Chiral Synthesis of Polyketide-derived Natural Products. Part 5.[1] Synthesis of a Chiral Segment Corresponding to the C-1—C-5 Unit of Erythromycin A from D-Glucose

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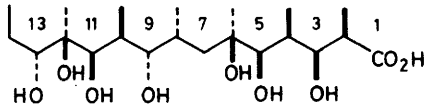
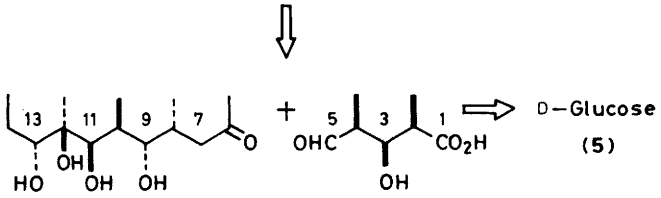
As a right-hand segment with three consecutive chiral centres corresponding to the C-1—C-5 unit of erythromycin A (**1**), (2*S*,3*R*,4*S*)-3,5-isopropylidenedioxy-2,4-dimethylpentanal (**32**) was synthesized from D-glucose (**5**) by application of MPM (4-methoxybenzyl) protection for an hydroxy function and some fairly stereoselective reactions, hydroboration and hydrogenation.

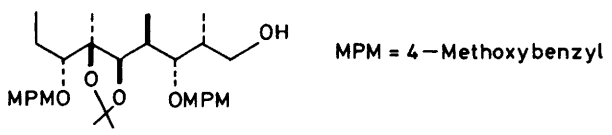
In the preceding papers[1,2] we described a stereocontrolled synthesis of an important chiral synthon (**6**) for the total synthesis of erythromycin A (**1**) from D-glucose (**5**) by means of the MPM (*p*-methoxyphenylmethyl) protection of hydroxy groups and some stereoselective reactions, *e.g.* the Wittig reaction, OsO_4 oxidation and epoxidation. Compound (**6**) is a synthetic equivalent of the left-hand segment i (**3**) of dihydroerythronolide A seco-acid (**2**) because it has the same six consecutive chiral centres with correct configurations. In this paper we report a stereocontrolled synthesis of another segment, the right-hand segment ii (**4**) corresponding to the C-1—C-5 unit of (**1**) with three consecutive chiral centres, from D-glucose (**5**) (Scheme 1).



Dihydroerythronolide A seco-acid (2)



Segment i (3) Segment ii (4)

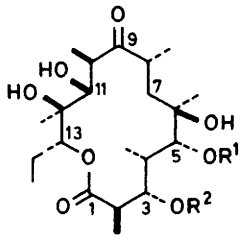


(6)

Scheme 1.

Results and Discussion

The ketone (**7**), derived from (**5**) as described in a previous paper,[2] was treated with methylenetriphenylphosphorane in order to obtain the olefinic compound (**8**). Wittig reaction in dimethyl sulphoxide (DMSO)[3] at room temperature proceeded quite smoothly to give an olefinic product which was, however, a 1:2 mixture of the expected olefin (**8**) and its isomer at the C-4 position, probably because the starting ketone (**7**) isomerized[4] to the more stable isomer before being attacked by the Wittig



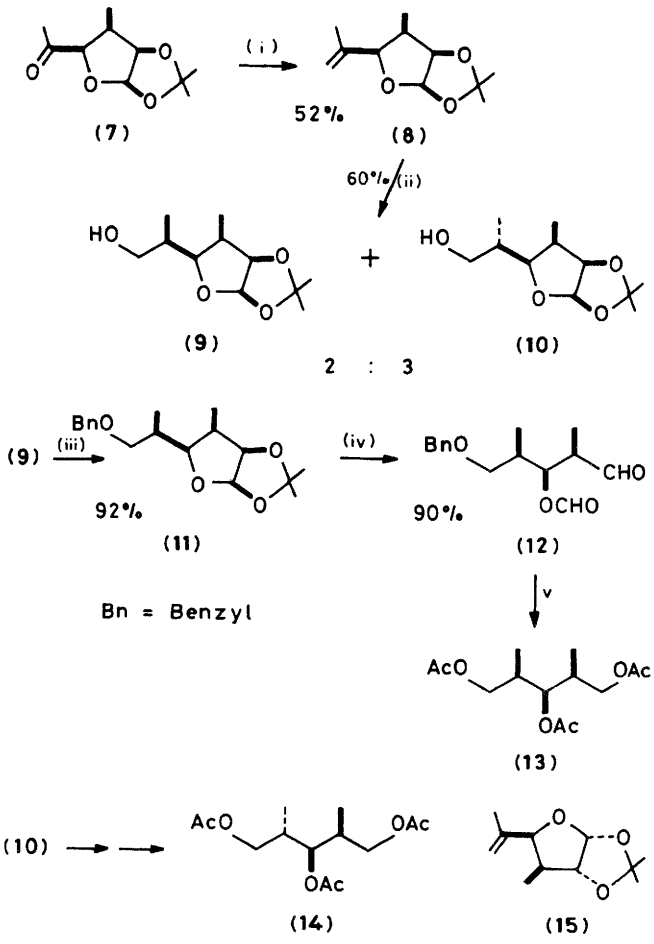
Erythromycin A (1)
R^1 = D—desosaminyl
R^2 = L—cladinosyl

reagent under basic conditions in the polar solvent. When (**7**) was treated with the Wittig reagent in tetrahydrofuran (THF) at −70 °C and the mixture was allowed to warm to 0 °C for a period of 9 h, olefin (**8**) was isolated as the sole product, though only in 52% yield with 14% recovery of the starting material (**7**).

Hydroboration of (**8**) in THF at between 0 °C and room temperature, followed by hydrogen peroxide oxidation, gave a 2:3 diastereoisomeric mixture of compounds (**9**) and (**10**), which were readily separated by silica gel column chromatography. The structures of both compounds were determined through conversion into their respective triacetates (**13**) and (**14**) in a sequence of conventional reactions. The minor alcohol (**9**) was protected as the benzyl ether (**11**), and then the isopropylidene group was removed by treatment with trifluoroacetic acid (TFA), followed by lead tetra-acetate oxidation to give the aldehyde (**12**). Lithium aluminium hydride reduction of (**12**) gave the diol, which was hydrogenated to remove the benzyl group and then the resultant triol was acetylated to afford the oil triacetate (**13**). The ^1H n.m.r. spectrum clearly showed that (**13**) was a *meso* compound, because only one methyl signal, at δ 0.96, was observed as a doublet (*J* 7 Hz, 6 H). The structure of compound (**13**) was finally confirmed by comparison of its spectral data with those of a degradation product of natural erythromycin A (**1**) which will be reported in the following paper.[4] The major alcohol (**10**) was converted into the isomeric triacetate (**14**) in the same way (Scheme 2). In its ^1H n.m.r. spectrum, two methyl groups were observed as two doublets at δ 0.94 and 0.99 with the same coupling constant (*J* 7.0 Hz), and hence (**10**) was not the expected compound.

Hydroboration of (**15**), isometic with (**8**) at C-3 and C-4, was reported[5] to occur stereoselectively and to give a single product, but compound (**8**) gave by this method a mixture of alcohols and, moreover, the expected alcohol (**9**) was the minor product. Therefore, an alternative route for the synthesis of segment ii (**4**) was next examined.

The alcohol (**16**)[6] derived readily from D-glucose (**5**) was first protected with the MPM group by treatment with MPM chloride and dimsylsodium in THF. The resultant MPM ether



Scheme 2. *Reagents:* (i) $Ph_3P{=}CH_2$, THF; (ii) BH_3–THF, then H_2O_2; (iii) NaH, BnCl; (iv) CF_3CO_2H, then $Pb(OAc)_4$; (v) (a) $LiAlH_4$, (b) H_2/Pd–C, (c) Ac_2O

(**17a**) was converted quite easily into the ketone (**21a**) by a method rather similar to that described in the earlier paper[2] *via* a series of conventional reactions. Selective removal of the 5,6-isopropylidene protection of (**17a**) with 2% sulphuric acid, followed by toluene-*p*-sulphonation of the primary hydroxy group[7] of the resultant diol gave the mono-toluenesulphonate (**18a**), which was cyclized into the epoxide (**19a**) by treatment with potassium carbonate. Alcoholysis with sodium benzyl alcoholate in THF gave the hydroxyether (**20a**), and finally the secondary hydroxy group in (**20a**) was oxidized with pyridinium chlorochromate (PCC) in the presence of molecular sieves[8] to afford the ketone (**21a**).

In contrast with (**7**), ketone (**21a**) gave solely the stereochemically pure olefin (**22a**) by the usual Wittig reaction in DMSO at room temperature, because compound (**21a**), with a 4-β-keto* group, is more stable than the corresponding 4-α-keto compound.

Hydroboration of olefin (**22a**) proceeded fairly stereoselectively even under the usual conditions, *e.g.* diborane in THF at room temperature, and a diastereoisomeric mixture (**23a**) of the expected alcohol as the main product and its isomer was obtained in moderate yield. The mixture (**23a**) without further purification, was converted into the methanesulphonate, followed by lithium aluminium hydride reduction to afford a diastereoisomeric mixture of deoxy compounds (**24a**), again in moderate yield. Although the separation of the mixture into its components was quite difficult, the ratio was easily determined to be 6.6:1 by means of the C-5 methyl signals in its ^1H n.m.r. spectrum. This means that the above hydroboration proceeded at a diastereoselection of the same ratio. The mixture (**24a**) was also obtained almost quantitatively directly from the olefin (**22a**) by catalytic reduction in the presence of rhodium on alumina at 0 °C, though the stereoselectivity was only modest (2.8:1). This direct reduction was nevertheless more convenient and efficient than the method *via* the hydroboration.

