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Note

Syntheses of D-rubranitrose and methyl α-D-tetronitroside by cyanomesylation of hexopyranosid-3-uloses*

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D-Rubranitrose[2] (**1**) and D-tetronitrose (kijanose[3], **2**) belong to a family of 2,3,6-trideoxy-3-*C*-methyl-3-nitrohexose and have the same D-*xylo* configuration. The only difference is in the substituent at C-4, methoxyl for the former and methoxycarbonylamino for the latter. In this paper, these branched-chain sugars were synthesised from D-galactose and D-glucose, respectively, via the corresponding hexopyranosid-3-uloses having the D-*threo* configuration. Cyanomesylation of the glycosidulose, followed by reductive spiroaziridine formation and reductive ring-opening to a methyl-branched amino sugar, and finally oxidation to the nitro sugar, is a well established synthetic method for such methyl-branched amino and nitro sugars as D- and L-evernitrose[4], L-vancosamine[5], L-rubranitrose[6], and a methyl-branched amino sugar[7,8] of antibiotic A35512B. Because the stereoselectivity in the cyanomesylation is not yet well understood, data for the α-D-*threo* isomers may provide an explanatory clue.

In a previous paper[6], the authors synthesised L-rubranitrose and confirmed the absolute configuration of natural rubranitrose, a component of the antibiotic rubradirin, to be D as revised[3] by comparison of the chirooptical data with those of tetronitrose. Synthesis of D-rubranitrose was first achieved through the inversion of configuration at C-4 of methyl 2,3,6-trideoxy-3-trifluoroacetamido-3-*C*-methyl-α-D-*ribo*-hexopyranoside[9]. Methyl tetronitroside, a component of such antibiotics as tetrocarcins, was synthesised through ring opening of methyl 2,3,4,6-tetradeoxy-3,4-epimino-3-*C*-methyl-α-D-*ribo*-hexopyranoside with azide anion[10].

For the synthesis of **1** through the aforementioned pathway, methyl 2,6-dideoxy-4-*O*-methyl-α-D-*threo*-hexopyranosid-3-ulose (**3**) was considered to be the most suitable key intermediate. A direct precursor of **3**, methyl 2,6-dideoxy-4-*O*-methyl-α-D-*lyxo*-hexopyranoside (**5**), could be obtained in improved yield from

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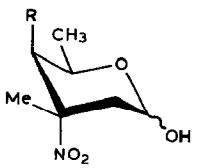
methyl 2,6-dideoxy-α-D-*lyxo*-hexopyranoside through selective 3-*O*-benzylation by the stannylene procedure[11], followed by 4-*O*-methylation and 3-*O*-debenzylation. Oxidation of **5** with dimethyl sulfoxide and oxalyl chloride[12] gave the glycosidulose **3** in quantitative yield. Cyanomesylation of **3**, with hydrogen cyanide at 0° in dichloromethane containing triethylamine, gave a cyanohydrin mixture of D-*xylo* (**6**) and D-*lyxo* isomers (**7**) in the ratio 1.4:1 in 90% yield. These were separated by column chromatography on silica gel. Under the conventionally used conditions of kinetic control (hydrogen cyanide in pyridine) the reaction proceeded in a more-complex manner to give the cyanohydrin mixture in low yield with a similar isomer ratio. The stereoselectivity of cyanide addition is thus diferent from that of methyl 4,6-*O*-benzylidene-2-deoxy-α-D-*threo*-hexopyranoside-3-ulose[13]. On the other hand, under conditions of thermodynamic control (potassium cyanide and sodium hydrogencarbonate in dichloromethane–water at room temperature), the D-*xylo* isomer **6** was obtained exclusively, as observed for the foregoing D-*threo*-hexopyranosid-3-ulose. Treatment of **6** in dichloromethane containing 4-dimethylaminopyridine with methanesulfonyl chloride–triethylamine gave the cyanomesyl derivative **8** quantitatively, whose stereochemistry was assigned as follows. Treatment of methyl 3-*C*-cyano-2,6-dideoxy-3-*O*-methylsulfonyl-4-*O*-methyl-α-L-*xylo*-hexopyranoside[6] with ion-exchanger in boiling methanol gave a mixture of α,β-glycosides whose ^{1}H-n.m.r. spectrum was exactly superposable on that obtained from **8**. Treatment of **7** in dichloromethane and triethylamine with hydrogen cyanide at 0° gave the corresponding methanesulfonate **9** quantitatively. Reaction of **9** with lithium aluminium hydride gave the spiroaziridine **12** in 50%

TABLE I

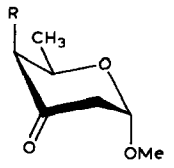
^{1}H- AND ^{13}C-N.M.R. DATA OF D-RUBRANITROSE (**1**) AND ITS METHYL GLYCOSIDE (**11**) IN $CDCl_3$

