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THE CHEMISTRY OF SOME METHYL ANHYDROGLYCOSIDULOSES*

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ABSTRACT

Methyl anhydroglycosiduloses containing an $\alpha\beta$-epoxy carbonyl unit have been readily prepared by the oxidation of methyl 2,3-anhydro-β-L-ribopyranoside and methyl 3,4-anhydro-6-deoxy-α-L-mannopyranoside with ruthenium tetraoxide. The reactions of these epoxyketones at either the oxirane or carbonyl function with hydrogen-over-palladium, hydrochloric acid, hydrobromic acid, nitromethane, or diazomethane illustrate their versatility, and their application to the synthesis of amino and deoxy sugars is described, including a derivative of colitose.

INTRODUCTION

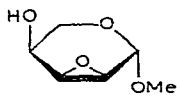
As part of a programme of studies of the chemistry of glycosiduloses[1], we have been investigating the reactions of a novel class of carbohydrate derivatives which possess vicinal carbonyl and oxirane functional groups[2]. Such derivatives, which may be prepared readily by the oxidation of simple anhydroglycosides with ruthenium tetraoxide, show considerable promise as intermediates for the synthesis of a variety of modified sugars. Recent communications from Paulsen's group[3,4] on this class of compound, together with a report of the synthesis and borohydride reduction of the epoxyketone **2** and its D-enantiomer[5], prompts this account of the synthesis of some α-epoxyketones and their reactions with a number of different reagents, particularly illustrating their value for the synthesis of deoxy and amino sugars. In a subsequent paper, we will discuss more-extensive studies of the reactions with arylhydrazines leading, *inter alia*, to diamino sugars.

RESULTS AND DISCUSSION

Treatment of methyl 2,3-anhydro-β-L-ribopyranoside (**1**) with ruthenium tetraoxide in carbon tetrachloride, according to a procedure originally reported from these laboratories[6], readily gave crystalline methyl 2,3-anhydro-β-L-*erythro*-pento-

*Dedicated to the memory of Professor Edward J. Bourne.

pyranosid-4-ulose (**2**) in 70% yield. Methyl 3,4-anhydro-6-deoxy-α-L-talopyranoside (**3**) similarly yielded crystalline methyl 3,4-anhydro-6-deoxy-α-L-*lyxo*-hexopyranosid-2-ulose (**4**) in 72% yield*. Both these epoxyketones exhibited infrared absorption at 1750 cm^{-1}, and gave a positive Ross-test for epoxides[7].



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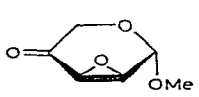

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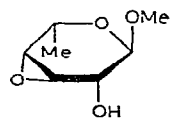

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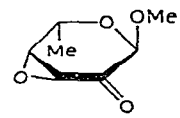

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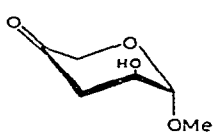
Hydrogenation of the epoxyketone **2** over palladium-on-charcoal gave a high yield of methyl 3-deoxy-β-L-*glycero*-pentopyranosid-4-ulose (**5**), characterised by its infrared and n.m.r. spectra; it showed ν_{max} at 1700 cm^{-1} (C=O), and in the n.m.r. spectrum the H-3 protons appeared as an octet centred at δ 2.70, with J_{gem} 17 Hz and both $J_{2,3}$ values 4 Hz, indicating that H-2 is equatorial. The signal for H-2 was hidden under the H-5 resonances, but H-1 could be clearly seen as a doublet at δ 4.71, $J_{1,2}$ 2.5 Hz, consistent with a diequatorial arrangement for H-1 and H-2. The utility of this method of synthesising 3-deoxy sugars was demonstrated by the hydrogenation of the 6-deoxy sugar **4** to give methyl 3,6-dideoxy-α-L-*threo*-hexopyranosid-2-ulose (**6**, >90%), which showed ν_{max} at 1765 cm^{-1} and gave n.m.r. signals for the H-3 protons at δ 3.01 (quartet) and at 2.53 (octet), with J_{gem} 15 Hz, and $J_{3,4}$ values of 3.5 and 3.0 Hz, respectively; the upfield proton also showed long-range coupling to H-5 of 0.5 Hz, consistent with H-5 and this H-3 proton both being axial. Reduction of **6** with sodium borohydride, followed by acetylation, gave a 63% yield of methyl 2,4-di-*O*-acetyl-3,6-dideoxy-α-L-*xylo*-hexopyranoside (**7**), which has the same configuration as colitose, a 3,6-dideoxyhexose occurring in the cell-wall polysaccharide obtained from a strain of *E. coli*[8]. The configuration of **7** followed from the vicinal coupling constants for the ring protons. Values for $J_{2,3}$ of 6.0 and 11.0 Hz require H-2 to be axial to account for the higher value which is indicative of a pair of diaxially related protons, and the $J_{1,2}$ value of 2.5 Hz (in chloroform) in turn requires H-1 to be equatorial if H-2 is axial, which confirms the expected $^1C_4$ conformation for this sugar. The reduction of the ketone **6** therefore occurred stereoselectively to give the equatorial alcohol, which is the usual orientation observed from reduction with sodium borohydride of cyclohexanone derivatives lacking bulky axial substituents in the β-position; the β-axial hydroxyl group may actually assist attack of the carbonyl group from the axial side by complex formation with the borohydride anion.

