Branched-chain Sugars. Part IV.[1] Synthesis of Derivatives of Aldgarose, a Component of Aldgamycin E[2]

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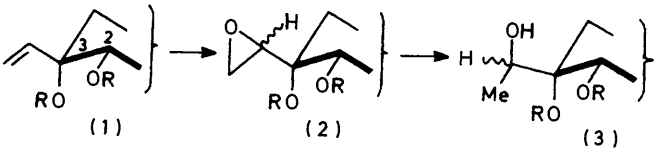
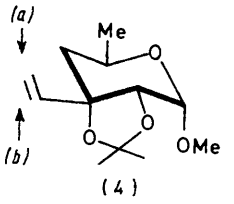
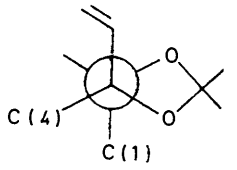
Methyl 4,6-dideoxy-3-*C*-[(*S*)-1-hydroxyethyl]-β-D-*ribo*-hexopyranoside 3,3[1]-cyclic carbonate (methyl aldgaroside B) (14) has been synthesised and shown to be identical with one of the anomeric glycosides obtained from aldgamycin E by methanolysis. The key step in the synthesis involved the epoxidation of methyl 4,6-dideoxy-2,3-*O*-isopropylidene-3-*C*-vinyl-α-D-*ribo*-hexopyranoside (4) to yield principally the (*S*)-epoxide (10).

METHYL ALDGAROSIDES A and B are obtained[3,4] by methanolysis of aldgamycin E, a neutral, macrolide antibiotic isolated from culture filtrates of *Streptomyces lavendulae*.[5] Chemical and spectroscopic evidence has established[4] that methyl aldgarosides A and B are the α- and β-anomers, respectively, of methyl 4,6-dideoxy-3-*C*-(1-hydroxyethyl)-D-*ribo*-hexopyranoside 3,3[1]-cyclic carbonate, but did not reveal the configuration of the asymmetric carbon atom in the chain branch. The parent sugar, aldgarose, represents the first sugar cyclic carbonate to be isolated from natural sources, although two other neutral, macrolide antibiotics, megacidin[6] and bandamycin,[7] show an i.r. absorption band at *ca.* 1800 cm^{-1} indicative of the presence of a cyclic carbonate group; indeed, spectroscopic evidence suggests a close relationship amongst the three antibiotics. It has also been suggested that aldgarose is likely to be related biogenetically to the branched-chain octose isolated from isoquinocycline A.[8]

A judicious choice of route for the synthesis of methyl aldgaroside A or B might permit the configuration of the hydroxyethyl branch to be decided. A route involving the epoxidation of an appropriately derivatised *C*-vinyl sugar [partial structure (1)] was considered







Newman projection along the C(3)-C(2) bond

to offer the best chance of achieving a degree of control over the stereochemistry of the epoxide(s) (2) formed; reductive ring-opening of the epoxide would then furnish the hydroxyethyl branch (3). It is well established in steroid and other fields that the stereochemistry of epoxidation of olefinic bonds with peroxy-acids

[1] Part III, J. S. Brimacombe and A. J. Rollins, *J.C.S. Perkin I*, 1974, 1568.

[2] Preliminary communication, J. S. Brimacombe, C. W. Smith, and J. Minshall, *Tetrahedron Letters*, 1974, 2997.

[3] M. P. Kunstmann, L. A. Mitscher, and N. Bohonos, *Tetrahedron Letters*, 1966, 839.

[4] G. A. Ellestad, M. P. Kunstmann, J. E. Lancaster, L. A. Mitscher, and G. Morton, *Tetrahedron*, 1967, **23**, 3893; the structure of methyl aldgaroside B was revised in this report.

[5] M. P. Kunstmann, L. A. Mitscher, and E. L. Patterson, 'Antimicrobial Agents and Chemotherapy,' Braun-Bromfield, Ann Arbor, Michigan, 1964, p. 87.

[6] L. Ettlinger, E. Gaümann, R. Hutter, W. Keller-Schierlein, F. Kradolfer, L. Neipp, V. Prelog, P. Reusser, and H. Zähner, *Monatsh.*, 1957, **88**, 989.

[7] S. Kondo, J. M. J. Sakamoto, and H. Yumoto, *J. Antibiotics*, 1961, **14A**, 365.

