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THE SYNTHESIS OF EVERNITROSE AND 3-*epi*-EVERNITROSE*

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ABSTRACT

Evernitrose (2,3,6-trideoxy-3-*C*-methyl-4-*O*-methyl-3-nitro-L-*arabino*-hexopyranose) was synthesized from methyl 2,6-dideoxy-4-*O*-methyl-α-L-*erythro*-hexopyranosid-3-ulose (**2**) through introduction of an amino group attached to the tertiary branching carbon by the method of Bourgeois, and subsequent oxidation of the amino group by *m*-chloroperoxybenzoic acid to a nitro group. 3-Cyano-3-*O*-mesylation of **2** by Bourgeois's method gave exclusively the desired product having the L-*ribo* configuration; furthermore, the β anomer of **2** gave the L-*ribo* and L-*arabino* products in the ratio of 1:2. The latter compound was converted into 3-*epi*-evernitrose by a similar sequence of reactions.

INTRODUCTION

Evernitrose (**1**) is the first reported, naturally occurring, branched–chain nitro sugar, and is found[2] in the oligosaccharide antibiotics everninomicin B, C, and D. The structure of **1** was recently revised to 2,3,6-trideoxy-3-*C*-methyl-4-*O*-methyl-3-nitro-L-*arabino*-hexopyranose, from the previously assigned L-*ribo* configuration[3], by X-ray analysis of the corresponding 3-acetamido derivative[4]. For synthesis of **1**, introduction of the unique nitro group attached to the tertiary, branching carbon atom seemed to be the key point. Recently, we communicated[5] the synthesis of **1** and its enantiomer, through oxidation with hydroperoxide of the corresponding branched-chain amino sugars, which were obtained by application of Bourgeois's method[6] with appropriate hexopyranosid-3-uloses. We also reported in detail on the synthesis of the enantiomer[7].

This paper describes the synthesis of **1** and its 3-epimer from methyl 2,6-dideoxy-4-*O*-methyl-α- (**2**) and -β-L-*erythro*-hexopyranosid-3-ulose (**3**), respectively.

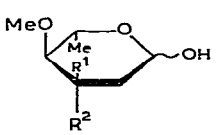
RESULTS AND DISCUSSION

Previous work has shown that successive reaction of hydrogen cyanide and

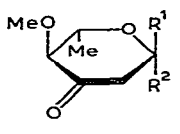
*Branched-chain Sugars, Part XIV. For Part XIII, see ref. 1.

methanesulfonyl chloride with methyl 4,6-*O*-benzylidene-2-deoxy-α-D-*erythro*-hexopyranosid-3-ulose gave the corresponding 3-cyano-3-*O*-mesyl derivatives having the desired D-*ribo* and undesired D-*arabino* configuration in the ratio of 21 : 1; the former was converted[7] into the enantiomer of **1**. The stereoselectivity in this cyanomesylation suggested that **2** would be the most suitable starting material for synthesis of **1**. However, we have also synthesized **3** to examine the effect of anomeric configuration on the stereoselectively in the addition of hydrogen cyanide to these glycos-3-uloses. Methyl 2,3-*O*-benzylidene-6-deoxy-4-*O*-methyl-α-L-mannopyranoside, which was used for the preparation of **2** according to the method of Clode *et al.*[8], was *O*-debenzylidenated with 70% acetic acid for 1 h at 95°; subsequent acetolysis of the product (**4**) gave 1,2,3-tri-*O*-acetyl-6-deoxy-4-*O*-methyl-α-L-mannopyranose (**5**) almost quantitatively. Conversion of **5** into the corresponding glycal (**6**) was achieved in 63% yield, by subsequent treatment[9] with hydrogen bromide in glacial acetic acid and then with zinc powder–acetic acid at −5 to −10°. Compound **6** is a volatile liquid, and its conformation was deduced to be $^5H_4$ by first-order analysis of its n.m.r. spectrum. Addition of bromine to **6** in dichloromethane and subsequent reaction of the product with methanol and silver carbonate gave a mixture of four products from which the main one, methyl 3-*O*-acetyl-2-bromo-2,6-dideoxy-4-*O*-methyl-β-L-mannopyranoside (**7**), was isolated pure by column chromatography on silica gel. Hydrogenation of the foregoing mixture by the procedure of Lemieux and Fraser-Reid[10], and separation of the products (α:β anomer = 1:4) on a column of silica gel, gave methyl 2,6-dideoxy-4-*O*-methyl-β-L-*arabino*-hexopyranoside (**8**) in 62% yield. Oxidation of **8** with chromium trioxide–pyridine in dichloromethane gave **3** in 87% yield.

