Synthetic Studies of Rifamycins. VIII.[1] An Improved Practical Synthesis of the Ansa-chain Compounds for the Rifamycin W Synthesis

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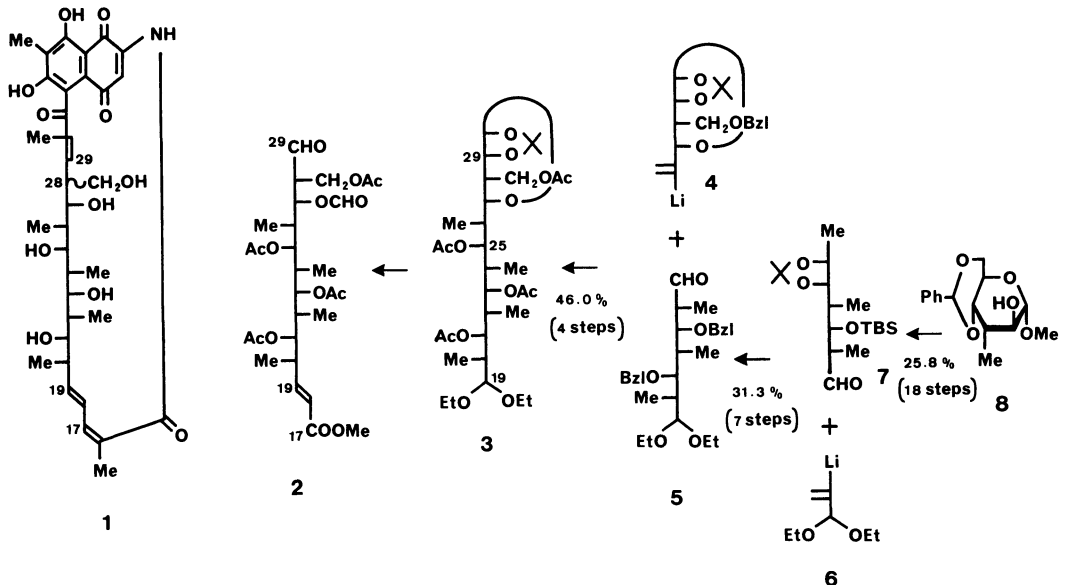
The improved practical synthesis of 6,8,10-tri-*O*-acetyl-3-*C*-(acetoxymethyl)-3,5,7,9,11-pentadeoxy-1,2-*O*-isopropylidene-5,7,9,11-tetra-*C*-methyl-L-*erythro*-D-*altro*-β-L-*talo*-dodecodialdofuranose-(1,4) 12-(diethyl acetal) (**3**), a useful synthetic segment for the rifamycin W ansa-chain, is described. The key intermediate, 3-*O*-benzyl-2,4,7-trideoxy-5,6-*O*-isopropylidene-2,4-di-*C*-methyl-*aldehydo*-D-*glycero*-D-*allo*-heptose (**22**), was synthesized in a 29.4% yield from methyl 4,6-*O*-benzylidene-3-deoxy-3-*C*-methyl-α-D-altropyranoside (**8**) in 15 steps. The coupling of **22** with the lithium reagent prepared from butyllithium and 3-*C*-(benzyloxymethyl)-3,5,6-trideoxy-5-iodo-1,2-*O*-isopropylidene-α-D-ribo-5-hexenofuranose afforded only the "Cram" product **24** in a 61% yield. The homogeneous hydrogenation of **24** with [$RhCl(Ph_3P)_3$] gave 8-*O*-benzyl-3-*C*-(benzyloxymethyl)-3,5,7,9,12-pentadeoxy-1,2:5,6-di-*O*-isopropylidene-5,7,9-tri-*C*-methyl-D-*erythro*-D-*altro*-L-*talo*-dodecofuranose-(1,4) (**25**) and its C-5 epimer in 95 and 3.8% yields respectively. 6,8-Di-*O*-benzyl-3-*C*-(benzyloxymethyl)-3,5,7,9-tetradeoxy-1,2-*O*-isopropylidene-5,7,9-tri-*C*-methyl-D-*altro*-β-L-*talo*-decodialdofuranose-(1,4), derived from **25** in a 91% yield, was subjected to coupling with 3,3-diethoxy-2-lithio-1-propene to afford about 1.7:1 excess of the "Cram" product (**30**, 59% yield). The conversion of **30** into **3** was accomplished by the sequence of reactions involving homogeneous hydrogenation, debenzylation, and acetylation in a 75% yield. The 24-step synthesis of **3** from **8** was achieved in a 7% overall yield.

