Identification of Variose as 2,6-Dideoxy-3-*O*-methyl-D-*ribo*-hexose (D-Cymarose)[1]

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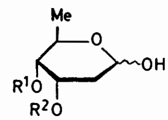
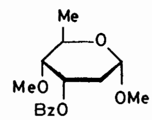
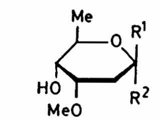
Variose, a sugar component of the antibiotic variamycin, has been identified as 2,6-dideoxy-3-*O*-methyl-D-*ribo*-hexose (*i.e.* D-cymarose). This assignment is based on the conversion of D-cymarose into, *inter alia*, methyl 2,6-dideoxy-3-*O*-methyl-α-D-*ribo*-hexofuranoside (6) and then into the 5-benzoate (8), which proved to be identical with methyl varioside benzoate. The α-cymarofuranoside (6) was also prepared by a less direct route that involved reaction of methyl 5-*O*-benzyl-6-deoxy-α-D-allofuranoside (10) with *NN*-dimethyl-α-chlorobenzylidene-ammonium chloride (11) to give methyl 2-*O*-benzoyl-5-*O*-benzyl-3-chloro-3,6-dideoxy-α-D-glucofuranoside (19). Reductive cleavage of the α-*allo*-epoxide (20) derived from (19), followed by methylation and debenzylation, gave the desired product.

VARIOSE is one of several 2,6-dideoxyhexoses found [2] in the anti-neoplastic antibiotic variamycin isolated from fermentation broths of *Actinomyces olivovariables* nova.[3] The antibiotic is a member of the same family as the chromomycins and olivomycins. Variose was originally assigned [4] the structure 2,6-dideoxy-4-*O*-methyl-D-*ribo*-hexose (1), based primarily on the characterization of methyl varioside benzoate, supposedly (2), by ^{1}H n.m.r. spectroscopy. However, two independent syntheses [5] of (2) showed that it is not identical to the varioside benzoate. Reassignment of the ^{1}H n.m.r. spectrum of the latter compound suggested [5] it is that of a methyl 5-*O*-benzoyl-2,6-dideoxy-3-*O*-methylhexofuranoside, since the low-field resonance ascribed to H-5, which lies downfield of the anomeric-proton resonance, cannot otherwise be accounted for satisfactorily.

The isomeric 2,6-dideoxy-3-*O*-methyl-D-hexoses are well known as constituents of the cardiac glycosides and, unlike variose, they have been isolated in crystalline form.[6] Consideration of their optical rotations suggested that variose {$[\alpha]_D$ + 53° (final, H_2O) [4]} might be identical to D-cymarose {$[\alpha]_D$ +55° (final, H_2O) [7]} or, possibly, D-diginose {$[\alpha]_D$ +60° (final, H_2O) [8]}, which are 2,6-dideoxy-3-*O*-methyl-D-*ribo*- and -D-*lyxo*-hexose, respectively. Since the former structure seemed more likely, we undertook to convert D-cymarose (3) into the anomeric methyl D-cymarofuranoside benzoates so that they could be compared with methyl varioside benzoate.