When **6** was treated with *N*-bromosuccinimide and methanol and the product then reduced with tributylstannane[11], the ratio of α- and β-glycosides produced was 9:2, and methyl 2-*O*-acetyl-2,6-dideoxy-4-*O*-methyl-α-L-*arabino*-hexopyranoside (**9**)



1 R^1 = Me, R^2 = NO_2
29 R^1 = NO_2, R^2 = Me



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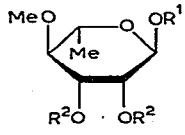
3 R^1 = H, R^2 = OMe



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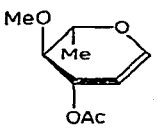

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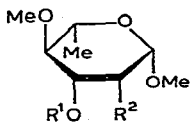
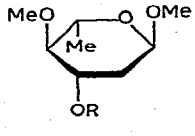


7 R^1 = Ac, R^2 = Br
8 R^1 = R^2 = H



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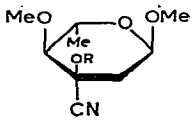
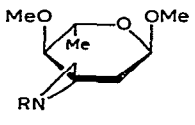
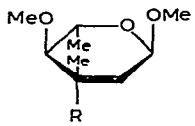
10 R = H



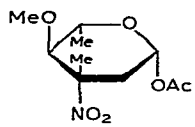
11 R = H
12 R = Ms



13 R = H
14 R = Ac



15 R = NH_2
16 R = NHAc
17 R = NO_2



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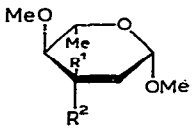
was obtained pure. Zemplén deacetylation of **9** in methanol gave compound **10**. Oxidation of **10** as for **8** gave **2** in good yield.

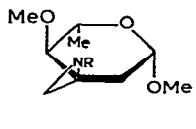
As expected, cyanomesylation of **2** gave exclusively the L-*ribo* epimer of the corresponding 3-cyano-3-*O*-mesyl derivative (**12**), plus the cyanohydrin **11**, in 80 and 10% yields, respectively. Reduction of **12** with lithium aluminum hydride gave the corresponding spiro-aziridine (**13**) having the L-*arabino* configuration, in 93% yield, presumably by an intramolecular, SN2 mechanism[12]; the product was characterized as *N*-acetyl derivative (**14**). Hydrogenation of **13** in the presence of Raney nickel gave the corresponding branched-chain amino sugar (**15**) quantitatively; it was also characterized as *N*-acetyl derivative (**16**).

Comparison of the physical properties of **16** and the enantiomeric methyl 3-acetamido-2,6-dideoxy-3-*C*-methyl-4-*O*-methyl-α-D-*arabino*-hexopyranoside (see Table I)[7] proved the structure of **16** unambiguously. Oxidation of **15** by adding it to a boiling solution of *m*-chloroperoxybenzoic acid in dichloromethane[13] gave the corresponding, branched-chain nitro sugar (**17**) in 52% yield. No nitroso dimer[14] could be detected in the products of this oxidation. This result may be attributed to the absence of a free hydroxyl group vicinal to the amino group in **15**. Hydrolysis of **17** in 0.05M sulfuric acid gave **1**, which was then converted into the 1-acetate (**18**).

In contrast, cyanomesylation of **3** gave a 1:2 mixture of 3-epimers in 66% yield, from which only a small amount of the desired L-*ribo* (**19**, minor) and the undesired L-*arabino* (**20**, major) derivatives were isolated pure. Reduction of **20** with lithium aluminum hydride gave the corresponding spiro-aziridine (**21**), which



	R^1	R^2
19	OMs	CN
20	CN	OMs
23	Me	NH_2
24	NH_2	Me
25	Me	NHAc
26	NHAc	Me
27	Me	NO_2
28	NO_2	Me



21 R = H
22 R = Ac

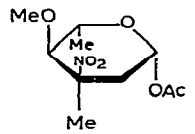


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TABLE I

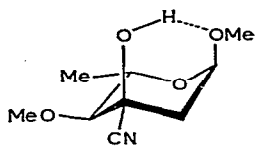
PHYSICAL PROPERTIES OF COMPOUNDS **16–18** AND **25–30**

Compound	*M.p.*	$[\alpha]_D^{22}$	*Chemical shifts (δ in $CDCl_3$) and coupling constants (Hz)*									
	(degrees)	*(in $CHCl_3$)*	*H-1* ($J_{1,2e}$)	*H-2e* ($J_{1,2a}$)	*H-2a* (J_{gem})	*H-4* ($J_{4,5}$)	*H-5* ($J_{5,6}$)	*H-6*	*OMe*	*CMe*	*NAc (OAc)*	*NH*
16	140–141	−75°	4.69 (0)	1.77 (4.5)	2.98 (13.2)	3.90 (10.0)	3.65 (6.0)	1.29	3.50 3.29	1.35	1.94	5.34
enantiomer of **16**	136–138	+73°	4.68 (0)	1.77 (4.5)	2.97 (13.6)	3.90 (10.0)	3.64 (5.9)	1.28	3.49 3.28	1.35	1.94	5.36
17	syrup	−103°	4.74 (1.5)	2.13 (4.5)	2.43 (13.5)	3.77 (9.7)	3.64 (5.3)	1.34	3.39 3.29	1.74	—	—
enantiomer of **17**	syrup	+95°	4.74 (1.5)	2.14 (4.5)	2.46 (13.5)	3.78 (9.5)	3.64 (5.4)	1.34	3.40 3.31	1.74	—	—
25	157–159	+56.4°	4.51 (2.3)	1.99 (8.5)	2.55 (13.5)	3.74 (9.2)	3.62 (6.0)	1.36	3.51 3.46	1.32	1.96	5.50
enantiomer of **25**	159–160	−57°	4.50 (2.5)	1.95 (8.9)	2.55 (13.5)	3.75 (8.8)	3.54 (6.0)	1.34	3.49 3.44	1.30	1.93	5.54
26	107–108	+35.4°	4.43 (1.9)	3.39 (9.3)	1.25 (15.5)	2.60 (9.5)	3.57 (6.2)	1.32	3.54 3.43	1.42	1.97	5.68
27	syrup	+33.6°	4.46 (3.2)	2.14 (8.1)	2.32 (13.0)	3.78 (9.1)	3.43 (6.1)	1.40	3.48 3.42	1.69		
28	syrup	−10.5°	5.04 (2.8)	2.39 (9.0)	1.80 (15.0)	2.96 (9.0)	4.08 (6.0)	1.36	3.58 3.50	1.74		
29	135–137	−57°	5.50 (2.5)	2.46 (9.1)	1.74 (15.5)	2.96 (9.5)	4.13 (6.1)	1.34	3.58	1.75		
30	123–124	−43°	6.32 (3.1)	2.43 (9.5)	1.88 (15.2)	2.96 (8.9)	4.14 (6.0)	1.30	3.56	1.74	2.07 (OAc)	
18	syrup	−19°	5.76 (3.0)	2.18 (10.0)	2.44 (13.0)	3.77 (9.5)	3.58 (6.0)	1.38	3.43	1.73	2.10 (OAc)	

