $J_{7,6}$ 9.5, $J_{7,8a}$ 2.4, $J_{7,8b}$ 4.3 Hz, H-7), 4.49 (dd, 1 H, $J_{8a,8b}$ −12.2 Hz, H-8a), 4.48 (br d, 1 H, H-3), 4.27 (dd, 1 H, H-8b), 4.12 (dd, 1 H, H-6), 3.86 (s, 3 H, CO_2CH_3), 3.56 (s, 3 H, OCH_3), 2.10 (s, 3 H), 2.09 (s, 3 H), 2.08 (s, 3 H), 2.00 (s, 3 H, 4 CH_3CO), and 1.60 (s, 3 H, *exo*-CH_3).

Further elution of the column afforded **21** as a syrup; yield, 35 mg (32%); $[\alpha]_D^{20}$ +28.5° (*c* 0.5, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$): δ 5.32 (dt, 1 H, $J_{5,6}$ 1.0 Hz, H-5), 5.20 (t, 1 H, $J_{4,3}$, $J_{4,5}$ 3.8 Hz, H-4), 5.15 (ddd, 1 H, $J_{7,6}$ 9.5, $J_{7,8a}$ 2.3, $J_{7,8b}$ 4.3 Hz, H-7), 4.65 (dd, 1 H, $^4J_{3,5}$ 1.1 Hz, H-3), 4.46 (dd, 1 H, $J_{8a,8b}$ −12.3 Hz, H-8a), 4.30 (dd, 1 H, H-8b), 4.20 (dd, 1 H, H-6), 3.88 (s, 3 H, CO_2CH_3), 3.35 (s, 3 H, OCH_3), 2.12 (s, 3 H), 2.09 (s, 6 H), 2.01 (s, 3 H, 4 CH_3CO), and 1.79 (s, 3 H, *endo*-CH_3). Anal. Calcd for $C_{20}H_{28}O_{14}$: C, 48.78; H, 5.73. Found: C, 48.97; H, 5.87.

Further elution of the column furnished **23** as a syrup; yield, 13 mg (12%); $[\alpha]_D^{20}$ +37° (*c* 0.6, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$): δ 5.48 (dd, 1 H, $J_{3,4}$ 3.7, $^4J_{3,5}$ 1.0 Hz, H-3), 5.38 (t, 1 H, $J_{4,5}$ 3.8 Hz, H-4), 5.37 (ddd, 1 H, H-7), 5.34 (ddd, 1 H, H-5), 4.68 (dd, 1 H, $J_{8a,7}$ 2,3, $J_{8a,8b}$ −12.4 Hz, H-8a), 4.26 (dd, 1 H, $J_{8b,7}$ 3.4 Hz, H-8b), 4.19 (dd, 1 H, $J_{6,5}$ 1.7, $J_{6,7}$ 9.9 Hz, H-6), 3.79 (s, 3 H, CO_2CH_3), 3.28 (s, 3 H, OCH_3), 2.08 (s, 3 H), 2.07 (s, 3 H), 2.05 (s, 3 H), 1.99 (s, 3 H), and 1.97 (s, 3 H, 5 CH_3CO). Anal. Calcd for $C_{20}H_{28}O_{14}$: C, 48.78; H, 5.73. Found: C, 49.12; H, 5.89.

Orthoester rearrangement.—A suspension of **21** (50 mg, 0.1 mmol), Me_3Si triflate (30 μL), and 4A molecular sieves (200 mg) in dry CH_2Cl_2 (6 mL) was

stirred under N_2 for 3 h. Solid $NaHCO_3$ (200 mg) was added, the mixture was filtered over Celite and washed with CH_2Cl_2 (50 mL). The organic layer was washed with $NaHCO_3$, dried (Na_2SO_4), and taken to dryness. The residue was purified by chromatography (*A*, 1:1 toluene–EtOAc) which gave **23** as a syrup; yield, 13 mg (26%).

