Chiral Synthesis of Polyketide-derived Natural Products. Part 6.[1] Chemical Correlation of Chiral Synthons, Derived from D-Glucose for the Synthesis of Erythromycin A, with Chemical Cleavage Products of the Natural Antibiotic

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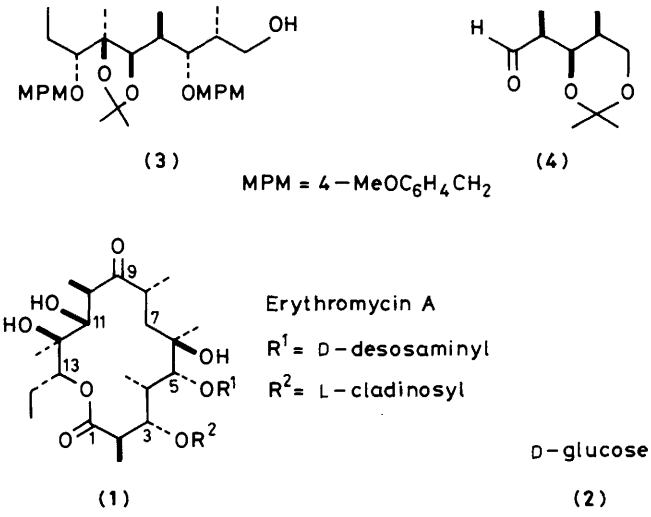
In order to prove unequivocally the structures and configurations of the two synthesized segments, (**3**) and (**4**), for the synthesis of erythromycin A (**1**) from D-glucose (**2**), chemical cleavage of dihydroerythronolide A (**5**) at the lactone and the 5,6-vicinal diol positions was examined *via* selective protection of hydroxy groups, lithium aluminium hydride reduction, and lead tetra-acetate oxidation. The two segments derived from (**5**), (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 (**3**) and (2*S*,3*R*,4*S*)-3,5-isopropylidenedioxy-2,4-dimethylpentanal (**4**), were completely identical in their spectral data with the respective synthesized segments.

As part of our continuing efforts to synthesize the well known antibiotic erythromycin A (**1**) from D-glucose (**2**), one of the most readily available chiral starting materials, two chiral synthons, (**3**) and (**4**), corresponding to the left-hand (C-7—C-15) and the right-hand (C-1—C-5) segments of dihydroerythronolide A (**5**), respectively, were synthesized by virtue of some stereoselective reactions in acyclic systems and MPM (4-methoxyphenylmethyl) protection of hydroxy functions.[2] Although details of the synthesis of (**3**) and (**4**) have been reported in the preceding papers,[1,3] it was still necessary to prove unequivocally their structures and, in particular, configurations.

The chemical correlation of the synthesized segments (**3**) and (**4**) with the segments derived from natural erythromycin A (**1**) itself by selective cleavage at the lactone and 5,6-vicinal diol positions of compound (**5**) was expected to provide conclusive proof. In order to obtain the segments, it was first necessary either to protect selectively another vicinal diol group at C-11 and C-12 or to remove selectively the protection for the 5,6-diol group in the case where both vicinal groups were previously protected. We report here a chemical cleavage of compound (**1**) into the desired segments *via* the latter method for the purpose of chemical correlation with the synthesized segments (**3**) and (**4**).



Results and Discussion

When dihydroerythronolide A (**5**),[4] derived from erythromycin A (**1**) *via a* four-step conversion, was treated with 4-methoxyacetophenone dimethyl acetal[5] in the presence of camphor-10-sulphonic acid (CSA) at room temperature, acetalization of (**5**) proceeded quite smoothly to give the mono-*p*-methoxyphenyl (MP)-ethylidene acetal (**6**) as the sole product. A vicinal diol group either at C-5 and C-6 or at C-11 and C-12 was protected, because the three remaining secondary hydroxy groups of compound (**6**) were readily acetylated to give the triacetate (**7**) by treatment with acetic anhydride in the presence of 4-dimethylaminopyridine (DMAP). If the acetal group was located either at C-3 and C-5 or at C-9 and C-11, the remaining two secondary hydroxy groups would have been acetylated to give a diacetate. The position of the acetal group was finally determined as follows. The unprotected vicinal diol group of (**6**) was cleaved with lead tetra-acetate, followed by acetylation of the resultant tricarbonyl compound (**8**) to give the monoacetate (**9**). If the acetal group in (**6**) was present at C-11 and C-12, a hemiacetal (**10**) would have been obtained. In the n.m.r. spectrum of (**9**), two low-field singlet methyl signals at δ_H 2.12 and 2.15 assignable to acetate and methyl ketone groups, respectively, were observed. Such signals could not be expected for compound (**10**).

Selective protection of the remaining vicinal diol group at C-11 and C-12 was next examined, and the isopropylidene group was found to be favourable because it is rather stable under weakly acidic conditions for removal of the MP-ethylidene protection at C-5 and C-6. When compound (**6**) was treated with acetone dimethyl acetal in acetone in the presence of CSA at 20 °C for 2.5 h, the acetonide (**11**) was obtained in high yield, but prolonged treatment under the same conditions was responsible for the acetal exchange at C-5 and C-6 to give gradually a diacetonide.† The two remaining secondary hydroxy groups in (**11**) were readily acetylated to afford the diacetate, thus confirming the position of the isopropylidene group.

The lactone ring of diol (**11**) was then cleaved by treatment with lithium aluminium hydride and the open-chain tetraol (**12**)

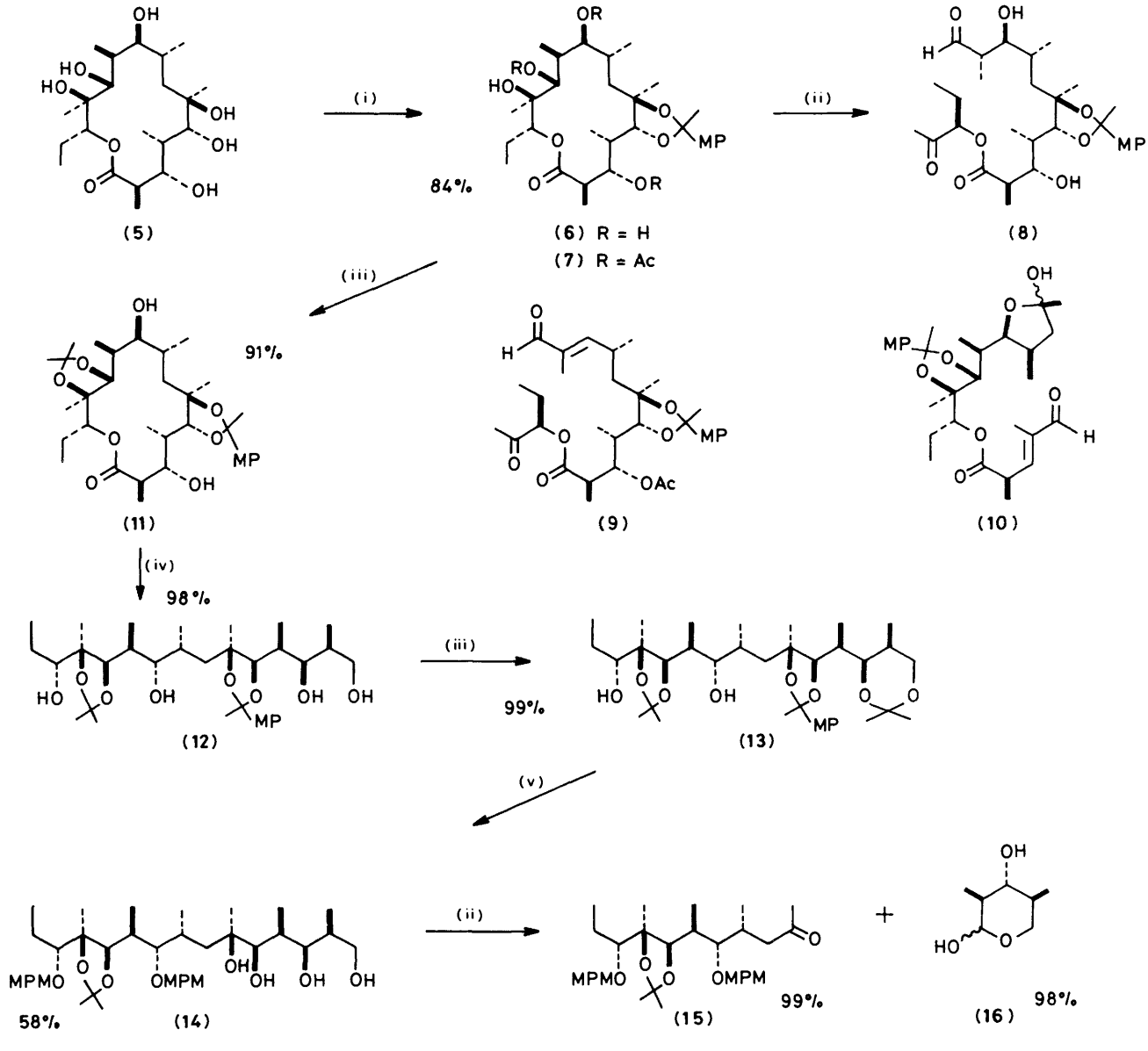
† The 5,6:11,12-di-*O*-isopropylidene derivative of dihydroerythronolide A (**5**) was synthesized by Woodward *et al.*, though no conditions were given; R. B. Woodward *et al.*, *J. Am. Chem. Soc.*, 1981, **103**, 3213.