The synthesis of aminodeoxy sugars from our epoxyketone intermediates was demonstrated by the sequential oximation, hydrogenation, and acetylation of the deoxyglycosidulose **5**, which afforded an epimeric mixture of acetamidodideoxy sugars in a 3:1 ratio, from which methyl 4-acetamido-2-*O*-acetyl-3,4-dideoxy-β-L-*erythro*-pentopyranoside (**8**) could be isolated in 56% yield by crystallisation. The

*These oxidations were first carried out by R. D. King in these laboratories[2a].



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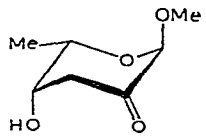

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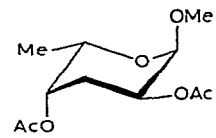

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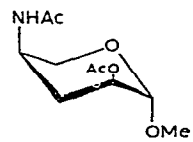

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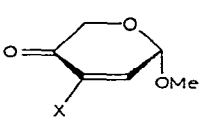
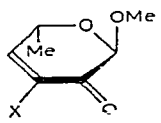
configuration assigned to **8** was deduced from p.m.r. evidence: the signal for H-1 was a broad singlet, suggesting that H-1 and H-2 are diequatorial and not diaxial; H-4 showed only a small coupling of 1.5 Hz to both H-5 protons, which requires it to be equatorial; and whilst the signal for one of the H-3 protons was masked by the acetyl resonances, the other H-3 proton could be clearly seen as a pair of triplets centred at δ 1.87, with J_{gem} 16 Hz and $J_{3,2} = J_{3,4} = 4.0$ Hz, confirming that both H-2 and H-4 are equatorial. The catalytic hydrogenation of the oxime derived from **5** therefore gave the axial amine preferentially, as expected. An alternative route to aminodeoxy sugars from epoxyketones *via* arylhydrazone intermediates will be described elsewhere.

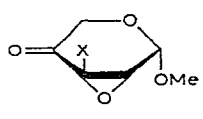
Treatment of the epoxyketone **2** with conc. hydrochloric acid in acetone gave a 60% yield of 4-chloro-2,6-dihydro-6-(*S*)-methoxy-3-oxopyran (**9**), and a similar reaction with hydrobromic acid gave the corresponding bromo sugar (**10**). Analogously, the epoxyketone **4** gave the halo-unsaturated sugars **11** and **12**; Paulsen obtained



9 X = Cl
10 X = Br



11 X = Cl
12 X = Br

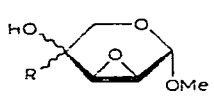


13 X = Cl
14 X = Br

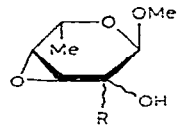
these derivatives from the epoxyketones by using the corresponding lithium halide[3]. The halo-unsaturated ketones **9**–**12** were further characterised as the crystalline oximes. Treatment of **9** or **10** with sodium hypochlorite in tetrahydrofuran readily yielded crystalline epoxide derivatives that are assigned the structures **13** and **14**, respectively. The indicated stereochemistry of these compounds is suggested by $J_{1,2}$ values of 1.0 and 1.2 Hz, respectively, as the corresponding protons in a number of 2,3-anhydro sugar derivatives show values in the range 0.8–2.5 Hz when *cis*-related, but no coupling when *trans*-related[9–11]. More-definitive evidence for the stereochemistry of **13** and **14** has not yet been obtained, however, and the opposite isomer would be formed if the epoxidation occurred *trans* to the methoxyl group as expected on steric grounds, in line with the general behaviour of cyclohexene derivatives and other unsaturated sugars having alkoxyl groups adjacent to the double bond.

In contrast to the reactions involving the epoxide ring, treatment of the epoxyketone **2** with alkaline nitromethane gave a quantitative yield of a branched-chain

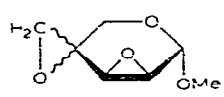
sugar epoxide, methyl 2,3-anhydro-4-*C*-nitromethyl-α-D-lyxo- or -β-L-ribo-pyranoside (**15**) which, although syrupy, appeared to be stereochemically homogeneous from chromatographic and spectroscopic evidence; however, the configuration at C-4 could not be deduced from this evidence. Catalytic hydrogenation of **15** over Raney



15 R = CH_2NO_2
16 R = CH_2NH_2



17 R = CH_2NO_2
18 R = CH_2NH_2



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nickel gave a crystalline, branched-chain, amino sugar that is assigned the structure methyl 4-*C*-aminomethyl-2,3-anhydro-α-D-lyxo- or -β-L-ribo-pyranoside (**16**), again with uncertain configuration at C-4. Similarly, the epoxyketone **4** yielded methyl 3,4-anhydro-6-deoxy-2-*C*-nitromethyl-α-L-galacto- or -talo-pyranoside (**17**) as a syrup which yielded the crystalline aminomethyl sugar **18** on hydrogenation; here again the configuration at the branch carbon has not yet been established, but work is continuing on this problem.