RESULTS AND DISCUSSION

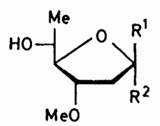
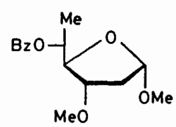
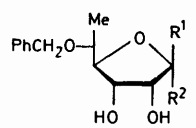
D-Cymarose [7] (3) was obtained by acidic hydrolysis of methyl 2,6-dideoxy-3-*O*-methyl-α-D-*ribo*-hexopyranoside (4), which was synthesized from the readily available methyl 4,6-*O*-benzylidene-2-deoxy-α-D-*erythro*-hexopyranosid-3-ulose [9] by a route essentially similar to one recently reported by Monneret *et al.*[10] Kinetically controlled glycosidation of D-cymarose (3) with methanol containing a catalytic amount of concentrated sulphuric acid at 4 °C gave, after careful chromatography on silica gel, an inseparable mixture of the methyl β-furanoside (7) [δ 5.08 (1 H, quartet, $J_{1,2}$ 3, $J_{1,2'}$ 5 Hz, H-1)] and the known methyl β-pyranoside [10] (5) [δ 4.55 (1 H, quartet, $J_{1,2ax}$ 9, $J_{1,2eq}$ 2 Hz, H-1)], as well as the pure methyl α-furanoside (6) [δ 5.04 (1 H, triplet, $J_{1,2}$ and $J_{1,2'}$ *ca.* 3 Hz)]. The anomeric configurations assigned to the methyl D-cymarofuranosides (6) and (7) are based on an independent synthesis of the α-anomer (see later).

(1) R^1 = Me; R^2 = H
(3) R^1 = H; R^2 = Me

(2)

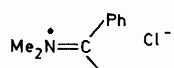
(4) R^1 = H; R^2 = OMe
(5) R^1 = OMe; R^2 = H

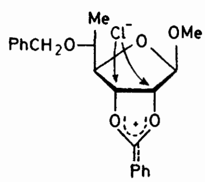
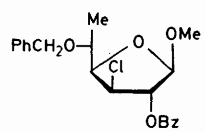
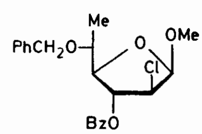
(6) R^1 = H; R^2 = OMe
(7) R^1 = OMe; R^2 = H

(8)

(9) R^1 = OMe; R^2 = H
(10) R^1 = H; R^2 = OMe



(11)

(12) (13) (14)

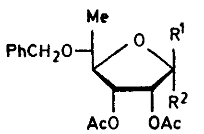
Benzoylation of the α-furanoside (6) gave the 5-benzoate (8) {$[\alpha]_D$ +60° (*c* 1 in $CHCl_3$)}, whose ^{1}H n.m.r. spectrum was indistinguishable from that recorded [4] for methyl varioside benzoate {$[\alpha]_D$ +60 ± 2° (*c* 0.2 in $CHCl_3$)}. Variose and D-cymarose are clearly one and the same sugar, so that the structure proposed [2] for variamycin must be amended accordingly.

Although the values for the optical rotation of the methyl glycofuranosides (6) and (8) are indicative of the α-configuration, it was not possible to obtain irrefutable evidence in support of their structures from ^{1}H n.m.r.

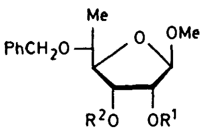
spectroscopy. We sought, therefore, to synthesize the methyl cymarofuranosides (6) and (7) from methyl 5-*O*-benzyl-6-deoxy-α-D-allofuranoside (10) and the corresponding β-anomer (9), respectively, by their reaction with *NN*-dimethyl-α-chlorobenzylideneammonium chloride [11] (11). According to the mechanism proposed by Barton *et al.*,[11] the latter reaction, for example, might yield the chlorohydrin benzoate (13) or (14), or both, from S_N2 displacement by chloride ion on the benzoxonium ion (12). Literature precedents [12] suggested that the 2-chloro-derivative (14) would be readily transformed into methyl β-D-cymarofuranoside (7) *via* reductive dechlorination, *etc.*

Acetylation of a mixture of methyl 5-*O*-benzyl-6-deoxy-α- and -β-D-allofuranosides (prepared [13] in six steps from L-rhamnose) gave, after chromatography on silica gel, the pure diacetates (15) and (16) in the ratio of roughly 2 : 1. *O*-Deacetylation then gave the diols (9) and (10). The anomeric configurations of these compounds were readily established, since acetonation of the diol (9) gave methyl 5-*O*-benzyl-6-deoxy-2,3-*O*-isopropylidene-β-D-allofuranoside,[13] whose anomeric configuration was known. Attempts to separate the diols (9) and (10) in the original mixture [13] by preparative t.l.c. were unrewarding.

