Total Synthesis of Erythronolide A[1)]

Masaya NAKATA,* Masayuki ARAI, Katsuhiko TOMOOKA,
Naoki OHSAWA, and Mitsuhiro KINOSHITA*
Department of Applied Chemistry, Faculty of Science and Technology, Keio University,
Hiyoshi, Kohoku-ku, Yokohama 223
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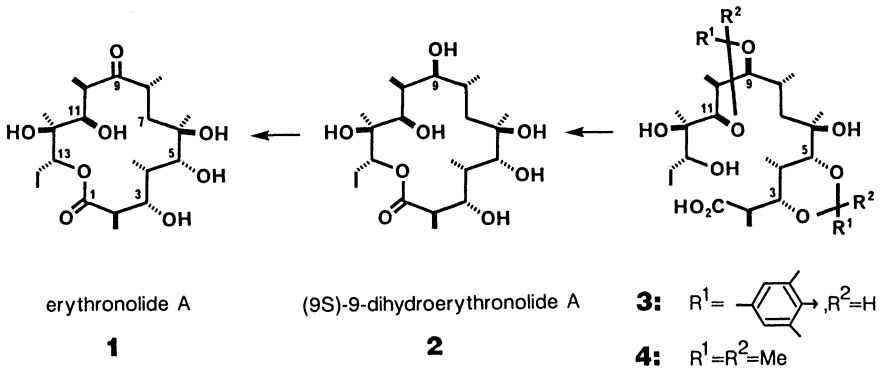
The enantiospecific total synthesis of erythronolide A (**1**) through (9*S*)-9-deoxo-9-hydroxyerythronolide A (**2**) from the chiral C1—C6, C7—C9, and C10—C13 synthetic segments is described. The C10—C13 segment, (3*R*,4*R*,5*R*)-5-*O*-benzyl-2-iodo-3,4-*O*-isopropylidene-4-methyl-1-heptene-3,4,5-triol (**11**) was synthesized in 16 steps and an 8.3% overall yield from D-ribose. The C7—C9 segment, (*S*)-(+)-2-(2-bromo-1-methylethyl)-1,3-dioxolane (**47**) was prepared from methyl (*S*)-(+)-3-hydroxy-2-methylpropionate in 8 steps and a 49% overall yield. The coupling of the Grignard reagent, prepared from magnesium and **47**, and the C1—C6 segment, 3,5,7-tri-*O*-benzyl-1,4,6-trideoxy-4,6-di-*C*-methyl-*keto*-L-*ido*-2-heptulose (**13**), afforded 5,7,9-tri-*O*-benzyl-2,3,6,8-tetradeoxy-2,4,6,8-tetra-*C*-methyl-L-*threo*-L-*ido*-nonose ethylene acetal (**48**) and its C4-epimer in 79% and 8% yields, respectively. 5,7,9-Tri-*O*-benzyl-4-*O*-*t*-butyldimethylsilyl-2,3,6,8-tetradeoxy-2,4,6,8-tetra-*C*-methyl-L-*threo*-L-*ido*-nonose (**12**), derived from **48**, was subjected to coupling reaction with the lithium reagent prepared from **11** to afford about 5 : 1 excess of the "Cram" product **50**. The homogeneous hydrogenation of **50** with [ClRh(Ph$_3$P)$_3$] gave 1,3,5,13-tetra-*O*-benzyl-6-*O*-*t*-butyldimethylsilyl-2,4,7,8,10,14,15-heptadeoxy-11,12-*O*-isopropylidene-2,4,6,8,10,12-hexa-*C*-methyl-D-*arabino*-D-*gluco*-L-*ido*-pentadecitol (**54**) and its C10-epimer in 41% and 7% yields from **12**, respectively. The conversion of **54** to **2** was accomplished by a sequence of reactions including the Corey-Nicolaou lactonization method in a 17% overall yield. Selective 3,5-*O*-benzylidenation of **2** followed by PCC oxidation and debenzylidenation gave **1** in 52% yield.

During the last decade, the total syntheses of various types of macrolide antibiotics have been achieved and well documented.[2)] Of these macrolides, erythromycin A is an extremely important 14-membered macrolide antibiotic.

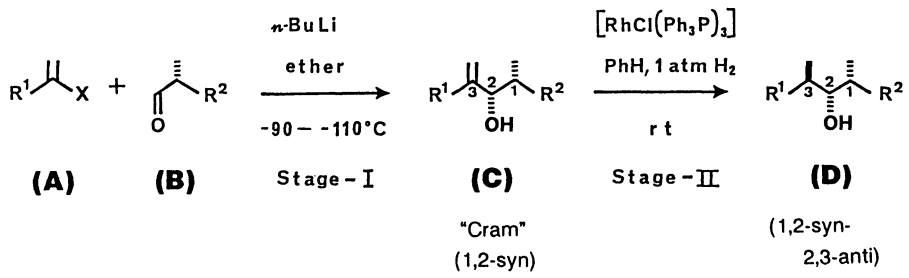
The only total synthesis of erythromycin A has been accomplished by Woodward and collaborators.[3)] After the first completion of the total synthesis of erythronolide A, aglycone of erythromycin A, by Corey et al. in 1979,[4)] several groups have succeeded in the synthesis of erythronolide A or the key intermediate carbamate in Woodward's total synthesis of erythromycin A.[5)] We wish to report in this full account[6)] the details of the total synthesis of erythronolide A.

Synthetic Strategy. We chose (9*S*)-9-deoxo-9-hydroxyerythronolide A (**2**) as a synthetic precursor of erythronolide A (**1**) by anticipating that the former could be converted into the latter through straightforward short steps (Scheme 1). Moreover, in the previous syntheses of erythronolide A,[4,5)] **2** has never been utilized as a practical synthetic precursor. The first crucial step for the synthesis of **2** should be the macrolactonization of the suitably protected seco-acid. In that sense, Woodward et al.[3)] had investigated extensively the structure-reactivity relationships of the lactonization. They concluded that *S*-configuration at C9 and cyclic protecting groups at C3/C5 and C9/C11 are required for efficient lactonization. Indeed, they realized good yield of lactonization of the naturally derived (9*S*)-9-hydroxy seco-acid 3,5 : 9,11-bis(cyclic acetal) derivative **3** by the Corey-Nicolaou method.[7)] By this fact, we thought the diacetonide **4** would be also a good precursor for the Corey-Nicolaou macrolactonization method, giving **2**.

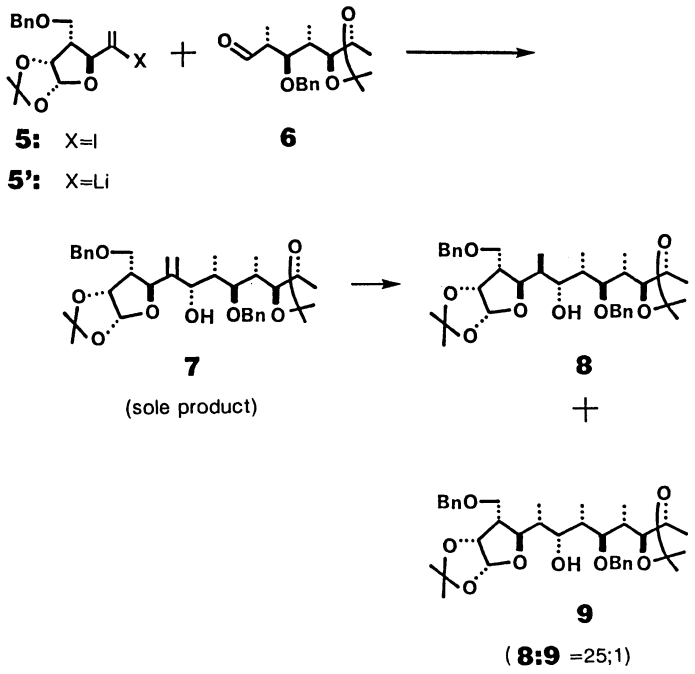
The next crucial step should be the effectively stereocontrolled enantiospecific synthesis of the key intermediate **4**. This seemed to be solved by the synthetic plan which was guided by our "two-stage coupling process."



Scheme 1.



Scheme 2.

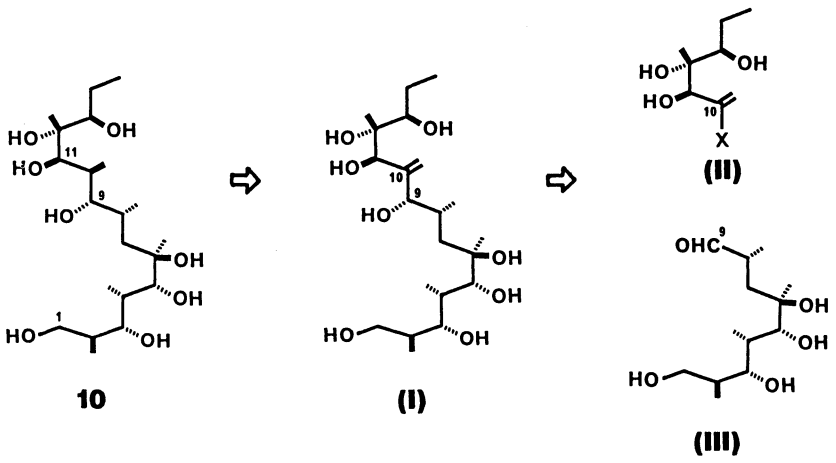


Scheme 3.

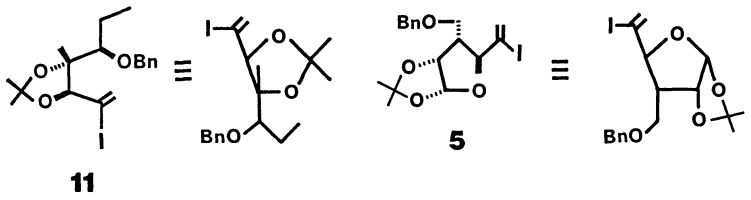
This new coupling process consists of two consecutive reaction stages (Scheme 2). The first stage is the "Cram (1,2-syn)" selective coupling reaction of a chiral vinyl halide (**A**) with a chiral α-methyl aldehyde (**B**) and the second one is the highly 2,3-anti-selective homogeneous hydrogenation of the major Cram type intermediary coupling product (**C**) with Wilkinson's catalyst. Consequently, the coupling of (**A**) and (**B**) by this process affords preferencially the final product (**D**) with 1,2-syn-2,3-anti configuration. In fact, this process was practicable in the enantiospecific synthesis of the ansa-chain portion of rifamycin W.[8] One example is showen in Scheme 3. The reaction of the chiral vinyllithium reagent **5'** prepared from the vinyl iodide **5** and the chiral (2*R*)-2-methyl aldehyde **6** gave a sole coupling product **7** (61% yield), which was subsequently hydrogenated homogeneously to give the anti-product **8** (95% yield) and the syn-product **9** (3.8% yield).

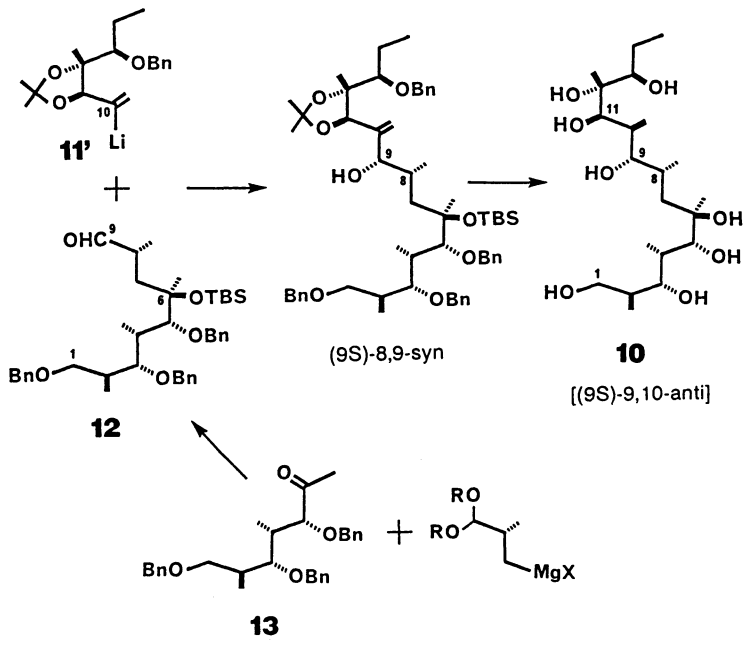
We can see in the polyol **10**, which is the hypothetical precursor of **4**, the three consecutive carbon chain (C8 to C10) having a 1,2-syn-2,3-anti configuration (Scheme 4). Therefore, a "two-stage coupling process" disconnection of the C9–C10 bond affords two subunits, **II** and **III**, through the vinylidene compound **I**. As the perspective view of the strategic vinyl iodide **11**, corresponding to the suitablly protected subunit **II**, seemed to be similar to that of **5** (Scheme 5), the reaction of the vinyllithium reagent **11'**, prepared from **11**, and (2*R*)-2-methyl aldehyde **12**, corresponding to the subunit **III**, would provide predominantly the "Cram" type of (9*S*)-8,9-syn-product, which could be homogeneously hydrogenated to produce selectively the (9*S*)-9,10-anti-product convertible into the desired polyol **10**. The aldehyde **12**, with the desired C6 chiral center, would be formed predominantly by the α-chelation controlled addition reaction,[9] of an appropriately protected chiral Grignard reagent to the chiral methyl ketone **13**,[10] which was previously synthesized in our laboratories as a versatile C1—C6 segment of **1**.

Preparation of Vinyl Iodide 11. The acetonide **14**[11] was obtained in 83% yield by treatment of D-ribose in acetone with 2,2-dimethoxypropane and a catalytic



Scheme 4.





Scheme 5.

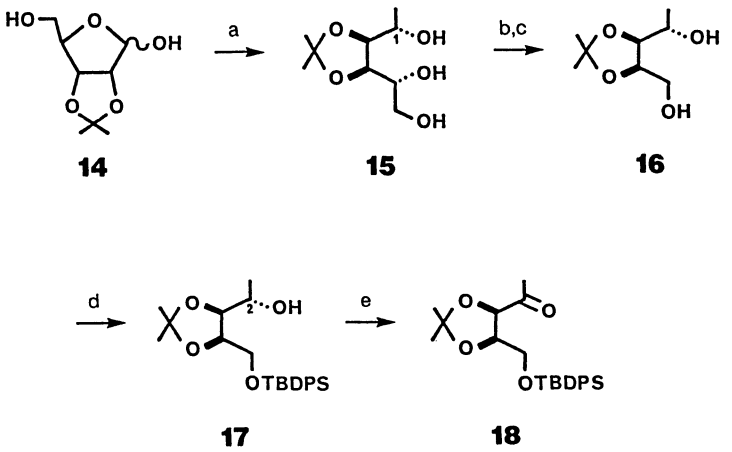
amount of H_2SO_4 (Scheme 6). The Grignard reaction of **14** with excess methylmagnesium iodide in diethyl ether afforded the alcohol **15** as a sole product in 73% yield. Regardless of the configuration at the newly formed Cl-stereocenter, the alcohol **15** can be used in the synthetic route since at a later stage this alcohol function is oxidized to a methyl ketone. We determined, however, its Cl-configuration (vide infra).

Oxidative cleavage of the glycol function in **15** with $NaIO_4$ followed by $LiAlH_4$ reduction of the resulting aldehyde afforded the alcohol **16** in 97.5% yield, whose primary alcohol was protected as its *t*-butyldiphenylsilyl (TBDPS) ether **17** (97%). Oxidation of **17** with PCC provided the methyl ketone **18** in a quantitative yield.

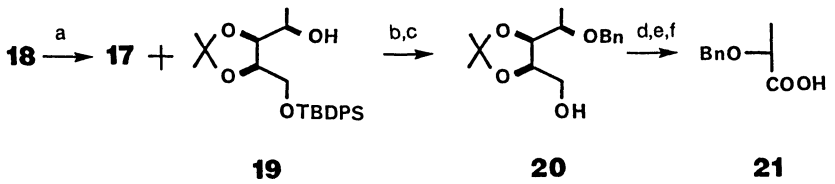
Since the attempts of 2-*O*-benzylation of **17** for the

purpose of straightforward determination of its (2*S*)-configuration was unsuccessful, the C2-epimer **19** was prepared (57%) along with **17** (28%) by $LiAlH_4$ reduction of **18** (Scheme 7). The 2-*O*-benzylation of **19** followed by removal of the silyl ether protecting group afforded the alcohol **20** in 91% yield. After treatment of **20** with aqueous acetic acid, the resulting triol was oxidized successively with $NaIO_4$ and CrO_3 to afford (*R*)-(+)-2-benzyloxypropionic acid **21**. The acid **21** was proved to be the enantiomer of the reported (*S*)-(−)-2-benzyloxypropionic acid[12] (see Experimental section).