[8] A. Tulinsky, *J. Amer. Chem. Soc.*, 1964, **86**, 5368; J. S. Webb, R. W. Broschard, D. B. Cosulich, J. H. Mowat, and J. E. Lancaster, *ibid.*, 1962, **84**, 3183.

is influenced by the nature of substituents at allylic and remote positions.[9] Thus, a bulky substituent in an allylic position on one side of the olefinic bond shields the approach of a peroxy-acid from that side,[10] whereas an allylic hydroxy-group tends to deliver the peroxy-acid on the same side of the double bond as it is substituted.[11] Related observations have been made in the epoxidation of unsaturated sugars.[12] The situation is a little more complex in the case under consideration, since it is necessary to know the conformation(s) of the vinyl branch about the bond attaching it to the tertiary centre.* However, it was envisaged that acetalisation or appropriate substitution of the hydroxy-groups in the neighbourhood of the vinyl branch might allow the preferred conformation to be predicted on the basis of accepted principles of conformational analysis.

The choice of a suitable target molecule was resolved in the initial phase of our work when Paulsen and Redlich,[14] using an entirely different synthetic approach, established that the hydroxyethyl branch of aldgarose possesses the *S*-configuration. This information directed our efforts towards a synthesis of methyl 4,6-dideoxy-2,3-*O*-isopropylidene-3-*C*-vinyl-α-D-*ribo*-hexopyranoside (4). Molecular models of this compound suggested that the vinyl branch should adopt a conformation close to that shown in (4) so as to minimise non-bonded interactions with the dioxolan ring [this is best seen by viewing the molecule along the C(3)–C(2) bond]; conformations in which the olefinic bond is oriented over the top of the dioxolan ring system are expected to be much less favourable. The *cis*-fused dioxolan ring has another role in that it should encourage the peroxy-acid to approach the olefinic bond from the direction (*a*) in order to avoid steric interactions engendered in the approach from direction (*b*). If the situation visualised obtains, then the resulting epoxide will have the *S*-configuration. The test of this conjecture and subsequent synthetic manipulations leading to a synthesis of methyl aldgaroside B are reported below.

Methyl 4,6-dideoxy-α-D-*xylo*-hexopyranoside (5), prepared from methyl α-D-glucopyranoside according to the procedure of Jones *et al.*,[15] was used as a convenient starting point. Treatment of this diol with *N*-benzoylimidazole [16] yielded a mixture of benzoates from which the 2-benzoate (6) was recovered following chromatography over silica gel. The site of benzoylation was revealed by the next step in the synthetic sequence in which the monoester (6) was oxidised (ruthenium tetraoxide in carbon tetrachloride [17]) to methyl 2-*O*-benzoyl-4,6-dideoxy-α-D-*erythro*-hexopyranosid-3-ulose (7) in near quantitative yield. The n.m.r. spectrum ($CDCl_3$) of this hexopyranosidulose showed the anomeric proton signal as a doublet ($J_{1,2}$ *ca.* 4 Hz) at τ 4·76 mutually coupled to the doublet of H-2 at τ 4·47. These assignments were confirmed by spin-decoupling experiments; thus, irradiation at τ 4·76 caused the doublet at τ 4·47 to collapse to a singlet, and *vice versa*. The observed splitting pattern would only be encountered if the carbonyl group is situated at C-3.

Treatment of the hexopyranosidulose (7) with an excess of vinylmagnesium bromide in ether gave, with concomitant debenzoylation, methyl 4,6-dideoxy-3-*C*-vinyl-α-D-*ribo*-hexopyranoside (8) in a highly stereoselective addition. The configuration of the newly-created asymmetric centre at C-3 was established by catalytic hydrogenation of the olefinic bond to yield methyl 4,6-dideoxy-3-*C*-ethyl-α-D-*ribo*-hexopyranoside (9). The c.d. spectrum of the cuprammonium complex (Cupra A solution) of this diol exhibited a negative band at *ca.* 590 nm indicative of a positive torsion angle between the hydroxy-groups at C-2 and -3.[18] This evidence is compatible with the *ribo*-configuration assigned or with a *lyxo*-configuration; the latter can reasonably be discarded since it requires epimerisation of the hydroxy-group at C-2 from an equatorial to an axial disposition, which seems unlikely.

The *C*-vinyl glycoside (8) was next treated with 2,2-dimethoxypropane in the presence of toluene-*p*-sulphonic acid to give methyl 4,6-dideoxy-2,3-*O*-isopropylidene-3-*C*-vinyl-α-D-*ribo*-hexopyranoside (4), which on treatment with *m*-chloroperbenzoic acid in methylene chloride yielded a 3 : 1 mixture (g.l.c. evidence) of the two possible epoxides. The major epoxide formed was identified as methyl 4,6-dideoxy-2,3-*O*-isopropylidene-3-*C*-[(*S*)-oxiran-2-yl]-α-D-*ribo*-hexopyranoside (10), on the basis of the predictions previously outlined, and the minor epoxide (11) was assigned the *R*-configuration. The formation of both epoxides indicates that the provisos made for epoxidation of the *C*-vinyl derivative (4) are not completely fulfilled, owing to attack of the reagent either from the direction (*b*) or on an alternative conformation from the direction (*a*).