Compound	*Chemical shifts (δ) and coupling constants (Hz) in ^{1}H-n.m.r.*							
	H-1 ($J_{1,2a}$)	*H-2a* ($J_{1,2e}$)	*H-2e* ($J_{2a,2e}$)	*H-4* ($J_{4,5}$)	*H-5* ($J_{5,6}$)	*H-6* ($J_{2e,4}$)	*CMe* ($J_{1,OH}$)	*OMe*
α-**1** (natural)[2]	5.28dd (2.5)	2.05dd (3.5)	2.67dd (14.5)	3.71bs (<1.0)	4.40bq (6.5)	1.33d	1.67s	3.62s
α-**1**	5.26bs (3.6)	2.02dd (1.6)	2.64ddd (14.6)	3.70bs (<1.0)	4.40bq (6.5)	1.33d (1.0)	1.64s	3.62s
β-**1**	4.78ddd (9.4)	1.77dd (2.0)	2.64ddd (14.4)	3.53bs (<1.0)	3.50bq (6.5)	1.32d (1.0)	1.66s (7.0)	3.64s
11	4.72dd (3.6)	2.04dd (1.0)	2.65dt (14.8)	3.74bs (1.0)	4.20bq (6.5)	1.33d (1.0)	1.63s	3.65s 3.27s
	Chemical shifts (p.p.m.) in ^{13}C-n.m.r.							
	C-1	*C-2*	*C-3*	*C-4*	*C-5*	*C-6*	*CMe*	*OMe*
α-**1**	90.50	34.55	85.69	79.45	69.87	16.82	25.88	63.46
β-**1**	92.58	37.19	90.37	79.67	69.87	16.82	25.14	62.98
11	96.83	34.55	85.46	79.31	62.67	16.69	25.92	60.32

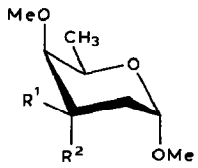
yield, and this was converted into methyl rubranitroside (**11**) *via* the methyl-branched amino sugar **10** in good yield, by successive catalytic hydrogenolysis and oxidation with *m*-chloroperoxybenzoic acid. Finally, hydrolysis of **11** in 0.05M sulfuric acid gave **1**, m.p. 160–162°, $[\alpha]_D$ +123→+86° (*c* 0.6, EtOH, 24 h); lit.[2] m.p. 150–153°, $[\alpha]_D$ +127→+86° (*c* 1.0, EtOH, 24 h) in quantitative yield. In Table I, ^{1}H- and ^{13}C-n.m.r. data for **11**, α-**1** and β-**1** are summarized. The ^{13}C-n.m.r. data show the presence of an equatorially oriented *C*-methyl group. Thus, the physical data for the synthetic rubranitrose are identical with those reported for the natural product.



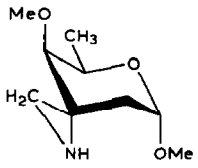
1 R = OMe
2 R = $NHCO_2Me$



3 R = OMe
4 R = $NHCO_2Me$



5 R^1 = OH, R^2 = H
6 R^1 = CN, R^2 = OH
7 R^1 = OH, R^2 = CN
8 R^1 = CN, R^2 = OMs
9 R^1 = OMs, R^2 = CN
10 R^1 = CH_3, R^2 = NH_2
11 R^1 = CH_3, R^2 = NO_2



12

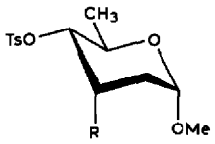
The key intermediate for the synthesis of **2**, methyl 2,4,6-trideoxy-4-methoxycarbonylamino-α-D-*threo*-hexopyranosid-3-ulose (**4**), was synthesized as follows. Methyl 2,6-dideoxy-α-D-*ribo*-hexopyranoside[14], in eight steps from D-glucose, was transformed into the 4-*O*-*p*-tolylsulfonyl derivative **13** in 67% yield. The substitution of **13** with sodium azide at 80° in *N*,*N*-dimethylformamide proceeded smoothly to give the corresponding 4-azido derivative **15** in 80% yield, and this was quantitatively reduced to the 4-amino sugar **16** with hydrogen in the presence of palladium-on-charcoal. Reaction of **16** with methyl chloroformate in methanol containing sodium hydrogencarbonate gave the corresponding methyl carbamate **17** quantitatively. Oxidation of **17** with dimethyl sulfoxide and oxalyl chloride gave the glycosidulose **4**, quantitatively. One-flask cyanomesylation of **4** by treatment with hydrogen cyanide in dichloromethane containing triethylamine at 0° and then with methanesulfonyl chloride gave an epimeric mixture of cyanomesylates (**18**) in the ratio 1.2:1 in 95% yield; these could not be separated. A similar selectivity was obtained with a two-phase reaction namely, potassium cyanide–sodium hydrogencarbonate in dichloromethane–water. Reduction of the mixture **18** with lithium aluminium hydride in dry diethyl ether at 0° gave in 39% yield the spiroaziridines **19**, which also could not be separated. By successive catalytic hydrogenolysis and oxidation with *m*-chloroperoxybenzoic acid, **19** was transformed into methyl α-D-tetronitroside (**21**) and its 3-epimer (**22**). Although

TABLE II

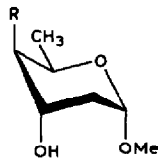
^{1}H-N.M.R. DATA OF METHYL α-TETRONITROSIDE (**21**) AND ITS 3-EPIMER (**22**) IN $CDCl_3$

Compound	*Chemical shifts (δ) and coupling constants (Hz)*									
	H-1 ($J_{1,2a}$)	*H-2a* ($J_{1,2e}$)	*H-2e* ($J_{2a,2e}$)	*H-4* ($J_{4,5}$)	*H-5* ($J_{5,6}$)	*H-6* ($J_{2e,4}$)	*NH* ($J_{NH,4}$)	*CMe*	*OMe*	*NCO_2Me*
21 (natural)[3]	4.59dd (4.0)	1.78dd (1.0)	2.71dd (15.0)	4.40dd (1.0)	4.22q (6.0)	1.19d	5.00d (10.0)	1.52s	3.19s	3.70s
21 (synthetic)[10]	4.65d (4.0)	1.79dd (0)	2.77d (15.6)	4.49d (0)	4.27q (6.5)	1.20d	5.00bd (9.5)	1.54s	3.24s	3.73s
21 (this paper)	4.67d (4.0)	1.80dd (0)	2.80d (15.6)	4.48d (0)	4.27q (6.5)	1.20d	5.00bd (10.0)	1.54s	3.25s	3.75s
22	4.84d (4.6)	2.46dd (1.0)	2.08d (14.5)	4.22d (1.0)	4.10q (6.4)	1.20d	4.95bd (10.0)	1.89s	3.37s	3.70s

