Syntheses towards the Carbohydrate Moiety of Lincomycin

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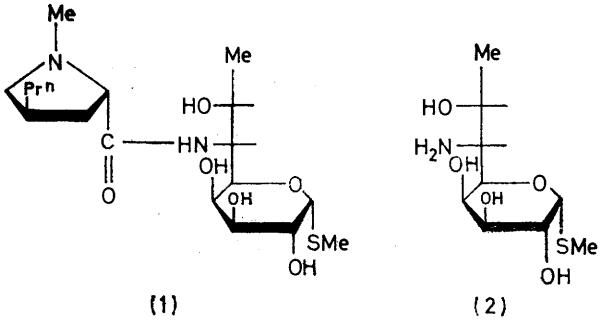
A key intermediate in the synthesis of the antibiotic lincomycin, 6-acetamido-6,8-dideoxy-1,2:3,4-di-*O*-isopropylidene-α-D-*erythro*-D-*galacto*-octopyranose (10), has been synthesised from *cis*-6,7,8-trideoxy-1,2:3,4-di-*O*-isopropylidene-7-*C*-nitro-α-D-*galacto*-oct-6-enose (3). The amino-group at C-6 was introduced by two different procedures.

LINCOMYCIN (1), an antibiotic produced by *Streptomyces lincolnensis* var. *lincolnensis*,[1] has been shown to be effective against most of the common gram-positive pathogens. A number of syntheses towards the carbohydrate moiety of the antibiotic have been published,[2-7] and a total synthesis of the sugar portion, methyl 6-amino-6,8-dideoxy-1-thio-α-D-*erythro*-D-*galacto*-octopyranoside (2), has been described.[8] A synthesis of the amino-acid component of lincomycin has been reported [9,10] and compound (2) was acylated [11] with this amino-acid to produce the antibiotic (1).

The starting material in the present synthesis, *cis*-6,7,8-trideoxy-1,2:3,4-di-*O*-isopropylidene-7-*C*-nitro-α-D-*galacto*-oct-6-enose (3), prepared [5] from D-galactose, was epoxidised with alkaline hydrogen peroxide to give a mixture of two isomers in the ratio 5 : 1. Column chromatography on silica gel resulted in total separation of the two nitro-epoxides. The preponderant isomer has been tentatively assigned the L-configuration (4) and the minor compound the D-configuration (5). These assignments are based on c.d. spectra, which show that stereochemically C-6 and C-7 in these products are mirror



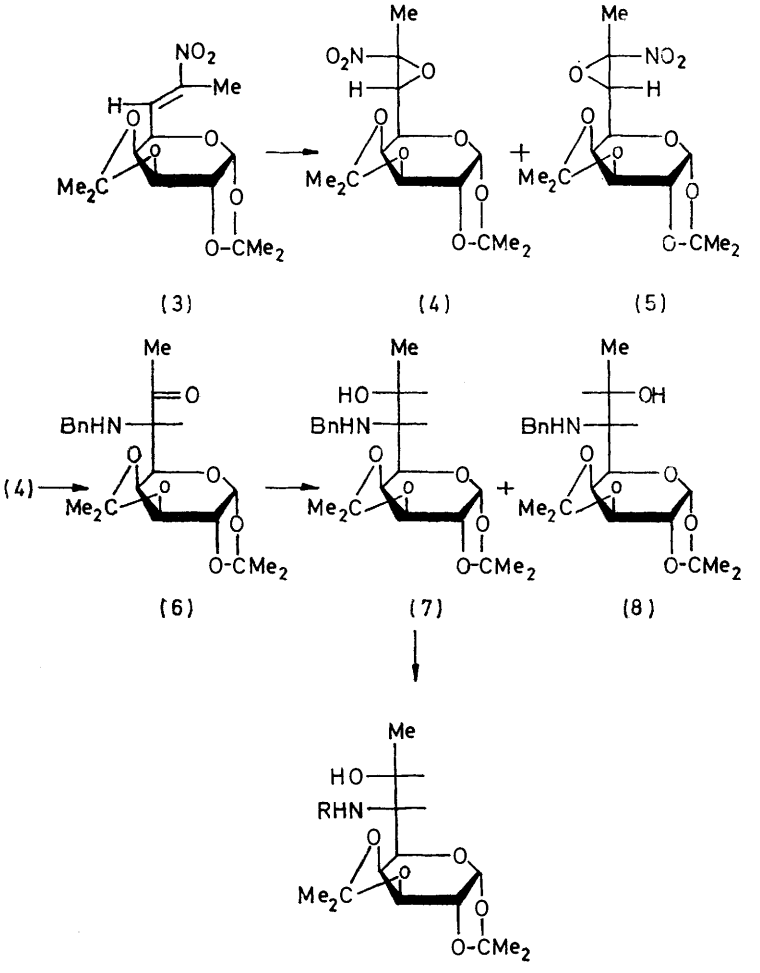
images, and on the configuration of the product of the reaction of compound (4) with benzylamine (Scheme 1).

