Support Studies for Formulating the Nine Contiguous Chiral Centres of Streptovaricin A Ansa Chain

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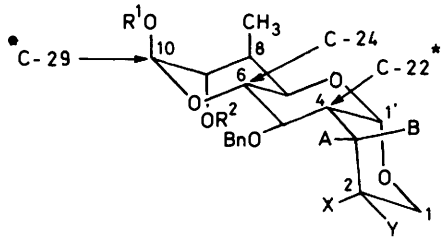
The tripyranoside (**1b**), which had been previously prepared as a key intermediate for the synthesis of the streptovaricin A ansa chain, lacks synthons for the C-24-CO_2Me and C-28 tertiary alcohol of the antibiotic [C-6 and C-10, respectively of (**1b**)]. The 'upper' acetal ring of (**1b**) has been cleaved selectively, an exocyclic methylene is developed at C-6, and a hydroboration sequence has been used to install an axial hydroxymethyl group as the synthon for the CO_2Me group. In order to provide a self-consistent means of structure verification, both epimers of the C-10 tertiary alcohol have been prepared by utilizing empirically determined strategies for acyclic stereoselection.

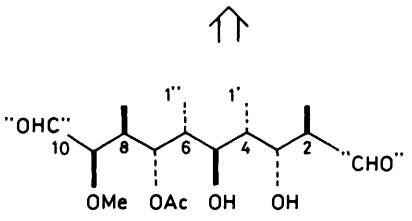
The strategy of pyranosidic homologation,[1] as applied to the synthesis of the ansamycin antibiotics, requires the fabrication of a tripyranose derivative [*e.g.*, (**1**)], which may be transformed into the corresponding acyclic target, (**2**), by cleavage of acetal linkages, followed by functional group adjustments. As the first plateau in the development of this strategy, we have recently described the synthesis of the tricyclic derivatives[2] (**1a**) and (**1b**), required for the acyclic fragments of rifamycin S (**2a**) and streptovaricin A (**2b**), respectively. A key aspect of our retrosynthetic planning was the utilization of the acetal entities for internal 'protection', a concomitant advantage being the conformational bias of the resulting fused systems. The eight contiguous asymmetric centres of (**1a**) and (**1b**) were thereby securely established and verified.

The remaining operations involved in the transformation of (**1b**) into (**2b**) were (*a*) introduction of the axial one-carbon residue at C-6,[2b] (*b*) formulation of the 'off template' tertiary alcohol at C-10, and (*c*) cleavage of the internal acetal. It was desirable that steps (*a*) and (*b*) precede (*c*), and in this paper, we address these two problems areas as they apply to (**1b**), the tricyclic intermediate of streptovaricin A.

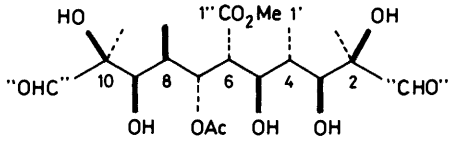


Tricyclic Intermediate for:		R^1	R^2	A	B	X	Y
Rifamycin S	(**1a**)	MeO	Me	BnO	H	Me	H
Streptovaricin A	(**1b**)	PMB	Bn	H	BnO	BnO	Me

* Ansamycin numbering (ref. 2b)



(**2a**) Rifamycin S Ansa Chain



(**2b**) Streptovaricin A Ansa Chain

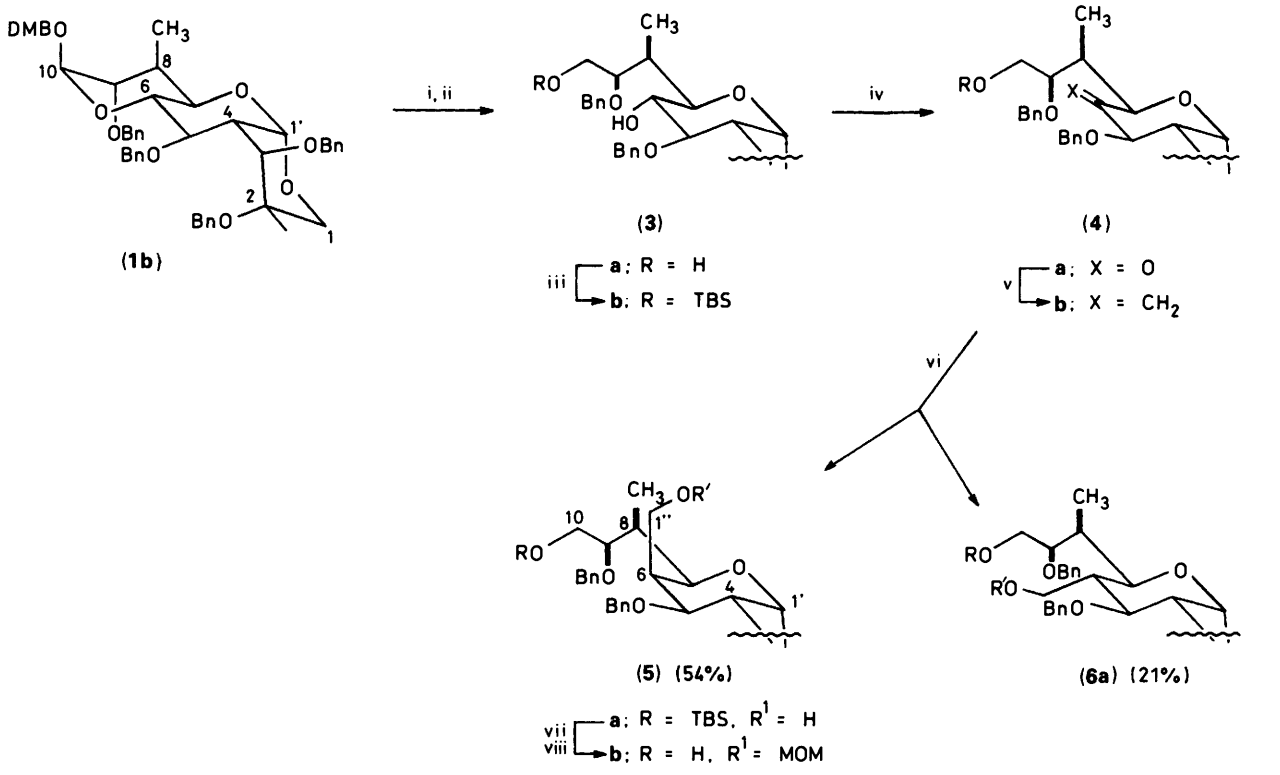
Scheme 1.

Results and Discussion

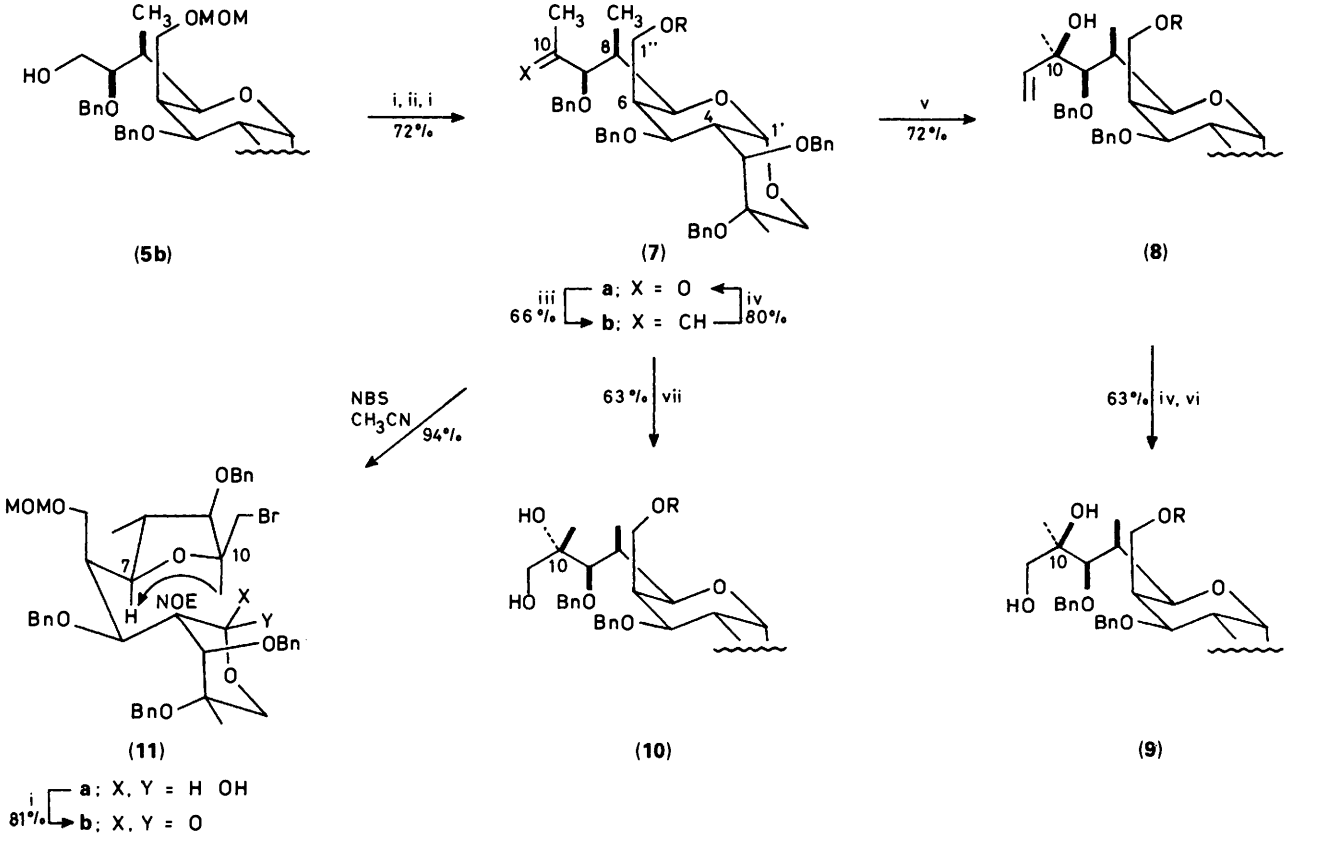
We first turned our attention to the introduction of the axial one-carbon appendage at C-6, which was destined to become the C-24-carboxymethyl group of the antibiotic. This operation required selective access to the 6-hydroxy group, and our use[2] of dimethoxybenzyl alcohol for glycosidation of the 'top' ring had been designed to facilitate cleavage of this acetal *via* oxidation with dichloro-5,6-dicyano-1,4-benzoquinone,[3,4] while leaving the other acetal of (**1b**) unaffected. Subsequent reduction of the resultant lactol, and selective protection of the primary alcohol produced thereby afforded the C-6 alcohol (**3b**).