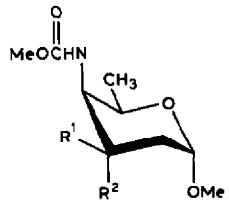
the epimers **18, 19,** and **20** could not be separated, their ^{1}H-n.m.r. data are described in the experimental section. Separation of the oxidation product was effected by preparative t.l.c. (1:1 ethyl acetate–hexane) to give α-D-tetronitroside **21** as syrup, $[\alpha]_D$ +134.5° (*c* 0.24, $CHCl_3$) [lit.[3] $[\alpha]_D$ +130° (MeOH); lit.[10] $[\alpha]_D$ +152° ($CHCl_3$); lit.[15] $[\alpha]_D$ +138° ($CHCl_3$)]; and its 3-epimer **22** as syrup, $[\alpha]_D$ +119.4 (*c* 0.3, $CHCl_3$). In Table II, ^{1}H-n.m.r. data of **21** and **22** are summarized along with those reported for **21**. The path reported here provides a convenient synthesis of **2**.



13 R = OH
14 R = OTs



15 R = N_3
16 R = NH_2
17 R = $NHCO_2Me$



18 R^1, R^2 = CN, OMs
19 R^1, R^2 = $-NHCH_2-$
20 R^1, R^2 = NH_2, CH_3
21 R^1 = CH_3, R^2 = NO_2
22 R^1 = NO_2, R^2 = CH_3

EXPERIMENTAL

General methods. — Melting points are uncorrected. Optical rotations were measured with JASCO DIP-4 polarimeter in chloroform, and ^{1}H- and ^{13}C-n.m.r. spectra recorded in chloroform-*d* with JEOL PS-100 and JEOL FX-90Q spectrometers, respectively, with tetramethylsilane as the internal standard.

*Methyl 2,6-dideoxy-4-*O*-methyl-α-*D*-*lyxo*-hexopyranoside* (**5**). — A mixture of methyl 2,6-dideoxy-α-D-*lyxo*-hexopyranoside (4.16 g, 25.7 mmol) and dibutyltin oxide (6.38 g, 25.7 mmol) in benzene (100 mL) was boiled under reflux overnight with azeotropic removal of water, and evaporated to ~25 mL. Tetrabutylammonium iodide (9.47 g, 25.7 mmol) and benzyl bromide (8.77 g, 51.3 mmol) were added to the solution, the mixture was boiled under reflux overnight, and evaporated. Separation of the residue on a silica gel column (1:2 ethyl acetate–hexane) gave methyl 2,6-dideoxy-3-*O*-benzyl-α-D-*lyxo*-hexopyranoside (5.44 g, 84%).

An ice-cold suspension of the foregoing benzyl derivative (1.91 g, 7.58 mmol) and sodium hydride (400 mg, 16.7 mmol) in $HCONMe_2$ (20 mL) was stirred for 30 min, and then methyl iodide (5.38 g, 37.9 mmol) was added dropwise to it. After stirring for 1 h, the starting material disappeared on t.l.c. Conventional processing of the mixture gave methyl 2,6-dideoxy-3-*O*-benzyl-4-*O*-methyl-α-D-*lyxo*-hexopyranoside (1.72 g, 86%) as a syrup.

To a suspension of aforementioned syrup and 10% palladium-on-carbon (200 mg) in ethanol (20 mL) hydrogen gas was passed with efficient stirring until the starting material was completely consumed; conventional isolation gave **5** (1.1 g) quantitatively; m.p. 97–99° (hexane), $[\alpha]_D$ +179° (*c* 1.0) [lit.[16] m.p. 96–97°; $[\alpha]_D$ +174° (*c* 1.2, ethanol)]; ^{1}H-n.m.r. δ 4.76 (dd, 1 H, $J_{1,2a}$ 3.0, $J_{1,2e}$ 2.0 Hz, H-1), 4.00 (m, 1 H, $J_{2e,3}$ 3.0, $J_{2a,3}$ 10.0 Hz, H-3), 3.86 (dd, 1 H, $J_{4,5}$ 1.0, $J_{5,6}$ 6.0 Hz, H-5), 3.60 and 3.30 (each s, 6 H, OMe × 2), 3.20 (dd, 1 H, $J_{3,4}$ 3.0 Hz, H-4), 2.20 (bs, 1 H, OH), 1.95 and 1.60 (m, 2 H, H-2a and H-2e), and 1.28 (d, 3 H, H-6).

*Methyl 2,6-dideoxy-4-*O*-methyl-α-*D*-threo-*hexopyranosid-3-ulose* (**3**). — To a cooled solution of dimethyl sulfoxide (2.2 g, 28.2 mmol) in dry dichloromethane (30 mL) at −78° was added dropwise oxalyl chloride (2.16 g, 17.0 mmol) in dry dichloromethane (2 mL) with stirring under argon. After 20 min, a solution of **5** (1.00 g, 5.68 mmol) in dry dichloromethane (5 mL) was gradually added to the solution. The mixture was quenched after 20 min by careful addition of triethylamine, poured into ice–water, and extracted with dichloromethane. Conventional processing of the extract gave **3** (980 mg) quantitatively as a syrup $[\alpha]_D$ +133° (*c* 1.0, $CHCl_3$); ν_{max}^{NaCl} 1730 cm^{-1} (C=O); ^{1}H-n.m.r. δ 5.07 (bd, 1 H, $J_{1,2a}$ 4.0, $J_{1,2e}$ 1.0 Hz, H-1), 4.14 (dq, 1 H, $J_{4,5}$ 1.0 Hz, H-5), 3.37 (s, 6 H, OMe × 2), 3.18 (bs, 1 H, H-4), 3.08 (dd, 1 H, $J_{2a,2e}$ 15.0 Hz, H-2e), 2.14 (dd, 1 H, $J_{2e,3}$ 1.0 Hz, H-2a), and 1.34 (d, 3 H, $J_{5,6}$ 6.5 Hz, H-6).