The mixture (**24a**) obtained by the catalytic reduction was treated with 4M-hydrochloric acid to remove the 1,2-isopropylidene protection, followed by oxidative cleavage with lead tetraacetate of the resultant vicinal diol group to afford a diastereoisomeric mixture of formyloxyaldehydes (**25a**). Lithium aluminium hydride reduction in ether, followed by silica gel column chromatography, gave the expected alcohol (**26a**) (64%) and its diastereoisomer (**27a**) (23%).

The major alcohol (**26a**) was treated with tosyl chloride and then reduced with lithium aluminium hydride in the usual way to afford the dimethyl compound (**28a**). The stereochemical configuration of (**28a**) was confirmed by its conversion into the *meso* dimethyltriacetate (**13**) (Scheme 3). Both the MPM and benzyl protecting groups were removed by treatment with sodium metal in liquid ammonia to afford the trihydroxy compound, which was acetylated in the usual manner. The resultant triacetate (**13**) was completely identical in its spectral data with both the abovementioned compound (**13**) synthesized from (**7**) and the degradation product of erythromycin A (**1**).

The antipodal dimethyl compound (**28b**) was next synthesized from (**16**) basically in the same way as was its isomer (**28a**). Benzylation of the alcohol (**16**), followed by a series of conventional reactions as described above, gave the olefin (**22b**) *via* intermediates (**17b**)—(**21b**) (**b** series). Catalytic reduction of the alkene (**22b**) over rhodium–alumina at 0 °C gave a 3:1 mixture of diastereoisomers (**24b**) as determined by the C-5 methyl signals in its ^1H n.m.r. spectrum. Then the fully protected furanose (**24b**) was converted into a mixture of diols *via* (**25b**), and chromatographic separation on a silica gel column gave the expected diol (**26b**) (53%) and its diastereoisomer (**27b**) (17%). The primary hydroxy group of (**26b**) was excellently reduced to afford the dimethyl compound (**28b**), the enantiomer of (**28a**), and the n.m.r. and mass spectral data of both compounds were completely identical.

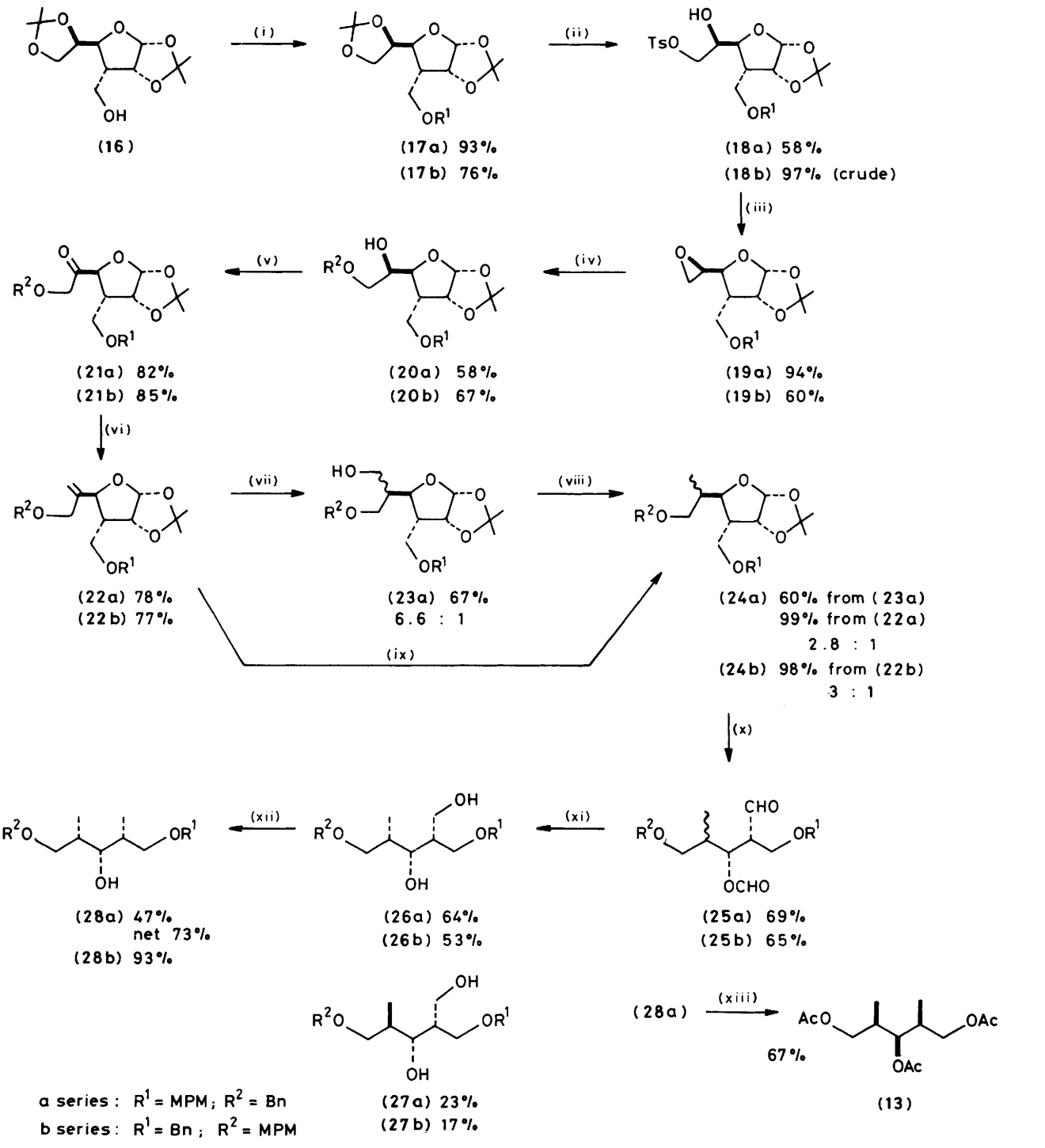
The MPM protecting group of (**28b**) was then selectively removed quite smoothly by treatment with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) in dichloromethane containing a small amount of water at room temperature according to the procedure described earlier.[9] The resultant diol (**29**) was protected as the six-membered acetonide (**30**) in the usual way, and the benzyl protection was removed by catalytic hydrogenolysis over palladium on charcoal to afford the alcohol (**31**). Finally, PCC oxidation of the primary hydroxy group of (**31**) gave the oily aldehyde (**32**), which is synthetically equivalent to the segment ii (**4**) (Scheme 4). Compound (**32**) was completely identical in its spectral data and specific optical rotation with a degradation product of natural erythromycin A (**1**) which will be reported in the following paper.[4]

Further studies on the coupling reaction of compound (**32**) with some derivatives of the segment i to give seco-acids and their cyclization to erythronolide A derivatives are currently in progress.

Experimental

M.p.s were measured on a Yamato MP-1 micro melting point apparatus and are uncorrected. Optical rotations were

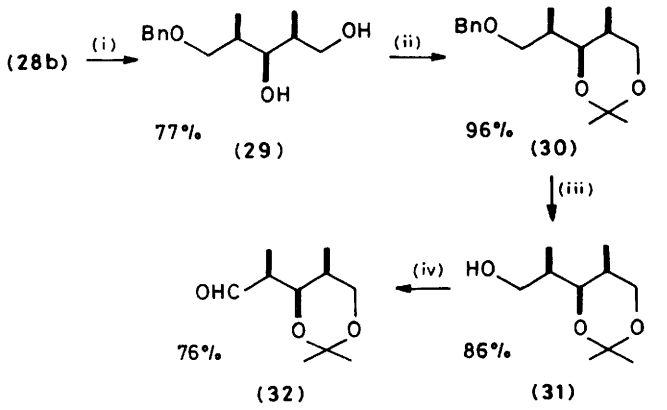
* The terms α and β are used with reference to each atom or group which lies behind the plane of the molecule and in front of it, respectively, as for steroids, as well to denote anomeric configurations.



Scheme 3. *Reagents:* (i) NaH, R^1Cl; (ii) 2% H_2SO_4, then TsCl, Py; (iii) K_2CO_3; (iv) R^2ONa; (v) PCC; (vi) $Ph_3P{=}CH_2$, DMSO; (vii) BH_3, then H_2O_2; (viii) MsCl, then $LiAlH_4$; (ix) $H_2/Rh{-}Al_2O_3$; (x) 4M-HCl, then $Pb(OAc)_4$; (xi) $LiAlH_4$; (xii) TsCl–Py, then $LiAlH_4$; (xiii) Na–liq. NH_3, then Ac_2O. Wavy bonds indicate mixtures of diastereoisomers

measured with a JASCO DIP-4 digital polarimeter. I.r. spectra were recorded on a JASCO IRA-2 spectrophotometer. Low- and high-resolution mass spectra were taken on a JEOL JMS D-300 or JEOL JMS-01 SG spectrometer. ^1H N.m.r. spectra were recorded on a JEOL JNM FX-100 or JEOL JNM FX-200 instrument.