Methyl {4,5,7,8-tetra-O-*acetyl-2,3*-O-*[(1*-exo-*methoxy)-4-nitrobenzylidene]-β*-D-glycero-D-talo-*2-octulopyranos}onate* (**22**).—A suspension of **17** (33 mg, 0.051 mmol), Ag triflate (25 mg, 0.1 mmol), 4A molecular sieves (200 mg), and MeOH (40 μL) in CH_2Cl_2 (10 mL) was stirred for 2 h at room temperature. The mixture was diluted with CH_2Cl_2 (50 mL) and filtered over Celite. The filtrate was washed with 5% aq $Na_2S_2O_3$, sat aq $NaHCO_3$, and dried ($MgSO_4$). Chromatography of the residue obtained upon concentration (*B*, 1:1 toluene–EtOAc) gave **22** as a syrup; yield, 16 mg (52%); $[\alpha]_D^{20}$ −44° (*c* 1.1, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$): δ 8.28–7.90 (m, 4 H, arom H), 5.32–5.29 (m, 2 H, H-4,5), 4.99 (ddd, 1 H, $J_{7,6}$ 9.4, $J_{7,8a}$ 2.2, $J_{7,8b}$ 4.4 Hz, H-7), 4.89 (dd, 1 H, $J_{3,4}$, 3.2, $^4J_{3,5}$ 1.6 Hz, H-3), 4.39 (dd, 1 H, H-8b), 4.18 (dd, 1 H, $J_{8a,8b}$ −12.4 Hz, H-8a), 4.21 (dd, 1 H, H-8b), 4.18 (dd, 1 H, $J_{6,5} < 1.0$ Hz, H-6), 3.92 (s, 3 H, CO_2CH_3), 3.42 (s, 3 H, OCH_3), 2.11 (s, 3 H), 2.08 (s, 3 H), 1.98 (s, 3 H), and 1.86 (s, 3 H, 4 CH_3CO). Anal. Calcd for $C_{25}H_{29}NO_{16}$: C, 50.09; H, 4.88; N, 2.34. Found: C, 50.89; H, 4, 91; N, 2.10.

Methyl [methyl 4,5,7,8-tetra-O-*acetyl-3*-O-*(4-nitrobenzoyl)-α*-D-glycero-D-talo-*2-octulopyranosid]onate* (**24**).—A suspension of **22** (25 mg, 0.04 mmol) 4A molecular sieves (200 mg), and trimethylsilyl triflate (40 μL) in dry CH_2Cl_2 (5 mL) was stirred for 90 min at room temperature under N_2. Workup and purification of the residue as described for **23** (orthoester rearrangement) afforded **24** as a syrup; yield, 10 mg (40%); $[\alpha]_D^{20}$ −27° (*c* 1.0, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$): δ 8.34–8.27 (m, 4 H, arom H), 5.73 (dd, 1 H, $J_{3,4}$ 3.7, $^4J_{3,5}$ 0.9 Hz, H-3), 5.52 (t, 1 H, $J_{4,5}$ 3.7 Hz, H-4), 5.47 (ddd, 1 H, $J_{7,6}$ 10.1, $J_{7,8a}$ 2.3, $J_{7,8b}$ 3.5 Hz, H-7), 5.43 (ddd, 1 H, $J_{5,6}$ 1.8 Hz, H-5), 4.72 (dd, 1 H, $J_{8a,8b}$ −12.3 Hz, H-8a), 4.30 (dd, 1 H, H-8b), 4.28 (dd, 1 H, H-6), 3.66 (s, 3 H, CO_2CH_3), 3.33 (s, 3 H, OCH_3), 2.11 (s, 3 H), 2.01 (s, 3 H), 1.94 (s, 3 H), and 1.91 (s, 3 H, 4 CH_3CO). Anal. Calcd for $C_{25}H_{29}NO_{16}$: C, 50.09; H, 4.88; N, 2.34. Found: C, 49.96; H, 4.67; N, 2.10.

Sodium (methyl α-D-glycero-D-talo-*2-octulopyranosid)onate* (**25**).—A solution of **23** (8 mg) in MeOH (3 mL) was stirred with 0.1 M methanolic NaOMe (0.1 mL) for 24 h at room temperature. The pH of the solution was made neutral by adding Dowex 50 (H^+) resin, and the mixture was filtered and evaporated. A solution of the residue in water (2 mL) was stirred with 0.2 M NaOH (4 mL) for 2 h at room temperature. Processing of the solution as described for **11** gave **25** as amorphous solid; yield, 4.6 mg (≈ 100%); $[\alpha]_D^{20}$ +50° (*c* 0.4, H_2O); ^1H NMR (300 MHz, D_2O): δ 4.07 (dd, 1 H, H-5), 4.03 (ddd, 1 H, $J_{7,6}$ 8.4, $J_{7,8a}$ 3.0, $J_{7,8b}$ 6.3 Hz, H-7), 3.98 (dd, 1 H, $J_{8a,8b}$ −11.7 Hz, H-8a), 3.94 (dd, 1 H, $^4J_{3,5}$ 1.4, $J_{3,4}$ 3.3 Hz, H-3), 3.91 (t, 1 H, $J_{4,5}$ 3.3 Hz, H-4), 3.72 (dd, 1 H, H-8b), 3.60 (dd, 1 H, $J_{6,5}$ 1.0 Hz, H-6), and 3.17 (s, 3 H, OCH_3).

