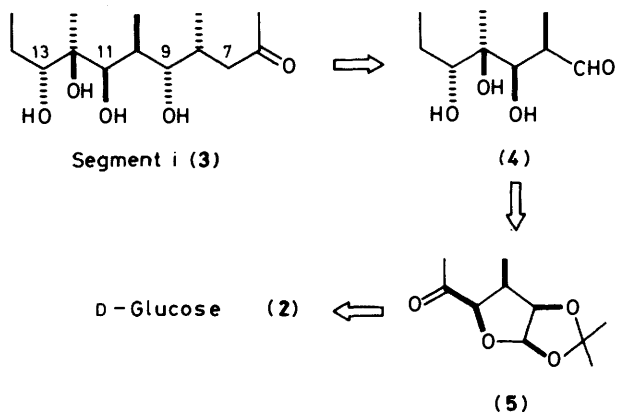
Chiral Synthesis of Polyketide-derived Natural Products. Part 4.[1] Synthesis of a Left-hand Segment with Six Consecutive Chiral Centres of Dihydroerythronolide A for the Total Synthesis of Erythromycin A from D-Glucose

Yuji Oikawa, Takao Nishi, and Osamu Yonemitsu *
Faculty of Pharmaceutical Sciences, Hokkaido University, Sapporo 060, Japan

For the purpose of the total synthesis of erythromycin A (**1**) from D-glucose (**2**) with the aid of stereochemical control in acyclic systems and *p*-methoxyphenylmethyl (MPM) protection, (2*R*,3*S*,4*S*,5*R*,6*R*,7*R*)-1-hydroxy-5,6-isopropylidenedioxy-3,7-bis(4-methoxybenzyloxy)-2,4,6-trimethylnonane (**55**), a left-hand segment corresponding to the C-7—C-15 segment of 9-dihydroerythronolide A, was synthesized from D-glucose (**2**) through some stereoselective reactions in open-chain systems, *e.g.* the Wittig reaction, OsO_4 oxidation, and epoxidation.

Because of its complex chemical structure and potent biological activity, the well known macrolide antibiotic erythromycin A (**1**), isolated from *Streptomyces erythreus*,[2] has stimulated intensive studies of its total synthesis,[3] which primarily requires new synthetic methodologies for the control of stereochemistry in acyclic systems. Recently, we planned to synthesize (**1**) from D-glucose (**2**), the most readily available chiral starting material, with the aid of the recently developed MPM (*p*-methoxyphenylmethyl) protection[4] and some stereocontrolled reactions in acyclic systems. In the preceding paper,[1] as the first step for the total synthesis of (**1**), we reported the synthesis of the chiral synthon (**5**) corresponding to both the C-1—C-4 and C-9—C-12 fragments of (**1**) (Scheme 1). In this paper we report the

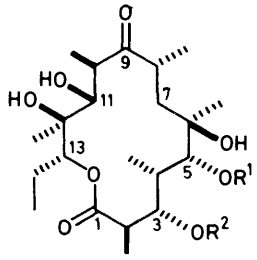


Scheme 1.

stereocontrolled synthesis of the key intermediate (**55**),[5] corresponding to the left-hand segment i (**3**) having six consecutive chiral centres, from (**2**) *via* (**5**).

Results and Discussion

Synthesis of the C-9—C-15 *Fragment.*—The Wittig reaction of the ketone (**5**)[1] with excess of propylidenetriphenylphosphorane occurred stereoselectively to give the *Z*-olefin (**6**) as the sole product, which was treated with *N*-methylmorpholine *N*-oxide (NMO) and osmium tetraoxide[6] to give a diastereoisomeric mixture of diols in 90% yield again with excellent stereoselection (23:1). Chromatographic separation of the mixture on silica gel readily gave the expected diol (**7**).

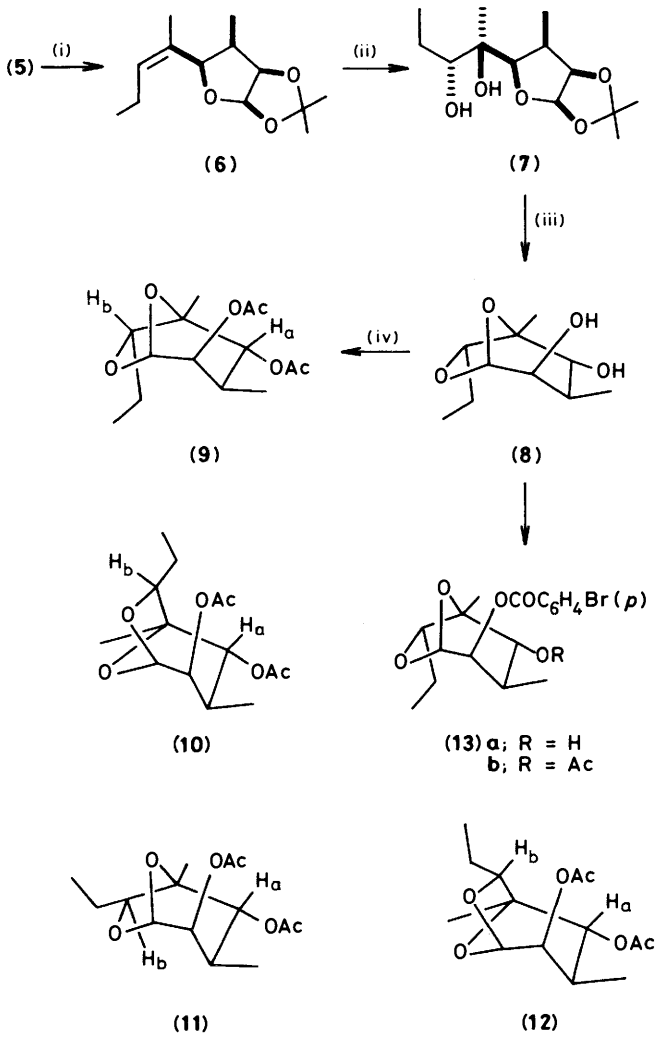


(1)
Erythromycin A
R^1 = D-desosaminyl
R^2 = L-cladinosyl

The stereochemical configuration of (**6**) and (**7**) was determined in the following way. When the isopropylidene group of (**7**) was cleaved with toluene-*p*-sulphonic acid, ring rearrangement and intramolecular acetal formation occurred to give the bicyclic dihydroxyacetal (**8**) in high yield. In order to confirm the structure, compound (**8**) was converted into the diacetate (**9**), and in its n.m.r. spectrum the long-range coupling (1.5 Hz) due to the W-configuration[7] between H_a (δ 5.02) and H_b (δ 3.54) was clearly observed. Among four possible isomers (**9**)—(**12**) arising from the configurational differences of the two hydroxy groups in (**7**) only structure (**9**) has the W-arrangement of the four σ-bonds between H_a and H_b. Therefore, it was clear that the double bond of (**6**) has the *Z*-configuration and that it was attacked with osmium tetraoxide selectively from its β-side * to afford compound (**7**). The structures (**6**) and (**7**) were then unequivocally established by *X*-ray analysis of the *p*-bromobenzoate (**13b**) which was derived from (**8**) (Scheme 2) and which crystallized in the orthorhombic space group $P2_12_12_1$ [*a* 9.327(4), *b* 10.117(5), and *c* 21.764(9) Å].[8]

Since the position of the secondary carbinol group of (**7**) corresponds to that at C-13 of (**1**), it was absolutely necessary to choose a protecting group which is not only stable under various conditions for elongation of the carbon chain to the seco-acid of (**1**) but also removable selectively among many protecting groups prior to macrolactonization of the seco-acid at the final stage of the total synthesis of (**1**). The MPM group seemed to be most suitable because it is usually stable under

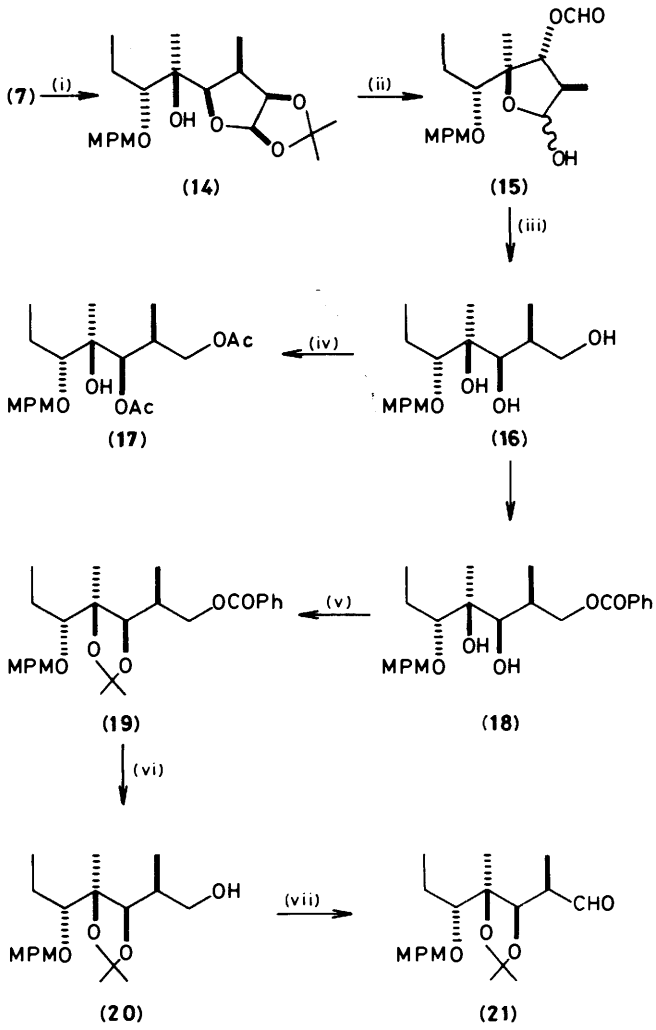
* The terms α and β are used with reference to each atom or group which lies behind the plane of the molecule and in front of it, respectively, as for steroids, as well as to denote anomeric configurations.



Scheme 2. *Reagents and conditions:* (i) $Ph_3P{=}CHEt$, THF, −70 to 0 °C; (ii) OsO_4, NMO-H_2O, Me_2CO–water; (iii) TsOH, water, CH_2Cl_2; (iv) Ac_2O, DMAP–TEA, CH_2Cl_2

both acidic and basic conditions, but removable selectively by 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) oxidation. Treatment of compound (**7**) with MPM chloride in the manner reported earlier[4] gave the mono-MPM ether (**14**) in excellent yield. The isopropylidene group of compound (**14**) was selectively removed with 4M-hydrochloric acid in tetrahydrofuran (THF), then lead tetra-acetate oxidation of the resultant vicinal diol group gave the hemiacetal (**15**) which was readily reduced with lithium aluminium hydride to give the acyclic triol (**16**), with four consecutive chiral centres, as an oil. Acetylation of (**16**) with excess of acetic anhydride gave the diacetate (**17**) even in the presence of 4-dimethylaminopyridine (DMAP) because of steric hindrance of the tertiary alcohol group of (**16**).

In order to convert (**16**) into a key intermediate (**21**) the primary hydroxy group of (**16**) was first benzoylated, followed by protection of the remaining diol group of (**18**) as its acetonide (**19**). The primary hydroxy group was then recovered by selective removal of the benzoyl protecting group under alkaline conditions. The resultant alcohol (**20**) was finally oxidized with pyridinium chlorochromate (PCC) in the presence of molecular sieves[9] and the key intermediary aldehyde (**21**) was isolated as an oil in excellent yield. Thus the ketone (**5**) with two chiral centres corresponding to the C-10—C-11 moiety of (**1**) was successfully and efficiently converted into the aldehyde (**21**), with four consecutive chiral centres corresponding to C-10—C-12, through the two stereoselective reactions in acyclic systems, the Wittig reaction, and the oxidation with OsO_4 (Scheme 3).