was readily obtained in almost quantitative yield. The tetraol character of this compound was confirmed by the preparation of a tetra-acetate.

In order to split the carbon chain selectively between C-5 and C-6 of compound (**12**) and to lead to the left-hand segment (**3**), the 1,3-diol at C-1 and C-3 was first protected as the six-membered acetonide (**13**), followed by *p*-methoxybenzyl (MPM) protection of the two isolated hydroxy groups at C-9 and C-13 by treatment with *p*-methoxybenzyl chloride (MPMCl) in the presence of dimsylsodium.[2] The resultant fully protected compound was then treated with a rather dilute acid [a mixture of 0.4M-hydrochloric acid and tetrahydrofuran (THF)] at 50 °C to remove selectively the MP-ethylidene protection at C-5 and C-6. Although the six-membered acetonide at C-1 and C-3 was also cleaved under these conditions, the five-membered acetonide at C-11 and C-12 as well as two MPM groups at C-9 and C-13 remained unchanged, and the tetraol (**14**) was obtained in reasonable yield.

Treatment of (**14**) with lead tetra-acetate gave almost quantiatively two segments, the ketone (**15**) consisting of the C-6—C-15 unit and the hemiacetal (**16**) consisting of the C-1—C-5 unit. As expected, selective cleavage of the carbon chain between C-5 and C-6 was thus achieved (Scheme 1).

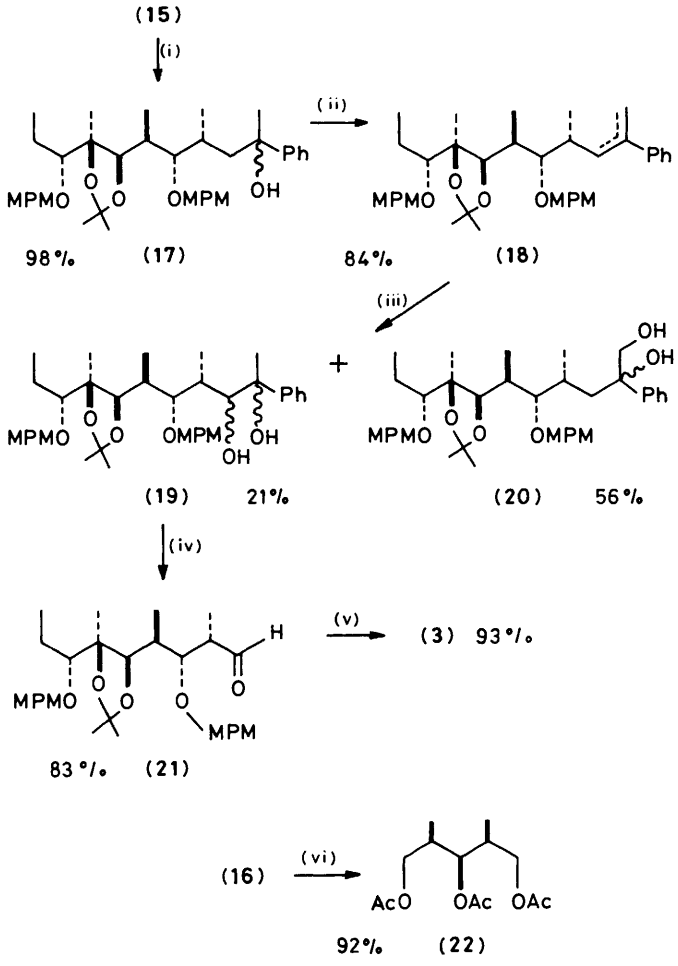
Baeyer–Villiger oxidation seemed at first to provide the most convenient way for the conversion of (**15**) into the required segment (**3**). However, all attempts with peracids were unsuccessful and only complex mixtures were obtained. Treatment of (**15**) with phenylmagnesium bromide in THF gave almost quantitatively a crude mixture of benzyl alcohols (**17**) which, without further purification, was readily dehydrated into a mixture of olefins (**18**) on heating with trifluoroacetic anhydride in the presence of DMAP in benzene. According to



Scheme 1. *Reagents:* (i) $MeC(OMe)_2$·MP, CSA, CH_2Cl_2; (ii) $Pb(OAc)_4$, PhH; (iii) $Me_2C(OMe)_2$; (iv) $LiAlH_4$; (v) MPMCl, NaH then 0.4M-HCl, THF

its n.m.r. spectrum, the ratio of the *exo* (δ_H 5.03, 5.30) and the expected *endo* (δ_H 5.82) isomers was 2.4:1.

Since ozonolysis followed by sodium borohydride treatment gave only complex products, the olefin mixture (**18**) was then subjected to OsO_4 oxidation. Treatment with osmium tetraoxide and *N*-methylmorpholine *N*-oxide (NMO) in aqueous acetone,[6] followed by column chromatography on silica gel, gave the expected diol (**19**) and its isomer (**20**) in 21 and 56% yield, respectively. The vicinal diol (**19**) was cleaved with lead tetra-acetate and the resultant aldehyde (**21**) was reduced with sodium borohydride to afford the alcohol (**3**) as an oil (Scheme 2). The n.m.r. and mass spectra and specific optical



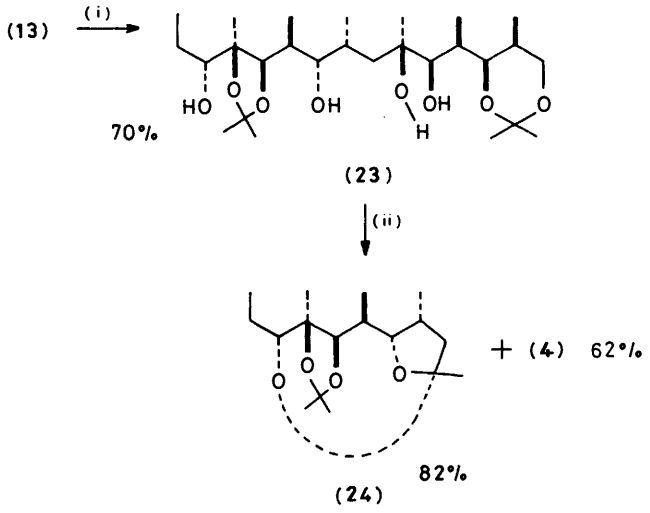
Scheme 2. *Reagents:* (i) PhMgBr; (ii) $(CF_3CO)_2O$, DMAP; (iii) OsO_4, NMO; (iv) $Pb(OAc)_4$; (v) $NaBH_4$; (vi) $LiALH_4$, then Ac_2O, DMAP. Wavy bond indicates diastereoisomeric mixture

rotation of compound (**3**) were completely identical with those of the alcohol (**3**) synthesized from D-glucose (**2**) as shown in the previous papers.[3]

The hemiacetal (**16**) is a synthetic equivalent of the aldehyde (right-hand segment) (**4**) and its structure was confirmed by conversion into the *meso*-triacetate (**22**)[1] *via* lithium aluminium hydride reduction and acetylation.