In accord with out studies on related systems,[5] we envisaged that the axial hydroxymethyl substituent could be introduced *via* hydroboration of the exocyclic olefin (**4b**). To this end, the alcohol (**3b**) was uneventfully transformed to the desired olefin, which afforded a 75% yield and 5:2 ratio of axial ($J_{5,6}$ 5.1 Hz) and equatorial ($J_{5,6}$ 11.4, $J_{6,7}$ 10.2 Hz) primary alcohols (**5a**) and (**6a**), respectively. Attempts to improve this selectivity by utilizing different hydroboration conditions were unsuccessful (*vide infra*).

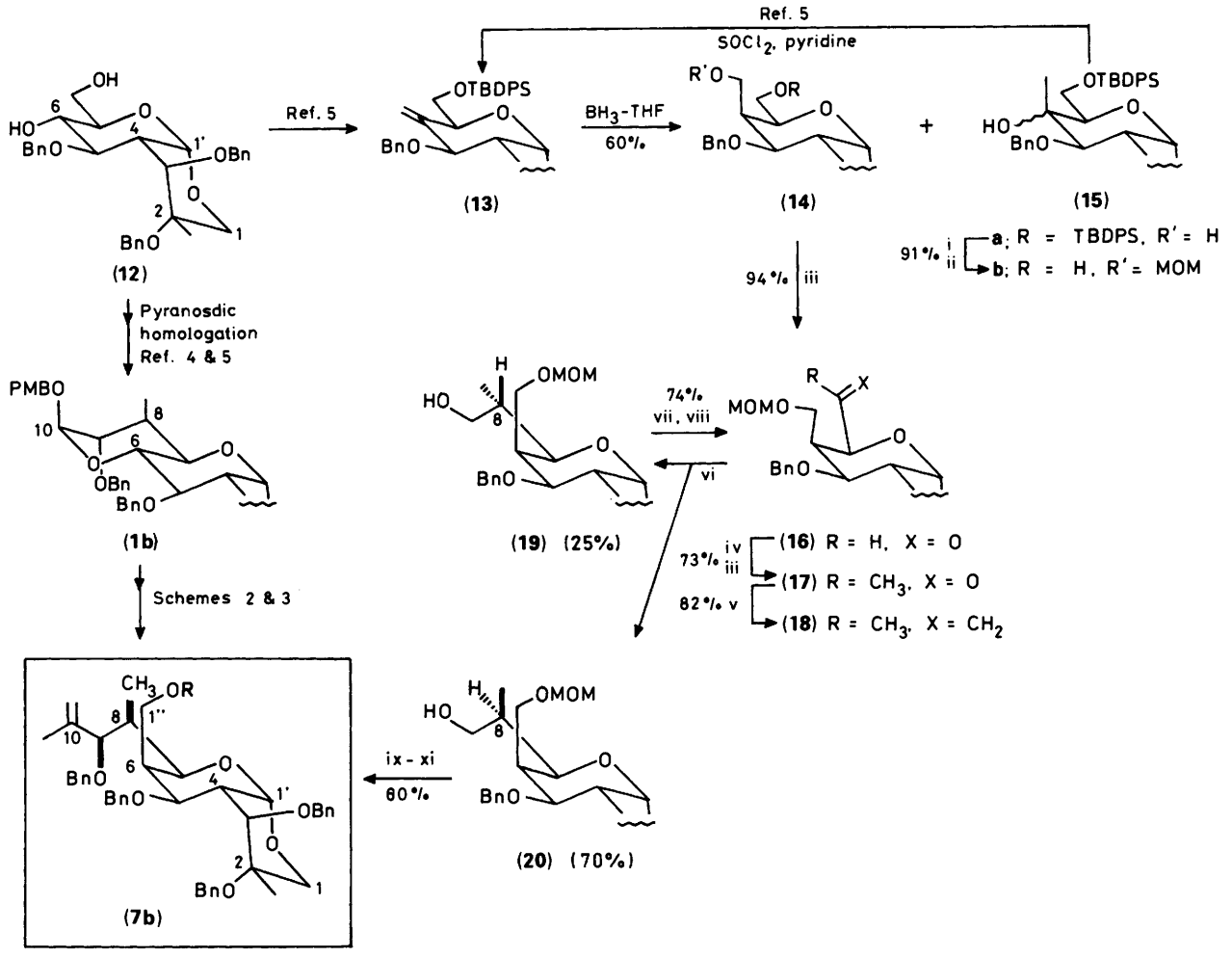
With provisions for the C-6 carboxymethyl group made, we directed out efforts to the formulation of the 'off template' tertiary alcohol at C-10. Owing to the difficulties involved in making stereochemical assignments at such centres, it was considered desirable to prepare both C-10 diastereoisomeric alcohols in order to effect comparisons. With our earlier studies as a model,[4] the protecting groups of the alcohol (**5a**) were adjusted, and the resulting primary alcohol (**5b**) was transformed to the versatile methyl ketone (**7a**) in three straightforward steps (Scheme 3). Addition of vinylmagnesium



Scheme 2. *Reagents and conditions:* i, DDQ, CH_2Cl_2–*p*-dioxane–H_2O; ii, $NaBH_4$, EtOH (i, ii, 66%); iii, TBDMSCl, Et_3N, DMAP, CH_2Cl_2 (75%); iv, Swern's Ox., (94%); v, $Ph_3P{=}CH_2$, THF (95%); vi, BH_3·THF, 0 °C; vii, MOMCl, Hunig's base, CH_2Cl_2; viii, Bu_4NF, THF (vii, viii, 77%).



Scheme 3. i, Swern's Ox; ii, MeMgCl, THF, −78 °C; iii, $Ph_3P{=}CH_2$, THF; iv, O_3, MeOH–$CHCl_3$, −78° then Me_2S; v, vinylmagnesium bromide, THF; vi, $NaBH_4$, EtOH, 0 °C; vii, OsO_4 (cat), NMNO; acetone–H_2O.



Scheme 4. i, MOMCl, Hunig's base; ii, CsF, 18-C-6 DMSO, 60 °C; iii, Swern's Ox; iv, MeMgCl, THF, 78 °C; v, $Ph_3P{=}CH_2$; vi, 9-BBN, THF, then Na_2O_2; vii, Bu_3P, NPSP, THF; viii, MCPBA, 0 °C, CH_2Cl_2 then Et_3N, heat; ix, PCC, CH_2Cl_2; x, isopropenylmagnesium bromide, THF, −90 °C; xi, BnBr, NaH, Bu_4NI, DMF.

bromide to (**7a**) afforded a single Grignard adduct, (**8**), to which a C-10 *S* configuration was assigned, based on the Cram chelation model[6,7] for nucleophilic addition to α-alkoxy carbonyls.

The utility of the vinyl group as a viable hydroxymethyl equivalent was verified by conversion of the olefin (**8**) into the diol (**9**) in two steps. Alternatively, osmium tetraoxide mediated hydroxylation of the olefin (**7b**), derived from methyl ketone (**7a**), afforded a single product that was different from the diol (**9**) obtained *via* the Grignard process. The structure of the second diol was therefore assigned as (**10**). This result is consistent with Kishi's observations[8] concerning the selectivity of osmium tetraoxide induced hydroxylation of allylic alcohol derivatives.

The formation of the epimers (**9**) and (**10**) from the ketone (**7b**) thereby provided a self-consistent method for assignment of the C-9 configurations of these tertiary alcohols.

Owing to the nature of the operations involved in the transformation of the acetal (**1b**) into the key methyl ketone (**7a**) and the olefin (**7b**), we were concerned about the stereochemical integrity of the C-9 benzyloxy group. That the configuration at this position has been unaffected throughout the sequence was verified by ^1H NMR analysis of the bromotetrahydrofuran lactone (**11b**), available by oxidation of the lactol (**11a**).[9] The latter was obtained by reaction of (**7b**) with *N*-bromosuccinimide.[9] A strong NOE enhancement of 7-H upon irradiation of 9-H of (**11b**) indicated a *syn* relationship between these protons and confirmed that the configuration at C-9 had been preserved.

By utilization of the concept of pyranosidic homologation, the configurations of all nine stereocentres in the intermediates (**9**) and (**10**) have, therefore, been securely established. However, owing to the length of the procedure and the poor selectivity in the formulation of the C-6 stereocentre in Scheme 2, a more efficient route to these compounds was sought. We had previously observed[5] that hydroboration of the olefin (**13**) [available from the key precursor (**12**)] had given the axial hydroxymethyl product (**14a**) only, in contrast with the result reported above for the more elaborate analogue (**4b**). A further advantage of this fortuitous occurrence was the fact that the by-product obtained in this reaction was the tertiary alcohol (**15**), which could be efficiently recycled by dehydration with thionyl chloride to regenerate the alkene (**13**).

The subsequent transformation of the primary alcohol (**14a**) into the olefin (**7b**) was accomplished efficiently, albeit, fortuitously and certainly unpredictably. Thus (**14a**) was uneventfully transformed over six steps in 51% overall yield to the olefin (**18**), which gave a 2:7 ratio of the alcohols (**19**) and (**20**), respectively, when subjected to hydroboration conditions using 9-borabicyclo[3.3.1]nonane. The major product (**20**) was oxidized to the corresponding aldehyde, which was treated with isopropenylmagnesium bromide. Benzylation of the Grignard product gave the required olefin (**7b**) exclusively in 60% overall

yield from (**20**). The olefin (**7b**) was transformed to the methyl ketone (**7a**) *via* ozonolysis, and therefore becomes a common progenitor to the key diols (**9**) and (**10**).