3,5,6-*Trideoxy*-1,2-O-*isopropylidene*-3,6-*di*-C-*methyl*-β-L-lyxo-*hex*-5-*enofuranose* (**8**).—To a stirred THF solution of methylenetriphenylphosphorane, prepared from methyltriphenylphosphonium bromide (1.77 g, 4.95 mmol) in THF (15 ml) and a 1.6M hexane solution of n-BuLi (2.7 ml, 4.32 mmol) at room temperature under argon, was added a solution of the ketone (**7**) (300 mg, 1.5 mmol) in THF (1.5 ml) at −70 °C. The stirred reaction mixture was allowed to warm to 0 °C during 9 h, then was poured into ice–aqueous NH_4Cl and extracted with CH_2Cl_2. The extract was washed with water, dried (Na_2SO_4), and evaporated under reduced pressure. The residue was



Scheme 4. *Reagents:* (i) DDQ, CH_2Cl_2–H_2O; (ii) CSA, $Me_2C(OMe)_2$; (iii) H_2/Pd–C; (iv) PCC

chromatographed on a silica gel column with n-hexane–EtOAc (3:1) as eluant to afford two fractions. The first fraction was the title compound (**8**) as an oil (155 mg, 52%), $\delta_H(CDCl_3)$ 0.98 (3 H, d, *J* 7.0 Hz), 1.35 (3 H, s), 1.56 (3 H, s), 1.74 (3 H, s), 2.53 (1 H, sextet, *J* 7.0 Hz), 4.47 (1 H, d, *J* 8.0 Hz), 4.66 (1 H, dd, *J* 6.5, 4.0 Hz), 4.95 (1 H, br s), 5.11 (1 H, br s), and 5.73 (1 H, d, 4.0 Hz).

The second fraction was recovered (**7**) (42 mg, 14%).

Hydroboration of Compound (**8**).—A 1M THF solution of BH_3 (4 ml, 4.0 mmol) was added dropwise to a stirred THF (1 ml) solution of alkene (**8**) (200 mg, 1.01 mmol) at 0—5 °C under argon. After 1 h, the reaction mixture was allowed to warm to room temperature, and the mixture was stirred for further 1 h. MeOH (0.5 ml), 3M-NaOH (0.6 ml), and 30% H_2O_2 (0.6 ml) were then added successively, and the mixture was stirred for 30 min at 50 °C and then extracted with CH_2Cl_2. The extract was washed successively with 2M-HCl and brine, dried (Na_2SO_4), and evaporated to leave an oil, which was chromatographed on a silica gel column with n-hexane–EtOAc (3:1) as eluant to give two fractions. The first fraction was oily 3,5-dideoxy-1,2-*O*-isopropylidene-3,5-di-*C*-methyl-β-L-mannofuranose (**10**) (78 mg, 36%), $\delta_H(CDCl_3)$ 0.81 (3 H, d, *J* 6.5 Hz), 1.20 (3 H, d, *J* 7.5 Hz), 1.31 (3 H, s), 1.60 (3 H, s), 2.15—2.60 (2 H, m), 3.13 (1 H, dd, *J* 7.5, 4.5 Hz), 3.35—3.90 (3 H, m), 4.60 (1 H, dd, *J* 6.5, 4.0 Hz), and 5.76 (1 H, d, *J* 4.0 Hz).

The second fraction was the oily isomer 3,5-dideoxy-1,2-*O*-isopropylidene-3,5-di-*C*-methyl-α-D-gulofuranose (**9**) (53 mg, 24%), $\delta_H(CDCl_3)$ 1.12 (3 H, d, *J* 6.5 Hz), 1.19 (3 H, d, *J* 6.5 Hz), 1.31 (3 H, s), 1.53 (3 H, s), 1.70 (1 H, br s), 1.95—2.60 (2 H, m), 3.20—3.70 (2 H, m), 3.92 (1 H, t, *J* 8.0 Hz), 4.57 (1 H, dd, *J* 6.0, 4.0 Hz), and 5.72 (1 H, d, *J* 4.0 Hz).

6-O-*Benzyl*-3,5-*dideoxy*-1,2-O-*isopropylidene*-3,5-*di*-C-*methyl*-α-D-*gulofuranose* (**11**).—A THF (1 ml) solution of compound (**9**) (52 mg, 0.24 mmol) was added to a stirred solution of dimsylsodium, prepared from NaH (7 mg, 0.29 mmol) and DMSO (2 ml), at room temperature. After 30 min, benzyl chloride (37 mg, 0.292 mmol) was added and the mixture was stirred for 1 h, and then was poured into ice–aqueous NH_4Cl and extracted with CH_2Cl_2. The extract was washed with water, dried (Na_2SO_4), and evaporated to leave an oil, which was chromatographed on a silica gel column with n-hexane–EtOAc (3:1) as eluant to afford the protected furanose (**11**) as an oil (68 mg, 92%), $\delta_H(CDCl_3)$ 1.10 (3 H, d, *J* 7.0 Hz), 1.14 (3 H, d, *J* 6.5 Hz), 1.31 (3 H, s), 1.52 (3 H, s), 2.05—2.55 (2 H, m), 3.10—3.60 (2 H, m), 3.88 (1 H, dd, *J* 9.0, 7.5 Hz), 4.49 (2 H, s), 4.57 (1 H, dd, *J* 4.5, 4.0 Hz), 5.70 (1 H, d, *J* 4.0 Hz), and 7.32 (5 H, s).

(2R,3S,4R)-5-*Benzyloxy*-3-*formyloxy*-2,4-*dimethylpentanal* (5-O-*Benzyl*-2,4-*dideoxy*-3-O-*formyl*-2,4-*di*-C-*methyl*-D-xylo-*pentose*) (**12**).—To a stirred solution of the furanose (**11**) (68 mg, 0.222 mmol) were added water (0.5 ml) and TFA (1 ml) at room temperature. After 1 h, the reaction mixture was neutralized with $NaHCO_3$, and concentrated under reduced pressure. The residue was extracted with CH_2Cl_2, and the extract was washed with brine, dried (Na_2SO_4), and evaporated to leave an oil (61 mg). This oil, without purification, was dissolved in benzene (2 ml) and treated with $Pb(OAc)_4$ (113 mg, 0.229 mmol) at room temperature. After 15 min, the mixture was chromatographed on a silica gel column with n-hexane–EtOAc (3:1) as eluant to give the oily aldehyde (**12**) (53 mg, 90%), $\delta_H(CDCl_3)$ 0.98 (3 H, d, *J* 7.0 Hz), 1.12 (3 H, d, *J* 7.0 Hz), 2.12 (1 H, quintet, *J* 7.0 Hz), 2.75 (1 H, quintet, *J* 7.0 Hz), 3.34 (1 H, s), 3.40 (1 H, s), 4.47 (2 H, s), 5.55 (1 H, dt, *J* 5.5, 1.0 Hz), 7.32 (5 H, s), 8.08 (1 H, d, *J* 0.5 Hz), and 9.65 (1 H, d, *J* 1.0 Hz).

(2R,3r,4S)-1,3,5-*Triacetoxy*-2,4-*dimethylpentane* (1,3,5-*Tri*-O-*acetyl*-2,4-*dideoxy*-2,4-*di*-C-*methyl*-D-xylo-*pentitol*) (**13**).—(*a*) Compound (**12**) (53 mg, 0.2 mmol) was dissolved in Et_2O (2 ml) and treated with $LiAlH_4$ (19 mg, 0.5 mmol) at 0 °C for 2 h under argon. Work-up and chromatography on a silica gel column with n-hexane–EtOAc (2:1) as eluant gave the oily diol (19 mg), which was hydrogenated in EtOAc (2 ml) in the presence of 10% Pd–C (4 mg) at ordinary pressure for 2 h. After removal of the catalyst by filtration, evaporation of the solvent gave the oily triol (6 mg). This oil in CH_2Cl_2 (2 ml) was acetylated with Ac_2O (33 mg) in the presence of Et_3N (48 mg) and 4-dimethylaminopyridine (DMAP) (2 mg) at room temperature. After 30 min, the reaction mixture was concentrated under reduced pressure and chromatographed on a silica gel column with n-hexane–EtOAc (2:1) as eluant to afford the oily triacetate (**13**) (6 mg) (Found: $M^+ - CH_3CO_2H$, 214.1228. $C_{11}H_{18}O_4$ requires *m/z*, 214.1200); $\delta_H(CDCl_3)$ 0.96 (6 H, d, *J* 7.0 Hz), 2.06 (6 H, s), 2.07 (3 H, s), 2.05—2.20 (2 H, septet, *J* 6.5 Hz), 3.85—4.03 (4 H, dABq, *J* 11.0, 6.5 Hz), and 5.04 (1 H, t, *J* 6.0 Hz); *m/z* 214 ($M^+ - 60$, 0.2%), 173 (10), 131 (20), 113 (20), 71 (30), and 43 (100).

(*b*) To stirred liquid NH_3 (*ca.* 2 ml) was added a THF (0.5 ml) solution of compound (**28a**) (see below) (7.0 mg) and then Na (*ca.* 40 mg) at −50 °C. After 1 h, the mixture was neutralized with NH_4Cl, and the NH_3 was allowed to evaporate off. The residue was extracted with Et_2O. The extract was dried and evaporated to leave an oil, which was dissolved in CH_2Cl_2 (0.2 ml) and acetylated as described above to afford the triacetate (**13**) as an oil (3.6 mg, 68%).