Treatment of the nitro-epoxide (4) with benzylamine in dimethylformamide (DMF) afforded only one benzylamino-ketone, 6-benzylamino-6,8-dideoxy-1,2:3,4-di-*O*-isopropylidene-α-D-*glycero*-D-*galacto*-octos-7-ulose (6). Reduction of compound (6) with sodium borohydride

[1] D. J. Mason, A. Dietz, and C. De Boer, 'Antimicrobial Agents and Chemotherapy, 1962,' American Society for Microbiology, Ann Arbor, Michigan, 1963, p. 554.
[2] T. Atsumi, T. Fukumaru, and M. Matsui, *Agric. and Biol. Chem.* (*Japan*), 1973, **37**, 2627.
[3] B. J. Magerlein, *Tetrahedron Letters*, 1970, 33.
[4] H. Saeki and E. Ohki, *Chem. and Pharm. Bull.* (*Japan*), 1970, **18**, 789.
[5] T. Atsumi, T. Fukumaru, T. Ogawa, and M. Matsui, *Agric. and Biol. Chem.* (*Japan*), 1973, **37**, 2621.
[6] G. B. Howorth, D. G. Lance, W. A. Szarek, and J. K. N. Jones, *Canad. J. Chem.*, 1969, **47**, 75.
[7] G. B. Howorth, W. A. Szarek, and J. K. N. Jones, *Chem. Comm.*, 1969, 1339.
[8] G. B. Howorth, W. A. Szarek, and J. K. N. Jones, *J. Chem. Soc.* (*C*), 1970, 2218.
[9] G. Slomp and F. A. Mackeller, *J. Amer. Chem. Soc.*, 1967, **89**, 2454.
[10] B. J. Magerlein, R. D. Birkenmeyer, R. R. Herr, and F. Kagan, *J. Amer. Chem. Soc.*, 1967, **89**, 2459.
[11] W. Schroeder, B. Bannister, and H. Hoeksema, *J. Amer. Chem. Soc.*, 1967, **89**, 2448.

and chromatographic separation of the products on silica gel gave the D-*erythro*- (7) and L-*threo*- (8) benzylamino-alcohols in the ratio 12 : 1. This result differs from that of Atsumi *et al.*,[2] who report that reduction of the *N*-acetyl derivatives of compound (6) afforded mainly the L-*threo*-isomer. De-*N*-benzylation of compound (7) by catalytic hydrogenation afforded 6-amino-6,8-dideoxy-1,2:3,4-di-*O*-isopropylidene-α-D-*erythro*-D-*galacto*-octopyranose (9). di-*O*-isopropylidene-7-*C*-nitro-β-L-*erythro*-D-*galacto*-octopyranose.

The reaction of the nitro-epoxide (4) with sodium azide in DMF (Scheme 2) afforded a mixture which was separated on silica gel to give the 6-azido-6,8-dideoxy-1,2:3,4-di-*O*-isopropylidene-α-D-and-β-L-*glycero*-D-*galacto*-octos-7-uloses (11) and (12) in the ratio 6 : 1. Treatment of either compound (11) or (12) with sodium azide, under