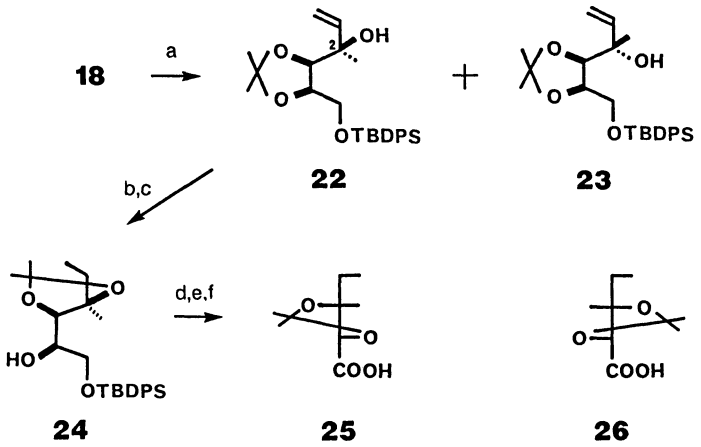
The chelation controlled Grignard reaction of **18** with vinylmagnesium bromide in THF provided the products **22** and **23** in 94% yield as a 77:1 mixture of epimers (^1H NMR). Silica-gel chromatography separated **22** (85%) and **22**+**23** (8%; 5.7:1 mixture in favor of **22**) (Scheme 8). The (2*R*)-configuration of



Scheme 6. (a) MeMgI, ether; (b) $NaIO_4$, aq acetone; (c) $LiAlH_4$, THF; (d) TBDPSCl, imidazole, DMF; (e) PCC, MS 3AP, CH_2Cl_2.



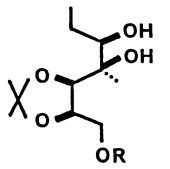
Scheme 7. (a) $LiAlH_4$, ether, −78 °C; (b) NaH, BnBr, THF; (c) TBAF, THF; (d) 75% AcOH, 80 °C; (e) $NaIO_4$, aq acetone: (f) CrO_3-AcOH-Py.



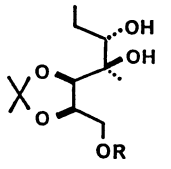
Scheme 8. (a) CH_2=CHMgBr, THF; (b) H_2/[ClRh-(Ph_3P)$_3$], benzene; (c) $ZnBr_2$, CH_2Cl_2; (d) TBAF, THF; (e) $NaIO_4$, aq acetone; (f) KIO.

22 was confirmed by the following manner. Reduction of double bond followed by $ZnBr_2$-promoted acetonide migration afforded **24**. After removal of the silyl ether protecting group, the diol was oxidized successively with $NaIO_4$ and KIO to give the carboxylic acid **25**, which was proved to be the epimer of **26**[13] by comparing optical rotation and ^1H NMR spectrum.

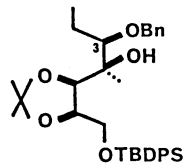
Ozonolysis of **22** followed by addition of ethylmagnesium bromide to the resulting aldehyde gave a ca. 1.6 : 1 mixture of the desired **27** and its epimer **28** in 63.5% combined yield. Since chromatographic separation of **27** and **28** was quite difficult, the isomeric



27: R=TBDPS
29: R=H



28: R=TBDPS
30: R=H



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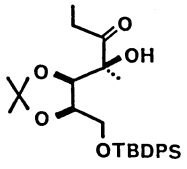

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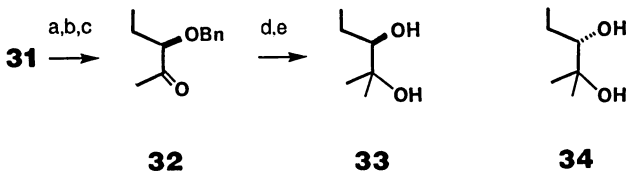
ratio was assumed based on the isolated yields of the chromatographycally separable products, **29** and **30**, obtained by desilylation of the epimeric mixture.

Direct *O*-benzylation of the mixture, **27** and **28**, with NaH and benzyl bromide in THF afforded fortunately only one isomeric *O*-benzyl derivative **31** (55%), and a 1 : 4.9 mixture of **27** and **28** was recovered (28%). The (3*R*)-configuration of **31** was confirmed by the following manner (Scheme 9). After desilylation of **31**,



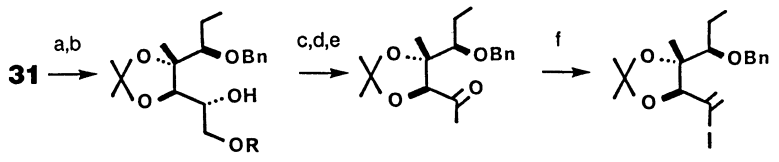
32 **33** **34**

Scheme 9. (a) TBAF, THF; (b) 50% AcOH, 115 °C; (c) $NaIO_4$, aq acetone; (d) MeMgI, ether; (e) H_2/Pd, *t*-BuOH.

acidic hydrolysis of acetonide protecting group followed by $NaIO_4$ oxidation gave methyl ketone **32**. The Grignard reaction of **32** with methylmagnesium iodide followed by debenzylation gave the diol **33**. This diol (*R*)-(+)-**33** was proved to be the enantiomer of the reported (*S*)-(−)-**34**.[14] From this result, the configurations of the compounds **27**—**31** were established as depicted.

The aforesaid unchanged epimeric mixture in favor of the (3*S*)-epimer **28** was converted into the ketone **35** by DMSO-oxidation in 90% yield. $LiAlH_4$ reduction of **35** in diethyl ether at −78 °C gave a 5 : 1 epimeric mixture in preponderance of **27**, which was again benzylated to afford **31** in 55% yield from **35**; the total yield of **31** from **22** amounted to 43.8%. Brief exposure of **31** to 0.5 equiv of $FeCl_3$ in acetone led to the isomeric acetonide **36** (95%), which was desilylated to give **37** in 92% yield. Oxidative cleavage of the glycol function in **37** with $NaIO_4$ followed by successive treatment of the resulting aldehyde with methylmagnesium iodide and PCC provided the methyl ketone **38** in a 92% overall yield, which was converted through its hydrazone into the vinyl iodide **11** according to the improved procedure of Barton et al.[15] (Scheme 10).

Preparation of Aldehyde 12. With the chiral vinyl iodide **11**, C10—C13 segment of **1**, in hand, we turned our attention to the synthesis of the second requisite **12**, C1—C9 segment of **1**. For the purpose of synthesizing **12** from the previously prepared C1—C6 segment **13**,[10] an adequate C7—C9 segment had first to be inquired. After many unsuccessful attempts, the



36: R=TBDPS
37: R=H

38 **11**

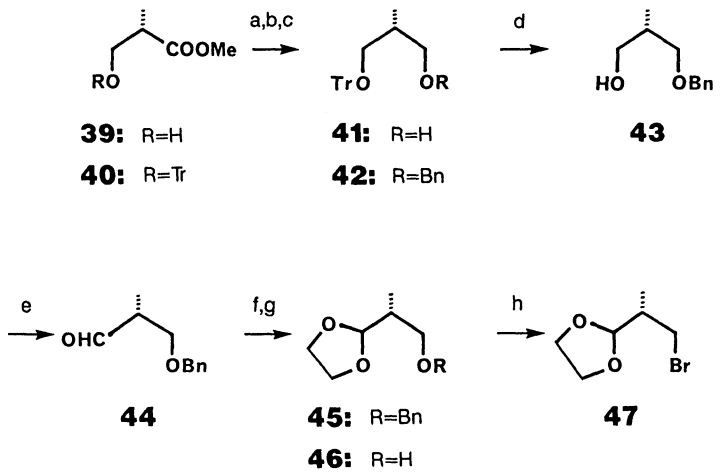
Scheme 10. (a) $FeCl_3$, acetone; (b) TBAF, THF; (c) $NaIO_4$, aq acetone; (d) MeMgI, ether; (e) PCC, MS 3AP, CH_2Cl_2; (f) 1) $NH_2NH_2 \cdot H_2O$, Et_3N, EtOH, 70 °C. 2) I_2, tetramethylguanidine, toluene, 0 °C.

most adequate synthetic segment was found to be (*S*)-(+)-2-(2-bromo-1-methylethyl)-1,3-dioxolane **47**.

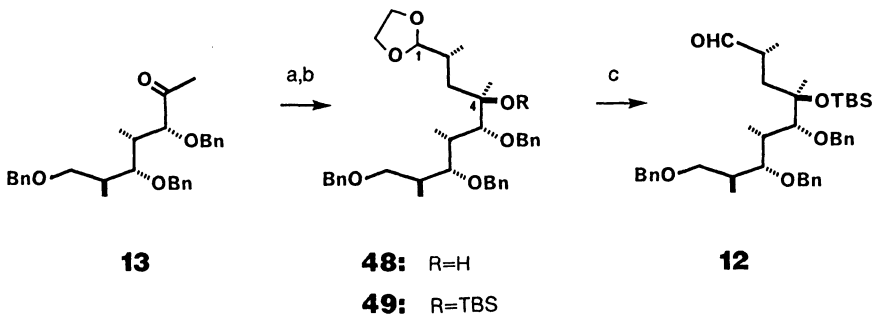
As detailed below (Scheme 11), **47** was efficiently constructed from the known aldehyde **44**,[16] which in turn was prepared from the commercially available methyl (*S*)-(+)-3-hydroxy-2-methylpropionate **39**. Tritylation of **39** followed by $LiAlH_4$ reduction of the resulting unpurified **40** gave the alcohol **41**. Benzylation of **41** with NaH and benzyl bromide in THF gave **42**, which was hydrolyzed with Amberlyst 15 in methanol to afford the alcohol **43**. Swern oxidation of **43** gave the aldehyde **44**, which was directly acetalized with ethylene glycol and *p*-toluenesulfonic acid in acetonitrile to provide **45**. After hydrogenolysis of **45**, the resulting alcohol **46** was transformed into the desired bromide **47** by treating with ethyl bromid-triphenylphosphine and diethyl azodicarboxylate[17] in THF in a 49% overall yield from **39**.

The methyl ketone **13** was treated in diethyl ether with an excess Grignard reagent prepared from 13 equiv of magnesium and 4.3 equiv of **47** to afford the alcohol **48** and its C4-epimer in 79% and 8% isolated yield, respectively (Scheme 12). The configuration at the newly formed C4-stereocenter was assumed to be (*R*) by considering the α-chelation controlled Grignard addition reaction,[9] and established at a later stage. Thus obtained **48** was silylated with *t*-butyldimethylsilyl triflate (TBSOTf) and 2,6-lutidine in CH_2Cl_2 to give **49** in 89% yield. The last step in the synthesis of the aldehyde **12** was to remove the acetal protecting group in **49**. This transformation proved to be troublesome to some extent. Among a wide variety of conditions employed, tin(II) chloride-acetone combination gave satisfactory yield of **12** (72%).

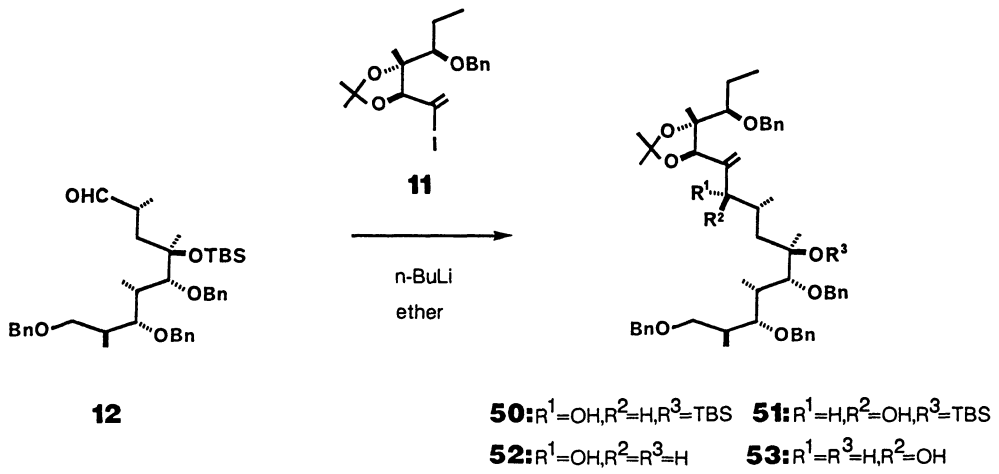
Preparation of Polyol Derivative 56. The stage was now set for us to examine the feasibility of the stereocontrolled coupling between **11** and **12** (Scheme 13). A 1.9 M ethereal solution (1 M=1 mol dm^{-3}) of **11** (3 equiv) was lithiated with 3 equiv of butyllithium at −100 °C for 15 min under argon. To this solution was added a 0.3 M etherial solution of **12** (1 equiv) and stirred at −100 °C for 1 h. Quenching with saturated aqueous NH_4Cl followed by chromatographic isolation afforded the major coupling product **50** (ca. 50%



Scheme 11. (a) TrCl, Et_3N, DMAP, CH_2Cl_2; (b) $LiAlH_4$, THF; (c) NaH, BnBr, THF; (d) Amberlyst 15, MeOH, 50 °C; (e) $(COCl)_2$, DMSO, CH_2Cl_2, Et_3N, −78 °C; (f) $HOCH_2CH_2OH$, *p*-TSA, MeCN; (g) H_2/Pd, MeOH; (h) EtBr, Ph_3P, DEAD, THF.



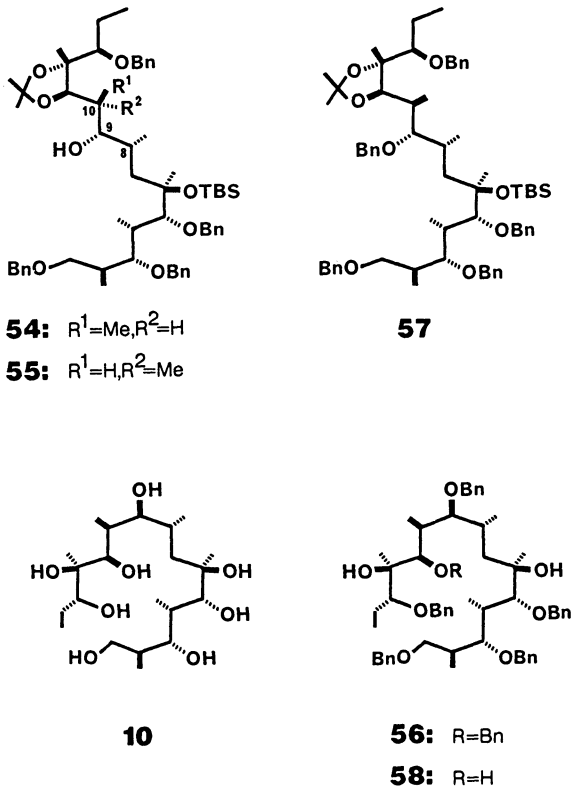
Scheme 12. (a) **47**, Mg, ether, then add **13**; (b) TBSOTf, 2,6-lutidine, CH_2Cl_2; (c) $SnCl_2$, acetone.



Scheme 13.

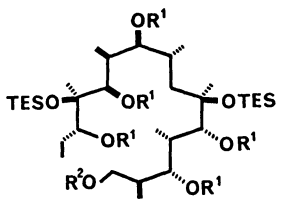
yield from **12**) contaminated with a by-product, probably one of the by-products originated from **11**, and the pure minor one **51** (10% yield from **12**). The yield of **50** was assumed based on the yield of **51** and on a ratio (5 : 1) of the corresponding separable desilylation products (**52** and **53**), derived from the crude mixture of **50** and **51**. The next step was homogeneous hydrogenation of the desired Cram type coupling product **50**. Usually this type of reaction is carried out smoothly at room temperature and 1 atm H_2 in benzene solution with 0.25 equiv of [ClRh(Ph_3P)$_3$] as catalyst for several hours.[8] However, hydrogenation of **50** under the usual conditions was very slow. After several experiments, we found that the crude **50** was homogeneously hydrogenated in benezene with 0.25 equiv of [ClRh(Ph_3P)$_3$] under 50 atm H_2 at 24 °C for 5 d to afford **54** 41% from **12**) and its C10-epimer **55** (7% from **12**). Hydrogenation of **50** was also carried out using [Rh(NBD(DIPHO-4)]BF_4[18] instead of the Wilkinson's catalyst, but no improvements in the reaction rate and the isomeric ratio were observed. The configuration of **54** was confirmed by the following manner. After desilylation and deacetonization of **54** with 46% aqueous HF-acetonitrile, the resulting alcohol was benzylated with 4 equiv of benzyl chloride and 8 equiv of KOH in DMF at 24 °C for 5 h to give **56** in 81% yield. Direct benzylation of **54** gave **57** in 84% yield. On the other hand, $LiAlH_4$ reduction of the naturally derived **2**[19,20] gave **10** in 72% yield, which was benzylated to afford **56** and **58**. The ratio of **56** and **58** depended on the reaction conditions used for benzylation (see Experimental section).