(2S,4S)-1,3,5-*Triacetoxy*-2,4-*dimethylpentane* (1,3,5-*Tri*-O-*acetyl*-2,4-*dideoxy*-2,4-*di*-C-*methyl*-L-arabino-*pentitol*) (**14**).—Compound (**10**) was converted into triacetate (**14**) as described for the preparation of (**13**) from (**9**). Benzylation of the furanose (**10**) (75 mg, 0.36 mmol) with benzyl alcohol (0.05 ml, 0.43 mmol) and 50% NaH (20 mg, 0.43 mmol) in DMSO (1 ml) and THF (1 ml) gave the oily benzyl ether (109 mg, quant.), δ_H 0.99 (3 H, d, *J* 6.5 Hz), 1.16 (3 H, d, *J* 7.5 Hz), 1.30 (3 H, s), 1.50 (3 H, s), 2.10—2.60 (2 H, m), 3.38—3.90 (3 H, m), 4.52 (2 H, s), 4.55 (1 H, t, *J* 4.0 Hz), 5.70 (1 H, d, *J* 4.0 Hz), and 7.31 (5 H, s).

The benzyl ether (109 mg) was hydrolysed with TFA to give the diol (91 mg) (96%) which was treated with $Pb(OAc)_4$ to give the oily aldehyde (76 mg, 84%), $\delta_H(CDCl_3)$ 1.03 (3 H, d, *J* 7.0 Hz), 1.12 (3 H, d, *J* 7.0 Hz), 1.95—2.30 (1 H, m), 2.60—2.90 (1 H, m), 3.10—3.60 (2 H, m), 4.45 (2 H, s), 5.48 (1 H, dd, *J* 8.0, 4.0 Hz), 7.31 (5 H, s), 8.02 (1 H, s), and 9.66 (1 H, d, *J* 0.5 Hz).

The aldehyde (76 mg) was reduced with $LiAlH_4$ (27 mg) to give the diol (31 mg, 45%). Hydrogenolysis of the diol (31 mg) gave the triol (15 mg, 78%), which was finally converted into the oily triacetate (**14**) (27 mg, 97%), δ_H 0.94 (3 H, d, *J* 7.0 Hz), 0.99 (3

H, d, *J* 7.0 Hz), 2.05 (3 H, s), 2.06 (6 H, s), 2.00—2.35 (2 H, m), 3.90—4.10 (4 H, m), and 4.99 (1 H, dd, *J* 9.0, 3.5 Hz).

3-*Deoxy*-1,2:5,6-*di*-O-*isopropylidene*-3-C-(4-*methoxybenzyloxymethyl*)-α-D-*allofuranose* (**17a**).—To a stirred suspension of NaH (1.1 g) in DMSO (72 ml) was added dropwise a THF (15 ml) solution of compound (**16**) (5.80 g) at room temperature. After evolution of H_2 had ceased a THF (3 ml) solution of MPM chloride (3.68 g) was added. The mixture was stirred for 2 h at room temperature, then poured into cold saturated aqueous NH_4Cl (*ca.* 150 ml) and extracted with CH_2Cl_2. The extract was washed with water, dried (Na_2SO_4), and evaporated under reduced pressure. The residue was chromatographed on a silica gel column with n-hexane–EtOAc (2:1) as eluant to afford crystals of the *title compound* (**17a**) (7.79 g, 93.4%), m.p. 75.5—76.5 °C (from n-hexane–Et_2O) (Found: C, 64.1; H, 7.8. $C_{21}H_{30}O_7$ requires C, 63.94; H, 7.66%).

3-*Deoxy*-1,2-O-*isopropylidene*-3-C-(4-*methoxybenzyloxymethyl*)-6-O-(*tosyl*-α-D-*allofuranose* (**18a**).—A solution of compound (**17a**) (3.52 g) in MeOH (43 ml) and 2% H_2SO_4 (18 ml) was kept at room temperature for 15 h. The reaction mixture was neutralized with $NaHCO_3$ and evaporated under reduced pressure. The residue was taken up in CH_2Cl_2 and the solution was washed with water, dried (Na_2SO_4), and evaporated under reduced pressure, and the residue was chromatographed on a short silica gel column with n-hexane–EtOAc (1:2) as eluant to afford the diol as an oil (2.716 g, 86.5%), which was subjected to the next reaction without further purification.

The diol (2.715 g) was dissolved in pyridine (16 ml) and TsCl (1.46 g) was added. The mixture was stirred at room temperature overnight. Work-up gave crude, oily (**18a**), which was chromatographed on a silica gel column with n-hexane–EtOAc (2:1) as eluant to afford the pure tosyl ester (**18a**) as an oil (2.60 g, 66.8%), $\delta_H(CDCl_3)$ 1.27 (3 H, s), 1.46 (3 H, s), 2.0—2.3 (1 H, m), 2.43 (3 H, s), 3.5—4.5 (9 H, m), 3.81 (3 H, s), 4.64 (1 H, t, *J* 4.5 Hz), 5.71 (1 H, d, *J* 4.5 Hz), 6.88 (2 H, d, *J* 8.5 Hz), 7.23 (2 H, d, *J* 8.5 Hz), 7.30 (2 H, d, *J* 8.5 Hz), and 7.80 (2 H, d, *J* 8.5 Hz).

5,6-*Anhydro*-3-*deoxy*-1,2-O-*isopropylidene*-3-C-(4-*methoxybenzyloxymethyl*)-α-D-*allofuranose* (**19a**).—K_2CO_3 (0.8 g) was added to a MeOH (50 ml) solution of the tosyl ester (**18a**) (2.6 g) and the mixture was stirred at room temperature for 40 min. After evaporation of the solvent, the residue was dissolved in CH_2Cl_2 and the solution was washed successively with water, aqueous NH_4Cl, and brine, dried (Na_2SO_4), and evaporated under reduced pressure to leave the oily epoxide (**19a**) (1.62 g, 94%), $[\alpha]_D^{13}$ +35.1° (*c* 0.928 in $CHCl_3$); $\delta_H(CDCl_3)$ 1.33 (3 H, s), 1.48 (3 H, s), 2.2—2.4 (1 H, m), 2.66—2.74 (1 H, dd, *J* 5.0, 2.5 Hz), 2.73—2.82 (1 H, dd, *J* 5.0, 4.0 Hz), 3.00—3.12 (1 H, m), 3.54—3.87 (3 H, m), 3.80 (3 H, s), 4.49 (2 H, s), 4.75 (1 H, t, *J* 4.0 Hz), 5.81 (1 H, d, *J* 4.0 Hz), 6.88 (2 H, d, *J* 9.0 Hz), and 7.28 (2 H, d, *J* 9.0 Hz); *m/z* 336 (M^+, 0.7%), 278 (0.3), 152 (11), 137 (42), 135 (14.5), and 121 (100).

6-O-*Benzyl*-3-*deoxy*-1,2-O-*isopropylidene*-3-C-(4-*methoxybenzyloxymethyl*)-α-D-*allofuranose* (**20a**).—A THF (1.5 ml) solution of benzyl alcohol (0.79 g, 7.3 mmol) was added dropwise to a stirred suspension of NaH (0.17 g, 7.08 mmol) in DMSO (8 ml) at room temperature. After evolution of H_2 had ceased, a THF (4 ml) solution of the epoxide (**19a**) (1.61 g, 4.8 mmol) was added dropwise at room temperature and the mixture was stirred for 40 h. The reaction mixture was then poured into cold aqueous NH_4Cl (*ca.* 50 ml) and extracted with CH_2Cl_2. The extract was washed with water, dried, and evaporated under reduced pressure, and the residue was chromatographed on a silica gel column with n-hexane–Et_2O (1:1) as eluant to afford compound (**20a**) as an oil (1.233 g, 58%), $\delta_H(CDCl_3)$ 1.30 (3 H, s), 1.49 (3 H, s), 2.0—2.3 (1 H, m), 3.5—4.2 (6 H, m), 3.80 (3 H, s), 4.35—4.62 (2 H, ABq, *J* 12 Hz), 4.58 (2 H, s), 4.68 (1 H, t, *J* 4.0 Hz), 5.60 (1 H, d, *J* 4.0 Hz), 6.86 (2 H, d, *J* 9.0 Hz), and 7.19—7.38 (7 H, m); *m/z* 444 (M^+, 0.5%), 295 (5), 265 (5), 121 (100), and 91 (40).