Another chemical cleavage of diol (**13**) gave the aldehyde (**4**) itself as follows. In order to obtain (**4**) from (**13**), it was necessary to remove the MP-ethylidene protection at C-5 and C-6 while leaving intact the six-membered acetonide at C-1 and C-3. When compound (**13**) was treated with a large excess of sodium in liquid ammonia, the MP-ethylidene group was selectively removed to yield the tetraol (**23**), which gave a triacetate under the usual acetylation conditions in the presence of DMAP since one tertiary hydroxy group at C-6 remained unacetylated.

Lead tetra-acetate oxidation of tetraol (**23**) gave the intramolecular acetal (**24**) and the expected aldehyde (**4**) as oils (Scheme 3). The acetal (**24**) has neither carbonyl- nor hydroxy-



Scheme 3. *Reagents:* (i) Na–liq. NH_3; (ii) $Pb(OAc)_4$

group bands in its i.r. spectrum, and is a rather rigid molecule with reasonable coupling constants for the hydrogens at C-9 (dd, *J* 2.5 and 11.0 Hz) and C-11 (d, *J* 9.0 Hz) as expected from inspection of stereomodels. The aldehyde (**4**) is completely identical in its i.r. and n.m.r. spectra and specific optical rotation with the aldehyde (**4**) synthesized from D-glucose (**2**) as shown in the preceding paper.[1]

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- 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.

5,6-O-[1-(4-*Methoxyphenyl*)*ethylidene*]*dihydroerythronolide A* (**6**).—A mixture of dihydroerythronolide A (**5**) (6.0 g, 14.3 mmol), *p*-methoxyacetophenone dimethyl acetal (10.0 g, 51.0 mmol), and CSA (2.0 g) in CH_2Cl_2 (600 ml) was stirred at room temperature for 20 h, after which time the reaction mixture was neutralized with Et_3N and evaporated under reduced pressure. The residue was chomatographed on a silica gel column with n-hexane–EtOAc (2:1) as eluant to give the product (**6**) as an amorphous solid (6.6 g, 83.7%) (Found: $M^+ - CH_3$, 537.3024. $C_{29}H_{45}O_9$ requires *m/z*, 537.3051); $[\alpha]_D^{20}$ +13.8° (*c* 1.8 in $CHCl_3$); $\nu_{max.}$ ($CHCl_3$) 1 700 cm^{-1}; δ_H ($CDCl_3$–D_2O) 0.82 (3 H, s), 0.91 (3 H, t, *J* 7.5 Hz), 1.04 (3 H, s), 1.05 (3 H, d, *J* 6.5 Hz), 1.25 (3 H, d, *J* 7.0 Hz), 1.31 (3 H, d, *J* 6.5 Hz), 1.34 (3 H, d, *J* 6.5 Hz), 1.60 (3 H, s), 1.45—1.82 (5 H, m), 1.85—2.20 (2 H, m) 2.80, (1 H, dq, *J* 8.0, 10.0 Hz), 3.06 (1 H, dd, *J* 2.5, 9.0 Hz), 3.48 (1 H, br s), 3.80 (3 H, s), 3.92 (1 H, d, *J* 10.0 Hz), 4.15 (1 H, br s), 4.74 (1 H, dd, *J* 2.0, 10.5 Hz), 6.84 (2 H, d, *J* 9.0 Hz), and 7.39 (2 H, d, *J* 9.0 Hz); *m/z* 537 ($M^+ - 15$, 13%), 519 (5), 402 (4.5), 241 (14), 151 (90), and 135 (100).

3,9,11-*Tri*-O-*acetyl*-5,6-O-[1-(4-*methoxyphenyl*)*ethylidene*]-*dihydroerythronolide A* (**7**).—A mixture of the tetraol (**6**) (10 mg), Ac_2O (2 drops, 24 mg), DMAP (2 mg), and Et_3N (3 drops, 33 mg) in CH_2Cl_2 (0.5 ml) was stirred at room temperature for 5 h. After decomposition of excess of Ac_2O by the addition of MeOH, the mixture was evaporated under reduced pressure, and the residue was chromatographed on a silica gel column with n-hexane–EtOAc (3:2) as eluant to give the *triacetate* (**7**) as an amorphous solid (12 mg), $\nu_{max.}$ ($CHCl_3$) 1 735 and 1 720sh cm^{-1}; δ_H ($CDCl_3$) 0.83 (3 H, s), 0.87 (3 H, t, *J* 7.5 Hz), 1.06 (3 H, d, *J* 6.5 Hz), 1.11 (6 H, d, *J* 7.0 Hz), 1.15 (3 H, d, *J* 7.5 Hz), 1.20 (3 H, s), 1.2—2.1 (5 H, m), 1.47 (3 H, s), 2.03 (3 H, s), 2.13 (3 H, s), 2.14 (3 H, s), 2.15—2.70 (3 H, m), 2.86 (1 H, dq, *J* 7.5, 10.0 Hz), 3.80 (3 H, s), 4.30 (1 H, s), 4.70 (1 H, dd, *J* 3.0, 10.5 Hz), 4.78 (1 H, dd, *J* 3.0, 9.0 Hz), 5.04 (1 H, s), 5.65 (1 H, dd, *J* 1.5, 10.5 Hz), 6.84 (2 H, d, *J* 9.0 Hz), and 7.40 (2 H, d, *J* 9.0 Hz); *m/z* 678 (M^+, 0.7%), 677 (0.9), 663 (53), 151 (32), 135 (100), and 43 (75).

(R)-1-*Ethyl*-2-*oxopropyl* (2R,3S,4S,5R,6R,8R,9S,10S)-3,9-*Dihydroxy*-5,6-[1-(4-*methoxyphenyl*)*ethylidenedioxy*]-2,4,6,8,10-*pentamethyl*-11-*oxoundecanoate* (**8**).—A mixture of compound (**6**) (20 mg, 0.036 mmol) and $Pb(OAc)_4$ (32 mg, 0.072 mmol) in benzene (1 ml) was stirred at room temperature for 25 min, after which time the reaction mixture was chromatographed on a silica gel column with n-hexane–EtOAc (1:1) as eluant to give the oily keto-aldehyde (**8**) (8 mg), δ_H ($CDCl_3$) 0.95 (3 H, d, *J* 6.5 Hz), 0.97 (3 H, s), 0.98 (3 H, t, *J* 8.0 Hz), 1.05 (3 H, d, *J* 7.0 Hz), 1.14 (3 H, d, *J* 7.0 Hz), 1.33 (3 H, d, *J* 7.0 Hz), 1.4—2.2 (6 H, m), 1.57 (3 H, s), 2.15 (3 H, s), 2.56 (1 H, m), 2.82 (1 H, quintet, *J* 8.0 Hz), 3.18 (1 H, br s) 3.81 (3 H, s), 3.90 (1 H, m), 3.92 (1 H, d, *J* 5.0 Hz), 4.15 (1 H, m) 4.97 (1 H, dd, *J* 5.0, 7.5 Hz), 6.85 (2 H, d, 9.0 Hz), 7.36 (2 H, d, *J* 9.0 Hz), and 9.87 (1 H, d, *J* 2.5 Hz).

(R)-1-*Ethyl*-2-*oxopropyl* (2R,3S,4S,5R,6R,8R)-3-*Acetoxy*-5,6-[1-(4-*methoxyphenyl*)*ethylidenedioxy*]-2,4,6,8,10-*pentamethyl*-11-*oxoundec*-9(E)-*enoate* (**9**).—Compound (**8**) (8 mg) was acetylated as described above for 20 h. After decomposition of Ac_2O with MeOH, the mixture was passed through a short silica gel column [n-hexane–EtOAc (1:1)]. Evaporation of the solvent left an oil, which was subjected to preparative t.l.c. on silica gel to give the oily monoacetate (**9**) (3 mg), $\nu_{max.}$ ($CHCl_3$) 1 733 and 1 720sh cm^{-1}; δ_H ($CDCl_3$) 0.86 (3 H, s), 0.98 (3 H, t, *J* 7.5 Hz), 1.10 (3 H, d, *J* 7.0 Hz), 1.13 (3 H, d, *J* 7.0 Hz), 1.19 (3 H, d, *J* 7.0 Hz), 1.35—2.20 (2 H, m), 1.42 (3 H, s), 1.83 (3 H, d, *J* 1.5 Hz), 2.12 (3 H, s), 2.15 (3 H, s), 2.96 (1 H, dq, *J* 7.0, 10.0 Hz), 3.75 (1 H, d, *J* 3.5 Hz), 3.78 (3 H, s), 4.99 (1 H, dd, *J* 5.0, 8.0 Hz), 5.25 (1 H, dd, *J* 2.0, 9.5 Hz), 6.53 (1 H, dd, *J* 2.0, 10.0 Hz), 6.80 (2 H, d, *J* 9.0 Hz), 7.28 (2 H, d, *J* 9.0 Hz), and 9.49 (1 H, s).