Methyl {{4,5,7,8-tetra-O-*acetyl-2,3*-O-*{1*-exo-*[allyl 2-acetamido-2-deoxy-3,4-*

*O-(1,1,3,3-tetraisopropyldisiloxan-1,3-diyl)-6-yl-β-D-glucopyranoside]-4-nitrobenzylidene}-β-D-*glycero-D-talo-*2-octulopyranos}}onate* (**27**).—A solution of **17** (63.5 mg, 0.01 mmol) in dry acetonitrile (5 mL) was added to a suspension of **26** (120 mg, 0.24 mmol), 4A molecular sieves (500 mg), and Ag triflate (80 mg, 0.3 mmol) in dry acetonitrile (10 mL). The suspension was stirred at 70°C for 4 h, then filtered over Celite, and washed with CH_2Cl_2 (50 mL). The filtrate was washed with 5% aq $Na_2S_2O_3$, satd aq $NaHCO_3$, and dried (Na_2SO_4). Evaporation to dryness and purification of the residue on a column of silica gel (*B*, 1:2 toluene–EtOAc) gave **27** as a syrup; yield, 64 mg (63%); $[\alpha]_D^{20}$ −7° (*c* 1.0, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.25–7.96 (m, 4 H, arom H), 5.90 (m, 1 H, =CH–), 5.53 (d, 1 H, $J_{2,NH}$ 7.8 Hz, NH), 5.34–5.30 (m, 2 H, H-4′,5′), 5.27 (dq, 1 H, $=CH_{2trans}$), 5.19 (dq, 1H, $=CH_{2cis}$), 5.01 (ddd, 1 H, H-7′), 5.00 (d, 1 H, $J_{1,2}$ 8.4 Hz, H-1), 4.86 (dd, 1 H, $J_{3',4'}$ 3.7, $^4J_{3',5'}$ 1.1 Hz, H-3′), 4.40 (dd, 1 H, $J_{8'a,7'}$ 2.2, $J_{8'a,8'b}$ −12.5 Hz, H-8′a), 4.32 (m, 1 H, OCH_2), 4.22 (dd, 1 H, $J_{8'b,7'}$ 4.3 Hz, H-8′b), 4.16 (dd, 1 H, H-3), 4.15 (dd, 1 H, $J_{6',7'}$ 9.5 Hz, H-6′), 4.10 (m, 1 H, OCH_2), 3.90 (s, 3 H, CO_2CH_3), 3.92–3.86 (m, 2 H, H-6a,6b), 3.74 (ddd, 1 H, $J_{5,4}$ 5.6 Hz, H-5), 3.52 (dd, 1 H, H-4), 3.24 (dt, 1 H, $J_{2,3}$ 8.1 Hz, H-2), 2.09 (s, 3 H), 2.07 (s, 3 H), 1.99 (s, 3 H), 1.97 (s, 3 H), 1.83 (s, 3 H, 4 CH_3CO, NHAc), and 1.06–0.92 [m, 28 H, 4 $SiCH(CH_3)_2$]. Anal. Calcd for $C_{47}H_{70}N_2O_{22}Si_2$: C, 52.70; H, 6.58; N, 2.61. Found: C, 52.76; H, 6.56; N, 3.07.