Scheme 3. *Reagents:* (i) MPMCl, NaH, DMF; (ii) (a) 4M-HCl, (b) $Pb(OAc)_4$, PhH; (iii) $LiAlH_4$; (iv) Ac_2O, DMAP; (v) TsOH, $Me_2C(OMe)_2$, Me_2CO; (vi) 1M-KOH, MeOH, (vii) PCC, molecular sieves, CH_2Cl_2

Alternative Synthesis of the C-9—C-15 *Fragment.*—An alternative synthesis of (**21**) *via* the stereoselective Wittig reaction and epoxidation of an aldehyde (**25**) with two chiral centres corresponding to the C-12—C-13 moiety was next examined. The diol (**22**)[1] derived from (**2**) was treated with tosyl (toluene-*p*-sulphonyl) chloride in the presence of DMAP to give the di(toluenesulphonate), which was converted into the olefin (**23**) by treatment with sodium iodide in refluxing methyl ethyl ketone.[10] Compound (**23**) was then converted into the aldehyde (**25**) in almost quantitative yield *via* three conventional reactions, catalytic hydrogenation over palladium–charcoal to give (**24**), removal of the isopropylidene protection with trifluoroacetic acid, and oxidation with lead tetra-acetate. The conventional Wittig reaction of (**25**) gave solely the *E*-olefin (**26**) in high yield, and its lithium aluminium hydride reduction

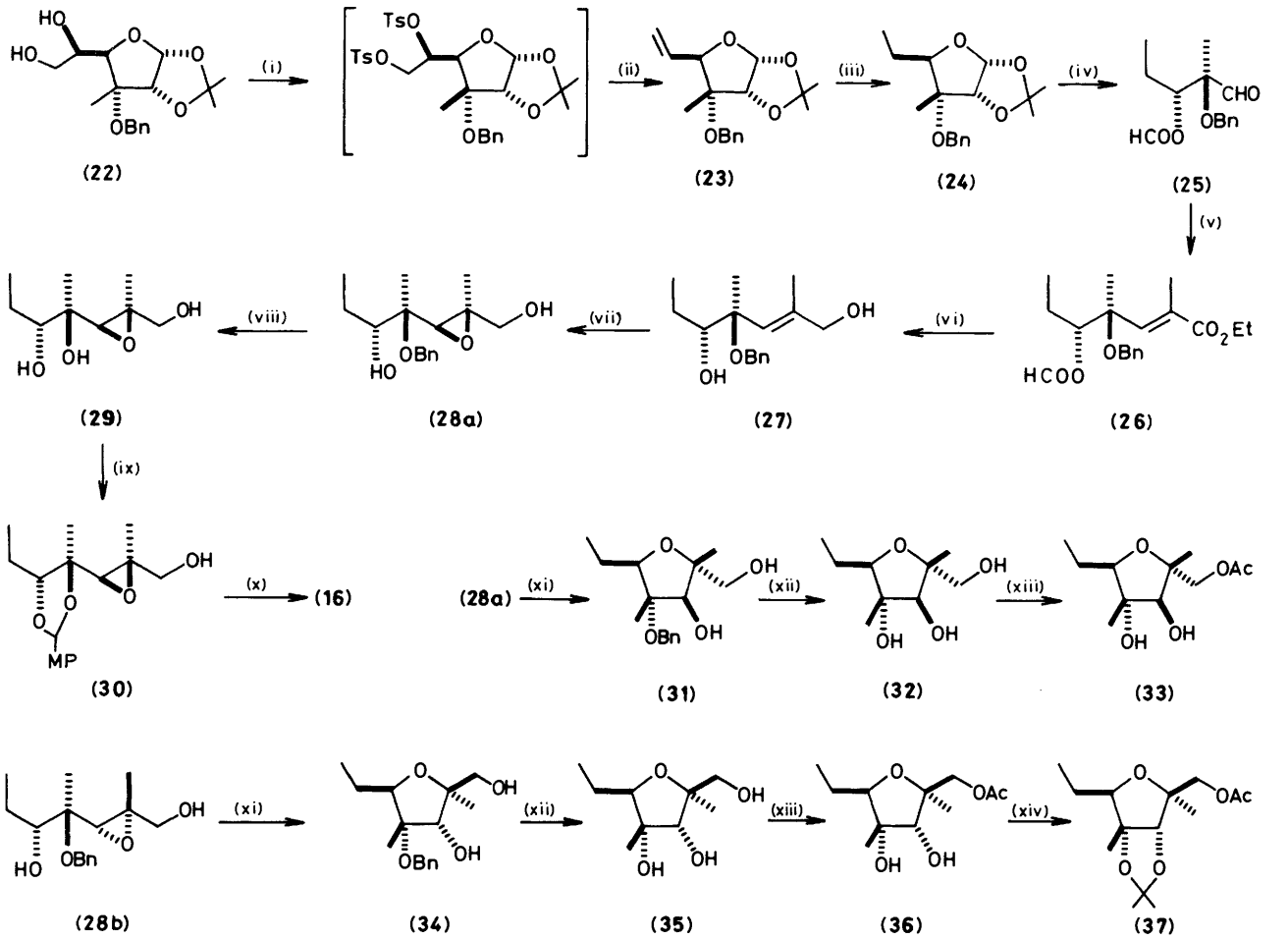
readily gave the allyl alcohol (**27**), which was characterized as the diacetate.

Epoxidation of (**27**) with *m*-chloroperbenzoic acid (*m*-CPBA) at −5 °C occurred highly stereoselectively to give almost pure β-epoxide (**28a**),[11] though the reaction with t-butyl hydroperoxide in the presence of vanadyl acetylacetonate gave a 5:4 mixture of the β- (**28a**) and α-epoxide (**28b**). The configurations of (**28a**) and (**28b**) were determined as follows. When treated with camphor-10-sulphonic acid (CSA) at room temperature, the epoxide (**28a**) was readily converted[12] into the dihydroxytetrahydrofuran (**31**), which was debenzylated to give quantitatively the trihydroxytetrahydrofuran (**32**) by catalytic hydrogenolysis over palladium–charcoal. After protection of the primary hydroxy group of compound (**32**) by acetylation, the vicinal hydroxy group of the acetate (**33**) was treated with acetone dimethyl acetal and toluene-*p*-sulphonic acid to examine whether an acetonide could be formed or not. No detectable formation of any acetonide was observed. On the other hand, the isomeric dihydroxy compound (**36**) derived from (**28b**) *via* (**34**) and (**35**) in the same manner was readily converted into its acetonide (**37**). The configurations of the vicinal diol groups of (**33**) and (**36**) were thus shown to be *trans* and *cis*, respectively. Therefore, (**28a**) was shown to have a β-epoxy group.

The benzyl group of (**28a**) was removed by catalytic hydrogenolysis over palladium–charcoal in the presence of sodium hydrogen carbonate to avoid undesirable opening of the epoxide ring by catalytic amounts of acidic impurities in the catalyst, since both (**28a**) and the expected triol (**29**) were unstable to acid. In order to convert (**29**) conveniently into (**16**) we chose a route *via* the acetal (**30**). We were unable to use the conventional acid-catalysed acetalization to protect the vicinal diol group of (**29**), but the recently developed kinetic acetalization with *p*-methoxyphenylmethyl methyl ether (MPMME) and DDQ[13] proceeded quite smoothly under neutral conditions to give a diastereoisomeric mixture of (**30**) with high stereoselection (12:1). When compound (**30**) was treated with aluminium hydride in ether, reductive cleavage[14] of both the acetal and the epoxide occurred to give (**16**), which was easily converted into (**21**) as described above. This alternative route to (**21**) is more convenient than that *via* (**5**) though the overall yield was not appreciably improved. These reactions are shown in Scheme 4.

Synthesis of the C-7—C-15 *Fragment.*—As a model experiment in order to elongate stereoselectively the skeletal chain by the two-carbon unit corresponding to C-7 and C-8, the Wittig reaction and epoxidation of aldehyde (**39**) were examined. Introduction of an α-hydroxy group at the position corresponding to C-9 in (**1**) is very important, because only 9-dihydroseco-acids with a 9-*S*(α)-hydroxy group are able to cyclize to the corresponding erythronolides.[3b]

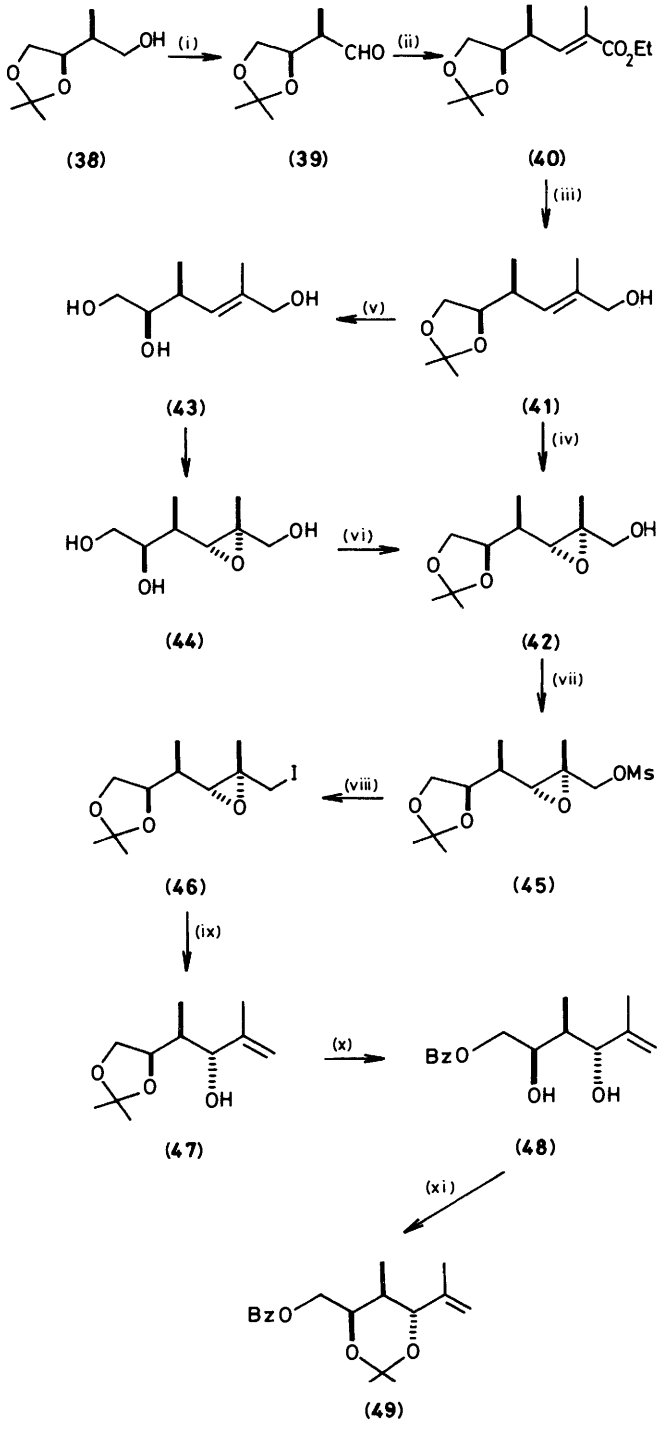
The model aldehyde (**39**)[15] derived from (**38**)[16] by PCC oxidation was subjected to the usual Wittig reaction followed



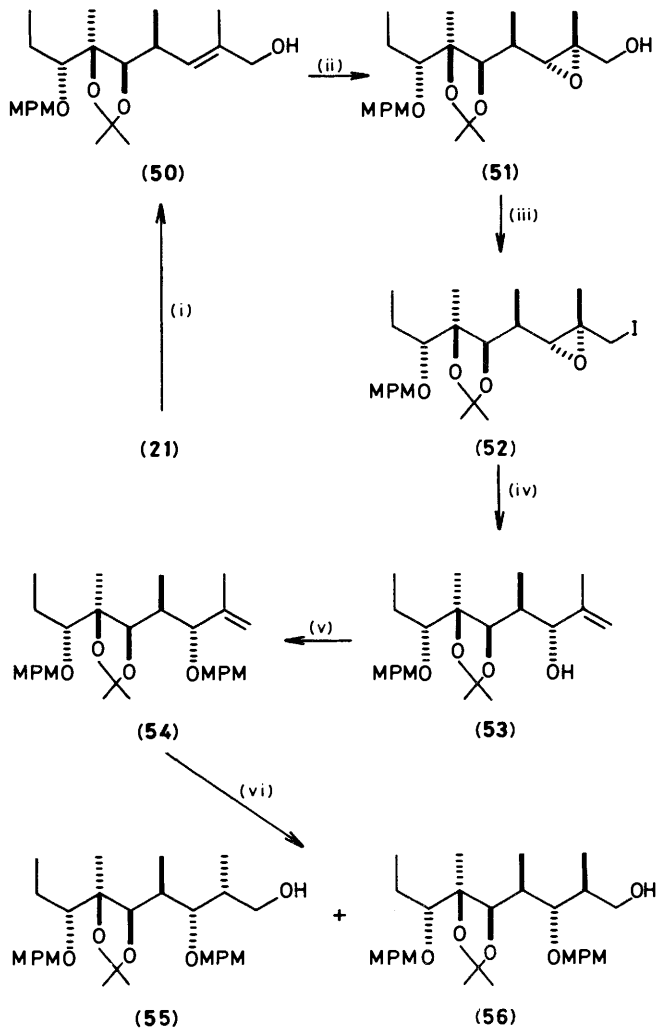
Scheme 4. *Reagents:* (i) TsCl, DMAP, TEA–CH_2Cl_2; (ii) NaI, MeCOEt; (iii) H_2/Pd–C, AcOEt, (iv) (a) TFA, THF–water, (b) $Pb(OAc)_4$, PhH; (v) $Ph_3P{=}C(Me)CO_2Et$, $ClCH_2CH_2Cl$; (vi) $LiAlH_4$, Et_2O; (vii) *m*-CPBA, CH_2Cl_2; (viii) H_2/Pd–C, EtOH ($NaHCO_3$); (ix) DDQ, MPMME, CH_2Cl_2; (x) AlH_3, Et_2O; (xi) CSA, CH_2Cl_2; (xii) H_2/Pd–C; (xiii) Ac_2O, Py, CH_2Cl_2; (xiv) $Me_2C(OMe)_2$, TsOH, Me_2CO

by lithium aluminium hydride reduction, to give the *E*-allyl alcohol (**41**) stereoselectively. Peracid oxidation of (**41**) with *m*-CPBA gave a 4:1 mixture of epoxides in excellent yield. The main α-epoxide (**42**) was also obtained as the sole product by the roundabout route *via* (**43**) and (**44**). The configuration of the epoxide group of (**42**) was determined as follows: the primary hydroxy group was converted into the iodide (**46**) *via* the methanesulphonate (**45**) in the usual manner, and then reductive ring opening[17] of the epoxide group with zinc–copper couple gave the terminal olefinic compound (**47**), which was easily converted into the six-membered acetonide (**49**) *via* the dihydroxy ester (**48**) (Scheme 5). In the n.m.r. spectrum the coupling constant between 3-H and 4-H was observed to be 8.5 Hz, clearly showing a *trans*-diaxial relationship between both hydrogens. Therefore, the epoxidation of (**41**) was shown to occur mainly at its α-side.[11]