was characterized as the *N*-acetyl derivative (**22**). The configurations of **19**–**22** were determined from the following experiments. The foregoing mixture was reduced with lithium aluminum hydride and then hydrogenolyzed with Raney nickel to give the corresponding branched-chain amino sugars (**23** and **24**) in 88% yield. These were separated on a column of silica gel, and then characterized as the *N*-acetyl derivatives (**25** and **26**), respectively. The configuration of the minor product (**25**) was determined to be L-*arabino* by comparison of its physical properties with those of the enantiomeric methyl 3-acetamido-2,6-dideoxy-3-*C*-methyl-4-*O*-methyl-β-D-*arabino*-hexopyranoside[7] (see Table I). Similar oxidation of **23** and **24** gave the corresponding branched-chain nitro sugars (**27** and **28**), respectively, and these were hydrolyzed to give **1** and its 3-epimer (**29**). Acetylation of **29** gave the corresponding 1-acetate (**30**).

As shown in Table I, the physical constants of the derivatives (**16**, **17**, and **25**) synthesized here and those of their enantiomers are in reasonable agreement, except for the signs of their specific rotations. However, the 3-epimers in the β series (**25** and **26**, **27** and **28**) are different. It is a characteristic feature that axial protons (H-2a and H-4) vicinal to equatorial 3-acetamido or 3-nitro groups in the L-*arabino* derivatives (**16**, **17**, **25**, **27**, and **18**) are so deshielded that the H-2a signals resonate downfield from that of H-2e. Such an abnormal phenomenon was not observed in the case of nonbranched derivatives[15], nor in branched-chain sugars having an alkoxyl group at the branch point[16]. It is noteworthy that comparison of the chemical shift of the axial H-1 and H-5 in **28**–**30** to those of **26** indicates that the deshielding effect of an axial 3-nitro group is stronger than that of a 3-acetamido group.

Although trifling differences in the m.p. and n.m.r. spectrum of **18** remained between the reported[3] values and those of the products here synthesized, we consider that evernitrose and 3-*epi*-evernitrose have been synthesized in this work.



A

The difference in the stereoselectivity of cyanomesylation between **2** and **3** may be explained as follows. In this reaction, the first step (cyanohydrin formation) is an equilibration reaction and the second step (mesylation) fixes the configuration of the cyanohydrins. Under the conditions used here (see Experimental), the kinetically controlled, initial cyanohydrin, which is probably the product of equatorial attack[17] by cyanide anion on the carbonyl function, is subsequently equilibrated to a mixture of epimers, as proved in the case of a hexofuranos-3-ulose[18].

In the case of **2**, the configuration of the product of equatorial attack might be stabilized by hydrogen bonding between the axial 3-hydroxyl and axial 1-methoxyl groups, as shown in (A), and the configuration is then fixed by the subsequent mesylation step, giving only **12**. Because no axial 1-methoxyl group is present in

3, the 3-epimeric cyanohydrins in equilibrium undergo mesylation to give a mixture of **19** and **20**.

EXPERIMENTAL

General methods. — Melting points are uncorrected. Solutions were evaporated under diminished pressure at a bath temperature not exceeding 45°. Specific rotations were measured in a 0.5-dm tube with a Carl Zeiss LEP-Al polarimeter, with chloroform as the solvent unless otherwise stated. I.r. spectra were recorded with a Hitachi Model EPI-G2 spectrometer. N.m.r. spectra were taken with a JEOL PS-100 MHz spectrometer with tetramethylsilane as the internal standard, in chloroform-*d* unless otherwise stated. Chemical shifts and coupling constants were recorded in δ and Hz units, and i.r. frequencies in cm^{-1}.

Methyl 6-deoxy-4-O-methyl-α-L-mannopyranoside (**4**). — A solution of methyl 2,3-*O*-benzylidene-6-deoxy-4-*O*-methyl-α-L-mannopyranoside (40 g, 0.14 mol) in 70% acetic acid (400 mL) and methanol (400 mL) was heated for 1 h at 90–95°, and then extracted with petroleum ether to remove benzaldehyde. Evaporation of the water layer gave a syrup (26.3 g, 96%), a small portion of which was purified by t.l.c. (4:1 benzene–acetone); $[\alpha]_D^{22}$ −76.4° (*c* 1.05); ν_{max}^{NaCl} 3500 (OH).

