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SYNTHESIS OF 6-AZIDO- AND 6-AMINO-2,3,6-TRIDEOXY-D-*erythro*-HEXOSE*

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ABSTRACT

The synthesis of 6-azido- and 6-amino-2,3,6-trideoxy-D-*erythro*-hexose (**19** and **22**) and several of their derivatives is described. Hydrogenation and hydrogenolysis of methyl 4,6-*O*-benzylidene-2,3-dideoxy-α-D-*erythro*-hex-2-enopyranoside (**1**) gave methyl 2,3-dideoxy-α-D-*erythro*-hexopyranoside (**3**), which was transformed into methyl 6-azido-2,3,6-trideoxy-α-D-*erythro*-hexopyranoside (**9**) *via* the 6-tosylate or the 6-*O*-tris(dimethylamino)phosphonium bromide derivative. The 4-acetate (**8**) of **9** was also prepared from methyl 4-*O*-acetyl-2,3-dideoxy-6-*O*-toluene-*p*-sulphonyl-α-D-*erythro*-hexopyranoside (**7**). Hydrogenation of **8** in methanol–acetic anhydride gave the diacetate **12**. Reduction of **8** in methanol gave a mixture (1:2) of unstable 4-*O*-acetyl-6-amino-2,3,6-trideoxy-α-D-*erythro*-hexopyranoside (**10**) and methyl 6-acetamido-2,3,6-trideoxy-α-D-*erythro*-hexopyranoside. Reduction of **9** afforded methyl 6-amino-2,3,6-trideoxy-α-D-*erythro*-hexopyranoside (**13**). Transformation of **1**, *via* the 6-bromo-4-*O*-benzoyl derivative **15**, into methyl 6-azido-4-*O*-benzoyl-2,3,6-trideoxy-α-D-*erythro*-hexopyranoside (**16**), followed by *O*-debenzoylation, afforded **9**. Hydrogenation of **16** in the presence of acetic anhydride gave methyl 6-acetamido-4-*O*-benzoyl-2,3,6-trideoxy-α-D-*erythro*-hexopyranoside (**17**), which yielded **11** on *O*-debenzoylation. Acid hydrolyses of **3** and **9** liberated the corresponding free sugars **18** and **19**. Hydrolysis of **11** gave 6-acetamido-2,3,6-trideoxy-D-*erythro*-hexopyranose (**20**) and minor amounts of the 1,6-anhydro derivative **21**. Acetolysis of **11** afforded 6-acetamido-4-*O*-acetyl-1,6-anhydro-2,3,6-trideoxy-β-D-*erythro*-hexopyranose (**22**), the *O*-deacetylation of which yielded a mixture of the bicyclic compound **21** (major product) and **20**.

INTRODUCTION

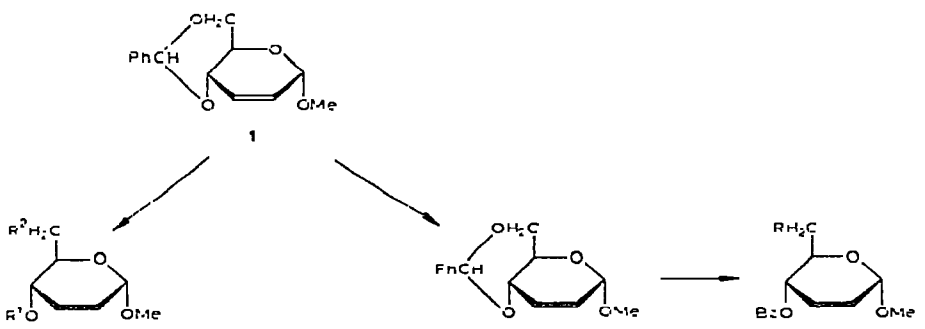
The chemistry of aminopolydeoxyhexoses has not been systematically investigated, although they are components of some antibiotics[1] and of polysaccharides

*Amino Sugars: Part I.

of biological interest[2]. We now report the preparation of 6-amino-2,3,6-trideoxy-D-*erythro*-hexopyranose.

RESULTS AND DISCUSSION

Methyl 4,6-*O*-benzylidene-2,3-dideoxy-α-D-*erythro*-hex-2-enopyranoside[3] (**1**) was catalytically hydrogenated (palladium catalyst) to yield syrupy methyl 2,3-dideoxy-α-D-*erythro*-hexopyranoside (**3**). The reaction goes through the intermediates **14** and the 4-benzyl ether **2** which can be isolated if the hydrogenation is stopped before completion. The structure of **2** was ascertained by using n.m.r. spectroscopy and the shift reagent[4] Eu(fod)$_3$. Treatment of **3** with 1 mol. of toluene-*p*-sulphonyl chloride in pyridine gave crystalline methyl 2,3-dideoxy-6-*O*-toluene-*p*-sulphonyl-α-D-*erythro*-hexopyranoside (**6**, 65%); a 77% yield was obtained by using *N*-tosylimidazole. Ready displacement of the toluene-*p*-sulphonyloxy group in **7** occurred with sodium azide in *N*,*N*-dimethylformamide, affording methyl 4-*O*-acetyl-6-azido-2,3,6-trideoxy-α-D-*erythro*-hexopyranoside (**8**). Reduction of **8** over palladium–charcoal in methanol containing acetic anhydride gave **12**; if the acetic anhydride was omitted, a 1:2 mixture of methyl 4-*O*-acetyl-6-amino-2,3,6-trideoxy-α-D-*erythro*-hexopyranoside (**10**) and methyl 6-acetamido-2,3,6-trideoxy-α-D-*erythro*-hexopyranoside (**11**) was obtained. The rearrangement **10** → **11** occurred spontaneously.