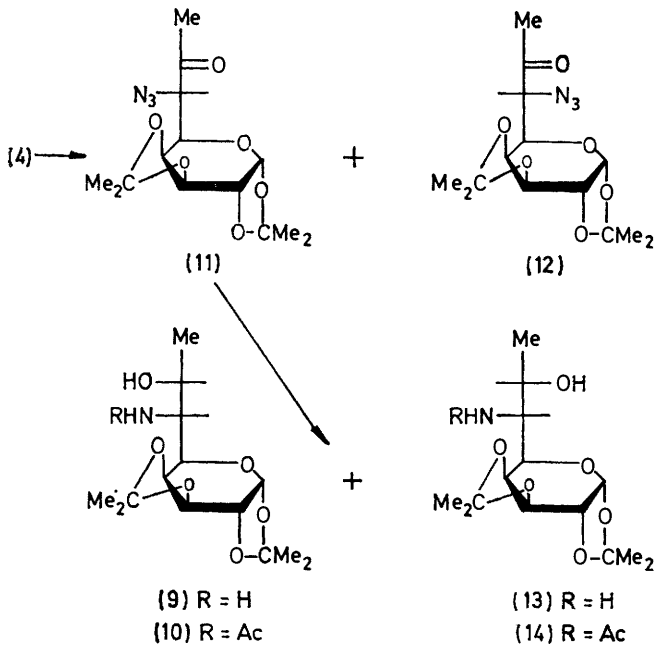


SCHEME 1 Bn = $PhCH_2$

N-Acetylation of compound (9) gave 6-acetamido-6,8-dideoxy-1,2:3,4-di-*O*-isopropylidene-α-D-*erythro*-D-*galacto*-octopyranose (10), identical with the D-*erythro*-isomer previously synthesised.[8] Since no racemisation occurs during the reduction of benzylamino-ketones,[2] compounds (6)—(9) must have the same configuration at C-6 as compound (10), *i.e.* the D-configuration. Compound (7) is therefore 6-benzylamino-6,8-dideoxy-1,2:3,4-di-*O*-isopropylidene-α-D-*erythro*-D-*galacto*-octopyranose. Nucleophilic substitution of nitro-epoxides is known to occur *via* an S_N2 transition state,[12] and, as the benzylamino-ketone (6) has the D-configuration at C-6, the intermediate (4) must be 6,7-anhydro-8-deoxy-1,2:3,4-conditions identical with that used for their preparation from compound (4), gave a mixture which was judged by t.l.c. to have the two azido-ketones present in the same proportions as was found in the original synthesis. The major isomer in each mixture was isolated and shown by c.d. to be identical with the D-*glycero*-azide (11). Compound (12) must therefore be formed by racemization of the azido-ketone (11) during the treatment of the nitro-epoxide (4) with sodium azide. Treatment of the azido-ketone (11) with sodium borohydride in propan-1-ol[13]

[12] H. Newman and R. B. Angier, *Tetrahedron*, 1970, **26**, 825.
[13] L. F. Fieser and M. Fieser, ' Reagents for Organic Synthesis,' Wiley, New York, 1967, p. 1052.

resulted in an initial, rapid reduction to the two azido-alcohols, followed by a slower reduction of the azido-group. The mixture of amino-alcohols (9) and (13) was



SCHEME 2

N-acetylated and the products were chromatographed on silica gel to give the 6-acetamido-6,8-dideoxy-1,2:3,4-di-*O*-isopropylidene-α-D-*erythro*- and -β-L-*threo*-D-*galacto*-octopyranoses (10) [8] and (14) [4] in the ratio 1.8 : 1.

EXPERIMENTAL

M.p.s were determined with a Kofler micro hot-stage apparatus. Optical rotations were measured with a Bendix-NPL Automatic Polarimeter type 143D for chloroform solutions at 20 °C. I.r. spectra were recorded with a Perkin-Elmer 237 spectrophotometer for 4% dispersion in potassium bromide or 3% solutions in chloroform. N.m.r. spectra were measured at 35 °C with a Varian HA-100 spectrometer for 10% solutions in deuteriochloroform with tetramethylsilane as internal reference. Coupling constants are quoted as observed spacings. C.d. spectra were recorded with a JASCO J-20 automatic recording spectropolarimeter (concentrations given as mol l^{-1}). T.l.c. was performed on 0.1 mm pre-coated Silica Gel 60 F-254 (Merck) plates, and Silica Gel 60 (70—230 mesh) (Merck) was used for column chromatography. The term 'light petroleum' refers to the fraction of b.p. 60—80°. The following chromatographic solvents were used: *a*, chloroform–ethyl acetate (30 : 1); *b*, light petroleum–ethyl acetate (3 : 1); *c*, ethyl acetate–methanol (20 : 1); *d*, light petroleum–ethyl acetate (7 : 1); *e*, ethyl acetate–methanol (5 : 1); and *f*, ethyl acetate–light petroleum (2 : 1). G.l.c. (Packard 805) was performed at a carrier gas (nitrogen) rate of *ca.* 40 ml min^{-1}, on a glass column (180 × 0.3 cm) of 1.5% (w/w) neopentyl glycol succinate supported on Chromosorb W (80—100 mesh), at either 185 or 210 °C. Retention times (t_R) are quoted relative to 1,3,5-trinitrobenzene (t_R = 1.00). Mass spectra were recorded with an A.E.I. MS9 instrument by the direct-insertion method.