Anal. Calc. for $C_8H_{16}O_5$: C, 49.99; H, 8.39. Found: C, 49.89; H, 8.47.

1,2,3-Tri-O-acetyl-6-deoxy-4-O-methyl-α-L-mannopyranose (**5**). — A solution of **4** (11.1 g, 58 mmol) in acetic anhydride (28 mL) and conc. sulfuric acid (0.14 mL) was kept for 3 days at room temperature, and then poured into cold, saturated sodium hydrogencarbonate. The resulting mixture was extracted with chloroform. The extracts were dried (magnesium sulfate), and evaporated to a syrup (17.1 g, 98%), a part of which was purified on a column of silica gel (4:1 benzene–ether); $[\alpha]_D^{22}$ −57° (*c* 1.0); ν_{max}^{NaCl} 1730–1780 (ester); n.m.r.: 5.94 (d, $J_{1,2}$ 1.5, H-1), 5.21 (q, $J_{2,3}$ 3.3, H-2), 5.18 (q, $J_{3,4}$ 10.0, H-3), 3.82 (dq, $J_{5,6}$ 6.0, H-5), 3.48 (OMe), 3.24 (t, $J_{4,5}$ 10.0, H-4), 2.15, 2.12, and 2.06 (3 OAc), and 1.25 (d, H-6).

Anal. Calc. for $C_{13}H_{20}O_8$: C, 51.31; H, 6.63. Found: C, 51.36; H, 6.48.

1,5-Anhydro-3-O-acetyl-2,6-dideoxy-4-O-methyl-L-arabino-*hex-1-enitol* (**6**). — To an ice-cooled solution of **5** (17.1 g, 56.3 mmol) in acetic acid (36 mL) and acetic anhydride (24 mL) was added ice-cooled, 30% hydrogen bromide in acetic acid (36 mL), and the mixture was refrigerated overnight.

To a solution of sodium acetate trihydrate (50 g) in 50% acetic acid (120 mL) cooled to −10° was subsequently added zinc powder (36 g) and a solution of cupric sulfate pentahydrate (3.6 g) in water (11 mL) with vigorous stirring. Just after the evolution of hydrogen gas began, the solution of glycosyl bromide was added dropwise to the suspension during 20 min, keeping the temperature at −10 to −5°, and this temperature was maintained for a further 2–3 h with stirring. The suspension was filtered under direct cooling with crushed ice, and the residue washed with 50% acetic acid. The combined filtrate and washings was extracted with chloroform, and the extract was washed thoroughly with water and cold, saturated, sodium hydrogen-

carbonate, dried (calcium chloride), and then evaporated to a syrup, which was distilled at 52–54°/0.2–0.25 mmHg; yield, 63%, $[\alpha]_D^{22}$ +119° (*c* 1.0); ν_{max}^{NaCl} 1740 (ester), and 1640 cm^{-1} (C=C); n.m.r.: 6.35 (q, $J_{1,2}$ 5.6, $J_{1,3}$ 1.7, H-1), 5.28 (septet, $J_{3,4}$ 6.2, H-3), 4.72 (q, $J_{2,3}$ 3.2, H-2), 4.00 (dq, $J_{5,6}$ 6.3, H-5), 3.54 (OMe), 3.28 (q, $J_{4,5}$ 8.2, H-4), 2.12 (OAc), and 1.42 (d, H-6).

Anal. Calc. for $C_9H_{14}O_4$: C, 58.05; H, 7.58. Found: C, 58.04; H, 7.47.

Methyl 3-O-acetyl-2-bromo-2,6-dideoxy-4-O-methyl-β-L-mannopyranoside (7) *and its diastereomers.* — To a solution of **6** (10 g, 54 mmol) in dried chloroform was added dropwise a solution of bromine in chloroform (0.05 g/mL) at 0° until the consumption of bromine has ceased (~172 mL). After refrigeration overnight, the mixture was evaporated, and a suspension of the residual syrup and silver carbonate (31.6 g) in methanol (200 mL) was stirred overnight. The mixture was filtered, and the filtrate evaporated to a syrup (14 g, 88%). Separation of this mixture of four diastereomers on a column of silica gel (4:1 benzene–acetone) gave only **7** as a pure syrup (1.87 g, 11.7%) from the second fractions; $[\alpha]_D^{22}$ −18.4° (*c* 1.0); n.m.r.: 5.04 (q, $J_{3,4}$ 8.8, H-3), 4.84 (d, $J_{1,2}$ 1.5, H-1), 4.47 (q, $J_{2,3}$ 3.6, H-2), 3.75 (dq, $J_{5,6}$ 6.2, H-5), 3.52 and 3.38 (2 OMe), 3.30 (t, $J_{4,5}$ 9.6, H-4), 2.14 (OAc), and 1.34 (d, H-6).

Anal. Calc. for $C_{10}H_{17}BrO_5$: C, 40.42; H, 5.77. Found: C, 40.36; H, 5.68.