Anal. Calc. for $C_8H_{14}O_4$: C, 55.16; H, 8.10. Found C, 54.94; H, 8.53.

Cyanohydrin formation from **3** *under kinetic and thermodynamic conditions.* — *(a) Kinetic conditions.* To a cooled solution of **3** (980 mg, 5.63 mmol) and triethylamine (2 mL) in dry dichloromethane (50 mL) at 0°, was added in excess a 10% (v/v) solution of hydrogen cyanide in dry dichloromethane with efficient stirring. After monitoring the disappearance of the starting material (30 min) by t.l.c. (2:1 hexane–ethyl acetate), the solution was evaporated under diminished pressure at a bath temperature <20°, and the residual syrup was separated by

column chromatography on silica gel (4:1 hexane–ethyl acetate) to give methyl 3-*C*-cyano-2,6-dideoxy-4-*O*-methyl-α-D-*xylo*-hexopyranoside (**6**, 600 mg) and the D-*lyxo* isomer (**7**, 433 mg) as crystals in 52 and 38% yields, respectively. Compound **6** had m.p. 132–133° (chloroform–hexane), $[\alpha]_D$ +183° (*c* 1.0, $CHCl_3$); ^{1}H-n.m.r. δ 4.88 (dd, 1 H, $J_{1,2a}$ 4.0, $J_{1,2e}$ 2.0 Hz, H-1), 4.17 (bq, 1 H, $J_{4,5}$ 1.0, $J_{5,6}$ 6.4 Hz, H-5), 2.44 (dd, 1 H, $J_{2a,2e}$ 14.0 Hz, H-2a), 2.10 (dd, 1 H, H-2e), and 1.30 (d, 3 H, H-6).

Anal. Calc. for $C_9H_{15}NO_4$: C, 53.72; H, 7.51; N, 6.96. Found: C, 53.60; H, 7.37; N, 6.75.

Compound **7** had m.p. 83–84° (chloroform–hexane), $[\alpha]_D$ +111° (*c* 1.0, $CHCl_3$); ^{1}H-n.m.r. δ 4.76 (dd, 1 H, $_{1,2a}$ 3.4, $J_{1,2e}$ 2.0 Hz, H-1), 4.15 (dq, 1 H, $J_{4,5}$ 1.0, $J_{5,6}$ 6.4 Hz, H-5), 3.62 and 3.33 (each s, 6 H, OMe × 2), 3.32 (bs, 1 H, H-4), 2.23 (dd, 1 H, $J_{2a,2e}$ 13.4 Hz, H-2e), 2.06 (dd, 1 H, H-2a), and 1.33 (d, 3 H, H-6).

Anal. Calc. for $C_9H_{15}NO_4$: C, 53.72; H, 7.51; N, 6.96. Found: C, 53.57; H, 7.26; N, 6.83.

(b) Thermodynamic conditions. — A two-phase solution of **3** (100 mg, 0.57 mmol), potassium cyanide (111 mg, 1.70 mmol), and sodium hydrogencarbonate (143 mg, 1.70 mmol) in 4:1 dichloromethane–water (5 mL) was vigorously stirred at room temperature for 1 h, two layers were separated, and the water layer was extracted with dichloromethane. Conventional processing of the combined organic layers gave **6** (100 mg, 87%) as crystals.

Methyl 3-C-cyano-2,6-dideoxy-3-O-methylsulfonyl-4-O-methyl-α-D-xylo-hexopyranoside (**8**). — To an ice-cooled solution of **6** (100 mg, 0.33 mmol) in dry dichloromethane (5 mL) containing triethylamine (100 mg, 0.99 mmol) and a catalytic amount of 4-dimethylaminopyridine was added with stirring methanesulfonyl chloride (76 mg, 0.66 mmol) dropwise, and the solution was kept for 1 h at room temperature; conventional isolation gave syrupy **8** (136 mg) quantitatively; $[\alpha]_D$ +91° (*c* 1.62, $CHCl_3$); ^{1}H-n.m.r. δ 4.80 (bd, 1 H, $J_{1,2e}$ 4.0, $J_{1,2e}$ 2.0 Hz, H-1), 4.17 (bq, 1 H, $J_{4,5}$ 1.0, $J_{5,6}$ 6.4 Hz, H-5), 3.76, 3.37 and 3.27 (each s, 9 H, OMe × 3), 3.50 (bs, 1 H, H-4), 2.73 (dd, 1 H, $J_{2a,2e}$ 12.0 Hz, H-2e), 2.43 (dd, 1 H, H-2a), and 1.32 (d, 3 H, H-6).

Anal. Calc. for $C_{10}H_{17}NO_6S$: C, 43.01; H, 6.14; N, 5.02: S, 11.46. Found: C, 42.85: H, 5.82; N, 4.74; S, 11.01.