In conclusion, the tertiary alcohol (**9**), which constitutes a key intermediate for synthesis of the ansa chain of streptovaricin A has been prepared. All nine contiguous chiral centres have been assembled in a highly selective fashion. Eight of those have been introduced by utilizing the stereochemical biases of the fused pyranoside systems, and the configurations of the newly formed stereocentres were unambiguously assigned by routine ^{1}H NMR analysis. However, the ultimate test of the methodology described here depends in the reliability with which these highly functionalized cyclic acetals could be converted into acyclic polyol derivatives. Our current efforts are directed toward this area of investigation, and these results will be reported in due course.

Experimental

General Procedures.—M.p.s were determinedly in capillary tubes using a Buchi Model 510 melting point apparatus and are uncorrected. Elemental analyses were performed by M-H-W Laboratories. IR spectra were recorded on Perkin-Elmer Model 298 spectrometer with sodium chloride plates for thin films of liquids, syrups, or solids in Nujol mulls. Optical rotations were determined at the sodium D line with a Perkin-Elmer 241 polarimeter. ^{1}H NMR spectra were determined on Bruker WM-250 and Varian XL-300 spectrometers. Unless otherwise stated, the solvent used was $CDCL_3$ with internal tetramethylsilane or $CHCl_3$ as the standard. The coupling constants were verified by homonuclear decoupling experiments. For the purpose of ^{1}H NMR interpretation, compound structures have been numbered in the schemes. The progress of all reactions was monitored by TLC, which was performed on aluminium plates precoated with silica gel HF-254 (0.2 mm layers) containing a fluorescent indicator (Merck, 5539). The following solvent systems were used: EtOAc–light petroleum mixtures: A = 1:9, B = 1:4, C = 3:7, D = 1:1, and E = 5% ether in dichloromethane. Detection was first by UV (254 nm), then charring with sulphuric acid spray, or charring with a solution of ammonium molybdate(VI), tetrahydrate (12.5 g), and cerium(IV) sulphate tetrahydrate (5.0 g) in 10% aqueous sulphuric acid (500 ml). Flash chromatography was performed using Kiesselgel 60 (230–400 mesh, E. Merck).

Standard Procedures

Swern's Oxidation.—A solution of dimethyl sulphoxide (2 mmol/mmol of alcohol) in dry methylene dichloride (2.5 ml/mmol) was added dropwise to a cooled (−78 °C) solution of oxalyl chloride (1.5 equiv.) in dry methylene dichloride (5 ml/mol) under an argon atmosphere. The solution was stirred for 20 min at −78 °C and then a solution of the alcohol in methylene dichloride (2.5 ml/mmol) was added, dropwise. The reaction was stirred for 25 min and dry triethylamine (4 mmol/mmol of alcohol) was added dropwise. The reaction mixture was warmed to 0 °C, diluted with a saturated aqueous sodium hydrogen carbonate, and extracted with ether. The combined extracts were washed with brine, dried (Na_2SO_4), filtered, and evaporated under reduced pressure. The residue was purified by flash chromatography.

Hydroboration of Olefins.—A solution of the appropriate borane (5 mmol/mmol of olefin) in tetrahydrofuran was added at 0 °C to a solution of the olefin in dry tetrahydrofuran (10 ml/mmol). The reaction mixture was stirred at 0 °C (room temperature when 9 borabicyclo[3.3.1]nonane was used) and the progress of the reaction followed by TLC. Upon completion, 3M aqueous sodium hydroxide (3 mmol/mmol of borane) was slowly added at 0 °C, followed by an equal volume of 30% aqueous hydrogen peroxide. This mixture was stirred at 0 °C for 45 min and then diluted with brine and extracted with ether and ethyl acetate. The combined organic extracts were washed with brine, dried (Na_2SO_4), filtered, and evaporated under reduced pressure. The residue was purified by flash chromatography.

Wittig Reactions using Methylenetriphenylphosphorane.—A 1M stock solution of methylenetriphenylphosphorane was prepared by the addition of butyl-lithium (1.0 equiv. of a hexane solution) to a suspension of methyltriphenylphosphonium bromide (1.1 equiv.) in dry tetrahydrofuran (2 ml/mmol) at 0 °C under an argon atmosphere. The reaction mixture was warmed to room temperature and stirred for an additional 20 min. An aliquot (1.5 mmol/mmol of ketone) of the prepared solution was added *via* a syringe to a solution of the ketone in tetrahydrofuran (1 ml/mmol) at room temperature under an argon atmosphere. The reaction was usually complete within 10 min, after which time the mixture was diluted with wet ether and filtered through a pad of Celite. The filtrate was concentrated under reduced pressure and the residue purified by flash chromatography.

2,3,5,9-*Tetra*-O-*benzyl*-4,8-*dideoxy*-4-C-(1′-*formyl*)-1′S)-2,8-*di*-C-*methyl*-L-talo-L-altro-1′,1-*bipyranoside-decitol.*—The 3,4-dimethoxybenzyl glycoside (**1b**) (440 mg, 0.605 mmol) was dissolved in a mixture of methylene dichloride (25 ml), *p*-dioxane (0.5 ml), and water (0.05ml). 2-3-Dichloro-5,6-dicyano-1,4-benzoquinone (150 mg, 0.66 mmol) was added and the reaction mixture was stirred for 4 h at room temperature. During this time, the initially formed dark green solution faded to pale yellow and TLC indicated the presence of a less polar product (R_F 0.2 [E]). Excess of reagent was decomposed by the addition of 3,4-dimethoxybenzyl alcohol and stirring for 30 min. The reaction mixture was filtered through a Celite pad and the filtrate concentrated under reduced pressure to give a brown oil.

The crude mixture obtained in the previous step was dissolved in ethanol (5 ml) and sodium borohydride (20 mg, 0.54 mmol) added to the solution. The reaction mixture was stirred at room temperature for 12 h and then cooled to 0 °C and quenched by the addition of acetic acid. The volatiles were removed under reduced pressure and the residue after flash chromatography gave the diol (**3a**) [270 mg, 66% from (**1b**)]: R_F 0.14 (E); $[\alpha]_D^{20}$ + 72° (*c* 0.95, $CHCl_3$); ν_{max} (neat) 3 420 cm^{-1}; (300 MHz, $CDCl_3$) 1.13 (d, 3 H, *J* 7.2 Hz, 8-CH_3), 1.16 (s, 3 H, 2-CH_3), 2.08 (dt, 1 H, $J_{1',4} = J_{3,4}$ 3.9, $J_{4,5}$ 9.0 Hz, 4-H), 2.38 (m, 2 H, 8-H, 10-OH), 2.70 (d, 1 H, *J* 2.4 Hz, 6-OH), 3.70 (m, 7 H), 4.17 (m, 2 H, 1eq-H, 5-H), 4.42 (m, 4 H), 4.51 (m, 4 H), 5.08 (d, 1 H, *J* 3.9 Hz, 1′-H), 7.30 (m, 20 H, *Ph*CH_2 × 4) (Found: C, 73.6; H, 7.4. $C_{41}H_{48}O_8$ requires C, 73.63; H, 7.23%).

2,3,5,9-*Tetra*-O-*benzyl*-4,6,8-*trideoxy*-4-C-(1′-*formyl*)-(1′S)-2,8-*di*-C-*methyl*-10-O-*t*-*butyldimethylsilyl*-L-lyxo-L-altro-6-*eno*-1′1-*bipyranoside-decitol* (**4b**).—t-Butyldimethylsilyl chloride (90 mg, 0.60 mmol) was added to a solution of triethylamine (0.95 ml, 0.68 mmol), 2,4-dimethylaminopyridine (5 mg, 0.04 mmol), and the alcohol (**3a**) (278 mg, 0.40 mmol) in dry methylene dichloride (10 ml). The reaction was stirred for 16 h at room temperature, at which time the solution was diluted with methylene dichloride and washed successively with saturated aqueous sodium hydrogen carbonate and brine. The organic phase was dried (Na_2SO4), filtered, and evaporated under reduced pressure.

Flash chromatography of the crude reaction mixture gave the silyl ether (**3b**) (304 mg, 75%) as a clear syrup, R_F 0.41 (B); ν_{max}(neat) 3 410 cm^{-1}; δ(300 MHz, $CDCl_3$) 0.01 [s, 6 H,

$Si(CH_3)_2$], 0.85 [s, 9 H, $SiC(CH_3)_3$], 1.04 (d, 3 H, *J* 7.5 Hz, 8-CH_3), 1.09 (s, 3 H, 2-CH_3), 2.00 (dt, 1 H, $J_{1',4} = J_{3,4}$ 3.9, $J_{4,5}$ 10.5 Hz, 4-H), 2.45 (m, 1 H, 8-H), 3.48 (m, 2 H), 3.64 (m, 3 H), 3.76 (m, 2 H), 4.07 (br d, 1 H, J_{gem} 13.2 Hz, 1eq-H), 4.15 (dd, 1 H, $J_{4,5}$ 10.5, $J_{5,6}$ 8.7 Hz, 5-H), 4.28, 4.36, and 4.40 (all d of ABq, *J* 11.1, 11.7, 11.1, respectively, PhC*H* × 3), 4.58 (m, 4 H, PhC*H* × 4), 4.74 (d of ABq, *J* 12.3 Hz, PhC*H*), 5.01 (d, 1 H, *J* 3.9 Hz, 1'-H), 7.23 (m, 20H, *Ph*CH_2 × 4).

The alcohol (**3b**) (304 mg, 0.39 mmol) was subjected to the standard Swern's oxidation procedure and gave the ketone (**4a**) (286 mg, 94%) as clear syrup, R_F 0.33 (B); $[\alpha]_D^{20}$ + 88° (*c* 0.82, $CHCl_3$); ν_{max}(neat) 1 735 cm^{-1}; δ(300 MHz, $CDCl_3$) 0.01 [s, 6 H, $Si(CH_3)_2$], 0.81 [br s, 12 H, $SiC(CH_3)_3$, 8-CH_3], 1.12 (s, 3 H, 2-CH_3), 2.22 (m, 1 H, 8-H), 2.50 (dt, 1 H, $J_{1',4} = J_{3,4}$ 3.9, $J_{4,5}$ 10.8 Hz, 4-H), 3.55 (dd, 1 H, $J_{9,10}$ 5.4, J_{gem} 10.2 Hz, 10a-H), 3.69 (m, 3 H, 1ax-H, 3-H, 10b-H), 3.88 (m, 2 H, 9-H, PhC*H*), 4.11 (dd, 1 H, $J_{1eq,3}$ 0.5, J_{gem} 12.0 Hz, 1eq-H), 4.45 (m, 6 H, PhC*H* × 5, 7-H), 4.70 (br s, 2 H, PhCH_2), 4.85 (d, 1 H, *J* 10.8 Hz, 5-H), 5.17 (d, 1 H, *J* 3.9 Hz, 1'-H), 7.30 (m, 20 H, PhCH_2 × 4).