Treatment of **2** with either diazomethane or dimethyl sulphoxonium methylide yielded a crystalline diepoxide, assigned the structure **19**. The n.m.r. spectrum of **19** in deuteriobenzene exhibited three sets of 2-proton AB quartets, with some additional small splitting due to long-range coupling. The signals for H-2 and H-3 appeared at δ 2.75 and 2.97, respectively ($J_{2,3}$ 3.8 Hz), H-5*a* and H-5*b* at 3.78 and 2.96 (J_{gem} 11.5 Hz), and H-1′*a* and H-1′*b* at 2.53 and 2.18 (J_{gem} 4.7 Hz). Further coupling could be seen with $J_{1,2}$ 0.6, $J_{3,5b}$ 0.9, and $J_{1'a,5a}$ 1.5 Hz. However, whilst some preference for the D-*lyxo* configuration might be expected from the consideration of possible steric interactions by inspection of models, the n.m.r. data unfortunately do not give a clear indication of this configuration, which is now being explored by chemical methods.

EXPERIMENTAL

General methods. — T.l.c. was performed on microscope slides coated with Kieselgel G or G_{254} (fluorescent type) (Merck), using (*a*) dichloromethane; (*b*) dichloromethane–ethyl acetate (4:1, v/v); (*c*) benzene. For column chromatography, either silicagel (M.F.C., Hopkins and Williams) or Kieselgel (0.05–0.2 mm, Merck) was used. I.r. spectra were recorded on a Perkin–Elmer Infracord 137 spectrometer. P.m.r. spectra were measured with Varian A-60 D or Jeol JNM-MH-100 spectrometers, for solutions in chloroform-*d* (internal Me_4Si) unless otherwise stated.

*Methyl 2,3-anhydro-β-*L-erythro-*pentopyranosid-4-ulose* (**2**). — Methyl 2,3-anhydro-β-L-ribopyranoside {**1**, 10 g; m.p. 52–53°, $[\alpha]_D$ +52° (*c* 0.9, ethanol); prepared from methyl 2-*O*-toluene-*p*-sulphonyl-β-L-arabinopyranoside by the method

described by Kent *et al.*[12] for the D enantiomer} in carbon tetrachloride (50 ml) was treated with a solution of ruthenium tetraoxide in carbon tetrachloride (350 ml) prepared from ruthenium dioxide (13 g) by the method of Beynon *et al.*[6]. After 2 h, 2-propanol (10 ml) was added and the mixture stirred for 1 h. The solution was filtered and concentrated to yield a crystalline residue which was recrystallised from ethyl ether–light petroleum (b.p. 40–60°) to give colourless needles (7.1 g, 70%), m.p. 45–46°, $[\alpha]_D$ +239° (*c* 2.1, chloroform), ν_{max} 1750 cm^{-1} (C=O). P.m.r. data: δ 5.10 (*s*, 1H, H-1), 4.13 (*s*, 2H, H-5*a*,5*b*), 3.70–3.35 (*m*, 5H, OMe, H-2,3); lit.[5] m.p. 45–46°, $[\alpha]_D$ +107° (methanol).

Anal. Calc. for $C_6H_8O_4$: C, 50.0; H, 5.6. Found: C, 50.35; H, 5.7.

*Methyl 3,4-anhydro-6-deoxy-α-*L*-lyxo-hexopyranosid-2-ulose* (**4**). — Methyl 3,4-anhydro-6-deoxy-α-L-talopyranoside[13] (**3**, 5.5 g) was oxidised by the procedure used for **2** to give **4** as colourless needles (4.0 g, 72%) which, when crystallised from isopropyl ether–light petroleum (b.p. 40–60°), had m.p. 53–54°, $[\alpha]_D$ +143° (*c* 2.0, dichloromethane), ν_{max} 1750 cm^{-1} (C=O). P.m.r. data: δ 4.57 (*s*, 1H, H-1), 4.35 (*q*, 1H, H-5), 3.52–3.30 (*m*, 5H, OMe, H-3,4), 1.45 (*d*, 3H, $J_{5,6}$ 6.5 Hz, CMe).

Anal. Calc. for $C_7H_{10}O_4$: C, 53.2; H, 6.4. Found: C, 53.3; H, 6.2.