	R^1	R^2
2	Bn	OH
3	H	OH
4	Ac	OAc
5	*p*-$O_2N \cdot C_6H_4 \cdot CO$	*p*-$O_2N \cdot C_6H_4 \cdot CO_2$
6	H	TsO
7	Ac	TsO

	R^1	R^2
8	Ac	N_3
9	H	N_3
10	Ac	NH_2
11	H	NHAc
12	Ac	NHAc
13	H	NH_2

14

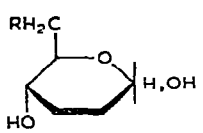
15 R = Br
16 R = N_3
17 R = NHAc

The azido compound **9** was obtained by reaction of **6** with sodium azide in *N*,*N*-dimethylformamide (56% yield from **1**) or by treatment of **3** in *N*,*N*-dimethylformamide with hexamethylphosphoric triamide and carbon tetrabromide[5] followed by azide displacement of the resulting phosphonium compound (76% yield from **1**).

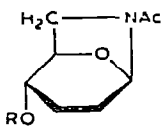
Catalytic reduction of **9** gave 6-amino-2,3,6-trideoxy-α-D-*erythro*-hexopyranoside (**13**) as the crystalline hydrochloride (61.6% overall yield by the phosphonium route).

An alternative route involved azide displacement on methyl 4-*O*-benzoyl-6-bromo-2,3,6-trideoxy-α-D-*erythro*-hexopyranoside[6] (**15**) to give the 6-azido-4-*O*-benzoyl derivative **16** which, upon catalytic *O*-debenzoylation, produced **9** (31% from **1**, *cf.* 76% by the route described above). Hydrogenation of **16** in methanol–acetic anhydride gave methyl 6-acetamido-4-*O*-benzoyl-2,3,6-trideoxy-α-D-*erythro*-hexopyranoside (**17**), *O*-debenzoylation of which gave **11**.

Acid hydrolysis of **3** and **9** produced the free sugars **18** and **19**, but **11** gave two products that were separated by column chromatography. The main component was a reducing syrup for which the elemental analysis and i.r. and p.m.r. spectroscopic data were consistent with the acetamidotrideoxyhexopyranose structure **20**. The minor product was crystalline and non-reducing, and was formulated as 6-acetamido-1,6-anhydro-2,3,6-trideoxy-β-D-*erythro*-hexopyranose (**21**) since the i.r. and n.m.r. spectroscopic data (see Experimental) were characteristic of a sugar having a tertiary acetamido group built into a ring[7]. Both **20** and **21** gave the same 2,4-dinitrophenylhydrazone.



18 R = OH
19 R = N_3
20 R = NHAc



21 R = H
22 R = Ac

Acid hydrolysis of **13** gave a complex mixture of products.

Attempted acetolysis of **3** and **9** gave the acetylated methyl glycosides **4** and **8**, respectively. Complex mixtures resulted when concentrations of acid higher than 1% were used. Acetolysis of **11** gave **22**, catalytic *O*-deacetylation of which gave a mixture of the hexopyranose **20** and its 1,6-anhydro derivative **21**, the latter being the main product.

EXPERIMENTAL

General methods. — Melting points are uncorrected. Solutions were dried with anhydrous sodium sulphate, and concentrated under diminished pressure at <40°. Light petroleum refers to the fraction having b.p. 60–80°. Identification of products was based on mixture m.p. and comparison of i.r. spectra and chromatographic mobilities. T.l.c. was performed on Silica Gel HF_{254} (Merck) or Silica Gel chromatoplates (Eastman Kodak). Detection was effected by charring with sulphuric acid or by

exposure to u.v. light of 254 nm. Optical rotations at 5461 Å were determined for solutions in chloroform with a Bendix NPL polarimeter; $[\alpha]_D$ values were measured with a Bellingham and Stanley Ltd. instrument. I.r. spectra were obtained with a Perkin–Elmer 621 spectrophotometer. The p.m.r. spectra (100 MHz) were recorded for solutions in chloroform-*d* (internal Me_4Si), unless otherwise stated, with a Varian XL spectrometer.

Acetates, *p*-nitrobenzoates, and 2,4-dinitrophenylhydrazones were prepared by conventional procedures.