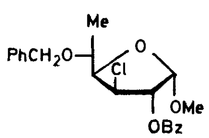
Methyl 5-*O*-benzyl-6-deoxy-β-D-allofuranoside (9) on reaction with the imidoyl chloride [11] (11) gave, after



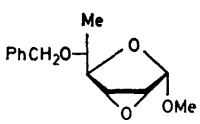
(15) R^1 = OMe ; R^2 = H
(16) R^1 = H ; R^2 = OMe



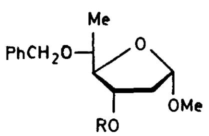
(17) R^1 = Bz ; R^2 = H
(18) R^1 = H ; R^2 = Bz



(19)



(20)



(21) R = H
(22) R = Me

preparative chromatography, the chlorohydrin benzoate (13) (27.5%) and the monobenzoates (17) (15%) and (18) (23%). These assignments are based on elemental analyses and the expectation of finding the resonance of the proton geminal to the benzoyloxy-group at a lower field than those of the other ring protons in the ^{1}H n.m.r. spectra. Spectral assignments (see Experimental section) were confirmed by decoupling experiments. In the ^{1}H n.m.r. spectrum of the chlorohydrin benzoate (13), H-1 and H-2 appeared as singlets at δ 5.08 and 5.49, respectively, consistent with the *trans*, *trans* arrangement of H-1—H-3 and the D-*gluco*-configuration. *O*-Debenzoylation of the monobenzoates (17) and (18) gave the diol (9). The compounds (13), (17), and (18) presumably arise from the 2,3-benzoxonium ion (12) either by S_N2 displacement by chloride ion at C-3 or by *cis*-opening with water during work-up. The S_N2 process appears to be sluggish (*cf.* the α-anomer), while attack at C-3 of the 2,3-benzoxonium ion (12) would be favoured electronically and, possibly, sterically. The propensity of ribonucleoside 2′,3′-acyloxonium ions to undergo nucleophilic opening at C-3′ is well documented,[12,14] although a heterocyclic base at C-1′ would exert a larger steric effect on an incoming nucleophile to C-2′ than does the 1-methoxy-group of (12).

Under comparable conditions, methyl 5-*O*-benzyl-6-deoxy-α-D-allofuranoside (10) reacted with the imidoyl chloride [11] (11) to give, after preparative chromatography, the chlorohydrin benzoate (19) in 62% yield. The H-2 resonance of (19), assigned on the basis of decoupling experiments, appeared as a quartet ($J_{1,2}$ *ca.* 4, $J_{2,3}$ *ca.* 2 Hz) at δ 5.53 to low field of the anomeric-proton resonance (doublet at δ 5.38). Since, in this case, the approach of chloride ion to C-2 of the benzoxonium ion intermediate would not be impeded by the 1-methoxy-group, with which it would have a *trans*-relationship, we conclude that electronic, rather than steric, effects are responsible for preferential nucleophilic attack at C-3. This might also be true of the regioselectivity observed in nucleophilic opening of benzoxonium ion (12) by chloride ion, although, in this case, electronic and steric effects would reinforce one another.