* Most treatments of steric effects in epoxidations are based on the reasonable assumption, first made by Rickborn and Lwo,[13] that the conformation in the transition state is very similar to that of the starting alkene since there is only little change in geometry in passing from the alkene to the epoxide.

[9] A. J. Fudge, C. W. Shoppee, and G. H. R. Summers, *J. Chem. Soc.*, 1954, 958; C. Djerassi and J. Fishman, *J. Amer. Chem. Soc.*, 1955, **77**, 4291; H. B. Henbest and B. Nicholls, *J. Chem. Soc.*, 1957, 4608; for a useful commentary see E. L. Eliel, 'Stereochemistry of Carbon Compounds,' McGraw-Hill, New York, 1962, p. 292.

[10] H. B. Henbest and B. Nicholls, *J. Chem. Soc.*, 1959, 221; H. B. Henbest, B. Nicholls, W. R. Jackson, R. A. L. Wilson, N. S. Crossley, M. B. Meyers, and R. S. McElhinney, *Bull. Soc. chim. France*, 1960, 1365.

[11] H. B. Henbest and R. A. L. Wilson, *J. Chem. Soc.*, 1957, 1958.

[12] H. B. Wood, jun., and H. G. Fletcher, jun., *J. Amer. Chem. Soc.*, 1957, **79**, 3234; R. J. Ferrier and N. Prasad, *J. Chem. Soc.* (*C*), 1969, 575; P. A. Levene and R. S. Tipson, *J. Biol. Chem.*, 1931, **93**, 631.

[13] B. Rickborn and S.-Y. Lwo, *J. Org. Chem.*, 1965, **30**, 2212.

[14] H. Paulsen and H. Redlich, *Angew. Chem. Internat. Edn.*, 1972, **11**, 1021; *Chem. Ber.*, 1974, **107**, 2992.

[15] B. T. Lawton, W. A. Szarek, and J. K. N. Jones, *Carbohydrate Res.*, 1970, **14**, 255.

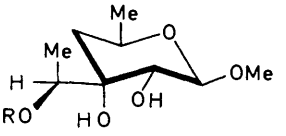
[16] H. A. Staab, *Angew. Chem. Internat. Edn.*, 1962, **1**, 351.

[17] P. J. Beynon, P. M. Collins, P. T. Doganges, and W. G. Overend, *J. Chem. Soc.* (*C*), 1966, 1131.

[18] S. T. K. Bukhari, R. D. Guthrie, A. I. Scott, and A. D. Wrixon, *Chem. Comm.*, 1968, 1580; *Tetrahedron*, 1970, **26**, 3653.