6,7-*Anhydro*-8-*deoxy*-1,2:3,4-*di*-O-*isopropylidene*-7-C-*nitro*-β-L- *and* -α-D-erythro-D-galacto-*octopyranoses* [(4) *and* (5)].—A solution of *cis*-6,7,8-trideoxy-1,2:3,4-di-*O*-isopropylidene-7-*C*-nitro-α-D-*galacto*-oct-6-enose (3) [6] (5.51 g) in methanol (80 ml) at 0 °C was stirred with hydrogen peroxide (30%; 10 ml) and 2M-sodium hydroxide (15 ml).[12] After 0.5 h, when g.l.c. (185°) showed the absence of starting material (t_R 0.68), the clear mixture was poured into iced M-sulphuric acid and extracted into ether. The extracts were washed with saturated sodium hydrogen carbonate solution and water, dried (Na_2SO_4), and evaporated to give a syrup (5.01 g). The product was fractionated on silica gel (1.5 kg) (solvent *a*). The *L-isomer* (4), eluted first, crystallised from light petroleum as needles (4.0 g), m.p. 83—84°; R_F 0.60 (solvent *a*); t_R 0.63 (185 °C); $[\alpha]_D$ −132° (*c* 1.79); $\lambda_{max.}$ ($CHCl_3$) 6.40 (C–NO_2), and 7.22 and 7.27 μm (CMe_2); c.d. (*c* 7.65 × 10^{-4}; 22 °C; MeOH): Δε (385 nm)0, (322) — 0.26, (310)0, (279)2.10, and (244)0; τ 4.49 (1 H, d, $J_{1,2}$ 5.0 Hz, H-1), 5.67 (1 H, q, $J_{2,3}$ 2.4 Hz, H-2), 5.35 (1 H, q, $J_{3,4}$ 8.0 Hz, H-3), 5.68 (1 H, q, $J_{4,5}$ 1.8 Hz, H-4), 6.44 (1 H, q, $J_{5,6}$ 7.3 Hz, H-5), 6.16 (1 H, d, H-6), 7.98 (3 H, s, 7-Me), and 8.51, 8.52, 8.63, and 8.67 (each 3 H, s, 2 × CMe_2); *m/e* 316 (M^+ − 15) (Found: C, 51.0; H, 6.3; N, 4.4. $C_{14}H_{21}NO_8$ requires C, 50.8; H, 6.4; N, 4.25%).

The D-*isomer* (5) (770 mg) crystallised as fine needles (from light petroleum), m.p. 123—124°; R_F 0.57 (solvent *a*); t_R 0.81 (185 °C); $[\alpha]_D$ −36° (*c* 1.01); $\lambda_{max.}$ ($CHCl_3$) 6.40 (C–NO_2), and 7.22 and 7.27 μm (CMe_2); c.d. (*c* 9.54 × 10^{-4}; 22 °C; MeOH) : Δε (385 nm)0, (322)0.24, (310)0, (279) — 2.07, and (238)0; τ 4.43 (1 H, d, $J_{1,2}$ 5.0 Hz, H-1), 5.64 (1 H, q, $J_{2,3}$ 2.6 Hz, H-2), 5.36 (1 H, q, $J_{3,4}$ 7.8 Hz, H-3), 5.79 (1 H, q, $J_{4,5}$ 1.9 Hz, H-4), 6.36 (1 H, q, $J_{5,6}$ 6.4 Hz, H-5), 6.24 (1 H, d, H-6), 7.99 (3 H, s, 7-Me), and 8.52 (3 H, s), 8.54 (3 H, s), and 8.67 (6 H, s) (2 × CMe_2); *m/e* 316 (M^+ − 15) (Found: C, 50.45; H, 6.2; N, 4.1%).