Methyl 2,3-dideoxy-α-D-erythro-*hexopyranoside* (**3**). — A solution of methyl 4,6-*O*-benzylidene-2,3-dideoxy-α-D-*erythro*-hex-2-enopyranoside (**1**; 50 g, 0.2 mol) in dry methanol (1 litre) containing 10% palladium-on-charcoal (9 g) was hydrogenated at 4 atmos. at room temperature. After 1 h, t.l.c. (ethyl acetate) showed that no starting material (R_F 0.85) remained and that methyl 4,6-*O*-benzylidene-2,3-dideoxy-α-D-*erythro*-hexopyranoside (**14**, R_F 0.67) was present. A second product, methyl 4-*O*-benzyl-2,3-dideoxy-α-D-*erythro*-hexopyranoside (**2**, R_F 0.57) appeared subsequently. After 48 h, **3** (R_F 0.18) was the only product detected. The mixture was filtered, and concentrated to yield a syrup (32.0 g, 98%) which was eluted from silica gel with ethyl acetate–ethanol (8:1) to give **3**, $[\alpha]_{5461}^{22}$ +115° (*c* 1.6), R_F 0.10 (chloroform) and 0.37 (ethyl acetate–ethanol, 8:1); ν_{max}^{film} 3390 (OH), 1644, 1212, 1202, 1123, 1070, 1040, 995, 971, 941, 900, 878, 862, and 839 cm^{-1}. P.m.r. data: δ 1.80 (m, 4 H, H-2,2′,3,3′), 2.86 (bm, OH), 3.32 (s, 3 H, OMe), 3.55 (m, 2 H, H-4,5), 3.79 (m, 2 H, H-6,6′), and 4.67 (m, 1 H, H-1).

Anal. Calc. for $C_7H_{14}O_4$: C, 51.86; H, 8.70. Found: C, 51.95; H, 8.80.

When the hydrogenation was stopped after 2 h and the reaction mixture was worked-up as indicated above, **14** (85%) was obtained; m.p. 82–84° (from ether–hexane), $[\alpha]_{5461}^{21}$ +125° (*c* 0.52); lit.[6], m.p. 82–84°, $[\alpha]_D$ +118°.

When the mixture, after hydrogenation for 18 h, was worked-up and the product eluted from silica gel with ethyl acetate, syrupy **2** (80%) was obtained; $[\alpha]_D^{20}$ +151° (*c* 1.2); $\nu_{max}^{CHCl_3}$ 3440 (OH), 1490, 1450, 1370, 1217, 1175, 1130, 1085, 1050, 978, 950, 910, 885 870, and 845 cm^{-1}. P.m.r. data: δ 1.78 (m, 4 H, H-2,2′,3,3′), 2.17 (bs, 1 H, OH), 3.33 (s, 3 H, OMe), 3.67 (m, 2 H, H-4,5), 3.76 (m, 2 H, H-6,6′), 4.55 (q, 2 H, PhCH_2), 4.66 (m, 1 H, H-1), and 7.32 (s, 5 H, Ph).

The benzyloxy group was shown to be at C-4 by the use of $Eu(fod)_3$ (europium 1,1,1,2,2,3,3-heptafluoro-7,7-dimethyl-4,6-octanedionate) as shift reagent in the chloroform-*d* solution of **2**.

Anal. Calc. for $C_{14}H_{21}O_4$: C, 66.38; H, 8.36. Found: C, 66.26; H, 8.50.

The 4,6-diacetate (**4**) of **3** had b.p. 100°/2 Torr; $[\alpha]_D^{20}$ +109°, $[\alpha]_{5461}^{22}$ +157° (*c* 1); R_F 0.60 (ethyl acetate); ν_{max}^{film} 1745 (AcO), 1227 (AcO), 1170, 1122, 1077, 1040, 990, 950, and 843 cm^{-1}. P.m.r. data: δ 1.80 (m, 4 H, H-2,2′,3,3′), 2.03, 2.07 (2 s, 6 H, 2 AcO), 3.35 (s, 3 H, OMe), 3.87 (m, 2 H, H-4,5), 4.20 (m, 2 H, H-6,6′), and 4.70 (m, 1 H, H-1).

Anal. Calc. for $C_{11}H_{18}O_6$: C, 53.65; H, 7.37. Found: C, 53.50; H, 7.45.

The 4,6-bis(*p*-nitrobenzoate) (**5**) of **3** had m.p. 153–155° (from benzene), $[\alpha]_{5461}^{21}$ +185° (*c* 0.5).

Anal. Calc. for $C_{21}H_{20}N_2O_{10}$: C, 54.78; H, 4.39; N, 6.12. Found: C, 54.90; H, 4.48; N, 6.32.

2,3-Dideoxy-D-erythro-*hexopyranose* (**18**). — A solution of **3** (0.6 g) in 0.1M HCl (15 ml) was heated at 100° for 25 min. The cooled mixture was neutralized with Amberlite IR-400(CO_3^{2-}) resin, filtered, and concentrated. The syrupy residue (0.5 g, 97%) was eluted from silica gel with ether–methanol (9:1) to give **18** (0.24 g, 43%): $[\alpha]_{5461}^{20}$ +38°, $[\alpha]_D^{20}$ +35.5° (*c* 0.54); R_F 0.25 (ether–methanol, 9:1); ν_{max}^{film} 3350 (OH), 1640, 1436, 1307, 1207, 1112, 1054, 974, 930, 903, 862, 840, and 818 cm^{-1}.

Anal. Calc. for $C_6H_{12}O_4$: C, 48.64; H, 8.16. Found: C, 48.61; H, 7.92.

The 2,4-dinitrophenylhydrazone of **18** had m.p. 134–135° (from ethanol), $[\alpha]_{5461}^{25}$ −10° (*c* 0.5, pyridine).

Anal. Calc. for $C_{12}H_{16}N_4O_7$: C, 43.90; H, 4.91; N, 17.07. Found: C, 43.97; H, 5.10; N, 17.27.