*Methyl 3-deoxy-β-*L*-glycero-pentopyranosid-4-ulose* (**5**). — Compound **2** (1.0 g) in ethyl acetate (15 ml) was added to a preactivated suspension of 10% palladium-on-charcoal (0.5 g) in ethyl acetate (10 ml) and shaken with hydrogen until uptake was complete. Filtration and removal of solvent yielded a syrupy product which was purified on a silica gel column to give compound **5** (0.8 g, 80%) as a colourless syrup, $[\alpha]_D$ +153.3° (*c* 0.6, chloroform); ν_{max} 3300 (OH) and 1700 cm^{-1} (C=O). P.m.r. data: δ 4.71 (*d*, 1H, $J_{1,2}$ 2.5 Hz, H-1), 4.35–3.95 (*m*, 3H, H-2,5*a*,5*b*), 3.9–3.7 (*s*, 1H, OH), 3.51 (*s*, 3H, OMe), and 2.70 (*o*, 2H, H-3*a*,3*b*).

Anal. Calc. for $C_6H_{10}O_4$: C, 49.3; H, 6.9. Found: C, 49.8; H, 6.8.

*Methyl 3,6-dideoxy-α-*L*-threo-hexopyranosid-2-ulose* (**6**). — Compound **4** (1.6 g) in methanol (10 ml) was hydrogenated over 10% palladium-on-charcoal (0.4 g) in methanol (15 ml), as described for compound **2**. The syrupy product was purified by silica gel column chromatography (solvent *b*) to give compound **6** (1.47 g, 91%) as a colourless syrup, $[\alpha]_D$ −116.4°, (*c* 0.86, chloroform); ν_{max} 3300 (OH) and 1765 cm^{-1} (C=O). P.m.r. data: δ 4.49 (*s*, 1H, H-1), 4.40 (*o*, 1H, $J_{5,4}$ 1.5, $J_{5,Me}$ 6.5 Hz, H-5), 4.28–3.97 (*m*, 1H, H-4), 3.47 (*s*, 3H, OMe), 3.37–3.15 (*m*, 1H, OH), 3.01 (*q*, 1H, $J_{3a,3b}$ 15.0, $J_{3a,4}$ 3.5 Hz, H-3*a*), 2.53 (*o*, 1H, $J_{3b,4}$ 3.0 Hz, $J_{3b,5}$ 0.5 Hz, H-3*b*), 1.3 (*d*, 3H, CMe).

Anal. Calc. for $C_7H_{12}O_4$: C, 52.5; H, 7.55. Found: C, 51.9; H, 7.7.

*Methyl 2,4-di-*O*-acetyl-3,6-dideoxy-α-*L*-xylo-hexopyranoside* (**7**). — Compound **6** (1.0 g) in methanol (10 ml) was treated with sodium borohydride (0.2 g) for 0.5 h, and then acetic acid (0.1 ml) was added. The mixture was concentrated to a syrupy residue, to which pyridine (15 ml) and acetic anhydride (2 ml) were added. After 4 h, the reaction mixture was worked up in the usual way and the product purified by silica gel column chromatography (solvent *b*) to yield **7** as a colourless syrup (0.97 g, 63%), b.p. 80–82°/0.3 mmHg, $[\alpha]_D$ −94.6° (*c* 1.85, chloroform). P.m.r. data: δ 4.83

(*d*, 1H, $J_{1,2}$ 2.5 Hz, H-1); (benzene-d_6): δ 5.27 (*o*, 1H, $J_{1,2}$ 3.0, $J_{2,3a}$ 6.0, $J_{2,3b}$ 11.0 Hz, H-2), 5.0–4.8 (*m*, 2H, H-1,4), 3.71 (*o*, 1H, $J_{5,4}$ 1.5, $J_{5,Me}$ 6.5 Hz, H-5), 3.10 (*s*, 3H, OMe), 2.2–1.9 (*m*, 2H, H-3*a*,3*b*), 1.67 (*s*, 6H, 2AcO), 1.03 (*d*, 3H, $J_{Me,5}$ 6.5 Hz, CMe); lit.[14] for D enantiomer, $[\alpha]_D$ +95° (chloroform), and in agreement with n.m.r. in chloroform-*d* at 60 MHz.

Anal. Calc. for $C_{11}H_{18}O_6$: C, 53.7; H, 7.3. Found: C, 54.6; H, 7.4.

*Methyl 4-acetamido-2-O-acetyl-3,4-dideoxy-β-*L-erythro-*pentopyranoside* (**8**). — Compound **5** (1.0 g) in methanol (20 ml) was treated with hydroxylamine hydrochloride (0.5 g) and pyridine (0.2 ml), and the mixture was stirred at room temperature. After 3 h, when all starting material had been consumed, the solution was added to a suspension of Raney nickel (1.0 g) in methanol (15 ml), and the mixture was shaken under hydrogen at room temperature and pressure until uptake was complete (5 h). The residue obtained after filtration and removal of solvent was acetylated in the usual way with acetic anhydride (0.5 ml) in pyridine (10 ml). The semi-crystalline product was twice recrystallised from ethyl ether–light petroleum (b.p. 40–60°) to give **8** as colourless needles (0.88 g, 56%), m.p. 109–110°, $[\alpha]_D$ +86° (*c* 0.16, chloroform); ν_{max} 3250 (N–H) and 1735 cm^{-1} (C=O). P.m.r. data (benzene-d_6): δ 6.2–5.8 (*s*, 1H, NH), 4.66 (*m*, 1H, H-2), 4.34 (*s*, 1H, H-1), 3.9 (*m*, 1H, H-4), 3.57 (*q*, 1H, $J_{5a,5b}$ 12.0, $J_{5a,4}$ 1.5 Hz, H-5*a*), 3.27 (sxt, 1H, $J_{5b,4}$ 1.5, $J_{5b,3b}$ 0.5 Hz, H-5*b*), 2.94 (*s*, 3H, OMe), 1.87 (sxt, 1H, J_{gem} 16, $J_{3,4} = J_{3,2} = 4.0$ Hz, H-3), 1.60 (*s*, 3H, NAc), 1.56 (*s*, 3H, OAc).