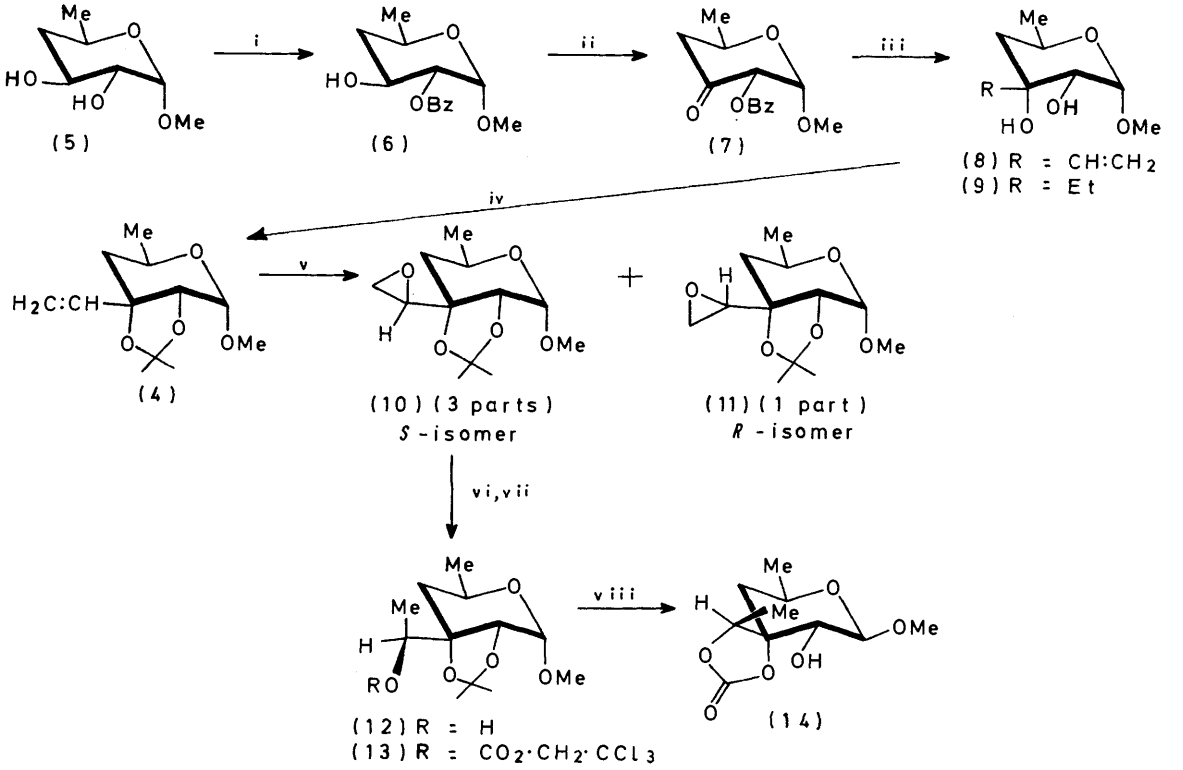
The correctness of the assignments made was demonstrated (see later) by conversion of the epoxide (10) into methyl aldgaroside B (14).

Following ring opening of the major epoxide (10) with lithium aluminium hydride in ether to give methyl 4,6-dideoxy-3-*C*-[(*S*)-1-hydroxyethyl]-2,3-*O*-isopropylidene-α-D-*ribo*-hexopyranoside (12), it remained to introduce the cyclic carbonate group. This was achieved in two ways. The first method used the 'active ester' procedure that has been applied so successfully to the preparation of nucleoside cyclic carbonates.[19] Treatment of the branched-chain glycoside (12) with 2,2,2-trichloroethoxycarbonyl chloride in chloroform–pyridine afforded the 3[1]-carbonate ester (13), which was heated with methanolic hydrogen chloride to remove the protecting acetal group. This treatment led directly to methyl aldgaroside B (14) (*i.e.* the β-glycoside), which was isolated in low yield following chromatography on silica gel. Presumably



(15) R = $CO_2 \cdot CH_2 \cdot CCl_3$
(16) R = H

the β-glycoside (15) resulting from methanolysis is cyclised to the 3,3[1]-cyclic carbonate (14) during the isolation or chromatographic procedures used, although the low yield of the final product suggests that this process, which is normally effected with a base,[19] may be incomplete. The low yield of methyl aldgaroside B obtained by this procedure caused us to employ an alternative, though less equivocal, means of completing the synthesis. Methanolysis of the glycoside acetal (12) gave principally methyl 4,6-dideoxy-3-*C*-[(*S*)-1-hydroxyethyl]-β-D-*ribo*-hexopyranoside (16); preparative chromatography gave the pure β-glycoside having an n.m.r. spectrum ($CDCl_3$) indistinguishable from that



Reagents: i, *N*-benzoylimidazole; ii, RuO_4–CCl_4; iii, CH_2:CHMgBr; iv, $Me_2C(OMe)_2$–H^+; v, *m*-$ClC_6H_4 \cdot CO_3H$; vi, $LiAlH_4$; vii, $Cl_3C \cdot CH_2 \cdot O \cdot COCl$; viii, MeOH–HCl

recorded[4] for the decarbonated form of methyl aldgaroside B. On treatment with an equimolar proportion of phosgene in pyridine, the triol (16) gave preferentially methyl aldgaroside B (14) (85%); this substitution pattern is easily reconciled with the greater reactivity of the secondary hydroxy-group at C-3[1] over that at C-2.

The physical constants and n.m.r. spectrum of methyl aldgaroside B (14) obtained by either route proved to be indistinguishable from those recorded for the glycoside derived from aldgamycin E[4] and from the synthetic material of Paulsen and Redlich.[14] In the foregoing synthesis of methyl aldgaroside B, a reasonable degree of stereoselectivity is afforded in the introduction of the asymmetric centres at C-3 (by Grignard addition) and C-3[1] (by epoxidation of the vinyl chain branch).