*Methyl 2,3-dideoxy-6-*O*-toluene*-p*-*sulphonyl*-α-D-erythro-*hexopyranoside* (**6**). — (*a*) A mixture of **3** (31 g, 0.191 mol) and toluene-*p*-sulphonyl chloride (36.29 g, 0.191 mol) in dry pyridine (150 ml) was stored at room temperature for 0.5 h. Water (2 ml) was then added, and the solvents were evaporated to give a syrup that was partitioned between water and ether (1:1, 500 ml). The aqueous layer was extracted with ether (3 × 50 ml), and the extracts were dried, concentrated to a small volume, and stored at 0°. The product was collected, washed with light petroleum, dried *in vacuo* at 45°, and recrystallised from benzene–light petroleum to give **6** (39.2 g, 65%), m.p. 100–102.5°, $[\alpha]_D^{20}$ +78° (*c* 1), R_F 0.55 (ethyl acetate); $\nu_{max}^{CDCl_3}$ 3520 (OH), 1595 (phenyl), 1190 and 1175 (–SO_2–), 1130, 1055, 950, 910, and 815 cm^{-1}. P.m.r. data: δ 1.75 (m, 4 H, H-2,2′,3,3′), 2.43 (s, 3 H, Ph–*Me*), 3.27 (s, 3 H, OMe). 3.60 (m, 2 H, H-4,5), 4.27 (m, 2 H, H-6,6′), 4.60 (m, 1 H, H-1), 7.35 (m, 2 H, aromatic), and 7.80 (m, 2 H, aromatic).

Anal. Calc. for $C_{14}H_{20}O_6S$: C, 53.16; H, 6.37; S, 10.12. Found: C, 53.26; H, 6.57; S, 10.39.

(*b*) A mixture of **3** (3.24 g, 20 mmol) and toluene-*p*-sulphonylimidazole (4.16 g, 20 mmol) in dry *p*-dioxane (25 ml) was stirred for 3 h at 35°. Evaporation of the solvent and treatment of the residue with water gave an oil that was extracted with ether (3 × 20 ml). The extracts were dried, concentrated to a small volume, and stored at 0° overnight. The product was recrystallized from benzene–light petroleum to give **6** (4.74 g, 75%), m.p. 100–102.5°, R_F 0.55 (ethyl acetate).

The 4-acetate (**7**) of **6** had m.p. 92–94° (from benzene–light petroleum), $[\alpha]_D^{20}$ +117° (*c* 1): R_F 0.72 (ethyl acetate), 0.64 (3:1, chloroform–ethyl acetate); $\nu_{max}^{CHCl_3}$ 1730 (AcO), 1595 (phenyl), 1230 (AcO), 1190 and 1175 (–SO_2–), 1130, 1050 (glycoside), 960, 880, and 670 cm^{-1}. P.m.r. data: δ 1.75 (m, 4 H, H-2,2′,3,3′), 1.95 (s, 3 H, AcO), 2.45 (s, 3 H, CH_3–Ph–), 3.30 (s, 3 H, OMe), 3.90 (m, 2 H, H-4,5), 4.12 (m, 2 H, H-6,6′), 4.60 (t, 1 H, H-1), 7.30 (m, 2 H, aromatic), and 7.78 (m, 2 H, aromatic).

Anal. Calc. for $C_{16}H_{22}O_7S$: C, 53.62; H, 6.18; S, 8.94. Found: C, 53.84; H, 6.30; S, 9.13.

*Methyl 4-O-acetyl-6-azido-2,3,6-trideoxy-α-*D*-*erythro*-hexopyranoside* (**8**). — A solution of **7** (0.5 g, 1.4 mmol) and sodium azide (0.3 g, 4.6 mmol) in dry *N,N*-dimethylformamide (10 ml) was stirred at 80° for 16 h, and then concentrated (1 Torr). The residue was partitioned between water (20 ml) and chloroform (3 × 50 ml). The extracts were washed with water (3 × 25 ml), dried, and concentrated, and the residue was distilled to give **8** (0.28 g, 87%), b.p. 120°/1 Torr; $[\alpha]_D^{22}$ +122°, $[\alpha]_{5461}^{20}$ +165° (*c* 1), R_F 0.25 (chloroform) and 0.65 (ethyl acetate); ν_{max}^{film} 2095 (N_3), 1740 (AcO), 1282, 1235 (AcO), 1173, 1126, 1095, 1041, 1000, 951, 913, 885, and 818 cm^{-1}. P.m.r. data: δ 1.84 (m, 4 H, H-2,2',3,3'), 2.02 (s, 3 H, AcO), 3.30 (m, 2 H, H-6,6'), 3.38 (s, 3 H, OMe), 3.86 (quintuplet, 1 H, $J_{4,5} \simeq 9$, $J_{5,6} \simeq J_{5,6'} \simeq 5$ Hz, H-5), 4.60 (m, 1 H, H-4), and 4.69 (t, 1 H, H-1).

Anal. Calc. for $C_9H_{15}N_3O_4$: C, 47.15; H, 6.60; N, 18.33. Found: C, 47.07; H, 6.75; N, 18.50.