Anal. Calc. for $C_{10}H_{17}NO_5$: C, 52.0; H, 7.4; N, 6.1. Found: C, 52.05; H, 7.3; N, 6.0.

4-Chloro-2,6-dihydro-6-(S)*-methoxy-3-oxopyran* (**9**). — Conc. hydrochloric acid (2 ml) was slowly added dropwise to a solution of **2** (1.0 g) in acetone (20 ml) at 0°, and the resulting solution was then kept at room temperature. T.l.c. indicated that no starting material remained after 12 h, and two products were present. On addition of ice–water, the major product crystallised. This was combined with further material obtained after column chromatography of the residue which was isolated from the aqueous solution by extraction with dichloromethane. Recrystallisation of the combined material from ethanol afforded **9** as colourless needles (0.63 g, 56%), m.p. 104–105°, $[\alpha]_D$ +43° (*c* 0.5, chloroform); λ_{max} 242 nm, ε 4,770; ν_{max} 1695 (C=O) and 1610 cm^{-1} (C=C). P.m.r. data: δ 7.01 (*d*, 1H, $J_{2,1}$ 3.9 Hz, H-2), 5.19 (*d*, 1H, H-1), 4.40 (*q*, 2H, $J_{5a,5b}$ 16.5 Hz, H-5*a*,5*b*), 3.50 (*s*, 3H, OMe).

Anal. Calc. for $C_6H_7ClO_3$: C, 44.2; H, 4.3; Cl, 21.8. Found: C, 44.0; H, 4.3; Cl, 21.8.

Compound **9** (0.48 g) in methanol (15 ml) was treated with a solution of hydroxylamine hydrochloride (0.26 g, 1.2 equivalents) in methanol (15 ml) containing pyridine (0.2 ml) at room temperature. After 30 min, water (20 ml) was added to give 4-chloro-2,6-dihydro-6-(*S*)-methoxy-3-oximinopyran as a white, crystalline precipitate (0.37 g, 71%), m.p. 104–105°, $[\alpha]_D$ +2.4° (*c* 0.5, chloroform); λ_{max} 231 nm, ε 10,500; ν_{max} 3150 (N–OH) and 1680 cm^{-1} (C=C and C=N). P.m.r. data: δ 11.10

(*s*, 1H, N–OH), 6.48 (*d*, 1H, $J_{2,1}$ 4.0 Hz, H-2), 5.20 (*d*, 1H, H-1), 4.80 (*q*, 2H, $J_{5a,5b}$ 16.5 Hz, H-5*a*,5*b*), 3.46 (*s*, 3H, OMe).

Anal. Calc. for $C_6H_8ClNO_3$: C, 40.45; H, 4.5; Cl, 20.0; N, 7.8. Found: C, 40.25; H, 4.4; Cl, 21.5; N, 7.6.

4-Bromo-2,6-dihydro-6-(S)*-methoxy-3-oxopyran* (**10**). — This substance was obtained from **2** (0.5 g) by a procedure similar to that described for the preparation of **9**, but using conc. hydrobromic acid. The product was recrystallised from ethanol to give the bromo derivative **10** as colourless needles (0.4 g, 56%), m.p. 91–92°, $[\alpha]_D$ +13.3° (*c* 1.3, chloroform); λ_{max} 250 nm, ε 4,185; ν_{max} 1685 (C=O) and 1600 cm^{-1} (C=C). P.m.r. data: δ 7.30 (*d*, 1H, $J_{2,1}$ 3.2 Hz, H-2), 5.12 (*d*, 1H, H-1), 4.45 (*q*, 2H, $J_{5a,5b}$ 16.5 Hz, H-5*a*,5*b*), 3.51 (*s*, 3H, OMe).

Anal. Calc. for $C_6H_7BrO_3$: C, 34.8; H, 3.4; Br, 38.2. Found: C, 34.6; H, 3.5; Br, 38.1.