The ketone (**4a**) (286 mg, 0.367 mmol) was subjected to the standard Wittig methylenation procedure. Flash chromatography of the crude product gave the olefin (**4b**) (272 mg, 95%) as a clear syrup; R_F 0.35 (B); $[\alpha]_D^{25}$ + 24° (*c* 0.58, $CHCl_3$); ν_{max}(neat) 845 and 935 cm^{-1}; δ(300 MHz, $CDCl_3$) 0.01 and 0.02 [both s, 3 H each, $Si(CH_3)_2$], 0.81 (d, 3 H, *J* 6.8 Hz, 8-CH_3), 0.82 [s, 9 H, $SiC(CH_3)_3$], 1.48 (s, 3 H, 2-CH_3), 2.21 (m, 1 H, 4-H), 2.60 (m, 1 H, 8-H), 3.53 (dd, 1 H, $J_{9,10a}$ 7.2, J_{gem} 10.0 Hz, 10a-H), 3.66 (d, 1 H, J_{gem} 11.4 Hz, 1ax-H), 3.73 (m, 2 H, 3-H, 10b-H), 4.03 (m, 2 H, 9-H, PhC*H*), 4.28 (m, 3 H, 1eq-H, 7-H, PhC*H*), 4.49 (m, 3 H, 5-H, PhC*H* × 2), 5.58 (ABq, 2 H, *J* 11.1 Hz, Δδ = 0.05 ppm, PhCH_2), 4.73 (ABq, 2 H, *J* 12.3 Hz, Δδ = 0.03 ppm; PhCH_2), 4.87 (m, 2 H, 7'a-H, PhC*H*), 5.09 (br s, 1 H, 7'b-H), 5.37 (d, 1 H, *J* 3.3 Hz 1'-H), 7.30 (m, 20 H, *Ph*CH_2 × 4). (Found: C, 73.6; H, 8.05. $C_{48}H_{62}O_7Si$ requires C, 74.00; H, 8.02%).

2,3,5,9-*Tetra*-O-*benzyl*-4,6,8-*trideoxy*-4-C-(1'-*formyl*)-(1'S)-6-C-(1''-*hydroxymethyl*)-2,8-*di*-C-*methyl*-10-O-*t*-*butyldimethylsilyl*-L-galacto- *and* L-talo-L-altro-1',1-*bipyranoside*-*decitol* (**5a**) *and* (**6a**).—The olefin (**4b**) (202 mg, 0.26 mmol) was subjected to the standard hydroboration conditions using borane-tetrahydrofuran. The reaction was maintained at 0 °C for 7 h to afford a mixture of two products (**5**) (111 mg, 54%) and (**6a**) (43 mg, 21%). For (**5a**): R_F 0.36 (B); $[\alpha]_D^{20}$ + 53° (*c* 0.60, $CHCl_3$); ν_{max}(neat) 3 480 cm^{-1}; δ(300 MHz, $CDCl_3$) 0.01 [s, 6 H, $Si(CH_3)_2$], 0.78 (d, 3 H, *J* 6.3 Hz, 8-CH_3), 0.83 [br s, 9 H, $SiC(CH_3)_3$], 1.10 (s, 3 H, 2-CH_3), 1.76 (m, 1 H, 8-H), 2.13 (m, 1 H, 6-H), 2.30 (m, 1 H, 4-H), 3.20 (br d, 1 H, *J* 9.3 Hz, OH), 3.51 (dd, 1 H, $J_{9,10a}$ 6.3, J_{gem} 10.5 Hz, 10a-H), 3.68 (m, 4 H, 1ax-H, 3-H, 1''a-H, 10b-H), 4.0 (m, 4 H,, 1eq-H, 7-H, 1''b-H, 9-H), 4.09 (ABq, 2 H, *J* 10.2 Hz, Δδ = 0.27 ppm; PhCH_2), 4.39 (ABq, 2 H, *J* 10.5 Hz, Δδ = 0.06 ppm; PhCH_2), 4.47 (dd, 1 H, $J_{4,5}$ 12.6, $J_{5,6}$ 5.1 Hz, 5-H), 4.50 (ABq, 2 H, *J* 12.0 Hz, Δδ 0.15 ppm, PhCH_2), 4.72 (br s, 2 H, PhCH_2), 5.10 (d, 1 H, *J* 3.0 Hz, 1'-H), 7.22 (m, 20 H, *Ph*CH_2 × 4) (Found: C, 72.25; H, 8.3. $C_{48}H_{64}O_8Si$ requires C, 72.33; H, 8.09%).

For (**6a**) R_F 0.27 (B); $[\alpha]_D^{20}$ + 68.5° (*c* 1.10, $CHCl_3$); ν_{max}(neat) 3 480 cm^{-1}; δ(300 MHz, $CDCl_3$) 0.02 [s, 6 H, $Si(CH_3)_2$], 0.88 [s, 9 H, $SiC(CH_3)_3$], 1.15 (d, 3 H, *J* 6.5 Hz, 8-CH_3), 1.19 (s, 3 H, 2-CH_3), 1.66 (m, 1 H, OH), 1.73 (m, 1 H, 6-H), 2.05 (m, 1 H, 4-H), 2.26 (m, 1 H, 8-H), 3.67 (m, 7 H, 1ax-H, 3-H, 1''-CH_2, 9-H, 10-CH_2), 3.97 (dd, 1 H, $J_{6,7}$ 10.2, $J_{7,8}$ 2.4 Hz, 7-H), 4.17 (dd, 1 H, $J_{1eq,3}$ 1.5, J_{gem} 15.6 Hz, 1_{eq}-H), 4.28 (ABq, 2 H, *J* 11.4 Hz, Δδ 0.36 ppm; PhCH_2), 4.34 (t, 1 H, $J_{4,5} = J_{5,6}$ 11.4 Hz, 5-H), 4.41 (m, 2 H, PhC*H* × 2), 4.53 (m, 4 H, PHC*H* × 4), 5.14 (d, 1 H, *J* 3.9 Hz, 1'-H), 7.30 (m, 20 H, *Ph*CH_2 × 4) (Found: C, 72.2; H, 8.35. $C_{48}H_{64}O_8Si$ requires C, 72.33; H, 8.09%).

2,3,5,9-*Tetra*-O-*benzyl*-4,6,8-*trideoxy*-4-C-(1'-*formyl*)(1'S)-6-C-(1''-*methoxymethoxymethyl*)-2,8-*di*-C-*methyl*-L-galacto-L-altro-1',1-*bipyranoside*-*decitol* (**5b**).—Chloromethyl methyl ether (0.05 ml, 0.63 mmol) was added to a solution of the alcohol (**5a**) (103 mg, 0.129 mmol) and *N*,*N*-di-isopropylethylamine (0.15 ml, 0.86 mmol) in dry methylene dichloride (2 ml) at 0 °C. The reaction mixture was warmed to room temperature and stirred for 16 h. The mixture was diluted with methylene dichloride (30 ml), washed with saturated aqueous sodium hydrogencarbonate (2 × 10 ml), dried (Na_2SO_4), filtered, and evaporated under reduced pressure.

The crude residue obtained above was dissolved in tetrahydrofuran (5 ml), and tetrabutylammonium fluoride (1M solution in tetrahydrofuran; 0.15 ml, 0.15 mmol) was added to the solution. The reaction mixture was stirred for 6 h at room temperature and then evaporated under reduced pressure and the residue subjected to flash chromatography to give (**5b**) (70 mg, 77% from (**5a**)) as a clear gum, R_F 0.05 (B); $[\alpha]_D^{20}$ + 69° (*c* 0.90, $CHCl_3$); ν_{max}(neat) 3 400 cm^{-1}; δ(300 MHz, $CDCl_3$), 0.95 (d, 3 H, 6.5 Hz, 8-CH_3), 1.11 (s, 3 H, 2-CH_3), 1.90 (m, 1 H, 4-H), 1.98 (m, 1 H, 8-H), 2.30 (m, 1 H, 6-H), 3.29 (s, 3 H, CH_3OCH_2), 3.72 (m, 5 H, 3-H, 1''-CH_2, 10-CH_2), 3.79 (br s, 1 H, OH), 3.96 (d of ABq, 1 H, *J* 12.3 Hz, PhC*H*), 4.01 (m, 3 H, 1eq-H, 7-H, 9-H), 4.49 (m, 3 H, 5-H, PhC*H* × 2), 4.45 (ABq, 2 H, *J* 10.8 Hz, Δδ 0.04 ppm; PhCH_2), 4.55 (br s, 2 H, CH_2OCH_3), 4.61 (d of ABq, 1 H, *J* 12.0 Hz, PhC*H*), 4.80 (ABq, 2 H, *J* = 10.2 Hz, Δδ = 0.09 ppm; PhCH_2), 5.13 (d, 1 H, *J* 3.3 Hz, 1'-H), 7.30 (m, 20 H *Ph*CH_2 × 4) (Found: C, 72.65; H, 7.55. $C_{44}H_{54}O_9$ requires C, 72.70; H, 7.49%).