Since the model experiments had been successfully carried out, the stereoselective elongation of (**21**) was next examined. Wittig reaction and lithium aluminium hydride reduction gave quantitatively the allyl alcohol (**50**), which was subjected to epoxidation. Its stereoselection was significantly superior to that in the case of the model experiment and only the α-epoxide (**51**) was isolated, in almost quantitative yield. The conversion of (**51**) into the terminal olefinic compound (**53**) with an α-hydroxy group at the position corresponding to C-9 of (**1**) was readily and efficiently carried out *via* the iodide (**52**) as described in the above model experiments. Thus the construction of the five consecutive chiral centres with desired configurations was accomplished. The sixth and final chiral centre was introduced by hydroboration as follows. The hydroxy group of the enol (**53**) was first protected as the MPM ether (**54**), and the compound was then treated with diborane in THF in the usual manner; no



Scheme 5. *Reagents:* (i) PCC; (ii) $Ph_3P{=}C(Me)CO_2Et$; (iii) $LiAlH_4$; (iv) *m*-CPBA, CH_2Cl_2; (v) 2M-HCl; (vi) $Me_2C(OMe)_2$, CSA; (vii) MsCl; (viii) NaI; (ix) Zn–Cu couple; (x) (a) 2M-HCl, MeOH, (b) PhCOCl, Py; (xi) $Me_2C(OMe)_2$, TsOH. The compounds prepared by this Scheme appear to be racemates (see Experimental section)



Scheme 6. *Reagents:* (i) (a) $Ph_3P{=}C(Me)CO_2Et$, (b) $LiAlH_4$; (ii) *m*-CPBA; (iii) (a) MsCl, Py, (b) NaI; (iv) Zn–Cu couple, EtOH; (v) MPMCl, NaH; (vi) (a) BH_3, CH_2Cl_2, (b) H_2O_2, NaOH

hydroboration occurred. Treatment, however, with diborane in methylene dichloride prepared *in situ* from tetra-n-butylammonium borohydride and methyl iodide[18] at room temperature gave a mixture of the expected alcohol (**55**) and its isomer (**56**), though both the yield and the stereoselection were very unsatisfactory. Compound (**55**), easily purified by silica gel chromatography as an oil, was completely identical in its i.r., n.m.r., and mass spectra and specific rotation with the degradation product[19] of natural erythromycin A. Since compound (**55**) has all of the six consecutive chiral centres with correct configurations expected for segment i (**3**), the most important intermediate in our synthetic plan became available as described in this paper, although the yield in the final step of Scheme 6 needs to be improved.

Experimental

M.p.s were measured on a Yamato MP-1 micro melting point apparatus and are uncorrected. Optical rotations were measured with a JASCO DIP-4 digital polarimeter. I.r. spectra were recorded on a JASCO IRA-2 spectrophotometer. Low-resolution, field-desorption, and high-resolution mass spectra were taken on a JEOL JMS D-300 or JEOL JMS-01 SG spectrometer. ^{1}H N.m.r. spectra were recorded on a JEOL JNM FX-100 or JEOL JNM FX-200 instrument.

(Z)-3,5,6,7,8-*Pentadeoxy*-1,2-O-*isopropylidene*-3,5-*di*-C-*methyl*-β-L-lyxo-*oct*-5-*enofuranose* (**6**).—A 1.6M hexane solution (15.6 ml, 25 mmol) of n-BuLi was added dropwise to a stirred suspension of n-propyltriphenylphosphonium bromide (10.6 g, 27.5 mmol) at −70 °C under argon, and then a solution of the ketone (**5**) (1.0 g, 5.0 mmol) in THF (2 ml) was added at the same temperature. The reaction mixture was allowed to warm to 0 °C during 9 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 under reduced pressure to leave an oil, which was chromatographed on a silica gel column with n-hexane–EtOAc (5:1) as eluant to afford two fractions. The first fraction was the title compound (**6**) as an oil (576 mg, 51%; net yield 98.6%); $[\alpha]_D^{17}$ +49° (*c* 0.84 in $CHCl_3$); δ_H ($CDCl_3$) 0.95 (3 H, t, *J* 7.5 Hz), 0.95 (3 H, d, *J* 7.5 Hz), 1.37 (3 H, s), 1.60 (3 H, s), 1.78 (3 H, d, *J* 1.0 Hz), 1.78—2.15 (2 H, m), 2.35—2.76 (1 H, m), 4.63 (1 H, dd, *J* 6.5, 3.5 Hz), 4.96 (1 H, d, *J* 9.0 Hz), 5.15—5.45 (1 H, m), and 5.67 (1 H, d, *J* 3.5 Hz); *m/z* 226 (M^+, 4.2%), 211 (8.1), 197 (4.1), 168 (7.0), 139 (5.8), 123 (14), 109 (22), 99 (98), and 59 (100).

The second fraction was recovered (**5**) (483 mg, 48.3%).

3,7,8-*Trideoxy*-1,2-O-*isopropylidene*-3,5-*di*-C-*methyl*-α-D-glycero-D-gulo-*octofuranose* (**7**).—*N*-Methylmorpholine *N*-oxide (NMO) monohydrate (380 mg, 2.8 mmol) and OsO_4 (130 mg, 0.51 mmol) were added to a stirred solution of compound (**6**) (580 mg, 2.56 mmol) in Me_2CO–water (10:3; 13 ml) at 0 °C. The reaction mixture was allowed to warm to room temperature and was stirred for 15 h. $Na_2S_2O_4$ (700 mg) was added and the mixture was stirred for a further 1 h. Insoluble materials were filtered off through a Celite pad and the filtrate was extracted with CH_2Cl_2. The extract was washed successively with 2% H_2SO_4, brine, saturated $NaHCO_3$, and brine, then dried (Na_2SO_4), and evaporated under reduced pressure. The residue was chromatographed on a short silica gel column with n-hexane–EtOAc (1:1) as eluant to give a solid 23:1 mixture of the title compound (**7**) and its isomer (602 mg, 90.2%). The mixture (525 mg) was chromatographed on a silica gel column with CH_2Cl_2–MeOH (40:1) as eluant to give two fractions.

The first fraction was compound (**7**) as a solid (415 mg), which was recrystallized from ether to afford *needles*, m.p. 131.5—132 °C (Found: C, 59.8; H, 9.4. $C_{13}H_{24}O_5$ requires C, 59.98; H, 9.29%); $[\alpha]_D^{18}$ −18° (*c* 0.72 in $CHCl_3$); δ_H ($CDCl_3$) 1.04 (3 H, t, *J* 7.0 Hz), 1.12 (3 H, s), 1.36 (3 H, s), 1.39 (3 H, d, *J* 7.5 Hz), 1.63 (3 H, s), 1.20—1.80 (2 H, m), 2.53 (1 H, d, *J* 8.0 Hz), 2.50—2.83 (1 H, m), 3.42 (1 H, ddd, *J* 10.0, 8.0, 2.0 Hz), 3.79 (1 H, s), 4.26 (1 H, d, *J* 8.5 Hz), 4.61 (1 H, dd, *J* 5.5, 4.0 Hz), and 5.71 (1 H, d, *J* 4.0 Hz); *m/z* 245 (M^+ − 15, 3.6%), 201 (7.7), 184 (9.2), 157 (13), 143 (92), 85 (89), and 43 (100).

The second fraction was a solid diastereoisomer of (**7**) (18 mg), δ_H ($CDCl_3$) 1.01 (3 H, t, *J* 7.0 Hz), 1.25 (3 H, s), 1.35 (3 H, d, *J* 7.5 Hz), 1.36 (3 H, s), 1.62 (3 H, s), 1.20—1.96 (2 H, m), 2.13 (1 H, d, *J* 5.0 Hz), 2.42—2.83 (1 H, m), 3.10 (1 H, s), 3.35—3.62 (1 H, m), 4.30 (1 H, d, *J* 8.5 Hz), 4.61 (1 H, dd, *J* 5.5, 4.0 Hz), and 5.71 (1 H, d, *J* 4.0 Hz).

(1S,2R,3R,4R,5R,7R)-7-*Ethyl*-2,4-*dihydroxy*-1,3-*dimethyl*-6,8-*dioxabicyclo*[3.2.1]*octane* (**8**).—Toluene-*p*-sulphonic acid monohydrate (25 mg) was added to a stirred solution of the diol (**7**) (50 mg) in CH_2Cl_2 (2.5 ml) at room temperature. After 12 h, the reaction mixture was neutralized with Et_3N and evaporated under reduced pressure. The residue was chromatographed on a silica gel column with CH_2Cl_2–MeOH (24:1) as eluant to give a solid residue of compound (**8**) (32 mg, 82%), which was recrystallized from n-hexane–EtOAc to afford *needles*, m.p. 180—181.5 °C (Found: C, 59.5; H, 9.1. $C_{10}H_{18}O_4$ requires C, 59.38; H, 8.97%); $[\alpha]_D^{11}$ +49° (*c* 1.08 in $CHCl_3$); δ_H($CDCl_3$–D_2O) 1.06 (3 H, t, *J* 7.5 Hz), 1.11 (3 H, d, *J* 7.0 Hz), 1.40 (3 H, s), 1.60—2.00 (2 H, m), 2.02—2.42 (1 H, m) 3.30—3.68 (3 H, m), and 5.25 (1 H, d, *J* 2.0 Hz); *m/z* 202 (M^+, 0.25%), 184 (0.25), 156 (6.1), 144 (35), 98 (83), and 43 (100).

(1R,2R,3R,4R,5R,7R)-2,4-*Diacetoxy*-7-*ethyl*-1,3-*dimethyl*-6,8-*dioxabicyclo*[3.2.1]*octane* (**9**).—Ac_2O (12 mg), Et_3N (24 mg), and DMAP (2 mg) were added to a stirred solution of the diol (**8**) (10 mg) in CH_2Cl_2 (1 ml) at room temperature. After 1 h, the solution was evaporated under reduced pressure and the residue was chromatographed on a silica gel column with CH_2Cl_2–MeOH (24:1) as eluant to afford the diacetate (**9**) as an oil (13 mg, 92%), $\nu_{max.}$ (neat) 1 740 cm^{-1}; δ_H($CDCl_3$) 0.84 (3 H, d, *J* 7.0 Hz), 1.07 (3 H, t, *J* 7.5 Hz), 1.27 (3 H, s), 1.64—2.02 (2 H, m), 2.10 (3 H, s), 2.12 (3 H, s), 2.42—2.66 (1 H, m), 3.54 (1 H, ddd, *J* 10.0, 5.0, 1.5 Hz), 4.89 (1 H, dd, *J* 5.0, 2.0 Hz), 5.02 (1 H, dd, *J* 11.0, 1.5 Hz), and 5.30 (1 H, d, *J* 2.0 Hz); *m/z* 286 (M^+, 0.6%), 243 (2.2), 198 (1.4), 186 (15), 144 (31), 109 (24), 98 (23), and 43 (100).

(1S,2R,3R,4R,5R,7R)-4-(4-*Bromobenzoyloxy*)-7-*ethyl*-2-*hydroxy*-1,3-*dimethyl*-6,8-*dioxabicyclo*[3.2.1]*octane* (**13a**).—A solution of the diol (**8**) (37 mg, 0.18 mmol), 4-bromobenzoyl chloride (88 mg, 0.4 mmol), and pyridine (0.2 ml) in CH_2Cl_2 (1 ml) was stirred at room temperature for 1 h. After addition of CH_2Cl_2 (20 ml) the solution was washed successively with aqueous $KHSO_4$, aqueous $NaHCO_3$, and water, dried (Na_2SO_4), and evaporated under reduced pressure. The residue was chromatographed on a silica gel column with CH_2Cl_2 (40:1) as eluant to give compound (**13a**) as a solid (64 mg, 91%), which was recrystallized from di-isopropyl ether to afford *fine needles*, m.p. 171—171.5 °C (Found: C, 53.0; H, 5.5. $C_{17}H_{21}BrO_5$ requires C, 53.00; H, 5.49%); δ_H ($CDCl_3$) 1.06 (3 H, d, *J* 6.0 Hz), 1.09 (3 H, t, *J* 7.0 Hz), 1.45 (3 H, s), 1.79 (1 H, d, *J* 5.5 Hz), 1.60—2.10 (2 H, m), 2.35—2.75 (1 H, m), 3.46—3.76 (2 H, m), 5.08 (1 H, dd, *J* 4.5, 2.0 Hz), 5.39 (1 H, d, *J* 4.5 Hz), 7.58 (2 H, d, *J* 9.0 Hz), and 7.92 (2 H, d, *J* 9.0 Hz).