11,12-O-*Isopropylidene*-5,6-O-[1-(4-*methoxyphenyl*)*ethylidenedihydroerythronolide A* (**11**).—Acetone dimethyl acetal (2.5 ml, 20.3 mmol) and CSA (0.35 g, 1.51 mmol) were added to a stirred acetone (50 ml) solution of compound (**6**) (1.04 g 1.88 mmol) at 20 °C. After 2.5 h, the reaction mixture was neutralized with Et_3N, and evaporated under reduced pressure, and the residue was chromatographed on a silica gel column with n-hexane–EtOAc (3:1) as eluant to give the title compound (**11**) as an amorphous solid (1.01 g, 90.6%) (Found: $M^+ - CH_3$, 577.3418. $C_{32}H_{49}O_9$ requires *m/z*, 577.3363); $[\alpha]_D^{18}$ +14.3° (*c* 2.28 in $CHCl_3$); $\nu_{max.}$ ($CHCl_3$) 1 725 cm^{-1}; δ_H ($CDCl_3$) 0.78 (3 H, s), 0.93 (3 H, t, *J* 7.5 Hz), 1.01 (3 H, d, *J* 7.0 Hz), 1.25 (3 H, d, *J* 7.0 Hz), 1.27 (3 H, s), 1.30—2.35 (8 H, m), 1.42 (3 H, s), 1.43 (3 H, d, *J* 7.5 Hz), 1.44 (3 H, d, *J* 6.5 Hz), 1.52 (3 H, s), 1.63 (3 H, s), 2.67 (1 H, d, *J* 9.5 Hz), 2.73 (1 H, dq *J* 7.0, 10.0 Hz), 3.04 (1 H, dt, *J* 2.5, 9.5 Hz), 3.80 (3 H, s), 3.98 (1 H, d, *J* 10.0 Hz), 4.26 (1 H, s), 4.32 (1 H, s), 4.98 (1 H, dd, *J* 3.0, 10.0 Hz), 6.84 (2 H, d, *J* 9.0 Hz), and 7.42 (2 H, d, *J* 9.0 Hz); *m/z* 577 ($M^+ - 15$, 31%), 501 (4), 349 (7), 223 (13), 151 (63), and 135 (100).

The diacetate of compound (**11**) was an amorphous solid, δ_H ($CDCl_3$) 0.76 (3 H, s), 0.92 (3 H, t, 7.5 Hz), 1.07 (6 H, d, *J* 7.0 Hz), 1.18 (3 H, d, 6.0 Hz), 1.24 (3 H, d, *J* 6.0 Hz), 1.26 (3 H, s), 1.35—2.35 (7 H, m), 1.39 (3 H, s), 1.40 (3 H, s), 1.49 (3 H, s), 2.11 (3 H, s), 2.16 (3 H, s), 2.90 (1 H, dq, *J* 7.5, 10.0 Hz), 3.80 (3 H, s), 4.15 (1 H, s), 4.30 (1 H, s), 4.77 (1 H, dd, *J* 3.0, 9.0 Hz), 5.02 (1 H, dd, *J* 3.0, 10.0 Hz), 5.47 (1 H, dd, *J* 2.0, 10.5 Hz), 6.83 (2 H, d, *J* 9.0 Hz), and 7.40 (2 H, d, *J* 9.0 Hz); *m/z* 661 ($M^+ - 15$, 45%), 151 (25), and 135 (100); $\nu_{max.}$ ($CHCl_3$) 1 735sh, 1 730, and 1 720 cm^{-1}.

(2S,3R,4S,5R,6R,8R,9S,10S,11R,12R,13R)-1,3,9,13-*Tetrahydroxy*-11,12-*isopropylidenedioxy*-5,6-[1-(4-*methoxyphenyl*)*ethylidenedioxy*]-2,4,6,8,10,12-*hexamethylpentadecane* (**12**).—$LiAlH_4$ (3.0 g, 79 mmol) was added to a stirred solution of the lactone (**11**) (5.6 g, 9.45 mmol) in THF (300 ml) at 0 °C under argon. After 1.5 h, excess of $LiAlH_4$ was decomposed by the successive addition of water, 15% aqueous NaOH, and more water. Precipitated inorganic salts were filtered off and the filtrate was concentrated under reduced pressure to leave a solid, which was chromatographed on a silica gel column with CH_2Cl_2–MeOH (24:1) as eluant to give the tetraol (**12**) as an amorphous solid (5.5 g, 97.6%) (Found: $M^+ - CH_3$, 581.3735. $C_{32}H_{53}O_9$ requires *m/z*, 581.3675; δ_H ($CDCl_3$–D_2O) 0.88 (3 H, d, *J* 6.5 Hz), 0.97 (3 H, s), 0.975 (3 H, d, *J* 7.0 Hz), 1.02 (3 H, t, *J* 6.5 Hz), 1.10 (3 H, d, *J* 7.0 Hz), 1.11 (3 H, d, *J* 7.0 Hz), 1.14 (3 H, s), 1.3—2.1 (8 H, m), 1.40 (3 H, s), 1.46 (3 H, s), 1.59 (3 H, s), 3.49 (1 H, dd, *J* 2.0, 10.0 Hz), 3.63 (2 H, d, *J* 5.0 Hz), 3.80 (3 H, s), 3.89 (1 H, d, *J* 6.0 Hz), 3.95 (1 H, dd, *J* 2.0, 11.0 Hz), 4.28 (1 H, d, *J* 1.5 Hz), 4.78 (1 H, br s), 6.83 (2 H, d, *J* 9.0 Hz), and 7.35 (2 H, d, *J* 9.0 Hz); *m/z* 581 ($M^+ - 15$, 20%), 447 (6), 379 (7), 241 (20), 151 (86), and 135 (100).

The tetra-acetate of the tetraol (**12**) was an oil, $\nu_{max.}$ ($CHCl_3$) 1 735sh, 1 725, and 1 720 cm^{-1}; δ_H ($CDCl_3$) 0.90 (3 H, t, *J* 7.5 Hz), 0.90 (3 H, s), 0.97 (3 H, d, *J* 7.0 Hz), 1.02 (3 H, d, *J* 7.0 Hz), 1.08 (3 H, d, *J* 7.0 Hz), 1.10 (3 H, d, *J* 7.0 Hz), 1.21 (3 H, s), 1.26 (3 H, s), 1.3—2.1 (8 H, m), 1.42 (3 H, s), 1.50 (3 H, s), 2.04 (3 H, s), 2.10 (3 H, s), 2.11 (3 H, s), 2.13 (3 H, s), 3.51 (1 H, m), 3.73 (1 H, d, *J* 5.5 Hz), 3.80 (3 H, s), 3.90—3.98 (1 H, dd, *J* 5.5, 12.0 Hz), 4.00—4.09 (1 H, dd, *J* 6.5, 12.0 Hz), 4.85 (1 H, dd, *J* 3.0, 9.5 Hz), 4.95 (1 H, dd, *J* 4.0, 7.0 Hz), 5.12 (1 H, dd, *J* 2.0, 10.0 Hz), 6.83 (2 H, d, 9.0 Hz), and 7.41 (2 H, d, *J* 9.0 Hz); *m/z* 749 ($M^+ - 15$, 55%) and 135 (100).