Although the formation of the 3-chloro-derivatives (13) and (19) thwarted any attempts to prepare 2-deoxy-derivatives *via* reductive dechlorination procedures, we sought to prepare the 2-deoxy-derivative (21) from the epoxide (20), which was readily obtained when (19) reacted with sodium methoxide in methanol. This approach was founded on the knowledge [15,16] that, for steric reasons, nucleophilic ring-opening of α-*ribo*-epoxides, unlike that of the corresponding β-*ribo*-epoxides, occurs preferentially at C-2 to yield α-D-*arabino*-derivatives. Factors governing the opening of such epoxides have been discussed by Williams.[15] Cleavage of the α-*allo*-epoxide (20) with lithium aluminium hydride in refluxing tetrahydrofuran, followed by methylation [17] of the resulting alcohol (21), gave a product that was undoubtedly methyl 5-*O*-benzyl-2,6-dideoxy-3-*O*-methyl-α-D-*ribo*-hexofuranoside (22). Assignment of the constitution of (22) followed from elemental analysis and ^{1}H n.m.r. spectroscopy [δ 5.09 (1 H, quartet, $J_{1,2}$ *ca.* 2, $J_{1,2'}$ *ca.* 4 Hz, H-1) and 2.07 (2 H, m, H-2 and H-2′)]. Both ^{1}H n.m.r. spectroscopy and t.l.c. of the crude reaction mixture indicated that little, if any, ring-opening of the epoxide (20) occurred at C-3. Catalytic hydrogenolysis of (22) then gave methyl 2,6-dideoxy-3-*O*-methyl-α-D-*ribo*-hexofuranoside (6), which was indistinguishable (t.l.c. and ^{1}H n.m.r. spectroscopy) from the pure methyl glycofuranoside isolated from glycosidation of D-cymarose (3).

EXPERIMENTAL

T.l.c. was performed on Kieselgel G, and spots were detected with vanillin-sulphuric acid.[18] I.r. spectra were recorded for Nujol mulls or films with a Perkin-Elmer Infracord spectrophotometer. ^{1}H N.m.r. spectra were measured with a Brucker Spectrospin (90 MHz) spectrometer. A Perkin-Elmer Model 141 polarimeter and 1-dm tubes were used for the measurement of specific rotations. Melting points are uncorrected. Light petroleum refers to the fraction of b.p. 60—80 °C.

Methyl 2,3-*Di*-O-*acetyl*-5-O-*benzyl*-6-*deoxy*-β- *and* -α-D-*allofuranosides* (15) *and* (16).—To a mixture of methyl 5-*O*-benzyl-6-deoxy-α- and -β-D-allofuranosides [13] (0.9 g) in pyridine (10 ml) was added acetic anhydride (2 ml), after which the reaction mixture was set aside overnight before it was diluted with chloroform. The solution was then washed successively with dilute hydrochloric acid, a solution of sodium hydrogencarbonate, and water. Concentration of the dried ($MgSO_4$) solution and chromatography of the residue on silica gel [eluant benzene–ether–light petroleum (9 : 2 : 1)] gave the β-*diacetate* (15) (0.7 g, 59%), b.p. 147 °C (bath) at 0.05 mmHg; $[\alpha]_D$ −26° (*c* 1 in $CHCl_3$) (Found: C, 61.8; H, 6.6. $C_{18}H_{24}O_7$ requires C, 61.35; H, 6.9%); δ 7.33 (5 H, m, aromatic), 5.49 (1 H, q, $J_{2,3}$ 6 Hz, H-3), 5.24 (1 H, q, $J_{1,2}$ *ca.* 1.5 Hz, H-2), 4.91 (1 H, d, H-1), 4.57 (2 H, AB q, J_{AB} 12 Hz, PhCH_2), 4.04 (1 H, t, $J_{4,5}$ 6 Hz, H-4), 3.61 (1 H, m, H-5), 3.38 (3 H, s, OMe), 2.08 and 1.96 (6 H, s, 2 × OAc), and 1.30 (3 H, d, $J_{5,6}$ 6 Hz, HC*Me*).

Further elution gave the α-*diacetate* (16) (0.38 g, 32%), b.p. 168 °C (bath) at 0.01 mmHg; $[\alpha]_D$ +106° (*c* 1 in $CHCl_3$) (Found: C, 61.6; H, 6.7%); δ 7.33 (5 H, m, aromatic), 5.47 (1 H, q, $J_{2,3}$ *ca.* 7 Hz, H-3), 5.20—4.92 (2 H, m, H-1 and H-2), 4.60 (2 H, AB q, J_{AB} 12 Hz, PhCH_2), 4.09 (1 H, t, $J_{3,4}$ and $J_{4,5}$ 3 Hz, H-4), 3.74 (1 H, m, H-5), 3.44 (3 H, s, OMe), 2.11 and 2.09 (6 H, s, 2 × OAc), and 1.22 (3 H, d, $J_{5,6}$ 6.5 Hz, HC*Me*).

