Convenient Syntheses of L-Digitoxose, L-Cymarose, and L-Ristosamine [1]

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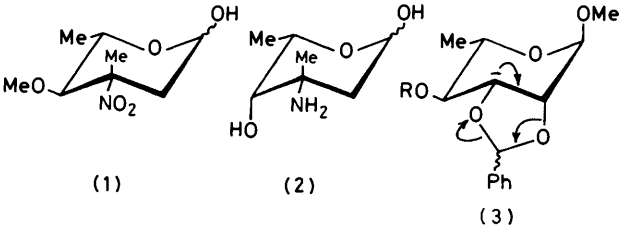
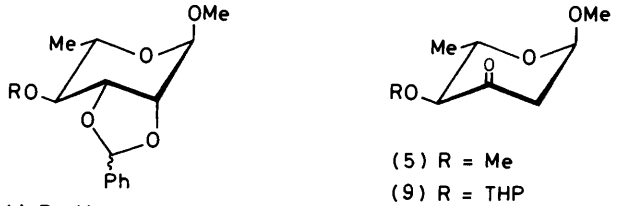
Methyl 2,3-*O*-benzylidene-6-deoxy-4-*O*-(2-methoxyethoxymethyl)-α-L-mannopyranoside (10) and the 4-*O*-(methoxymethyl) analogue (11) reacted with butyl-lithium to give the 4-*O*-substituted methyl 2,6-dideoxy-α-L-*erythro*-hexopyranosid-3-uloses (12) and (13), respectively. Appropriate transformations on these keto-sugars afforded practical syntheses of 2,6-dideoxy-L-*ribo*-hexopyranose (L-digitoxose) (15), its 3-*O*-methyl analogue (17) (L-cymarose), and 3-acetamido-2,3,6-trideoxy-L-*ribo*-hexose (*N*-acetyl-L-ristosamine).

A slight amendment to one of the sugar residues in published structures of the orthosomycin antibiotics flambamycin and avilamycins is indicated.

In considering synthetic routes to a number of sugar components of antibiotics, particularly the branched-chain sugars L-evernitrose [2] (1) and L-vancosamine [3] (2), we concluded that methyl 2,6-dideoxy-α-L-*erythro*-hexopyranosid-3-ulose bearing a temporary protecting group at position 4 would serve as a versatile intermediate. Such a compound might be derived from a suitably protected methyl 2,3-*O*-benzylidene-α-L-rhamnopyranoside by excision of benzaldehyde through the action of organolithium compounds [formally as shown in structure (3)]. Although methyl 2,3-*O*-benzylidene-4-*O*-methyl-α-L-rhamnopyranoside (4), for example, reacts with butyl-lithium in tetrahydrofuran (THF) at −30 °C to give the ketone (5) in acceptable yield, neither the hydroxylated compound (6) nor the benzyl ether (7) undergo analogous transformations, presumably because either formation of the 4-oxyanion or abstraction of a proton from the benzyl group impedes deprotonation of the dioxolan ring.[4] The use of tetrahydropyran-2-yl as a protecting group allows the transformation (8) ⟶ (9) (40%) to be accomplished [5] with s-butyl-lithium in THF at −30 °C, but protection of the hydroxy-group in this way introduces a new chiral centre. Scattered reports in the literature suggested that either of the protected derivatives (10) or (11) might be better suited for our purpose, although it was known that 2-methoxyethoxymethyl [6] and other [7] ethers are cleaved slowly by organolithium reagents at ambient temperature.