Methyl 2,6-dideoxy-4-O-methyl-β-L-arabino-hexopyranoside (**8**). — A suspension of the foregoing mixture of diastereomers (9.6 g, 32 mmol) and palladium-on-charcoal (5%, 3 g) in a 10:9:1 mixture (150 mL) of methanol, water, and triethylamine was hydrogenated for two days until the theoretical amount of hydrogen (724 mL) had been absorbed. The mixture was filtered, and the filtrate evaporated. A solution of the residue in water was extracted with chloroform, and the extract was washed with water, dried (magnesium sulfate), and then evaporated to give crystals (4.5 g, $\alpha:\beta$ = 1:4). Resolution on a column of silica gel (4:1 benzene–acetone) gave **8** (3.5 g, 62%) from the second fractions; m.p. 121–122°, $[\alpha]_D^{22}$ +19° (*c* 1.0); ν_{max}^{KBr} 3300 cm^{-1} (OH); n.m.r.: 4.36 (q, $J_{1,2e}$ 2.0, $J_{1,2a}$ 9.5, H-1), 3.60 (sex, $J_{3,4}$ 9.2, H-3), 3.62 and 3.51 (2 OMe), 3.25 (dq, $J_{5,6}$ 6.2, H-5), 2.71 (t, $J_{4,5}$ 9.2, H-4), 2.46 (OH), 2.18 (dq, J_{gem} 12.4, $J_{2e,3}$ 5.0, H-2e), 1.58 (dt, $J_{2a,3}$ 9.4, H-2a), and 1.38 (d, H-6).

Anal. Calc. for $C_8H_{16}O_4$: C, 54.53; H, 9.15. Found: C, 54.74; H, 9.12.

Methyl 3-O-acetyl-2,6-dideoxy-4-O-methyl-α-L-arabino-hexopyranoside (**9**). — To an ice-cooled mixture of abs. methanol (19 g) and **6** (76 g, 0.41 mol) in distilled acetonitrile (700 mL) was added *N*-bromosuccinimide (87 g). The mixture was stirred for 3 h at 0° and then evaporated. The resulting syrup was purified on a column of silica gel (50:1 benzene–acetone) to give a syrup (107 g, 88%) that was reduced in benzene (1 L) with tributylstannane (113 g) and a small amount of azobis-(isobutyronitrile) by boiling under reflux for 2 h on an oil-bath. The mixture was evaporated, and the resulting syrup ($\alpha:\beta$ = 9:2) was resolved on a column of silica gel (1:1 hexane–benzene) to give pure **9** (1 g, 1.3%) at first and then a syrupy mixture of anomers (65 g, 88%).

Compound **9** had $[\alpha]_D^{22}$ −87.4° (*c* 1.0); n.m.r.: 5.18 (oct, $J_{2e,3}$ 5.0, $J_{2a,3}$ 11.0, H-3), 4.70 (q, $J_{1,2e}$ 1.3, $J_{1,2a}$ 4.0, H-1), 3.71 (dq, $J_{5,6}$ 6.5, H-5), 3.31 and 3.49 (2 OMe),

2.91 (t, $J_{4,5} = J_{3,4} = 9.3$, H-4), 2.25 (oct, J_{gem} 13.2, H-2e), 2.07 (OAc), 1.60 (oct, H-2a), and 1.30 (d, H-6).

Anal. Calc. for $C_{10}H_{18}O_5$: C, 55.03; H, 8.31. Found: C, 55.31; H, 8.04.

*Methyl 2,6-dideoxy-4-*O*-methyl-α-*L*-arabino-hexopyranoside* (**10**). — Sodium metal (1 g) was added to a solution of the foregoing α,β mixture (65 g, 312 mmol) in methanol (800 mL) and the solution was boiled under reflux for 5–6 h, and then evaporated. The resulting syrup was resolved on a column of silica gel (50:1 benzene–acetone) to give in turn **10** (33.5 g, 61%), a mixture of anomers (12.5 g, 23%, $\alpha:\beta$ = 4.9:2.6), and **8** (4 g, 7.2%).

Compound **10** had m.p. 70–72°, $[\alpha]_D^{22}$ −132.7° (*c* 0.9); n.m.r.: 4.74 (q, $J_{1,2e}$ 1.7, $J_{1,2a}$ 4.1, H-1), 3.96 (oct, $J_{2e,3}$ 6.0, $J_{2a,3}$ 11.0, $J_{3,4}$ 10.0, H-3), 3.78–3.48 (m, $J_{5,6}$ 6.3, H-5), 3.58 and 3.31 (2 OMe), 2.88 (OH), 2.74 (t, $J_{4,5}$ 10.0, H-4), 2.15 (oct, J_{gem} 13.6, H-2e), 1.70 (oct, H-2a), and 1.32 (d, H-6).

Anal. Calc. for $C_8H_{16}O_4$: C, 54.53; H, 9.15. Found: C, 54.61; H, 9.10.