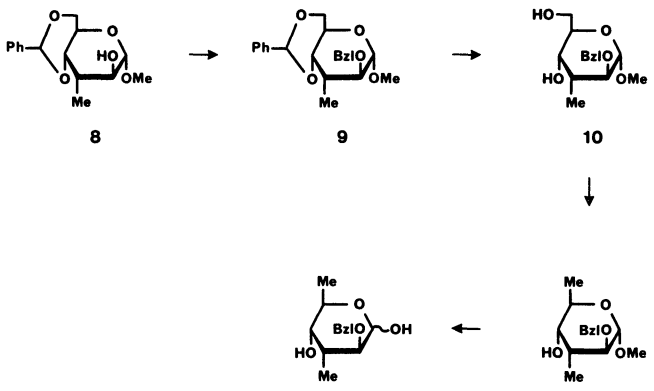
For the purpose of synthesizing practically the optically active natural macrolides such as rifamycins and erythronolides which contain a long chain consisting of many consecutive chiral carbon atoms, it is indispensable to realize the highly diastereoselective connections between the selected chiral carbon chain segments which can be effectively synthesized from appropriate chiral compounds, but on the other hand each resulting coupling product must naturally be transformed into each target compound as effectively as possible. In the studies directed toward the total synthesis of rifamycin W (**1**), the selected ansa-chain compound **2**[2] corresponding to the C-17 - C-29 portion of **1** was first synthesized from the sugar derivative **8** in our laboratories. In this synthesis, the precursor **3** of **2** was prepared in good yield from **5** by the sequence of reactions involving the highly diastereoselective coupling of **4** and **5** followed by the stereospesific homogeneous hydrogenation of the major "Cram" product and two successive transformations. However, the 7-steps synthesis of **5** from **7**, involving the coupling of **6** with **7** followed by the stereospecific homogeneous hydrogenation of the desilylated compound of the major "Cram" product and four successive transformations, was not satisfactory because of the low overall yield caused by the requirement of many steps of transformation not directly neccessary for the connection of carbon chains in the synthetic route. Moreover, the long way (18 steps) to **7** from **8** was also undesirable for the large scale preparation of **7**. In our recent synthetic studies of **3** directed at the total synthesis of rifamycin W, it was found that a modified synthetic route which was shorter by five steps than the old route effected a 2-fold improvement in the overall



Scheme 1.

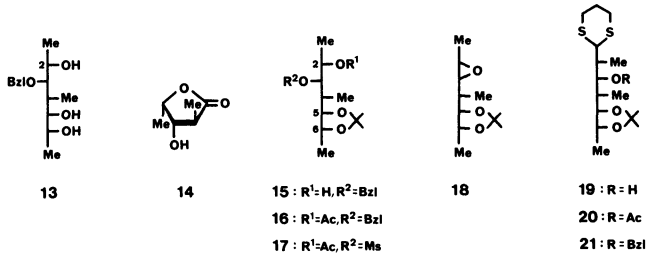
yield of **3** from the starting material **8** with no sacrifice in the stereoselectivities of the peculiar carbon chain connections which we have termed a "two stage coupling," and were effectively used in the old route. In this paper, we wish to report the improved practical synthesis of **3**, the most important key intermediate for the rifamycin W ansa-chain synthesis.

The starting material, methyl 4,6-*O*-benzylidene-3-deoxy-3-*C*-methyl-α-D-altropyranoside (**8**)[3,4] was *O*-benzylated and the resulting **9** was treated with 75% dichloroacetic acid (DCA) to afford the crystalline derivative **10**. The selective 6-*O*-mesylation of **10** followed by reduction with lithium aluminium hydride gave **11**. The acetolysis of **11** followed by the hydrolysis yielded **12** in a 71% overall yield from **8**.