2,3,5,9-*Tetra*-O-*benzyl*-4,6,8,11-*tetradeoxy*-4-C-(1'-*formyl*)-(1'S)-6-C-(1''-*methoxymethoxymethyl*)-2,8-*di*-C-*methyl*-L-galacto-L-altro-10-*ulo*-1',1-*bipyranoside*-*decitol* (**7a**).—The primary alcohol (**5b**) (74 mg, 0.10 mmol) was subjected to the standard Swern's oxidation conditions. The resultant aldehyde (67 mg, 91%) was obtained as a clear gum, R_F 0.42 (B); ν_{max}(neat) 1 725 cm^{-1}; δ(300 MHz, $CDCl_3$) 0.84 (d, 3 H, *J* 6.9 Hz, 8-CH_3), 1.08 (s, 3 H, 2-CH_3), 1.81 (m, 1 H, 4-H), 2.18 (m, 1 H, 6-H), 2.35 (m, 1 H, 8-H), 3.26 (s, 3 H, CH_2OCH_3), 3.68 (m, 3 H, 1ax-H, 1''-CH_2), 3.79 (m, 1 H, 3-H), 3.92 (d of ABq, 1 H, *J* 11.1 Hz, PhC*H*), 4.01 (m, 2 H, 1eq-H, 7-H), 4.30 (d, 1 H, overlapped by m, *J* 2.7 Hz, 9-H), 4.32 (m, 4 H, 5-H, PhC*H* × 3), 4.49 (m, 4 H, CH_2OCH_3, PhC*H* × 2), 4.69 (ABq, 2 H, *J* 10.8 Hz, Δδ = .03 ppm; PhCH_2), 5.05 (d, 1 H, *J* 3.3 Hz, 1'-H), 7.22 (m, 20 H, *Ph*CH_2 × 4), and 9.68 (s, 1 H, 10-H).

Methylmagnesium chloride (2.8M solution in tetrahydrofuran; 0.07 ml, 0.20 mmol) was added at −78 °C to a solution of the above aldehyde (67 mg, 0.093 mmol) in dry tetrahydrofuran (5 ml) under an argon atmosphere. The solution was warmed to 0 °C and diluted with saturated aqueous ammonium chloride (10 ml). The reaction mixture was extracted with ether (3 × 15 ml) and the combined extracts were dried (Na_2SO_4), filtered, and evaporated under reduced pressure. The yellow residue was dissolved in toluene, dried by the azeotropic removal of water, and used directly in the subsequent step.

The crude alcohol mixture obtained was subjected to Swern's oxidation conditions, as described earlier. The methyl ketone (**7a**) [53 mg, 72% from (**5b**)] was obtained a a clear syrup, R_F 0.27 (B); $[\alpha]_D^{20}$ + 78° (*c* 0.97, $CHCl_3$); ν_{max}(neat) 1 710 cm^{-1}; δ(300 MHz, $CDCl_3$) 0.80 (d, 1 H, *J* 6.9 Hz, 8-CH_3), 1.07 (s, 3 H, 2-CH_3), 1.81 (m, 1 H, 4-H), 2.15 (s, 3 H, 10-CH_3), 2.16 (m, 1 H, overlapped by s, 6-H), 2.32 (m, 1 H, 8-H), 3.27 (s, 3 H, CH_2OCH_3), 3.68 (m, 3 H, 1ax-H, 1''-CH_2), 3.79 (br s, 1 H, 3-H), 3.89 (d of ABq, 1 H, *J* 11.1 Hz, PhC*H*), 3.98 (dd, 1 H, $J_{1eq,3}$ 0.5, J_{gem} 13.5 Hz, 1eq-H), 4.01 (br d, 1 H, $J_{7,8}$ 10.2 Hz, 7-H), 4.31 (m, 5 H, 5-H, 9-H, PhC*H* × 3), 4.50 (m, 4 H, CH_2OCH_3, PhC*H* × 2), 4.63 (ABq, 2 H, *J* 11.0 Hz, Δδ .01 ppm; PhCH_2), 5.06 (d, 1 H, *J* 3.6 Hz, 1'-H), and 7.27 (m, 20 H, *Ph*CH_2 × 4) (Found: C, 73.1; H, 7.33. $C_{45}H_{54}O_9$ requires C, 73.15; H, 7.37%).

2,3,5,9-*Tetra*-O-*benzyl*-4,6,8-*trideoxy*-4-C-(1′-*formyl*)-(1′S)-6-C-(1″-*methoxymethoxymethyl*)-2,8,10-*tri*-C-*methyl*-D-glycero-L-galacto-L-altro-1,1′:1′:7-*bipyranoside-undecitol* (**9**).—A solution of the methyl ketone (**7a**) (10 mg, 0.014 mmol) in dry tetrahydrofuran (1 ml) was added slowly at 78 °C to a solution of vinylmagnesium bromide (1M solution in tetrahydrofuran; 0.05 ml,) in tetrahydrofuran (2 ml). The reaction mixture was allowed to warm to room temperature when it was diluted with a saturated aqueous ammonium chloride. The mixture was extracted with ether and the organic extract washed with brine, dried (Na_2SO_4), filtered, and concentrated under reduced pressure. Flash chromatography of the crude residue afforded a single Grignard adduct (**8**) (8 mg, 72%): R_F 0.28 (E); $[\alpha]_D^{20}$ +86° (*c* 0.80, $CHCl_3$); ν_{max}(neat) 3 450 cm^{-1} δ(300 MHz, $CDCl_3$) 1.04 (d, 3 H, *J* 7.0 Hz 8-CH_3), 1.11, 1.28 (both s, each 3 H, 2-CH_3 and 10-CH_3), 1.89 (m, 1 H, 4-H), 2.19 (m, 1 H, 8-H), 2.33 (m, 1 H, 6-H), 2.78 (s, 1 H, OH), 3.31 (s, 3 H, CH_2OCH_3), 3.64 (d, 1 H, J_{gem} 12.0 Hz, 1ax-H), 3.69 (br d, 1 H, J_{gem} 8.6 Hz, 1″a-H), 3.78 (dd, 1 H, $J_{6,1''b}$ 6.5, J_{gem} 8.6 Hz, 1″b-H), 3.84 (br s, 1 H, 3-H), 4.00 (m, 4 H, 1eq-H, 7-H, 9-H, PhC*H*), 4.32 (dd, 1 H, overlapped by m, $J_{4,5}$ 8.0, $J_{5,6}$ 5.1 Hz, 5-H), 4.39 (m, 4 H, PhC*H* × 4), 4.56 (br s, 2 H, CH_2OCH_3), 4.60 (d of ABq, 1 H, *J* 11.2 Hz, PhC*H*), 4.83 (ABq, 2 H, *J* 10.8 Hz, Δδ = 0.21 ppm, $PhCH_2$), 5.11 (dd, 1 H, J_{gem} 1.5, J_{cis} 12.0 Hz, 12-*cis*-H), 5.12 (d, 1 H, *J* 4.3 Hz, 1′-H), 5.35 (dd, 1 H, J_{gem} 1.5, J_{trans} = 15 Hz, 12-*trans*-H), 6.09 (dd, 1 H, J_{cis} 12.0, J_{trans} 15.0 Hz, 11-H), and 7.26 (m, 20 H, *Ph*CH_2 × 4).

A solution of the Grignard adduct (**8**) (8 mg, 0.010 mmol) in methylene dichloride (1 ml) was treated with a saturated solution of ozone in methanol at −78 °C and the reaction mixture warmed to room temperature with TLC (C) monitoring. After 30 min, dimethyl sulphide (0.05 ml) was added and the reaction mixture was stirred for an additional 30 min; the volatiles were then removed under reduced pressure. The crude aldehyde displayed the following physical characteristics: R_F 0.30 (C); ν_{max}(neat) 3 400 and 1 710 cm^{-1}; δ(250 MHz, $CDCl_3$) 0.89 (d, 3 H, *J* 7.3 Hz, 8-CH_3), 1.11, 1.28 (both s, each 3 H, 2-CH_3, 10-CH_3), 1.88 (m, 1 H, 4-H), 2.31 (m, 2 H, 6-H, 8-H), 3.30 (s, 3 H, CH_2OCH_3), 3.49 (br s, 1 H, OH), 3.72 (m, 3 H, 1ax-H, 3-H, 1″a-H), 3.82 (m, 2 H, 1″b-H, PhC*H*), 3.98 (m, 3 H, 1eq-H, 7-H, 9-H), 4.39 (m, 6 H, 5-H, PhC*H* × 5), 4.56 (m, 3 H, PhC*H*, CH_2OCH_3), 4.99 (d of ABq, 1 H, *J* 10.4 Hz, PhC*H*), 5.16 (d, 1 H, *J* 3.6 Hz, 1′-H), 7.30 (m, 20 H PhC*H* × 4), 9.68 (s, 1 H, C*H*O).

Sodium borohydride (2 mg, 0.053 mmol) was added at 0 °C to a solution in ethanol (2 ml) of the crude aldehyde obtained in the previous step. The reaction mixture was stirred at this termperature for 5 min and then quenched by the addition of acetic acid (0.02 ml). The volatiles were removed under reduced pressure and the resulting residue triturated with ethyl acetate. The mixture was filtered and the filtrate was evaporated under reduced pressure. The crude product yielded, after flash chromatography, the diol (**9**) [5 mg, 63% from (**8**)] as a clear gum; R_F 0.10 (C); $[\alpha]_D^{20}$ + 58° (*c* 0.44, $CHCl_3$); ν_{max}(neat) 3 450 cm^{-1}; δ(300 MHz, $CDCl_3$) 1.05 (d, 3 H, *J* 6.9 Hz, 8-CH_3), 1.09, 1.14 (both s, each 3 H, 2-CH_3, 10-CH_3), 1.89 (m, 1 H, 4-H), 2.18 (m, 1 H, 8-H), 2.32 (m, 1 H, 6-H), 2.48 (dd, 1 H, $J_{11a,OH}$, 9.9, $J_{11b,OH}$, 3.3 Hz, 11-OH), 2.75 (s, 1 H, 10-OH), 3.31 (s, 3 H, CH_2OCH_3), 3.37 (dd, 1 H, $J_{11a,OH}$, 9.9, J_{gem} 11.0 Hz, 11a-H), 3.59 (dd, 1 H, $J_{11b,OH}$, 3.3, J_{gem} 9.9 Hz, 11b-H), 3.63 (d, 1 H, J_{gem} 13.5 Hz, 1ax-H), 3.67 (br d, 1 H, $J_{6,1''a}$ O, J_{gem} 9.9 Hz, 1″a-H), 3.75 (dd, 1 H, $J_{6,1''b}$ 6.9, J_{gem} 9.9 Hz, 1″b-H), 3.83 (br s, 1 H, 3-H), 3.94 (m, 2 H, 7-H, PhC*H*), 4.02 (m, 2 H, 1eq-H, 9-H), 4.30 (dd, 1 H, overlapped by m, $J_{4,5}$ 11.7, $J_{5,6}$ 4.8 Hz, 5-H), 4.41 (m, 4 H, PhC*H* × 4), 4.55 (br s, 2 H, CH_2OCH_3), 4.58 (d of ABq, 1 H, *J* 11.7 Hz, PhC*H*), 4.77 (ABq, 2 H, *J* 11.4 Hz, Δδ = 0.21 ppm, $PhCH_2$), 5.11 (d, 1 H, *J* 3.6 Hz, 1′-H), 7.28 (m, 20 H, *Ph*CH_2 × 4) (Found: C, 71.9; H, 7.55. $C_{46}H_{58}O_{10}$ requires C, 71.66; H, 7.58%).