The oxime of **10** was prepared by the procedure used for the chloro analogue. In this way, **10** (0.5 g) gave 4-bromo-2,6-dihydro-6-(*S*)-methoxy-3-oximinopyran as colourless needles (0.42 g, 79%), m.p. 117–118° (dec.), $[\alpha]_D$ +13.8° (*c* 0.2, chloroform); λ_{max} 239 nm, ε 11,100; ν_{max} 3180 (N–OH) and 1675 cm^{-1} (C=C and C=N). P.m.r. data: δ 11.10 (*s*, 1H, N–OH), 6.72 (*d*, 1H, $J_{2,1}$ 4.0 Hz, H-2), 5.15 (*d*, 1H, H-1), 4.70 (*q*, 2H, $J_{5a,5b}$ 16.5 Hz, H-5*a*,5*b*), 3.4 (*s*, 3H, OMe).

Anal. Calc. for $C_6H_8BrNO_3$: C, 32.4; H, 3.6; N, 6.3; Br, 36.0. Found: C, 32.9; H, 3.6; N, 6.3; Br, 35.85.

*Methyl 2,3-anhydro-3-chloro-β-*L-threo-*pentopyranosid-4-ulose** (**13**). — Compound **9** (1.5 g) in tetrahydrofuran (20 ml) was treated with aqueous sodium hypochlorite (10–14% available chlorine, 5 ml). The mixture was stirred at room temperature for 12 h, when t.l.c. indicated that **9** was no longer present. Water (20 ml) was added and the solution concentrated to remove most of the organic solvent; the aqueous residue was extracted with dichloromethane (3 × 50 ml), and the extracts were dried ($MgSO_4$) and concentrated. Purification of the crystalline residue by column chromatography on silica gel (solvent *a*) gave the anhydride **13** as colourless needles (1.05 g, 64%), m.p. 67–68°, $[\alpha]_D$ +202° (*c* 1.0, chloroform), ν_{max} 1730 cm^{-1} (C=O). P.m.r. data: δ 5.11 (*d*, 1H, $J_{1,2}$ 1.0 Hz, H-1), 4.23 (*s*, 2H, H-5*a*,5*b*), 3.83 (*d*, 1H, H-2), 3.51 (*s*, 3H, OMe).

Anal. Calc. for $C_6H_7ClO_4$: C, 40.5; H, 4.0; Cl, 20.0. Found: C, 41.25; H, 4.1; Cl, 20.6.

*Methyl 2,3-anhydro-3-bromo-β-*L-threo-*pentopyranosid-4-ulose* (**14**). — This compound, prepared from **10** (1.2 g) by the procedure described for **13**, was obtained as colourless needles (0.8 g, 62%), m.p. 127–128°, $[\alpha]_D$ +147° (*c* 1.4, chloroform),

*The nomenclature of compounds **13** and **14** is based on the proposals of the Chemical Society Carbohydrate Nomenclature Committee for naming geminally disubstituted sugar derivatives, which recommend that the substituent defining the configuration be chosen by the Cahn–Ingold–Prelog sequence rule; in this instance, halogen takes precedence over oxygen at C-3, so that these are both L-*threo*-pentose derivatives.

ν_{max} 1725 cm^{-1} (C=O). P.m.r. data: δ 5.09 (*d*, 1H, $J_{1,2}$ 1.2 Hz, H-1), 4.24 (*s*, 2H, H-5*a*,5*b*), 3.86 (*d*, 1H, H-2), 3.51 (*s*, 3H, OMe).

Anal. Calc. for $C_6H_7BrO_4$: C, 32.3; H, 3.1; Br, 35.85. Found: C, 33.0; H, 3.2; Br, 36.3.

*Methyl 3-chloro-3,4,6-trideoxy-α-*L*-glycero-hex-3-enopyranosid-2-ulose* (**11**). — Conc. hydrochloric acid (2 ml) was slowly added dropwise to a solution of **4** (1.2 g) in acetone (20 ml) at 0°. The mixture was then stored at room temperature for 15 h, after which t.l.c. indicated that there was no residual **4**. Ice–water (20 ml) was added, and the products were extracted with dichloromethane (3 × 50 ml). The extracts were washed successively with aqueous sodium hydrogen carbonate and water, dried ($MgSO_4$), and concentrated. Column chromatography of the syrupy residue on silica gel yielded the unsaturated chloro derivative **11** as colourless needles (0.76 g, 58%), m.p. 52–53°, $[\alpha]_D$ −133° (*c* 1.1, chloroform); λ_{max} 246 nm, ε 7,235; ν_{max} 1710 (C=O) and 1600 cm^{-1} (C=C). P.m.r. data: δ 7.03 (*d*, 1H, $J_{4,5}$ 1.5 Hz, H-4), 4.87 (*s*, 1H, H-1), 4.80 (*o*, 1H, $J_{5,Me}$ 6.5 Hz, H-5), 3.53 (*s*, 3H, OMe), 1.42 (*d*, 3H, CMe).

Anal. Calc. for $C_7H_9ClO_3$: C, 47.45; H, 5.1; Cl, 20.0. Found: C, 47.7; H, 5.2; Cl, 19.9.