*Allyl O-{methyl [4,5,7,8-tetra-*O*-acetyl-3-*O*-(4-nitrobenzoyl)-α-*D*-*glycero*-D-talo-2-octulopyranosyl]onate}-(2 → 6)-2-acetamido-2-deoxy-3,4-*O*-(1,1,3,3-tetraisopropyldisiloxan-1,3-diyl)-β-*D*-glucopyranoside* (**28**).—A suspension of **27** (135 mg, 0.126 mmol), 4A molecular sieves (300 mg), and Me_3Si triflate (30 μL) in dry CH_2Cl_2 (5 mL) was stirred for 2 h at room temperature under N_2. Pyridine (10 mL), 4-dimethylaminopyridine (15 mg), and Ac_2O (0.5 mL) were added at 0°C, and the mixture was kept for 15 h at room temperature. The suspension was filtered over Celite and washed with CH_2Cl_2 (50 mL). The filtrate was extracted with satd aq $NaHCO_3$, dried (Na_2SO_4), and evaporated. Purification of the residue by chromatography (*B*, 1:1 toluene–EtOAc) gave **28** as a syrup; yield, 95 mg (70%); $[\alpha]_D^{20}$ −7.5° (*c* 0.8, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.34–8.28 (m, 4 H, arom H), 5.90 (m, 1 H, =CH–), 5.77 (dd, 1 H, $J_{3',4'}$ 3.6, $^4J_{3',5'}$ 0.7 Hz, H-3′), 5.52 (d, 1 H, $J_{NH,2}$ 8.8 Hz, NH), 5.50 (t, 1 H, $J_{4',5'}$ 3.8 Hz, H-4′), 5.47 (ddd, 1 H, H-7′), 5.39 (ddd, 1 H, H-5′), 5.34 (dq, 1 H, $=CH_{2trans}$), 5.22 (dq, 1 H, $=CH_{2cis}$), 4.96 (d, 1 H, $J_{1,2}$ 8.5 Hz, H-1), 4.74 (dd, 1 H, $J_{8'a,7'}$ 2.5, $J_{8'a,8'b}$ −12.3 Hz, H-8′a), 4.45 (dd, 1 H, $J_{6',5'}$ 1.7, $J_{6',7'}$ 10.0 Hz, H-6′), 4.34 (m, 1 H, OCH_2), 4.25 (dd, 1 H, $J_{8'b,7'}$ 4.3 Hz, H-8′b), 4.14 (m, 1 H, OCH_2), 4.12 (t, 1 H, H-3), 3.80 (dd, 1 H, $J_{6a,6b}$ −10.0, $J_{6a,5} < 1.0$ Hz, H-6a), 3.68 (t, 1 H, $J_{6b,5}$ 9.5 Hz, H-6b), 3.61 (s, 3 H, CO_2CH_3), 3.60 (ddd, 1 H, H-5), 3.42 (t, 1 H, $J_{4,5}$ 7.9 Hz, H-4), 3.29 (dt, 1 H, $J_{2,3}$ 8.1 Hz, H-2), 2.12 (s, 3 H), 2.00 (s, 3 H), 1.98 (s, 3 H), 1.93 (s, 3 H), and 1.90 (s, 3 H, 4 CH_3CO, NHAc), and 1.06–0.98 [m, 28 H, 4 $SiCH(CH_3)_2$]. Anal. Calcd for $C_{47}H_{70}N_2O_{22}Si_2$: C, 52.70; H, 6.58; N, 2.62. Found: C, 52.95; H, 5.97; N, 3.05.

*Allyl O-[methyl (3,4,5,7,8-penta-*O*-acetyl-α-*D*-*glycero*-D-talo-2-octulopyranosyl) onate]-(2 → 6)-2-acetamido-3,4-di-*O*-acetyl-2-deoxy-β-*D*-glucopyranoside* (**29**).—A

solution of **28** (75 mg, 0.07 mmol) in dry oxolane (10 mL) was stirred with 1.1 M tetrabutylammonium fluoride (0.3 mL) in oxolane for 6 h at room temperature. The solution was evaporated and the residue was dissolved in dry MeOH (5 mL) and 0.1 M methanolic NaOMe (1 mL). The solution was stirred for 12 h at room temperature and the base neutralized by addition of Dowex 50-WX8 (H^+) resin. The mixture was filtered and evaporated. A solution of the residue in dry pyridine (6 mL) was stirred with 4-dimethylaminopyridine (5 mg) and Ac_2O (0.25 mL) for 5 h at room temperature. The solution was evaporated and the residue was dissolved in EtOAc. The organic layer was washed with satd aq $NaHCO_3$ solution, dried ($MgSO_4$), and evaporated. Purification of the residue on the column of silica gel (*B*, 1:2 toluene–EtOAc, then EtOAc) gave **29** (43 mg, 76%) as colorless needles; mp 108°C (EtOAc–Et_2O); $[\alpha]_D^{20}$ +26° (*c* 0.8, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$); δ 5.88 (m, 1 H, =CH–), 5.49 (dd, 1 H, $J_{3',4'}$ 3.6, $^4J_{3',5'}$ 0.8 Hz, H-3′), 5.44 (d, 1 H, $J_{2,NH}$ 8.9 Hz, NH), 5.38 (t, 1 H, $J_{4',5'}$ 3.7 Hz, H-4′), 5.35 (m, 1 H, H-7′), 5.32 (dq, 1 H, $=CH_{2trans}$), 5.31 (ddd, 1 H, H-5′), 5.22 (dq, 1 H, $=CH_{2cis}$), 5.21 (dd, 1 H, H-3), 4.87 (t, 1 H, $J_{3,4}$ 9.6 Hz, H-4), 4.72 (dd, 1 H, $J_{8'a,7'}$ 2.5, $J_{8'a,8'b}$ 12.5 Hz, H-8′a), 4.64 (d, 1 H, $J_{1,2}$ 8.3 Hz, H-1), 4.35 (m, 1 H, OCH_2), 4.30 (dd, 1 H, $J_{6',5'}$ 1.9, $J_{6',7'}$ 10.0 Hz, H-6′), 4.17 (dd, 1 H, $J_{8'b,7'}$ 3.9 Hz, H-8′b), 4.11 (m, 1 H, OCH_2), 3.91 (dt, 1 H, $J_{2',3'}$ 10.7 Hz, H-2′), 3.77 (s, 3 H, CO_2CH_3), 3.71–3.63 (m, 2 H, H-5, 6a), 3.36 (dd, 1 H, $J_{6a,6b}$ −13.5, $J_{6b,5}$ 6.5 Hz, H-6b), 2.14 (s, 3 H, NHAc), 2.06 (s, 3 H), 2.05 (s, 3 H), 2.04 (s, 6 H), 1.99 (s, 3 H), and 1.96 (s, 6 H, 7 CH_3CO). Anal. Calcd for $C_{34}H_{47}NO_{21}$: C, 50.68; H, 5.87; N, 1.73. Found: C, 49.96; H, 5.73; N, 1.68.