6-O-*Benzyl*-3-*deoxy*-1,2-O-*isopropylidene*-3-C-(4-*methoxybenzyloxymethyl*)-α-D-ribo-*hexofuranos*-5-*ulose* (**21a**).—PCC (1.4 g) and powdered molecular sieves 4A (4.5 g) were added to a stirred solution of compound (**20a**) (1.233 g, 2.77 mmol) in CH_2Cl_2 (30 ml) at room temperature. After 3 h, the reaction mixture was filtered, and the filtrate was concentrated under reduced pressure and chromatographed on a silica gel column with n-hexane–EtOAc (2:1) as eluant to afford the oily *ketone* (**21a**) (1.0 g, 82%) (Found: M^+, 442.1983. $C_{25}H_{30}O_7$ requires *M*, 442.2023); $\delta_H(CDCl_3)$ 1.33 (3 H, s), 1.49 (3 H, s), 2.30—2.44 (1 H, m), 3.63—3.70 (1 H, dd, *J* 10.0, 6.0 Hz), 3.73—3.86 (1 H, dd, *J* 10.0, 9.0 Hz), 3.79 (3 H, s), 4.28 (1 H, d, *J* 11.0 Hz), 4.39 (2 H, s), 4.44 (2 H, s), 4.47—4.61 (2 H, ABq, *J* 12.0 Hz), 4.73 (1 H, t, *J* 4.0 Hz), 5.86 (1 H, d, *J* 3.5 Hz), 6.86 (2 H, d, *J* 8.5 Hz), 7.24 (2 H, d, *J* 8.5 Hz), and 7.33 (5 H, s); *m/z* 442 (M^+, 0.25%), 293 (2), 227 (1.5), 137 (4), 121 (100), and 91 (20).

5-C-(*Benzyloxymethyl*)-3,5,6-*trideoxy*-1,2-O-*isopropylidene*-3-C-(4-*methoxybenzyloxymethyl*)-α-D-ribo-*hex*-5-*enofuranose* (**22a**).—To a stirred solution of methylenetriphenylphosphorane, prepared from NaH (0.161 g, 6.7 mmol) in DMSO (13 ml) and methyltriphenylphosphonium bromide (2.7 g, 7.56 mmol), was added dropwise a THF (3.5 ml) solution of the ketone (**21a**) (0.99 g, 2.24 mmol) at room temperature. After 8 h, the reaction mixture was poured into ice–water (*ca.* 50 ml) and extracted with CH_2Cl_2. The extract was washed with water, dried, and evaporated under reduced pressure, and the residue was chromatographed on a silica gel column with n-hexane–EtOAc (2:1) as eluant to afford the product (**22a**) as an *oil* (0.768 g, 78%) (Found: M^+, 440.2150. $C_{26}H_{32}O_6$ requires *M*, 440.2190); $\delta_H(CDCl_3)$ 1.34 (3 H, s), 1.51 (3 H, s), 2.32—2.47 (1 H, m), 3.44 (1 H, dd, *J* 9.0, 4.5 Hz), 3.73 (1 H, t, *J* 9.0 Hz), 3.79 (3 H, s), 3.97—4.17 (2 H, ABq, *J* 13.0 Hz), 4.31 (1 H, d, *J* 11.0 Hz), 4.36—4.49 (2 H, ABq, *J* 11.5 Hz), 4.41—4.55 (2 H, ABq, *J* 12.0 Hz), 4.74 (1 H, t, *J* 4.0 Hz), 5.22 (1 H, s), 5.31 (1 H, d, *J* 1.5 Hz), 5.80 (1 H, d, *J* 4.0 Hz), 6.85 (2 H, d, *J* 9.0 Hz), 7.31 (5 H, s), and 7.33 (2 H, d, *J* 9.0 Hz); *m/z* 440 (M^+, 0.15%), 425 (0.3), 349 (1.2), 332 (3), 291 (4), 215 (2.5), 121 (100), and 91 (55).

Hydroboration of the Alkene (**22a**).—To a stirred solution of compound (**22a**) (40 mg, 0.091 mmol) in THF (0.5 ml) was added a 1M solution of BH_3 in THF (0.28 ml) at room temperature. After 4 h, 3M-NaOH (0.5 ml) and 30% H_2O_2 (0.5 ml) were added, and the mixture was vigorously stirred for 30 min, and then extracted with Et_2O. The extract was washed with water, dried ($MgSO_4$), evaporated under reduced pressure, and chromatographed on a silica gel column with n-hexane–EtOAc (1:1) as eluant to afford the oily product (**23a**) as a mixture of 6-*O*-benzyl-3,5-dideoxy-5-*C*-hydroxymethyl-1,2-*O*-isopropylidene-3-*C*-(4-methoxybenzyloxymethyl)-β-L-talofuranose and 6-*O*-benzyl-3,5-dideoxy-5-*C*-hydroxymethyl-1,2-*O*-isopropylidene-3-*C*-(4-methoxybenzyloxymethyl)-α-D-allofuranose (28 mg, 67%) (Found: M^+, 458.2274. $C_{26}H_{34}O_7$ requires *M*, 458.2295); *m/z* 458 (M^+, 0.25%), 400 (0.5), 309 (3.5), 291 (1.2), 279 (1.5), 173 (3), 121 (100), and 91 (60).

Reduction of Compound (**23a**) via *the Methanesulphonate*.—To a stirred ice-cold solution compound of (**23a**) (24 mg, 0.05 mmol) in benzene (0.8 ml) were added Et_3N (20 mg) and mesyl chloride (8 mg, 0.07 mmol). After being stirred at room temperature for 15 min, the reaction mixture was diluted with

benzene (5 ml), washed with water, dried (Na_2SO_4), and evaporated to leave the oily *methanesulphonate* (22.5 mg, 80%) (Found: M^+, 536.2051. $C_{27}H_{36}O_9S$ requires M, 536.2069); m/z 536 (M^+, 0.2%), 401 (1), 387 (5), 348 (1.5), 121 (60), and 91 (100).

The oil (22.5 mg) without further purification, was dissolved in Et_2O (1 ml), $LiAlH_4$ (4 mg) was added, and the mixture was stirred at room temperature for 1.5 h. Work-up and chromatography on a silica gel column with n-hexane–EtOAc (4:1) as eluant gave, as an oil (14 mg, 76%), a 6.6:1 mixture of diastereoisomeric deoxy compounds (**24a**), 6-*O*-benzyl-3,5-dideoxy-1,2-*O*-isopropylidene-3-*C*-(4-methoxybenzyloxymethyl)-5-*C*-methyl-β-L-talofuranose and 6-*O*-benzyl-3,5-dideoxy-1,2-*O*-isopropylidene-3-*C*-(4-methoxybenzyloxymethyl)-5-*C*-methyl-α-D-allofuranose (Found: M^+, 442.2378. $C_{26}H_{34}O_6$ requires M, 442.2346); $\delta_H(CDCl_3)$ 0.90 (2.6 H, d, J 7.0 Hz), 1.02 (0.4 H, d, J 7.0 Hz), 1.49 (3 H, s), 1.59 (3 H, s), 2.0—2.3 (2 H, m), 3.3—3.5 (3 H, m), 3.68—3.77 (1 H, m), 3.80 (3 H, s), 3.86 (0.14 H, dd, J 10.0, 3.5 Hz), 4.06 (0.86 H, dd, J 10.5, 2.5 Hz), 4.38—4.52 (4 H, m), 4.69 (1 H, t, J 4.0 Hz), 5.73 (0.14 H, d, J 4.0 Hz), 5.75 (0.86 H, d, J 4.0 Hz), 6.86 (2 H, d, J 9.0 Hz), and 7.23—7.33 (7 H, m); m/z 442 (M^+, 0.2%), 427 (0.2), 384 (0.7), 293 (5), 230 (6.5), 121 (100), and 91 (65).

Catalytic Reduction of Alkene (**22a**).—An ethanolic solution of alkene (**22a**) (538 mg in 45 ml) was hydrogenated in the presence of 5% Rh–Al_2O_3 catalyst (150 mg) at 0 °C for 2 h. Removal of the catalyst by filtration, followed by evaporation of the solvent, gave an oily 2.8:1 mixture of the mixed products (**24a**) (532 mg, 98.5%), m/z 442 (M^+, 0.25%), 427 (0.25), 293 (4.5), 230 (6), 121 (100), and 91 (65).

HCl *Hydrolysis and* $Pb(OAc)_4$ *Oxidation of Compound* (**24a**).—The 2.8:1 mixture of diastereoisomers (**24a**) (517 mg) was dissolved in dioxane (6 ml) and 4M-HCl (3 ml) and the solution was stirred at 45 °C for 2 h. After neutralization with $NaHCO_3$, the solvent was evaporated under reduced pressure, and the residue was extracted with CH_2Cl_2. The extract was dried (Na_2SO_4), evaporated, and chromatographed on a silica gel column with n-hexane–EtOAc (1:2) as eluant to afford the oily diol (331 mg, 70.4%).

The oil (327 mg) was oxidized with $Pb(OAc)_4$ (441 mg) in benzene (5 ml) at 8—10 °C for 10 min, and the reaction mixture was poured onto a silica gel column; elution with n-hexane–EtOAc (1:1) gave the oily diastereoisomers (**25a**), a mixture of (2*R*,3*R*,4*R*)- and (2*R*,3*R*,4*S*)-5-benzyloxy-3-formyloxy-2-(4-methoxybenzyloxymethyl)-4-methylpentanal [5-*O*-benzyl-2,4-dideoxy-3-*O*-formyl-2-*C*-(4-methoxybenzyloxymethyl)-4-*C*-methyl-D-*ribo*-and -L-*lyxo*-pentose, respectively] (320 mg, 98%), $\nu_{max.}$(neat) 1 720 and 1 175 cm^{-1}; $\delta_H(CDCl_3)$ 0.94 (2.2 H, d, J 7.0 Hz), 1.01 (0.8 H, d, J 7.0 Hz), 2.0—2.3 (1 H, m), 2.9—3.1 (1 H, m), 3.3—3.5 (2 H, m), 3.6—3.77 (2 H, m), 3.80 (3 H, s), 4.40—4.47 (4 H, m), 5.44 (0.26 H, t, J 6.0 Hz), 5.59 (0.74 H, t, J 5.5 Hz), 6.85 (1.48 H, d, J 9.0 Hz), 6.87 (0.52 H, d, J 9.0 Hz), 7.21 (2 H, d, J 9.0 Hz), 7.28—7.38 (5 H, m), 8.06 (0.26 H, s), 8.07 (0.74 H, s), 9.70 (0.74 H, d, J 2.5 Hz), and 9.71 (0.26 H, d, J 2.5 Hz); m/z 309 (M^+ − 91, 0.5%), 291 (1), 263 (0.7), 137 (45), 121 (70), and 91 (100).