Methyl 3-C-cyano-2,6-dideoxy-3-O-methylsulfonyl-4-O-methyl-α-D-lyxo-hexopyranoside (**9**). — Methylsulfonylation of **7** (300 mg, 1.49 mmol) as in the preceding experiment, and purification of the product on a short column of silica gel (2:1 hexane–ethyl acetate) gave **9** (410 mg) quantitatively as needles; m.p. 87° (chloroform–hexane), $[\alpha]_D$ +163° (*c* 1.0, $CHCl_3$); ^{1}H-n.m.r. δ 4.86 (dd, 1 H, $J_{1,2a}$ 4.0, $J_{1,2e}$ 2.0 Hz, H-1), 4.24 (q, 1 H, $J_{4,5}$ 0, $J_{5,6}$ 6.4 Hz, H-5), 3.71, 3.38 and 3.28 (each s, 9 H, OMe × 3), 3.02 (s, 1 H, H-4), 2.50 (m, 2 H, H-2a and H-2e), and 1.34 (d, 3 H, H-6).

Anal. Calc. for $C_{10}H_{17}NO_6S$: C, 43.01; H, 6.14; N, 5.02; S, 11.46. Found: C, 42.69; H, 5.78; N, 4.81; S, 11.74.

Spiro[aziridine-2,3'-(methyl 2,3,6-trideoxy-4-O-methyl-α-D-xylo-hexopyrano-

side)] (**12**). — A suspension of **9** (160 mg, 0.57 mmol) and lithium aluminium hydride (32 mg, mmol) in anhydrous ether (20 mL) boiled under reflux for 3 h, the excess of reagent was decomposed by adding cold ethyl acetate–water, and the mixture was filtered. The precipitate was washed with ethanol. The combined filtrate and washings were evaporated to give a syrup, which was purified by column chromatography on silica gel (5:1 ethyl acetate–ethanol) to give **12** (53 mg, 50%) as a syrup; $[\alpha]_D$ +172° (*c* 1.0, $CHCl_3$); ^{1}H-n.m.r. δ 4.83 (bd, 1 H, $J_{1,2a}$ 4.0, $J_{1,2e}$ 1.0 Hz, H-1), 4.28 (dq, 1 H, $J_{4,5}$ 1.6, $J_{5,6}$ 6.4 Hz, H-5), 3.47 and 3.39 (each s, 6 H, OMe × 2), 3.38 (bs, 1 H, H-4), 2.70 (dd, 1 H, $J_{2a,2e}$ 14.4 Hz, H-2a), 2.44 (bs, 1 H, NH), 1.78 and 1.74 (each s, 2 H, NCH_2), 1.24 (d, 3 H, H-6), and 0.95 (dd, 1 H, H-2e).

Anal. Calc. for $C_9H_{17}NO_3$: C, 57.73; H, 9.15; N, 7.48. Found: C, 57.46; H, 8.62; N, 7.17.

*Methyl 2,3,6-trideoxy-3-*C*-methyl-4-*O*-methyl-3-nitro-α-*D*-xylo-hexopyranoside* (**11**). — A solution of **12** (150 mg, 0.80 mmol) in methanol (20 mL) was hydrogenolyzed under 90 atm pressure of hydrogen in the presence of Raney nickel (1.0 g) for 3 days. The mixture was filtered, and the filtrate evaporated to give 3-amino-2,3,6-trideoxy-3-*C*-methyl-4-*O*-methyl-α-D-*xylo*-hexopyranoside (**10**) as a syrup in good yield. To a solution of the syrup in dichloromethane (2 mL) was added *m*-chloroperoxybenzoic acid (515 mg, 3.00 mmol) in three portions, and the mixture was boiled under reflux for 40 min, poured into 10% sodium sulfite solution and extracted with chloroform. Conventional processing of the extract, and purification of the product by preparative t.l.c. (4:1 benzene–methanol) gave **11** (71 mg) in 41% overall yield. It was recrystallized from hexane; m.p. 84–87°, $[\alpha]_D$ +174° (*c* 1.0, $CHCl_3$); ν_{max}^{KBr} 1545 cm^{-1} (NO_2), ^{1}H-n.m.r. δ 4.72 (dd, 1 H, $J_{1,2a}$ 3.6, $J_{1,2e}$ 1.0 Hz, H-1), 4.20 (bq, 1 H, $J_{3,5}$ 1.0, $J_{5,6}$ 6.5 Hz, H-5), 3.74 (bs, 1 H, H-4), 3.65 and 3.27 (each s, H, OMe × 2), 2.65 (dt, 1 H, $J_{2e,4}$ 1.0, $J_{2a,2e}$ 14.8 Hz, H-2e), 2.04 (dd, 1 H, H-2a), 1.63 (s, 3 H, CMe), and 1.33 (d, 3 H, H-6).

Anal. Calc. for $C_9H_{17}NO_5$: C, 49.30; H, 7.82; N, 6.39. Found: C, 49.17; H, 7.61; N, 6.47.

D-*Rubranitrose* (**1**). — A solution of **11** (31.4 mg, 0.14 mmol) in 1,4-dioxane (3 mL) and 0.05M sulfuric acid (3 mL) was kept for 6 h at 85°, made neutral with sodium hydrogencarbonate, and extracted with chloroform. Conventional processing of the extract gave syrupy **1** quantitatively, and it was crystallized from dichloromethane–hexane. The physical properties of **1** have already been given.