Acetonization of **58** followed by silylation provided **57**. The synthetic **56** and **57** were spectroscopically and chromatographycally identical with the corresponding materials obtained by the aforesaid transformations starting from naturally derived **2**. Consequently the structure showed for **48**, **49**, **12**, **50**, **54**, and **55** were determined and the anti-selectiveity in homogeneous hydrogenation of the "Cram" product **50** was also confirmed.

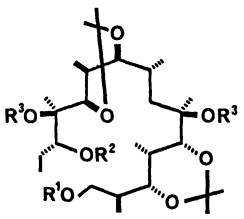


Preparation of Erythronolide A. Having thus prepared the polyol derivative **56**, which has the entire chiral sequence of (9*S*)-9-deoxo-9-hydroxyerythronolide A (**2**) in the proper absolute configuration, attention was directed toward the facile transformation of **56** into **2**. Protection of the tertiary alcohol function of **56** with triethylsilyl triflate and 2,6-lutidine provided all protected polyol **59** in 93% yield. Hydrogenolysis of **59** over palladium-black in ethanol furnished **60**. After the protection of the primary alcohol function of **60** with TBDPSCl and imidazole,

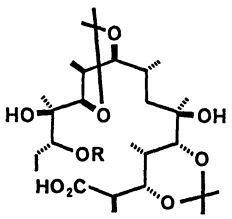
selective acetonization[4] of the resulting **61** with 2-methoxypropene and pyridinium *p*-toluenesulfonate (PPTS) in CH_2Cl_2 afforded the desired 3,5:9,11-



59: $R^1=R^2=Bn$
60: $R^1=R^2=H$
61: $R^1=H, R^2=TBDPS$



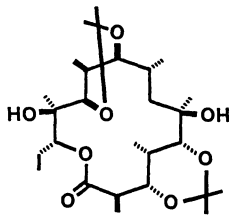
62: $R^1=TBDPS, R^2=H, R^3=TES$
63: $R^1=TBDPS, R^2=Ac, R^3=TES$
64: $R^1=R^3=H, R^2=Ac$



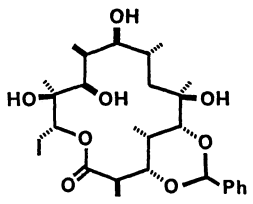
65: R=Ac
4: R=H

diacetonide **62** in 64% yield from **59**. The standard acetylation of **62** followed by desilylation of the acetate **63** with tetrabutylammonium fluoride (TBAF) in THF at 60 °C furnished **64** in 70% yield from **62**. Oxidation of **64** with 4 equiv of PDC in the presence of 3A Molecular Sieves in DMF afforded the acid **65**, which was deacetylated with 1-M NaOH-dioxane (1:1) to give the seco-acid 3,5:9,11-diacetonide **4** in 82% yield. Treatment of **4** with 1.5 equiv of triphenylphosphine and 1.5 equiv of di-(2-pyridyl) disulfide in THF yielded the 2-pyridinethiol ester, which was purified by silica-gel column chromatography (95% yield). This ester was subjected to lactonization by the modified Corey-Nicolaou method[7] using toluene instead of xylene to give the intramolecular cyclization product **66** in 65% yield. The protected lactone **66** was treated with 50% aqueous acetic acid to afford (9*S*)-9-deoxo-9-hydroxyerythronolide A (**2**) in quantitative yield. The synthetic sample of **2** was identical in all respects with a sample of the naturally derived **2**.[20] The overall yield of **2** from **56** was 21.1% in 11 steps.

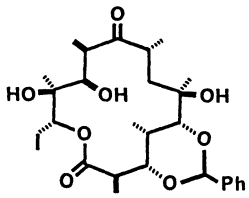
The lactone **2** was led to **1** by the straightforward transformation. Selective 3,5-*O*-benzylidenation[3] of **2** with benzaldehyde dimethyl acetal and 10-camphorsulfonic acid (CSA) in CH_2Cl_2 gave **67** in 80% yield. Selective oxidation[21] of **67** followed by



66



67



68

hydrogenolysis of the resulting ketone **68** with palladium-black in methanol furnished erythronolide A (**1**) in 66% yield. The synthetic sample of **1** was identical in all respects with naturally derived erythronolide A.[22]

Thus the new synthetic route to erythlonolide A through (9*S*)-9-deoxo-9-hydroxyerythronolide A from **13** was completed.

Experimental

Melting points were determined on a micro hot-stage Yanaco MP-S3 and were uncorrected. Optical rotations were measured on a JASCO DIP-360 photoelectric polarimeter in chloroform unless otherwise noted. IR spectra were recorded on a Hitachi Perkin-Elmer 225 spectrometer and ^1H NMR spectra on either a Varian EM-390 or a Bruker WM 250 spectrometer in $CDCl_3$ using TMS as internal standard. Mass spectra were recorded on Hitachi M-80 mass spectrometer. Silica-gel TLC and column chromatography were performed on Merck TLC 60F-254 and Merck Kieselgel 60, respectively. In general, organic solvents were purified and dried by the appropriate procedure, and evaporation and concentration were carried out under reduced pressure below 30 °C, unless otherwise noted.

2,3-*O*-Isopropylidene-D-ribofuranose (14).[11] To a stirred solution of D-ribose (25.0 g, 0.167 mol) and 2,2-dimethoxypropane (21.5 ml, 0.175 mol) in dry acetone (500 ml) at 0 °C was added concd H_2SO_4 (0.025 ml). After being stirred in a refrigerator (5 °C) for 20 h, the reaction mixture was neutralized with solid Na_2CO_3 and the insoluble materials were filtered off and washed with acetone. The combined filtrate and washings were concentrated. The residue was chromatographed on silica gel (1.6 kg) with 10:1 chloroform-methanol to afford **14** [26.2 g, 83%; R_f=0.39 (10:1 chloroform-methanol)] as a practically pure pale yellow syrup and 3,4-*O*-isopropylidene-D-ribopyranose [1.70 g, 5.5%; R_f=0.26 (10:1 chloroform-methanol)] as colorless needles.

2,3-*O*-Isopropylidene-1-*C*-methyl-D-allitol (15). To a stirred solution of methylmagnesium iodide [prepared from 33.5 g 1.38 mol) of magnesium powder and 94.3 ml (1.51 mol) of iodomethane] in dry diethyl ether (1050 ml) at 0 °C was added dropwise a solution of **14** (26.2 g, 0.138 mol) in dry diethyl ether (524 ml). The reaction mixture was stirred at 23 °C for 3.5 h. Saturated aqueous NH_4Cl (100 ml) was added to the ice-cooled reaction mixture. The phases were separated and the aqueous layer was thoroughly extracted with ethyl acetate. The combined organic layers were washed with saturated aqueous NaCl, dried, and concentrated. The residue was chromatographed on silica gel (1.7 kg) with 1 : 4 benzene-ethyl acetate to afford **15** (26.5 g, 73%) as colorless crystals and 2.20 g (7.9%) of **14** was recovered: R_f=0.28 (1 : 4 benzene-ethyl acetate); mp 72—73 °C (needles, ether-hexane); $[\alpha]_D^{15}$ +27.5° (*c* 1.00); ^{1}H NMR (90 MHz) δ=1.32 (3H, d, 1-Me, *J*=6.0 Hz), 1.35 and 1.39 (each 3H, each s, CMe_2), 3.3—4.9 (9H, m).

Found: C, 52.64; H, 8.59%. Calcd for $C_9H_{18}O_5$: C, 52.41; H, 8.80%.

1-Deoxy-3,4-*O*-isopropylidene-D-ribitol (16). To a stirred solution of **15** (19.0 g, 0.0921 mol) in acetone (380 ml) at 0 °C was added dropwise a solution of $NaIO_4$ (59.1 g, 0.276 mol) in water (590 ml). The reaction mixture was stirred at 24 °C for 1 h. Acetone was removed under reduced pressure and the aqueous layer was extracted with ethyl acetate. The combined organic layers were washed with saturated aqueous NaCl, dried, and concentrated. The residue (16.0 g) was dissolved in dry THF (640 ml) and then cooled to 0 °C. To this was added portionwise $LiAlH_4$ (3.83 g, 0.101 mol) and the reaction mixture was stirred at 20 °C for 20 min. Wet diethyl ether (300 ml) and water (200 ml) were added carefully to the ice-cooled reaction mixture and the insoluble materials were filtered through Celite and washed with ethyl acetate. The combined filtrate and washings were concentrated and the residue was chromatographed on silica gel (330 g) with 1 : 1 benzene-ethyl acetate to afford **16** (15.8 g, 97.5%) as colorless crystals: R_f=0.34 (1 : 1 benzene-ethyl acetate); mp 47—49 °C (cubes, ether-petroleum ether); ^{1}H NMR (90 MHz) δ=1.31 (3H, d, 3×H-1, *J*=6.0 Hz), 1.34 and 1.39 (each 3H, each s, CMe_2), 2.90—3.60 (2H, br, 2×OH), 4.26 (1H, dq, H-2, $J_{2,3}$=7.2 Hz).

Found: C, 54.64; H, 8.93%. Calcd for $C_8H_{16}O_4$: C, 54.53; H, 9.15%.

5-*O*-(*t*-Butyldimethylsilyl)-1-deoxy-3,4-*O*-isopropylidene-D-ribitol (17). To a stirred solution of **16** (15.7 g, 89.1 mmol) in dry DMF (157 ml) were added at 0 °C imidazole (7.87 g, 116 mmol) and *t*-butylchlorodiphenylsilane (27.8 ml, 107 mmol). The reaction mixture was stirred at 24 °C for 2 h 40 min. The reaction mixture was poured into cold water (150 ml) and the mixture was extracted with ethyl acetate. The extracts were washed with saturated aqueous NaCl, dried, and concentrated. The residue was chromatographed on silica gel (1.5 kg) with 25 : 1 benzene-ethyl acetate to afford **17** (35.6 g, 97%) as a colorless syrup: R_f=0.41 (25:1 benzene-ethyl acetate); $[\alpha]_D^{19}$ +8.0°, $[\alpha]_{365}^{19}$ +29° (*c* 1.12); ^{1}H NMR (90 MHz) δ=1.07 (9H, s, *t*-Bu), 1.28 and 1.30 (each 3H, each s, CMe_2), 1.34 (3H, d, 3×H-1, *J*=7.0 Hz), 3.58 (1H, dd, H-5, J_{gem}=10.2 and $J_{4,5}$=3.9 Hz), 3.81 (1H, d, H-5′, $J_{4,5'}$=0 Hz), 3.95—4.5 (4H, m), 7.3—7.8 (10H, m, 2×Ph).

Found: C, 69.24; H, 8.05%. Calcd for $C_{24}H_{34}O_4Si$: C, 69.52; H, 8.27%.

5-*O*-(*t*-Butyldiphenylsilyl)-1-deoxy-3,4-*O*-isopropylidene-*keto*-D-*erythro*-2-pentulose (18). To a stirred suspension of PCC (71.7 g, 332 mmol) and Molecular Sieves 3A powder (MS3AP) (83.1 g) in dry CH_2Cl_2 (208 ml) was added dropwise at 0 °C a solution of **17** (34.5 g, 83.2 mmol) in dry CH_2Cl_2 (138 ml). After 2 h at 22 °C, the reaction mixture was diluted with diethyl ether (200 ml) and the resulting suspension was transferred to a column filled with silica gel (930 g). The column was eluted with diethyl ether and the eluant was concentrated to give practically pure sample of **18** (34.3 g, 100%) as a pale yellow syrup. A portion of this was chromatographed on silica gel with 40 : 1 benzene-ethyl acetate to afford an analytically pure sample of **18**: R_f=0.55 (25 : 1 benzene-ethyl acetate); $[\alpha]_D^{22}$ +49.0° (*c* 0.97); IR ($CHCl_3$) 1712 cm^{-1}; ^{1}H NMR (90 MHz) δ=1.03 (9H, s, *t*-Bu), 1.37 and 1.57 (each 3H, each s, CMe_2), 2.27 (3H, s, 3×H-1), 3.72 (2H, d, 2×H-5, $J_{4,5}$=3.0 Hz), 4.30—4.60 (2H, m), 7.3—7.8 (10H, m, 2×Ph).

Found: C, 69.60; H, 7.63%. Calcd for $C_{24}H_{32}O_4Si$: C, 69.87; H, 7.82%.

$LiAlH_4$ Reduction of 18: To a stirred suspension of $LiAlH_4$ (50.0 mg, 1.32 mmol) in dry diethyl ether (1 ml) at −78 °C was added a solution of **18** (543 mg, 1.32 mmol) in dry diethyl ether (5.4 ml). After 2 h at −78 °C, wet diethyl ether was added to the reaction mixture. The insoluble materials were filtered through Celite and washed with ethyl acetate. The combined filtrate and washings were concentrated and the residue was chromatographed on silica gel (40 g) with 25 : 1 benzene-ethyl acetate to afford **17** (154 mg, 28%) and **19** (313 mg, 57%) as colorless syrups. **19**: R_f=0.27 (25 : 1 benzene-ethyl acetate); $[\alpha]_D^{20}$ 0°, $[\alpha]_{365}^{20}$ +15° (*c* 1.01); ^{1}H NMR (90 MHz) δ=1.08 (9H, s, *t*-Bu), 1.27 (3H, d, 3×H-1, *J*=4.5 Hz), 1.35 and 1.43 (each 3H, each s, CMe_2), 2.62 (1H, d, OH, *J*=3.0 Hz), 3.6—4.3 (5H, m), 7.3—7.8 (10H, m, 2×Ph).

Found: C, 69.80; H, 8.21%. Calcd for $C_{24}H_{34}O_4Si$: C, 69.52; H, 8.27%.

Transformation of 19 to (*R*)-2-Benzyloxypropinoic Acid (21). To a stirred solution of **19** (122 mg, 0.294 mmol) in dry THF (0.61 ml) at 0 °C was added NaH (19 mg, 0.44 mmol; 55% dispersion in mineral oil). After 0.5 h at room temperature, the mixture was cooled to 0 °C and benzyl bromide (0.052 ml, 0.44 mmol) was added. After being stirred at room temperature for 8 h, ice-water was added and the mixture was extracted with ethyl acetate. The extracts were washed with saturated aqueous NaCl, dried and concentrated. The crude residual syrup (148 mg) was dissolved in THF (1.5 ml) and cooled to 0 °C. 1M solution of TBAF in THF (0.585 ml) was added to the above solution. After 2 h at 0 °C, ice-water was added and the mixture was extracted with ethyl acetate. The extracts were washed with saturated aqueous NaCl, dried, and concentrated. The residue was chromatographed on silica gel (2.5 g) with 3 : 1 toluene-ethyl acetate to afford **20** (70.7 mg, 91% from **19**) as a colorless syrup, which was dissolved in 75% aqueous acetic acid (1.4 ml) and the mixture was heated at 80 °C for 10 h. The reaction mixture was concentrated and the residual triol (60.1 mg) was dissolved in acetone (1.4 ml) and cooled to 0 °C. A solution of $NaIO_4$ (125 mg, 0.584 mmol) in water (1.25 ml) was added and the mixture was stirred at 24 °C for 3 h. Acetone was removed under reduced pressure (50 mmHg; 1 mmHg≈133.322 Pa, 0 °C) and the aqueous phase was extracted with diethyl ether. The extracts were washed with saturated aqueous NaCl, dried, and concentrated. The residue was chromatographed on silica gel (0.5 g) with

6:1 hexane-ethyl acetate to afford (*R*)-2-benzyloxypropanal (43.6 mg, 100%) as a colorless syrup [^{1}H NMR (90 MHz) δ=1.31 (3H, d, 3×H-3, J=6.9 Hz), 3.88 (1H, dq, H-2, J=1.5 and 6.9 Hz) , 4.63 (2H, s, OC$\underline{H}_2$Ph), 7.37 (5H, s, Ph), and 9.69 (1H, d, CHO, J=1.5 Hz)]. This aldehyde (43.6 mg) was dissolved in a solution of CrO_3 in acetic acid and pyridine (3.5 ml; prepared from 1 g of CrO_3, 30 ml of acetic acid, and 1 ml of pyridine). After 3 h at 23 °C, ice-water was added and the mixture was extracted with diethyl ether. The etracts were washed with saturated aqueous $KHSO_4$, NaCl, dried, and concentrated (0 °C, 50 mmHg). The residue was chromatographed on silica gal (5 g) with 30:10:1 hexane-ethyl acetate-acetic acid to afford **21** (24.0 mg, 50% from **20**) as a colorless syrup: R_f=0.21 (30:10:1 hexane-ethyl acetate-acetic acid); $[\alpha]_D^{18}$ +54°, $[\alpha]_{546}^{18}$ +85° (c 2.30, benzene) [(*S*)-(−)-2-benzyloxypropionic acid: $[\alpha]_{546}$ −78.6° (c 2.3, benzene)[12]]; ^{1}H NMR (90 MHz) δ=1.47 (3H, d, 3×H-3, J=7.2 Hz), 4.12 (1H, q, H-2, J=7.2 Hz), 4.52 and 4.71 (each 1H, ABq, J=12.0 Hz), 7.37 (5H, s, Ph), and 8.0—8.4 (1H, br, COOH).