(1R,2R,3R,4R,5R,7R)-2-*Acetoxy*-4-(4-*bromobenzoyloxy*)-7-*ethyl*-1,3-*dimethyl*-6,8-*dioxabicyclo*[3.2.1]*octane* (**13b**).—Compound (**13a**) (59 mg) was acetylated as described for the preparation of (**9**) to give the acetate (**13b**) as a solid (57 mg, 88%) which was recrystallized from n-hexane to afford *plates*,

m.p. 137—137.5 °C (Found: C, 53.3; H, 5.45; Br, 18.7. $C_{19}H_{23}BrO_6$ requires C, 53.41; H, 5.43; Br, 18.70%); δ_H ($CDCl_3$) 0.91 (3 H, d, *J* 7.0 Hz), 1.10 (3 H, t, *J* 7.5 Hz), 1.31 (3 H, s), 1.62—2.10 (2 H, m), 2.12 (3 H, s), 2.48—2.90 (1 H, m), 3.59 (1 H, ddd, *J* 9.0, 5.0, 1.5 Hz), 5.10 (1 H, dd, *J* 11.0, 1.5 Hz), 5.11 (1 H, dd, *J* 5.0, 2.0 Hz), 5.42 (1 H, d, *J* 2.0 Hz), 7.60 (2 H, d, *J* 9.0 Hz), and 7.95 (2 H, d, *J* 9.0 Hz).

3,7,8-*Trideoxy*-1,2-O-*isopropylidene*-6-O-(4-*methoxybenzyl*)-3,5-*di*-C-*methyl*-α-D-glycero-D-gulo-*hexofuranose* (**14**).—50% NaH dispersion (26 mg, 0.55 mmol) was added to a stirred solution of compound (**7**) (130 mg, 0.5 mmol) in dimethylformamide (DMF) (3 ml) at room temperature. After 30 min, 4-methoxybenzyl chloride (MPMCl) (112 mg, 0.6 mmol) was added and the mixture was stirred for 2 h, and then 50% NaH dispersion (26 mg) and MPMCl (50 mg) were again added. After being stirred at 50 °C for 1 h, the reaction mixture was poured into ice–aqueous NH_4Cl and extracted with ether. The extract was washed with brine, dried ($MgSO_4$), and evaporated to leave an oil, which was chromatographed on a silica gel column with n-hexane–EtOAc (3:1) as eluant to give compound (**14**) as an oil (177 mg, 93.2%), $[\alpha]_D^{20}$ −31° (*c* 0.5 in $CHCl_3$); δ_H ($CDCl_3$) 1.04 (3 H, t, *J* 7.5 Hz), 1.15 (3 H, s), 1.33 (3 H, d, *J* 7.5 Hz), 1.37 (3 H, s), 1.61 (3 H, s), 1.55—2.1 (2 H, m), 2.45—2.82 (1 H, m), 3.31 (1 H, s), 3.56 (1 H, dd, *J* 8.5, 3.0 Hz), 3.79 (3 H, s), 4.31 (1 H, d, *J* 8.0 Hz), 4.61 (2 H, s), 4.62 (1 H, dd, *J* 6.0, 4.0 Hz), 5.72 (1 H, d, *J* 4.0 Hz), 6.81—6.92 (2 H, m), and 7.18—7.35 (2 H, m); *m/z* 264 (M^+ −116, 1.1%), 221 (2.6), 201 (15), 143 (84), and 121 (100); *m/z* (FD) 380 (M^+, 100%), 381 (97), 201 (60), and 121 (52).

(2S,3R,4S,5R)-1,3,4-*Trihydroxy*-5-(4-*methoxybenzyloxy*)-2,4-*dimethylheptane* [2,6,7-*Trideoxy*-5-O-(4-*methoxybenzyl*)-2,4-*di*-C-*methyl*-D-gluco-*heptitol*] (**16**).—(*a*) A solution of compound (**14**) (150 mg) in 4M-HCl (1 ml) and THF (2 ml) was stirred at room temperature for 1 h. After neutralization with $NaHCO_3$, the reaction mixture was evaporated under reduced pressure and the residue was chromatographed on a silica gel column with n-hexane–EtOAc (1:1) as eluant to give an oil (118 mg). This oil was dissolved in benzene (2 ml) and $Pb(OAc)_4$ (171 mg) was added. The mixture was stirred at room temperature for 15 min, and then the supernatant of the reaction mixture was poured onto a silica gel column. Elution with n-hexane–EtOAc (3:2) gave an oily 1:1 mixture of the anomers of (**15**) (116 mg, 87%), $\nu_{max.}$(neat) 1 720 cm^{-1}; *m/z* 338 (M^+, 0.2%), 320 (0.5), 262 (0.6), 216 (0.7), 159 (11), 122 (30), and 121 (100).

$LiAlH_4$ (78 mg, 2.06 mmol) was added to a stirred solution of the anomers of compound (**15**) (116 mg, 0.34 mmol) in ether (2 ml) at 0 °C under argon. After 2 h, EtOAc, water, 15% NaOH, and more water were successively added, and then the mixture was extracted with ether. The extract was dried and evaporated to leave an oil, which was chromatographed on a silica gel column with n-hexane–EtOAc (3:2) as eluant to afford the heptitol (**16**) as an oil (93 mg, 87%). The oil solidified with time, m.p. 63—64 °C (from ether–hexane) (Found: C, 65.55; H, 9.0. $C_{17}H_{28}O_5$ requires C, 65.36; H, 9.03%); δ_H ($CDCl_3$) 1.06 (3 H, t, *J* 7.5 Hz), 1.07 (3 H, d, *J* 7.0 Hz), 1.10 (3 H, s), 1.60—1.95 (3 H, m), 2.42 (1 H, s), 3.15 (1 H, s), 3.34 (1 H, dd, *J* 7.5, 5.0 Hz), 3.50—4.04 (4 H, m), 3.80 (3 H, s), 4.63 (2 H, s), 6.88 (2 H, d, *J* 9.0 Hz), and 7.26 (2 H, d, *J* 9.0 Hz); *m/z* 236 (M^+ −76, 0.5%), 206 (0.3), 180 (0.9), 173 (1.4), 133 (14), 122 (50), and 121 (100); *m/z* (FD) 312 (M^+, 100%), 313 (30), and 121 (11); $[\alpha]_D^{16}$ +23° (*c* 1.20 in $CHCl_3$).

(*b*) A solution of compound (**30**) (3.12 g, 10.1 mmol) in ether (75 ml) was added dropwise to a stirred solution of AlH_3 prepared from $AlCl_3$ (3.5 g, 26 mmol) and $LiAlH_4$ (2.27 g, 59.7 mmol) in ether (150 ml) at room temperature. After 1 h, excess of AlH_3 was decomposed with MeOH (7 ml). The mixture was diluted with ether (50 ml) and then stirred and treated with 15% NaOH (12 ml) at 0 °C. Precipitated salts were filtered off and the filtrate was dried (Na_2SO_4), evaporated under reduced pressure, and chromatographed on a silica gel column to give the heptitol (**16**) (2.273 g, 72%).

(2S,3R,4R,5R)-1,3-*Diacetoxy*-4-*hydroxy*-5-(4-*methoxybenzyloxy*)-2,4-*dimethylheptane* [1,3-*Di*-O-*acetyl*-2,6,7-*trideoxy*-5-O-(4-*methoxybenzyl*)-2,4-*di*-C-*methyl*-D-gluco-*heptitol*] (**17**).—Compound (**16**) (9 mg) was acetylated as described for the preparation of (**9**) to afford compound (**17**) as an oil (11 mg), δ_H 1.03 (3 H, d, *J* 7.0 Hz), 1.08 (3 H, t, *J* 7.0 Hz), 1.19 (3 H, s), 1.48—1.90 (2 H, m), 1.87 (3 H, s), 2.03 (3 H, s), 2.18—2.40 (1 H, m), 2.59 (1 H, s), 3.11 (1 H, t, *J* 5.5 Hz), 3.80 (3 H, s), 3.80 and 3.87 (1 H each, ABq, *J* 2.5 Hz), 4.30 and 4.47 (1 H each, ABq, *J* 8.5 Hz), 5.27 (1 H, d, *J* 2.0 Hz), 6.86 (2 H, d, *J* 9.0 Hz), and 7.27 (2 H, d, *J* 9.0 Hz).

(2S,3R,4S,5R)-1-*Benzoyloxy*-3,4-*dihydroxy*-5-(4-*methoxybenzyloxy*)-2,4-*dimethylheptane* [1-O-*Benzoyl*-2,6,7-*trideoxy*-5-O-(4-*methoxybenzyl*)-2,4-*di*-C-*methyl*-D-gluco-*heptitol*] (**18**).—A solution of compound (**16**) (171 mg, 0.547 mmol), pyridine (0.15 ml), and benzoyl chloride (152 mg, 1.08 mmol) in CH_2Cl_2 (5 ml) was stirred at room temperature for 1 h. After addition of CH_2Cl_2 (20 ml), the solution was washed successively with aqueous $KHSO_4$ and 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 benzoate (**18**) as an oil (216 mg, 95%) (Found: M^+ −CH_3, 441.2263. $C_{26}H_{33}O_6$ requires *m/z*, 441.2268); $\nu_{max.}$ (neat) 1 715 cm^{-1}; δ_H 1.05 (3 H, t, *J* 7.5 Hz), 1.10 (3 H, d, *J* 7.0 Hz), 1.12 (3 H, s), 1.40—1.80 (2 H, m), 2.05—2.36 (1 H, m), 3.10 (1 H, s), 3.35 (1 H, dd, *J* 7.5, 4.0 Hz), 3.50 (1 H, s), 3.78 (3 H, s), 3.97 (1 H, t, *J* 2.0 Hz), 4.18 (1 H, dd, *J* 9.0, 6.5 Hz), 4.36 (1 H, dd, *J* 9.0, 8.5 Hz), 4.61 (2 H, s), 6.82 (2 H, d, *J* 9.0 Hz), 7.21 (2 H, d, *J* 9.0 Hz), 7.30—7.64 (3 H, m), and 8.02 (2 H, dd, *J* 8.0, 1.5 Hz); *m/z* 237 (M^+ −179, 15%), 219 (2.9), 193 (5.6), 138 (5.6), 122 (45), and 121 (100).

(2S,3R,4R,5R)-1-*Benzoyloxy*-3,4-*isopropylidenedioxy*-5-(4-*methoxybenzyloxy*-2,4-*dimethylheptane* [1-O-*Benzoyl*-2,6,7-*trideoxy*-3,4-O-*isopropylidene*-5-O-(4-*methoxybenzyl*)-2,4-*di*-C-*methyl*-D-gluco-*heptitol*] (**19**).—A solution of compound (**18**) (206 mg, 0.495 mmol), 2,2-dimethoxypropane (acetone dimethyl acetal) (57 mg, 0.544 mmol), and TsOH (20 mg) in Me_2CO (10 ml) was stirred at room temperature for 30 h. After addition of CH_2Cl_2 (30 ml), the solution was washed successively with aqueous $NaHCO_3$ and water, dried (Na_2SO_4), and evaporated under reduced pressure to leave compound (**19**) as an oil (213 mg, 94%), $[\alpha]_D^{18}$ +12° (*c* 1.2 $CHCl_3$); $\nu_{max.}$ (neat) 1 730 cm^{-1}; δ_H 0.95 (3 H, t, *J* 7.0 Hz), 1.15 (3 H, d, *J* 6.5 Hz), 1.24 (3 H, s), 1.34 (3 H, s), 1.44 (3 H, s), 1.40—1.80 (2 H, m), 2.08—2.40 (1 H, m), 3.27 (1 H, dd, *J* 7.5, 4.5 Hz), 3.75 (3 H, s), 4.15 (1 H, d, *J* 4.0 Hz), 4.19 and 4.26 (1 H each, ABq, *J* 2.0 Hz), 4.54 and 4.60 (1 H each, ABq, *J* 11.0 Hz), 6.79 (2 H, d, *J* 8.0 Hz), 7.21 (2 H, d, *J* 8.0 Hz), 7.30—7.62 (3 H, m), and 7.90—8.08 (2 H, m); *m/z* 456 (M^+, 0.1%), 441 (1.1), 277 (18), 219 (100), 155 (51), and 121 (99).

(2S,3R,4R,5R)-1-*Hydroxy*-3,4-*isopropylidene*-5-(4-*methoxybenzyloxy*)-2,4-*dimethylheptane* [2,6,7-*Trideoxy*-3,4-O-*isopropylidene*-5-O-(4-*methoxybenzyl*)-2,4-*di*-C-*methyl*-D-gluco-*heptitol*] (**20**).—A solution of compound (**19**) (213 mg) in 1M-KOH (2 ml) and MeOH (7.5 ml) was stirred at room temperature. After 1 h, the reaction mixture was concentrated under reduced pressure and extracted with CH_2Cl_2. The extract was washed with water, dried (Na_2SO_4), and evaporated to leave compound (**20**) as an oil (164 mg, 100%), $[\alpha]_D$ −4.9° (*c* 1.76 in $CHCl_3$); δ_H ($CDCl_3$) 1.03 (3 H, t, *J* 7.0 Hz), 1.04 (3 H, d, *J* 7.0 Hz), 1.21 (3 H, s), 1.34 (3 H, s), 1.42 (3 H, s), 1.50—2.12 (4 H, m),

3.32 (1 H, dd, *J* 7.5, 4.5 Hz), 3.49 (2 H, t, *J* 5.5 Hz), 3.80 (3 H, s), 3.98 (1 H, d, *J* 4.5 Hz), 4.58 (2 H, s), 6.87 (2 H, d, *J* 9.0 Hz), and 7.27 (2 H, d, *J* 9.0 Hz); *m/z* 337 ($M^+ - 15$, 0.5%), 217 (0.5), 180 (1.1), 173 (35), 121 (98), and 115 (100).