(1) (2) (3)



(4) R = Me
(6) R = H
(7) R = CH_2Ph
(8) R = tetrahydropyran-2-yl (THP)
(10) R = $CH_2OCH_2CH_2OMe$ (MEM)
(11) R = CH_2OMe

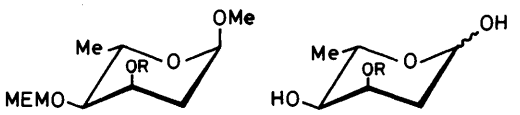
(5) R = Me
(9) R = THP
(12) R = MEM
(13) R = CH_2OMe

Results and Discussion

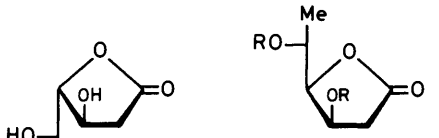
Each of the derivatives (10) and (11) was obtained as a distillable mixture of diastereoisomers when methyl 2,3-*O*-benzylidene-α-L-rhamnopyranoside [4] (6) was allowed to react at room temperature with either 2-methoxyethoxymethyl chloride [8] or methoxymethyl chloride in methylene dichloride containing ethyldi-isopropylamine. Both compounds (10) and (11) reacted with butyl-lithium at −30 °C or below to give, after careful chromatography, the crystalline keto-sugars (12) (41%) and (13) (38%), respectively. In practice we found the methoxymethyl derivative (13) much easier to purify. The somewhat modest yields of the ketones (12) and (13), which are comparable to those obtained in similar reactions,[4,5] are offset by the directness of the route (*i.e.* four steps from L-rhamnose).

The usefulness of compounds (12) and (13) in the synthesis of rare sugars is demonstrated by the following examples. L-Digitoxose (2,6-dideoxy-L-*ribo*-hexopyranose) (15), a component of kijanimicin [9] and other antibiotics,[10] is available by borohydride reduction of the ketone (12) *via* the axial alcohol (14), which yielded the crystalline free sugar on hydrolysis in refluxing acetic acid. Similarly, acidic hydrolysis of the methylated derivative (16) furnished L-cymarose (2,6-dideoxy-3-*O*-methyl-L-*ribo*-hexopyranose) (17) which was identified by comparison with the D-enantiomer.[11]

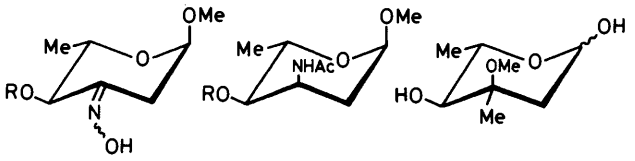
The distillable γ-lactone (18), $\nu_{max.}$ 1 788 cm^{-1}, resulting from oxidation of L-digitoxose (15) with bromine water, was found to have $[\alpha]_D$ +30 ± 2° (*c*, 0.4 in Me_2CO), indicating that the 3,5-dihydroxy-γ-caprolactone, $[\alpha]_D$ +50° (in EtOH), obtained on hydrolysis of the antibiotic flambamycin,[12] cannot have the enantiomeric D-*ribo*-configuration previously assigned to it. Since 2,6-dideoxy-L-*arabino*-hexono-1,4-lactone is reported [13] to have $[\alpha]_D$ −52.5 ± 2° (*c*, 1.2 in Me_2CO), it seemed likely that the flambamycin-derived lactone [12] is its D-enantiomer (19). This has been confirmed both by our [14] syntheses of D- (19) or L-(19) [mirror image of structure (19) as drawn] and their crystalline 3,5-diacetates [*e.g.* (20)] (see Experimental section) and independently by Pedersen and his co-workers.[15] Thus, the configuration at position 18 of the published structure of flambamycin [12,16] should be inverted, giving the sugar residues labelled B and C the same absolute



(14) R = H (15) R = H
(16) R = Me (17) R = Me



(18) (19) R = H
(20) R = Ac



(21) R = MEM (23) R = MEM (25)
(22) R = CH_2OMe (24) R = CH_2OMe

stereochemistry. Since sugar residue C of the avilamycins [17] was also characterised as the (then unidentified) diacetate (20),[18] it too must possess the D-*arabino*-configuration and, in view of close similarities of structure and the absence of decisive *chemical* evidence, it is not unreasonable to assume that sugar residue C of the everninomicins [16,19] also has the same configuration.