*Methyl 6-azido-4-O-benzoyl-2,3,6-trideoxy-α-*D*-*erythro*-hexopyranoside* (**16**). — A solution of methyl 4-*O*-benzoyl-6-bromo-2,3,6-trideoxy-α-D-*erythro*-hexopyranoside[6] (**15**; 23.3 g, 70.7 mmol) and sodium azide (10 g, 153 mmol) in dry *N,N*-dimethylformamide (200 ml) was stirred at 60–70° for 36 h. After evaporating the solvent (1 Torr), the residue was diluted with water (200 ml) and extracted with dichloromethane (3 × 100 ml). The combined extracts were washed with water, dried, and concentrated to give a syrupy product (18.7 g, 91%) which was pure enough for the subsequent step. Purification by t.l.c. gave **16**, $[\alpha]_{5461}^{24}$ +152° (*c* 0.3, ethanol); ν_{max}^{film} 2100 (N_3), 1720 (BzO), 1600 and 1585 (phenyl), 1355, 1315, 1260, 1220, 1175, 1110, 1050, 1030, 1010, 1000, 955, 890, 850, 710, and 685 cm^{-1}. P.m.r. data: δ 1.96 (m, 4 H, H-2,2',3,3'), 3.36 (m, 2 H, H-6,6'), 3.42 (s, 3 H, OMe), 4.04 (m, 1 H, H-5), 4.73 (t, 1 H, $J_{1,2} \simeq J_{1,2'} \simeq 2$ Hz, H-1), 4.92 (t, 1 H, H-4), 7.40 (m, 3 H, aromatic), and 7.97 (m, 2 H, aromatic).

Anal. Calc. for $C_{14}H_{17}N_3O_4$: C, 57.72; H, 5.88; N, 14.42. Found: C, 57.56; H, 5.64; N, 14.70.

*Methyl 6-azido-3,2,6-trideoxy-α-*D*-*erythro*-hexopyranoside* (**9**). — (*a*) A solution of **6** (10 g, 31.6 mmol) and sodium azide (6 g, 92 mmol) in *N,N*-dimethylformamide (120 ml) was stirred at 80° for 24 h and then concentrated (1 Torr), and the residue was partitioned between water (50 ml) and chloroform (3 × 100 ml). The extracts were washed with water (3 × 50 ml), dried, and concentrated, and the residue was distilled to give **9** (5.2 g, 82%), b.p. 110–120°/0.1 Torr; $[\alpha]_D^{20}$ +118°, $[\alpha]_{5461}^{20}$ +157° (*c* 1), R_F 0.62 (ethyl acetate) and 0.46 (chloroform–ethanol, 15:1); ν_{max}^{film} 3420 (OH), 2099 (N_3), 1262, 1200, 1189, 1146, 1112, 1034, 984, 972, 935, 895, 867, 853, 840, and 827 cm^{-1}. P.m.r. data: δ 1.80 (m, 4 H, H-2,2',3,3'), 2.23 (bs, 1 H, OH), 3.16 (s, 3 H, OMe), 3.50 (m, 2 H, H-6,6'), 3.60 (m, 2 H, H-4,5), and 4.70 (t, 1 H, H-1).

Anal. Calc. for $C_7H_{13}N_3O_3$: C, 44.91; H, 7.00; N, 22.44. Found: C, 44.66; H, 7.05; N, 22.15.

(*b*) A mixture of **3** (1.62 g, 10 mmol), hexamethylphosphoric triamide (1.78 g,

11 mmol), carbon tetrabromide (3.32 g, 10 mmol), and dry *N,N*-dimethylformamide (15 ml) was stirred at −50° for 2 h. Sodium azide (1.30 g, 20 mmol) was then added, and the mixture was stirred at 60° for 12 h, concentrated (1 Torr), and diluted with water (30 ml). The solution was extracted with chloroform (3 × 30 ml), and the combined extracts were washed with water (2 × 25 ml) and concentrated. Distillation of the syrupy residue gave **9** (1.5 g, 78%), b.p. 120°/0.1 Torr, $[\alpha]_D^{20}$ +118° (*c* 1). R_F 0.62 (ethyl acetate) and 0.32 (chloroform).

(*c*) A solution of **16** (1.45 g, 5 mmol) in methanol (20 ml) containing sodium methoxide (0.1 g) was stored overnight. After neutralization with Amberlite IR-120(H^+) resin, the mixture was filtered and concentrated. The residual syrup was repeatedly extracted with light petroleum to remove methyl benzoate. The crude product (0.45 g, 48%), which was pure enough (R_F 0.31, chloroform) to be used in the next step, when further purified by elution from silica gel with chloroform, gave a product which was identical with that described in (*a*).

6-Azido-2,3,6-trideoxy-D-erythro-*hexose* (**19**). — A solution of **9** (1 g) in 0.1M HCl (20 ml) was heated at 100° for 0.5 h, then cooled, neutralized with Amberlite IR-400(CO_3^{2-}) resin, filtered, and concentrated. The syrupy residue (0.9 g, 97%) was eluted from silica gel with chloroform–ethanol mixtures to give **19**, $[\alpha]_{5461}^{25}$ +56° (*c* 0.6, water); R_F 0.06 (chloroform–ethanol, 93:7); ν_{max}^{film} 3360 (OH), 2092 (N_3), 1210, 1115, 1060, 970, 900, 875, 865, and 815 cm^{-1}.

Anal. Calc. for $C_6H_{11}N_3O_3$: C, 41.61; H, 6.40; N, 24.26. Found: C, 41.75; H, 6.29; N, 24.35.

The 2,4-dinitrophenylhydrazone of **19** had m.p. 142–143° (from ethanol), $[\alpha]_{5461}^{25}$ +13° (*c* 0.5, pyridine).