6-*Benzylamino*-6,8-*dideoxy*-1,2:3,4-*di*-O-*isopropylidene*-α-D-glycero-D-galacto-*octos*-7-*ulose* (6).—A solution of the preponderant epoxy-isomer (4) (1.0 g) in DMF (40 ml) was treated with benzylamine (5 ml). T.l.c. after 0.5 h (solvent *a*) showed that the reaction was complete. The mixture was applied to a column of silica gel (150 g) and eluted with solvent *d*. The *benzylamino-ketone* (6) (820 mg) crystallised as needles (from light petroleum), m.p. 115.5—117°; R_F 0.77 (solvent *c*); t_R 2.07 (210 °C); $[\alpha]_D$ −7° (*c* 0.91); $\lambda_{max.}$ (KBr) 2.99 (N–H of secondary amine), 5.88 (C=O), and 7.22 and 7.25 μm (CMe_2); τ 4.57 (1 H, d, $J_{1,2}$ 5.0 Hz, H-1), 5.75 (1 H, q, $J_{2,3}$ 2.0 Hz, H-2), 5.40 (1 H, q, $J_{3,4}$ 8.0 Hz, H-3), 5.50 (1 H, q, $J_{4,5}$ 1.0 Hz, H-4), 6.58 (2 H, m, H-5 and -6), 7.85 (3 H, s, 7-Me), 7.95br (1 H, s, D_2O-exchangeable, 6-NH), 2.73 (5 H, m, Ph), 6.58 (2 H, benzyl CH_2), and 8.54 (6 H, s), 8.64 (3 H, s), and 8.72 (3 H, s) (2 × CMe_2); *m/e* 376 (M^+ − 15) (Found: C, 64.4; H, 7.6; N, 3.7. $C_{21}H_{29}NO_6$ requires C, 64.45; H, 7.45; N, 3.6%).

6-*Benzylamino*-6,8-*dideoxy*-1,2:3,4-*di*-O-*isopropylidene*-α-D-erythro- *and* -β-L-threo-D-galacto-*octopyranoses* [(7) *and* (8)].—The benzylamino-ketone (6) (770 mg) was dissolved in methanol–water (2 : 1; 7 ml) and reduced with sodium borohydride (600 mg) for 4 h. Acetone was added to decompose the sodium borohydride and, after removal of the solvent and addition of water, the product was extracted into chloroform. The chloroform was washed with water and dried (Na_2SO_4); removal of the solvent afforded the two