(2R,3R,4R,5R)-3,4-O-*Isopropylidene*-5-(4-*methoxybenzyloxy*-2,4-*dimethylheptanal* [2,6,7-*Trideoxy*-3,4-O-*isopropylidene*-5-O-(4-*methoxybenzyl*)-2,4-*di*-C-*methyl*-D-gluco-*heptose*] (**21**).—Pyridinium chlorochromate (PCC) (303 mg, 1.4 mmol) and powdered molecular sieves 3A (450 mg) was added to a stirred solution of alcohol (**20**) (165 mg, 0.468 mmol) in CH_2Cl_2 (10 ml) at room temperature. After 15 min, the reaction mixture was poured onto a silica gel column and elution with ether gave *compound* (**21**) as an oil (149 mg, 91%) (Found: M^+, 350.2083. $C_{20}H_{30}O_5$ requires *M*, 350.2095); $[\alpha]_D^{11}$ −7.0° (*c* 1.32 in $CHCl_3$); $\nu_{max.}$(neat) 1 720 cm^{-1} (CHO); δ_H ($CDCl_3$) 1.03 (3 H, t, *J* 7.0 Hz), 1.16 (3 H, s), 1.20 (3 H, d, *J* 7.0 Hz), 1.34 (3 H, s), 1.41 (3 H, s), 1.50—1.82 (2 H, m), 2.70 (1 H, ddd, *J* 7.5, 7.0, 2.5 Hz), 3.30 (1 H, dd, *J* 7.0, 5.0 Hz), 3.80 (3 H, s), 4.26 (1 H, d, *J* 6.0 Hz), 4.46 and 4.56 (1 H each, ABq, *J* 11.0 Hz), 6.86 (2 H, d, *J* 8.5 Hz), 7.23 (2 H, d, *J* 8.5 Hz), and 9.45 (1 H, d, *J* 2.5 Hz); *m/z* 350 (M^+, 2.2%), 171 (53), and 121 (100).

3-O-*Benzyl*-5,6-*dideoxy*-1,2-O-*isopropylidene*-3-C-*methyl*-α-D-ribo-*hex*-5-*enofuranose* (**23**).—DMAP (10 mg), Et_3N (1 ml), and TsCl (538 mg, 2.82 mmol) were added to a stirred solution of the diol (**22**) (436 mg, 1.34 mmol) in CH_2Cl_2 (5 ml) at 0 °C. After being stirred at room temperature for 40 h, the reaction mixture was poured into ice–water and extracted with CH_2Cl_2. The extract was washed successively with 1M-HCl, saturated aqueous $NaHCO_3$, and water, dried (Na_2SO_4), and evaporated under reduced pressure. The residue was chromatographed on a silica gel column with CH_2Cl_2–MeOH (100:1) as eluant to give, as a pale yellow solid, 3-*O*-benzyl-1,2-*O*-isopropylidene-3-*C*-methyl-5,6-ditosyloxy-α-D-allofuranose (717 mg, 84.3%).

This solid (717 mg) was dissolved in methyl ethyl ketone (15 ml) and NaI (680 mg, 4.53 mmol) was added. The mixture was refluxed for 1.5 h, and then evaporated under reduced pressure. The residue was extracted with CH_2Cl_2. The extract was washed successively with aqueous $Na_2S_2O_3$ and water, dried (Na_2SO_4), and evaporated under reduced pressure to leave a solid, which was chromatographed on a silica gel column with n-hexane–EtOAc (3:1) as eluant to give compound (**23**) as a pale yellow solid (243 mg, 73.9%). Recrystallization from n-hexane gave the *hexenofuranose* as needles, m.p. 90.5—92 °C (Found: C, 70.1; H, 7.7. $C_{17}H_{22}O_4$ requires C, 70.32; H, 7.62%); δ_H ($CDCl_3$) 1.29 (3 H, s), 1.35 (3 H, s), 1.60 (3 H, s), 4.33 (1 H, d, *J* 3.5 Hz), 4.63 (1 H, d, *J* 8.0 Hz), 4.67 (2 H, s), 5.15—5.60 (2 H, m), 5.72 (1 H, d, *J* 3.5 Hz), 5.62—5.98 (1 H, m), and 7.20—7.42 (5 H, m); *m/z* 275 ($M^+ - 15$, 2.0%), 191 (3.8), 176 (3.1), 143 (97), and 91 (100).

3-O-*Benzyl*-5,6-*dideoxy*-1,2-O-*isopropylidene*-3-C-*methyl*-α-D-ribo-*hexofuranose* (**24**).—A solution of compound (**23**) (1.9 g) in EtOAc (50 ml) was hydrogenated in the presence of 10% Pd–C (0.19 g) at ordinary temperature and pressure for 2 h. After removal of the catalyst by filtration, the filtrate was evaporated under reduced pressure to leave the *saturated product* (**24**) as a solid (1.9 g, 100%), m.p. 71—71.5 °C (from n-hexane) (Found: C, 70.1; H, 8.2. $C_{17}H_{24}O_4$ requires C, 69.83; H, 8.27%); $[\alpha]_D^{15}$ + 49° (*c* 0.77 in $CHCl_3$); δ_H ($CDCl_3$) 1.02 (3 H, t, *J* 7.0 Hz), 1.18 (3 H, s), 1.35 (3 H, s), 1.60 (3 H, s), 1.35—1.70 (2 H, m), 3.97 (1 H, dd, *J* 8.0, 5.5 Hz), 4.34 (1 H, d, *J* 4.0 Hz), 4.56 and 4.64 (1 H each, ABq, *J* 11.0 Hz), 5.73 (1 H, d, *J* 4.0 Hz), and 7.19—7.48 (5 H, m).

(2R,3R)-2-*Benzyloxy*-3-*formyloxy*-2-*methylpentanal* (2-O-*Benzyl*-4,5-*dideoxy*-3-O-*formyl*-2-C-*methyl*-D-erythro-*pentose*) (**25**).—Water (30 ml) and trifluoroacetic acid (TFA) (40 ml) were added to a stirred solution of compound (**24**) (1.92 g, 6.57 mmol) in THF (40 ml) at room temperature. After 40 h, the solution was neutralized with $NaHCO_3$ and evaporated under reduced pressure to leave an oil, which was extracted with CH_2Cl_2. The extract was washed with water, dried (Na_2SO_4), and evaporated to give the 2,4-diol (1.70 g), which was oxidized with $Pb(OAc)_4$ (3.3 g) in benzene (30 ml) as indicated for the preparation of compound (**15**) to afford the oily aldehyde (**25**) (1.6 g, 97.3%), δ_H 0.92 (3 H, t, *J* 7.0 Hz), 1.37 (3 H, s), 1.50—1.90 (2 H, m), 4.44 and 4.60 (1 H each, ABq, *J* 11.0 Hz), 5.29 (1 H, dd, *J* 9.0, 4.5 Hz), 7.33 (5 H, s), 8.13 (1 H, s), and 9.63 (1 H, s); *m/z* 221 ($M^+ - 29$, 5%) and 91 (100).

Ethyl (2E,4S,5R)-4-*Benzyloxy*-5-*formyloxy*-2,4-*dimethylhept*-2-*enoate* [*Ethyl* (E)-4-O-*Benzoyl*-2,3,6,7-*tetradeoxy*-5-O-*formyl*-2,4-*di*-C-*methyl*-D-erythro-*hept*-2-*enonate*] (**26**).—A stirred solution of compound (**25**) (378 mg, 1.51 mmol) and α-ethoxycarbonylethylidenetriphenylphosphorane (2.19, 6.05 mmol) in ethylene dichloride (35 ml) was refluxed for 17 h. After removal of the solvent under reduced pressure, the residue was chromatographed on a silica gel column with n-hexane–EtOAc (3:1) as eluant to afford the oily ester (**26**) (449 mg, 88.9%), δ_H ($CDCl_3$) 0.92 (3 H, t, *J* 7.0 Hz), 1.30 (3 H, t, *J* 7.0 Hz), 1.48 (3 H, s), 1.50—2.00 (2 H, m), 2.05 (3 H, d, *J* 1.5 Hz), 4.09 (2 H, q, *J* 7.0 Hz), 4.34 and 4.50 (1 H each, ABq, *J* 11.0 Hz), 5.24 (1 H, dd, *J* 10.0, 2.5 Hz), 6.61 (1 H, q, *J* 1.5 Hz), 7.29 (5 H, s), and 8.15 (1 H, s).

(2E,4S,5R)-4-*Benzyloxy*-1-*hydroxy*-2,4-*dimethylhept*-2-*ene* [(E)-4-O-*Benzyl*-2,3,6,7-*tetradeoxy*-2,4-*di*-C-*methyl*-D-erythro-*hept*-2-*enitol*] (**27**).—Compound (**26**) (449 mg) was reduced with $LiAlH_4$ (128 mg) in ether (35 ml) as described for the preparation of compound (**16**) to give compound (**27**) as a solid (321 mg, 90.4%). Recrystallization from ether–hexane gave *needles*, m.p. 90—91 °C (Found: C, 72.8; H, 9.2. $C_{16}H_{24}O_3$ requires C, 72.69; H, 9.15%); δ_H ($CDCl_3$) 1.00 (3 H, t, *J* 7.0 Hz), 1.40 (3 H, s), 1.81 (3 H, d, *J* 1.5 Hz), 1.6—2.0 (2 H, m), 2.02 (1 H, br s), 2.43 (1 H, dt, *J* 4.0 Hz), 3.40—3.80 (1 H, m), 4.02 (2 H, d, *J* 5.0 Hz), 4.30—4.57 (2 H, ABq, *J* 12.0 Hz), 5.45 (1 H, s), and 7.31 (5 H, s); *m/z* 205 ($M^+ - 59$, 10%), 145 (15), and 91 (100). The diacetate was an oil, δ_H ($CDCl_3$) 0.88 (3 H, t, *J* 7.5 Hz), 1.39 (3 H, s), 1.40—1.95 (2 H, m), 1.84 (3 H, d, *J* 1.0 Hz), 2.06 (3 H, s), 2.08 (3 H, s), 4.37 and 4.47 (1 H each, ABq, *J* 11.5 Hz), 4.43 (2 H, s), 5.13 (1 H, dd, *J* 10.5, 3.0 Hz), and 7.31 (5 H, s).

(2S,3R,4R,5R)-4-*Benzyloxy*-2,3-*epoxy*-1,5-*dihydroxy*-2,4-*dimethylheptane* (2,3-*Anhydro*-4-O-*benzoyl*-6,7-*dideoxy*-2,4-*di*-C-*methylheptitol*) (**28a**).—85% *m*-Chloroperbenzoic acid (*m*-CPBA) (3.97 g, 19.6 mmol) was added to a stirred solution of compound (**27**) (3.97 g, 15 mmol) in CH_2Cl_2 (250 ml) at −5 °C. After 2.5 h, the reaction mixture was washed successively with aqueous Na_2SO_3, aqueous $NaHCO_3$, and water, dried (Na_2SO_4), and evaporated under reduced pressure to leave an oil, which was chromatographed on a silica gel column with ether–CH_2Cl_2 (10:1) as eluant to afford the oily epoxide (**28a**) (3.21 g, 76.2%), δ_H ($CDCl_3$) 1.05 (3 H, t, *J* 7.0 Hz), 1.32 (3 H, s), 1.40 (3 H, s), 1.3—1.82 (2 H, m), 2.11 (1 H, t, *J* 6.5 Hz), 2.56 (1 H, d, *J* 6.0 Hz), 3.24 (1 H, s), 3.39—3.60 (1 H, m), 3.59 (2 H, d, *J* 6.5 Hz), 4.63 (2 H, s), and 7.32 (5 H, s); *m/z* 249 ($M^+ - 31$, 2.2%), 221 (1.0), 191 (2.4), 113 (3.2), and 91 (100).

Epoxidation of Compound (**27**) *with* t-BuOOH.—A 2.35M solution of t-butyl hydroperoxide in ethylene dichloride (5 ml, 1.18 mmol) was added to a stirred solution of (**27**) (100 mg, 0.38 mmol) and vanadyl acetylacetonate (5 mg) in CH_2Cl_2 (20 ml) at room temperature. After 1 h, the reaction mixture was diluted with CH_2Cl_2 (30 ml), washed successively with aqueous Na_2SO_3, and water, dried (Na_2SO_4), and evaporated under

reduced pressure to leave an oil, which was chromatographed on a silica gel column with ether–CH_2Cl_2 (10:1) as eluant to give two fractions. The first fraction was the oily epoxide (**28a**) (48 mg, 45%).

The second fraction was the oily isomer (**28b**) (38 mg, 36%), δ_H ($CDCl_3$) 1.05 (3 H, t, *J* 7.0 Hz), 1.45 (3 H, s), 1.51 (3 H, s), 1.35—1.95 (2 H, m), 2.40 (1 H, s), 3.09 (1 H, s), 3.42—3.70 (4 H, m), 4.59 and 4.68 (1 H each, ABq, *J* 11.5 Hz), and 7.31 (5 H, s); *m/z* 249 ($M^+ - 31$, 6.5%), 191 (3.7), 143 (12), and 91 (100).