Methyl 5-O-*Benzyl*-6-*deoxy*-β-D-*allofuranoside* (9).—To a solution of the β-diacetate (15) (2.8 g) in methanol (60 ml) was added a small piece of sodium, after which the solution was set aside for 2 h at room temperature. After removal of the solvent, the residue was taken up in chloroform (100 ml), which was washed with water (3 × 50 ml), dried ($MgSO_4$), and concentrated. Chromatography of the residue on silica gel [eluant benzene–ether–light petroleum (9 : 2 : 1)] gave the diol (9) (1.84 g, 86%), m.p. 79—81 °C (from ether–light petroleum); $[\alpha]_D$ −106° (*c* 1 in $CHCl_3$); $\nu_{max.}$ 3 500 cm^{-1} (br, OH) (Found: C, 62.7; H, 7.8. $C_{14}H_{20}O_5$ requires C, 62.7; H, 7.5%); δ 7.33 (5 H, m, aromatic), 4.81 (1 H, s, H-1), 4.58 (2 H, AB q, J_{AB} 12 Hz, PhCH_2), 4.41—3.40 (4 H, H-2—H-5), 3.31 (3 H, s, OMe), and 1.28 (3 H, d, $J_{5,6}$ 6 Hz, HC*Me*).

Acetonation of the diol (9), using the procedure of Singh *et al.*,[19] gave, after chromatography on silica gel and distillation, methyl 5-*O*-benzyl-6-deoxy-2,3-*O*-isopropylidene-β-D-allofuranoside (identified by comparison with an authentic sample [13]).

Methyl 5-O-*Benzyl*-6-*deoxy*-α-D-*allofuranoside* (10).—This diol (81%), $[\alpha]_D$ +76° (*c* 1 in $CHCl_3$), was obtained as a syrup by *O*-deacetylation of the α-diacetate (16) and chromatography on silica gel [eluant ethyl acetate–chloroform–methylene chloride (5 : 2 : 2)] essentially as described in the previous experiment (Found: C, 63.0; H, 7.2%); δ 7.29 (5 H, m, aromatic), 4.89 (1 H, d, $J_{1,2}$ *ca.* 3 Hz, H-1), 4.55 (2 H, AB q, J_{AB} 12 Hz, PhCH_2), 4.11—3.91 (3 H, m, H-2—H-4), 3.66 (1 H, m, H-5), 3.44 (3 H, s, OMe), and 1.20 (3 H, d, $J_{5,6}$ 6 Hz, HC*Me*).