benzylamino-alcohols [(7) and (8)] (595 mg). Chromatography of the mixture on silica gel (solvent *f*) gave the L-threo-*isomer* (8) (20 mg), a syrup, R_F 0.66 (solvent *f*); t_R 3.85 (185 °C); $[\alpha]_D$ −31° (*c* 1.4); $\lambda_{max.}$ (KBr) 2.92 (OH, NH), and 7.25 and 7.30 μm (CMe_2); τ 4.44 (1 H, d, $J_{1,2}$ 5.0 Hz, H-1), 5.69 (1 H, q, $J_{2,3}$ 2.0 Hz, H-2), 5.38 (1 H, q, $J_{3,4}$ 8.0 Hz, H-3), 5.53 (1 H, q, $J_{4,5}$ 1.5 Hz, H-4), 6.17 (1 H, q, $J_{5,6}$ 8.0 Hz, H-5), 7.16 (1 H, q, $J_{6,7}$ 4.2 Hz, H-6), 8.77 (3 H, d, $J_{7,8}$ 6.5 Hz, 7-Me), 7.51br (2 H, s, D_2O-exchangeable, 6-NH, 7-OH), 6.04 (2 H, d, benzyl CH_2), 2.74 (5 H, m, Ph), and 8.49, 8.56, 8.67, and 8.74 (each 3 H, s, 2 × CMe_2); *m/e* 378 (M^+ − 15). The D-erythro-*isomer* (7) (235 mg) crystallised from light petroleum with m.p. 102—104°; R_F 0.60 (solvent *f*); t_R 3.60(185 °C); $[\alpha]_D$ −36° (*c* 1.02); $\lambda_{max.}$ (KBr) 2.91 (OH), 3.01 (N–H of secondary amine), and 7.22 and 7.25 μm (CMe_2); τ 4.49 (1 H, d, $J_{1,2}$ 5.0 Hz, H-1), 5.72 (1 H, q, $J_{2,3}$ 2.1 Hz, H-2), 5.38 (1 H, q, $J_{3,4}$ 7.8 Hz, H-3), 5.53 (1 H, q, $J_{4,5}$ 1.5 Hz, H-4), 5.28 (1 H, q, $J_{5,6}$ 8.6 Hz, H-5), 7.02 (1 H, q, $J_{6,7}$ 4.4 Hz, H-6), 5.98 (1 H, o, $J_{7,8}$ 6.5 Hz, H-7), 8.82 (3 H, d, 7-Me), 7.82br (2 H, s, D_2O-exchangeable, 6-NH, 7-OH), 6.10 (2 H, d, benzyl CH_2), 2.71 (5 H, m, Ph), and 8.49, 8.55, 8.64, and 8.69 (each 3 H, s, 2 × CMe_2); *m/e* 378 (M^+ − 15) (Found: C, 64.35; H, 8.05; N, 3.7. $C_{21}H_{31}NO_6$ requires C, 64.1; H 7.95; N, 3.55%).

6-*Acetamido*-6,8-*dideoxy*-1,2:3,4-*di*-O-*isopropylidene*-α-D-erythro-D-galacto-*octopyranose* (10).—The benzylamino-alcohol (7) (60 mg) in methanol (10 ml) containing 5% palladium–charcoal (15 mg), was reduced with hydrogen at atmospheric pressure. After uptake had ceased (1 h), t.l.c. (solvent *c*) showed that the starting material had all reacted to give the amino-alcohol (9). The catalyst was filtered off and the filtrate concentrated to a syrup (42 mg), R_F 0.21 (solvent *e*); τ 4.50 (1 H, d, $J_{1,2}$ 5.0 Hz, H-1), 5.69 (1 H, q, $J_{2,3}$ 2.2 Hz, H-2), 5.37 (1 H, q, $J_{3,4}$ 8.0 Hz, H-3), 5.56 (1 H, q, $J_{4,5}$ 1.6 Hz, H-4), 6.39br (1 H, d, $J_{5,6}$ 8.6 Hz, H-5), 6.82br (1 H, s, H-6), 5.94br (1 H, s, H-7), 8.82 (3 H, d, $J_{7,8}$ 6.5 Hz, 7-Me), 7.43br (3 H, s, D_2O-exchangeable, 6-NH_2 and 7-OH), and 8.48, 8.55, 8.64, and 8.68 (each 3 H, s, 2 × CMe_2); *m/e* 288 (M^+ − 15). The amino-alcohol (9) (40 mg) was dissolved in methanol (10 ml) containing acetic anhydride (0.5 ml) and kept at room temperature for 2 h. After addition of pyridine (1 ml) the *N*-acetylated product was recovered as described previously.[8] The product (10) had m.p. and mixed m.p. (with authentic sample) 166—167°; R_F 0.30 (solvent *c*); t_R 3.08 (210 °C); $[\alpha]_D$ −53° (*c* 0.98); $\lambda_{max.}$ (KBr) 2.9—3.2 (amide NH and OH), 6.1 (amide I, C=O), 6.41 (amide II, N–H), and 7.22 and 7.25 μm (CMe_2); τ 4.50 (1 H, d, $J_{1,2}$ 5.0 Hz, H-1), 5.71 (1 H, q, $J_{2,3}$ 2.1 Hz, H-2), 5.38 (1 H, q, $J_{3,4}$ 8.0 Hz, H-3), 5.53br (1 H, d, H-4), 8.78 (3 H, d, $J_{7,8}$ 6.0 Hz, 7-Me), 3.09 (1 H, d, D_2O-exchangeable, $J_{NH,6}$ 7.1 Hz, 6-NH), 6.41 (1 H, d, D_2O-exchangeable, $J_{OH,7}$ 4.7 Hz, 7-OH), 8.02 (3 H, s, NAc), and 8.49, 8.52, 8.66, and 8.69 (each 3 H, s, 2 × CMe_2); *m/e* 330 (M^+ − 15).