(2S,3S,4R,5R)-2,3-*Epoxy*-1,4,5-*trihydroxy*-2,4-*dimethylheptane* (2,3-*Anhydro*-6,7-*dideoxy*-2,4-*di*-C-*methyl*-D-gluco-*heptitol*) (**29**).— Compound (**28a**) (4.74 g) in EtOH (350 ml) was hydrogenated over 10% Pd–C (2.0 g) in the presence of $NaHCO_3$ (0.4 g) at ordinary temperature and pressure for 5 h. After removal of the catalyst by filtration, the filtrate was evaporated to leave an oil, which was chromatographed on a silica gel column with EtOAc as eluant to give two fractions. The first fraction was the free triol (**29**) as an oil (2.78 g, 86.6%), δ_H 1.06 (3 H, t, *J* 7.0 Hz), 1.26 (3 H, s), 1.51 (3 H, s), 1.30—1.82 (2 H, m), 2.30 (2 H, s), 2.62 (1 H, s), 3.17 (1 H, s), 3.30 (1 H, dd, *J* 11.0, 2.5 Hz), and 3.62 and 3.64 (1 H each, ABq, *J* 13 Hz); *m/z* 159 ($M^+ - 31$, 9.4%), 101 (34), 71 (47), and 43 (100).

The second fraction was the furanose (**32**) (331 mg, 10.3%).

(2S,3R,4R,5R)-2,3-*Epoxy*-1-*hydroxy*-4,5-(4-*methoxybenzylidenedioxy*-2,4-*dimethylheptane* [2,3-*Anhydro*-6,7-*dideoxy*-4,5-O-[4-*methoxybenzylidene*)-2,4-*di*-C-*methyl*-D-gluco-*heptitol*] (**30**).—DDQ (9.92 g, 43.8 mmol) was added to a stirred solution of compound (**29**) (2.78 g, 14.6 mmol) and 4-methoxybenzyl methyl ether (MPMME) (9.96 g, 65.7 mmol) in CH_2Cl_2 (150 ml) at 16 °C. After 25 min, water (15 ml) was added and the mixture was stirred for further 35 min at room temperature. A precipitate was removed by filtration, and the filtrate was washed with 5% aqueous $NaHCO_3$, dried (Na_2SO_4), and evaporated under reduced pressure to leave an oil, which was chromatographed on a silica gel column with n-hexane–EtOAc (1:1) as eluant to afford *compound* (**30**) (12:1 mixture) as an oil (3.12 g, 69.3%) (Found: M^+, 308.1608. $C_{17}H_{24}O_5$ requires *M*, 308.1617); δ_H ($CDCl_3$) 1.12 (3 H, t, *J* 7.5 Hz), 1.38 (3 H, s), 1.43 (3 H, s), 1.60—2.00 (3 H, m), 3.05 (1 H, s), 3.5—3.9 (3 H, m), 3.80 (3 H, s), 5.76 (0.92 H, s), 6.06 (0.08 H, s), 6.88 (2 H, d, *J* 8.0 Hz), and 7.51 (2 H, d, *J* 8.0 Hz); *m/z* 308 (M^+, 15%), 307 (25), 221 (25), 178 (25), 137 (85), and 135 (100).

2,5-*Anhydro*-6,7-*dideoxy*-2,4-*di*-C-*methyl*-D-manno-*heptitol* (**32**).—Camphor-10-sulphonic acid (CSA) (2 mg) was added to a stirred solution of compound (**28a**) (48 mg) in CH_2Cl_2 (4 ml) at room temperature. After 30 min, the reaction mixture was neutralized with Et_3N and evaporated under reduced pressure. The residue was chromatographed on a silica gel column with CH_2Cl_2–MeOH (96:4) as eluant to give oily 2,5-anhydro-4-*O*-benzyl-6,7-dideoxy-2,4-di-*C*-methyl-D-*manno*-heptitol (**31**) (47 mg), which was dissolved in MeOH (2 ml) and hydrogenated as described for the preparation of triol (**29**) to give the oily triol (**32**) (33 mg, 100%), *m/z* 159 ($M^+ - 31$, 29%), 101 (14), 85 (21), 71 (24), and 43 (100). The triacetate was an oil, δ_H ($CDCl_3$) 1.00 (3 H, t, *J* 7.0 Hz), 1.14 (3 H, s), 1.42 (3 H, s), 1.35—1.75 (2 H, m), 2.00 (3 H, s), 2.10 (3 H, s), 2.15 (3 H, s), 3.95 (1 H, dd, *J* 8.0, 5.0 Hz), 4.10 and 4.22 (1 H each, ABq, *J* 11.0 Hz), and 5.39 (1 H, s); *m/z* 243 ($M^+ - 73$, 2.5%), 197 (3.1), 183 (27), 141 (36), 99 (20), and 43 (100).

1-O-*Acetyl*-2,5-*anhydro*-6,7-*dideoxy*-2,4-*di*-C-*methyl*-D-manno-*heptitol* (**33**).—A solution of compound (**32**) (33 mg, 0.17 mmol), pyridine (0.05 ml), and Ac_2O (24 mg, 0.25 mmol) in CH_2Cl_2 (1 ml) was stirred at room temperature for 1 h, and then chromatographed on a silica gel column with CH_2Cl_2–MeOH (10:1) as eluant to give two fractions. The first fraction was an oily diacetate (17 mg). The second fraction was the oily acetate (**33**) (25 mg, 62%), δ_H ($CDCl_3$) 0.99 (3 H, t, *J* 7.0 Hz), 1.17 (3 H, s), 1.21 (3 H, s), 1.25—1.70 (2 H, m), 2.11 (3 H, s), 2.24 (2 H, s), 3.56 (1 H, dd, *J* 7.5, 5.5 Hz), 4.01 (1 H, s), and 4.03 and 4.11 (1 H each, ABq, *J* 12.0 Hz).

2,5-*Anhydro*-6,7-*dideoxy*-2,4-*di*-C-*methyl*-D-allo-*heptitol* (**35**).—The free triol (**35**) was obtained as an oil (20 mg) from compound (**28b**) (38 mg) *via* intermediate (**34**) as described for the preparation of the anomer (**32**). The triacetate was an oil, δ_H ($CDCl_3$) 1.02 (3 H, t, *J* 7.0 Hz), 1.15 (3 H, s), 1.52 (3 H, s), 1.30—1.75 (2 H, m), 2.04 (3 H, s), 2.06 (3 H, s), 2.09 (3 H, s), 3.91 (1 H, dd, *J* 8.0, 5.0 Hz), 3.99 and 4.15 (1 H each, ABq, *J* 11.5 Hz), and 5.24 (1 H, s); *m/z* 243 ($M^+ - 73$, 9.6%), 197 (4.3), 183 (3.6), 141 (21), 99 (31), and 43 (100).

1-O-*Acetyl*-2,5-*anhydro*-6,7-*dideoxy*-2,4-*di*-C-*methyl*-D-allo-*heptitol* (**36**).—Compound (**35**) (20 mg) was acetylated as described for the preparation of the acetate (**33**) to give a diacetate (8 mg) and the monoacetate (**36**) as an oil (15 mg), δ_H ($CDCl_3$) 1.00 (3 H, t, *J* 7.0 Hz), 1.24 (3 H, s), 1.26 (3 H, s), 1.35—1.80 (2 H, m), 2.09 (3 H, s), 2.38 (1 H, br s), 2.74 (1 H, br s), 3.45—3.74 (2 H, m), and 3.97 and 4.06 (1 H each, ABq, *J* 11.5 Hz).

1-O-*Acetyl*-2,5-*anhydro*-6,7-*dideoxy*-3,4-O-*isopropylidene*-2,4-*di*-C-*methyl*-D-allo-*heptitol* (**37**).—The isopropylidene acetate (**37**) (4 mg) was obtained as an oil from compound (**36**) (5 mg) as described for the preparation of benzoate (**19**) (Found: $M^+ - CH_3$, 257.1374. $C_{13}H_{21}O_5$ requires *m/z*, 257.1383); δ_H ($CDCl_3$) 0.97 (3 H, t, *J* 7.5 Hz), 1.28 (3 H, s), 1.37 (3 H, s), 1.38 (3 H, s), 1.53 (3 H, s), 1.25—1.62 (2 H, m), 2.10 (3 H, s), 3.68 (1 H, t, *J* 7.0 Hz), 3.95 and 4.05 (1 H each, ABq, *J* 11.5 Hz), and 4.14 (1 H, s); *m/z* 272 (M^+, 0.09%), 257 (8.1), 199 (36), 114 (47), and 43 (100).

(2RS,3RS)-3,4-*Isopropylidenedioxy*-2-*methylbutanal* (2-*Deoxy*-3,4-O-*isopropylidene*-2-C-*methyl*-threo-*tetrose*) (**39**).—Compound (**38**) (1.15 g, 7.2 mmol) was oxidized with PCC (4.65 g, 21.6 mmol) and molecular sieves (3.3 g) in CH_2Cl_2 (20 ml) as described for the preparation of the aldehyde (**21**) to give compound (**39**) as an oil (0.97 g, 85.4%), $\nu_{max.}$ ($CHCl_3$) 1 710 cm^{-1}; δ_H ($CDCl_3$) 1.21 (3 H, d, *J* 7.0 Hz), 1.36 (3 H, s), 1.42 (3 H, s), 2.60 (1 H, quint, *J* 7.0 Hz), 3.60 (1 H, m), 4.06—4.42 (2 H, m), and 9.73 (1 H, s); *m/z* 159 ($M^+ + 1$, 25%), 97 (57), and 43 (100).

Ethyl (2E,4SR,5RS)-5,6-O-*Isopropylidene*-2,4-*dimethyl*-threo-*hex*-2-*enoate* (*Ethyl* 2,3,4-*Trideoxy*-5,6-O-*isopropylidene*-2,4-*di*-C-*methylhex*-2-*enonate*) (**40**).—A solution of compound (**39**) (405 mg, 2.56 mmol) and α-ethoxycarbonylethylidenetriphenylphosphorane (1.86 g, 5.12 mmol) in ethylene dichloride (8 ml) was stirred and refluxed for 2 h. Work-up as described for the preparation of ester (**26**) gave a compound (**40**) as an oil (437 mg, 70.4%), δ_H ($CDCl_3$) 1.11 (3 H, d, *J* 6.5 Hz), 1.30 (3 H, t, *J* 7.0 Hz), 1.35 (3 H, s), 1.42 (3 H, s), 1.88 (3 H, d, *J* 1.0 Hz), 2.45—2.90 (1 H, m), 3.45—3.75 (1 H, m), 3.80—4.10 (2 H, m), 4.19 (2 H, q, *J* 7.0 Hz), and 6.51 (1 H, dq, *J* 11.0, 1.0 Hz).

(2E,4SR,5RS)-1-*Hydroxy*-5,6-*isopropylidenedioxy*-2,4-*dimethylhex*-2-*ene* [(E)-2,3,4-*Trideoxy*-5,6-O-*isopropylidene*-2,4-*di*-C-*methyl*-threo-*hex*-2-*enitol*] (**41**).—$LiAlH_4$ (273 mg, 7.18 mmol) was added to a stirred solution of the ester (**40**) (435 mg, 1.79 mmol) in THF (16 ml) at 0 °C under argon. After 15 min, work-up gave the enol (**41**) as an oil (345 mg, 96%), δ_H ($CDCl_3$) 1.05 (3 H, d, *J* 6.5 Hz), 1.35 (3 H, s), 1.42 (3 H, s), 1.69 (3 H, d, *J* 1.0 Hz), 1.81 (1 H, br s), 2.40—2.75 (1 H, m), 3.40—3.72 (1 H, m), 3.75—4.20 (4 H, m), and 5.20 (1 H, dq, *J* 10.0, 1.0 Hz).

(2RS,3RS,4RS,5RS)-2,3-*Epoxy*-1-*hydroxy*-5,6-*isopropylidenedioxy*-2,4-*dimethylhexane* (2,3-*Anhydro*-4-*deoxy*-5,6-O-*isopropylidene*-2,4-*di*-C-*methyl*-galacto-*hexitol*) (**42**).—(*a*) 2,2-Dimethoxypropane (0.1 ml) and CSA (2 mg) were added to a stirred solution of the triol (**44**) (see below) (35 mg) in Me_2CO (1 ml) at room temperature. After 15 min, the reaction mixture was neutralized with Et_3N, evaporated under reduced pressure, and chromatographed on a silica gel column with CH_2Cl_2–MeOH (10:1) as eluant to give compound (**42**) as an oil (38 mg, 89%), δ_H ($CDCl_3$) 1.05 (3 H, d, *J* 7.0 Hz), 1.31 (3 H, s), 1.38 (3 H, s), 1.42 (3 H, s), 1.81 (1 H, s), 1.90—2.00 (1 H, m), 2.88 (1 H, d, *J* 9.0 Hz), 3.55—3.90 (3 H, m), and 4.05—4.20 (2 H, m).

(*b*) Compound (**41**) was oxidized with *m*-CPBA as described for the preparation of compound (**18a**) to give an oily 4:1 mixture of the epoxide (**42**) and its isomer (92.6%).

(2E,4SR,5RS)-1,5,6-*Trihydroxy*-2,4-*dimethylhex*-2-*ene* [(E)-2,3,4-*Trideoxy*-2,4-*di*-C-*methyl*-threo-*hexitol*] (**43**).—A solution of compound (**41**) (211 mg) in 2M-HCl (1 ml) and MeOH (6 ml) was stirred at room temperature. After 30 min, the solution was neutralized with $NaHCO_3$ and evaporated under reduced pressure. The residue was chromatographed on a silica gel column with CH_2Cl_2–MeOH (10:1) as eluant to give the oily ene-triol (**43**) (165 mg, 97.8%), *m/z* 142 ($M^+ - 18$, 11%), 127 (6.1), 111 (3.6), and 82 (100).