2S,3R,4S,5R,6R,8R,9S,10S,11R,12R,13R)-9,13-*Dihydroxy*-1,3:11,12-*bis*(*isopropylidenedioxy*)-5,6-[1-(4-*methoxylphenyl*)*ethylidenedioxy*]-2,4,6,8,10,12-*hexamethylpentadecane* (**13**).—Acetone dimethyl acetal (300 mg) and CSA (20 mg) were added to a stirred solution of compound (**12**) (175 mg) in acetone (10 ml) at room temperature. After 10 min, work-up gave the diol (**13**) as an oil (184 mg, 98.5%) (Found: $M^+ - CH_3$, 621.3970. $C_{35}H_{57}O_9$ requires *m/z*, 621.3987); $[\alpha]_D^{23}$ −42.0° (*c* 1.6 in $CHCl_3$); δ_H ($CDCl_3$–D_2O) 0.86 (3 H, d, *J* 6.5 Hz), 0.94 (3 H, s), 0.96 (3 H, d, *J* 7.0 Hz), 1.03 (3 H, t, *J* 7.5 Hz), 1.05 (3 H, d, *J* 6.5 Hz), 1.13 (3 H, d, *J* 7.0 Hz), 1.14 (3 H, s), 1.3—2.1 (8 H, m), 1.40 (3 H, s), 1.41 (3 H, s), 1.46 (6 H, s), 1.57 (3 H, s), 3.51 (1 H, dd, *J* 2.0, 10.0 Hz), 3.67 (1 H, dd, *J*, 1.5, 12.0 Hz), 3.77 (1 H, d, *J* 1.5 Hz), 3.81 (3 H, s), 3.91 (1 H, dd, *J* 2.0, 10.0 Hz), 3.93 (1 H, dd, *J* 2.0, 12.0 Hz), 4.18 (1 H, dd, *J* 3.0, 12.0 Hz), 4.29 (1 H, d, *J* 2.0 Hz), 6.83 (2 H, d, *J* 9.0 Hz), and 7.36 (2 H, d, *J* 9.0 Hz); *m/z* 621 ($M^+ - 15$, 30%) 151 (60), 135 (88), and 43 (100).

The diacetate of compound (**13**) was an oil, $\nu_{max.}$ ($CHCl_3$) 1 735 sh and 1 725 cm^{-1}; δ_H ($CDCl_3$) 0.90 (3 H, t, *J* 7.5 Hz), 0.90 (3 H, s), 1.01 (3 H, d, *J* 7.0 Hz), 1.03 (3 H, d, *J* 7.0 Hz), 1.06 (3 H, d, *J* 7.0 Hz), 1.11 (3 H, d, *J* 7.0 Hz), 1.20 (3 H, s), 1.3—2.1 (8 H, m), 1.42 (6 H, s), 1.46 (3 H, s), 1.52 (3 H, s), 1.59 (3 H, s), 2.09 (6 H, s), 3.38 (1 H, d, *J* 2.5 Hz), 3.63 (1 H, dd, *J* 1.5, 11.5 Hz), 3.76 (1 H, br s), 3.80 (3 H, s), 3.88 (1 H, dd, *J* 2.5, 9.0 Hz), 4.15 (1 H, dd, *J* 2.0, 11.5 Hz), 4.85 (1 H, dd, *J* 3.0, 9.5 Hz), 5.19 (1 H, dd, *J* 2.0, 10.0

Hz), 6.84 (2 H, d, *J* 9.0 Hz), and 7.44 (2 H, d, *J* 9.0 Hz); *m/z* 705 (M^+ − 15, 65%), 151 (40), 135 (100), and 129 (90).

(2S,3R,4S,5R,6R,8R,9S,10S,11R,12R,13R)-1,3,5,6-*Tetrahydroxy*-11,12-*isopropylidenedioxy*-9,13-*bis*(4-*methoxybenzyloxy*)-2,4,6,8,10,12-*hexamethylpentadecane* (**14**).—A THF (1 ml) solution of compound (**13**) (406 mg, 0.64 mmol) was added to a stirred dimsylsodium solution prepared from 50% NaH (245 mg, 5.1 mmol) and dimethyl sulphoxide (10 ml) at room temperature under argon. After 1 h, a THF (1 ml) solution of MPMCl (798 mg, 5.1 mmol) was added in five portions at 50 °C during 40 min. The reaction mixture was stirred at 50 °C for an additional 1.5 h, then poured into ice–water containing 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 chromatographed on a silica gel column with benzene–EtOAc (10:1) as eluant to give the di-MPM ether of compound (**13**) (210 mg) and mono-MPM ethers (two isomers, 307 mg). The mixture of mono-MPM ethers was treated again with MPMCl as described above to give the di-MPM ether (398 mg) as an oil, δ_H ($CDCl_3$) 0.91 (3 H, d, *J* 7.0 Hz), 0.91 (3 H, s), 0.93 (3 H, t, *J* 7.5 Hz), 1.02 (6 H, d, *J* 6.5 Hz), 1.10 (3 H, d, *J* 7.0 Hz), 1.22 (3 H, s), 1.38 (3 H, s), 1.40—2.38 (8 H, m), 1.41 (3 H, s), 1.45 (3 H, s), 1.48 (3 H, s), 1.50 (3 H, s), 3.21 (1 H, dd, *J* 4.5, 8.0 Hz), 3.64 (1 H, d, *J* 12.0 Hz), 3.72—3.89 (3 H, m), 3.76 (3 H, s), 3.78 (3 H, s), 3.80 (3 H, s), 4.17 (1 H, dd, *J* 2.0, 12.0 Hz), 4.38 (1 H, d, *J* 11.0 Hz), 4.48 (1 H, s), 4.57—4.71 (2 H, ABq, *J* 11.0 Hz), 4.69 (1 H, d, *J* 11.0 Hz), 6.77 (4 H, d, *J* 9.0 Hz), 6.85 (2 H, d, *J* 9.0 Hz), 7.18 (2 H, d, *J* 9.0 Hz), 7.25 (2 H, d, *J* 9.0 Hz), and 7.45 (2 H, d, *J* 9.0 Hz); *m/z* 861 (M^+ − 15, 0.3%), 755 (0.3), 619 (0.6), and 121 (100).

The combined di-MPM ether (608 mg) was dissolved in THF (25 ml) and 0.4M-HCl (10 ml), and the solution was stirred at 50 °C for 6 h. The reaction mixture was neutralized with $NaHCO_3$ and evaporated under reduced pressure. The residue was chromatographed on a silica gel column with EtOAc as eluant to give the oily product (**14**) (262 mg, 58.3%) (Found: M^+ + H, 705.4562. $C_{40}H_{65}O_{10}$ requires *m/z*, 705.4560) (Found: M^+ − CH_3, 689.4254. $C_{39}H_{61}O_{10}$ requires *m/z*, 689.4248); $[\alpha]_D^{23}$ + 20.6° (*c* 3.92 in $CHCl_3$); δ_H ($CDCl_3$–D_2O) 0.95 (3 H, t, *J* 7.5 Hz), 0.98 (6 H, d, *J* 7.0 Hz), 1.00 (3 H, d, *J* 7.5 Hz), 1.04 (3 H, d, *J* 7.0 Hz), 1.16 (3 H, s), 1.20 (3 H, s), 1.37 (3 H, s), 1.4—2.2 (8 H, m), 1.46 (3 H, s), 3.18 (1 H, dd, *J* 6.0, 7.0 Hz), 3.35 (1 H, dd, *J* 2.0, 9.0 Hz), 3.44 (1 H, br s), 3.58 (1 H, s), 3.61 (1 H, s), 3.71 (1 H, dd, *J* 3.0, 7.0 Hz), 3.77 (3 H, s), 3.78 (3 H, s), 4.37 (1 H, d, *J* 11.0 Hz), 4.47 (1 H, s), 4.52 (2 H, s), 4.69 (1 H, d, *J* 11.0 Hz), 6.74 (2 H, d, *J* 8.5 Hz), 6.81 (2 H, d, *J* 8.5 Hz), 7.21 (2 H, d, *J* 8.5 Hz), and 7.24 (2 H, d, *J* 8.5 Hz); *m/z* 705 (M^+ + 1, 0.0002%), 689 (0.003), 447 (0.1), 341 (0.4), 279 (1.4), 149 (41), and 121 (100).