*Methyl 3-chloro-3,4,6-trideoxy-α-*L*-glycero-hex-3-enopyranosid-2-ulose oxime.* — Compound **11** (0.65 g) in methanol (12 ml) was treated with hydroxylamine hydrochloride (0.35 g) and pyridine (0.2 ml), and the mixture was stored at room temperature for 3 h. Water (15 ml) was added, and the product extracted into dichloromethane. The usual work-up afforded a semi-crystalline product which was purified by sublimation to give colourless needles (0.42 g, 60%) of the title compound, m.p. 55–56°, $[\alpha]_D$ −153° (*c* 0.94, chloroform); λ_{max} 241 nm, ε 13,300; ν_{max} 3210 (OH), 1630 and 1610 cm^{-1} (C=C and C=N). P.m.r. data: δ 10.16 (*s*, 1H, OH), 6.27 (*d*, 1H, $J_{4,5}$ 1.5 Hz, H-4), 5.82 (*s*, 1H, H-1), 4.65 (*o*, 1H, $J_{5,Me}$ 6.5 Hz, H-5), 3.53 (*s*, 3H, OMe), 1.33 (*d*, 3H, CMe).

Anal. Calc. for $C_7H_{10}ClNO_3$: C, 44.0; H, 5.2; Cl, 18.6; N, 7.3. Found: C, 44.45; H, 5.3; Cl, 18.2; N, 7.0.

*Methyl 3-bromo-3,4,6-trideoxy-α-*L*-glycero-hex-3-enopyranosid-2-ulose* (**12**). — This compound was prepared from **4** (0.8 g), as described for **11** but using conc. hydrobromic acid. The product was recrystallised from ethanol to give the unsaturated bromo derivative **12** as colourless needles (0.59 g, 53%), m.p. 49–50°, $[\alpha]_D$ −162° (*c* 1.1, chloroform); λ_{max} 255 nm, ε 7,670; ν_{max} 1705 (C=O) and 1595 cm^{-1} (C=C). P.m.r. data: δ 7.33 (*d*, 1H, $J_{4,5}$ 1.5 Hz, H-4), 4.80 (*s*, 1H, H-1), 4.77 (*o*, 1H, $J_{5,Me}$ 7.0 Hz, H-5), 3.53 (*s*, 3H, OMe), 1.41 (*d*, 3H, CMe).

Anal. Calc. for $C_7H_9BrO_3$: C, 38.0; H, 4.1; Br, 36.2. Found: C, 38.2; H, 4.1; Br, 36.5.

The oxime of **12** was prepared as described for the oxime of **11**. Compound **12** (0.5 g) afforded needles (0.29 g, 55%) of methyl 3-bromo-3,4,6-trideoxy-α-L-*glycero*-hex-3-enopyranosid-2-ulose oxime, m.p. 51–52°, $[\alpha]_D$ −127° (*c* 1.2, chloroform); λ_{max} 242 nm, ε 11,000; ν_{max} 3200 (OH), 1620 and 1600 cm^{-1} (C=C and C=N). P.m.r.

data: δ 10.2 (*s*, 1H, N–OH), 6.51 (*d*, 1H, $J_{4,5}$ 1.5 Hz, H-4), 5.83 (*s*, 1H, H-1), 4.63 (*o*, 1H, H-5), 3.52 (*s*, 3H, OMe), 1.32 (*d*, 3H, CMe).

Anal. Calc. for $C_7H_{10}BrNO_3$: C, 35.6; H, 4.2; Br, 33.9; N, 6.0. Found: C, 35.9; H, 4.3; Br, 34.3; N, 6.05.

*Methyl 2,3-anhydro-4-*C*-nitromethyl-α-*D*-lyxo-(or β-*L*-ribo)-pyranoside* (**15**). — Compound **2** (1.0 g) in nitromethane (10 ml) was treated with a solution of sodium methoxide (0.2 g) in nitromethane (10 ml) at room temperature. T.l.c. examination indicated that complete reaction had occurred after 2 h, with formation of a single product. Water (20 ml) was then added, and the solution extracted with dichloromethane (3 × 50 ml). After drying ($MgSO_4$), the extract was concentrated to afford **15** as a colourless syrup (1.3 g, 92%), $[\alpha]_D$ +76.3° (*c* 0.55, chloroform); ν_{max} 3550 (OH) and 1550 cm^{-1} (NO_2). P.m.r. data: δ 4.85 (*s*, 1H, H-1), 4.72 (*q*, 2H, J_{gem} 14.0 Hz, CH_2-NO_2), 3.76 (*s*, 1H, OH), 3.65–3.40 (*m*, 6H, H-3,5*a*,5*b*, OMe), 3.20 (*d*, 1H, $J_{2,3}$ 4.0 Hz, H-2).

Anal. Calc. for $C_7H_{11}NO_6$: C, 41.0; H, 5.4; N, 6.8. Found: C, 41.6; H, 5.4; N, 6.5.