Both the ketones (12) and (13) afforded nicely crystalline oximes [(21) and (22), respectively], which were transformed into the acetamido-derivatives (23) and (24) on catalytic hydrogenation in the presence of acetic anhydride. ^{1}H N.m.r. spectroscopy of the crude reaction products indicated that little, if any, of the 3-equatorial isomer was formed. Mild acidic hydrolysis of either compound (23) or (24) gave *N*-acetyl-L-ristosamine (3-acetamido-2,3,6-trideoxy-L-*ribo*-hexose) which was identified by comparison (m.p.,$[\alpha]_D$) with the D-enantiomer.[20] This synthesis of a derivative of L-ristosamine,[21] a component of the antibiotic ristomycin A,[22] compares favourably with others [23] in the literature.

Doubtless other antibiotic sugars could be obtained from the ketones (12) and (13) either directly [*e.g.* L-cladinose [24] (25)] or by manipulation of the configuration and functionality at C-4 after removal of the protecting group at a later stage of the synthesis. Syntheses of L-evernitrose [2] (1) and L-vancosamine [3] (2) along these lines will be reported in due course.

Experimental

Thin-layer chromatography (t.l.c.) was performed on Kieselgel G, and spots were detected with 1% aqueous sulphuric acid. I.r. spectra were recorded for Nujol mulls or films with a Perkin-Elmer Infracord spectrophotometer. ^{1}H N.m.r. spectra were measured with a Bruker Spectrospin (90 MHz) spectrometer. A Perkin-Elmer Model 141 polarimeter and 1 dm tubes were used for the measurement of specific optical rotations. M.p.s are uncorrected. Light petroleum refers to the fraction boiling in the range 60—80 °C.

Methyl 2,3-O-*Benzylidene*-6-*deoxy*-4-O-(2-*methoxyethoxymethyl*)-α-L-*mannopyranoside* (10).—A solution of the acetals [4] (6) (4.6 g) in methylene dichloride (35 ml) containing ethyldiisopropylamine (5 g) and 2-methoxyethoxymethyl chloride [8] (5 g) was stirred overnight at room temperature and the solvent was then removed under reduced pressure. The resulting syrup was dissolved in methylene dichloride and the solution was washed in turn with dilute hydrochloric acid and water and dried ($MgSO_4$). Removal of the solvent under reduced pressure and chromatography of the residue on silica gel [diethyl ether–light petroleum (2 : 3) as eluant] gave the *MEM derivative* (10) (5.5 g, 90%) as a mixture of diastereoisomers (δ_H 6.17 and 5.88, s, PhC*H*) that was suitable for use in the next step.

An analytical sample of compound (10), obtained by distillation [b.p. 120—150 °C (bath) at 0.05 mmHg], had $[\alpha]_D$ −22° (*c*, 1 in $CHCl_3$) (Found: C, 60.7; H, 7.3. $C_{18}H_{26}O_7$ requires C, 61.0; H, 7.4%).

Methyl 2,3-O-*Benzylidene*-6-*deoxy*-4-O-(*methoxymethyl*)-α-L-*mannopyranoside* (11).—A mixture of the diastereoisomers of the title compound (2.03 g, 76%) was obtained after the usual work-up procedure when a solution of the alcohol (6) (2.3 g) in anhydrous methylene dichloride (18 ml) containing ethyldi-isopropylamine (2.5 g) was treated for 40 h at room temperature with methoxymethyl chloride (1.7 g). The *product* had b.p. 136—138 °C at 0.1 mmHg; δ_H 6.42 and 6.14 (s, PhC*H*) (Found: C, 61.8; H, 7.1. $C_{16}H_{22}O_6$ requires C, 61.9; H, 7.1%).