5-*O*-(*t*-Butyldiphenylsilyl)-1-deoxy-3,4-*O*-isopropylidene-2-*C*-vinyl-D-ribitol (22) and arabinitol (23). To a stirred solution of vinylmagnesium bromide [prepared from 343 mg (14.1 mmol) of magnesium powder and 0.99 ml (14.0 mmol) of vinyl bromide] in dry THF (36 ml) at 0 °C was added dropwise a solution of **18** (582 mg, 1.41 mmol) in dry THF (12 ml). After 3 h at room temperature, water was carefully added to the ice-cooled reaction mixture. The insoluble materials were filtered through Celite and washed with ethyl acetate. The combined filtrate and washings were washed with saturated aqueous NaCl, dried, and concentrated. The residue was chromatographed on silica gel (50 g) with 10:1 hexane-ethyl acetate to afford **22** (527 mg, 85%) and a mixture of **22** and **23** (50 mg, 8.0%) as colorless syrups. The ratio of **22** and **23** of this mixture by ^{1}H NMR was 5.7:1. Therefore, the ratio of **22** and **23** was 77:1. **22**: R_f=0.37 (10:1 hexane-ethyl acetate); $[\alpha]_D^{24}$ +32.5° (c 1.00); ^{1}H NMR (90 MHz) δ=1.06 (9H, s, t-Bu), 1.30, 1.35, and 1.37 (each 3H, each s, 3×Me), 3.54 (1H, dd, H-5, $J_{4,5}$=3.6 and J_{gem}=10.5 Hz), 3.95—4.4 (4H, m) , 5.12 (1H, dd, C=CH (cis) J=1.8 and 10.5 Hz), 5.52 (1H, dd, C=CH (trans), J=1.8 and 17.7 Hz), 6.36 (1H, dd, C$\underline{H}$=CH$_2$), and 7.3—7.75 (10H, m, 2×Ph) [^{1}H NMR (90 MHz) of the mixture of **22** and **23** showed the following additional peaks; 5.06 (dd, C=CH) (cis), J=1.8 and 10.5 Hz), 5.31 (dd, C=CH (trans), J=1.8 and 17.7 Hz), 5.98 (dd, C$\underline{H}$=CH$_2$), which were attributed to **23**].

Found: C, 70.27; H, 8.05%. Calcd for $C_{26}H_{36}O_4Si$: C, 70.55; H, 8.20%.

Transformation of 22 to (4*S*,5*R*)-(−)-5-Ethyl-2,2,5-trimethyl-1,3-dioxolane-4-carboxylic Acid (25). A mixture of **22** (147 mg, 0.334 mmol), [ClRh(Ph$_3$P)$_3$] (61.8 mg, 0.668 mmol), and benzene (7.4 ml) was stirred at 23 °C for 4 h under atmospheric pressure of H_2. The reaction mixture was concentrated and the residue was passed through Florisil (11 g) with diethyl ether. The eluant was concentrated to give a colorless syrup (137 mg, 93%) [R_f=0.47 (10:1 toluene-ethyl acetate); ^{1}H NMR (90 MHz) δ=0.96 (3H, t, J=7.5 Hz), 1.08 (9H, s, t-Bu), 1.28, 1.32, and 1.37 (each 3H, each s, 3×Me), 1.71 (2H, q), 3.33 (1H, s, OH), 3.59 (1H, dd, J=3.9 and 10.2 Hz), 3.9—4.35 (3H, m), and 7.3—7.8 (10H, m, 2×Ph)]. To a stirred solution of this syrup (130 mg, 0.294 mmol) in dry CH_2Cl_2 (1.3 ml) was added $ZnBr_2$ (66.4 mg, 0.295 mmol) at 0 °C and the mixture was stirred at 0 °C for 2 h. Saturated aqueous Na_2CO_3 solution was added and the mixture was extracted with ethyl acetate. The extracts were washed with saturated aqueous NaCl, dried, and concentrated. The residue was chromatographed on silica gel (15 g) with 20:1 toluene-ethyl acetate to afford **24** (108 mg, 83%) as a colorless syrup [R_f=0.44 (30:1 toluene-acetone); ^{1}H NMR (90 MHz) δ=1.00 (3H, t, J=7.5 Hz), 1.09 (9H, s, t-Bu), 1.24, 1.30, and 1.36 (each 3H, each s, 3×Me), 1.50—1.85 (2H, m), 2.48 (1H, d, OH, J=5.7 Hz), 3.6—3.95 (4H, m), and 7.3—7.8 (10H, m, 2×Ph)]. To a stirred solution of **24** (104 mg, 0.235 mmol) in dry THF (1.0 ml) was added at 0 °C TBAF (0.47 ml). After 1.5 h at 0 °C, ice-water was added and the mixture was extracted with ethyl acetate. The extracts were washed with saturated aqueous NaCl, dried, and concentrated. The residue was chromatagraphed on silica gel (5 g) with 3.5:1 chloroform-acetone to give a colorless syrup (47.8 mg, 99%) [R_f=0.48 (1:3 toluene-ethyl acetate); ^{1}H NMR (90 MHz) δ=0.98 (3H, t, J=7.5 Hz), 1.23, 1.33, and 1.40 (each 3H, each s, 3×Me), 1.5—1.85 (2H, m), 2.5—2.85 (2H, br, 2×OH), 3.6—4.0 (4H, m)]. To a stirred solution of this syrup (45.6 mg, 0.223 mmol) in acetone (1.4 ml) was added at 0 °C a solution of $NaIO_4$ (95.5 mg, 0.446 mmol) in water (1 ml). After 1 h at 26 °C, acetone was removed by evaporation and the residue was extracted with ethyl acetate. The extracts were washed with saturated aqueous NaCl, dried, and concentrated to afford an aldehyde (12.0 mg, 31%; the low yield might be attributed to the volatility of the sample.) as a colorless syrup [R_f=0.76 (3:1 chloroform-acetone); ^{1}H NMR (90 MHz) δ=0.98 (3H, t, J=7.5 Hz), 1.16, 1.38, and 1.54 (each 3H, each s, 3×Me), 1.5—1.85 (2H, m), 4.12 (1H, d, J=2.0 Hz), and 9.75 (1H, d, J=2.0 Hz)]. To a solution of this aldehyde (12.0 mg, 0.070 mmol) in dioxane (0.3 ml) were added at 27 °C water (0.1 ml), K_2CO_3 (60.9 mg, 0.44 mmol), a solution of $KHCO_3$ (44.2 mg, 0.44 mmol) in water (0.49 ml), iodine (52.0 mg, 0.200 mmol), and a solution of KI (68.6 mg, 0.41 mmol) in water (0.06 ml), successively. After 2 h at 27 °C, solid $Na_2S_2O_3$ (102 mg, 0.41 mmol) was added and the mixture was extracted with diethyl ether. The aqueous phase was acidified (pH 2—3) with 10% aqueous H_2SO_4 under ice-cooling and immediately extracted with chloroform. The extracts were washed with saturated aqueous NaCl, dried, and concentrated to afford almost pure sample of **25** (6.8 mg, 52%) as colorless crystals: R_f=0.30 (80:5:1 chloroform-ethanol-acetic acid); $[\alpha]_D^{18}$ −27°, (c 0.84), ^{1}H NMR 90 MHz) δ=1.02 (3H, t, J=7.5 Hz), 1.22, 1.39, and 1.54 (each 3H, each s, 3×Me), 1.6—2.0 (2H, m), 4.43 (1H, s), and 8.2—8.65 (1H, br, COOH). The ^{1}H NMR of the authentic (+)-**26**[13] [$[\alpha]_D^{20}$ +26°, (c 0.84)] was identical with the above one.

3-*O*-Benzyl-7-*O*-(*t*-butyldiphenylsilyl)-1,2-dideoxy-5,6-*O*-isopropylidene-4-*C*-methyl-D-*manno*-heptitol (31). A solution of **22** (0.850 g, 1.93 mmol) in dry CH_2Cl_2 (43 ml) was stirred at −78 °C under bubbling with ca. 2% O_3 in O_2 (4300 ml, ca. 3.8 mmol). Dimethyl sulfide (1.42 ml, 19.3 mmol) was added and the mixture was warmed gradually to room temperature. The mixture was washed with water and saturated aqueous NaCl, dried, and concentrated. The residue was chromatographed on silica gel (130 g) with 5:1 hexane-ethyl acetate to afford an aldehyde (0.620 g, 73%) as a colorless syrup [^{1}H NMR (90 MHz) δ=1.09 (9H, s), 1.29 (3H, s), 1.37 (3H, s), 1.40 (3H, s), 9.81 (1H, s)]. To a stirred solution of ethylmagnesium bromide [prepared from magnesium powder (0.27 g, 11 mmol) and ethyl bromide (0.84 ml, 11 mmol) in dry diethyl ether (19 ml) at 0 °C was added a

solution of the above aldehyde (0.620 g, 1.40 mmol) in dry diethyl ether (19 ml). After 1.5 h at room temperature, $Na_2SO_4 \cdot 10H_2O$ was added carefully to the ice-cooled reaction mixture. The insoluble materials were filtered through Celite and washed with ethyl acetate. The combined filtrate and washings were washed with saturated aqueous NaCl, dried, and concentrated. The residue was chromatographed on silica gel (35 g) with 4 : 1 hexane-ethyl acetate to afford an inseparable mixture of **27** and **28** (0.580 g, 88%) as a colorless syrup. To a solution of the above mixture in dry THF (2.9 ml) were added at 0 °C NaH (65 mg, 2.70 mmol) and benzyl bromide (0.22 ml, 1.84 mmol) and the mixture was stirred at 21 °C for 4 h. Ice-water was added and the mixture was extracted with ethyl acetate. The extracts were washed with saturated aqueous NaCl, dried, and concentrated. The residue was chromatographed on silica gel (28 g) with 20 : 1 hexane-ethyl acetate to afford **31** (380 mg, 55%) as a colorless syrup. The column was further eluted with 4 : 1 hexane-ethyl acetate to afford a mixture of **27** and **28** (162 mg, 28%). **31**: R_f=0.43 (6 : 1 hexane-ethyl acetate); $[\alpha]_D^{29}$ +7.5°, $[\alpha]_{365}^{29}$ +27.5° (*c* 1.00); ^{1}H NMR (90 MHz) δ=1.08 (12H, s, *t*-Bu involving 3×H-1), 1.29 and 1.39 (6H and 3H, each s, 4-Me and CMe_2), 1.5—2.1 (2H, m), 3.5—4.5 (6H, m), 4.72 (2H, s, $OC\underline{H}_2Ph$), and 7.2—8.0 (15H, m, 3×Ph).

Found: C, 72.27; H, 8.09%. Calcd for $C_{34}H_{46}O_5Si$: C, 72.56; H, 8.24%.

Desilylation of a Mixture of 27 and 28. (a) The mixture of **27** and **28** (12.4 mg, 0.0262 mmol) obtained from the Grignard reaction was dissolved in THF (0.124 ml) and solution of 1 M TBAF in THF (0.053 ml) was added under ice-cooling. After 1 h at 0 °C, ice-water was added and the mixture was extracted with ethyl acetate. The extracts were washed with saturated aqueous NaCl, dried, and concentrated. The residue was chromatographed on silica gel (0.75 g) with 25 : 1 chloroform-methanol to afford **29** (3.6 mg, 59%) and **30** (2.3 mg, 37%) as colorless syrups. **29**: R_f=0.45 (25:1 chloroform-methanol); ^{1}H NMR (90 MHz) δ=1.0—1.3 (6H, m), 1.26, 1.37, and 1.49 (each 3H, each s, 4-Me and CMe_2). **30**: R_f=0.36 (25 : 1 chloroform-methanol); ^{1}H NMR (90 MHz) δ=0.9—1.2 (6H, m), 1.22, 1.37, and 1.49 (each 3H, each s, 4-Me and CMe_2).

(b) The mixture of **27** and **28** recovered after the benzylation reaction was desilylated as in the case of (a) to afford **29** and **30** in a ratio of 1:4.9.

(c) The mixture of **27** and **28** prepared from ketone **35** by $LiAlH_4$ reduction (vide infra) was desilylated as in the case of (a) to afford **29** and **30** in a ratio of 5 : 1.

Transformation of 31 to (*R*)-2-Methylpentane-2,3-diol (33). 1 M TBAF in THF (0.314 ml) was added to a stirred, ice-cooled solution of **31** (88.5 mg, 0.157 mmol), in dry THF (0.89 ml). After 1 h at 0 °C, ice-water was added and the mixture was extracted with ethyl acetate. The extracts were washed with saturated aqueous NaCl, dried, and concentrated. The residue was chromatographed on silica gel (5 g) with 1 : 1 hexane-ethyl acetate to afford a diol (49.1 mg, 96%) as colorless needles [mp 94.5—100.5 °C; R_f=0.15 (3 : 1, hexane-ethyl acetate); ^{1}H NMR (90 MHz) δ=1.04 (3H, t, 3×H-1, J=7.2 Hz), 1.23 (3H, s, 4-Me), 1.35 and 1.52 (each 3H, each s, CMe_2), 1.5—2.0 (2H, m) , 2.6—2.9 (2H, br, 2×OH), 3.47 (1H, dd, H-3, J=3.6 and 9.0 Hz), 3.7—3.85 (2H, m), 4.21 (1H, dt, H-6, $J_{6,7}$=6.0 Hz), 4.41 (1H, d, H-5, $J_{5,6}$=6.0 Hz), 4.68 (1H, s, $OC\underline{H}_2Ph$), and 7.35 (5H, s, Ph)]. A mixture of the above diol (45.0 mg, 0.139 mmol) and 50% aqueous acetic acid (0.9 ml) was heated at 115 °C for 2 h, then concentrated. The residue was chromatographed on silica gel (6 g) with 10 : 1 chloroform-methanol to afford a tetrol (37.5 mg, 95%) as colorless needles [mp 88—89.5 °C; R_f=0.19 (1:3 hexane-ethyl acetate); $[\alpha]_D^{24}$ +75° (*c* 1.00); ^{1}H NMR (90 MHz) δ=1.10 (3H, t, 3×H-1, J=7.0 Hz), 1.23 (3H, s, 4-Me), 1.5—1.9 (3H, m) , 2.7—3.0 (2H, br, 2×OH), 3.4—3.9 (6H, m), 4.64 and 4.76 (each 1H, ABq, $OC\underline{H}_2Ph$, J=10.5 Hz), and 7.35 (5H, s, Ph)]. A solution of $NaIO_4$ (65.3 mg, 0.305 mmol) in water (0.65 ml) was added to a stirred, ice-cooled solution of the above tetrol (26.3 mg, 0.0925 mmol) in acetone (0.53 ml). After 1.5 h at room temperature, the reaction mixture was filtered and the filtrate was concentrated. The residue was chromatographed on silica gel (1 g) with 30 : 1 toluene-ethyl acetate to afford **32** (14.9 mg, 84%) as a colorless syrup [^{1}H NMR (90 MHz) δ=0.95 (3H, t, 3×H-5, J=7.0 Hz), 1.68 (2H, dq, 2×H-4, $J_{3,4}$=$J_{4,5}$=7.0 Hz), 2.17 (3H, s, 3×H-1), 3.71 (1H, t, H-3), 4.47 and 4.60 (each 1H, ABq, $OC\underline{H}_2Ph$, J=12.0 Hz), and 7.38 (5H, s, Ph)]. A solution of **32** (13.4 mg, 0.0697 mmol) in dry diethyl ether (0.27 ml) was added to a solution of methylmagnesium iodide [prepared from magnesium powder (20.3 mg, 0.836 mmol) and iodomethane (0.0564 ml, 0.906 mmol)] in dry diethyl ether (0.58 ml) under ice-cooling. After 2 h at 20 °C, saturated aqueous NH_4Cl was added and the mixture was extracted with ethyl acetate. The extracts were washed with saturated aqueous NaCl, dried, and concentrated. The residue was chromatographed on silica gel (1 g) with 10 : 1 benzene-ethyl acetate to afford (*R*)-3-benzyloxy-2-methyl-2-pentanol (13.1 mg, 90%) as a colorless syrup [R_f=0.19 (20 : 1 benzene-ethyl acetate); $[\alpha]_D^{19}$ −7.7°, $[\alpha]_{365}^{19}$ −25.5° (*c* 0.98); ^{1}H NMR (90 MHz) δ=1.04 (3H, t, 3×H-5, J=6.3 Hz), 1.15 and 1.20 (each s, each 3H, 2-Me and 3×H-1), 1.4—1.8 (2H, m), 2.18 (1H, s, OH), 3.12 (1H, dd, H-3, J=4.5 and 6. 0 Hz), 4.61 and 4.73 (each 1H, ABq, $OC\underline{H}_2Ph$, J=10.5 Hz), and 7.35 (5H, s, Ph); Found: C, 74.72; H, 9.45%. Calcd for $C_{13}H_{20}O_2$: C, 74.96; H, 9.68%]. A mixture of the above alcohol (13.0 mg, 0.0624 mmol), palladium black, and *t*-BuOH (0.3 ml) was stirred at 28 °C for 0.5 h under bubbling with H_2. Catalyst was filtered off and the filtrate was concentrated to afford **33** (7.4 mg, 100%) as a colorless syrup: R_f=0.40 (10 : 1 chloroform-methanol); $[\alpha]_D^{18.5}$ +27.3° (*c* 1.10, ether) ; ^{1}H NMR (90 MHz) δ=1.03 (3H, t, 3×H-5, J=6.0 Hz), 1.15 and 1.20 (each 3H, each s, 3×H-1 and 2-Me), 2.45—2.65 (2H, br, 2×OH), 3.28 (1H, dd, H-3, J=3.0 and 9.0 Hz). The product **33** was proved to be the enantiomer of **34** by comparing its optical rotation with that of **34** [$[\alpha]_D$ −32.6° (*c* 1.10, diethyl ether)].[14]

7-*O*-(*t*-Butyldiphenylsilyl)-1,2-dideoxy-5,6-*O*-isopropylidene-4-*C*-methyl-*keto*-D-*arabino*-3-heptulose (35). To a mixture of **27** and **28** (0.720 g, 1.52 mmol), dry benzene (5 ml), dry DMSO (1.17 ml, 16.4 mmol), and dry pyridine (0.117 ml, 1.45 mmol) at 0 °C were successively added trifluoroacetic acid (0.062 ml, 0.81 mmol) and a solution of DCC (952 mg, 4.61 mmol) in dry benzene (3.24 ml). After 5 h at room temperature, the reaction mixture was filtered and the filtrate was washed with saturated aqueous $KHSO_4$, $NaHCO_3$, and NaCl solutions, dried, and concentrated. The residue was chromatographed on silica gel (85 g) with 10 : 1 pet. ether-diethyl ether to afford **35** (650 mg, 90%) as a colorless syrup: R_f=0.53 (10 : 1 toluene-ethyl acetate); $[\alpha]_D^{29}$ 0°, $[\alpha]_{365}^{29}$ −17.5° (*c* 1.00); IR (0.15 M in $CHCl_3$) 1713 cm^{-1}; ^{1}H NMR (90 MHz) δ=1.06 (3H, t, 3×H-1, J=7.5 Hz), 1.08

(9H, s, *t*-Bu), 1.27 and 1.36 (3H and 6H, each s, 4-Me and CMe_2), 2.69 (2H, q, 2×H-2), 3.65—4.45 (5H, m), and 7.3—7.85 (10H, m, 2×Ph).