Allyl O-*[sodium (α-*D-glycero-D-talo-*2-octulopyranosyl)onate]-(2 → 6)-2-acetamido-2-deoxy-β-*D-*glucopyranoside* (**30**).—A solution of **29** (23 mg, 0.03 mmol) in dry MeOH (5 mL) was stirred with 0.1 M methanolic NaOMe (1 mL) for 3 h at room temperature. The solution was deionized by addition of Dowex 50-WX8 (H^+) cation-exchange resin, filtered, and evaporated. A solution of the residue in water (6 mL) was treated with 0.2 M NaOH (4 mL) for 12 h at room temperature. The pH of the solution was adjusted to 8.5 by addition of Dowex 50-WX8 (H^+) resin. Filtration and lyophilization gave a residue, which was purified on Bio-Gel P-2 (2.6 × 100 cm, water) to afford **30** (14.8 mg, 98%) as an amorphous solid; $[\alpha]_D^{20}$ +6° (*c* 1.0, H_2O); ^1H NMR (360 MHz, D_2O): δ 5.90 (m, 1 H, =CH–), 5.30 (dq, 1 H, $=CH_{2trans}$), 5.26 (dq, 1 H, $=CH_{2cis}$), 4.56 (d, 1 H, $J_{1,2}$ 8.8 Hz, H-1), 4.31 (m, 1 H, OCH_2), 4.15 (m, 1 H, OCH_2), 4.10 (ddd, 1 H, $J_{5',6'}$, $^4J_{3',5'}$ 1.4 Hz, H-5′), 4.06 (ddd, 1 H, $J_{7',8'}$ 2.8 Hz, H-7′), 4.01 (dd, 1 H, $J_{3',4'}$ 3.4 Hz, H-3′), 4.00 (dd, 1 H, $J_{8'a,8'b}$ −10.8 Hz, H-8′a), 3.96 (dd, 1 H, $J_{4',5'}$ 3.2 Hz, H-4′), 3.71 (dd, 1 H, $J_{2,3}$ 8.9 Hz, H-2), 3.70 (dd, 1 H, $J_{6',7'}$ 9.0 Hz, H-6′), 3.69 (dd, 1 H, $J_{8'b,7'}$ 7.0 Hz, H-8′b), 3.57 (m, 2 H, H-5, 6b), 3.51 (dd, 1 H, $J_{3,4}$ 9.0 Hz, H-3), 3.46 (dd, 1 H, $J_{4,5}$ 8.8 Hz, H-4), 2.04 (s, 3 H, $NHCOCH_3$). Anal. Calcd for $C_{19}H_{30}NNaO_{14} \cdot 1.5H_2O$: C, 41.76; H, 6.09; N, 2.56. Found: C, 41.72; H, 5.92; N, 2.34.

ACKNOWLEDGMENTS

The authors are grateful to Dr. Gerhard Schulz from Sandoz-Forschungsinstitut Vienna for recording the 250 MHz-spectra and Anja Stoffers for technical assistance. This work was supported by a grant from the Bundesministerium für Wissenschaft and Forschung, Wien.

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