Scheme 2.

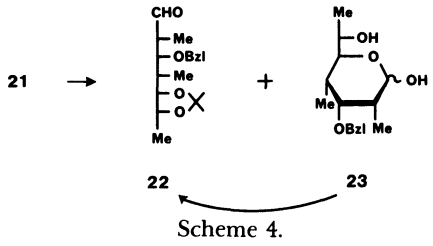
The Grignard reaction of **12** with 10 equimolar amounts of methylmagnesium iodide in ether gave **13** in an 86% yield as a sole product. The (2S)-configuration of **13** was confirmed by conversion to the known 1,4-lactone **14**[5] by the sequence of reactions involving periodate-oxidation, debenzylation, and bromine-oxidation. The isopropylidenation of **13** with 2,2-dimethoxypropane (DMP) in acetone containing a catalytic amounts of concd sulfuric acid gave the 5,6-isopropylidene derivative **15** without the



Scheme 3.

formation of the undesired 2,5-isopropylidene derivative.[2] Subsequent acetylation of **15** gave the crystalline derivative **16** in an 89% yield from **13**. The hydrogenolysis of **16** was reproducibly carried out with an atmospheric pressure of hydrogen and a freshly prepared palladium black in a 9:1 mixture of ethyl acetate–methanol. The resulting debenzylated product was immediately mesylated to afford **17** in a 95% yield. The mesylate **17** was then treated with sodium methoxide in chloroform to afford the epoxide **18** in an 81% yield after distillation. The nucleophilic addition of 2-lithio-1,3-dithiane to the *cis*-epoxide **18** gave regiospecifically only the desired C-6-adduct **19** in a 93% yield. The structure of **19** could be determined by the coupling feature (double doublet) of the acetoxymethine proton in the ^{1}H-NMR spectrum of its acetate **20**. The reason for this high regioselectivity in ring-opening of the *cis*-epoxide has been reasonably explained in the preceding paper.[2]

The benzylation of **19** provided, in a 91% yield, the benzyl ether **21**, whose dithioacetal group was cleaved with a 1:1 mixture of mercury(II) chloride and red mercury(II) oxide to generate the aldehyde **22** in a 65% yield together with the 27% yield of the deisopropylidenation heptopyranose **23**. The latter could

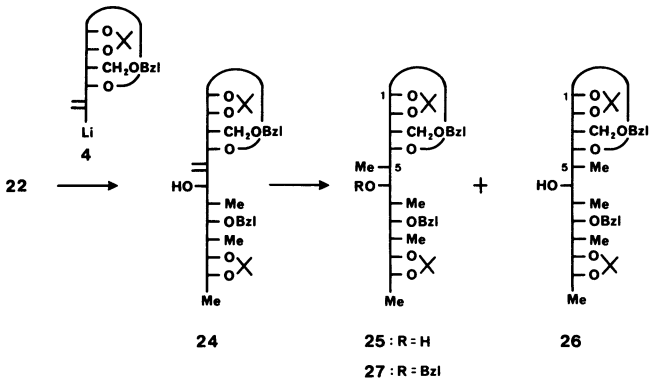


Scheme 4.

be converted to the former, in a 67% yield, by a sequence of reactions involving sodium borohydride reduction, isopropylidenation, and Swern oxidation, therefore the yield of **22** from **21** amounted to an 83% (or to a 29.4% overall yield from**8**).