(2S,3R,4R)-1-*Benzyloxy*-3-*hydroxy*-4-*hydroxymethyl*-5-(4-*methoxybenzyloxy*-2-*methylpentane* [1-O-*Benzyl*-2,4-*dideoxy*-4-C-(4-*methoxybenzyloxymethyl*)-2-C-*methyl*-L-arabino-*pentitol*] (**26a**) *and* (2R,3R,4R)-1-*Benzyloxy*-3-*dihydroxy*-4-*hydroxymethyl*-5-(4-*methoxybenzyloxy*-2-*methylpentane* [5-O-*Benzyl*-2,4-*dideoxy*-2-C-*hydroxymethyl*-1-O-(4-*methoxybenzyl*)-4-C-*methyl*-D-arabino-*pentitol*] (**27a**).—The oily diastereoisomeric mixture (**25a**) (305 mg, 0.76 mmol) was reduced with $LiAlH_4$ (58 mg, 1.53 mmol) in ether (8 ml) at 0 °C for 1 h. Work-up and chromatography on a silica gel column with n-hexane–EtOAc (1:1) as eluant gave two fractions. The first fraction was the oily arabino-*pentitol* (**27a**) (64 mg, 23%) (Found: M^+, 374.2090. $C_{20}H_{30}O_5$ requires M, 374.2085); $[\alpha]_D^{16}$ −14.3° (c 0.964 in $CHCl_3$); $\delta_H(CDCl_3)$ 0.86 (3 H, d, J 7.0 Hz), 1.8—2.2 (3 H, m), 3.21 (1 H, br s), 3.4—4.0 (7 H, m), 3.80 (3 H, s), 4.47 (2 H, s), 4.52 (2 H, s), 6.87 (2 H, d, J 9.0 Hz), 7.31 (2 H, d, J 9.0 Hz), and 7.32 (5 H, s); m/z 374 (M^+, 0.25%), 356 (0.25), 265 (8.5), 238 (4.5), 137 (40), 121 (100), and 91 (75).

The second fraction was the oily xylo-*pentitol* (**26a**) (182 mg, 63.9%) (Found: M^+, 374.2098. $C_{22}H_{30}O_5$ requires M, 374.2085); $[\alpha]_D^{22}$ −3.8° (c 1.27 in $CHCl_3$); δ_H ($CDCl_3$) 1.00 (3 H, d, J 7.0 Hz), 1.7—2.1 (3 H, m), 3.15 (1 H, br s), 3.48 (2 H, d, J 7.0 Hz), 3.53 (2 H, d, J 5.0 Hz), 3.80 (3 H, s), 3.80—4.06 (3 H, m), 4.40 (2 H, s), 4.50 (2 H, s), 6.85 (2 H, d, J 9.0 Hz), 7.21 (2 H, d, J 9.0 Hz), and 7.32 (5 H, s); m/z 374 (M^+, 0.3%), 356 (0.5), 283 (1), 265 (1.5), 137 (40), 121 (100), and 91 (70).

(2S,3R,4R)-1-*Benzyloxy*-3-*hydroxy*-5-(4-*methoxybenzyloxy*)-2,4-*dimethylpentane* [1-O-*Benzyl*-2,3-*dideoxy*-5-O-(4-*methoxybenzyl*)-2,4-*di*-C-*methyl*-D-xylo-*pentitol*] (**28a**).—Compound (**26a**) (132 mg, 0.353 mmol) was treated with TsCl (81 mg, 0.42 mmol) in pyridine (1.2 ml) at room temperature for 12 h as described for the preparation of the ester (**18a**). Chromatography on a silica gel column with n-hexane–EtOAc (1:1) as eluant gave two fractions. The first fraction was a colourless oil of (2*S*,3*R*,4*S*)-1-benzyloxy-3-hydroxy-4-(4-methoxybenzyloxymethyl)-2-methyl-5-(*p*-tosyloxy)pentane (88 mg, 47%; net yield 73%); $\delta_H(CDCl_3)$ 0.93 (3 H, d, J 7.0 Hz), 1.7—2.2 (2 H, m), 2.40 (3 H, s), 2.89 (1 H, br s), 3.3—3.6 (4 H, m), 3.80 (3 H, s), 3.82 (1 H, m), 4.30 (2 H, d, J 4.0 Hz), 4.32 (2 H, s), 4.46 (2 H, s), 6.83 (2 H, d, J 9.0 Hz), 7.15 (2 H, d, J 9.0 Hz), 7.29 (2 H, d, J 8.5 Hz), 7.30 (5 H, s), and 7.77 (2 H, d, J 8.5 Hz); m/z 386 (M^+ − 142, 0.5%), 265 (5.5), 257 (3.5), 137 (40), 121 (50), 107 (55), and 91 (100).

The second fraction was recovered diol (**26a**) (47 mg, 36%).

The toluenesulphonate (86 mg, 0.162 mmol) was treated with $LiAlH_4$ (23 mg, 0.605 mmol) in Et_2O (5 ml) at 0 °C for 15 min and then at room temperature for 2 h. Work-up and chromatography on a silica gel column with n-hexane–Et_2O (1:1) as eluant gave compound (**28a**) as an *oil* (58 mg, 99%) (Found: M^+, 358.2151. $C_{22}H_{30}O_4$ requires M, 358.2136); $[\alpha]_D$ −0.54° (c 2.04 in $CHCl_3$); $\delta_H(CDCl_3)$ 1.01 (3 H, d, J 7.0 Hz), 1.02 (3 H, d, J 7.0 Hz), 1.7—2.1 (2 H, m), 2.75 (1 H, d, J 3.0 Hz), 3.42 (2 H, d, J 5.0 Hz), 3.44 (2 H, d, J 5.0 Hz), 3.62—3.78 (1 H, m), 3.80 (3 H, s), 4.41 (2 H, s), 4.48 (2 H, s), 6.86 (2 H, d, J 9.0 Hz), 7.23 (2 H, d, J 9.0 Hz), and 7.31 (5 H, s); m/z 358 (M^+, 0.5%), 249 (9.5), 204 (3.5), 150 (3.5), 137 (35), 121 (100), and 91 (70).

3-C-*Benzyloxymethyl*-3-*deoxy*-1,2:5,6-*di*-O-*isopropylidene*-α-D-*allofuranose* (**17b**).—Compound (**16**) (3.88 g, 14.05 mmol) was benzylated as described for the preparation of compound (**11**) to afford the oily benzyl ether (**17b**) (3.927 g, 76.2%), $\delta_H(CDCl_3)$ 1.35 (6 H, s), 1.38 (3 H, s), 1.52 (3 H, s), 2.1—2.4 (1 H, m), 3.78 (2 H, d, J 7.0 Hz), 3.9—4.2 (4 H, m), 4.57 (2 H, s), 4.79 (1 H, t, J 4.0 Hz), 5.79 (1 H, d, J 4.0 Hz), and 7.35 (5 H, s); m/z 364 (M^+, 1%), 349 (6.4), and 91 (100).

3-C-*Benzyloxymethyl*-3-*deoxy*-1,2-O-*isopropylidene*-6-O-*tosyl*-α-D-*allofuranose* (**18b**).—Compound (**17b**) (3.91 g) was converted into the oily diol (3.29 g, 94.5% as described in the preparation of compound (**18a**). The diol showed m/z 324 (M^+, 1.2%), 309 (0.15), and 91 (100).

The diol (3.28 g) was treated with toluene-*p*-sulphonyl chloride and pyridine as described for the preparation of (**18a**) to afford the crude oily tosyl ester (**18b**) (4.95 g), 10 mg of which was purified by t.l.c.; $\delta_H(CDCl_3)$ 1.27 (3 H, s), 1.46 (3 H, s), 2.0—2.3 (1 H, m), 2.43 (3 H, s), 3.5—4.1 (5 H, m), 4.35 (2 H, m), 4.53 (1 H, s), 4.57 (1 H, s), 4.65 (1 H, t, J 6.0 Hz), 5.72 (1 H, d, J 6.5 Hz),

7.29 (2 H, d, *J* 8.0 Hz), 7.33 (5 H, s), and 7.80 (2 H, d, *J* 8.0 Hz); *m/z* 478 (M^+, 0.5%), 463 (0.5), 420 (0.25), and 91 (100).