Methyl 2,6-*Dideoxy*-4-O-(2-*methoxyethoxymethyl*)-α-L-erythro-*hexopyranosid*-3-*ulose* (12).—A stirred solution of the acetal (10) (2.5 g, 7 mmol) in anhydrous THF (70 ml) under nitrogen was cooled to −40 °C prior to the addition of butyllithium in hexane (1.55M; 27 ml, 42 mmol) while the internal temperature of the mixture was kept ≤ −30 °C. After 1 h, t.l.c. [light petroleum–diethyl ether (3 : 2)] showed that no starting material remained and that several products were present. The mixture was allowed to warm to −10 °C before being poured into ice–water (50 ml) containing ammonium chloride (5 g). The aqueous solution was extracted thoroughly with chloroform and the extract was washed with water and dried ($MgSO_4$). Removal of the solvents under reduced pressure and chromatography of the residue on silica gel [light petroleum–diethyl ether (3 : 2) and then ether as eluant] gave the *keto-sugar* (12) (0.7 g, 40%) as a syrup that was suitable for use in subsequent experiments.

An analytical sample was obtained by cooling a solution of compound (12) in diethyl ether–light petroleum with solid carbon dioxide. The product was filtered off and had m.p. 42—44 °C; $[\alpha]_D$ −235° (*c*, 1 in $CHCl_3$); $\nu_{max.}$ 1 730 cm^{-1} (C=O) (Found: C, 53.4; H, 7.8. $C_{11}H_{20}O_6$ requires C, 53.2; H, 8.1%); δ_H 5.04 (1 H, dd, $J_{1,2}$ *ca.* 4, $J_{1,2'}$ *ca.* 2 Hz, 1-H), 4.84 (2 H, ABq, J_{AB} 8 Hz, OCH_2O), 4.06—3.47 (total 6 H, 4- and 5-H and OCH_2CH_2O), 3.38 and 3.33 (total 6 H, s, 2 × OMe), 2.77 (1 H, dd, J_{gem} 14 Hz, 2-H), 2.53 (1 H, dd, 2′-H), and 1.41 (3 H, d, $J_{5,6}$ 6 Hz, 5-Me).

Methyl 2,6-*Dideoxy*-4-O-(*methoxymethyl*)-α-L-erythro-*hexopyranosid*-3-*ulose* (13).—In a typical experiment, a stirred solution of the acetal (11) (11.2 g, 36 mmol) in anhydrous THF (240 ml) under nitrogen was cooled to −40 °C prior to the gradual addition of butyl-lithium in hexane (1.55M; 71 ml, 110 mmol) while the internal temperature of the mixture was kept at ≤ −30 °C. After 1 h, the mixture was worked up as described in the previous experiment. Chromatography on silica gel [methylene dichloride–acetone (20 : 1) as eluant] gave the *keto-sugar* (13) (2.8 g, 38%), m.p. 73—

74.5 °C (from light petroleum); $[\alpha]_D$ −344° (*c*, 1 in $CHCl_3$); $\nu_{max.}$ 1 730 cm^{-1} (C=O) (Found: C, 53.0; H, 7.9. $C_9H_{16}O_5$ requires C, 52.9; H, 7.9%); δ_H 5.05 (1 H, dd, 1-H), 4.78 (2 H, ABq, J_{AB} 7 Hz, OCH_2O), 4.11—3.76 (total 2 H, m, 4- and 5-H), 3.45 and 3.36 (total 6 H, s, 2 × OMe), 2.80 (1 H, dd, $J_{1,2}$ *ca.* 4, J_{gem} 14 Hz, 2-H), 2.56 (1 H, dd, $J_{1,2'}$ *ca.* 1.5 Hz, 2'-H), and 1.46 (3 H, d, $J_{5,6}$ 5 Hz, 5-Me).