[19] J. R. Tittensor, *J. Chem. Soc.* (*C*), 1971, 2656; J. R. Tittensor and P. Mellish, *Carbohydrate Res.*, 1972, **25**, 531.

Notably, the epoxidation of methyl 4,6-dideoxy-2,3-*O*-isopropylidene-3-*C*-vinyl-α-D-*ribo*-hexopyranoside (4) gives the epoxide (10) having the required *S*-configuration as the major product.

EXPERIMENTAL

T.l.c. was performed on Kieselgel G; spots were located with vanillin–sulphuric acid.[20] I.r. spectra were usually recorded for Nujol mulls on a Perkin-Elmer Infracord spectrophotometer, and n.m.r. spectra were measured with a Perkin-Elmer R-10 spectrometer for solutions in deuteriochloroform with tetramethylsilane as internal reference. Optical rotations were measured at ambient temperature with a Perkin-Elmer 141 automatic polarimeter. G.l.c. was carried out on a Pye 104 chromatograph (nitrogen carrier gas, 7 lb in^{-2}, flame-ionisation detector) using a column of 25% silicone gum on Celite at an operating temperature of 160°. Light petroleum refers to the fraction having b.p. 60—80°.

Methyl 2-O-*Benzoyl*-4,6-*dideoxy*-α-D-xylo-*hexopyranoside* (6).—Benzoyl chloride (28·2 g) was added slowly with cooling to a solution of imidazole (27·2 g) in redistilled chloroform (200 ml), after which the solution was filtered to remove imidazole hydrochloride. The filtrate was added to a solution of the diol [15] (5) (32 g) in chloroform (200 ml) and the mixture was heated under reflux for 12 h. When cool, the solution was washed with saturated sodium hydrogen carbonate solution and water, and dried ($MgSO_4$). Removal of the solvent and chromatography of the residue on silica gel (elution with light petroleum–acetone, 4 : 1) afforded an oil, which was dissolved in hot light petroleum. On cooling, this solution deposited crystals of the 2-*benzoate* (6) (15·5 g, 30%), m.p. 107—108°, $[\alpha]_D$ +153° (*c* 2·9 in $CHCl_3$), $\nu_{max.}$ 3400 (OH) and 1740 cm^{-1} (benzoate) (Found; C, 62·9; H, 7·0. $C_{14}H_{18}O_5$ requires C, 63·1; H, 6·8%); τ *ca.* 2·00 (5H, m, aromatic), 4·96 and 5·20 (2H, each d, $J_{1,2}$ *ca.* 3·5 Hz, H-1 and -2), 6·63 (3H, s, OMe), and 8·77 (3H, d, $J_{5,6}$ *ca.* 7 Hz, HC*Me*).

Methyl 2-O-*Benzoyl*-4,6-*dideoxy*-α-D-erythro-*hexopyranosid*-3-*ulose* (7).—The monobenzoate (6) (19·2 g) in carbon tetrachloride (500 ml) was stirred for 2 h at room temperature with a solution of ruthenium tetraoxide in carbon tetrachloride (800 ml) [prepared from ruthenium dioxide dihydrate (10 g) and sodium periodate (150 g) in water (600 ml) [17]]. Propan-2-ol (200 ml) was then added and stirring was continued for a further 30 min. Ruthenium dioxide was filtered off and washed thoroughly with chloroform, and the combined filtrate and washings were dried ($MgSO_4$). Removal of the solvent furnished the *hexosidulose* (7) (18·6 g, 98%), $[\alpha]_D$ +66° (*c* 1·8 in $CHCl_3$), $\nu_{max.}$ (film) 1725 cm^{-1} (C=O) (Found: C, 63·4; H, 6·1. $C_{14}H_{16}O_5$ requires C, 63·6; H, 6·1%); τ *ca.* 2·10 (5H, m, aromatic), 4·47 (1H, d, $J_{2,1}$ *ca.* 4 Hz, H-2), 4·76 (1H, d, $J_{1,2}$ *ca.* 4 Hz, H-1), 6·53 (3H, s, OMe), 7·43 (2H, m, H-4 and 4′), and 8·65 (3H, d, $J_{5,6}$ *ca.* 7 Hz, HC*Me*).

Methyl 4,6-*Dideoxy*-3-C-*vinyl*-α-D-ribo-*hexopyranoside* (8).—Sufficient dry tetrahydrofuran was added to cover clean and dry magnesium turnings (25·8 g) contained in a three-necked flask; vinyl bromide (*ca.* 5 ml) was then added and the mixture was stirred at room temperature. After the reaction had started, ether–tetrahydrofuran (1 : 1 v/v; 350 ml) was added, followed by vinyl bromide (70 ml) in dry ether (100 ml) at such a rate that moderate reflux was maintained. Stirring was continued throughout the addition and until most of the metal had reacted.