Anal. Calc. for $C_{12}H_{15}N_7O_6$: C, 40.79; H, 4.28; N, 27.75. Found: C, 40.97; H, 4.36; N, 27.70.

*Methyl 6-acetamido-4-*O*-benzoyl-2,3,6-trideoxy*-α-D-erythro-*hexopyranoside* (**17**). — A solution of the azido derivative **16** (16.5 g) in methanol (100 ml) containing acetic anhydride (25 ml) and 10% palladium-on-charcoal (1.5 g) was hydrogenated at 1.5 atmos. for 4 h at room temperature, then filtered, and concentrated to yield **17** (8.1 g), m.p. 173–175°. A second crop (2.3 g; total yield, 60%) was obtained upon concentration of the mother liquors. Recrystallization from methanol gave the pure product, m.p. 176–178°, $[\alpha]_{5461}^{23}$ +170° (*c* 0.5, methanol), R_F 0.36 (chloroform–ethanol, 15:1); ν_{max}^{KBr} 3260 (NH), 1715 (BzO), 1640 (Amide I), 1560 (Amide II), 1320, 1270, 1260, 1222, 1203, 1179, 1130, 1110, 1070, 1050, 1027, 1010, 999, 954, 922, 898, 880, 863, 845, 800, and 710 cm^{-1}. P.m.r. data: δ 1.94 (s, 3 H, NAc), 1.95 (t, 4 H, H-2,2′,3,3′), 3.18 (m, 1 H, H-5), 3.24 (s, 3 H, OMe), 3.82 (m, 2 H, H-6,6′), 4.69 (t, 1 H, H-1), 4.80 (m, 1 H, H-4), 5.94 (bs, 1 H, NH), 7.40 (m, 3 H, aromatic), and 8.00 (m, 2 H, aromatic).

Anal. Calc. for $C_{16}H_{21}NO_5$: C, 62.53; H, 6.88, N, 4.55. Found: 62.72; H, 6.67; N, 4.53.

*Methyl 4-*O*-acetyl-6-amino-2,3,6-trideoxy*-α-D-erythro-*hexopyranoside* (**10**) *and methyl 6-acetamido-2,3,6-trideoxy*-α-D-erythro-*hexopyranoside* (**11**). — (*a*) A solution

of **17** (3 g) in dry methanol (70 ml) containing sodium methoxide (0.1 g) was stored overnight. The mixture was neutralized with Amberlite IR-120(H^+) resin and concentrated. The residue crystallized on treatment with ether, and the product (2 g), m.p. 115–117°, was recrystallized from chloroform–ether to give **11**, m.p. 117–118°; ν_{max}^{KBr} 3400 (OH), 3320 (NH), 1640 (Amide I), 1540 (Amide II), 1280 (Amide III), 1220, 1205, 1165, 1125, 1105, 1087, 1077, 1050, 1029, 1000, 983, 955, 900, 864, 846, and 822 cm^{-1}. P.m.r. data: δ 1.77 (m, 4 H, H-2,2',3,3'), 2.03 (s, 3 H, NAc), 3.04 (dq, 2 H, $J_{6,6'} \simeq 14$, $J_{5,4} \simeq 3.0$, $J_{5,6} \simeq 3.5$ Hz, H-6,6'), 3.29 (s, 3 H, OMe), 3.51 (dt, 1 H, $J_{4,5} \simeq 9.0$ Hz, H-5), 3.98 (dq, 1 H, $J_{3,4} \simeq 3.0$, $J_{3',4} \simeq 12$ Hz, H-4), 4.19 (bs, 1 H, OH), 4.58 (t, 1 H, H-1), and 6.56 (bs, 1 H, NH).

Anal. Calc. for $C_9H_{17}NO_4$: C, 53.18; H, 8.43; N, 6.89. Found: C, 53.08; H, 8.53; N, 6.73.

(*b*) A solution of **8** (1 g, 4.4 mmol) in dry methanol (100 ml) was hydrogenated over 10% palladium-on-charcoal (0.4 g) at 2.5 atmos. for 2 h at 20°, then filtered, and concentrated. The syrupy residue contained (t.l.c.; chloroform–methanol–ammonia, 20:6:1) two products, R_F 0.34 (**10**) and 0.82 (**11**). Trituration of the syrup with ether gave **11** (0.53 g, 60%), m.p. 116–118°, which was identical with the product prepared in (*a*). On concentration of the mother liquors to a small volume and storage at room temperature, the conversion **10** → **11** occurred, as revealed by t.l.c.

*Methyl 6-acetamido-4-O-acetyl-2,3,6-trideoxy-α-*D-erythro-*hexopyranoside* (**12**). — (*a*) A solution of **8** (2 g, 8.8 mmol) in dry methanol (100 ml) containing acetic anhydride (5 ml) was hydrogenated at 2.5 atmos. for 2 h at 20° over palladium-on-charcoal (0.4 g), then filtered, and concentrated. Crystallization of the residue from ether–hexane at 0° gave **12** (1.73 g, 80%), m.p. 97–98°, $[\alpha]_{5461}^{20}$ +135° (*c* 0.5), R_F 0.50 (ethyl acetate–ethanol, 8:1) and 0.95 (chloroform–methanol–ammonia, 20:6:1); ν_{max}^{KBr} 3328 (NH), 1725 and 1715 (AcO), 1640 (Amide I), 1550 (Amide II), 1294 (Amide III), 1270, 1240 (AcO), 1219, 1194, 1169, 1125, 1097, 1047, 1030, 1009, 990, 941, 920, 910, 874, and 847 cm^{-1}. P.m.r. data: δ 1.82 (bm, 4 H, H-2,2',3,3'), 1.96 and 2.04 (2 s, 6 H, NAc and AcO), 3.32 (s, 3 H, OMe), 3.58 (bm, 3 H, H-5,6,6'), 4.52 (m, 1 H, H-4), 4.64 (t, 1 H, H-1), and 5.82 (bs, 1 H, NH).