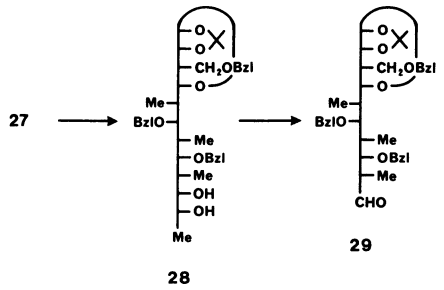
With the aldehyde **22** corresponding to the central portion of the rifamycin W ansa-chain now in hand, the next stage was elaboration of it to the key intermediate **3** using our "two stage coupling." The coupling of **22** with the lithium reagent **4**, prepared from the corresponding iodide[2] (3 equiv) and butyllithium (2.8 equiv) in ether at −95—−90 °C, was carried out in ether at −95—−90 °C to afford a sole coupling product **24** in a 61% yield based on **22**. The homogeneous hydrogenation of **24** with 0.25 equimolar amounts of chlorotris(triphenylphosphine)rhodium(I) in benzene under an atmospheric pressure of hydrogen gave the hydrogenated products **25** and **26** in 95 and 3.8% yields respectively. We could confidently predict the structures of **24**, **25**, and **26** as depicted in Scheme 5 by the fact that in the old synthetic route (Scheme 1)[2] the "two stage coupling" of **4** and **5** gave predominantly the precursor of **3**. This prediction was confirmed in the later stage of this ansa-chain synthesis.

The benzylation of **25** followed by the selective deisopropylidenation of the resulting benzyl ether **27** afforded **28**, which was subjected to the periodate-oxidation to give the aldehyde **29** in a 91% yield from



Scheme 5.

25. The coupling of **29** with the lithium reagent **6**, prepared from 3 equiv of 2-bromo-3,3-diethoxy-1-propene[2,6] and 2.5 equiv of butyllithium in THF at −110—−108°C, was performed in THF at −110—−108°C to afford, after column-chromatographic separation, **30** and **31** in 59 and 35% yields respectively based on **29**. The homogeneous hydrogenation of the



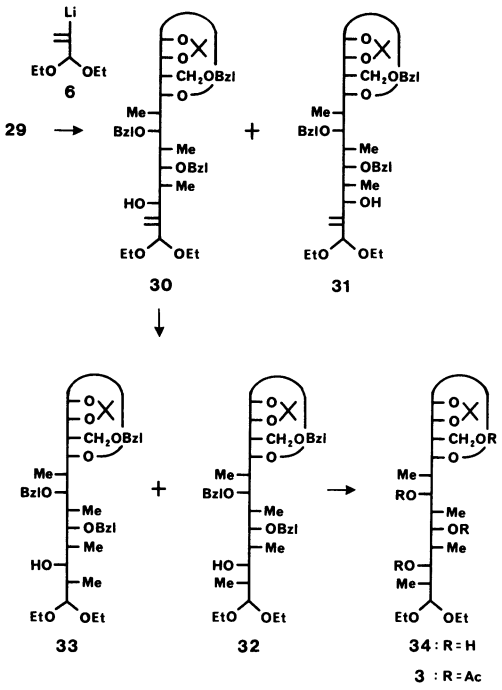
Scheme 6.

major product **30** with 0.25 equimolar amounts of rhodium catalyst gave **32** and its C-11 epimer **33** in 83 and 3.6% yields respectively. The major product **32** was debenzylated with lithium in liquid ammonia to afford **34**, which was acetylated with acetic anhydride and 4-dimethylaminopyridine (DMAP) in ethyl acetate to give the target key intermediate **3** in a 90% yield from **32**. The ^{1}H-NMR spectrum, R_f-value on TLC, and mp of **3** were identical with those of the authentic sample.[2] This result established the structures of **30—33**, together with those of the first "two stage coupling" products **24—26**. The overall yield of **3** from **8** (24 steps) thus amounted to a 7%, whereas the 29 steps overall yield of **3** from **8** in the old route was 3.5%.

Having achieved improved practical synthesis of **3**, we now undertake the total synthesis of rifamycin W.

Experimental

Melting points were determined on a micro hot-stage Yanaco MP-S3 and were uncorrected. The specific rotations were measured with a Carl Zeiss or JASCO DIP-360 photoelectric polarimeter in chloroform unless stated otherwise. IR spectra were recorded on a Hitachi Perkin-



Scheme 7.

Elmer 225 spectrometer and ^{1}H-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 Wakogel C-200, respectively. In general, evaporation of solvents was carried out under reduced pressure below 35°C.