*Methyl 2,6-dideoxy-4-*O*-methyl-β-*L*-erythro-hexopyranosid-3-ulose* (**3**). — To a mixture of pyridine (4.26 g, 54 mmol) and dichloromethane (60 mL) was added chromium trioxide (2.4 g, 16 mmol) in two portions, and the mixture was stirred for 20 min. To the mixture was added **8** (0.38 g, 2.2 mmol) and it was stirred for 20 min until **8** had disappeared in t.l.c. (5:1 benzene–acetone). The mixture was poured into saturated sodium hydrogencarbonate, and the organic layer was processed conventionally to give crystals (0.33 g, 87%) that were recrystallized from hexane; m.p. 97.5–99.5°, $[\alpha]_D^{22}$ −96.2° (*c* 0.85); ν_{max}^{KBr} 1720 cm^{-1} (C=O); n.m.r.: 4.56 (q, $J_{1,2e}$ 3.5, $J_{1,2a}$ 8.0, H-1), 3.55 (dq, $J_{5,6}$ 5.6, H-5), 3.55 (2 OMe), 3.48 (d, $J_{4,5}$ 8.8, H-4), 2.74 (q, J_{gem} 14.0, H-2e), 2.63 (q, H-2a), and 1.46 (d, H-6).

Anal. Calc. for $C_8H_{14}O_4$: C, 55.16; H, 8.10. Found: C, 55.21; H, 8.08.

*Methyl 2,6-dideoxy-4-*O*-methyl-α-*L*-erythro-hexopyranosid-3-ulose* (**2**). — Oxidation of **10** with chromium trioxide as just described gave **2** in 83.8% yield; m.p. 69–70°, $[\alpha]_D^{22}$ −294° (*c* 0.9) (lit.[8], m.p. 71–72°, $[\alpha]_D^{22}$ −301°).

*Methyl 3-*C*-cyano-2,6-dideoxy-4-*O*-methyl-α-*L*-ribo-hexopyranoside* (**11**) *and its 3-methanesulfonate* (**12**). — A solution of **2** (1.3 g, 7.5 mmol) and an excess of hydrogen cyanide in pyridine (10 mL) was kept overnight at room temperature, and then methanesulfonyl chloride (5 g, 44 mmol) was added with stirring. After 2 days at room temperature, the mixture was evaporated to a syrup that was resolved on a column of silica gel (5:1 hexane–ether) to give **12** (1.6 g, 77%) and **11** (0.15 g, 10%) as crystals from early and later fractions, respectively.

Compound **11** had m.p. 82–86°, $[\alpha]_D^{22}$ −161° (*c* 1.0); ν_{max}^{KBr} 3370 (OH) and 2240 cm^{-1} (CN).

Anal. Calc. for $C_9H_{15}NO_4$: C, 53.72; H, 7.51; N, 6.96. Found: C, 53.80; H, 7.47; N, 6.91.

Compound **12** had m.p. 105–106°, $[\alpha]_D^{22}$ −134° (*c* 1.0); ν_{max}^{KBr} 2230 (CN), 1360 and 1180 (OMs); n.m.r.: 4.74 (d, $J_{1,2e}$ 0, $J_{1,2a}$ 4.2, H-1), 4.05 (dq, $J_{5,6}$ 7.0, H-5), 3.77 and 3.40 (2 OMe), 3.26 (OMs), 3.24 (d, $J_{4,5}$ 10.0, H-4), 3.18 (d, J_{gem} 15.0, H-2e), 2.23 (q, H-2a), and 1.38 (d, H-6).

Anal. Calc. for $C_{10}N_{17}NO_6S$: C, 43.01; H, 6.14; N, 5.02; S, 11.71. Found: C, 42.86; H, 6.08; N, 4.81; S, 11.80.

*Spiro[aziridine-2,3'-(methyl 2,3,6-trideoxy-4-*O*-methyl-α-*L*-*arabino*-hexopyranoside)]* **(13)** *and its* N*-acetyl derivative* **(14)**. — To a suspension of **12** (8.4 g, 30 mmol) in abs. ether (160 mL) was gradually added lithium aluminum hydride (1.7 g) in small portions, and the mixture was kept spontaneously boiling for 4 h under reflux. The excess of reductant was inactivated by the addition of ethyl acetate–water, and then the mixture was filtered. The filtrate was evaporated, and the residue extracted conventionally with chloroform to give syrupy **13** (5.2 g, 93%). Acetylation of a small amount of **13** with pyridine–acetic anhydride, and purification of the syrupy product by t.l.c. (5:1:1 benzene–ethanol–acetate) gave pure **14** almost quantitatively.

Compound **14** had $[\alpha]_D^{22}$ −82.5° (*c* 1.6); n.m.r.: 4.76 (d, $J_{1,2a}$ 4.0, H-1), 3.73 (dq, $J_{5,6}$ 6.0, H-5), 3.35 and 3.33 (2 OMe), 3.26 (d, $J_{4,5}$ 9.8, H-4), 2.58 and 2.16 (s, CH_2), 2.47 (q, J_{gem} 13.5, H-2a), 2.10 (NAc), 1.47 (d, H-2e), and 1.34 (d, H-6).

Anal. Calc. for $C_{11}H_{19}NO_4$: C, 57.62; H, 8.35; N, 6.11. Found: C, 57.25; H, 8.62; N, 5.98.

*Methyl 3-amino-2,3,6-trideoxy-3-*C*-methyl-4-*O*-methyl-α-*L*-*arabino*-hexopyranoside* **(15)** *and its* N*-acetyl derivative* **(16)**. — A suspension of **13** (5.1 g, 27 mmol) and Raney nickel (8 g) in methanol (300 mL) was hydrogenolyzed for 3 days under hydrogen at 90 kg/cm^2, and then filtered. Evaporation of the filtrate gave syrupy **15** (5 g, 96%). Acetylation of a small amount of **15** as before, and purification of the product by t.l.c. (3:1 benzene–acetone) gave crystals that were recrystallized from hexane; m.p. 140–141°, $[\alpha]_D^{22}$ −75° (*c* 1.0).