*Methyl 4-*C*-aminomethyl-2,3-anhydro-α-*D*-lyxo-(or β-*L*-ribo)-pyranoside* (**16**). — Compound **15** (1.2 g) in methanol (20 ml) was hydrogenated over Raney nickel (0.5 g) in methanol (15 ml) until hydrogen uptake was complete (2 h). The solution was filtered and concentrated to a residue, which was crystallised from ethyl acetate–light petroleum (b.p. 40–60°) to give **16** as colourless needles (0.75 g, 73%), m.p. 93–94°, $[\alpha]_D$ +76° (*c* 0.3, chloroform); ν_{max} 3350 cm^{-1} (OH and NH). P.m.r. data: δ 4.75 (*s*, 1H, H-1), 3.45 (*s*, 4H, H-3, OMe), 3.35 (*q*, 2H, H-5*a*,5*b*), 3.19 (*d*, 1H, $J_{2,3}$ 4.0 Hz, H-2), 2.85 (*q*, 2H, J_{gem} 13.0 Hz, H-1′*a*,1′*b*), 2.7–2.5 (*m*, 3H, NH_2 and OH).

Anal. Calc. for $C_7H_{13}NO_4$: C, 48.0; H, 7.4; N, 8.0. Found: C, 48.0; H, 7.3; N, 8.1.

*Methyl 3,4-anhydro-6-deoxy-2-*C*-nitromethyl-α-*L*-galacto-(or -talo)-pyranoside* (**17**). — By the procedure described for the synthesis of compound **15**, **4** (1.0 g) was converted into **17**, which was obtained as a colourless syrup (1.37 g, 98%), $[\alpha]_D$ −76.6° (*c* 0.9, chloroform); ν_{max} 3400 (OH) and 1550 cm^{-1} (NO_2). P.m.r. data: δ 4.66 (*q*, 2H, J_{gem} 12.0 Hz, CH_2NO_2), 4.61 (*d*, 1H, $J_{1,2}$ 1.2 Hz, H-1), 4.10 (*q*, 1H, $J_{5,Me}$ 6.0 Hz, H-5), 3.38 (*d*, 1H, $J_{3,4}$ 3.0 Hz, H-3), 3.27 (*s*, 4H, OH and OMe), 3.18 (*d*, 1H, H-4), 1.32 (*d*, 3H, CMe).

Anal. Calc. for $C_8H_{13}NO_6$: C, 43.8; H, 6.0; N, 6.3. Found: C, 44.3; H, 5.9; N, 5.9.

*Methyl 2-*C*-aminomethyl-3,4-anhydro-6-deoxy-α-*L*-galacto-(or -talo)-pyranoside* (**18**). — Compound **17** (1.0 g) was hydrogenated as described for the synthesis of compound **16**, to yield **18** as colourless needles (0.69 g, 81%). When recrystallised from ethyl acetate–light petroleum (b.p. 40–60°), **18** had m.p. 118–119°, $[\alpha]_D$ −118° (*c* 0.56, chloroform); ν_{max} 3300 (NH and OH) and 1590 cm^{-1} (NH). P.m.r. data: δ 4.37 (*s*, 1H, H-1), 4.10 (*q*, 1H, $J_{5,Me}$ 6.0 Hz, H-5), 3.46 (*s*, 3H, OMe), 3.12 and

3.00 (AB*q*, 2H, $J_{3,4}$ 4.0 Hz, H-3,4), 2.74 (AB*q*, 2H, J_{gem} 12.0 Hz, CH_2), 2.48 (*s*, 3H, NH_2 and OH), 1.33 (*d*, 3H, CMe).

Anal. Calc. for $C_8H_{15}NO_4$: C, 50.8; H, 7.9; N, 7.4. Found: C, 50.7; H, 7.8; N, 7.5.

*Methyl 2,3:4,1'-dianhydro-4-C-hydroxymethyl-α-*D*-lyxo-(or β-*L*-ribo)-pyranoside* (**19**). — Compound **2** (0.6 g) in ethyl ether (10 ml) was treated with sufficient diazomethane in ethyl ether to give a persistent yellow colour. T.l.c. (solvent *c*) after 25 min indicated that reaction was complete, and removal of the solvent gave crystalline **19** (0.65 g, 100%). After recrystallisation from ethyl ether, **19** had m.p. 55–56°, $[\alpha]_D$ +72° (*c* 1.0, chloroform); ν_{max} 870 cm^{-1} (oxirane), no OH or C=O. P.m.r. data: (benzene-d_6) δ 4.63 (*d*, 1H, $J_{1,2}$ 0.6 Hz, H-1), 3.78 (*q*, 1H, J_{gem} 11.5, $J_{5a,1'a}$ 1.5 Hz, H-5*a*), 3.10 (*s*, 3H, OMe), 2.97 (*q*, 1H, $J_{2,3}$ 3.8 Hz, H-3), 2.96 (*q*, 1H, $J_{5b,3}$ 0.9 Hz, H-5*b*), 2.75 (*q*, 1H, H-2), 2.53 (*q*, 1H, J_{gem} 4.7 Hz, H-1'*a*), 2.18 (*d*, 1H, H-1'*b*). The product gave a positive Ross test[7] for oxirane.

Anal. Calc. for $C_7H_{10}O_4$: C, 53.2; H, 6.4. Found: C, 53.4; H, 6.4.

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