The hexopyranosid-3-ulose (7) (18·6 g) in dry ether (150 ml) was added dropwise to the solution of vinylmagnesium bromide, and the mixture was then heated under reflux for 4 h. Water was then added to decompose the excess of reagent and the solvents were removed. The residue was extracted with hot chloroform (3 × 300 ml), and the combined extracts were concentrated to an oil that was chromatographed on silica gel (elution with light petroleum–ethyl acetate, 2 : 1) to give the 3-C-*vinyl derivative* (8) (10·8 g, 81%), $[\alpha]_D$ +109° (*c* 1·2 in $CHCl_3$), $\nu_{max.}$ (film) 3350 (OH) and 1650 cm^{-1} ($CH=CH_2$) (Found: C, 58·0; H, 8·5. $C_9H_{16}O_4$ requires C, 57·4; H, 8·5%); τ 3·86—4·95 (3H, m, $CH=CH_2$), 5·20 (1H, d, $J_{1,2}$ *ca.* 3·5 Hz, H-1), 6·55 (3H, s, OMe), and 8·82 (3H, d, $J_{5,6}$ *ca.* 7 Hz, HC*Me*).

Methyl 4,6-*Dideoxy*-3-C-*ethyl*-α-D-ribo-*hexopyranoside* (9).—A solution of the *C*-vinyl compound (8) (0·15 g) in methanol (20 ml) containing platinum oxide (0·1 g) was shaken under a slight overpressure of hydrogen for 4 h. Removal of the catalyst and the solvent afforded the C-*ethyl compound* (9) (0·11 g, 74%), $[\alpha]_D$ +92·5° (*c* 0·7 in $CHCl_3$) (Found: C, 57·7; H, 9·7. $C_9H_{18}O_4$ requires C, 56·8; H, 9·5%); this compound did not decolourise a solution of bromine in carbon tetrachloride. The c.d. spectrum of (9) in Cupra A solution [18] revealed a negative band at *ca.* 590 nm, indicating a positive torsion angle between the two hydroxy-groups.

Methyl 4,6-*Dideoxy*-2,3-O-*isopropylidene*-3-C-*vinyl*-α-D-ribo-*hexopyranoside* (4).—A solution of the *C*-vinyl compound (8) (3 g) in dry acetone (20 ml) and 2,2-dimethoxypropane (40 ml) containing toluene-*p*-sulphonic acid (0·24 g) was stirred at room temperature for 3 days; it was then neutralised (solid $NaHCO_3$), filtered, and concentrated. Chromatography of the residue on silica gel (elution with light petroleum–acetone, 8 : 1) gave the 2,3-*acetal* (4) (2·75 g, 75%), b.p. 62—64° at *ca.* 12 mmHg, $[\alpha]_D$ +72° (*c* 3 in $CHCl_3$), $\nu_{max.}$ (film) 1380 cm^{-1} (CMe_2) (Found: C, 63·4; H, 8·9. $C_{12}H_{20}O_4$ requires C, 63·2; H, 8·85%); τ 3·67—4·93 (3H, m, $CH=CH_2$), 5·20 (1H, d, $J_{1,2}$ *ca.* 3 Hz, H-1), 5·79 (1H, d, $J_{2,1}$ *ca.* 3 Hz, H-2), 6·43 (3H, s, OMe), 8·43 and 8·60 (6H, each s, CMe_2), and 8·73 (3H, d, $J_{5,6}$ *ca.* 7 Hz, HC*Me*).

Methyl 4,6-*Dideoxy*-2,3-O-*isopropylidene*-3-C-[(S)- *and* (R)-*oxiran*-2-*yl*]-α-D-ribo-*hexopyranosides* [(10) *and* (11)].—A solution of the *C*-vinyl acetal (4) (2·65 g) in methylene chloride (50 ml) containing *m*-chloroperbenzoic acid (3·1 g) was stirred for 7 days at room temperature; t.l.c. (light petroleum–acetone, 9 : 1) then showed that most of the starting material had reacted. The excess of reagent was destroyed by the addition of 10% sodium sulphite solution until a test with starch–iodide paper was negative. The organic layer was then washed with sodium hydrogen carbonate solution and water, and dried ($MgSO_4$). Removal of the solvent left an oil (2·6 g), which g.l.c. showed to contain the two epoxides (ratio 3 : 1) and a small proportion of starting material. Chromatography on silica gel (elution with light petroleum–acetone, 9 : 1) afforded first the unchanged *C*-vinyl compound (4) (0·4 g) (identified by i.r. spectroscopy) and then the (R)-*epoxide* (11) (0·12 g, 5%), m.p. 67—69° (from ether), $[\alpha]_D$ +60° (*c* 2·8 in $CHCl_3$), $\nu_{max.}$ 805 cm^{-1} (epoxide) (Found: C, 58·6; H, 8·5. $C_{12}H_{20}O_5$ requires C, 59·0; H, 8·2%); τ 5·23