2,3,5,9-*Tetra*-O-*benzyl*-4,6,8,10,11-*pentadeoxy*-4-C-(1′-*formyl*)-(1′S)-6-C-(1″-*methoxymethyoxymethyl*)-2,8,10-*tri*-C-*methyl*-L-galacto-L-altro-10-*eno*-1,1′:1′,7-*bipyranoside-undecitiol* (**7b**).—The methyl ketone (**7a**) (10 mg, 0.14 mmol) was subjected to the standard Wittig methylenation conditions. The olefin (**7b**) (4 mg, 40%) and unchanged ketone (**7a**) (4 mg, 40%) were obtained after flash chromatography of the crude product. For (**7b**) clear gum; R_F 0.40 (A); $[\alpha]_D^{20}$ + 81° (*c* 0.78, $CHCl_3$); δ(300 MHz, $CDCl_3$) 0.77 (d, 3 H, *J* 6.6 Hz, 8-CH_3), 1.08 (s, 3 H, 2-CH_3), 1.67 (br s, 3 H, 10-CH_3), 1.86 (m, 2 H, 4-H, 8-H), 2.21 (m, 1 H, 6-H), 3.25 (s, 3 H, CH_2OCH_3), 3.61 (d , 1 H, *J* 13.5 Hz, 1ax-H), 3.65 (br d, 1 H, *J* 10.2 Hz, 1″a-H), 3.76 (dd, 1 H, $J_{6,1''b}$ 7.5, J_{gem} 13.5 Hz, 1″b-H), 3.79 (br s, 1 H, 3-H), 3.86 (d of ABq, 1 H, *J* 11.4 Hz, PhC*H*), 3.99 (dd, 1 H, $J_{1eq,3}$ 1.5, J_{gem} 13.5 Hz, 1eq-H), 4.14 (br d, 1 H, $J_{6,7}$ O, $J_{7,8}$ 10.2 Hz, 7-H), 4.35 (m, 5 H, 5-H, 9-H, PhC*H* × 3), 4.51 (6 H, PhC*H* × 4, CH_2OCH_3), 4.93, 5.06 (both br s, each 1 H, = CH_2), 5.08 (d, 1 H, *J* 3.6 Hz, 1′-H), and 7.22 (m, 20 H, PhC*H* × 4) (Found C, 75.1; H, 7.55. $C_{46}H_{56}O_8$ requires C, 74.97; H, 7.66.

When a solution of potassium t-butoxide in t-butyl alcohol and tetrahydrofuran was used as the base for the generation of the stock solution of the Wittig reagent, the ketone (**7a**) was completely converted into the olefin (**7b**) after 4 h at room temperature.

2,3,5,9-*Tetra*-O-*benzyl*-4,6,8-*trideoxy*-4-C-(1′-*formyl*)-(1′S)-6-C-(1″-*methoxymethoxymethyl*)-2,8,10-*tri*-C-*methyl*-L-glycero-L-galacto-L-altro-1,1′:1′7-*bipyranoside-undecitol* (**10**).—*N*-Methylmorpholine *N*-oxide (60 wt % in water; 0.01 ml, 0.05 mmol) and osmium tetroxide 2.5 wt % in butyl alcohol; (0.06 ml; 0.006 mmol) were added to a solution of (**7b**) (9 mg, 0.012 mmol) in acetone (2 ml). The reaction mixture was stirred for 12 h at room temperature. 0.5M Aqueous sodium bisulphite (0.02 ml) was added and the reaction mixture stirred for an additional 30 min. Most of the solvent was evaporated under reduced pressure and the residue diluted with water (2 ml) and extracted with ethyl acetate (3 × 5 ml). The combined organic extracts were dried (Na_2SO_4), filtered, and concentrated under reduced pressure. Flash chromatography of the residue gave the diol (**10**) (6 mg, 67%) as a clear gum; R_F 0.10 (C); $[\alpha]_D^{20}$ + 55° (*c* 0.40, $CHCl_3$); ν_{max}(neat) 3 430 cm^{-1}; δ(300 MHz, $CDCl_3$) 0.98 (d, 3 H, *J* 6.9 Hz, 8-CH_3), 1.08, 1.11 (both s, each 3 H, 2-CH_3, 10-CH_3), 1.82 (m, 1 H, 4-H), 2.15 (m, 1 H, 8-H), 2.28 (m, 1 H, 6-H), 2.35 (dd, 1 H, $J_{11a,OH}$ 7.2, $J_{11b,OH}$ 4.8 Hz, 11-OH), 2.82 (s, 1 H, 10-OH), 3.27 (s, 3 H, CH_2OCH_3), 3.36 (dd, 1 H, $J_{11a,OH}$ 7.2, J_{gem} 11.1 Hz, 11a-H), 3.64 (m, 3 H, 1ax-H, 1″a-H, 11b-H), 3.73 (dd, 1 H, $J_{6,1''b}$ 7.5, J_{gem} 9.6 Hz, 1″b-H), 3.80 (br s, 1 H, 3-H), 3.86 (br d, 1 H, $J_{6,7}$ 0, $J_{7,8}$ 10.8 Hz, 7-H), 3.93 (d of ABq, 1 H, *J* 10.8 Hz, PhC*H*), 4.03 (m, 2 H, 1eq-H, 9-H), 4.29 (dd, 1 H, overlapped by m, $J_{4,5}$ 12.0, $J_{5,6}$ 5.1 Hz, 5-H), 4.38 (m, 4 H, PhC*H* × 4), 4.52 (br s, 2 H, CH_2OCH_3), 4.55 (d of ABq, *J* 12.0 Hz, PhC*H*), 4.72 (ABq, 2 H, *J* 12.0 Hz, Δδ = 0.13 ppm, $PhCH_2$), 5.07 (d, 1 H, *J* 3.3 Hz, 1′-H), and 7.28 (m, 20 H, *Ph*CH_2 × 4) (Found: C, 71.8; H, 7.45. $C_{46}H_{58}O_{10}$ requires C, 71.66; H, 7.58%).

7,10-*Anhydro*-2,3,5-*tri*-O-*benzyl*-11-*bromo*-4,6,8,10,11-*pentadeoxy*-4-C-(1′-*formyl*)-6-C-(1″-*methoxymethoxymethyl*)-2,8,10-*tri*-C-*methyl*-D- *or* L-glycero-L-talo-L-altro-1′,1-*pyranose-undecitol* (**11a**).—*N*-Bromosuccinimide (155 mg, 0.876 mmol) was added at 0 °C to a mixture of sodium hydrogencarbonate (100 mg, 1.20 mmol) and the olefin (**7b**) (260 mg, 0.353 mmol) in acetonitrile (10 ml). The reaction mixture was stirred at 0 °C for 10 min and then quenched by the addition of 10% aqueous sodium thiosulphate solution (1 ml); it was then stirred for an additional 10 min at 0 °C. Most of the solvent was removed under reduced pressure at room temperature and the residue diluted with water (25 ml), and extracted with ether (4 × 25 ml).

The organic phase was washed with brine, dried (Na_2SO_4), filtered, and concentrated under reduced pressure to give a crude syrup. This was subjected to flash chromatography and gave the bromo lactol (**11a**) as a colourless, syrupy 4:1 anomeric mixture (275 mg, 94%); R_F 0.20 (C); ν_{max}(neat) 3 380 cm^{-1}; selected resonances δ(300 MHz, $CDCl_3$) 0.60 (d, 8-CH_3, minor anomer), 0.73 (d, 8-CH_3, major anomer), 1.23, 1.41, 1.48 (all s, 2-CH_3 and 10-CH_3), 2.00–2.30 (m, 4-H, 6-H, 8-H), 3.00 (d, OH, minor anomer), 3.15, 3.20, 3.31 (all d, 11-CH_2), 3.27 (CH_2OCH_3, major anomer), 3.28 (s, CH_2OCH_3, minor anomer), 3.48, 3.69 (both dd, 1″-CH_2, major anomer), 3.98 (d, OH, major anomer), and 5.16 (br t, 1′-H, minor anomer) (Found: C, 66.15; H, 6.7. $C_{46}H_{57}BrO_9$ requires C, 66.26; H, 6.89%).