Anal. Calc. for $C_{11}H_{21}NO_4$: C, 57.12; H, 9.15; N, 6.06. Found: C, 56.81; H, 8.94; N, 5.95.

*Methyl 2,3,6-trideoxy-3-*C*-methyl-4-*O*-methyl-3-*C*-nitro-α-*L*-*arabino*-hexopyranoside* **(17)**. — To a boiling solution of *m*-chloroperoxybenzoic acid (14 g, 81 mmol) in dichloromethane (200 mL) was added dropwise a solution of **15** (2 g, 11 mmol) in dichloromethane (50 mL) during 20 min, and heating was continued for 40 min. The mixture was subsequently washed with 10% sodium sulfite, saturated sodium carbonate and water, dried (magnesium sulfate), and then evaporated to a syrup that was purified on a column of silica gel (5:1 benzene–hexane); yield, 1.2 g (52%), $[\alpha]_D^{22}$ −103° (*c* 1.0); ν_{max}^{NaCl} 1540 and 1340 (NO_2).

Anal. Calc. for $C_9H_{17}NO_5$: C, 49.30; H, 7.82; N, 6.39. Found: C, 49.37; H, 7.66; N, 6.02.

*2,3,6-Trideoxy-3-*C*-methyl-4-*O*-methyl-3-*C*-nitro-*L*-arabino-hexose* **(1)**. — A solution of **17** (1.8 g, 8.2 mmol) in 0.05M sulfuric acid in 1:1 water–1,4 dioxane (100 mL) was maintained for 30 h at 90–95°, neutralized with barium carbonate, and the mixture then filtered. Evaporation of the filtrate and purification of the residual syrup on a column of silica gel (20:1 benzene–acetone) gave a syrup (1.4 g, 83%) that crystallized from benzene–hexane; m.p. 85–89°, $[\alpha]_D^{22}$ −22° (*c* 1.0, ethanol, 1 day) [lit.[3], m.p. 88–93°, $[\alpha]_D$ −19.4° (ethanol)]; ν_{max}^{KBr} 3400 (OH), 1540 and 1360

cm^{-1} (NO_2). The n.m.r. spectrum showed the presence of the α and β anomers in the ratio of 1:1.

*1-O-Acetyl-2,3,6-trideoxy-3-C-methyl-4-O-methyl-3-C-nitro-β-*L-arabino-*hexose* (**18**). — Conventional acetylation of **1** gave **18** as a syrup in 75% yield; $[\alpha]_D^{22}$ −20.5° (*c* 1.0) [lit.[3], m.p. 58–59°, $[\alpha]_D$ −20.5° (ethanol)]. The n.m.r. spectrum of this syrup showed the presence of the β anomer almost exclusively.

Anal. Calc. for $C_{10}H_{17}NO_6$: C, 48.58; H, 6.93; N, 5.67. Found: C, 48.83; H, 6.95; N, 5.67.

*Methyl 3-C-cyano-2,6-dideoxy-4-O-methyl-3-O-mesyl-β-*L-ribo- (**19**) *and* -arabino-*hexopyranoside* (**20**). — Cyanomesylation of **3** (7 g, 40 mmol) as for **2**, and separation of the products on a column of silica gel (5:1 hexane–ether) gave successively **19** (0.25 g), a mixture of 3-epimers (3.75 g; **19**:**20** = 1.4:1), and **20** (3.3 g); total yield, 66%.

Compound **19** had m.p. 107–109°, $[\alpha]_D^{22}$ −14.0° (*c* 1.0); n.m.r.: 4.73 (d, $J_{1,2e}$ 2.0, $J_{1,2a}$ 9.0, H-1), 3.81 (dq, $J_{5,6}$ 6.2, H-5), 3.72 and 3.47 (2 OMe), 3.27 (OMs), 3.19 (d, $J_{4,5}$ 9.4, H-4), 2.97 (q, J_{gem} 13.0, H-2e), 2.06 (q, H-2a), and 1.37 (d, H-6).

Anal. Calc. for $C_{10}H_{17}NO_6S$: C, 43.01; H, 6.14; N, 5.02; S, 11.71. Found: C, 42.95; H, 6.10; N, 4.75; S, 11.88.

Compound **20** had m.p. 97–99°, $[\alpha]_D^{22}$ −2.1° (*c* 1.0); ν_{max}^{KBr} 1360 and 1190 cm^{-1} (OMs); n.m.r.: 4.59 (q, $J_{1,2e}$ 1.2, $J_{1,2a}$ 9.8, H-1). 3.67 (dq, $J_{5,6}$ 6.2, H-5), 3.65 and 3.51 (2 OMe), 3.26 (OMs), 3.11 (d, $J_{4,5}$ 9.0, H-4), 3.05 (q, J_{gem} 13.0, H-2e), 2.17 (q, H-2a), and 1.40 (d, H-6).

Anal. Calc. for $C_{10}H_{17}NO_6S$: C, 43.01; H, 6.14; N, 5.02; S, 11.71. Found: C, 42.71; H, 6.15; N, 4.85; S, 11.42.