The 1,3,5-triacetate of (**14**) was an oil, $\nu_{max.}$ ($CHCl_3$) 1 735sh and 1 725 cm^{-1}; δ_H 0.89 (3 H, d, *J* 7.5 Hz), 0.91 (3 H, t, *J* 7.0 Hz), 0.92 (6 H, d, *J* 7.0 Hz), 0.99 (3 H, d, *J* 7.0 Hz), 1.18 (3 H, s), 1.20 (3 H, s), 1.38 (3 H, s), 1.4—2.2 (8 H, m), 1.46 (3 H, s), 2.02 (3 H, s), 2.05 (3 H, s), 2.06 (3 H, s), 3.20 (1 H, dd, *J* 5.0, 7.0 Hz), 3.39 (1 H, dd, *J* 2.0, 9.0 Hz), 3.78 (1 H, d, *J* 8.0 Hz), 3.77 (6 H, s), 3.89 (2 H, d, *J* 6.5 Hz), 4.39 (1 H, d, *J* 11.0 Hz), 4.46 (2 H, s), 4.57 (1 H, d, *J* 11.0 Hz), 4.67 (1 H, s), 4.69 (1 H, d, *J* 10.5 Hz), 4.97 (1 H, dd, *J* 5.0, 7.0 Hz), 6.75 (2 H, d, *J* 9.0 Hz), 6.80 (2 H, d, *J* 9.0 Hz), 7.20 (2 H, d, *J* 9.0 Hz), and 7.23 (2 H, d, *J* 9.0 Hz); *m/z* 505 (M^+ − 325, 0.5%), 371 (2), and 121 (100).

Lead Tetra-acetate Cleavage of Compound (**14**) *to give* (4R,5S,6S,7R,8R,9R)-7,8-*Isopropylidenedioxy*-5,9-*bis*(4-*methoxybenzyloxy*)-4,6,8-*trimethylundecan*-2-*one* (**15**) *and* 2,4-*Dideoxy*-2,4-*di*-C-*methyl*-α-and β-L-xylo-*pentopyranose* (**16**).—$Pb(OAc)_4$ (637 mg, 1.44 mmol) was added to a stirred benzene (13 ml) solution of compound (**14**) (675 mg, 0.96 mmol) at room temperature. After 15 min, the reaction mixture was chromatographed on a silica gel column with n-hexane–EtOAc (3:2) as eluant to give two fractions. The first fraction was the oily undecanone (**15**) (530 mg, 99.4%) (Found: M^+ − $CH_3OC_6H_4CH_2$, 435.2735. $C_{25}H_{39}O_6$ requires *m/z*, 435.2736); $[\alpha]_D^{18}$ +7.9° (*c* 1.84 in $CHCl_3$); $\nu_{max.}$ ($CHCl_3$) 1 710 cm^{-1}; δ_H 0.81 (3 H, d, *J* 6.5 Hz), 0.93 (3 H, t, *J* 7.5 Hz), 0.99 (3 H, d, *J* 7.0 Hz), 1.21 (3 H, s), 1.39 (3 H, s), 1.4—1.7 (2 H, m), 1.47 (3 H, s), 2.00 (1 H, m), 2.10 (3 H, s), 2.3—2.6 (3 H, m), 3.19 (1 H, t, *J* 8.0 Hz), 3.20 (1 H, dd, *J* 2.0, 8.0 Hz), 3.77 (3 H, s), 3.79 (3 H, s), 4.30 (1 H, d, *J* 10.5 Hz), 4.39 (1 H, d, *J* 11.5 Hz), 4.45 (1 H, s), 4.55 (1 H, d, *J* 11.5 Hz), 4.67 (1 H, d, *J* 10.5 Hz), 6.78 (2 H, d, *J* 9.0 Hz), 6.79 (2 H, d, *J* 9.0 Hz), 7.19 (2 H, d, *J* 9.0 Hz), and 7.24 (2 H, d, *J* 9.0 Hz); *m/z* 541 (M^+ − 15, 0.15%), 435 (0.3), 354 (0.2), 319 (0.6), 299 (2.8), 242 (1.5), and 121 (100).

The second fraction was the solid *pyranose* (**16**) (137 mg, 98%), which was recrystallized from Et_2O-light petroleum (b.p. 30—70 °C) to give granules, m.p. 112—114 °C (Found: C, 57.5; H, 9.5. $C_7H_{14}O_3$ requires C, 57.51; H, 9.65%); $[\alpha]_D^{24}$ −46.1° (*c* 5.4 in MeOH); δ_H ($CDCl_3$) 0.93 (1.5 H, d, *J* 7.0 Hz), 0.95 (1.5 H, d, *J* 7.0 Hz), 1.07 (1.5 H, d, *J* 7.0 Hz), 1.12 (1.5 H, d, *J* 7.0 Hz), 1.3—1.9 (3 H, m), 2.14 (0.5 H, br s), 2.82 (0.5 H, br s), 2.91 (0.5 H, t, *J* 10.0 Hz), 3.11 (0.5 H, t, *J* 11.5 Hz), 3.35 (0.5 H, t, *J* 10.0 Hz), 3.53 (0.5 H, dd, *J* 5.5, 12.0 Hz), 3.68 (0.5 H, t, *J* 11.5 Hz), 3.86 (0.5 H, dd, *J* 5.0, 12.0 Hz), 4.33 (0.5 H, d, *J* 8.5 Hz), and 5.14 (0.5 H, d, *J* 3.0 Hz).

2RS,4R,5S,6S,7R,8R,9R)-2-*Hydroxy*-7,8-*isopropylidenedioxy*-5,9-*bis*(4-*methoxybenzyloxy*)-4,6,8-*trimethyl*-2-*phenylundecane* (**17**).—An Et_2O (1.5 ml) solution of the undecanone (**15**) (100 mg, 0.37 mmol) was added dropwise to a stirred Et_2O (1 ml) solution of PhMgBr (0.91 mmol), prepared from phenyl bromide (143 mg, 0.91 mmol) and Mg (22 mg, 0.91 mg-atom), at 0 °C under argon. After 30 min, saturated aqueous NH_4Cl was added to quench the reaction, and the mixture was extracted with Et_2O. The extract was evaporated under reduced pressure and the residue was chromatographed on a silica gel column with n-hexane–EtOAc (3:1) as eluant to give the oily benzyl alcohol (**17**) (112 mg, 98.2%) (Found: M^+ − $CH_3OC_6H_4CH_2$, 513.3210. $C_{31}H_{45}O_6$ requires *m/z*, 513.3204); δ_H ($CDCl_3$) 0.78 (1.5 H, d, *J* 7.0 Hz), 0.82 (1.5 H, d, *J* 7.0 Hz), 0.89 (1.5 H, d, *J* 7.0 Hz), 0.92 (3 H, t, *J* 7.0 Hz), 0.94 (1.5 H, d, *J* 7.0 Hz), 1.16 (1.5 H, s), 1.21 (1.5 H, s), 1.32 (1.5 H, s), 1.34 (1.5 H, s), 1.4—2.2 (6 H, m), 1.44 (1.5 H, s), 1.45 (1.5 H, s), 1.46 (1.5 H, s), 1.53 (1.5 H, s), 3.10—3.21 (2 H, m), 3.26 (1 H, s), 3.76 (4.5 H, s), 3.77 (1.5 H, s), 4.32 (1 H, s), 4.37 (0.5 H, s), 4.40 (1 H, d, *J* 11.0 Hz), 4.41 (0.5 H, s), 4.43 (1 H, s), 4.63 (0.5 H, d, *J* 11.0 Hz), 4.73 (0.5 H, d, *J* 11.0 Hz), 6.71 (1 H, d, *J* 9.0 Hz), 6.76 (1 H, d, *J* 9.0 Hz), 6.79 (1 H, d, *J* 9.0 Hz), 6.81 (1 H, d, *J* 9.0 Hz), and 7.17—7.43 (9 H, m); *m/z* 513 (M^+ − 121, 0.25%), 437 (0.7), 379 (0.7), 301 (17), and 121 (100).