5,6-*Anhydro*-3-C-*benzyloxymethyl*-3-*deoxy*-1,2-O-*isopropylidene*-α-D-*allofuranose* (**19b**).—The crude oily ester (**18b**) (4.94 g) was treated with K_2CO_3 (1.0 g) in MeOH (65 ml) as described for the preparation of the MPM analogue (**19a**) and the mixture was chromatographed on a silica gel column with n-hexane–Et_2O (1:1) as eluant to afford the anhydride (**19b**) as an oil (1.898 g, 60%), $\delta_H(CDCl_3)$ 1.33 (3 H, s), 1.48 (3 H, s), 2.2—2.5 (1 H, m), 2.67—2.75 (1 H, dd, *J* 5.0, 3.0 Hz), 2.74—2.83 (1 H, dd, *J* 5.0, 4.0 Hz), 3.0—3.2 (1 H, ddd, *J* 5.5, 4.0, 3.0 Hz), 3.6—3.9 (3 H, m), 4.56 (2 H, s), 4.76 (1 H, t, *J* 4.0 Hz), 5.82 (1 H, d, *J* 3.5 Hz), and 7.34 (5 H, s); *m/z* 306 (M^+, 0.5%), 291 (3.5), and 91 (100).

3-C-*Benzyloxymethyl*-3-*deoxy*-1,2-O-*isopropylidene*-6-O-(4-*methoxybenzyl*)-α-D-*allofuranose* (**20b**).—To a stirred solution of sodium 4-methoxybenzyl alcoholate, prepared from 4-methoxybenzyl alcohol (1.30 g, 9.38 mmol) and NaH (226 mg) in DMSO (10 ml), was added dropwise a THF (4 ml) solution of the anhydride (**19b**) (1.89 g, 6.17 mmol) at room temperature. After 4.5 h, the reaction mixture was poured into cold aqueous NH_4Cl (0.2 g in 50 ml), and extracted with CH_2Cl_2. The extract was washed with water, dried (Na_2SO_4), and evaporated under reduced pressure, and the residue was chromatographed on a silica gel column with n-hexane–Et_2O (1:1) as eluant to afford the oily compound (**20b**) (1.837 g, 67%), $\delta_H(CDCl_3)$ 1.30 (3 H, s), 1.49 (3 H, s), 2.0—2.3 (1 H, m), 3.5—4.0 (7 H, m), 3.79 (3 H, s), 4.49 (2 H, s), 4.41—4.56 (2 H, ABq, *J* 12.0 Hz), 4.70 (1 H, t, *J* 4.0 Hz), 5.76 (1 H, d, *J* 3.5 Hz), 6.85 (2 H, d, *J* 9.0 Hz), 7.27 (2 H, d, *J* 9.0 Hz), and 7.32 (5 H, s); *m/z* 386 ($M^+ - 58$, 6%), 121 (95), and 91 (100).

3-C-*Benzyloxymethyl*-3-*deoxy*-1,2-O-*isopropylidene*-6-O-(4-*methoxybenzyl*)-α-D-ribo-*hexofuranos*-5-*ulose* (**21b**).—Compound (**20b**) (1.82 g, 4.1 mmol) was converted into the oily ketone (**21b**) (1.54 g, 85%) as described for the preparation of compound (**21a**); δ_H 1.34 (3 H, s), 1.49 (3 H, s), 2.2—2.6 (1 H, m), 3.61—3.89 (2 H, m), 3.80 (3 H, s), 4.28 (1 H, d, *J* 10.0 Hz), 4.36 (2 H, s), 4.48 (2 H, s), 4.51 (2 H, s), 4.75 (1 H, t, *J* 3.5 Hz), 5.87 (1 H, d, *J* 3.5 Hz), 6.86 (2 H, d, *J* 9.0 Hz), 7.27 (2 H, d, *J* 9.0 Hz), and 7.31 (5 H, s); *m/z* 306 ($M^+ - 136$, 2%), 248 (5.5), 121 (40), and 91 (100).

3-C-*Benzyloxymethyl*-3,5,6-*trideoxy*-1,2-O-*isopropylidene*-5-C-(4-*methoxybenzyloxymethyl*)-α-D-ribo-*hex*-5-*enofuranose* (**22b**).—Compound (**21b**) (1.54 g, 3.48 mmol) was converted into the oily alkene (**22b**) (1.177 g, 77%) as described for the preparation of its isomer (**22a**) (Found: $M^+ - C_3H_6O$, 382.1797. $C_{23}H_{26}O_5$ requires *m/z*, 382.1782); $\delta_H(CDCl_3)$ 1.35 (3 H, s), 1.51 (3 H, s), 2.3—2.6 (1 H, m), 3.45 (1 H, dd, *J* 10.0, 5.0 Hz), 3.80 (1 H, d, *J* 10.0 Hz), 4.02 (1 H, s), 4.07 (1 H, s), 4.31 (1 H, d, *J* 10.0 Hz), 4.40 (1 H, s), 4.42 (1 H, s), 4.50 (2 H, s), 4.76 (1 H, t, *J* 4.0 Hz), 5.21 (1 H, s), 5.30 (1 H, d, *J* 1.0 Hz), 5.81 (1 H, d, *J* 3.5 Hz), 6.84 (2 H, d, *J* 9.0 Hz), 7.25 (2 H, d, *J* 9.0 Hz), and 7.31 (5 H, s); *m/z* 425 ($M^+ - 15$, 0.15%), 382 (1.5), 121 (85), and 91 (100).

Catalytic Reduction of the Alkene (**22b**).—Compound (**22b**) (1.11 g) was hydrogenated over 5% Rh–Al_2O_3 (310 mg) as described for the preparation of the isomer (**24a**) to afford an oily 3:1 diastereoisomeric mixture of compounds (**24b**), 3-C-benzyloxymethyl-3,5-dideoxy-1,2-*O*-isopropylidene-6-*O*-(4-methoxybenzyl)-5-*C*-methyl-β-L-talofuranose and 3-C-benzyloxymethyl-3,5-dideoxy-1,2-*O*-isopropylidene-6-*O*-(4-methoxybenzyl)-5-*C*-methyl-α-D-allofuranose (1.083 g, 97.5%), $\delta_H(CDCl_3)$: the ratio of the C-5 methyl signals at δ 0.89 and 1.00 was 3:1. Other signals of the major product: δ 1.33 and 1.49 (s, isopropylidene Me), 3.79 (t, *J* 4.5 Hz, 3-H), 4.05 (dd, *J* 10.5, 2.5 Hz, 4-H), 4.42 (s, CH_2), 4.52 (s, CH_2), 4.70 (t, *J* 4.5 Hz, 2-H), 5.75 (d, *J* 4.0 Hz, 1-H), 6.85 (d, *J* 9.0 Hz), 7.25 (d, *J* 9.0 Hz), and 7.31 (s, Ph); *m/z* 384 ($M^+ - 58$, 4.2%), 121 (100), and 91 (65).

HCl *Hydrolysis and* $Pb(OAc)_4$ *Oxidation of Compound* (**24b**).—Compound (**24b**) (1.073 g) was hydrolysed to the diol (676 mg, 69.3%), *m/z* 384 ($M^+ - 18$, 1%), 293 (3), 121 (100), and 91 (55). The diol (670 mg) was oxidized with $Pb(OAc)_4$ (901 mg) to afford the oily aldehyde (**25b**) as a mixture of (2*R*,3*R*,4*R*)- and (2*R*,3*R*,4*S*)-2-benzyloxymethyl-3-formyloxy-5-(4-methoxybenzyloxy)-4-methylpentanal [2-*C*-benzyloxymethyl-2,4-dideoxy-5-*O*-(4-methoxybenzyl)-4-*C*-methyl-D-arabinose and -L-lyxose, respectively] (626 mg, 94%) as described for the preparation of the isomers (**25a**); $\delta_H(CDCl_3)$: the ratio of the C-4 methyl signals at δ 0.93 and 1.01 (both d, *J* 7.0 Hz) was 3:1. The aldehyde signals at δ 9.70 and 9.72 (both d, *J* 2.5 Hz) also have the same ratio.

(2R,3R,4S)-1-*Benzyloxy*-3-*hydroxy*-2-*hydroxymethyl*-5-(4-*methoxybenzyloxy*)-4-*methylpentane* [*4*-C-*Benzyloxymethyl*-2,4-*dideoxy*-1-O-(4-*methoxybenzyl*)-2-C-*methyl*-L-arabino-*pentitol*] (**26b**) *and* (2R,3R,4R)-1-*Benzyloxy*-3-*hydroxy*-2-*hydroxymethyl*-5-(4-*methoxybenzyloxy*)-4-*methylpentane* [1-O-*Benzyl*-2,4-*dideoxy*-2-C-*hydroxymethyl*-5-O-(4-*methoxybenzyl*)-4-C-*methyl*-D-arabino-*pentitol*] (**27b**).—Compound (**25b**) (440 mg) was reduced with $LiAlH_4$ (84 mg) as described for the preparation of the diols (**26a**) and (**27a**). Compound (**26b**) (218 mg, 53%) was an oil (Found: $M^+ - C_7H_7$, 283.1553. $C_{15}H_{23}O_5$ requires *m/z*, 283.1547. Found: $M^+ - C_7H_9O$, 265.1426. $C_{15}H_{21}O_4$ requires *m/z*, 265.1441); $\delta_H(CDCl_3)$ 1.00 (3 H, d, *J* 7.0 Hz), 1.7—2.0 (2 H, m), 2.98 (1 H, t, *J* 6.0 Hz), 3.20 (1 H, d, *J* 2.5 Hz), 3.4—3.6 (4 H, m), 3.80 (3 H, s), 3.8—4.0 (3 H, m), 4.43 (2 H, s), 4.47 (2 H, s), 6.87 (2 H, d, *J* 9.0 Hz), 7.23 (2 H, d, *J* 9.0 Hz), and 7.30 (5 H, s); *m/z* 374 (M^+, 0.3%), 283 (1.5), 137 (40), 121 (100), and 91 (70). Compound (**27b**) (68.5 mg, 16.6%) was also an oil, $\delta_H(CDCl_3)$ 0.85 (3 H, d, *J* 7.0 Hz), 1.9—2.0 (1 H, m), 2.0—2.2 (1 H, m), 3.4—4.1 (9 H, m), 3.80 (3 H, s), 4.45 (2 H, s), 4.54 (2 H, s), 6.88 (2 H, d, *J* 9.0 Hz), 7.23 (2 H, d, *J* 9.0 Hz), and 7.33 (5 H, s); *m/z* 374 (M^+, 0.25%), 283 (1), 265 (6), 137 (40), 121 (100), and 91 (75).