(2RS,3RS,4RS,5RS)-2,3-*Epoxy*-1,5,6-*trihydroxy*-2,4-*dimethylhexane* (2,3-*Anhydro*-4-*deoxy*-2,4-*di*-C-*methyl*-galacto-*hexitol*) (**44**).—$NaHCO_3$ (173 mg, 2.06 mmol) and *m*-CPBA (85%; 314 mg, 1.55 mmol) were added to a stirred solution of enol (**43**) (165 mg, 1.03 mmol) in CH_2Cl_2 (10 ml) at room temperature. After 30 min, the reaction mixture was passed through a silica gel column with CH_2Cl_2–MeOH (10:1) as eluant to give the oily epoxide (**44**) (167 mg, 92%). The triacetate was an oil, δ_H ($CDCl_3$) 0.99 (3 H, d, *J* 7.0 Hz), 1.33 (3 H, s), 1.6—1.9 (1 H, m), 2.04 (3 H, s), 2.09 (6 H, s), 2.72 (1 H, d, *J* 9.5 Hz), 3.95 (1 H, d, *J* 12.0 Hz), 4.20 (1 H, d, *J* 12.0 Hz), 4.11 (1 H, dd, *J* 12.0, 7.0 Hz), 4.42 (1 H, dd, *J* 12.0, 3.5 Hz), and 5.00—5.25 (1 H, m).

(2RS,3RS,4RS,5RS)-2,3-*Epoxy*-5,6-*isopropylidenedioxy*-2,4-*dimethyl*-1-*methylsulphonyloxyhexane* (2,3-*Anhydro*-4-*deoxy*-5,6-O-*isopropylidene*-2,4-*di*-C-*methyl*-1-O-*methylsulphonyl*-galacto-*hexitol*) (**45**).—Et_3N (35 mg) and mesyl chloride (28 mg, 0.48 mmol) were added to a stirred solution of compound (**42**) (52 mg, 0.24 mmol) in benzene (1 ml) at room temperature. After 10 min, the reaction mixture was diluted with ether (20 ml), washed with water, dried ($MgSO_4$), and evaporated to leave compound (**45**) as an oil (75 mg), δ_H ($CDCl_3$) 1.06 (3 H, d, *J* 7.0 Hz), 1.37 (3 H, s), 1.40 (3 H, s), 1.41 (3 H, s), 1.50—1.65 (1 H, m), 2.78 (1 H, d, *J* 9.5 Hz), 3.07 (3 H, s), 3.65—3.82 (1 H, m), 4.00 (3 H, m), and 4.25 (1 H, d, *J* 11.5 Hz).

(2SR,3RS,4RS,5RS)-2,3-*Epoxy*-1-*iodo*-5,6-*isopropylidenedioxy*-2,4-*dimethylhexane* (2,3-*Anhydro*-1,4-*dideoxy*-1-*iodo*-5,6-O-*isopropylidene*-2,4-*di*-C-*methylgalactitol*) (**46**).—A solution of compound (**45**) (12 mg) and NaI (36 mg) in Me_2CO (1 ml) was stirred at room temperature overnight. The reaction mixture was poured onto a silica gel column and eluted with n-hexane–ether (1:2) to give the iodide (**46**) as an oil [9.5 mg, 71% overall yields from (**42**)], δ_H ($CDCl_3$) 1.11 (3 H, d, *J* 7.0 Hz), 1.36 (3 H, s), 1.41 (3 H, s), 1.48 (3 H, s), 1.30—1.58 (1 H, m), 2.70 (1 H, d, *J* 9.5 Hz), 3.06 and 3.25 (1 H each, ABq, *J* 10.0 Hz), 3.65—3.82 (1 H, m), and 4.00—4.10 (2 H, m).

(3RS,4SR,5RS)-3-*Hydroxy*-5,6-*isopropylidenedioxy*-2,4-*dimethylhex*-1-*ene* (1,2,4-*Trideoxy*-5,6-O-*isopropylidene*-2,4-*di*-C-*methyl*-lyxo-*hex*-1-*enitol*) (**47**).—A mixture of Zn–Cu couple (190 mg) and the iodide (**46**) (9.5 mg) in EtOH (1 ml) was refluxed for 3 h, and then evaporated under reduced pressure. The residue was chromatographed on a silica gel column with n-hexane–ether (2:1) as eluant to give the oily enol (**47**) (4.5 mg, 77%), δ_H ($CDCl_3$) 0.87 (3 H, d, *J* 7.0 Hz), 1.35 (3 H, s), 1.44 (3 H, s), 1.72 (3 H, d, *J* 1.5 Hz), 1.85—1.96 (1 H, m), 2.59 (1 H, d, *J* 4.0 Hz), 3.75 (1 H, dt, *J* 8.0, 6.0 Hz), 3.95—4.10 (2 H, m), 4.30—4.40 (1 H, m), 4.92 (1 H, t, *J* 1.5 Hz), and 4.98 (1 H, t, *J* 1.0 Hz).

(3RS,4RS,5RS)-6-*Benzoyloxy*-3,5-*dihydroxy*-2,4-*dimethylhex*-1-*ene* (6-O-*Benzoyl*-1,2,4-*trihydroxy*-2,4-*di*-C-*methyl*-lyxo-*hex*-1-*enitol*) (**48**).—A solution of compound (**47**) (8 mg) in MeOH (0.7 ml) and 2M-HCl (0.1 ml) was stirred at room temperature. After 20 min, the solution was neutralized with $NaHCO_3$ and evaporated under reduced pressure, and then the residue was passed through a silica gel column with CH_2Cl_2–MeOH (10:1) as eluant to give an oil (6.5 mg). The oil was dissolved in CH_2Cl_2 (0.4 ml), then pyridine (24 mg) and benzoyl chloride (17 mg) were added, and the mixture was stirred at room temperature. After 4 h, the reaction mixture was diluted with CH_2Cl_2 (20 ml), washed successively with aqueous $KHSO_4$ and brine, dried (Na_2SO_4), and poured onto a silica gel column. Elution with CH_2Cl_2–MeOH (10:1) gave the oily benzoate (**48**) (7 mg), δ_H ($CDCl_3$) 1.02 (3 H, d, *J* 7.0 Hz), 1.73 (3 H, s), 1.80—2.15 (1 H, m), 2.20—3.00 (2 H, br s), 4.10—4.45 (4 H, m), 4.97 (1 H, t, *J* 1.0 Hz), 5.07 (1 H, t, *J* 1.0 Hz), 7.35—7.60 (3 H, m), and 8.06 (2 H, dd, *J* 8.5, 2.0 Hz).

(3RS,4SR,5RS)-6-*Benzoyloxy*-3,5-*isopropylidenedioxy*-2,4-*dimethylhex*-1-*ene* (6-O-*Benzoyl*-1,2,4-*trideoxy*-3,5-O-*isopropylidene*-2,4-*di*-C-*methyl*-lyxo-*hex*-1-*enitol*) (**49**).—Compound (**48**) (7 mg) in Me_2CO (0.5 ml) was treated with 2,2-dimethoxypropane (30 mg) and toluene-*p*-sulphonic acid (1 mg) as described for the preparation of compound (**19**) to give the derivative (**49**) as an oil (7.5 mg) (Found: $M^+ - CH_3$, 289.1455. $C_{17}H_{21}O_4$ requires *m/z*, 289.1434); $\nu_{max.}$ ($CHCl_3$) 1 730 cm^{-1}; δ_H ($CDCl_3$) 0.95 (3 H, d, *J* 7.0 Hz), 1.42 (6 H, s), 1.80 (3 H, s), 2.02—2.10 (1 H, m), 3.79 (1 H, d, *J* 8.5 Hz), 4.25—4.45 (3 H, m), 4.90 (1 H, t, *J* 1.5 Hz), 4.97 (1 H, t, *J* 1.0 Hz), 7.40—7.62 (3 H, m), and 8.05 (2 H, dd, *J* 8.5, 2.0 Hz); *m/z* 289 ($M^+ - 15$, 1.6%), 176 (34), and 105 (100).

(2E,4S,5R,6R,7R)-1-*Hydroxy*-5,6-*isopropylidenedioxy*-7-(4-*methoxybenzyloxy*)-2,4,6-*trimethylnon*-2-*ene* [(E)-2,3,4,8,9-*Pentadeoxy*-5,6-O-*isopropylidene*-7-O-(4-*methoxybenzyl*)-7,4,6-*tri*-C-*methyl*-D-gluco-*non*-2-*enitol*] (**50**).—A solution of compound (**21**) (120 mg, 0.342 mmol) and α-ethoxycarbonylethylidenetriphenylphosphorane (372 mg, 1.03 mmol) in ethylene dichloride (3 ml) was refluxed for 12 h. Work-up as described for the preparation of the ester (**26**) gave oily ethyl (2*E*,4*S*,5*R*,6*R*,7*R*)-5,6-isopropylidenedioxy-7-(4-methoxybenzyloxy)-2,4,6-trimethylnon-2-enoate (170 mg), which was dissolved in THF (6 ml), and $LiAlH_4$ (60 mg, 1.6 mmol) was added at 0 °C under argon. After 30 min, work-up gave the oily *enol* (**50**) (134 mg, 99.7%) (Found: M^+, 392.2574. $C_{23}H_{36}O_5$ requires *M*, 392.2553); δ_H ($CDCl_3$) 1.02 (3 H, t, *J* 7.5 Hz), 1.05 (3 H, d, *J* 7.0 Hz), 1.13 (3 H, s), 1.35 (3 H, s), 1.43 (3 H, s), 1.62 (3 H, d, *J* 1.5 Hz), 1.40—1.80 (3 H, m), 2.56—2.70 (1 H, m), 3.22 (1 H, dd, *J* 7.5, 4.5 Hz), 3.71 (1 H, d, *J* 9.5 Hz), 3.80 (3 H, s), 3.87 (2 H, s), 4.48 and 4.55 (1 H each, ABq, *J* 11.0 Hz), 5.12 (1 H, dd, 10.5, 1.5 Hz), 6.86 (2 H, d, *J* 9.0 Hz), and 7.26 (2 H, d, *J* 9.0 Hz); *m/z* 392 (M^+, 0.34%), 377 (0.6), 334 (0.4), 261 (0.7), 213 (18), 155 (45), and 121 (100).

(2R,3R,4S,5R,6R,7R)-2,3-*Epoxy*-1-*hydroxy*-5,6-*isopropylidenedioxy*-7-(4-*methoxybenzyloxy*)-2,4,6-*trimethylnonane* [2,3-*Anhydro*-4,8,9-*trideoxy*-5,6-O-*isopropylidene*-7-O-(4-*methoxybenzyl*)-2,4,6-*tri*-C-*methyl*-D-erythro-L-galacto-*nonitol*] (**51**).—

Compound (**50**) (120 mg, 0.306 mmol) in CH_2Cl_2 (5 ml) was oxidized with *m*-CPBA (158 mg, 0.917 mmol) at −15 to −10 °C as described for the preparation of the epoxide (**28a**) to give the oily epoxynonane (**51**) (122 mg, 97.7%) (Found: $M^+ - CH_3$, 393.2296. $C_{22}H_{33}O_6$ requires *m/z*, 393.2268); δ_H 1.01 (3 H, t, *J* 7.5 Hz), 1.06 (3 H, d, *J* 7.0 Hz), 1.23 (3 H, s), 1.26 (3 H, s), 1.36 (3 H, s), 1.44 (3 H, s), 1.52—1.90 (4 H, m), 2.92 (1 H, d, *J* 10.0 Hz), 3.39 (1 H, dd, *J* 7.0, 5.0 Hz), 3.45—3.73 (2 H, m), 3.79 (3 H, s), 4.03 (1 H, d, *J* 5.5 Hz), 4.54 and 4.66 (1 H each, ABq, *J* 11.0 Hz), 6.84 (2 H, d, *J* 9.0 Hz), and 7.30 (2 H, d, *J* 9.0 Hz); *m/z* 393 (M^+ − 15, 1.0%), 171 (41), and 121 (100).

(2S,3R,4S,5R,6R,7R)-2,3-*Epoxy*-1-*iodo*-5,6-*isopropylidenedioxy*-7-(4-*methoxybenzyloxy*)-2,4,6-*trimethylnonane* [2,3-*Anhydro*-1,4,8,9-*tetradeoxy*-1-*iodo*-5,6-O-*isopropylidene*-7-O-(4-*methoxybenzyl*)-2,4,6-*tri*-C-*methyl*-D-erythro-L-galacto-*nonitol*] (**52**).—A stirred solution of the alcohol (**51**) (115 mg, 0.282 mmol) in benzene (2 ml) was treated with Et_3N (85 mg, 0.85 mmol) and mesyl chloride (65 mg, 0.56 mmol) at room temperature. After 2 min, the reaction mixture was diluted with di-isopropyl ether (20 ml), washed with water, dried (Na_2SO_4), evaporated under reduced pressure, and chromatographed on a silica gel column with n-hexane–EtOAc (3:2) as eluant to give the oily methanesulphate (126 mg, 92%), δ_H ($CDCl_3$) 1.00 (3 H, t, *J* 7.5 Hz), 1.07 (3 H, d, *J* 7.0 Hz), 1.22 (3 H, s), 1.28 (3 H, s), 1.36 (3 H, s), 1.44 (3 H, s), 1.45—1.90 (3 H, m), 2.84 (1 H, d, *J* 9.5 Hz), 3.05 (3 H, s), 3.34 (1 H, dd, *J* 7.0, 5.0 Hz), 3.80 (3 H, s), 4.05 (1 H, d, *J* 4.0 Hz), 4.03 and 4.21 (1 H each, ABq, *J* 11.5 Hz), 4.54 and 4.62 (1 H each, ABq, *J* 11.0 Hz), 6.84 (2 H, d, *J* 9.0 Hz), and 7.28 (2 H, d, *J* 9.0 Hz); *m/z* 486 (M^+, 0.17%), 471 (0.5), 307 (5.9), 249 (22), 153 (35), and 121 (100).