Reaction of Methyl 5-O-*Benzyl*-6-*deoxy*-β-D-*allofuranoside* (9) *with the Imidoyl Chloride* (11).—*NN*-Dimethylbenzamide (1.6 g) was treated overnight with a 15% solution of phosgene in methylene chloride (10 ml), and the solvent and excess of reagent were then removed to give the imidoyl chloride (11) as a white solid. To a stirred solution of the imidoyl chloride in methylene chloride (10 ml) was added the diol (9) (0.825 g) and pyridine (1.3 g), after which the reaction mixture was stirred for 3 days at room temperature before it was diluted with chloroform, washed with water, and dried. Removal of the solvent and chromatography of the residue on silica gel [eluant toluene–hexane–acetone (5 : 1 : 1)] gave first methyl 2-*O*-benzoyl-5-*O*-benzyl-3-chloro-3,6-dideoxy-β-D-glucofuranoside (13) (0.33 g, 27.5%); $[\alpha]_D$ −4° (*c* 1 in $CHCl_3$); $\nu_{max.}$ 1 740 cm^{-1} (C=O) (Found: C, 64.7; H, 5.6; Cl, 8.9. $C_{21}H_{23}ClO_5$ requires C, 64.5; H, 5.9; Cl, 9.1%); δ 8.13—7.02 (10 H, m, aromatic), 5.49 (1 H, s, H-2), 5.08 (1 H, s, H-1), 4.57 (2 H, AB q, J_{AB} 12 Hz, PhCH_2), 4.56 (1 H, d, $J_{3,4}$ *ca.* 3 Hz, H-3), 4.36—3.87 (2 H, m, H-4 and H-5), 3.49 (3 H, s, OMe), and 1.43 (3 H, d, $J_{5,6}$ 6 Hz, HC*Me*). Further elution gave methyl 2-*O*-benzoyl-5-*O*-benzyl-6-deoxy-β-D-allofuranoside (17) (0.175 g, 15%), m.p. 104—105 °C; $[\alpha]_D$ −13° (*c* 1 in $CHCl_3$); $\nu_{max.}$ 3 400 (OH) and 1 730 cm^{-1} (C=O) (Found: C, 67.8; H, 6.6. $C_{21}H_{24}O_6$ requires C, 67.7; H, 6.5%); δ 8.18—7.13 (10 H, m, aromatic), 5.36 (1 H, d, $J_{2,3}$ *ca.* 5 Hz, H-2), 5.01 (1 H, s, H-1), 4.64 (2 H, AB q, J_{AB} 12 Hz, PhCH_2), 4.56 (1 H, q, H-3), 4.00 (1 H, t, $J_{3,4}$ and $J_{4,5}$ *ca.* 6 Hz, H-4), 3.67 (1 H, m, H-5), 3.39 (3 H, s, OMe), and 1.36 (3 H, d, $J_{5,6}$ 6 Hz, HC*Me*), followed by methyl 3-*O*-benzoyl-5-*O*-benzyl-6-deoxy-β-D-allofuranoside (18) (0.26 g, 23%); $[\alpha]_D$ −9° (*c* 0.7 in $CHCl_3$); $\nu_{max.}$ 3 400 (OH) and 1 730 cm^{-1} (C=O) (Found: C, 68.1; H, 6.4%); δ 8.11—7.02 (10 H, m, aromatic), 5.47 (1 H, t, $J_{2,3}$ and $J_{3,4}$ 5 Hz, H-3), 4.91 (1 H, d, $J_{1,2}$ *ca.* 1.5 Hz, H-1), 4.55 (2 H, AB q, J_{AB} 12 Hz, PhCH_2), 4.39 (1 H, q, H-2), 4.22 (1 H, t, $J_{4,5}$ 5 Hz, H-4), 3.63 (1 H, m, H-5), 3.38 (3 H, s, OMe), and 1.30 (3 H, d, $J_{5,6}$ 6 Hz, HC*Me*).

On *O*-debenzoylation, both (17) and (18) gave the diol (9) (m.p. and mixed m.p. 79—81 °C).

Methyl 2-O-*Benzoyl*-5-O-*benzyl*-3-*chloro*-3,6-*dideoxy*-α-D-*glucofuranoside* (19).—To a stirred solution of the imidoyl chloride [11] (11) [prepared from *NN*-dimethylbenzamide (2.5 g)] in methylene chloride (15 ml) containing pyridine (1.3 g) was added the diol (10) (1.12 g) and stirring was continued for 3 days at room temperature. The reaction mixture was then diluted with chloroform and the solution was washed with water, dried ($MgSO_4$), and concentrated. Chromatography on silica gel [eluant benzene–ether–light petroleum (9 : 2 : 1)] gave the *chloro-benzoate* (19) (1.01 g, 62%); $[\alpha]_D$ +111° (*c* 1.3 in $CHCl_3$); $\nu_{max.}$ 1 740 cm^{-1} (C=O) (Found: C, 64.8; H, 6.2; Cl, 8.8. $C_{21}H_{23}ClO_5$ requires C, 64.5; H, 5.9; Cl, 9.1%); δ 8.20—7.13 (10 H, m, aromatic), 5.53 (1 H, q, $J_{2,3}$ *ca.* 2 Hz, H-2), 5.38 (1 H, d, $J_{1,2}$ *ca.* 4 Hz, H-1), 4.69 (1 H, q, H-3), 4.60 (2 H, AB q, J_{AB} 12 Hz, PhCH_2), 4.30 (1 H, q, H-4), 3.92 (1 H, m, H-5), 3.40 (3 H, s, OMe), and 1.41 (3 H, d, $J_{5,6}$ 6 Hz, HC*Me*). The ^{1}H n.m.r. spectrum showed the presence of a trace of a second component, which could not be removed by chromatography.