Methyl 2,6-*Dideoxy*-4-O-(2-*methoxyethoxymethyl*)-α-L-ribo-*hexopyranoside* (14).—Sodium borohydride (0.32 g) was added in portions to a stirred solution of the ketone (12) (0.22 g) in methanol (10 ml) and, on completion of the addition, the mixture was stirred for a further 1 h and the solvent was then removed under reduced pressure. The residue was extracted with chloroform and the extract was washed with a little water and dried ($MgSO_4$). Removal of the solvent under reduced pressure and chromatography of the residue on silica gel [methylene dichloride–acetone (4 : 1) as eluant] gave the *axial alcohol* (14) (0.18 g, 81%), b.p. 95—100 °C (bath) at 0.2 mmHg; $[\alpha]_D$ −128° (*c*, 1 in $CHCl_3$); $\nu_{max.}$ 3 300 cm^{-1} (OH) (Found: C, 52.2; H, 8.6. $C_{11}H_{22}O_6$ requires C, 52.8; H, 8.9%); δ_H 4.84 and 4.73 (total 3 H, overlapping q, J_{AB} 7 Hz, 1-H and OCH_2O), 4.27—3.44 (total 7 H, 3-, 4-, and 5-H and OCH_2CH_2O), 3.39 and 3.38 (total 6 H, s, 2 × OMe), 2.16 (1 H, dq, $J_{1,2}$ *ca.* 2, $J_{2,3}$ *ca.* 4, J_{gem} 15 Hz, 2-H), 1.84 (1 H, dt, $J_{1,2'} = J_{2',3}$ *ca.* 3.5 Hz, 2'-H), and 1.29 (3 H, d, $J_{5,6}$ 6 Hz, 5-Me).

Methyl 2,6-*Dideoxy*-4-O-(2-*methoxyethoxymethyl*)-3-O-*methyl*-α-L-ribo-*hexopyranoside* (16).—A stirred solution of the alcohol (14) (2 g) in anhydrous THF (40 ml) was treated with oil-free sodium hydride (0.5 g) for 1 h, after which methyl iodide (10 ml) was added and the mixture was stirred for 24 h; t.l.c. [methylene dichloride–acetone (4 : 1)] then showed that the reaction was complete. Work-up in the usual way [25] and distillation gave the *methylated derivative* (16) (1.85 g, 88%), b.p. 75—80 °C (bath) at 0.05 mmHg; $[\alpha]_D$ −158° (*c*, 1 in $CHCl_3$) (Found: C, 54.6; H, 9.4. $C_{12}H_{24}O_6$ requires C, 54.5; H, 9.15%); δ_H 4.81 (2 H, ABq, J_{AB} 8 Hz, OCH_2O), 4.62 (1 H, dd, 1-H), 4.33—3.47 (total 7 H, 3-, 4-, and 5-H and OCH_2CH_2O), 3.42, 3.39, and 3.33 (total 9 H, s, 3 × OMe), 2.24 (1 H, dq, $J_{1,2}$ *ca.* 1.5, $J_{2,3}$ *ca.* 3.5, J_{gem} 15 Hz, 2-H), 1.71 (1 H, dt, $J_{1,2'} = J_{2',3}$ *ca.* 4 Hz, 2'-H), and 1.24 (3 H, d, $J_{5,6}$ 6 Hz, 5-Me).

2,6-*Dideoxy*-L-ribo-*hexopyranose* (L-*Digitoxose*) (15).—A solution of the protected sugar (14) (0.53 g) in a mixture of glacial acetic acid (5 ml) and water (12 ml) was heated under gentle reflux for 2 h after which time t.l.c. [ethyl acetate–methanol (9 : 1)] showed that no starting material remained. Removal of the solvents under reduced pressure (40 °C and 1 mmHg) and chromatography of the residue on silica gel [ethyl acetate–methanol (9 : 1) as eluant] gave a syrup that crystallised with time. Recrystallisation from acetone gave L-digitoxose (15) (0.22 g, 70%), m.p. 105—107 °C; $[\alpha]_D$ −47° (final; *c*, 1 in H_2O) (Found: C, 48.9; H, 7.9. $C_6H_{12}O_4$ requires C, 48.6; H, 8.2%). D-Digitoxose has m.p. 105—108 °C; $[\alpha]_D$ +47.8° (final; *c*, 1.06 in H_2O).[26]