[20] E. Merck A.G., ' Chromatography,' Darmstadt, 2nd edn., p. 30.

(1H, d, $J_{1.2}$ *ca.* 3 Hz, H-1), 5·76 (1H, d, $J_{2.1}$ *ca.* 3 Hz, H-2), 6·46 (3H, s, OMe), *ca.* 7·30 (3H, m, O·CH·CH_2), 8·47 and 8·61 (6H, each s, CMe_2), and 8·78 (3H, d, $J_{5.6}$ *ca.* 7 Hz, HC*Me*). Continued elution gave a mixture of the two epoxides (1·3 g, 54%), followed by a fraction containing the (S)-*epoxide* (10) (0·7 g, 29%), b.p. 45—50° (bath) at 0·3 mmHg, $[\alpha]_D$ +54° (*c* 1·2 in $CHCl_3$), $\nu_{max.}$ (film) 808 cm^{-1} (epoxide) (Found: C, 58·9; H, 8·6%); τ 5·36 (1H, d, $J_{1.2}$ *ca.* 3 Hz, H-1), 5·86 (1H, d, $J_{2.1}$ *ca.* 3 Hz, H-2), 6·47 (3H, s, OMe), 6·89—7·30 (3H, m, O·CH·CH_2), 8·48 and 8·57 (6H, each s, CMe_2), and 8·79 (3H, d, $J_{5.6}$ *ca.* 7 Hz, HC*Me*).

Further chromatography of the mixture of epoxides furnished additional quantities of pure materials, giving total yields of 70 and 13% for the (*S*)- and (*R*)-epoxides, respectively.

Methyl 4,6-*Dideoxy*-3-C-[(S)-1-*hydroxyethyl*]-2,3-O-*isopropylidene*-α-D-ribo-*hexopyranoside* (12).—A solution of the major epoxide (10) (0·62 g) in dry ether (50 ml) containing lithium aluminium hydride (0·23 g) was heated under gentle reflux for 1 h, after which t.l.c. (light petroleum–acetone, 9 : 1) showed that no starting material remained. Ethyl acetate (30 ml) and water (5 ml) were added cautiously to decompose undamaged hydride and this process was completed by heating the mixture under reflux for 20 min. Solids were filtered off and washed thoroughly with chloroform, and the combined filtrate and washings were dried ($MgSO_4$) and concentrated. Chromatography of the residue on silica gel (elution with light petroleum–acetone, 7 : 3) gave the *branched-chain sugar* (12) (0·59 g, 94%), m.p. 66—68° (from ether),$[\alpha]_D$ +71° (*c* 1·3 in $CHCl_3$), $\nu_{max.}$ 3400 cm^{-1} (OH) (Found: C, 58·5; H, 9·05. $C_{12}H_{22}O_5$ requires C, 58·5; H, 8·9%); τ 5·18 (1H, d, $J_{1.2}$ *ca.* 3 Hz, H-1), 5·68 (1H, d, $J_{2.1}$ *ca.* 3 Hz, H-2), 6·43 (3H, s, OMe), 8·44 and 8·58 (6H, each s, CMe_2), and 8·73 [6H, superimposed d, *J ca.* 7 Hz, HC(5)*Me* and HC(3^1)*Me*].

Methyl 4,6-*Dideoxy*-2,3-O-*isopropylidene*-3-C-[(S)-1-(2,2,2-*trichloroethoxycarbonyloxy*)*ethyl*]-β-D-ribo-*hexopyranoside* (13).—To a cooled (0°) solution of the hydroxyethyl derivative (12) (0·4 g) in dry pyridine (10 ml) was added, over 30 min, a solution of 2,2,2-trichloroethoxycarbonyl chloride (0·6 g) in chloroform (5 ml), and the mixture was then set aside for 3 days at room temperature. Water (5 ml) was then added and the solvents were removed after 1 h to furnish the *carbonate ester* (13) (0·6 g, 50%), m.p. 97—98° (from ether–light petroleum), $[\alpha]_D$ +25° (*c* 1·1 in $CHCl_3$), $\nu_{max.}$ 1770 cm^{-1} (carbonate) (Found: C, 42·7; H, 5·8. $C_{15}H_{23}Cl_3O_7$ requires C, 42·55; H, 5·45%); τ *ca.* 5·18 (2H, ABq, *J* 12 Hz, $CH_2{\cdot}CCl_3$), 6·48 (3H, s, OMe), 8·46 and 8·58 (6H, each s, CMe_2), 8·62 [3H, d, *J ca.* 7 Hz, HC(3^1)*Me*], and 8·78 [3H, d, $J_{5.6}$ *ca.* 7 Hz, HC(5)*Me*].