6-*Azido*-6,8-*dideoxy*-1,2:3,4-*di*-O-*isopropylidene*-α-D- *and* -β-L-glycero-D-galacto-*octos*-7-*uloses* [(11) *and* (12)].—The preponderant epoxide (4) (1.86 g) was dissolved in DMF (25 ml) containing sodium azide (4.02 g) and the mixture stirred at 40 °C for 8 h; t.l.c. (solvent *a*) showed the presence of some starting material together with a spot corresponding to the two azides. After filtration through a column of silica gel, the product was evaporated to dryness (*in vacuo*) and chromatographed on silica gel (solvent *a*) to give starting material (80 mg) and the azide mixture (1.40 g). The azides were chromatographed on silica gel (2 kg; solvent *b*) to give the D-glycero-*isomer* (11) (834 mg) and the L-glycero-*isomer* (12) (130 mg). Compound (11), a syrup, had b.p. *ca.* 90° at 4 × 10^{-5} mmHg; R_F 0.44 (solvent *b*); $[\alpha]_D$ −58° (*c* 1.29); $\lambda_{max.}$ ($CHCl_3$) 4.76 (CN_3), 5.80 (C=O), and 7.22 and 7.27 μm (CMe_2); c.d. (*c* 4.29 × 10^{-4}; 22 °C; MeOH): Δε (340 nm)0, (315) − 0.25, (306)0, (281) 0.81, and (241)0; τ 4.55 (1 H, d, $J_{1,2}$ 5.0 Hz, H-1), 5.65 (1 H, q, $J_{2,3}$ 2.5 Hz, H-2), 5.33 (1 H, q, $J_{3,4}$ 7.8 Hz, H-3), 5.66 (1 H, q, $J_{4,5}$ 1.6 Hz, H-4), 6.10 (1 H, q, $J_{5,6}$ 10.1 Hz, H-5), 5.92 (1 H, d, H-6), 7.73 (3 H, s, 7-Me), and 8.48, 8.54, 8.63, and 8.69 (each 3 H, s, 2 × CMe_2); *m/e* 312 (M^+ − 15) (Found: C, 51.15; H, 6.7; N, 12.65. $C_{14}H_{21}N_3O_6$ requires C, 51.35; H, 6.45; N, 12.85%). The L-*glycero*-isomer (12), a syrup, had b.p. *ca.* 95° at 1 × 10^{-3} mmHg; R_F 0.40 (solvent *b*); $[\alpha]_D$ −74° (*c* 1.13); $\lambda_{max.}$ ($CHCl_3$) 4.75 (CN_3), 5.81 (C=O), and 7.22 and 7.25 μm (CMe_2); c.d. (*c* 1.04 × 10^{-3}; 22 °C; MeOH): Δε (340 nm)0, (313) − 0.33, (306) − 0.28, (296) − 0.24, (275) − 0.37, and (241)0; τ 4.43 (1 H, d, $J_{1,2}$ 5.0 Hz, H-1), 5.66 (1 H q, $J_{2,3}$ 2.5 Hz, H-2), 5.38 (1 H, q, $J_{3,4}$ 7.7 Hz, H-3), 5.76 (1 H, q, $J_{4,5}$ 1.5 Hz, H-4), 5.97 (1 H, q, $J_{5,6}$ 11.1 Hz, H-5), 5.89 (1 H, d, H-6), 7.67 (3 H, s, 7-Me), and 8.45, 8.53, 8.66, and 8.86 (each 3 H, s, 2 × CMe_2); *m/e* 312 (M^+ − 15) (Found: C, 51.1; H, 6.6; N, 12.6%).