2,6-*Dideoxy*-3-O-*methyl*-L-ribo-*hexopyranose* (L-*Cymarose*) (17).—A solution of the glycoside (16) (0.15 g) in 0.05M-sulphuric acid (5 ml) was heated at 65—70 °C for 2 h, whereafter the hydrolysate was diluted with water (15 ml), neutralised ($BaCO_3$), filtered, and concentrated under reduced pressure. The residue was extracted with diethyl ether and the extract was filtered and concentrated to dryness under reduced pressure. Chromatography of the residue on silica gel [methylene dichloride–acetone (4 : 1) as eluant] gave L-cymarose (17) (70 mg, 76%) as a syrup that crystallised slowly with time. This material, which was not purified further, was indistinguishable [t.l.c., ^1H n.m.r. spectroscopy (D_2O)] from an authentic sample of crystalline D-cymarose.[11]

2,6-*Dideoxy*-L-ribo-*hexono*-1,4-*lactone* (18).—A stirred solution of L-digitoxose (15) (0.318 g) in water (3.2 ml) was treated with bromine (0.14 ml) in the dark at room temperature for 19 h, whereafter the excess of bromine was removed in a stream of air and the solution was adjusted to pH *ca.* 5 with freshly prepared silver carbonate. The mixture was filtered and hydrogen sulphide was bubbled through the filtrate to precipitate Ag^+ ions. The mixture was filtered again and the filtrate was concentrated under reduced pressure; a solution of the residue in ethanol was decolourised with charcoal. Removal of the solvent under reduced pressure and chromatography of the residue on silica gel [chloroform–methanol (4 : 1) as eluant], with sacrificial cuts, gave the γ-*lactone* (18) (0.147 g, 47%), b.p. 145—147 °C (bath) at 0.1 mmHg; $[\alpha]_D$ +30 ± 2° (*c*, 0.4 in Me_2CO) [lit.,[13] (D-enantiomer) $[\alpha]_D$ −32.1 ± 2° (*c*, 3 in Me_2CO)]. The i.r. spectrum of a 0.06M-solution of compound (18) in methylene dichloride was indistinguishable from that recorded [13] for D-digitoxonic acid lactone, showing a prominent absorption at 1 788 cm^{-1} (γ-lactone).

3,5-*Di*-O-*acetyl*-2,6-*dideoxy*-L-arabino-*hexono*-1,4-*lactone* [*Mirror Image of* (20)].—To a solution of methyl 3,4-di-*O*-acetyl-2,6-dideoxy-α-L-*arabino*-hexopyranoside [27] (3 g) in anhydrous methanol was added a small piece of sodium metal and the solution was kept at room temperature for 4 h, then neutralised (CO_2) and filtered, and the filtrate was concentrated under reduced pressure. A solution of the deacetylated compound (residue) in a mixture of glacial acetic acid (9 ml) and water (21 ml) was boiled under reflux for 90 min and the solvents were then removed under reduced pressure. Toluene was then added to, and distilled from, the residue several times. The residue was then dissolved in ethanol and decolourised (charcoal). Chromatography on silica gel [ethyl acetate–methanol (7 : 3) as eluant] then afforded 2,6-dideoxy-L-*arabino*-hexose (1.6 g, 89%) as a clear syrup that was used in the next step.

Oxidation of the free sugar (0.32 g) with bromine water and preparative chromatography, essentially as described for L-digitoxose (15), gave 2,6-dideoxy-L-*arabino*-hexono-1,4-lactone [mirror image of (19)] (71%), b.p. *ca.* 140 °C (bath) at 0.1 mmHg; $[\alpha]_D$ −51° (*c*, 0.8 in EtOH), −55 ± 2° (*c*, 1.8 in Me_2CO) [lit.,[13] b.p. 160 °C (bath at 0.01 mmHg; $[\alpha]_D$ −52.5° (Me_2CO)]. The ^1H n.m.r. data ([$^2H_5$]pyridine) for this lactone were essentially indistinguishable from those reported [12] for the 3,5-dihydroxy-γ-caprolactone, b.p. 144 °C at 0.15 mmHg; $[\alpha]_D$ +50° (EtOH), isolated from acidic hydrolysates of flambamycin.