Mixture (**18**) of (4R,5S,6S,7R,8R,9R)-7,8-*Isopropylidenedioxy*-5,9-*bis*(4-*methoxybenzyloxy*-4,6,8-*trimethyl*-2-*phenylundec*-1-*ene* and (2E,4R,5S,6S,7R,8R,9R)-7,8-*Isopropylidenedioxy*-5,9-*bis*(4-*methoxybenzyloxy*)-4,6,8-*trimethyl*-2-*phenylundec*-2-*ene*.—A benzene (12 ml) solution of compound (**17**) (270 mg, 0.425 mmol), Et_3N (300 mg, 2.96 mmol), $(CF_3CO)_2O$ (443 mg, 2.11 mmol), and DMAP (30 mg) was heated under reflux for 1 h. The reaction mixture was washed successively with dilute HCl and saturated 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–Et_2O (3:1) as eluant to give the oily mixture of alkenes (**18**) (220 mg, 83.9%). Mixture (**18**) was a 1:2.4 mixture of *endo* and *exo* isomers with respect to the olefinic double bond; δ_H ($CDCl_3$) 0.80 (2.1 H, d, *J* 7.0 Hz), 0.82 (2.1 H, d, *J* 7.0 Hz), 0.92 (3 H, t, *J* 7.5 Hz), 1.00 (0.9 H, d, *J* 7.5 Hz), 1.06 (0.9 H, d, *J* 7.0 Hz), 1.16 (2.1 H, s), 1.22 (0.9 H, s), 1.29 (2.1 H, s), 1.36 (0.9 H, s), 1.4—2.1 (3.7 H, m), 1.44 (2.1 H, s), 1.47 (0.9 H, s), 2.06 (0.9 H, d, *J*

1.0 Hz), 2.49 (0.7 H, dd, *J* 8.0, 14.0 Hz), 2.75 (0.7 H, dd, *J* 6.0, 14.0 Hz), 2.81—3.00 (0.3 H, m), 3.14 (0.7 H, dd, *J* 3.0, 8.0 Hz), 3.18 (0.3 H, t, *J* 6.5 Hz), 3.29 (0.7 H, dd, *J* 1.5, 10.0 Hz), 3.34 (0.3 H, dd, *J* 2.5, 10.0 Hz), 3.76, 3.77, 3.79 (total 6 H, each s), 4.34—4.69 (5 H, m), 5.03 (0.7 H,br s), 5.30 (0.7 H, d, *J* 1.5 Hz), 5.82 (0.3 H, dd, *J* 1.5, 9.5 Hz), 6.73—6.81 (4 H, m), and 7.18—7.37 (9 H, m); $\nu_{max.}$ ($CHCl_3$) 1 610 cm^{-1}.

(2RS,3RS,4R,5S,6S,7R,8R,9R)-2,3-*Dihydroxy*-7,8-*isopropylidenedioxy*-5,9-*bis*(4-*methoxybenzyloxy*)-4,6,8-*trimethyl*-2-*phenylundecane* (**19**) *and* (2RS,4R,5S,6S,7R,8R,9R)-1,2-*Dihydroxy*-7,8-*isopropylidenedioxy*-5,9-*bis*(4-*methoxybenzyloxy*)-4,6,8-*trimethyl*-2-*phenylundecane* (**20**).—NMO monohydrate (70 mg, 0.52 mmol) and OsO_4 (4 mg) were added to a stirred 4:1 acetone–water (5 ml) solution of alkenes (**18**) (220 mg, 0.357 mmol) at room temperature. The reaction mixture was stirred overnight and then quenched with $Na_2S_2O_4$. Precipitates were filtered off through a Celite pad, and the filtrate was extracted with CH_2Cl_2. The extract was washed successively with dilute HCl and water, and evaporated under reduced pressure. The residue was chromatographed on a silica gel column with n-hexane–EtOAc (3:1) as eluant to give two fractions. The first fraction was the diol (**19**) as an oil (49 mg, 21%) (Found: $M^+ - CH_3OC_6H_4CH_2$, 529.3205. $C_{31}H_{45}O_7$ requires *m/z*, 529.3153); *m/z* 529 ($M^+ - 121$, 0.15%), 511 (0.25), 374 (2), and 121 (100).

The second fraction was the isomeric diol (**20**) as an oil (130 mg, 56%) (Found: $M^+ - CH_3OC_6H_4CH_2$, 529.3173. $C_{31}H_{45}O_7$ requires *m/z*, 529.3153); *m/z* 529 ($M^+ - 121$, 0.15%), 511 (0.25), 395 (5), 393 (5), 374 (6), and 121 (100).

(2S,3R,4S,5R,6R,7R)-5,6-*Isopropylidenedioxy*-3,7-*bis*(4-*methoxybenzyloxy*)-2,4,6-*trimethylnonanal* (**21**).—$Pb(OAc)_4$ (98 mg, 0.22 mmol) was added to a stirred benzene solution (9 ml) of the diol (**19**) (130 mg, 0.2 mmol) at room temperature. After 10 min, the reaction mixture was chromatographed on a silica gel column with a n-hexane–Et_2O (3:1) as eluant to give the oily aldehyde (**21**) (87.7 mg, 82.7%) (Found: $M^+ - CH_3OC_6H_4CH_2$, 407.2438. $C_{23}H_{35}O_6$ requires *m/z*, 407.2424); δ_H ($CDCl_3$) 0.94 (3 H, t, *J* 8.0 Hz), 0.99 (3 H, d, *J* 7.0 Hz), 1.08 (3 H, d, *J* 7.0 Hz), 1.20 (3 H, s), 1.37 (3 H, s), 1.4—1.7 (2 H, m), 1.82 (1 H, m), 1.47 (3 H, s), 2.10 (1 H, quintet, *J* 8.0 Hz), 2.60 (1 H, dq, *J* 3.0, 6.5 Hz), 3.19 (1 H, dd, *J* 6.5, 8.0 Hz), 3.76 (6 H, s), 3.90 (1 H, dd, *J* 3.5, 9.0 Hz), 4.25 (1 H, d, *J* 10.0 Hz), 4.27 (1 H, d, *J* 10.0 Hz), 4.36 (1 H, s), 4.43 (1 H, d, *J* 10.0 Hz), 4.55 (1 H, d, *J* 10.0 Hz), 6.72 (2 H, d, *J* 8.5 Hz), 6.78 (2 H, d, *J* 3.5 Hz), 7.16 (2 H, d, *J* 8.5 Hz), 7.20 (2 H, d, *J* 8.5 Hz), and 9.78 (1 H, s); *m/z* 407 ($M^+ - 121$, 1%), 349 (0.5), and 121 (100).

(2R,3S,4S,5R,6R,7R))-1-*Hydroxy*-5,6-*isopropylidenedioxy*-3,7-*bis*(4-*methoxybenzyloxy*)-2,4,6-*trimethylnonane* (**3**).—$NaBH_4$ (4 mg, 0.11 mmol) was added to a stirred MeOH solution of the aldehyde (**21**) (28 mg, 0.053 mmol) at 0 °C. After 20 min, the MeOH was evaporated under reduced pressure, and the residue was taken up in CH_2Cl_2; the extract was washed successively with cold 2M-HCl and brine, and dried (Na_2SO_4). Evaporation of the solvent under reduced pressure left the oily alcohol (**3**) (26 mg, 93%) (Found: $M^+ - CH_3OC_6H_4CH_2$, 409.2557. Calc. for $C_{23}H_{37}O_6$: *m/z*, 409.2580); δ_H ($CDCl_3$) 0.83 (3 H, d, *J* 7.0 Hz), 0.94 (3 H, t, *J* 7.5 Hz), 0.97 (3 H, t, *J* 7.0 Hz), 1.22 (3 H, s), 1.40 (3 H, s), 1.4—1.7 (3 H, m), 1.47 (3 H, s), 1.93—2.18 (2 H, m), 3.20 (1 H, dd, *J* 4.5, 7.5 Hz), 3.51 (1 H, dd, *J* 2.0, 9.0 Hz), 3.60 (2 H, d, *J* 6.5 Hz), 3.76 (3 H, s), 3.77 (3 H, s), 4.37 (1 H, d, *J* 10.5 Hz), 4.41 (1 H, d, *J* 10.5 Hz), 4.45 (1 H, s), 4.56 (1 H, d, *J* 10.5 Hz), 4.69 (1 H, d, *J* 10.5 Hz), 6.76 (2 H, d, *J* 9.0 Hz), 6.80 (2 H, d, *J* 9.0 Hz), 7.21 (2 H, d, *J* 9.0 Hz), and 7.24 (2 H, d, *J* 9.0 Hz); *m/z* 409 ($M^+ - 121$, 0.75%), 351 (0.25), 349 (0.25), 273 (3), and 121 (100); $[\alpha]_D^{14}$ +12.8° (*c* 0.28 in $CHCl_3$).