Methyl 2,3-*Anhydro*-5-O-*benzyl*-6-*deoxy*-α-D-*allofuranoside* (20).—To a solution of the chloro-benzoate (19) (0.79 g) in methanol (30 ml) was added a small piece of sodium, after which it was kept for 3 h at room temperature; t.l.c. [benzene–ether–light petroleum (9 : 2 : 1)] then showed that a single product had been formed. The solvents were removed, the residue was extracted with chloroform, and the organic extract was filtered and concentrated. Chromatography on silica gel [eluant benzene–ether–light petroleum (9 : 2 : 1)] furnished the *anhydro sugar* (20) (0.38 g, 75%); $[\alpha]_D$ −35.5° (*c* 1 in $CHCl_3$) (Found: C, 67.5; H, 7.5. $C_{14}H_{18}O_4$ requires C, 67.2; H, 7.25%); δ 7.29 (5 H, m, aromatic), 5.10 (1 H, s, H-1), 4.50 (2 H, AB q, J_{AB} 12 Hz, PhCH_2), 4.11 and 3.76—3.49 (4 H, d and m, H-2—H-5), 3.43 (3 H, s, OMe), and 1.18 (3 H, d, $J_{5,6}$ 6 Hz, HC*Me*). Vacuum distillation of (20) resulted in slight decomposition.

Methyl 5-O-*Benzyl*-2,6-*dideoxy*-3-O-*methyl*-α-D-ribo-*hexofuranoside* (22).—A solution of the epoxide (20) (0.143 g) in tetrahydrofuran (15 ml) containing lithium aluminium hydride (0.1 g) was heated overnight under reflux before the excess of the reagent was destroyed with wet ethyl acetate. Work-up of the reaction mixture in the usual way, followed by chromatography on silica gel [eluant methylene chloride–acetone (10 : 1)], gave the 2,6-*dideoxy-derivative* (21) (68 mg, 47%); δ 7.33 (5 H, m, aromatic), 5.09 (1 H, narrow q, $J_{1,2}$ 4, $J_{1,2'} \leqslant 1.5$ Hz, H-1), 4.56 (2 H, AB q, J_{AB} 12 Hz, PhCH_2), 4.24 (1 H, m, H-3), 3.99 (1 H, q, H-4), 3.54 (1 H, m, H-5), 3.38 (3 H, s, O*Me*), 2.04 (2 H, m, H-2 and H-2′), and 1.22 (3 H, d, $J_{5,6}$ 6 Hz, HC*Me*), which was used in the next step with further purification.