Acetylation of the γ-lactone (0.2 g) with acetic anhydride (1 ml) in pyridine (3 ml) gave, after the usual work-up, the 3,5-*diacetate* [mirror image of (20)] (0.24 g, 76%), m.p. 102—103 °C (from benzene); $[\alpha]_D$ −27° (*c*, 1 in $CHCl_3$) (Found: C, 52.5; H, 6.0. $C_{10}H_{14}O_6$ requires C, 52.2; H, 6.1%); δ_H 5.65 (1 H, m, 3-H), 5.20 (1 H, dq, 5-H), 4.47 (1 H, dd, $J_{3,4}$ 4, $J_{4,5}$ 9 Hz, 4-H), 2.96 and 2.56 (total 2 H, ABX system, J_{AB} 18, J_{AX} 5.5, and J_{BX} 1 Hz, 2- and 2'-H), 2.05 and 2.01 (total 6 H, s, 2 × OAc), and 1.40 (3 H, d, $J_{5,6}$ 6 Hz, 5-Me). The ^1H n.m.r. spectrum of this diacetate was indistinguishable from that of the acetylated, flambamycin-derived γ-lactone [12] (diacetate m.p. 113 °C) which has been shown [15] (^1H n.m.r. spectroscopy) to be identical with a 3,5-diacetate [18] (m.p. 102 °C) similarly obtained from the avilamycins. The foregoing evidence establishes that the antibiotic-derived compound is 3,5-di-*O*-acetyl-2,6-dideoxy-D-*arabino*-hexono-1,4-lactone (20).

Methyl 2,6-*Dideoxy*-4-O-(2-*methoxyethoxymethyl*)-α-L-erythro-*hexopyranosid*-3-*ulose Oxime* (21).—A solution of the keto-sugar (12) (2 g) in methanol (150 ml) and water (1 ml) containing hydroxylamine hydrochloride (6 g) and potassium hydrogen-carbonate (7 g) was boiled under reflux for 1 h and was then evaporated to dryness under reduced pressure. The residual solid was extracted several times with hot chloroform and the combined extracts were filtered, dried ($MgSO_4$), and concentrated under reduced pressure. Chromatography of the residue on silica gel [diethyl ether–methylene dichloride (3 : 10) as eluant] furnished the *oxime* (21) (1.75 g, 83%), m.p. 78—81 °C (from light petroleum); $[\alpha]_D$ −320° (*c*, 1 in $CHCl_3$); $\nu_{max.}$ 1 660 cm^{-1} (C=N) (Found: C, 50.0; H, 7.9; N, 5.6. $C_{11}H_{21}NO_6$ requires C, 50.2; H, 8.0; N, 5.3%); δ_H 4.84 (total 3 H, overlapping q, 1-H and OCH_2O), 4.08—3.13 (total 6 H, 4- and 5-H and OCH_2CH_2O), 3.37 and 3.33 (total 6 H, s, 2 × OMe), 2.33 (1 H, dd, $J_{1,2}$ 4, J_{gem} 14 Hz, 2-H), and 1.33 (3 H, d, $J_{5,6}$ 6 Hz, 5-Me).

Methyl 2,6-*Dideoxy*-4-O-(*methoxymethyl*)-α-L-erythro-*hexopyranosid*-3-*ulose Oxime* (22).—In an identical manner, the ketone (13) yielded, without resort to chromatography, the *title compound* (79%), m.p. 130.5—132.5 °C (from chloroform–light petroleum); $[\alpha]_D$ −367° (*c*, 0.8 in $CHCl_3$); $\nu_{max.}$ 1 660 cm^{-1} (C=N) (Found: C, 49.3; H, 7.9; N, 6.4. $C_9H_{17}NO_5$ requires C, 49.3; H, 7.8; N, 6.4%); δ_H 4.82 (1 H, m, 1-H), 4.74 (2 H, ABq, J_{AB} 7 Hz, OCH_2O), 4.02—3.67 (total 2 H, m, 4- and 5-H), 3.41 and 3.36 (total 6 H, s, 2 × OMe), 3.31 (1 H, dd, $J_{1,2}$ *ca.* 1.5 Hz, 2-H), 2.33 (1 H, dd, $J_{1,2'}$ 4, J_{gem} 14 Hz, 2'-H), and 1.34 (3 H, d, $J_{5,6}$ 6 Hz, 5-Me).