Found: C, 68.68; H, 8.06%. Calcd for $C_{27}H_{38}O_5Si$: C, 68.90; H, 8.14%.

$LiAlH_4$ Reduction of 35 and Benzylation of the Resulting Mixture of 27 and 28. To a stirred suspension of $LiAlH_4$ (104 mg, 2.74 mmol) in dry diethyl ether (2.0 ml) at −78 °C was added a solution of **35** (1.25 g, 2.66 mmol) in dry diethyl ether (12 ml). After 2 h at −78 °C, wet diethyl ether was added to the reaction mixture and the mixture was warmed to room temperature. The insoluble materials were filtered off through Celite and washed with ethyl acetate. The combined filtrate and washings were concentrated and the residue was chromatographed on silica gel (35 g) with 6:1 toluene-ethyl acetate to afford a mixture of **27** and **28** (1.05 g, 83.6%). To a solution of this mixture in dry THF (5.3 ml) at 0 °C was added NaH (213 mg, 4.89 mmol, 55% dispersion in mineral oil). The mixture was stirred at 21 °C for 0.5 h. Benzyl bromide (0.40 ml, 3.36 mmol) was added to the above ice-cooled suspension and the mixture was stirred at 21 °C for 4.5 h. Ice was added and the mixture was extracted with ethyl acetate and the extracts were washed with saturated aqueous NaCl, dried, and concentrated. The residue was chromatographed on silica gel (120 g) with 20:1 hexane-ethyl acetate to afford **31** (845 mg, 68%) as a colorless syrup.

3-*O*-Benzyl-7-*O*-(*t*-butyldiphenylsilyl)-1,2-dideoxy-4,5-*O*-isopropylidene-4-*C*-methyl-D-*manno*-heptitol (36). To a stirred solution of **31** (1.47 g, 2.61 mmol) in dry acetone (37 ml) at 0 °C was added a solution of $FeCl_3$ (212 mg, 1.31 mmol) in dry acetone (7.4 ml). After 1 h at 29 °C, saturated aqueous $NaHCO_3$ was added to the reaction mixture. The insoluble materials were filtered through Celite and washed with ethyl acetate. The filtrate and washings were washed with saturated aqueous NaCl, dried, and concentrated. The residue was chromatographed on silica gel (75 g) with 100:1 toluene-acetone to afford **36** (1.39 g, 95%) as a colorless syrup: R_f=0.49 (60:1 toluene-ethyl acetate); $[\alpha]_D^{26}$ −17.5° (*c* 1.00); ^{1}H NMR (90 MHz) δ=1.06 (3H, t, 3×H-1, *J*=7.4 Hz), 1.08 (9H, s, *t*-Bu), 1.25 (3H, s, 4-Me), 1.31 and 1.36 (each 3H, each s, CMe_2), 1.73 (2H, q, 2×H-2), 3.38 (1H, dd, H-3, *J*=6.3 and 5.7 Hz), 3.6—4.25 (5H, m), 4.67 (2H, s, $OC\underline{H}_2Ph$), and 7.25—7.85 (15H, m, 3×Ph).

Found: C, 72.84; H, 8.11%. Calcd for $C_{34}H_{46}O_5Si$: C, 72.56; H, 8.24%.

3-*O*-Benzyl-1,2-dideoxy-4,5-isopropylidene-4-methyl-D-*manno*-heptitol (37). To a stirred solution of **36** (1.30 g, 2.31 mmol) in THF (13 ml) at 0 °C was added 1 M TBAF in THF (4.6 ml). After 1 h at 0 °C, ice was added and the mixture was extracted with chloroform. The extracts were washed with saturated aqueous NaCl, dried, and concentrated. The residue was chromatographed on silica gel (50 g) with 2:1 hexane-ethyl acetate to afford **37** (691 mg, 92%) as a colorless syrup: R_f=0.23 (6:1 hexane-ethyl acetate); $[\alpha]_D^{22}$ −45.0° (*c* 1.00); ^{1}H NMR (90 MHz) δ=1.10 (3H, t, 3×H-1, *J*=7.5 Hz), 1.23, 1.30, and 1.40 (each 3H, each s, 4-Me and CMe_2), 1.6—2.1 (3H, m, 2×H-2 and OH), 3.34 (1H, dd, H-3, *J*=5.5 and 5.5 Hz), 3.55—4.30 (5H, m), 4.53 and 4.76 (each 1H, ABq, $OC\underline{H}_2Ph$, *J*=10.8 Hz), 7.39 (5H, s, Ph).

Found: C, 66.52; H, 8.60%. Calcd for $C_{18}H_{24}O_5$: C, 66.64; H, 8.70%.

5-*O*-Benzyl-1,6,7-trideoxy-3,4-*O*-isopropylidene-4-*C*-methyl-keto-D-*arabino*-2-heptulose (38). To a solution of **37** (723 mg, 2.23 mmol) in acetone (14.5 ml) at 0 °C was added a solution of $NaIO_4$ (524 mg, 2.45 mmol) in water (5.2 ml). After 3 h at 27 °C, acetone was removed by evaporation and the residue was extracted with $CHCl_3$. The extracts were washed with saturated aqueous NaCl, dried, and concentrated. The residual aldehyde [652 mg, 100%; ^{1}H NMR (90 MHz) δ=4.45 (1H, s, H-2), 9.63 (1H, s, CHO)] was dissolved in dry diethyl ether (13 ml) and added to a stirred solution of methylmagnesium iodide [prepared from magnesium powder (0.54 g, 22 mmol) and iodomethane (1.53 ml, 24.6 mmol)] in dry diethyl ether (28 ml) under ice-cooling. After 2 h at 27 °C, $Na_2SO_4 \cdot 10H_2O$ was added to the ice-cooled reaction mixture and the insoluble materials were filtered off through Celite and washed with $CHCl_3$. The filtrate and washings were washed with saturated aqueous NaCl, dried, and concentrated. The residue was chromatographed on silica gel (70 g) with 6:1 hexane-ethyl acetate to afford **fr.1** (91.7 mg, 13.3%) and **fr.2** (531 mg, 77.3%) as colorless syrups, both of which are the desired alcohol: R_f=0.58 (fr. 1), 0.40 (fr.2) (4:1 hexane-ethyl acetate). This epimeric mixture (623 mg, 2.02 mmol) was dissolved in dry CH_2Cl_2 (2.5 ml) and added to a stirred suspension of PCC (1.72 g, 8.07 mmol), MS 3AP (2.02 g) in dry CH_2Cl_2 (5.0 ml) at 0 °C. The reaction mixture was stirred at 25 °C for 1.5 h. Diethyl ether (5 ml) was added and the suspension was transferred to a column filled with silica gel (23 g). The column was eluted with diethyl ether and the eluant was concentrated to give **38** (607 mg, 98%) as a colorless syrup: R_f=0.61 (6:1 hexane-ethyl acetate); $[\alpha]_D^{21}$ 0°, $[\alpha]_{365}^{21}$ +25.0° (*c* 1.00); IR ($CHCl_3$) 1720 cm^{-1}; ^{1}H NMR (90 MHz) δ=1.00 (3H, t, 3×H-7, *J*=7.0 Hz), 1.14 (3H s, 4-Me), 1.35 and 1.53 (each 3H, each s, CMe_2), 1.4—1.85 (2H, m), 2.23 (3H, s, 3×H-1), 3.38 (1H, dd, H-5, *J*=4.8 and 8.4 Hz), 4.51 (1H, s, H-3), 4.63 and 4.78 (each 1H, ABq, $OC\underline{H}_2Ph$, *J*=11.4 Hz), and 7.33 (5H, s, Ph).

Found: C, 70.44; H, 8.42%. Calcd for $C_{18}H_{26}O_4$: C, 70.56; H, 8.55%.

5-*O*-Benzyl-1,2,6,7-tetradeoxy-2-iodo-3,4-*O*-isopropylidene-4-*C*-methyl-D-*arabino*-1-heptenitol (11). To a stirred solution of **38** (520 mg, 1.70 mmol) in ethanol (0.58 ml) were added triethylamine (2.01 ml, 14.4 mmol) and $NH_2NH_2 \cdot H_2O$ (0.33 ml, 6.8 mmol). After 1 h at 70 °C, the reaction mixture was cooled to room temperature and diluted with CH_2Cl_2. The mixture was washed with water, saturated aqueous NaCl, dried, and concentrated. The residual pale yellow syrup (544 mg, 100%) was dissolved in dry toluene (19 ml) and added at 0 °C to a mixture of iodine (946 mg, 3.73 mmol), 1,1,3,3-tetramethylguanidine (10.6 ml, 84.5 mmol), and dry toluene (5.5 ml). After 0.5 h at 0 °C, the reaction mixture was diluted with diethyl ether, washed with saturated aqueous $Na_2S_2O_3$, 10% aqueous citric acid, and saturated aqueous NaCl, dried, and concentrated. The residue was chromatographed on silica gel (26 g) with 50:50:1 hexane-toluene-ethyl acetate to afford **11** (389 mg, 55%) as a colorless syrup: R_f=0.74 (6:1 hexane-ethyl acetate); $[\alpha]_D^{18.5}$ 0°, $[\alpha]_{365}^{18.5}$ −11.2° (*c* 1.12); ^{1}H NMR (90 MHz) δ=1.04 (3H, t, 3×H-7, *J*=7.2 Hz), 1.29 (3H, s, 4-Me), 1.37 and 1.52 (each 3H, each s, CMe_2), 1.55—1.7 (2H, m), 3.56 (1H, t, H-5, *J*=6.0 Hz), 4.52 (1H, s, H-3), 4.70 (2H, s, $OC\underline{H}_2Ph$), 6.08 and 6.62 (each 1H, each d, 2×H-1, *J*<1.0 Hz), and 7.32 (5H, s, Ph).

Found: C, 51.65; H, 5.87; I, 30.75%. Calcd for $C_{18}H_{25}O_3I$: C, 51.93; H, 6.05; I, 30.48%.

Methyl (*S*)-(+)-2-Methyl-3-triphenylmethoxypropionate

(40). A mixture of methyl (*S*)-(+)-3-hydroxy-2-methylpropionate (**39**) (2.00 g, 16.9 mmol), triphenylmethyl chloride (4.96 g, 17.8 mmol), triethylamine (3.54 ml, 25.4 mmol), DMAP (103 mg, 0.85 mmol), and dry CH_2Cl_2 (20 ml) was stirred at 23 °C for 15 h. The reaction mixture was poured into 50% aqueous NH_4Cl (20 ml). The phases were separated, and the aqueous layer was extracted with CH_2Cl_2 (20 ml×2). The combined organic layers were washed with saturated aqueous NaCl (20 ml), dried, and concentrated to give crude crystals (6.49 g, 100% up) of **40**, which was used without any further purification. A portion of this was chromatographed on silica gel with toluene to afford an analytically pure sample of **40**: mp 100—101 °C; R_f=0.38 (toluene); $[\alpha]_D^{31}$ +19.6° (*c* 1.00); IR (KBr) 1726 cm^{-1}; ^1H NMR (90 MHz) δ=1.13 (3H, d, 2-Me, *J*=6.6 Hz), 2.5—2.9 (1H, m, H-2), 3.05—3.45 (2H, m, 2×H-3), 3.70 (3H, s, OMe), and 7.1—7.55 (15H, m, Tr).

Found: C, 80.05; H, 6.78%. Calcd for $C_{24}H_{24}O_3$: C, 79.97; H, 6.71%.

(*R*)-(+)-2-Methyl-3-triphenylmethoxypropanol (41). To a stirred solution of the crude **40** (6.19 g) in dry THF (62 ml) at 0 °C was added $LiAlH_4$ (0.65 g, 17 mmol). After 50 min at room temperature, water (0.65 ml), 15% aqueous NaOH (0.65 ml), and water (1.95 ml) were added successively to the cooled (0 °C) reaction mixture. The insoluble materials were filtered off with Celite and washed with diethyl ether. The filtrate and washings were concentrated and the residue was chromatographed on silica gel (220 g) with 9 : 1 toluene-ethyl acetate to give **41** (4.89 g, 86% from **39**) as a pale yellow syrup, which on standing crystallized. An analytical sample was obtained by recrystallization from ethyl acetate-hexane: mp 74—76 °C; R_f=0.13 (8 : 1 hexane-acetone); $[\alpha]_D^{29}$ +28.4° (*c* 1.00); ^1H NMR (90 MHz) δ=0.84 (3H, d, 2-Me, *J*=6.9 Hz), 1.8—2.3 (1H, m), 2.21 (1H, d, OH, *J*=5.7 Hz), 2.9—3.35 (2H, m), 3.58 (2H, dd, 2×H-1, *J*=5.7 Hz), and 7.15—7.55 (15H, m, Tr).

Found: C, 82.59; H, 7.38%. Calcd for $C_{23}H_{24}O_2$: C, 83.10; H, 7.28%.