*Methyl 2,6-dideoxy-4-*O*-tolylsulfonyl-α-*D*-ribo-hexopyranoside* (**13**). — To an ice-cooled solution of methyl 2,6-dideoxy-α-D-*ribo*-hexopyranoside (1.0 g, 6.2 mmol) in dry pyridine (20 mL) was added slowly a solution of *p*-toluenesulfonyl chloride (1.3 g, 6.8 mmol) in dry pyridine (10 mL) with efficient stirring. The mixture was kept for 3 days at 0°. Conventional isolation gave a syrup that was purified by column chromatography to give crystalline mono- **13** and di-sulfonate **14** (methyl 2,6-dideoxy-3,4-di-*O*-*p*-tolylsulfonyl-α-D-*ribo*-hexopyranoside), in 67 (1.3 g) and 10% (0.29 g) yields, respectively. Compound **13** had m.p. 115–120°,

$[\alpha]_D$ +146.6° (*c* 1.0, $CHCl_3$) [lit.[17] m.p. 135°, $[\alpha]_D$ +145°]; ν_{max}^{KBr} 3840 (OH), 1360 cm^{-1} (SO_2); ^{1}H-n.m.r. δ 7.83 and 7.32 (each d, 4 H, *J* 8.0 Hz, Ph), 4.74 (dd, 1 H, $J_{1,2a}$ 3.0 Hz, H-1), 4.24 (dd, 1 H, $J_{3,4}$ 2.6 Hz, H-4), 4.08 (dq, 1 H, $J_{4,5}$ 9.8 Hz, H-5), 4.00 (ddt, 1 H, $J_{2a,3}$ 3.0 Hz, H-3), 3.40 (d, 1 H, $J_{3,OH}$ 10.0 Hz, OH), 3.37 (s, 3 H, OMe), 2.46 (s, 3 H, $PhCH_3$), 2.12 (ddd, 1 H, $J_{1,2e}$ 2.0, $J_{2a,2e}$ 15.0 Hz, H-2e), 1.87 (dt, 1 H, $J_{2e,3}$ 3.0 Hz, H-2a), and 1.17 (d, 1 H, $J_{5,6}$ 6.0 Hz, H-6).

Anal. Calc. for $C_{14}H_{20}O_6S$: C, 53.15; H, 6.37; S, 10.11. Found: C, 53.27; H, 6.19; S, 9.83.

Compound **14** had m.p. 86° (dec), $[\alpha]_D$ +115° (*c* 1.0, $CHCl_3$); ν_{max}^{KBr} 1360 and 1380 cm^{-1} (SO_2); ^{1}H-n.m.r. δ 7.80, 7.40, 7.28, and 7.28 (each d, 8 H, *J* 8.0 Hz, Ph), 4.93 (dt, 1 H, $J_{2a,3}$ 3.0 Hz, H-3), 4.60 (dd, 1 H, $J_{1,2a}$ 4.0 Hz, H-3 and H-4), 3.28 (s, 3 H, OMe), 2.44 (s, 6 H, $PhCH_3$), 2.30 (ddd, 1 H, $J_{1,2e}$ 1.0, $J_{2a,2e}$ 15.0 Hz, H-2e), 1.86 (ddd, 1 H, $J_{2e,3}$ 3.4 Hz, H-2a), and 0.98 (d, 1 H, $J_{5,6}$ 6.0 Hz, H-6).

Anal. Calc. for $C_{21}H_{26}O_8S_2$: C, 53.60; H, 5.57; S, 13.63. Found: C, 53.37; H, 5.61; S, 13.47.

*Methyl 4-azido-2,4,6-trideoxy-α-*D-xylo-*hexopyranoside* (**15**). — A mixture of **13** (3.0 g, 9.5 mmol) and sodium azide (3.09, 46 mmol) in dry *N,N*-dimethylformamide (40 mL) was heated overnight at 85°. The solvent was evaporated off under diminished pressure, and the residue was extracted with ether. The extract afforded a syrup that was purified by column chromatography to give **15** (1.42 g) in 80% yield; $[\alpha]_D$ +141° (*c* 1.0, $CHCl_3$); ν_{max}^{NaCl} 2130 cm^{-1} (N_3); ^{1}H-n.m.r. δ 4.81 (d, 1 H, $J_{1,2a}$ 3.0 Hz, H-1), 4.30 (dq, 1 H, $J_{4,5}$ 2.0 Hz, H-5), 4.04 (ddt, 1 H, $J_{2a,3}$ 4.0 Hz, H-3), 3.90 (d, 1 H, $J_{3,OH}$ 10 Hz, OH), 3.40 (s, 3 H, OMe), 3.40 (s, 1 H, $J_{3,4} = J_{2e,4}$ 1.3 Hz, H-4), 2.13 (dt, 1 H, $J_{2e,3}$ 4.0, $J_{2a,2e}$ 14.0 Hz, H-2a), 1.85 (ddd, 1 H, $J_{1,2e}$ 1.3 Hz; H-2e), and 1.32 (d, 1 H, $J_{5,6}$ 6.4 Hz, H-6).

Anal. Calc. for $C_7H_{13}N_3O_3$: C, 44.91; H, 7.00; N, 22.45. Found: C, 44.95; H, 6.73; N, 22.17.

*Methyl 4-amino-2,4,6-trideoxy-α-*D-xylo-*hexopyranoside* (**16**). — The azide **15** (2.5 g) was catalytically reduced in ethanol (50 mL) by bubbling hydrogen gas in the presence of 10% Pd/C (0.5 g). After 3 h, t.l.c. indicated the disappearance of starting material. The mixture was filtered and the filtrate evaporated to give **16** (2.0 g) in 93% yield, m.p. 61–62° (needles), $[\alpha]_D$ +142° (*c* 1.0, $CHCl_3$); ν_{max}^{KBr} 3330 and 3270 cm^{-1} (NH_2); ^{1}H-n.m.r. δ 4.77 (dd, 1 H, $J_{1,2a}$ 3.6 Hz, H-1), 4.28 (dq, 1 H, $J_{4,5}$ 2.0 Hz, H-5), 3.80 (dt, 1 H, $J_{2a,3}$ 3.6 Hz, H-3), 3.38 (s, 3 H, OMe), 2.67 (bs, 1 H, $J_{3,4}$ 3.0 Hz, H-4), 2.37 (bs, 3 H, OH and NH_2), 2.07 (dt, 1 H, $J_{1,2e}$ 1.0, $J_{2a,2e}$ 14.8 Hz, H-2e), 1.77 (ddd, 1 H, $J_{2e,3}$ 3.0 Hz, H-2a), and 1.22 (d, 1 H, $J_{5,6}$ 6.4 Hz, H-6).