*Spiro[aziridine-2,3'-(methyl 2,3,6-trideoxy-3-C-methyl-4-O-methyl-β-*L-ribo-*hexopyranoside)]* (**21**) *and its* N-*acetyl derivative* (**22**). — Reduction of **19** with lithium aluminum hydride as for **12** gave **21** (2 g, 89%) as a syrup that was characterized as its syrupy *N*-acetyl derivative (**22**); $[\alpha]_D^{22}$ +61° (*c* 0.75); n.m.r.: 4.45 (q, $J_{1,2e}$ 2.0, $J_{1,2a}$ 9.8, H-1), 3.62 (dq, $J_{5,6}$ 6.0, H-5), 3.48 and 3.36 (2 OMe), 3.19 (d, $J_{4,5}$ 9.5, H-4), 2.52 and 2.07 (s, CH_2), 2.26 (q, J_{gem} 13.5, H-2a), 2.11 (NAc), 1.50 (q, H-2e), and 1.38 (d, H-6).

Anal. Calc. for $C_{11}H_{19}NO_4 \cdot 0.5\ H_2O$: C, 55.44; H, 8.46; N, 5.87. Found: C, 55.26; H, 8.03; N, 5.59.

*Methyl 3-amino-2,3,6-trideoxy-3-C-methyl-4-O-methyl-β-*L-arabino- (**23**) *and* -ribo-*hexopyranoside* (**24**), *and their* N-*acetyl derivatives* (**25** *and* **26**). — The foregoing mixture of **19** and **20** (3.75 g; **19**:**20** = 1.4:1) was reduced with lithium aluminum hydride and the product hydrogenolyzed as before, to give a mixture of **23** and **24** in 88% (2.23 g) yield. The mixture was resolved on a column of silica gel (7:1:1 benzene–ethanol–ethyl acetate) to give successively **24** (0.83 g) and **23** (1.17 g) as syrups. The n.m.r. spectrum of each showed distinctive H-1 signals (**24**: δ 4.47, $J_{1,2e}$ 2.2, $J_{1,2a}$ 9.2; **23**: δ 4.71, $J_{1,2e}$ 2.7, $J_{1,2a}$ 9.1), but, only **24** gave reasonable analytical values (calc. for $C_9H_{19}NO_3 \cdot 0.5\ H_2O$: C, 54.52; H, 10.17; N, 7.06. Found: C, 54.51; H, 9.95; N, 6.69). Therefore, **23** and **24** were converted into their crystalline

N-acetyl derivatives (**25** and **26**), respectively, and then purified by t.l.c. (5:1:1 benzene–ethanol–ethyl acetate). Each product was recrystallized from hexane.

Compound **25** had m.p. 157–159°, $[\alpha]_D^{22}$ +56.4° (*c* 1.0); compound **26** had m.p. 107–108°, $[\alpha]_D^{22}$ +35.4° (*c* 0.8).

Anal. Calc. for $C_{11}H_{21}NO_4$: C, 57.12; H, 9.15; N, 6.06. Found (**25**): C, 56.84; H, 9.05; N, 5.83; (**26**): C, 56.76; H, 8.95; N, 5.91.

*Methyl 2,3,6-trideoxy-3-*C*-methyl-4-*O*-methyl-3-*C*-nitro-β-*L*-*arabino- (**27**) *and* -ribo-hexopyranoside* (**28**). — Oxidation of crude **23** and **24** with *m*-chloroperoxybenzoic acid as for **5** gave syrupy **27** and **28**, respectively, in 37 and 46%, yields after purification.

Compound **27** had $[\alpha]_D^{22}$ +33.6° (*c* 1.2).

Anal. Calc. for $C_9H_{17}NO_5$: C, 49.30; H, 7.82; N, 6.39. Found: C, 49.31; H, 7.65; N, 6.17.

Compound **28** had $[\alpha]_D^{22}$ −10.5° (*c* 1.0); ν_{max}^{NaCl} 1540 and 1380 cm^{-1} (NO_2).

Anal. Calc. for $C_9H_{17}NO_5$: C, 49.30; H, 7.82; N, 6.39. Found: C, 49.91; H, 7.55; N, 6.12.

*2,3,6-Trideoxy-3-*C*-methyl-4-*O*-methyl-3-*C*-nitro-*L*-ribo-hexopyranose* (**29**, *3-epi-evernitrose*) *and its β-1-*O*-acetyl derivative* (**30**). — Hydrolysis of **28** as for **17** gave **29** quantitatively; m.p. 135–137° (from benzene–petroleum ether), $[\alpha]_D^{22}$ −57° (*c* 1.6, ethanol, 1 day). The n.m.r. spectrum indicated that **29** exists almost exclusively as the β anomer.

Anal. Calc. for $C_8H_{15}NO_5$: C, 46.82; H, 7.37; N, 6.83. Found: C, 47.11; H, 7.35; N, 6.79.

Acetylation of **29** gave **30** in 83% yield; m.p. 123–124° (from benzene–hexane), $[\alpha]_D^{22}$ −43° (*c* 0.8).

Anal. Calc. for $C_{10}H_{17}NO_6$: C, 48.58; H, 6.93; N, 5.67. Found: C, 48.34; H, 6.74; N, 5.48.

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