(2R,3S,4S)-1-*Benzyloxy*-3-*hydroxy*-5-(4-*methoxybenzyloxy*)-2,4-*dimethylpentane* [5-O-*Benzyl*-2,4-*dideoxy*-1-O-(4-*methoxybenzyl*)-2,4-*di*-C-*methyl*-D-xylo-*pentitol*] (**28b**).—Compound (**26b**) was converted into compound (**28b**) *via* the primary toluenesulphonate as described for the preparation of the isomer (**28a**). Thus, compound (**26b**) (210 mg) was treated with TsCl (156 mg) in pyridine to afford oily (2*S*,3*R*,4*S*)-1-benzyloxymethyl-3-hydroxy-5-(4-methoxybenzyloxy)-4-methyl-2-(*p*-tosyloxymethyl)pentane (290 mg, 98%), $\delta_H(CDCl_3)$ 0.92 (3 H, d, *J* 7.0 Hz), 1.6—2.2 (2 H, m), 2.39 (3 H, s), 2.90 (1 H, br s), 3.4—3.6 (4 H, m), 3.80 (3 H, s), 3.82 (1 H, m), 4.31 (2 H, d, *J* 5.0 Hz), 4.38 (4 H, s), 6.86 (2 H, d, *J* 9.0 Hz), 7.2—7.3 (9 H, m), and 7.77 (2 H, d, *J* 9.0 Hz); *m/z* 468 ($M^+ - 60$, 0.25%), 420 (0.25), 390 (0.3), 357 (0.5), 348 (1), 172 (15), 137 (30), 121 (50), and 91 (100).

The toluenesulphonate (282 mg) was reduced with $LiAlH_4$ (75 mg) to afford the oily product (**28b**) (178 mg, 93%) (Found: M^+, 358.2141. $C_{22}H_{30}O_4$ requires *M*, 358.2146); $\delta_H(CDCl_3)$ 1.01 (3 H, d, *J* 6.0 Hz), 1.03 (3 H, d, *J* 7.0 Hz), 1.8—2.1 (2 H, m), 2.74 (1 H, d, *J* 3.0 Hz), 3.42 (2 H, d, *J* 5.0 Hz), 3.44 (2 H, d, *J* 5.0 Hz), 3.6—3.8 (1 H, m), 3.80 (3 H, s), 4.42 (2 H, s), 4.49 (2 H, s), 6.86 (2 H, d, *J* 9.0 Hz), 7.23 (2 H, d, *J* 9.0 Hz), and 7.31 (5 H, s); *m/z* 358 (M^+, 0.5%), 317 (0.4), 249 (0.6), 137 (35), 121 (100), and 91 (65).

2R,3R,4S)-1-*Benzyloxy*-3,5-*dihydroxy*-2,4-*dimethylpentane* (5-O-*Benzyl*-2,4-*dideoxy*-2,4-*di*-C-*methyl*-D-xylo-*pentitol*) (**29**).—To a stirred solution of the MPM ether (**28b**) (175 mg, 0.488 mmol) in CH_2Cl_2 (6 ml) were added water (0.3 ml) and DDQ (277 mg, 1.22 mol). The mixture was stirred at room

temperature for 1 h, then washed with saturated aqueous $NaHCO_3$, dried (Na_2SO_4), and evaporated to leave an oil, which was dissolved in MeOH (6 ml) and 20% KOH (0.5 ml). The reaction mixture was stirred at room temperature for 2 h, and then evaporated. The residue was extracted with Et_2O, and the extract was chromatographed on a silica gel column with n-hexane–EtAOc (1:1) as eluant to afford the oily diol (**29**) (91 mg, 77%) (Found: $M^+ - H_2O$, 220.1450. $C_{14}H_{20}O_2$ requires m/z 220.1458); $\delta_H(CDCl_3)$ 1.01 (3 H, d, J 7.0 Hz), 1.05 (3 H, d, J 7.0 Hz), 1.8—2.1 (3 H, m), 2.65 (1 H, d, J 4.0 Hz), 3.48 (2 H, d, J 5.0 Hz), 3.6—3.9 (3 H, m), 4.50 (2 H, s), and 7.32 (5 H, s); m/z 220 ($M^+ - 18$, 2.5%), 178 (2.2), 108 (42), and 91 (100).

2R,3S,4S)-1-*Benzyloxy*-3,5-*isopropylidenedioxy*-2,4-*dimethylpentane* (5-O-*Benzyl*-2,4-*dideoxy*-1,3-O-*isopropylidene*-2,4-*dimethyl*-D-xylo-*pentitol*) (**30**).—To a solution of the diol (**29**) (66.6 mg) in Et_2O (2 ml) and 2,2-dimethoxypropane (0.1 ml) was added camphor-10-sulphonic acid (3 mg), and the reaction mixture was kept at room temperature for 1 h. After neutralization with Et_3N, the solvent was evaporated under reduced pressure and the residue was chromatographed on a silica gel column with n-hexane–EtOAc (3:1) as eluant to afford the oily product (**30**) (75 mg, 96%) (Found: $M^+ - CH_3$, 263.1655. $C_{16}H_{23}O_3$ requires m/z, 263.16); $\delta_H(CDCl_3)$ 1.04 (3 H, d, J 6.5 Hz), 1.06 (3 H, d, J 6.0 Hz), 1.40 (3 H, s), 1.41 (3 H, s), 1.69—1.90 (2 H, m), 3.35 (2 H, d, J 5.0 Hz), 3.55 (1 H, dd, J 11.0, 1.5 Hz), 3.73 (1 H, dd, J 10.0, 2.0 Hz), 4.06 (1 H, dd, J 11.0, 2.5 Hz), 4.48 (2 H, s), and 7.32 (5 H, s); m/z 263 ($M^+ - 15$, 8.5%) and 91 (100).

(2R,3S,4S)-1-*Hydroxy*-1,3-*isopropylidenedioxy*-2,4-*dimethylpentane* (2,4-*Dideoxy*-1,3-O-*isopropylidene*-2,4-*dimethyl*-D-xylo-*pentitol*) (**31**).— Compound (**30**) (73 mg) was hydrogenated in EtOAc (6 ml) in the presence of 10% Pd–C (100 mg) at ordinary pressure and temperature for 2.5 h. After removal of the catalyst by filtration, evaporation of the solvent left the oily alcohol (**31**) (42.3 mg, 85.8%), $\delta_H(CDCl_3)$ 1.02 (3 H, d, J 7.0 Hz), 1.11 (3 H, d, J 7.0 Hz), 1.40 (3 H, s), 1.42 (3 H, s), 1.4—1.8 (3 H, m), 3.5—3.6 (3 H, m), 3.77 (1 H, dd, J 9.5, 2.5 Hz), and 4.09 (1 H, dd, J 11.0, 3.0 Hz); m/z 173 ($M^+ - 15$, 12.5%), 113 (11), and 59 (100).

(2S,3R,4S)-3,5-*Isopropylidenedioxy*-2,4-*dimethylpentanal* (2,4-*Dideoxy*-3,5-O-*isopropylidene*-2,4-*dimethyl*-L-xylo-*pentose*) (**32**).—To a stirred solution of the alcohol (**31**) (42 mg) in CH_2Cl_2 (5 ml) was added PCC (100 mg) at room temperature. After 30 min, the reaction mixture was concentrated and chromatographed on a silica gel column with n-hexane–EtOAc (3:1) as eluant to afford the oily pentose (**32**) (31.7 mg, 75.8%), $[\alpha]_D^{17}$ + 5.0 (c 1.2 in $CHCl_3$); $\delta_H(CDCl_3)$ 1.08 (3 H, d, J 6.5 Hz), 1.13 (3 H, d, J 7.0 Hz), 1.40 (3 H, s), 1.45 (3 H, s), 1.5—1.8 (1 H, m), 2.4—2.8 (1 H, m), 3.57 (1 H, dd, J 11.5, 2.0 Hz), 4.08 (1 H, dd, J 9.0, 2.0 Hz), 4.12 (1 H, dd, J 11.5, 2.5 Hz), and 9.75 (1 H, d, J 2.0 Hz).

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