Anal. Calc. for $C_{11}H_{19}NO_5$: C, 53.86; H, 7.81; N, 5.71. Found: C, 54.05; H, 7.98; N, 5.52.

(*b*) Acetylation of **11** also gave **12**, m.p. 97–98° (from ether–hexane), which was identical with the product described in (*a*).

*Methyl 6-amino-2,3,6-trideoxy-α-*D-erythro-*hexopyranoside hydrochloride* (**13**). — A solution of **9** (1.5 g, 8 mmol) in dry methanol containing 10% palladium-on-charcoal (0.4 g) was hydrogenated at 2.5 atmos. for 5 h (20°), then filtered, and concentrated. A solution of the syrupy residue (1.2 g) in dry methanol was treated with ethereal hydrogen chloride until precipitation was complete. The product (1.25 g, 79%) was recrystallized from methanol–ether to give **13**, m.p. 153–154° (dec.), $[\alpha]_{5461}^{22}$ +130° (*c* 1, water), R_F 0.65 (20:6:1, chloroform–methanol–ammonia); ν_{max}^{Nujol} 3130 (NH, OH), 1610 and 1580 (NH), 1210, 1120, 1070, 1050, 1015, 1015, 935, 790, and 660 cm^{-1}. P.m.r. data (D_2O): δ 1.80 (m, 4 H, H-2,2',3,3'), 3.10 (m, 2 H,

H-6,6'), 3.38 (s, 3 H, OMe), 3.5–3.9 (m, 2 H, H-4,5), and 4.80 (m, 1 H, H-1); ($CDCl_3$): δ 1.77, (m, 4 H, H-2,2',3,3'), 2.97 (m, 2 H, H-6,6'), 3.33 (s, 3 H, OMe), 3.47 (m, 2 H, H-4,5), and 4.63 (t, 1 H, H-1).

Anal. Calc. for $C_7H_{16}ClNO_3$: C, 42.53; H, 8.15; N, 7.08; Cl, 17.93. Found: C, 42.70; H, 8.01; N, 7.25; Cl, 18.16.

*6-Acetamido-2,3,6-trideoxy-*D-erythro-*hexopyranose* (**20**) *and 6-acetamido-1,6-anhydro-2,3,6-trideoxy-β-*D-erythro-*hexopyranose* (**21**). — A solution of **11** (0.3 g) in 0.1M HCl (6 ml) was heated at 100° for 20 min, then neutralised with Amberlite IR-400(CO_3^{2-}) resin, and concentrated. The syrupy residue (0.3 g) contained (t.l.c.; ethyl acetate–ethanol, 8:1) two components of R_F 0.20 (major) and 0.13. Elution from silica gel (50 g), with ether–methanol or ethyl acetate–ethanol mixtures, gave **20** (0.12 g, 39.5%), $[\alpha]_{5461}^{25}$ +50° (*c* 0.5 water); ν_{max}^{nujol} 3309 (OH), 3100 sh (NH), 1640 (Amide I), 1545 (Amide II), 1290 (Amide III), 1209, 1059, 970, 916, and 860 cm^{-1}. P.m.r. data (Me_2SO-d_6): δ 1.5–1.8 (m, 4 H, H-2,2',3,3'), 1.84 (s, 3 H, NAc), 3.20 (m, 3 H, H-5,6,6'), 4.60 (m, 1 H, H-4), 4.80 (m, 1 H, disappeared on deuterium exchange, HO-4), 5.02 and 5.32 (2 bm, 1 H, intensity ratio 4:3, H-1 of two anomeric isomers), 5.98 and 6.40 (m and d, 1 H, intensity ratio 4:3, signals disappeared on deuterium exchange, HO-1), and 7.80 (b, 1 H, NH).

Anal. Calc. for $C_8H_{15}NO_4$: C, 50.78; H, 7.99; N, 7.40. Found: C, 50.83; H, 8.03; N, 6.94.

Eluted second was **21** (16 mg, 6%), m.p. 125–126°, $[\alpha]_{5461}^{24}$ −32° (*c* 0.5, water); ν_{max}^{KBr} 3410 (OH), 1635 (Amide I), 1330, 1311, 1282, 1253, 1210, 1192, 1176, 1165, 1099, 1080, 1070 sh, 1042, 1032, 1013, 988, 944, 927, 874, 854, and 834 cm^{-1}. P.m.r. data: δ 1.82 (bm, 4 H, H-2,2',3,3'), 2.04 and 2.07 (2 s, 3 H, NAc of two rotational isomers), 2.91 (s, 1 H, disappeared on deuterium exchange, OH), 3.51 (m, 3 H, H-5,6,6'), 4.52 (m, 1 H, H-4), 5.44 and 5.71 (2 bs, 1 H, intensity ratio 7:9, H-1 of two rotational isomers); (pyridine-d_5 at room temperature): δ 1.82 and 1.85 (2 s, 3 H, NAc of two rotational isomers), 5.37 and 5.74 (2 bs, 1 H, intensity ratio 4:3, H-1 of two rotational isomers); (pyridine-d_5 at 70°): δ 1.83 (s, 3 H, NAc) and 5.65 (bs, 1 H, H-1).