Methyl 4,6-*Dideoxy*-3-C-[(S)-1-*hydroxyethyl*]-β-D-ribo-*hexopyranoside* (16).—To a solution of the acetal (12) (0·58 g) in dry methanol (25 ml) was added methanol (10 ml) containing 2% hydrogen chloride gas, whereafter the mixture was heated under reflux for 3 h, neutralised (solid $NaHCO_3$), and filtered. The residue remaining after removal of the solvent was extracted with hot chloroform (2 × 50 ml), and the combined extracts were filtered and concentrated. Chromatography of the residue on silica gel (elution with ethyl acetate–chloroform, 4 : 1) gave the β-*glycoside* (16) (0·25 g, 51%), $[\alpha]_D$ −46 ± 3° (*c* 1·3 in $CHCl_3$) {lit.,[4] $[\alpha]_D$ −37 ± 2·5° (*c* 1·2 in $CHCl_3$)}. The n.m.r. spectrum of this material was identical with that published [4] for the decarbonated form of methyl aldgaroside B.

Methyl 4,6-*Dideoxy*-3-C-[(S)-1-*hydroxyethyl*]-β-D-ribo-*hexopyranoside* 3,3^1-*Cyclic Carbonate* (*Methyl Aldgaroside B*) (14).—*Method* (*a*). A solution of the trichloroethoxycarbonyl derivative (13) (0·5 g) in methanol (30 ml) containing *ca.* 2% hydrogen chloride was heated under gentle reflux for 2 h, after which it was neutralised (solid $NaHCO_3$) and filtered. Removal of the solvent left an oil (0·13 g) that was chromatographed on silica gel (elution with light petroleum–ethyl acetate, 7 : 3) to give *methyl aldgaroside B* (14) (29 mg, 11%), m.p. 175—176° (from methylene chloride–ether), $[\alpha]_D$ −40 ± 2° (*c* 0·35 in MeOH), $\nu_{max.}$ 1770 cm^{-1} (cyclic carbonate) (Found: C, 51·9; H, 7·1. $C_{10}H_{16}O_6$ requires C, 51·7; H, 6·95%) {lit.,[4] m.p. 175—177°, $[\alpha]_D$ −41 ± 3° (*c* 1 in MeOH); lit.,[14] m.p. 178—180°, $[\alpha]_D$ −43·5° (MeOH)}; τ 5·52 (1H, d, $J_{1.2}$ *ca.* 7·5 Hz, H-1), 5·58 (1H, q, *J ca.* 7 Hz, H-3^1), 6·50 (3H, s, OMe), 8·48 [3H, d, *J ca.* 7 Hz, HC(3^1)*Me*], and 8·77 [3H, d, $J_{5.6}$ *ca.* 7 Hz, HC(5)*Me*]. The n.m.r. and i.r. (KBr disc) spectra of the synthetic sugar were indistinguishable from those of methyl aldgaroside B obtained from aldgamycin E[4] and by synthesis using an alternative route.[14]

Continued elution of the chromatographic column yielded a mixture (89 mg) of unidentified compounds. Attempts to isolate the intermediate carbonate ester (15) met with no success.

Method (*b*). A cooled (0°) solution of the triol (16) (0·21 g) in dry pyridine (5 ml) containing a 12% (w/w) solution of phosgene in benzene (1·2 ml) was set aside for 2 h at 0°; it was then poured into ice–water (15 ml) and the product was extracted with chloroform (3 × 5 ml). Evaporation of the extract and chromatography of the residue on silica gel (elution with carbon tetrachloride–acetone, 2 : 1) afforded methyl aldgaroside B (14) (0·2 g, 85%), m.p. 175—177° (from methylene chloride–ether), $[\alpha]_D$ −42° (*c* 1·1 in MeOH), which was indistinguishable (mixed m.p., and n.m.r. and i.r. spectra) from the material obtained using method (*a*).

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