(2R,4S)-1,3,5-*Triacetoxy*-2,4-*dimethylpentane* (**22**).—$LiAlH_4$ (12 mg, 0.33 mmol) was added to a stirred THF (1 ml) solution of the pyranose (**16**) (12 mg, 0.082 mmol) at room temperature under argon. After 2 h, water was added to decompose excess of $LiAlH_4$, and the reaction mixture was passed through a short silica gel column with CH_2Cl_2–MeOH (10:1) as eluant to give the oily triol (11 mg). The oil (10 mg) was acetylated as described above to give the triacetate (**22**) as an oil (17 mg, 92%), $[\alpha]_D^{20}$ 0° (*c* 0.68 in $CHCl_3$); $\nu_{max.}$ ($CHCl_3$) 1 730 cm^{-1}; δ_H ($CDCl_3$) 0.96 (6 H, d, *J* 7.0 Hz), 2.06 (6 H, s), 2.07 (3 H, s), 2.04—2.23 (2 H, m), 3.90, 3.97 (2 H each, dABq, *J* 7.0, 11.0 Hz), and 5.04 (1 H, t, *J* 5.5 Hz); *m/z* 173 ($M^+ - 101$, 14%), 131 (24), 113 (21), 71 (31), and 43 (100).

(2S,3R,4R,5R,6R,8R,9S,10S,11R,12R,13R)-5,6,9,13-*Tetrahydroxy*-1,3:11,12-*bis*(*isopropylidenedioxy*)-2,4,6,8,10,12-*hexamethylpentadecane* (**23**).—Na (0.42 g, 18 mg-atom) was added to a stirred liquid NH_3 (*ca.* 60 ml) solution of the diol (**13**) (1.2 g, 1.89 mmol) at between −60 and −55 °C. After 1 h, NH_4Cl (1.2 g) was added, and then the liquid NH_3 was allowed to evaporate. The residue was extracted with Et_2O, and the extract was evaporated under reduced pressure and chromatographed on a silica gel column with n-hexane–EtOAc (3:2) as eluant to give the tetraol (**23**) as an amorphous solid (665 mg, 69.9%) (Found: $M^+ - CH_3$, 489.3429. $C_{26}H_{49}O_8$ requires *m/z*, 489.3414); $[\alpha]_D^{23}$ −20.2° (*c* 4.8 in $CHCl_3$); δ_H ($CDCl_3$–D_2O) 0.86 (3 H, d, *J* 6.5 Hz), 0.97 (3 H, d, *J* 7.5 Hz), 0.99 (3 H, d, *J* 6.5 Hz), 0.99 (3 H, t, *J* 7.5 Hz), 1.08 (3 H, d, *J* 7.0 Hz), 1.12 (3 H, s), 1.26 (3 H, s), 1.33 (3 H, s), 1.4—2.1 (8 H, m), 1.41 (3 H, s), 1.43 (6 H, s), 3.35 (1 H, s), 3.40 (1 H, dd, *J* 2.0, 10.5 Hz), 3.61 (1 H, d, *J* 11.5 Hz), 3.80 (1 H, dd, *J* 2.5, 7.5 Hz), 3.85 (1 H, dd, *J* 1.5, 8.5 Hz), 4.10 (1 H, dd, *J* 2.5, 11.5 Hz), and 4.19 (1 H, d, *J* 1.5 Hz); *m/z* 489 ($M^+ - 15$, 0.2%), 369 (4.5), 299 (8), 244 (44), 59 (73), and 43 (100).

The triacetate of (**23**) was an oil, δ_H ($CDCl_3$) 0.89 (3 H, t, *J* 7.0 Hz), 0.91 (3 H, d, *J* 7.5 Hz), 1.03 (3 H, d, *J* 7.0 Hz), 1.05 (3 H, d, *J* 7.5 Hz), 1.08 (3 H, d, *J* 7.0 Hz), 1.19 (3 H, s), 1.22 (3 H, s), 1.24 (3 H, s), 1.37 (3 H, s), 1.38 (3 H, s), 1.39 (3 H, s), 1.4—2.3 (8 H, m), 2.08 (3 H, s), 2.11 (3 H, s), 2.16 (3 H, s), 2.64 (1 H, s), 3.42 (1 H, dd, *J* 2.0, 10.5 Hz), 3.56 (1 H, dd, *J* 1.5, 11.5 Hz), 3.69 (1 H, s), 4.00 (1 H, dd, *J* 2.5, 11.5 Hz), 4.64 (1 H, s), 4.83 (1 H, dd, *J* 3.0, 9.5 Hz), and 5.15 (1 H, dd, *J* 1.5, 10.5 Hz); *m/z* 615 ($M^+ - 15$, 5%), 453 (5.5), 451 (6.5), 283 (10), 223 (20), 129 (40), 97 (35), 86 (30), 59 (35), and 42 (100); $\nu_{max.}$ ($CHCl_3$) 1 720 cm^{-1}.

Lead Tetra-acetate Cleavage of Compound (**23**) *to give* (1S,3R,4R,5R,6S,7S,8R)-3-*Ethyl*-4,5-*isopropylidenedioxy*-1,4,6,8-*tetramethyl*-2,10-*dioxabicyclo*[5.2.1]*octane* (**24**) *and* (2S,3R,4S)-3,5-*Isopropylidenedioxy*-2,4-*dimethylpentanal* (**4**).—$NaHCO_3$ (370 mg, 4.4 mmol) and $Pb(OAc)_4$ (488 mg, 1.1 mmol) were added to a stirred benzene (10 ml) solution of the tetraol (**23**) (370 mg, 0.733 mmol) at room temperature. After 5 min, the reaction mixture was extracted with CH_2Cl_2 (30 ml). The extract was washed successively with 1M-HCl (3 times), dilute aqueous $NaHCO_3$, and water, and dried (Na_2SO_4). Evaporation of the solvent left an oil, which was chromatographed on a silica gel column with n-hexane–EtOAc (5:1) as eluant to give two fractions. The first fraction was the oily *bicycle* (**24**) (180 mg, 82%) (Found: M^+, 298.2164. $C_{17}H_{30}O_4$ requires *M*, 298.2136); $[\alpha]_D^{24}$ −1.2° (*c* 4.2 in $CHCl_3$); δ_H ($CDCl_3$) 0.93 (3 H, t, *J* 8.0 Hz), 0.96 (3 H, d, *J* 7.0 Hz), 1.08 (3 H, d, *J* 7.5 Hz), 1.13 (3 H, s), 1.33 (3 H, s), 1.36 (3 H, s), 1.41 (3 H, s), 1.50—1.90 (3 H, m), 2.00—2.26 (2 H, m), 2.55 (1 H, m), 3.50 (1 H, dd, *J* 2.5, 11.0 Hz), 3.73 (1 H, dd, *J* 7.5, 9.0 Hz), and 3.90 (1 H, d, *J* 9.0 Hz); *m/z* 298 (M^+, 5.5%), 283 (6), 240 (24), 99 (49), and 43 (100).

The second fraction was the oily pentanal (**4**) (84 mg, 62%); $[\alpha]_D^{24}$ +5.4 (*c* 3.2 in $CHCl_3$); $\nu_{max.}$ ($CHCl_3$) 1 720 cm^{-1}; δ_H ($CDCl_3$) 1.08 (3 H, d, *J* 6.5 Hz), 1.13 (3 H, d, *J* 7.5 Hz), 1.40 (3 H,

s), 1.45 (3 H, s), 1.5—1.8 (1 H, m), 2.55—2.67 (1 H, m), 3.57 (1 H, dd, *J* 2.0, 11.5 Hz), 4.08 (1 H, dd, *J* 2.0, 9.0 Hz), 4.12 (1 H, dd, *J* 2.5, 11.5 Hz), and 9.73 (1 H, d, *J* 2.0 Hz); *m/z* 171 ($M^+ - 15$, 22%), 111 (11), 83 (16), and 59 (100).

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Received 5*th October* 1983; *Paper* 3/1759