Anal. Calc. for $C_7H_{15}NO_3$: C, 52.15; H, 9.38; N, 8.69. Found: C, 52.29; H, 9.57; N, 8.90.

*Methyl 2,4,6-trideoxy-4-*O*-methoxycarbonylamino-α-*D-xylo-*hexopyranoside* (**17**). — To a solution of **16** (0.5 g, 3.1 mmol) and sodium hydrogencarbonate (1 g) in methanol (10 mL), was added methyl chloroformate (586 mg, 6.2 mmol) dropwise at 0° with stirring. After 3 h, the undissolved material was removed by

filtration, the filtrate evaporated under diminished pressure, and the residue extracted with chloroform. The extract was washed with water, dried over magnesium sulfate, and evaporated to a solid that was recrystallized from benzene to give **17** (0.65 g) in 96% yield; m.p. 100–102° (prisms), $[\alpha]_D$ +123° (*c* 1.0, $CHCl_3$); ν_{max}^{KBr} 3510 (OH), 3300 (NH), and 1720 cm^{-1} (C=O); ^{1}H-n.m.r. δ 5.04 (d, 1 H, $J_{4,NH}$ 9.0 Hz, NH), 4.77 (bs, 1 H, H-1), 4.41 (dq, 1 H, $J_{4,5}$ 1.6 Hz, H-5), 3.92 (ddt, 1 H, $J_{2a,3}$ 3.0 Hz, H-3), 3.70 (s, 3 H, Me in carbamoyl), 3.60 (bs, 1 H, $J_{3,4}$ 3.0 Hz, H-4), 3.57 (d, 1 H, $J_{3,OH}$ 9.0 Hz, OH), 3.37 (s, 3 H, OMe), 1.90 (m, 2 H, $J_{2e,3}$ 3.0 Hz, H-2a and H-2e), and 1.18 (d, 1 H, $J_{5,6}$ 6.4 Hz, H-6).

Anal. Calc. for $C_9H_{17}NO_5$: C, 49.30; H, 7.82; N, 6.39. Found: C, 49.25; H, 7.61; N, 6.47.

*Methyl 2,4,6-trideoxy-4-methoxycarbonylamino-α-*D-threo*-hexopyranosid-3-ulose* (**4**). — Reaction of **17** (200 mg, 0.91 mmol) in dichloromethane (5 mL) with oxalyl chloride (346 mg) in dichloromethane (2 mL) and dimethyl sulfoxide (355 mg, 4.5 mmol) dissolved in dichloromethane (20 mL) and subsequent treatment with triethylamine (460 mg, 4.5 mmol), as described for **3** gave syrupy **4** (195 mg) quantitatively; it crystallized on cooling; m.p. 59–60°, $[\alpha]_D$ +153° (*c* 1.1, $CHCl_3$); ν_{max}^{KBr} 1740 (C=O), and 1650 cm^{-1} (NHC=O); ^{1}H-n.m.r. δ 5.56 (d, 1 H, $J_{NH,4}$ 6.0 Hz, NH), 4.95 (t, 1 H, $J_{1,2a}$ 4.0 Hz, H-1), 4.70–4.20 (m, 2 H, H-4 and H-5), 3.68 (s, 3 H, $NHCO_2Me$), 3.40 (s, 3 H, OMe), 2.93 (dd, 1 H, H-2a), 2.54 (dd, 1 H, $J_{1,2e}$ 4.0, $J_{2a,2e}$ 15 Hz, H-2e), and 1.22 (d, 3 H, $J_{5,6}$ 6.4 Hz, H-6).

Anal. Calc. for $C_9H_{15}NO_5$: C, 49.76; H, 6.96; N, 6.45. Found: C, 49.93; H, 6.77; N, 6.47.

*Methyl 3-*C*-cyano-2,4,6-trideoxy-4-methoxycarbonylamino-3-*O*-methylsulfonyl-α-*D*-xylo and* lyxo*-hexopyranoside* (**18**). — *(a) Kinetic conditions.* Treatment of **4** (195 mg, 0.9 mmol) in dichloromethane (20 mL) containing triethylamine (0.05 mL) with a 10% (v/v) solution of hydrogen cyanide in dichloromethane, followed by methylsulfonylation with methanesulfonyl chloride in the presence of dimethylaminopyridine (catalytic) and triethylamine (270 mg), as described earlier, gave a syrupy mixture (1.2:1, by ^{1}H-n.m.r.) of cyanomesyl derivatives **18** (260 mg), in 95% yield; these could not be separated.