A cold (0 °C) solution of (21) (68 mg) in tetrahydrofuran (5 ml) containing sodium hydride (80 mg) was stirred for 30 min before methyl iodide (300 mg) was added dropwise. The reaction mixture was then stirred for 24 h at room temperature, after which the excess of reagents was destroyed by addition of methanol. Work-up in the usual way [17] and chromatography on silica gel [eluant methylene chloride–acetone (10 : 1)] gave the syrupy *methylated derivative* (22) (47 mg, 65.5%); $[\alpha]_D$ +86° (*c* 0.2 in $CHCl_3$) (Found: C, 67.3; H, 8.2. $C_{15}H_{22}O_4$ requires C, 67.6; H, 8.3%); δ 7.33 (5 H, m, aromatic), 5.09 (1 H, q, $J_{1,2}$ *ca.* 2, $J_{1,2'}$ *ca.* 4 Hz, H-1), 4.61 (2 H, AB q, J_{AB} 12 Hz, PhCH_2), 4.13—3.51 (3 H, m, H-3—H-5), 3.40 and 3.33 (6 H, s, 2 × OMe), 2.07 (2 H, m, H-2 and H-2′), and 1.22 (3 H, d, $J_{5,6}$ 6 Hz, HC*Me*).

Methyl 2,6-*Dideoxy*-3-O-*methyl*-α-D-ribo-*hexofuranoside* (6).—To a cooled (4 °C) solution of cymarose [7] (3) [0.476 g; prepared by acidic hydrolysis of methyl 2,6-dideoxy-3-*O*-methyl-α-D-*ribo*-hexopyranoside [10] (4)] in methanol (5 ml) was added a 1% solution of conc. H_2SO_4 in methanol (5 ml), and glycosidation was allowed to proceed at this temperature for 18 h. The solution was then neutralised with conc. ammonia solution, filtered, and concentrated to a syrup (0.444 g), which ^{1}H n.m.r. spectroscopy showed to contain three components. Careful chromatography on silica gel [eluant methylene chloride–acetone (4 : 1)] gave an inseparable mixture (0.1 g) of methyl β-D-cymarofuranoside (7) [δ 5.08 (1 H, q, $J_{1,2}$ 5, $J_{1,2'}$ 3 Hz, H-1)] and methyl β-D-cymaropyranoside [10] (5) [δ 4.55 (1 H, q, $J_{1,2ax}$ 9, $J_{1,2eq}$ 2 Hz, H-1)] followed by pure *methyl* α-D-*cymarofuranoside* (6) (0.12 g, 23%), b.p. 81 °C (bath) at 2 mmHg, $[\alpha]_D$ +175° (*c* 0.7 in $CHCl_3$) (Found: C, 54.2; H, 9.0. $C_8H_{16}O_4$ requires C, 54.5; H, 9.15%); δ 5.04 (1 H, t, $J_{1,2}$ and $J_{1,2'}$ *ca.* 3 Hz, H-1), 4.13—3.78 (3 H, m, H-3—H-5), 3.38 and 3.33 (6 H, s, 2 × OMe), 2.04 (2 H, m, H-2 and H-2′), and 1.20 (3 H, d, $J_{5,6}$ 6 Hz, HC*Me*).

Alternatively, hydrogenolysis of the benzylated derivative (22) (40 mg) in methanol (10 ml) containing 5% palladised carbon (150 mg) gave, after removal of the catalyst and solvent, the α-glycofuranoside (6) (79%), which was indistinguishable (^{1}H n.m.r. spectrum and t.l.c.) from the previous sample.

Methyl 5-O-*Benzoyl*-2,6-*dideoxy*-3-O-*methyl*-α-D-ribo-*hexofuranoside* (8).—To a solution of the α-furanoside (6) (70 mg) in pyridine (1 ml) was gradually added benzoyl chloride (0.15 g) in pyridine (2 ml), after which the reaction mixture was set aside at room temperature for 4 h; t.l.c. [methylene chloride–acetone (10 : 1)] then showed that no starting material remained. Work-up in the usual way and chromatography on silica gel gave the *benzoate* (8) (99 mg, 89%), $[\alpha]_D$ +60° (*c* 1 in $CHCl_3$). The ^{1}H n.m.r. spectrum of (8) (published in ref. 1) was indistinguishable from that recorded [4] for methyl varioside monobenzoate {$[\alpha]_D$ +60 ± 2° (*c* 0.2 in $CHCl_3$)}.

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