Methyl 3-*Acetamido*-2,3,6-*trideoxy*-4-O-(2-*methoxyethoxymethyl*)-α-L-ribo-*hexopyranoside* (23).—A solution of the oxime (21) (0.7 g) in anhydrous methanol (20 ml) containing acetic anhydride (1.5 ml) was hydrogenated over Adams' catalyst (0.6 g) under a slight overpressure of hydrogen at room temperature for 20 h. The catalyst was filtered off and the filtrate was evaporated to dryness under reduced pressure. Toluene was added to, and distilled from, the residue several times. Chromatography of the residue on silica gel [ethyl acetate–methanol (7 : 3) as eluant] gave a *ca.* quantitative yield of the *acetamido-derivative* (23), b.p. 128—132 °C (bath) at 0.1 mmHg; $[\alpha]_D$ −166° (*c*, 1.3 in $CHCl_3$) (Found: C, 53.2; H, 8.2; N, 4.6. $C_{13}H_{25}NO_6$ requires C, 53.6; H, 8.65; N, 4.8%); δ_H 4.80 (2 H, ABq, J_{AB} 7 Hz, OCH_2O), 4.72 (1 H, m, 1-H), 4.00—3.48 (total 6 H, m, 4- and 5-H and OCH_2CH_2O), 3.40 (total 6 H, s, 2 × OMe), 1.99 (3 H, s, NAc), 1.91 (total 2 H, m, 2- and 2'-H), and 1.29 (3 H, d, $J_{5,6}$ 6 Hz, 5-Me).

Methyl 3-*Acetamido*-2,3,6-*trideoxy*-4-O-(*methoxymethyl*)-α-L-ribo-*hexopyranoside* (24).—In a similar manner, the oxime (22) yielded the title compound (*ca.* 78%), b.p. 105—108 °C (bath) at 1 mmHg; $[\alpha]_D$ *ca.* −209° (*c*, 0.7 in $CHCl_3$); $\nu_{max.}$ 1 650 and 1 520 cm^{-1} (NHAc); δ_H 4.71 (total 3 H, m and ABq, J_{AB} 7 Hz, 1-H and OCH_2O), 3.40 (total 6 H, s, 2 × OMe), 2.00 (3 H, s, NAc), and 1.30 (3 H, d, $J_{5,6}$ 6 Hz, 5-Me).

Attempts to free this material from a persistent impurity, which did not appear to be the corresponding 3-equatorial isomer, were unsuccessful.

3-*Acetamido*-2,3,6-*trideoxy*-L-ribo-*hexose* (N-*Acetyl*-L-*ristosamine*).—A solution of the MEM derivative (23) (0.32 g) in water (5 ml) and acetic acid (2 ml) was boiled under reflux for 90 min. The mixture was then diluted with water and evaporated to dryness under reduced pressure. Chromatography of the residue on silica gel [ethyl acetate–methanol (7 : 3) as eluant] gave N-*acetyl*-L-*ristosamine* (0.15 g, 72%), m.p. 133—135 °C (from ethyl acetate); $[\alpha]_D$ −38° (final; *c*, 0.7 in H_2O) (Found: C, 51.0; H, 8.05; N, 7.3. $C_8H_{15}NO_4$ requires C, 50.8; H, 8.0; N, 7.4%) [lit.,[20] (D-enantiomer) m.p. 134 °C; $[\alpha]_D$ +39° (final; *c*, 0.5 in H_2O)].

Similar hydrolysis of the methoxymethyl analogue (24) gave an identical product in comparable yield.

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