Anal. Calc. for $C_8H_{13}NO_3$: C, 56.12; H, 7.65; N, 8.18. Found: C, 56.11; H, 7.92; N, 7.93.

*2,4-Dinitrophenylhydrazone of 6-acetamido-2,3,6-trideoxy-*D-erythro-*hexose.* — (*a*) Methyl 6-acetamido-2,3,6-trideoxy-α-D-*erythro*-hexopyranoside (**11**, 0.1 g) was heated with 2M hydrochloric acid (2 ml) at 100° for 0.5 h, and then treated with a hot solution of 2,4-dinitrophenylhydrazine (140 mg) in 2M hydrochloric acid (20 ml). The mixture was stored for 2 days. A few drops of acetone were added, and the product was collected, washed with water, and recrystallized from ethanol to give the title compound (0.11 g), m.p. 120–122°, $[\alpha]_{5461}^{25}$ −11° (*c* 0.3, pyridine).

Anal. Calc. for $C_{14}H_{19}N_5O_7$: C, 45.53; H, 5.18; N, 18.96. Found: C, 45.30; H, 4.95; N, 19.12.

(*b*) A solution of 6-acetamido-1,6-anhydro-2,3,6-trideoxy-β-D-*erythro*-hexopyranose (**21**, 0.1 g) in water (0.5 ml) was treated with 2,4-dinitrophenylhydrazine

(0.13 g) in hot 2M hydrochloric acid (20 ml). The product (0.14 g), when recrystallized from ethanol, had m.p. 120–121°, and was identical with the sample described in (*a*).

*6-Acetamido-4-O-acetyl-1,6-anhydro-β-*D-erythro-*hexopyranose* (**22**). — A solution of **11** (0.4 g) in acetic anhydride (5 ml) containing conc. sulphuric acid (0.05 ml) was stored at room temperature for 2 days, then poured onto ice, and neutralized to pH 6.5–7.0 with solid $NaHCO_3$. The suspension was filtered, the solid was washed with chloroform, and the filtrate was extracted with chloroform (5 × 5 ml). The combined organic liquors were washed with water, dried, and concentrated. The syrupy residue was thrice dissolved in ether, and the solution was concentrated. Recrystallization of the product (0.18 g, 42.6%) from ether then gave **22**, m.p. 69–70°, $[\alpha]_{5461}^{25}$ −46° (*c* 0.5), R_F 0.26 (ether–chloroform, 9:1); ν_{max}^{KBr} 1720 (AcO), 1633 (Amide I), 1324, 1309, 1259, 1238, 1210, 1194, 1173, 1105, 1064, 1036, 1020, 1004, 968, 948, 937, 894, 879, 858, 833, and 808 cm^{-1}. P.m.r. data: δ 1.82 (m, 4 H, H-2,2',3,3'), 2.04 and 2.07 (2 s, 3 H, NAc of two rotational isomers), 2.11 (s, 3 H, OAc), 3.52 (m, 2 H, H-6,6'), 4.63 (m, 2 H, H-4,5), 5.46 and 5.75 (2 bs, 1 H, intensity ratio 2:3, H-1 of two rotational isomers).

Anal. Calc. for $C_{10}H_{15}NO_4$: C, 56.32; H, 7.09; N, 6.57. Found: C, 56.60; H, 7.10; N, 6.69.

Treatment of **22** (1.8 g) with a solution of sodium methoxide (0.1 g) in dry methanol (25 ml) for 3 h was followed by neutralisation with Amberlite IR-120(H^+) resin, filtration, and concentration. The syrupy product (0.94 g) contained (t.l.c.; ethyl acetate–ethanol, 8:1) two components having R_F 0.13 and 0.20. Elution from silica gel (20 g) with ether–methanol (19:1) gave 6-acetamido-2,3,6-trideoxy-D-*erythro*-hexopyranose (**20**; 12 mg, 1.1%), R_F 0.20, which was identical with the product described above. 6-Acetamido-1,6-anhydro-2,3,6-trideoxy-*β*-D-*erythro*-hexopyranose (**21**; R_F 0.13, 0.33 g, 30%) was also obtained; m.p. 125–126°, $[\alpha]_{5461}^{25}$ −32° (*c* 0.5 water), which had the same characteristics as the product described above.

When **11** was treated with acetic anhydride containing 0.5% of sulphuric acid, the product (43%) was methyl 6-acetamido-4-*O*-acetyl-2,3,6-trideoxy-α-D-*erythro*-hexopyranoside (**12**), m.p. 93–94° (see above).

Attempted acetolyses of glycosides **3** *and* **9**. — Treatment of **3** with 1.8% sulphuric acid in acetic anhydride gave methyl 4,6-di-*O*-acetyl-α-D-*erythro*-hexopyranoside (**4**, 87%). Similar treatment of **9** with 0.15% sulphuric acid in acetic anhydride gave methyl 4-*O*-acetyl-6-azido-2,3,6-trideoxy-α-D-*erythro*-hexopyranoside (**8**, 75%). When the concentration of H_2SO_4 was raised to 1.8%, the products remained unchanged.

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