(*R*)-(−)-2-(2-Benzyloxy-1-methylethyl)-1,3-dioxolane (45). To a stirred solution of **41** (1.50 g, 4.51 mmol) in dry THF (15 ml) at 0 °C was added NaH (0.394 g, 9.02 mmol, 55% dispersion in mineral oil). After 1 h at room temperature, benzyl bromide (1.07 ml. 9.02 mmol) was added to the mixture under ice-cooling. The new mixture was heated under reflux (70 °C) for 2 h. The reaction mixture was cooled to 0 °C and ethanol (0.53 ml) was added and the mixture was stirred for 1 h. Cold water (20 ml) was added and extracted with diethyl ether. The extracts were washed with saturated aqueous NaCl, dried, and concentrated. The residue was chromatographed on silica gel (100 g) with 50 : 1 hexane-acetone to give a practically pure sample of **42** (1.91 g, 100%) as a pale yellow syrup [R_f=0.32 (50 : 1 hexane-acetone); $[\alpha]_D^{33}$ +4.3°, $[\alpha]_{365}^{33}$ +14.8° (*c* 0.88)]. This sample (1.73 g, 4.09 mmol) was dissolved in methanol (17.3 ml) and Amberlyst 15 (123 mg) was added. The mixture was heated at 50 °C for 3.5 h under vigorous stirring. The reaction mixture was filtered off and washed with methanol. The filtrate and washings were concentrated and the residue was chromatographed on silica gel (21 g) with 3.5 : 1 benzene-ethyl acetate to give **43** (612 mg, 83% from **41**) as a colorless syrup [R_f=0.32 (3.5 : 1 benezene-ethyl acetate); $[\alpha]_D^{33}$ −15.6° (*c* 1.37) [lit,[16] $[\alpha]_D$ −11.3° (*c* 16.05)]]. A solution of DMSO (0.469 ml, 6.61 mmol) in dry CH_2Cl_2 (1.2 ml) was added to a solution of oxalyl chloride (0.434 ml, 4.97 mmol) in dry CH_2Cl_2 (12 ml) at −78 °C under argon. After 3 min, a solution of **43** (551 mg, 3.06 mmol) in dry CH_2Cl_2 (3.6 ml) was added dropwise and the resulting suspension was stirred at −78 °C for 15 min. After addition of triethylamine (2.31 ml, 16.6 mmol), the mixture was gradually warmed to 0 °C for a period of 20 min. A mixture of 4 : 1 benzene-ether and water was added to the reaction mixture and phases were separated. The aqueous phase was extracted with 4 : 1 benzene-ether and the combined organic layers were washed with saturated aqueous NaCl, dried, and concentrated. The residual colorless aldehyde **44** was used without any further purification [R_f=0.64 (5 : 1 toluene-ethyl acetate) $[\alpha]_D^{33}$ −28.0° (*c* 1.40), [lit, [16] $[\alpha]_D$ −28° (*c* 1.40)]]. To a stirred mixture of **44** (514 mg, 2.88 mmol), ethylene glycol (1.60 ml, 28.8 mmol), and dry acetonitrile (5.14 ml) at 0 °C was added *p*-toluenesulfonic acid (45.1 mg, 0.288 mmol). After 35 h at 21 °C, the reaction mixture was poured into saturated aqueous $NaHCO_3$. The mixture was extracted with CH_2Cl_2 and the extracts were washed with saturated aqueous NaCl, dried, and concentrated. The residue was chromatographed on silica gel (30 g) with 15 : 1 toluene-ethyl acetate to give **45** (630 mg, 98%) as a colorless syrup: R_f=0.52 (10 : 1 toluene-ethyl acetate) $[\alpha]_D^{17}$ −3°, $[\alpha]_{365}^{17}$ +9° (*c* 0.81); ^1H NMR (90 MHz) δ=1.00 (3H, d, 2-Me, *J*=6.5 Hz), 1.85—2.3 (1H, m), 3.3—3.7 (2H, m) 3.7—4.0 (4H, m, OCH_2CH_2O), 4.52 (2H, s, OCH_2Ph), 4.86 (1H, d, H-1, $J_{1,2}$=5.4 Hz), 7.33 (5H, s, Ph).

Found: C, 70.15; H, 8.35%. Calcd for $C_{13}H_{18}O_3$: C, 70.25; H, 8.16%.

(*R*)-(−)-2-(2-Hydroxy-1-methylethyl)-1,3-dioxolane (46). A mixture of **45** (8.60 g, 38.7 mmol), palladium black, and methanol (86 ml) was vigorously stirred at room temperature for 1 h under bubbling with H_2. The catalyst was filtered off and washed with methanol. The filtrate and washings were concentrated to afford **46** (5.11 g, 100%) which was distilled under reduced pressure to give pure **46** (4.51 g, 88%) as a colorless oil: bp 69—71 °C (4 mmHg); $[\alpha]_D^{18}$ −6°, $[\alpha]_{365}^{18}$ −16.5° (*c* 1.21); ^1H NMR (90 MHz) δ=0.96 (3H, d, 2-Me, *J*=7.5 Hz), 1.8—2.2 (1H, m), 2.6—2.85 (1H, br t, OH), 3.5—3.8 (2H, m), 3.8—4.15 (4H, m, OCH_2CH_2O), and 4.77 (1H, d, H-1, $J_{1,2}$=7.3 Hz).

Found: C, 54.76; H 9.06%. Calcd for $C_6H_{12}O_3$: C, 54.53; H, 9.15%.

(*S*)-(+)-2-(2-Bromo-1-methylethyl)-1,3-dioxolane (47). To a stirred solution of **46** (970 mg, 7.34 mmol) and triphenylphosphine (2.89 g, 11.0 mmol) in dry THF (9.7 ml) at −5 °C was added dropwise diethyl azodicarboxylate (1.70 ml, 11.0 mmol). After 5 min at −5 °C, ethyl bromide (0.822 ml, 11.0 mmol) was added and the mixture was stirred at 20 °C for 2 h. The reaction mixture was concentrated under reduced pressure (120 mmHg) and the residue was chromatographed on silica gel (100 g) with 10 : 1 hexane-ethyl acetate to afford an oil (1.10 g, 77%) which was distilled to give a pure **47** (903 mg, 63%) as a colorless oil: bp 54—56 °C (3 mmHg); $[\alpha]_D^{16}$ +3°, $[\alpha]_{365}^{16}$ +11° (*c* 1.15); ^1H NMR (90 MHz) δ=1.09 (3H, d, 2-Me, *J*=6.5 Hz), 1.9—2.2 (1H, m), 3.29—3.4 (each 1H, each dd, H-3 and 3′, $J_{3,3'}$=9.3, $J_{2,3}$=7.0, and $J_{2,3'}$=4.5 Hz), 3.93 (1H, br s, OCH_2CH_2O), and 4.71 (1H, d, H-1, $J_{1,2}$=5.5 Hz).

Found: C, 37.10; H, 5.49; Br, 40.68%. Calcd for $C_6H_{11}O_2Br$: C, 36.95; H, 5.68; Br, 40.96%.

5,7,9-Tri-*O*-benzyl-2,3,6,8-tetradeoxy-2,4,6,8-tetra-*C*-methyl-L-*threo*-L-*ido*-nonose Ethylene Acetal (48) and Its C-4 Epimer. To a stirred suspension of magnesium powder

(687 mg, 28.3 mmol) in dry diethyl ether (50.5 ml) was added at room temperature 1,2-dibromoethane (0.244 ml, 2.83 mmol). After 0.5 h at room temperature, **47** (1.84 g, 9.43 mmol) in dry diethyl ether (92 ml) was added and the new mixture was stirred at room temperature for 1 h. To this was added **13** (1.01 g, 2.19 mmol) in dry diethyl ether (5.05 ml) and the mixture was stirred at room temperature for 2 h. Ice was added and the insoluble materials were filtered off with Celite and washed with ethyl acetate. The filtrate and washings were separated and the aqueous phase was extracted with ethyl acetate. The combined organic layers were washed with saturated aqueous NaCl, dried, and concentrated. The residue was chromatographed on silica gel (200 g) with 7 : 1 hexane-acetone to afford **48** (999 mg, 79%) and its C4-epimer (101 mg, 8.0%) as colorless syrups.

48: R_f=0.41 (15 : 1 benzene-acetone); $[\alpha]_D^{16}$ +3°, $[\alpha]_{365}^{16}$ +20° (*c* 0.64); ^{1}H NMR (90 MHz) δ=0.9—1.3 (12H, m), 1.5—2.5 (5H, m), 3.3—3.8 (5H, m), 3.8—4.1 (4H, m, OCH_2CH_2O), 4.56 and 4.67 (each 2H, each s, 2×OCH_2Ph), 4.5—4.95 (3H, m, H-1, OCH_2Ph), and 7.3—7.6 (15H, m, 3×Ph).

Found: C, 74.71; H, 8.44%. Calcd for $C_{36}H_{48}O$: C, 74.97; H, 8.38%.

C4-epimer of **48**: R_f=0.34 (15 : 1 benzene-acetone); ^{1}H NMR (90 MHz) δ=0.9—1.3 (12H, m, 4×Me), 1.4—2.7 (6H, m), 3.35—4.15 (8H, m), 4.53 and 4.59 (each 2H, each s, 2×OCH_2Ph), 4.4—5.15 (3H, m, H-1 and OCH_2Ph), and 7.3—7.6 (15H, m, 3×Ph).

5,7,9-Tri-*O*-benzyl-4-*O*-*t*-butyldimethylsilyl-2,3,6,8-tetradeoxy-2,4,6,8-tetra-*C*-methyl-L-*threo*-L-*ido*-nonose Ethylene Acetal (49). To a solution of **48** (1.06 g, 1.84 mmol), 2,6-lutidine (0.852 ml, 7.31 mmol) in dry CH_2Cl_2 (10.6 ml) was added at 0 °C TBDMSOTf (1.27 ml, 5.53 mmol). After 2 h standing at 25 °C, ice was added and the mixture was extracted with CH_2Cl_2. The extracts were washed with saturated aqueous NaCl, dried, and concentrated. The residue was chromatographed on silica gel (50 g) with 8 : 1 hexane-ethyl acetate to give **49** (1.13 g, 89%) as a colorless syrup: R_f=0.67 (3 : 1 hexane-ethyl acetate); $[\alpha]_D^{16}$ +0°, $[\alpha]_{365}^{16}$ +8° (*c* 0.64); ^{1}H NMR (90 MHz) δ=(9H, s, *t*-Bu), 0.8—1.15 (9H, m, 2, 6, and 8-Me), 1.35 (3H, s, 4-Me), 1.5—2.5 (5H, m), 3.26 (1H, d, *J*=2. 1 Hz), 3.4—3.7 (3H, m) , 3.8—4.1 (5H, m, OCH_2CH_2O+1H), 4.56 and 4.65 (each 2H, each s, 2×OCH_2Ph), 4.4—4.95 (3H, m, H-1, and OCH_2Ph), and 7.3—7.55 (15H, m, 3×Ph).

Found: C, 73.21; H, 8.92%. Calcd for $C_{42}H_{62}O_6Si$: C, 73.00; H, 9.04%.

1,3,5,13-Tetra-*O*-benzyl-6-*O*-*t*-butyldimethylsilyl-2,4,7,8,10,14,15-heptadeoxy-11,12-*O*-isopropylidene-2,4,6,8,12-penta-*C*-methyl-10-*C*-methylene-D-*erythro*-L-*ido*-L-*ido*-pentadecitol (50) and Its D-*erythro*-L-*ido*-L-*altro* Epimer 51. To a solution of **49** (406 mg, 0.588 mmol) in dry acetone (20 ml) was added $SnCl_2$ (112 mg, 0.588 mmol) and the mixture was stirred at 26 °C for 19 h. The reaction mixture was poured into a cold saturated aqueous $NaHCO_3$ and extracted with ethyl acetate. The extracts were washed with saturated aqueous NaCl, dried, and concentrated. The residue was chromatographed on silica gel (200 g) with 100 : 1 toluene-acetone to afford **12** (275 mg, 72%) as a colorless syrup [R_f=0.53 (8 : 1 hexane-ethyl acetate)]. To a cooled (−100 °C), stirred solution of **11** (531 mg, 1.28 mmol) in dry diethyl ether (0.667 ml) was added 1.38 M butyllithium in hexane (0.924 ml, 1.28 mmol) and the mixture was stirred at −100 °C for 15 min. To this was added the above aldehyde **12** (275 mg, 0.425 mmol) in dry diethyl ether (1.38 ml) and the mixture was stirred at −100 °C for 1 h. The reaction mixture was quenched with saturated aqueous NH_4Cl and extracted with ethyl acetate. The extracts were washed with saturated aqueous NaCl, dried, and concentrated. The residue was chromatographed on silica gel (80 g) with 25 : 1 toluene-ethyl acetate to afford **11** (32% recovered), and a mixture of **50**, **51**, and impurities (0.45 g). This mixture was re-chromatographed on silica gel (50 g) with 10 : 1 hexane-ethyl acetate to afford **50**+impurities (252 mg) and **51** (40.1 mg, 10%). This impure **50** was directly used to the next step. **50**: R_f=0.38 (25 : 1 toluene-acetone); ^{1}H NMR (250 MHz) δ=0.09 and 0.10 (each 3H, each s, $SiMe_2$), 0.88 (9H, s, *t*-Bu, containing one of the doublets of three methyls), 0.95—1.05 (9H, one t and two d, 3×Me), 1.14, 1.32, and 1.48 (3H, 6H, and 3H, each s, 4×Me), 1.55—1.8 (3H, m), 1.8—2.0 (1H, m), 2.01 (1H, br d, OH, *J*=3.8 Hz), 2.1—2.35 (2H, m), 3.19 (1H, d, *J*=1.8 Hz), 3.25—3.6 (4H, m), 3.92 (1H, br t, H-9, *J*=3.8 Hz), 4.3—4.75 (9H, m) , 5.33 and 5.47 (each 1H, each s), and 7.1—7.35 (20H, m), and some impurities' peaks. **51**: R_f=0.36 (25 : 1 toluene-acetone); $[\alpha]_D^{34}$ −6.5°, $[\alpha]_{365}^{34}$ −17.1° (*c* 1.00); ^{1}H NMR (250 MHz) δ=0.11 and 0.13 (each 3H, each s, $SiMe_2$), 0.88 (9H, s, *t*-Bu), 0.93, 1.04, and 1.06 (each 3H, each d, 2, 4, and 8-Me, *J*=6.8, 6.8, and 6.8 Hz), 1.03 (3H, t, 14-Me, *J*=7.5 Hz), 1.13, 1.30, 1.36, and 1.44 (each 3H, each s, 4×Me), 1.6—2.35 (7H, m), 3.21 (1H, d, *J*=2.0 Hz), 3.35 (1H, dd, *J*=6.8 and 9.0 Hz), 3.4—3.55 (3H, m), 4.05 (1H, br, H-9), 4.34 and 4.73 (each 1H, ABq, OCH_2Ph, *J*=12.5 Hz), 4.45 and 4.48 (each 1H, ABq, OCH_2Ph, *J*=12.5 Hz), 4.53 and 4.58 (each 1H, ABq, OCH_2Ph, *J*=11.3 Hz), 4.62 (2H, s, OCH_2Ph), 4.71 (1H, s, H-11), 5.16 and 5.31 (each 1H, each s, $C=CH_2$), and 7.1—7.35 (20H, m, 4×Ph).

Desilylation of the Coupling Products. The crude coupling products (220 mg) containing **50**, **51**, and impurities were dissolved in THF (4.4 ml) and to this was added 1 M solution of TBAF in THF (0.47 ml). After 2 h at 25 °C, ice-water was added and the mixture was extracted with ethyl acetate. The extracts were washed with saturated aqueous NaCl, dried and concentrated. The residue was chromatographed on silica gel (35 g) with 5 : 1 hexane-ethyl acetate to afford **52** (63.5 mg) and **53** (12.1 mg). **52**: R_f=0.36 (5 : 1 hexane-ethyl acetate); ^{1}H NMR (250 MHz) δ=0.82 (3H, d, *J*=7.0 Hz), 0.99 (3H, d, *J*=7.0 Hz), 1.01 (3H, t, *J*=7.0 Hz), 1.08 (3H, d, *J*=7.0 Hz), 1.11, 1.15, 1.36, and 1.50 (each 3H, each s, 4×Me), 1.55—2.3 (7H, m), 2.65—2.95 (2H, br), 3.15 (1H, d, *J*=2.3 Hz), 3.35—3.65 (4H, m), 4.25—4.75 (10H, m), 5.41 and 5.52 (each 1H, each s), and 7.2—7.35 (20H, m). **53**: R_f=0.31 (5 : 1 hexane-ethyl acetate); ^{1}H NMR (250 MHz) δ=0.86 (3H, d, *J*=6.3 Hz), 0.91 (3H, d, *J*=6.8 Hz), 0.98 (3H, t, *J*=74 Hz), 1.02 (3H, d, *J*=7.3 Hz), 1.06, 1.08, 1.28, and 1.41 (each 3H, each s, 4×Me), 1.5—2.25 (7H, m), 2.9—3.15 (2H, br), 3.25—3.45 (3H, m), 3.5—3.6 (2H, m), 4.3—4.7 (10H, m), 5.29 and 5.40 (each 1H, each s), and 7.15—7.35 (20H, m).

1,3,5,13-Tetra-*O*-benzyl-6-*O*-*t*-butyldimethylsilyl-2,4,7,8,10,14,15-heptadeoxy-11,12-*O*-isopropylidene-2,4,6,8,10,12-hexa-*C*-methyl-D-*arabino*-D-*gluco*-L-*ido*-pentadecitol (54) and Its D-*arabino*-L-*ido*-L-*ido* Epimer 55. A mixture of **50** (61.9 mg; contaminated with impurity), [$ClRh(PPh_3)_3$], and degassed benzene (3.1 ml) was placed in autoclave and stirred under 50 kg cm^{-2} at 24 °C for 5 d. The reaction mixture was concentrated and the residue was passed through Florisil (100—200 mesh, 2 g) with ether and again concentrated. The residue was chromatographed on silica

gel (6 g) with 100:1 toluene-acetone to afford **54** (39.9 mg, 41% from **12**) and **55** (6.5 mg, 7% from **12**) as colorless syrups.