7,10-*Anhydro*-2,3,5-*tri*-O-*benzyl*-11-*bromo*-4,6,8,11-*tetradeoxy*-4-C-(1′-*formyl*)-6-C-(1″-*methoxymethoxymethyl*)-2,8,10-*tri*-C-*methyl*-D *or* L-glycero-L-talo-L-altro-1′,1-*pyranose-undecitol* (**11b**).—The hemiacetal (**11a**) (93 mg, 0.11 mmol) was treated under standard conditions for Swern's oxidation and gave the lactone (**11b**) (75 mg, 81%) as a clear syrup, R_F 0.50 (C); $[\alpha]_D^{20}$ − 8.91° (*c* 2.11, $CHCl_3$); ν_{max}(neat) 1 740 cm^{-1}; δ(300 MHz, $CDCl_3$) 0.93 (d, 3 H, *J* 6.3 Hz, 8-CH_3), 1.31, 1.44 (both s, each 3 H, 2-CH_3, 10-CH_3), 2.12 (m, 1 H, 6-H), 2.35 (m, 1 H, 8-H), 3.06 (dd, 1 H, $J_{3,4}$ 6.3, $J_{4,5}$ 1.8 Hz, 4-H), 3.23 (s, 3 H, OCH_2OCH_3), 3.31 (ABq, 2 H, *J* 10.8 Hz, Δδ 0.10 ppm, 11-CH_2), 3.40 (dd, 1 H, overlapped by ABq, $J_{6,1''a}$ = 4.5, J_{gem} 11.0 Hz, 1″a-H), 3.70 (d, 1 H, *J* 10.0 Hz, 9-H), 3.79 (dd, 1 H, $J_{6,1''b}$ 6.3, J_{gem} 11.0 Hz, 1″b-H), 4.01 (br d, 1 H, $J_{7,8}$ 11.1 Hz, 7-H), 4.12 (d, 1 H, $J_{3,4}$ 6.3 Hz, 3-H), 4.18 (ABq, 2 H, *J* 11.1 Hz, Δδ = 0.05 ppm, 1-CH_2), 4.33 (dd, 1 H, $J_{4,5}$ 1.8, $J_{5,6}$ 10.5 Hz, 5-H), 4.41 (m, 2 H, OCH_2OCH_3), 4.45–4.64 (m, 6 H, PhC*H* × 6), 4.76, 4.82 (both d of ABq, *J* 11.1, 10.8 Hz respectively, PhC*H* × 2), and 7.30 (m, 20 H, *Ph*CH_2 × 4). Irradiation of the 7-H signal at δ 4.01 produced a significant NOE enhancement of the 9-H signal at δ 3.70 (Found: C, 66.35; H, 6.5. $C_{46}H_{55}BrO_9$ requires C, 66.42; H, 6.67%).

2,3,5-*Tri*-O-*benzyl*-4,6-*dideoxy*-4-C-(1′-*formyl*)-(1′S)-6-C-(1″-*methoxymethoxymethyl*)-2-C-*methyl*-8-*aldehydo*-D-talo-L-threo-1,1′:1,′7-*bipyranoside-ocitol* (**1b**).—The primary alcohol (**14a**)[5] (1.63 g, 2.10 mmol) was protected, as the methoxymethyl ether according to the procedure described in the preparation of (**5b**). The crude product was dissolved in dimethyl sulphoxide (10 ml) and caesium fluoride (385 mg, 2.53 mmol) and 18-crown-6 (25 mg, 0.095 mmol) added to the solution. The reaction mixture was stirred at 60 °C for 1 h and then diluted with water (50 ml) and extracted with ether (4 × 50 ml). The combined extracts were washed with brine (50 ml), dried (Na_2SO_4), filtered, and evaporated under reduced pressure. The crude product after flash chromatography gave the primary alcohol (**14b**) [1.1 g, 91% from (**14a**)] as a colourless syrup, R_F 0.08 (C); $[\alpha]_D^{20}$ 119° (*c* 1.36, $CHCl_3$); ν_{max}(neat) 3 500 and 1 600 cm^{-1}; δ(300 MHz, $CDCl_3$) 1.11 (s 3 H, 2-CH_3), 1.78 br d, 1 H, *J* 11.1 Hz, 4-H), 2.23 (m, 1 H, 6-H), 2.70 (t, 1 H, *J* 7.2 Hz, OH), 3.29 (s, 3 H, CH_2OCH_3), 3.57 (m, 1 H, 8a-H), 3.61 (dd, 1 H, J_{gem} 12.6 Hz, 1ax-H), 3.74 (m, 4 H, 3-H, 1″-CH_2, 8b-H), 4.07 (d, 1 H, $J_{1eq,3}$ 1.5, J_{gem} 12.6 Hz, 1eq-H), 4.08 (ABq, 2 H, *J* 11.7 Hz, Δδ 0.29 ppm, PhCH_2), 4.15 (dt, 1 H, $J_{6,7}$ 1.5, $J_{7,8a}$ $J_{7,8b}$ 5.1 Hz, 7-H), 4.38 (m, 3 H, 5-H, PhC*H* × 2), 4.55 (m, 4 H, PhC*H* × 2, CH_2OCH_3), 5.08 (d, 1 H, *J* 3.0 Hz, 1′-H), and 7.28 (m, 15 H, *Ph*CH × 3).

The primary alcohol (**14b**) (530 mg, 0.92 mmol) was oxidized according to the standard Swern's procedure. The aldehyde (**16**) (500 mg, 94%) was obtained after flash chromatography as a clear syrup; R_F 0.50 (C); $[\alpha]_D^{20}$ + 96° (*c* 0.70, $CHCL_3$); ν_{max}(neat) 1 718 cm^{-1}; δ(300 MHz, $CDCl_3$) 1.13 (s, 3 H, 2-CH_3), 2.01 (dt, 1 H, $J_{1',4}$ $J_{3,4}$ 2.7, $J_{4,5}$ 10.5 Hz, 4-H), 2.60 (m, 1 H, 6-H), 3.24 (s, 3 H, OCH_2OCH_3), 3.57 (m, 1 H, 1″a-H), 3.67 (d, 1 H, *J* 12.0 Hz, 1ax-H), 3.74 (m, 2 H, 3-H, 1″b-H), 4.05 (m, 2 H, 1eq-H, PhC*H*), 4.29 (d of ABq, 1 H, *J* 12.3 Hz, PhC*H*), 4.42 (m, 7 H, 5-H, 7-H, PhC*H* × 3) CH_2OCH_3), 4.59 (d of ABq, 1 H, *J* 10.8 Hz, PhC*H*), 5.25 (br s, 1 H, 1′-H), 7.25 (m, 15 H, *Ph*CH_2 × 3), and 9.51 (s, 1 H, 8-H) (Found: C, 70.9; H, 7.05. $C_{34}H_{40}O_8$ requires C, 70.81; H, 6.99%).

2,3,5-*Tri*-O-*benzyl*-4,6,9-*trideoxy*-4-C-(1′-*formyl*)-(1′S)-6-C-(1″-*methoxymethoxymethyl*)-2-C-*methyl*-8-ulo-D-talo-L-threo-1,1′:1′,7-*bipyranoside-nonitol* (**17**).—Methylmagnesium chloride (2.8 M solution in tetrahydrofuran; 0.5 ml, 1.4 mmol) was added to a solution of the aldehyde (**16**) (490 mg, 0.85 mmol) in dry tetrahydrofuran (10 ml) at −78 °C under an argon atmosphere. The reaction mixture was processed as described for the preparation of (**8**), the crude product dried under high vacuum, and subjected to Swern's oxidation conditions. The methyl ketone (**17**) [365 mg, 73% from (**16**)] was obtained after flash chromatography as a colourless oil; R_F 0.37 (C); $[\alpha]_D^{20}$ + 108° (*c* 0.83, $CHCl_3$); ν_{max}(neat) 1 720 and 1 600 cm^{-1}; δ(300 MHz, $CDCl_3$) 1.09 (s, 3 H, 2-CH_3), 1.99 (dt, 1 H, $J_{1',4}$ $J_{3,4}$ 2.1, $J_{4,5}$ 11.4 Hz, 4-H), 2.15 (s, 3 H, CH_3CO), 2.62 (m, 1 H, 6-H), 3.23 (s, 3 H, OCH_2OCH_3), 3.70 (m, 3 H, 1ax-H, 1″-CH_2), 3.87 (t, 1 H, $J_{1eq,3}$ = $J_{3,4}$ 2.1 Hz, 3-H), 4.01 (dd, 1 H, $J_{1eq,3}$ 2.1, J_{gem} 13.8 Hz, 1eq-H), 4.17 (ABq, 2 H, *J* 10.8 Hz, Δδ 0.31 ppm, $PhCH_2$), 4.43 (m, 5 H, 5-H, PhC*H* × 2, OCH_2 OCH_3), 4.50 (d, 1 H, *J* 6.0 Hz, 7-H), 4.54, 4.62 (both d of ABq, each 1 H, *J* 10.5, 11.7 Hz, respectively, PhC*H* × 2), 5.21 (d, 1 H, *J* 3.9 Hz, 1′-H), and 7.28 (m, 15 H, *Ph*CH_2 × 3) (Found: C, 71.95; H, 8.05. $C_{35}H_{42}O_8$ requires C, 72.09; H, 7.98%).

2.3.5-*Tri*-O-*benzyl*-4,6,8,9-*tetradeoxy*-4-C-(1′-*formyl*)-(1′S)-6-C-(1″-*methoxymethoxymethyl*)-2-8-*di*-C-*methyl*-D-talo-L-threo-8-*eno*-1,1′:1′,7-*bipyranoside-nonitol* (**18**).—A solution of methylenetriphenylphosphorane was prepared as described in the standard Wittig procedure by the addition of butyllithium (2.2M solution in hexane, 0.48 mmol, 0.22 ml) to a suspension of methyltriphenylphosphonium bromide (222 mg, 0.64 mmol) in dry tetrahydrofuran (5 ml). The methyl ketone (**17**) (95 mg, 0.16 mmol) was added to the solution of the ylide and the reaction processed as described for the standard procedure. The olefin (**18**) (78 mg, 82%) was obtained after flash chromatography as a white solid; R_F 0.55 (B); $[\alpha]_D^{20}$ + 131° (*c* 0.86, $CHCl_3$); ν_{max}($CHCl_3$) 1 600 and 910 cm^{-1}; δ(300 MHz, $CDCl_3$) 1.13 (s, 3 H, 2-CH_3), 1.74 (br s, 3 H, 8-CH_3), 1.92 (m, 1 H, 4-H), 2.35 (m, 1 H, 6-H), 3.27 (s, 3 H, OCH_2OCH_3), 3.55 (dd, 1 H, $J_{6,1''a}$ 6.0, J_{gem} 10.5 Hz, 1″a-H), 3.67 (dd, 1 H, $J_{6,1''b}$ 2.1, J_{gem} 10.5 Hz, 1″b-H), 3.70 (d, 1 H *J* 13.5 Hz, 1ax-H), 3.90 (m, 1 H, 3-H), 3.98 (d of ABq, 1 H, *J* 11.1 Hz, PhC*H*), 4.08 (dd, 1 H, $J_{1eq,3}$ 2.1, J_{gem} 10.5 Hz, 1eq-H), 4.45 (m, 7 H, 5-H, 7-H, PhC*H* × 3, OCH_2OCH_3), 4.56, 4.63 (both of d of ABq, each 1 H, *J* 11.7, 12.0 Hz, PhC*H* × 2), 4.89, 5.16 (both m, each 1 H CH_2), 5.17 (d, 1 H, *J* 3.3 Hz, 1′-H), and 7.28 (m, 15 H, *Ph*CH_2 × 3) (Found: C, 73.35; H, 7.5. $C_{36}H_{44}O_7$ requires C, 73.44; H, 7.53%).