A solution of the intermediate ester (126 mg, 0.259 mmol) and NaI (117 mg, 0.777 mmol) in MeOH (3 ml) was refluxed for 1 h, and then evaporated under reduced pressure. The residue was taken up in di-isopropyl ether, washed successively with aqueous $Na_2S_2O_3$ and water, dried (Na_2SO_4), evaporated under reduced pressure, and chromatographed on a silica gel column with n-hexane–EtOAc (3:2) as eluant to give the oily iodide (**52**) (131 mg, 97.6%) (Found: $M^+ - CH_3$, 503.1290. $C_{22}H_{32}O_5I$ requires *m/z* 503.1284), δ_H ($CDCl_3$) 1.00 (3 H, t, *J* 7.5 Hz), 1.12 (3 H, d, *J* 7.0 Hz), 1.21 (3 H, s), 1.35 (6 H, s), 1.44 (3 H, s), 1.50—1.92 (3 H, m), 2.77 (1 H, d, *J* 9.5 Hz), 3.00 and 3.21 (1 H each, ABq, *J* 10.0 Hz), 3.31 (1 H, dd, *J* 7.0, 5.0 Hz), 3.80 (3 H, s), 4.03 (1 H, d, *J* 5.0 Hz), 4.54 and 4.62 (1 H each, ABq, *J* 11.0 Hz), 6.84 (2 H, d, *J* 9.0 Hz), and 7.29 (2 H, d, *J* 9.0 Hz); *m/z* 503 (M^+ − 15, 1.0%), 392 (1.4), 339 (5.4), 281 (31), 197 (16), 169 (15), and 121 (100).

(3R,4S,5R,6R,7R)-3-*Hydroxy*-5,6-*isopropylidenedioxy*-7-(4-*methoxybenzyloxy*)-2,4,6-*trimethylnon*-1-*ene* [1,2,4,8,9-*Pentadeoxy*-5,6-O-*isopropylidene*-7-O-(4-*methoxybenzyl*)-2,4,6-*tri*-C-*methyl*-D-glycero-D-gulo-*non*-1-*enitol*] (**53**).—Compound (**52**) (120 mg, 0.231 mmol) was treated with Zn–Cu couple (600 mg) in refluxing EtOH (5 ml) for 20 min as described for the preparation of the enol (**47**) to give the oily product (**53**) (87 mg, 96%) (Found: $M^+ - CH_3$, 377.2308. $C_{22}H_{33}O_5$ requires *m/z*, 377.2319); δ_H ($CDCl_3$) 0.99 (3 H, d, *J* 7.0 Hz), 1.01 (3 H, t, *J* 7.0 Hz), 1.21 (3 H, s), 1.34 (3 H, s), 1.44 (3 H, s), 1.55 (3 H, s), 1.50—1.90 (2 H, m), 1.91—2.04 (1 H, m), 2.21 (1 H, d, *J* 6.0 Hz), 3.28 (1 H, dd, *J* 8.0, 4.0 Hz), 3.80 (3 H, s), 3.88 (1 H, t, *J* 6.0 Hz), 4.41 (1 H, s), 4.54 and 4.66 (1 H each, ABq, *J* 10.5 Hz), 4.89 (1 H, s), 4.98 (1 H, s), 6.86 (2 H, d, *J* 8.5 Hz), and 7.27 (2 H, d, *J* 8.5 Hz); *m/z* 377 (M^+ −15, 0.34%), 309 (0.2), 263 (0.4), 213 (6.9), 155 (61), and 121 (100).

(3R,4S,5R,6R,7R)-5,6-*Isopropylidenedioxy*-3,7-*bis*-(4-*methoxybenzyloxy*)-2,4,6-*trimethylnon*-1-*ene* [1,2,4,8,9-*Pentadeoxy*-3,7-*bis*-(O-4-*methoxybenzyl*)-2,4,6-*tri*-C-*methyl*-D-glycero-D-gulo-*non*-1-*enitol*] (**54**).—Compound (**53**) (89 mg) was treated with MPMCl as described for the preparation of compound (**14**) to afford the fully protected nonene (**54**) as an oil (103 mg, 89%) (Found: $M^+ - CH_3$, 497.2893. $C_{30}H_{41}O_6$ requires *m/z*, 497.2892), δ_H ($CDCl_3$) 0.81 (3 H, d, *J* 7.0 Hz), 0.97 (3 H, t, *J* 7.0 Hz), 1.18 (3 H, s), 1.30 (3 H, s), 1.42 (3 H, s), 1.58 (3 H, s), 1.50—2.00 (3 H, m), 3.20 (1 H, dd, *J* 8.0, 4.0 Hz), 3.56 (1 H, d, *J* 10.5 Hz), 3.74 (3 H, s), 3.79 (3 H, s), 4.16 and 4.41 (1 H each, ABq, *J* 12.0 Hz), 4.39 and 4.76 (1 H each, ABq, *J* 11.0 Hz), 4.57 (1 H, s), 4.93 (1 H, s), 5.03 (1 H, s), 6.62—6.94 (4 H, m), and 7.16—7.36 (4 H, m); *m/z* 497 (M^+ −15, 0.2%), 391 (3.2), 333 (3.3), 197 (2.0), 137 (3.2), and 121 (100).

Hydroboration of compound (**54**).—A CH_2Cl_2 (0.6 ml) solution of MeI (80 mg, 0.56 mmol) was added dropwise to a stirred, ice-cooled solution of $Bu^n_4NBH_4$ (126 mg, 0.49 mmol) in CH_2Cl_2 (0.6 ml). After 15 min, a solution of the nonene (**54**) (25.0 mg, 0.049 mmol) in CH_2Cl_2 (0.3 ml) was added dropwise, and the mixture was stirred at room temperature for 1.5 h. Then 3M-NaOH (0.21 ml) and 30% H_2O_2 (0.21 ml) were added and the mixture was stirred for further 1 h. The reaction mixture was then extracted with CH_2Cl_2. The extract was washed with water, dried (Na_2SO_4), and evaporated. The residue was passed through a silica gel column in n-hexane–EtOAc (3:1) to remove Bu^n_4NI, and the eluant was evaporated to leave an oil, which was purified by silica gel t.l.c. Development with n-hexane–EtOAc (3:1) gave the nonanols (**55**) (2.8 mg, 11%) and (**56**) (4.2 mg, 16%) as oils from lower and upper fractions, respectively.

(2R,3S,4S,5R,6R,7R)-1-*Hydroxy*-5,6-*isopropylidenedioxy*-3,7-*bis*-(4-*methoxybenzyloxy*)-2,4,6-*trimethylnonane* [2,4,8,9-*Tetradeoxy*-5,6-O-*isopropylidene*-3,7-*bis*-O-(4-*methoxybenzyl*)-2,4,6-*tri*-C-*methyl*-D-erythro-L-galacto-*nonitol*] (**55**) (Found: $M^+ - CH_3OC_6H_4CH_2$, 409.2618. $C_{23}H_{37}O_6$ requires *m/z*, 409.2580), δ_H ($CDCl_3$) 0.84 (3 H, d, *J* 7.5 Hz), 0.94 (3 H, t, *J* 7.5 Hz), 0.97 (3 H, d, *J* 7.0 Hz), 1.22 (3 H, s), 1.40 (3 H, s), 1.47 (3 H, s), 1.4—1.7 (3 H, m), 1.9—2.2 (2 H, m), 3.20 (1 H, dd, *J* 7.0, 5.0 Hz), 3.51 (1 H, dd, *J* 9.0, 2.0 Hz), 3.60 (2 H, d, *J* 6.5 Hz), 3.76 (3 H, s), 3.77 (3 H, s), 4.38 (1 H, d, *J* 11 Hz), 4.41 (1 H, d, *J* 11.0 Hz), 4.45 (1 H, s), 4.56 (1 H, d, *J* 11.0 Hz), 4.69 (1 H, d, *J* 11.0 Hz), 6.76 (2 H, d, *J* 8.5 Hz), 6.80 (2 H, d, *J* 8.5 Hz), 7.20 (2 H, d, *J* 8.5 Hz), and 7.24 (2 H, d, *J* 8.5 Hz); *m/z* 409 (M^+ −121, 0.75%), 351 (0.15), 293 (1), 273 (3), 121 (100); $[\alpha]_D^{14}$ +12.2° (*c* 0.10 in $CHCl_3$).

(2S,3S,4S,5R,6R,7R)-1-*Hydroxy*-5,6-*isopropylidenedioxy*-3,7-*bis*-(4-*methoxybenzyloxy*)-2,4,6-*trimethylnonane* [1,2,6,8-*Tetradeoxy*-4,5-O-*isopropylidene*-3,7-*bis*-O-(4-*methoxybenzyl*)-4,6,8-*tri*-C-*methyl*-L-erythro-L-gulo-*nonitol*] (**56**); δ_H ($CDCl_3$) 0.95 (3 H, t, *J* 7.5 Hz), 1.01 (3 H, d, *J* 7.5 Hz), 1.13 (3 H, d, *J* 7.5 Hz), 1.22 (3 H, s), 1.30—1.70 (3 H, m), 1.40 (3 H, s), 1.47 (3 H, s), 1.8—2.1 (2 H, m), 3.23 (1 H, dd, *J* 8.5, 4.0 Hz), 3.33 (1 H, dd, *J* 8.0, 4.0 Hz), 3.4—3.6 (2 H, m), 3.76 (3 H, s), 3.78 (3 H, s), 4.41 (1 H, d, *J* 10.5 Hz), 4.51 (1 H, d, *J* 10.5 Hz), 4.47 (1 H, d, *J* 10.5 Hz), 4.68 (1 H, d, *J* 10.5 Hz), 4.38 (1 H, s), 6.76 (2 H, d, *J* 9.0 Hz), 6.82 (2 H, d, *J* 9.0 Hz), 7.21 (2 H, d, *J* 9.0 Hz), and 7.23 (2 H, d, *J* 9.0 Hz).

References

1 Part 3, Y. Oikawa, T. Nishi, and O. Yonemitsu, preceding paper.

2 (*a*) Isolation; J. M. McGuire, R. L. Bunch, R. C. Anderson, H. E. Boaz, E. H. Flynn, H. M. Powell, and J. W. Smith, *Antibiot. Chemother.*, 1952, **2**, 281; (*b*) Structure; D. R. Harris, S. G. McGeachin, and H. H. Mills, *Tetrahedron Lett.*, 1965, 679.

3 (*a*) Erythronolide A; E. J. Corey, P. B. Hopkins, S. Kim, S. Yoo, K. P. Nambiar, and J. R. Falck, *J. Am. Chem. Soc.*, 1979, **101**, 7131; (*b*) Erythromycin A; *ibid.*, 1981, **103**, 3210, 3213, 3215.

4 Y. Oikawa, T. Yoshioka, and O. Yonemitsu, *Tetrahedron Lett.*, 1982, **23**, 885.

5 Preliminary communication, Y. Oikawa, T. Nishi, and O. Yonemitsu, *Tetrahedron Lett.*, 1983, **24**, 3635.
6 V. Ran Rheenen, R. C. Kelly, and D. Y. Cha, *Tetrahedron Lett.*, 1976, 1973; *Org. Synth.*, 1978, **58**, 44.
7 *Cf.* L. M. Jackman and S. Sternhell, 'Application of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry,' Pergamon Press, Oxford, 1969, p. 334.
8 M. Kido, unpublished results.
9 J. Herscovici and K. Antonaks, *J. Chem. Soc., Chem. Commun.*, 1980, 561.
10 W. A. Szarek, R. G. S. Ritchie, and D. M. Vyas, *Carbohydr. Res.*, 1978, **62**, 89.
11 *Cf.* M. R. Johnson and Y. Kishi, *Tetrahedron Lett.*, 1979, 4347.
12 *Cf.* T. Fukuyama, B. Vranesic, D. P. Negri, and Y. Kishi, *Tetrahedron Lett.*, 1978, 2741.
13 Y. Oikawa, T. Nishi, and O. Yonemitsu, *Tetrahedron Lett.*, 1983, **24**, 4037.
14 E. L. Eliel, *Rec. Chem. Prog.*, 1961, **22**, 129; N. M. Yoon and H. C. Brown, *J. Am. Chem. Soc.*, 1968, **90**, 2927.
15 R. H. Schlessinger and M. Poss, *J. Am. Chem. Soc.*, 1982, **104**, 357.
16 E. J. Corey and M. G. Bock, *Tetrahedron Lett.*, 1975, 2643.
17 *Cf.* E. W. Logusch, *Tetrahedron Lett.*, 1979, 3365.
18 A. Brandström, U. Junggren, and B. Lamm, *Tetrahedron Lett.*, 1972, 3173.
19 Y. Oikawa, T. Nishi, and O. Yonemitsu, *J. Chem. Soc., Perkin Trans. 1*, 1985, 27.

Received 5th October 1983; *Paper* 3/1757