6-*Acetamido*-6,8-*dideoxy*-1,2:3,4-*di*-O-*isopropylidene*-α-D-erythro- *and* -β-L-threo-D-galacto-*octopyranoses* [(10) *and* (14)].—A solution of 6-azido-6,8-dideoxy-1,2:3,4-di-*O*-isopropylidene-α-D-*glycero*-D-*galacto*-octos-7-ulose (11) (413 mg) in propan-2-ol (7 ml) containing sodium borohydride (600 mg) [13] was heated under reflux. After 10 min, t.l.c. (solvent *b*) showed total reduction of the carbonyl group, to give a mixture of azido-alcohols [R_F 0.28 and 0.25; $\lambda_{max.}$ ($CHCl_3$) 2.84(OH) and 4.76 μm (CN_3)]. After 16 h the sodium borohydride was decomposed with acetone and the mixture was poured into iced M-sulphuric acid (20 ml) and extracted with chloroform. The extract was washed with saturated sodium hydrogen carbonate solution and water, dried (Na_2SO_4), and evaporated. The residue (78 mg) was identical with starting material. The aqueous layer was made alkaline with M-sodium hydroxide and extracted with chloroform. This extract was washed with water, dried (Na_2SO_4), and evaporated to give two amino-alcohols [(9) and (13)] (275 mg) which were *N*-acetylated as described above. The product (243 mg) was chromatographed on silica gel (150 g; solvent *c*) to separate the two *N*-acetates. The L-threo-*isomer* (14)[4] crystallised as needles (from light petroleum–ethyl acetate) (70 mg), m.p. 153—154°; R_F 0.36 (solvent *c*); t_R 1.60 (210 °C); $[\alpha]_D$ −18° (*c* 2.19); $\lambda_{max.}$ (KBr) 2.9—3.15 (amide NH and OH), 6.08 (amide I, C=O), 6.45 (amide II, N–H), and 7.22 and 7.25 μm (CMe_2); τ 4.48 (1 H, d, $J_{1,2}$ 4.9 Hz, H-1), 5.22 (1 H, q, $J_{2,3}$ 2.2 Hz, H-2), 4.92 (1 H, q, $J_{3,4}$ 8.0 Hz, H-3), 5.13 (1 H, q, $J_{4,5}$ 1.5 Hz, H-4), 5.03 (1 H, q, $J_{5,6}$ 6.4 Hz, H-5), 8.86 (3 H, d, $J_{7,8}$ 6.5 Hz, 7-Me), 3.57 (1 H, d, D_2O-exchangeable, $J_{NH,6}$ 8.0 Hz, 6-NH), 6.05br (1 H, s, D_2O-exchangeable, 7-OH), 7.97 (3 H, s, NAc), and 8.52 (3 H, s), 8.54 (3 H, s), and 8.67 (6 H, s) (2 × CMe_2); *m/e* 330 (M^+ − 15) (Found: C, 55.5; H, 7.95; N, 4.2. $C_{16}H_{27}NO_7$ requires C, 55.65; H, 7.9; N, 4.05%).

The *N*-acetyl derivative (10), R_F 0.30 (solvent *c*) (123 mg), was shown (n.m.r. and mass spectra, t.l.c., m.p., and $[\alpha]_D$) to be identical with the isomer described above.

Treatment of 6-*Azido*-6,8-*dideoxy*-1,2:3,4-*di*-O-*isopropylidene*-α-D- *and* -β-L-glycero-D-galacto-*octos*-7-*uloses* [(11) *and* (12)] *with Sodium Azide*.—Compound (11) (23 mg) in DMF (0.35 ml) containing sodium azide (51 mg) was kept at 40 °C for 8 h. T.l.c. (solvent *b*) showed the presence of two compounds, R_F 0.40 and 0.44. The mixture was separated by

preparative layer chromatography (2 mm pre-coated Merck Silica Gel 60 F-254 plates; solvent *b*). The isomer having R_F 0.44 showed c.d. (*c* 1.10 × 10^{-3}; 20 °C; MeOH): Δε (337 nm)0, (315) — 0.20, (306)0, (281) 0.76, and (236)0.

Similar treatment of compound (12) (25 mg) with sodium azide gave a mixture identical (t.l.c., solvent *b*) with that obtained from compound (11). The major isomer, R_F 0.44, showed c.d. (*c* 1.07 × 10^{-3}; 20 °C; MeOH): Δε (337 nm)0, (315) — 0.23, (306)0, (281) 0.78, and (234)0.

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