54: R_f=0.67 (6:1 hexane-ethyl acetate); ^{1}H NMR (250 MHz) δ=0.12 and 0.13 (each 3H, each s, $SiMe_2$), 0.86 (9H, s, *t*-Bu), 0.62, 0.89, 1.02, 1.03, and 1.06 (each 3H, each d, 5×Me, J=7.0, 7.0, 7.5, 7.3, and 6.8 Hz), 1.02 (3H, t, 14-Me, J=7.5 Hz), 1.22, 1.33, 1.34, and 1.42 (each 3H, each s, 4-Me), 1.5—2.35 (8H, m), 3.19 (1H, d, J=1.5 Hz), 3.32 (1H, dd, J=7.3 and 4.0 Hz), 3.34 (1H, dd, J=7.3 and 10.0 Hz), 3.4—3.55 (3H, m), 4.11 and 4.71 (each 1H, ABq, $OC\underline{H}_2Ph$, J=12.5 Hz), 4.45 and 4.48 (each 1H, ABq, $OC\underline{H}_2Ph$, J=12.5 Hz), 4.53 (1H, d, J=0.5 Hz), 4.53 and 4.60 (each 1H, ABq, $OC\underline{H}_2Ph$, J=11.3 Hz), 4.63 and 4.71 (each 1H, ABq, $OC\underline{H}_2Ph$, J=12.5 Hz), and 7.1—7.35 (20H, m, 4×Ph).

55: R_f=0.60 (6:1 hexane-ethyl acetate); ^{1}H NMR (250 MHz) δ=0.08 (6H, s, $SiMe_2$), 0.87 (9H, s, *t*-Bu), 0.85—1.10 (15H, m, 5×Me), 1.20, 1.31, 1.39, and 1.43 (each 3H, each 5, 4×Me), 1.5—2.35 (8H, m), 3.07(1H, dd, J=11.3 and 6.0 Hz), 3.2—3.55 (7H, m), 4.35—4.75 (8H, m), and 7.15—7.35 (20H, m, 4×Ph).

1,3,5,9,11,13-Hexa-*O*-benzyl-2,4,7,8,10,14,15-heptadeoxy-2,4,6,8,10,12-hexa-*C*-methyl-D-*arabino*-D-*gluco*-L-*ido*-pentadecitol (56) and Its 11-Debenzylated Product 58. (a) To a stirred solution of **10** (1.69 g, 3.98 mmol) in dry DMF (68 ml) at 0 °C was added freshly powdered KOH (7.11 g, 127 mmol) and the mixture was stirred at 22 °C for 1 h. To this was added benzyl chloride (7.32 ml, 63.7 mmol) at 0 °C and the mixture was stirred at 22 °C for 6.5 h. Ice-water was added and the mixture was extracted with ethyl acetate and the extracts were washed with saturated aqueous NaCl, dried, and concentrated. The residue was chromatographed on silica gel (299 g) with 5:1 hexane-acetone to afford **56** (2.24 g, 58%), **58** (74 mg, 2%), and a mixture of partially benzylated products (1.12 g) as colorless syrups.

56: R_f=0.44 (5:1 hexane-acetone); $[\alpha]_D^{29}$ +7.1°, $[\alpha]_{365}^{29}$ +22.2° (*c* 0.90); ^{1}H NMR (250 MHz) δ=0.93 (3H, d, J=7.5 Hz), 0.97 (3H, t, 14-Me, J=7.5 Hz), 1.01 (3H, d, J=7.3 Hz), 1.07 (3H, d, J=7.0 Hz), 1.11 (3H, d, J=7.0 Hz), 1.17 and 1.21 (each 3H, each s, 6- and 12-Me), 1.39 (1H, dd, H-7′, $J_{7',8}$=5.0, $J_{7,7'}$=13.8 Hz), 1.57 (1H, ddq, H-14, $J_{14,15}$=$J_{13,14}$=7.5, $J_{14,14'}$=15.0 Hz), 1.76 (1H, ddq, H-14′, $J_{14',15}$=7.5, $J_{13,14'}$=3.8 Hz), 1.88 (1H, dd, H-7, $J_{7,7'}$=13.8, $J_{7,8}$=5.0 Hz), 2.0—2.3 (4H, m), 2.55 and 2.65 (each 1H, each s, 2×OH), 3.18 (1H, d, H-11, $J_{10,11}$=1.5 Hz), 3.30 (1H, dd, H-13), 3.33 (1H, dd, H-1, $J_{1,1'}$=9.3 and $J_{1,2}$=5.3 Hz), 3.43 (1H, dd, H-1′, $J_{1',2}$=9.3 Hz), 3.5—3.6 (2H, m, H-3 and 9), 4.04 (1H, d, H-5, $J_{4,5}$=0.5 Hz), 4.35—4.8 (12H, m, 6×$OC\underline{H}_2Ph$), and 7.15—7.35 (30H, m, 6×Ph).

Found: C, 78.65; H, 8.30%. Calcd for $C_{63}H_{80}O_8$: C, 78.39; H, 8.35%.

58: R_f=0.39 (5:1 hexane-acetone) $[\alpha]_D^{23}$ +15.0°, $[\alpha]_{365}^{23}$ +45.6° (*c* 1.00); ^{1}H NMR (90 MHz, characteristic peaks only), δ=2.34, 3.07, and 3.70 (each br s, each 1H, 3×OH), 4.4—4.8 (10H, m, 5×$OC\underline{H}_2Ph$), and 7.15—7.4 (25H, m, 5×Ph).

Found: C, 76.60; H, 8.39%. Calcd for $C_{56}H_{74}O_8$: C, 76.85; H, 8.52%.

(b) Treatment of a mixture of **10** (667 mg, 1.57 mmol), benzyl chloride (2.89 ml, 25.1 mmol), powdered KOH (2.82 g, 50.3 mmol), and DMF (10 ml) in a sonicator (65 W, 48 kHz) at room temperature for 3.5 h yielded **58** (436 mg, 29%), **56** (346 mg, 23%), and a mixture of partially benzylated products (844 mg).

1,3,5,9,13-Penta-*O*-benzyl-6-*O*-*t*-butyldimethylsilyl-2,4,7,8,10,14,15-heptadeoxy-11,12-*O*-isopropylidene-2,4,6,8,10,12-hexa-*C*-methyl-D-*arabino*-D-*gluco*-L-*ido*-pentadecitol (57). (a) To a stirred solution of **58** (276 mg, 0.315 mmol) and 2,2-dimethoxypropane (0.194 ml, 1.57 mmol) in dry acetone (5.51 ml) was added at 0 °C a 1 v/v% solution of concd H_2SO_4 in dry acetone (0.0276 ml). After 2.5 h at 20 °C, the mixtuere was neutralized with solid Na_2CO_3 and insoluble materials were filtered off and the filtrate was concentrated and chromatographed on silica gel (9 g) with 50:1 CH_2Cl_2-ethyl acetate to afford the acetonide (271 mg, 94%) as a clorless syrup [R_f=0.44 (5:1 hexane-ethyl acetate); $[\alpha]_D^{25}$ −6.2°, $[\alpha]_{365}^{25}$ −24.6° (*c* 100); Found: C, 77.19; H, 8.41%. Calcd for $C_{59}H_{78}O_8$: C, 77.43; H, 8.59%.]. To a stirred solution of this (247 mg, 0.270 mmol) in dry CH_2Cl_2 (0.27 ml) was added 2,6-lutidine (0.126 ml, 1.08 mmol) and cooled to 0 °C. To this was added TBDMSOTf (0.186 ml, 0.809 mmol) and the mixture was stirred at 20 °C for 2.5 h. Ice-water was added and the mixture was extracted with CH_2Cl_2. The extracts were washed with saturated aqueous NaCl, dried, and concentrated. The residue was chromatographed on silica gel (30 g) with 30:1 hexane-acetone to afford **57** (264 mg, 95%) as a colorless syrup: R_f=0.69 (4:1 hexane-ethyl acetate); $[\alpha]_D^{28}$ +10.4°, $[\alpha]_{365}^{28}$ +37.4° (*c* 1.00); ^{1}H NMR (250 MHz) δ=0.07 and 0.09 (each s, each 3H, $SiMe_2$), 0.83 (3H, d, J=6.8 Hz), 0.88 (9H, s, *t*-Bu), 0.89 (3H, t, 3×H-15, J=7.5 Hz), 0.95 (3H, d, J=6.5 Hz), 1.01 (3H, d, J=7.3 Hz), 1.03 (3H, d, J=7.5 Hz), 1.21, 1.36, and 1.46 (3H, 6H, and 3H, each s), 1.5—2.4 (8H, m), 3. 13 (1H, dd, J=6.3 and 6.3 Hz), 3.19 (1H, d, J=2.0 Hz), 3.25—3.55 (4H, m), 4.3—4.75 (11H, m, 5×$OC\underline{H}_2Ph$ and 1H), and 7.15—7.35 (25H, m, 5×Ph).

Found: C, 75.66; H, 8.86%. Calcd for $C_{65}H_{92}O_8Si$; C, 75.83; H, 9.01%.

(b) To a solution of **54** (17.2 mg, 0.0183 mmol) in dry DMF (0.86 ml) was added at 0 °C powdered KOH (2.1 mg, 0.037 mmol) and the mixture was stirred at 24 °C for 1 h. To this was added benzyl chloride (0.0042 ml, 0.037 mmol) at 0 °C and the mixture was stirred at 24 °C for 4 h. After work-up, the residue was chromatographed on silica gel (1 g) with 5:1 hexane-acetone to afford **57** (15.9 mg, 84%) as a coloress syrup. This synthetic sample of **57** was identical with naturally derived **57** by ^{1}H NMR, $[\alpha]_D$, and TLC.

Transformation of 54 to 56. **54** (23.9 mg, 0.0254 mmol) was dissolved in 1:2 (v/v) mixture of 46% aqueous HF-acetonitrile (0.72 ml) and the solution was stirred at 24 °C for 1 h. Water was added and the mixture was extracted with CH_2Cl_2. The extracts were washed with saturated aqueous NaCl, dried, and concentrated. The residue was chromatographed on silica gel (1 g) with 4:1 toluene-ethyl acetate to give a diol (18.9 mg, 95%) as a colorless syrup. 17.0 mg (0.0216 mmol) of this was dissolved in dry DMF (0.85 ml) and cooled to 0 °C. To this was added powdered KOH (9.7 mg, 0.17 mmol) and the mixture was stirred at 24 °C for 1 h. This mixture was cooled to 0 °C and benzyl chloride (0.0099 ml, 0.086 mmol) was added. The new mixture was stirred at 24 °C for 5 h. After work-up, the residue was chromatographed on silica gel (1.5 g) with 5:1 hexane-ethyl acetate to give **56** (17.9 mg, 81% from **54**) as a colorless syrup. This synthetic sample of **56** was identical with naturally derived **56** by ^{1}H NMR (250 MHz), $[\alpha]_D$, and TLC.

1,3,5,9,11,13-Hexa-*O*-benzyl-2,4,7,8,10,14,15-heptadeoxy-2,4,6,8,10,12-hexa-*C*-methyl-6,12-di-*O*-triethylsilyl-D-*arabino*-

D-*gluco*-L-*ido*-pentadecitol (59). To a stirred mixture of **56** (669 mg, 0.693 mmol), 2,6-lutidine (0.305 ml, 2.77 mmol), and dry CH_2Cl_2 (13.4 ml) was added at 0 °C triethylsilyl trifluoromethanesulfonate (0.426 ml, 2.08 mmol). After 1.5 h at 23 °C, ice-water was added and the mixture was extracted with CH_2Cl_2. The extracts were washed with saturated aqueous NaCl, dried, and concentrated. The residue was chromatographed on silica gel (40 g) with 30:1 hexane-ethyl acetate to give **59** (766 mg, 93%) as a colorless syrup: R_f=0.64 (5:1 hexane-acetone); $[\alpha]_D^{30}$ +19.4° (*c* 1.00); ^{1}H NMR (250 MHz) δ=0.5—0.7 (12H, m, 6×SiC<u>H</u>$_2$Me), 0.82 (3H, t, 3×H-15, *J*=7.5 Hz), 0.85—1.0 (24H, m, 6×SiCH$_2$<u>Me</u>, 8- and 10-Me), 1.01 (3H, d, 4-Me, *J*=7.0 Hz), 1.02 (3H, d, 2-Me, *J*=7.0 Hz), 1.31 and 1.33 (each 3H, each s, 6- and 12-Me), 1.4—1.95 (5H, m), 1.95—2.15 (1H, m, H-8), 2.15—2.4 (2H, m, H-2 and 4), 3.15—3.25 (3H, m, H-9, 11, and 13), 3.33 (1H, dd, H-1, J_{gem}=9.5, and $J_{1,2}$=7.0 Hz), 3.47 (1H, dd, H-1′, $J_{1',2}$=7.3 Hz), 3.51 (1H, dd, H-3, *J*=3.8, and 5.5 Hz), 3.78 (1H, s, H-5, $J_{4,5}$=0 Hz), 4.3—4.95 (12H, m, 6×OC<u>H</u>$_2$Ph), and 7.15—7.4 (30H, m, 6×Ph).

Found: C, 75.21; H, 9.01%. Calcd for $C_{75}H_{108}O_8Si_2$: C, 75.46; H, 9.12%.

1-*O*-*t*-Butyldiphenylsilyl-2,4,7,8,10,14,15-heptadeoxy-3,5:9,11-di-*O*-isopropylidene-2,4,6,8,10,12-hexa-*C*-methyl-6,12-di-*O*-triethylsilyl-D-*arabino*-D-*gluco*-L-*ido*-pentadecitol (62). A mixture of **59** (100 mg, 0.0839 mmol), palladium black, and ethanol (2.0 ml) was stirred at 20 °C for 0.5 h under bubbling with H_2, and the suspension was filtered. The filtrate was evaporated and the residue was chromatographed on silica gel (10 g) with 3:1 hexane-acetone to afford **60** (50.3 mg, 92%) as colorless foam. 46.6 mg (0.0714 mmol) of this sample was dissolved in dry DMF (4.66 ml) and imidazole (19.4 mg, 0.285 mmol) was added. This mixture was cooled to 0 °C and TBDPSCl (0.0742 ml, 0.285 mmol) was added and the new mixture was stirred at 25 °C for 3 h. The reaction mixture was poured into ice-water and extracted with ethyl acetate. The extracts were washed with saturated aqueous NaCl, dried, and concentrated. The residue was chromatographed on silica gel (10 g) with 4:1 toluene-ethyl acetate to give **61** (52.1 mg, 82%) as a colorless syrup [R_f=0.51 (3:1 hexane-acetone); ^{1}H NMR (90 MHz) δ=0.5—0.8 (12H, m, 6×SiC<u>H</u>$_2$Me), 0.8—1.15 (33H, m, 11×Me), 1.05 (9H, s, *t*-Bu), 1.17 (6H, s), 1.25—2.1 (8H, m), 2.75 (1H, d, OH, *J*=8.3 Hz), 3.00 (1H, d, OH, *J*=6.8 Hz), 3.13 (1H, d, OH, *J*=6.5 Hz), 3.30 and 3.60 (each 1H, each s, 2×OH), 3.25—3.9 (6H, m), 4.15 (1H, d, *J*=11.3 Hz), and 7.25—7.75 (10H, m, 2×Ph)]. 42.3 mg (0.0474 mmol) of this sample was dissolved in dry CH_2Cl_2 (0.85 ml) and 2-methoxypropene (0.025 ml, 0.24 mmol) was added. The mixture was cooled to 0 °C and PPTS (1.2 mg, 0.0047 mmol) was added and the new mixture was stirred at 25 °C for 3 h. The reaction mixture was neutralized with solid Na_2CO_3 and insoluble materials were filtered off. The filtrate was concentrated and the residue was chromatographed on silica gel (5 g) with 50:1 toluene-ethyl acetate to afford **62** (39.2 mg, 85%) as colorless foam: R_f=0.78 (8:1 hexane-ethyl acetate); $[\alpha]_D^{29}$ +31.2°, (*c* 1.00); ^{1}H NMR (250 MHz) δ=0.45—0.7 (12H, m, 6×SiC<u>H</u>$_2$Me), 0.8—1.1 (33H, m, 11×Me), 1.05 (9H, s, *t*-Bu), 1.17, 1.22, 1.27, 1.28, 1.40, and 1.41 (each 3H, each s, 6×Me), 1.50—2.0 (9H, m), 3.18 (1H, dd, *J*=1.5 and 7.0 Hz), 3.47 (1H, dd, *J*=10.3 and 6.0 Hz), 3.5—3.8 (5H, m), 7.1—7.25 and 7.35—7.55 (6H and 4H, m, 2×Ph).

Found: C, 67.80; H, 9.77%. Calcd for $C_{55}H_{98}O_8Si_3$: C, 67.99; H, 10.17%.