2,3,5-*Tri*-O-*benzyl*-4,6,8-*trideoxy*-4-C-(1′-*formyl*)-(1′S)-6-C-(1″-*methoxymethoxymethyl*)-2,8-*di*-C-*methyl*-L-galacto *and* D-altro-L-lyxo-1,1′:1′,7-*bipyranoside-nonitol* (**19**) and (**20**).—The olefin (**18**) (1.05 g, 1.79 mmol) was subjected to the standard conditions for hydroboration using 9-borabicyclo[3.3.1]nonane (2 equiv.) in tetrahydrofuran at room temperature for 1 h. Two compounds, (**19**) (245 mg, 23%) and (**20**) (750 mg, 70%), were obtained after flash chromatography of the crude product.

For (**19**): prisms (light petroleum–ethyl acetate), m.p. 113–114 °C; R_F 0.20 (C); $[\alpha]_D^{20}$ 119° (*c* 1.12, $CHCl_3$);ν_{max}($CHCl_3$)

3 480 cm^{-1}; δ(300 MHz, $CDCl_3$) 1.01 (d, 3 H, *J* 6.8 Hz, 8-CH_3), 1.09 (s, 3 H, 2-CH_3), 1.75 (m, 1 H, 4-H), 2.00 (m, 1 H, 8-H), 2.44 (m, 1 H, 6-H), 2.81 (t, 1 H, *J* 5.1 Hz, OH), 3.26 (s, 3 H, OCH_2OCH_3), 3.46, 3.56 (both m, each 1 H, 9-CH_2), 3.63 (d, 1 H, *J* 13.0 Hz, 1ax-H), 3.72 (m, 3 H, 1″-CH_2, 7-H), 3.79 (br s, 1 H, 3-H), 3.93 (d of ABq, 1 H, *J* 12.0 Hz, PhC*H*), 4.04 (dd, 1 H, $J_{1eq,3}$ 1.5, J_{gem} 13.0 Hz, 1eq-H), 4.30 (dd, 1 H, overlapped by m, $J_{4,5}$ 10.5, $J_{5,6}$ 5.1 Hz, 5-H), 4.36 (m, 3 H, PhCH × 3), 4.54 (m, 4 H, PhC*H* × 2, OCH_2OCH_3), 5.04 (d, 1 H, *J* 3.0 Hz, 1′-H), and 7.22 (m, 15 H, *Ph*CH_2 × 3) (Found: C, 71.4; H, 7.85. $C_{36}H_{46}O_8$ requires C, 71.26; H, 7.64%).

For (**20**): R_F 0.15 (C); $[\alpha]_D^{20}$ + 122° (*c* 0.97, $CHCl_3$); ν_{max}(neat) 3 400 cm^{-1}; δ(300 MHz, $CDCl_3$) 1.05 (d, 3 H, *J* 6.6 Hz 8-CH_3), 1.11 (s, 3 H, 2-CH_3), 1.83 (m, 1 H, 4-H), 2.01 (m, 1 H, 8-H), 2.11 (m, 1 H, 6-H), 2.90 (m, 1 H, OH), 3.31 (s, 3 H, OCH_2OCH_3), 3.65 (m, 3 H, 1ax-H, 9-CH_2), 3.74 (m, 2 H, 1″-CH_2), 3.83 (br d, 1 H, $J_{7,8}$ 8.4 Hz, 7-H), 3.84 (br s, overlapped m, 1 H, 3-H), 3.96 (d of ABq, 1 H, *J* 12.0 Hz, PhC*H*), 4.06 (dd, 1 H, $J_{1eq,3}$ 1.5, J_{gem} 14.0 Hz, 1eq-H), 4.31 (dd, 1 H, $J_{4,5}$ 12.0, $J_{5,6}$ 4.5 Hz, 5-H), 4.39 (m, 3 H, PhC*H* × 3), 4.56 (m, 4 H, PhC*H* × 2, OCH_2OCH_3), 5.07 (d, 1 H, *J* 3.3 Hz, 1′-H), 7.30 (m, 15 H, *Ph*CH_2 × 3) (Found: C, 71.35; H, 7.9. $C_{36}H_{46}O_8$ requires C, 71.26; H, 7.64%).

Preparation of the Olefin (**18**) *from the Primary Alcohol* (**19**).—Tributylphosphine (0.37 ml, 1.5 mmol) was added to a solution of the alcohol (**24**) (450 mg, 0.740 mmol) and *N*-phenylselenophthalimide (335 mg, 1.11 mmol) in dry tetrahydrofuran (10 ml) and 0 °C under an argon atmosphere. The reaction mixture was warmed to room temperature and after 30 min, was diluted with methylene dichloride (50 ml) and washed with saturated aqueous sodium hydrogencarbonate (25 ml). The organic phase was dried (Na_2SO_4), filtered, and evaporated under reduced pressure and the crude residue was purified by flash chromatography, using ethyl acetate–light petroleum mixtures of increasing polarity (0–10%).

The product obtained in the previous step was dissolved in dry methylene dichloride (20 ml) and treated at 0 °C with *m*-chloroperbenzoic acid (256 mg, 1.50 mmol). After 15 min, triethylamine (2 ml) was added to the solution and the reaction temperature raised to reflux for an additional 3 h. The mixture was then diluted with methylene dichloride (50 ml) and washed with a 10% aqueous sodium thiosulphate (50 ml) and saturated aqueous sodium hydrogencarbonate. The organic phase was dried (Na_2SO_4), filtered, and concentrated under reduced pressure. Flash chromatography of the residue afforded the olefin (**18**) [325 mg, 74% from (**19**)].

Preparation of the Olefin (**7b**) *from the Alcohol* (**20**).—Pyridinium chlorochromate (1.56 g, 7.26 mmol) was added to a mixture of Celite (2.80 g), anhydrous sodium acetate (1.00 g), Florisil (0.20 g), and the alcohol (**25**) (1.56 g, 2.62 mmol) in dry methylene dichloride (50 ml). The reaction mixture was stirred at room temperature for 1 h and then diluted with ether (200 ml) and filtered through a short column of Florisil. The column was eluted with additional ether and the filtrate concentrated under reduced pressure. Flash chromatography of the crude product afforded the corresponding aldehyde (1.35 g, 87%): clear gum; R_F 0.50 (F); $[\alpha]_D^{20}$ + 108° (*c* 1.06, $CHCl_3$); ν_{max}(neat) 1 720 cm^{-1}; δ(300 MHz, $CDCl_3$) 1.07 (d, 3 H, *J* 6.6 Hz, 8-CH_3), 1.15 (s, 3 H, 2-CH_3), 1.87 (m, 1 H, 4-H), 2.25 (m, 1 H, 6-H), 2.75 (m, 1 H, 8-H), 3.35 (s, 3 H, OCH_2OCH_3), 3.69 (d, 1 H, J_{gem} 13.0 Hz, 1ax-H), 3.80 (m, 2 H, 1″-CH_2), 3.88 (t, 1 H, $J_{1eq,3} = J_{3,4}$ 1.5 Hz, 3-H), 4.03 (d of ABq, 1 H, *J* 12.0 Hz, PhC*H*), 4.10 (dd, 1 H, $J_{1eq,3}$ 1.5, J_{gem} 13.0 Hz, 1eq-H), 4.19 (br d, 1 H, $J_{7,8}$ 10.5 Hz, 7-H), 4.43 (m, 4 H, 5-H, PhC*H* × 3), 4.60 (m, 4 H, PhC*H* × 2, OCH_2OCH_3), 5.07 (d, 1 H, *J* 3.0 Hz, 1′-H), 7.30 (m, 15 H, *Ph*CH_2 × 3), 9.76 (d, 1 H, *J* = 3.0 Hz, 9-H)(Found: C, 71.7; H, 7.5. $C_{36}H_{44}O_8$ requires C, 71.50; H, 7.33.

Isopropenylmagnesium bromide[10] (1M solution in tetrahydrofuran; 5.0 ml, 5.0 mmol) was added to a solution of the above aldehyde (1.35 g, 2.27 mmol) in dry tetrahydrofuran (20 ml) at −90 °C under an argon atmosphere. The reaction mixture was warmed to 0 °C, quenched by the addition of saturated aqueous ammonium chloride (50 ml) and extracted with ether (4 × 50 ml). The combined ethereal extracts were dried (Na_2SO_4), filtered, and evaporated under reduced pressure.

The above residue was dried under high vacuum and dissolved in dry *N*,*N*-dimethylformamide (20 ml). Sodium hydride (50% suspension in mineral oil washed with light petroleum; 200 mg, 4.17 mmol) and tetrabutylammonium iodide (25 mg, 0.068 mmol) was added to the solution at 0 °C. The slurry was stirred for 20 min at this temperature after which benzyl bromide (0.33 ml, 2.78 mmol) was added and the reaction mixture allowed to warm to room temperature. After 1 h, excess of sodium hydride was decomposed by addition of methanol and the reaction mixture diluted with water (100 ml), and extracted with ether (4 × 50 ml). The organic phase was washed with brine, dried (Na_2SO_4), filtered, and concentrated under reduced pressure. Flash chromatography of the resultant oil (E), afforded the benzyl ether (**7b**) [1.15 g, 69% from (**20**)]; TLC, $[\alpha]_D$, IR, and NMR data identical with those previously obtained for the compound.

Conversion of (**7b**) *into* (**7a**).—The olefin (**7b**) (15 mg, 0.20 mmol) was subjected to the ozonolysis procedure as described in the preparation of (**9**). Column chromatography of the crude reaction mixture gave the methyl ketone (**7a**) (12 mg, 80%), TLC $[\alpha]_D$, IR and NMR data, identical with those previously obtained for the compound.

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