(b) Thermodynamic conditions. A two-phase mixture of **4** (100 mg, 0.46 mmol), potassium cyanide (90 mg, 1.38 mmol) and sodium hydrogencarbonate (116 mg, 1.38 mmol) in 4:1 dichloromethane–water (5 mL) was vigorously stirred for 1 h at room temperature. The two layers were separated, and the water layer was extracted with dichloromethane. Conventional processing of the combined organic layers gave a syrupy mixture of cyanohydrin derivatives, which could not be separated. Treatment of the foregoing syrup with methanesulfonyl chloride (100 mg, 0.91 mmol) and triethylamine (140 mg, 1.38 mmol) in the presence of dimethylaminopyridine (catalytic) as already mentioned gave a syrupy mixture (1.2:1 by ^{1}H-n.m.r.) of cyanomesyl derivatives **18** (116 mg) in 79% yield from **4**; ^{1}H-n.m.r. δ 5.37 (d, 1 H, $J_{NH,4}$ 9.0 Hz, NH), 4.85 (d, 1 H, $J_{1,2e}$ 0, $J_{1,2a}$ 4.0 Hz, H-1), 4.47 (q, 1 H, $J_{4,5}$ 0, $J_{5,6}$ 6.4 Hz, H-5), 4.33 (d, 1 H, H-4), 3.76 (s, 3 H, Me in

carbamoyl), 3.40 (s, 3 H, OMe), 3.23 (s, 3 H, OMs), 3.82 (d, 1 H, $J_{2a,2e}$ 14.0 Hz, H-2e), 2.24 (dd, 1 H, H-2a), 1.27 (d, 3 H, H-6); δ 5.46 (d, 1 H, $J_{NH,4}$ 9.0 Hz, NH), 4.78 (d, 1 H, $J_{1,2e}$ 0, $J_{1,2a}$ 4.6 Hz, H-1), 4.45 (q, 1 H, $J_{4,5}$ 0, $J_{5,6}$ 6.4 Hz, H-5), 4.21 (d, 1 H, H-4), 3.80 (s, 3 H, Me in carbamoyl), 3.37 (s, 3 H, OMs), and 3.93 (d, 1 H, H-6).

*Methyl 2,3,4,6-tetradeoxy-4-methoxycarbonylamino-3-*C*-methyl-3-nitro-α-*D*-lyxo and* xylo*-hexopyranoside* (**21** and **22**). — A suspension of **18** (500 mg, 1.55 mmol) and lithium aluminium hydride (125 mg, 3.3 mmol) in anhydrous ether (60 mL) was kept overnight at 0°. Conventional isolation gave a syrup that was purified by column chromatography to give a mixture of spiro[aziridine-2,3′-(methyl 2,3,4,6-tetradeoxy-4-methoxycarbonylamino-α-D-*lyxo* and *xylo*-hexopyranosides] (**19**) as a syrup (138 mg) in 39% yield, which could not be separated; ^{1}H-n.m.r. δ 5.66 (d, 0.6 H, $J_{NH,4}$ 9.0 Hz, NH), 5.46 (d, 0.4 H, $J_{NH,4}$ 9.0 Hz, NH), 4.76 (d, 1 H, $J_{1,2e}$ 0, $J_{1,2a}$ 4.0 Hz, H-1), 4.25 (dq, 0.6 H, $J_{4,5}$ 1.5, $J_{5,6}$ 6.4 Hz, H-5), 4.42 (dq, 0.4 H, $J_{4,5}$ 1.5, $J_{5,6}$ 6.4 Hz, H-5), 3.67 (s, 3 H, Me in carbamoyl), 3.37 (s, 1.8 H, OMe), 3.33 (s, 1.2 H, OMe), 3.06 (bd, 0.6 H, H-4), 3.00 (bd, 0.4 H, H-4), 2.27 (dd, 0.6 H, $J_{2a,2e}$ 14.0 Hz, H-2a), 2.48 (dd, 0.4 H, $J_{2a,2e}$ 14.0 Hz, H-2a), 1.85 (bs, 1 H, NH in aziridine), 1.85 (s, 1.2 H, CH_2 in aziridine), 1.54 (s, 0.8 H, CH_2 in aziridine), 1.16 (d, 1.8 H, H-6), 1.14 (d, 1.2 H, H-6), 0.97 and 1.14 (each d, H-2e).

A solution of **19** (50 mg, 0.22 mmol) in methanol (5 mL) was hydrogenolyzed under 90 atm hydrogen in the presence of Raney nickel (1 g) for 3 days. The mixture was filtered and the filtrate evaporated to give an epimeric mixture of 3-amino-2,3,6-trideoxy-3-*C*-methyl-4-*O*-methyl-α-D-*lyxo* and *xylo*-hexopyranosides (**20**) as a syrup (40 mg) in 79% yield; ^{1}H-n.m.r. δ 5.10 (d, 1 H, $J_{NH,4}$ 10.0 Hz, NH), 4.70 (bd, 1 H, $J_{1,2e}$ 1.0, $J_{1,2a}$ 4.0 Hz, H-1), 4.18 (q, 1 H, $J_{5,6}$ 6.4 Hz, H-5), 3.73 (s, 3 H, Me in carbamoyl), 3.48 (s, 3 H, OMe), 3.35 (d, 1 H, H-4), 1.66 (d, 1 H, H-2e), 1.47 (dd, 1 H, $J_{2a,2e}$ 12.0 Hz, H-2a), 1.39 (s, 3 H, CMe), and 1.16 (d, 3 H, H-6).

To a solution of the methyl-branched amino sugars **20** (50 mg, 0.217 mmol) in dichloromethane (10 mL) was added *m*-chloroperoxybenzoic acid (110 mg, 0.65 mmol) in three portions, and the mixture was boiled under reflux for 35 min, poured into 10% sodium sulfate solution and extracted with chloroform. Conventional processing of the extract, and purification of the product by preparative t.l.c. (1:1 hexane–ethyl acetate) gave the corresponding methyl-branched nitro sugar derivatives **10** (11 mg) and **11** (15 mg) in 47% yield. The physical properties of **21** and **22** are described elsewhere.

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