13-*O*-Acetyl-2,4,7,8,10,14,15-heptadeoxy-3,5;9,11-di-*O*-isopropylidene-2,4,6,8,10,12-hexa-*C*-methyl-D-*arabino*-D-*gluco*-L-*ido*-pentadecitol (64). A mixture of **62** (58.3 mg, 0.0600 mmol), acetic anhydride (0.0283 ml, 0.300 mmol), 4-dimethylaminopyridine (0.7 mg, 0.006 mmol), and dry pyridine (1.17 ml) was heated at 60 °C for 20 h. Ice-water was added and the mixture was extracted with ethyl acetate and the extracts were washed with saturated aqueous NaCl, dried, and concentrated. The residue was chromatographed on silica gel (6 g) with 50:1 hexane-acetone to afford **63** (52.3 mg, 86%) as a colorless syrup [R_f=0.55 (20:1 hexane-ethyl acetate); ^{1}H NMR (90 MHz, representatives only) δ=2.08 (3H, s, OAc), 4.93 (1H, dd, H-13, *J*=2.3 and 9.0 Hz)]. 48.0 mg (0.0474 mmol) of this sample was dissolved in dry THF (0.96 ml) and to this was added 1 M TBAF in THF (0.284 ml). After 8 h at 60 °C, ice-water was added and the mixture was extracted with ethyl acetate. The extracts were washed with saturated aqueous NaCl, dried, and concentrated. The residue was chromatographed on silica gel (5 g) with 2:1 hexane-ethyl acetate to afford **64** (21.0 mg, 81%) as colorless foam: R_f=0.07 (4:1 hexane-ethyl acetate); $[\alpha]_D^{30}$ +29.8°, (*c* 1.00); IR ($CHCl_3$) 1729 cm^{-1}; ^{1}H NMR (250 MHz) δ=0.91 (3H, 14-Me, *J*=7.5 Hz), 0.97 (3H, d, *J*=7.0 Hz), 1.03 (3H, d, *J*=7.0 Hz), 1.04 (3H, d, *J*=7.0 Hz), 1.07 (3H, d, *J*=7.0 Hz), 1.16, 1.17, 1.26, 1.35, 1.41, and 1.42 (each 3H, each s, 6×Me), 1.4—1.65 (1H, m, H-14), 1.6—1.95 (8H, m), 2.09 (3H, s, OAc), 2.31 and 2.40 (each 1H, each br s, 2×OH), 3.31 (1H, dd, *J*=2.5 and 6.5 Hz), 3.5—3.65 (5H, m), 4.90 (1H, dd, H-13, *J*=3.3 and 9.0 Hz).

Found: C, 63.34; H, 9.56%. Calcd for $C_{29}H_{54}O_9$: C, 63.71; H, 9.95%.

3,5:9,11-Di-*O*-isopropylidene-(9*S*)-9-deoxo-9-hydroxy-erythronolide A (66). To a stirred suspension of PDC (188 mg, 0.499 mmol) and MS 3AP (125 mg) in dry CH_2Cl_2 (0.55 ml) was added at 0 °C a solution of **64** (68.2 mg, 0.125 mmol) in dry CH_2Cl_2 (0.27 ml). After 4 h at 22 °C, the reaction mixture was diluted with diethyl ether (0.5 ml) and the suspension was transferred to a column filled with silica gel (1 g). The column was eluted with diethyl ether and the eluant was concentrated. The residue was chromatographed on silica gel (2 g) with 60:20:1 hexane-ethyl acetate-acetic acid to afford **65** (59.2 mg, 85%) as a colorless syrup [R_f=0.48 (50:50:1 hexane-ethyl acetate-acetic acid); ^{1}H NMR (90 MHz, representitatives only) δ=2.07 (3H, s, OAc), 2.60 (1H, m), 3.28 (1H, dd, *J*=2.4 and 6.0 Hz), 3.52 (1H, d, *J*=1.5 Hz), 3.63 (1H, d, *J*=3.8 Hz), 3.83 (1H, dd, *J*=2.3 and 9.8 Hz), and 4.90 (1H, dd, H-13, *J*=3.8 and 9.0 Hz)]. This was dissolved in 1,4-dioxane (0. 13 ml) and 1 M aqueous NaOH (0.126 ml) was added. After 2 h at 23 °C, the reaction mixture was neutralised with CG 50 and filtered. The filtrate was concentrated and the residue was chromatographed on silica gel (2 g) with 2:1 hexane-acetone to afford **4** (52.4 mg, 96%) as a colorless syrup [R_f=0.23 (30:10:1 hexane-acetone-acetic acid)]. This was dissolved in dry THF (1.04 ml) and triphenylphosphine (39.4 mg, 0.150 mmol) and di-(2-pyridyl) disulfide (33.1 mg, 0.150 mmol) were added and stirred at 22 °C for 8 h. After concentration, the residue was chromatographed on silica gel (6.5 g) with 1:1 hexane-ethyl acetate to afford pyridyl ester of **4** (58.3 mg, 95%) as a colorless syrup, which was dissolved in dry toluene (5.83 ml) and this solution was slowly added to a refluxing dry toluene (41.2 ml) with

syringe pump during a period of 10 h under argon. After further 14 h standing at 110 °C, the mixture was concentrated and the residue was chromatographed on silica gel (3 g) with 5 : 1 hexane-acetone to afford **66** (31.0 mg, 65%) as a clorless foam: R_f=0.61 (3 : 1 hexane-acetone); $[\alpha]_D^{33}$ +12.1°, $[\alpha]_{365}^{33}$ +40.0° (*c* 0.66); IR ($CHCl_3$) 1720 cm^{-1}; 1H NMR (250 MHz) δ=0.84 (3H, t, 14-Me, *J*=7.5 Hz), 1.01 (3H, d, 4-Me, *J*=6.8 Hz), 1.14 and 1.23 (each 3H, each s, 6- and 12-Me), 1.18 (3H, d, 2-Me), 1.24 (3H, d, 10-Me), 1.28 (3H, d, 8-Me, *J*=6.0 Hz), 1.46, 1.48, and 1.49 (3H, 6H, and 3H, each s, 2×CMe_2), 1.5—1.65 (3H, m, H-4, 7′, and 14′), 1.82 (1H, dq, H-10, *J*=7.3, $J_{9,10}$=0, and $J_{10,11}$=1.8 Hz), 1.94 (1H, ddq, H-14, *J*=7.5, $J_{14,14'}$=14.8, and $J_{13,14}$=2.5 Hz), 2.05—2.25 (3H, m, H-7, 8, and OH), 2.75 (1H, dq, H-2, $J_{2,3}$=10.8, and $J_{2,Me}$=6.5 Hz), 2.96 (1H, s, OH), 3.12 (1H, d, H-9, $J_{8,9}$=11.0 Hz), 3.60 (1H, d, H-11), 3.78 (1H, dd, H-3, $J_{3,4}$=1.0 Hz), 3.97 (1H, d, H-5, $J_{4,5}$=1.5 Hz), and 5.06 (1H, dd, H-3, $J_{13,14'}$=11.3 Hz).

Found: *m/z*, 485.3110. Calcd for $C_{26}H_{45}O_8$: M^+−Me, 485.3111.

(9*S*)-9-Deoxo-9-hydroxyerythronolide A (2). A mixture of **66** (69.4 mg, 0.139 mmol) and 50% aqueous acetic acid (1.39 ml) was stirred at 24 °C for 4 h. After concentration, the residual sample of **2** (58.3 mg, 100%) was recrystallised from acetone-hexane to afford a pure sample of **2**. This sample was identical in all respects [mp, TLC, 1H NMR (250 MHz), and $[\alpha]_D$], with a sample of **2** prepared by the literature procedure.[20]

Data of 2: R_f=0.15 (3 : 1 hexane-ethyl acetate); mp 203—206 °C (acetone-hexane) [lit,[20a] 185—187 °C, lit,[20b] 199—200°C, mp of **2** prepared by the method of lit,:[20b] 202—205 °C (acetone-hexane)]; $[\alpha]_D^{27}$ +9.5°, $[\alpha]_{365}^{27}$ +24.7° (*c* 2.00, MeOH) lit,[20a] $[\alpha]_D^{27}$ +9.5° (*c* 2.00, MeOH), lit,[20b] $[\alpha]_D^{25}$ +9.5° (*c* 2.00, MeOH), $[\alpha]_D$ of **2** prepared by the method of lit,:[20b] $[\alpha]_D^{30}$ +9.5°, $[\alpha]_{365}^{30}$ +24.1° (*c* 200, MeOH)]; 1H NMR (250 MHz) δ=0.90 (3H, t, 3×H-15, *J*=7.3 Hz), 1.04 (3H, d, 4-Me, *J*=7.5 Hz), 1.05 (3H, s), 1.24 (3H, s), 1.24 (3H, d, 10-Me, *J*=7.3 Hz), 1.29 (6H, d, 2- and 8-Me, *J*=7.0 Hz) 1.2—1.35 (1H, m, H-7), 1.42 (1H, dd, H-7′, $J_{7,7'}$=15.0 and $J_{7',8}$=2.5 Hz), 1.45—1.65 (3H, m, H-4, 8, and 14), 1.95 (1H, ddq, H-14′, $J_{13,14'}$=2.3, $J_{14,14'}$=14.5 and $J_{14',Me}$=7.3 Hz), 2.0—2.1 (1H, m, H-10), 2.07 (1H, br s, OH), 2.63 (1H, br s, OH), 2.79 (1H, dq, H-2, $J_{2,3}$=10.3 and $J_{2,Me}$=7.0 Hz), 2.97 (1H, ddd, H-9, *J*=2.3, 9.0, and $J_{9,OH}$=9.0 Hz), 3.13 (1H, br s, OH), 3.48 (1H, dd, H-11, $J_{10,11}$=1.0 and $J_{11,OH}$=4.3 Hz), 3.57 (1H, d, 9-OH, *J*=9.0 Hz), 3.63 (1H, br s, OH), 3.85 (1H, d, H-3, $J_{2,3}$=10.3 and $J_{3,4}$=0 Hz), 3.95 (1H, br s, H-5, $J_{4,5}$=0 Hz), 4.30 (1H, d, 11-OH, *J*=4.3 Hz), and 4.64 (1H, dd, H-13).

Found: C, 59.73; H, 9.30%. Calcd for $C_{21}H_{40}O_8$: C, 59.98; H, 9.59%.

Erythronolide A (1). To a stirred mixture of **2** (37.6 mg, 0.0894 mmol), benzaldehyde dimethyl acetal (0.067 ml, 0.45 mmol), and dry CH_2Cl_2 (1.88 ml) was added at 0 °C CSA (2.1 mg, 0.0089 mmol). After 24 h at 0 °C, solid Na_2CO_3 was added and the insoluble materials were filtered off. The filtrate was concentrated and the residue was chromatographed on silica gel (9 g) with 3 : 2 hexane-ethyl acetate to afford **67** (36.5 mg, 80%) as colorless needles [R_f=0.68 (2 : 1 hexane-acetone); $[\alpha]_D^{26}$ +5.4°, $[\alpha]_{365}^{26}$ +11.2° (*c* 1.00); mp 128—130 °C (acetone-hexane); IR ($CHCl_3$) 1728 cm^{-1}; 1H NMR (250 MHz) δ=0.87 (3H, t, 14-Me, *J*=7.5 Hz), 1.13 and 1.31 (each 3H, each s, 6- and 12-Me), 1.15 (3H, d, 4-Me, *J*=7.0 Hz), 1.24 (3H, d, 10-Me, *J*=7.3 Hz), 1.27 (3H, d, 2-Me, *J*=7.7 Hz), 1.32 (3H, d, 8-Me, *J*=7.5 Hz), 1.4—2.1 (7H, m), 2.41 (1H, br, 12-OH), 2.81 (1H, d, 9-OH, *J*=4.5 Hz), 2.91 (1H, dq, H-2, $J_{2,3}$=10.8 Hz), 3.1—3.2 (1H, m, H-9) , 3.14 (1H, s, 6-OH), 3.73 (1H, br s, H-11, $J_{10,11}$<1.0 Hz), 3.79 (1H, dd, H-3, $J_{3,4}$=1.0 Hz), 3.96 (1H, d, H-5, $J_{4,5}$=1.0 Hz), 4.26 (1H, d, 11-OH, *J*=1.6 Hz), 5.13 (1H, dd, H-13, $J_{13,14}$=2.3 and $J_{13,14}$=11.0 Hz), 5.65 (1H, s, $OC\underline{H}_2Ph$), 7.35—7.45 and 7.45—7.55 (3H and 2H, each m, Ph)]. A solution of this sample **67** (19.5 mg, 0.0383 mmol) in dry CH_2Cl_2 (0.078 ml) was added to a stirred suspension of PCC (132 mg, 0.613 mmol), MS 3AP (153 mg), and dry CH_2Cl_2 (0.38 ml) at 0 °C. After 0.5 h at 0 °C, the reaction mixture was diluted with diethyl ether (0.5 ml) and the suspension was transferred to a column filled with silica gel (1 g). The column was eluted with diethyl ether and the eluant was concentrated. The residue was chromatogaphed on silica gel (1 g) with 1 : 1 hexane-ethyl acetate to afford **68** (15.6 mg, 80%) as a colorless syrup [R_f=0.60 (2 : 1 toluene-acetone); $[\alpha]_D^{22}$ −36.6°, (*c* 1.00, MeOH); IR ($CHCl_3$) 1705 cm^{-1}; 1H NMR (250 MHz) δ=0.90 (3H, t, 3×H-15, *J*=7.5 Hz), 1.10 (3H, s), 1.18 (3H, d, 4-Me, *J*=7.5 Hz) , 1.21 (3H, d, 10-Me, *J*=7.5 Hz), 1.25 (3H, s), 1.28 (3H d, 2-Me, *J*=6.5 Hz), 1.34 (3H, d, 8-Me, *J*=6.0 Hz), 1.59 (1H, ddq, H-14, $J_{13,14}$=10.3 and $J_{14,14'}$=14.8 Hz), 1.71 (2H, d, 2×H-7, $J_{7,8}$=7.3 Hz), 1.78 (1H, ddq, H-4, $J_{3,4}$=1.0 and $J_{4,5}$=1.3 Hz), 1.97 (1H, ddq, H-14′, $J_{13,14'}$=2.0 Hz), 2.31 (1H, br, OH), 2.60 (1H, br s, OH), 2.85—3.1 (3H, m), 3.29 (1H, d, 11-OH, *J*=5.0 Hz), 3.76 (1H, dd, H-11, *J*=5.0 and 5.0 Hz), 3.83 (1 H, dd, H-3, $J_{2,3}$=10.3 Hz), 4.01 (1H, d, H-5), 4.88 (1H, dd, H-13, *J*=2.0 and 10.3 Hz), 5.68 (1H, s, $OC\underline{H}_2Ph$), 7.3—7.45 and 7.45—7.55 (3H and 2H, m, Ph)]. A mixture of this sample **68** (23.5 mg, 0.0464 mmol), palladium black, and MeOH (0.71 ml) was stirred at 25 °C for 0.5 h under bubbling with H_2, and the suspension was filtered. The filtrate was concentrated and the residue was chromatographed on silica gel (1 g) with 2 : 1 toluene-acetone to afford **1** (15.9 mg, 82%) as colorless needles. The synthetic sample of **1** proved to be identical with the naturally derived erythronolide A[22] by spectroscopic means and mixed mp measurement: R_f=0.23 (2 : 1 hexane-acetone); mp 170—172 °C (acetone-hexane) [lit,[22] mp 172—173 °C, lit,[4] 168—172 °C, mp of **1** prepared by the method of lit,[22] 170—172 °C]; mix. mp 170—172 °C; $[\alpha]_D^{28}$ −36.7° (*c* 0.90, MeOH) [lit,[4] $[\alpha]_D^{25}$ −37° (*c* 0.90, MeOH) $[\alpha]_D$ of **1** prepared by the method of lit,:[22] −37.3 ° (*c* 0.90, MeOH)]; IR ($CHCl_3$) 1743 cm^{-1}; 1H NMR (250 MHz) δ=0.85 (3H, t, 3×H-15, *J*=7.5 Hz), 1.01 (3H, d, 4-Me, *J*=7.3 Hz), 1.16 (3H, d, 10-Me, *J*=7.3 Hz), 1.17 (3H, s), 1.19 (3H, d, *J*=6.5 Hz), 1.24 (3H, d, *J*=6.5 Hz), 1.36 (3H, s), 1.4—1.6 (2H, m), 1.8—2.05 (3H, m), 2.48 (1H, s, OH), 2.6—2.8 (2H, m), 2.84 (1H, d, OH, *J*=3.8 Hz), 3.07 (1H, br q, H-10, $J_{10,11}$=0 Hz), 3.13 (2H, br s, 2×OH), 3.55—3.7 (2H, m), 3.81 (1H, br s, H-11, $J_{11,OH}$=0 Hz), 3.93 (1H, d, OH, *J*=2.5 Hz), and 5.04 (1H, dd, H-13, $J_{13,14}$=2.3 and $J_{13,14'}$=10.8 Hz). After addition of D_2O, the signals of H-5, H-3, and H-11 changed to 3.56 (d, $J_{4,5}$=2.5 Hz), 3.62 (d, $J_{3,4}$=0 and $J_{2,3}$=10.5 Hz), and 3.81 (d, $J_{10,11}$=1.0 Hz), respectively.

Found: C, 60.20; H, 8.86%. Calcd for $C_{21}H_{38}O_8$: C, 60.27; H, 9.15%.

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