Methyl 2-O-Benzyl-4,6-O-benzylidene-3-deoxy-3-C-methyl-α-D-altropyranoside (9). To an ice-cold stirred solution of **8** (31.1 g, 111 mmol) in dry DMF (218 ml), sodium hydride (5.30 g, 221 mmol) was added portionwise. The mixture was stirred at room temperature for 1 h and then ice-cooled. Benzyl bromide (26.4 ml, 221 mmol) was added dropwise and the resulting mixture was stirred at room temperature for 2 h. The reaction mixture was poured into ice water (600 ml) and the resulting mixture was extracted with ethyl acetate (300 ml×3). The extracts were washed with a saturated aqueous NaCl solution, dried, and evaporated. The residue was chromatographed on silica gel (1.5 kg) with 40:1 benzene–ethyl acetate to afford **9** (40.1 g, 98%) as a colorless syrup: R_f=0.72 (5:1 benzene–ethyl acetate); $[\alpha]_D^{27}$ −24° (*c* 2.10); ^{1}H-NMR δ=1.17 (3H, d, 3-Me, *J*=7.0 Hz), 2.30—2.70 (1H, m, H-3), 3.33 (3H, s, OMe), 3.60—4.30 (5H, m, H-2, 4, 5,6, and 6′), 4.54 (2H, s, $OC\underline{H}_2Ph$), 4.62 (1H, s, H-1), 5.55 (1H, s, $C\underline{H}Ph$), and 7.38 (10H, s, 2×Ph).

Found: C, 71.38; H, 7.05%. Calcd for $C_{22}H_{26}O_5$: C, 71.33; H, 7.07%.

Methyl 2-O-Benzyl-3-deoxy-3-C-methyl-α-D-altropyranoside (10). To an ice-cold sample of **9** (35.0 g, 94.5 mmol) was added ice-cold 75% aqueous dichloroacetic acid (350 ml). After being stirred at 0°C for 0.5 h, the reaction mixture was poured into a cold saturated aqueous $NaHCO_3$ solution (3 l). The mixture was extracted with chloroform (1 l×3) and the extracts were washed with a saturated aqueous NaCl solution (1 l), dried, and evaporated. The crystalline residue was washed with cold hexane to remove benzalde-

hyde and a practically pure sample of **10** (22.1 g, 83%) was obtained: mp 68.0—69.0 °C (colorless plates from acetone); R_f=0.09 (3:1 benzene-ethyl acetate); $[\alpha]_D^{23}$ +42° (*c* 1.38); ^{1}H-NMR δ=1.09 (3H, d, 3-Me, *J*=7.0 Hz), 1.20—2.40 (3H, m, H-3 and 2×OH), 3.33 (3H, s, OMe), 3.45—4.30 (5H, m, H-2, 4, 5, 6, and 6′), 4.51 (2H, s, OC<u>H</u>$_2$Ph), 4.61 (1H, s, H-1), and 7.35 (5H, s, Ph).

Found: C, 63.76; H, 7.99%. Calcd for $C_{15}H_{22}O_5$: C, 63.81; H, 7.85%.

Methyl 2-O-Benzyl-3,6-dideoxy-3-C-methyl-α-D-altropyranoside (11). To an ice-cold solution of **10** (48.6 g, 172 mmol) in dry pyridine (486 ml) was added mesyl chloride (14.6 ml, 189 mmol) over a period of 5 min. After being stirred at 0 °C for 1 h, the reaction mixture was poured into cold water (450 ml) and the resulting mixture was extracted with ethyl acetate (400 ml×3). The extracts were evaporated and the residue was resolved in ethyl acetate (250 ml). The solution was washed successively with saturated aqueous $KHSO_4$ (100 ml), $NaHCO_3$ (100 ml), and NaCl (100 ml) solutions, dried, and evaporated. To an ice-cold stirred solution of this crude syrup (62.0 g) of the 6-mesylate in dry ether (930 ml), $LiAlH_4$ (14.4 g, 379 mmol) was added portionwise over a period of 10 min. After being stirred at room temperature for 2 h, $Na_2SO_4 \cdot 10H_2O$ (122 g, 379 mmol) was added to the reaction mixture, and the resulting insoluble matter was filtered and the filter cake was washed thoroughly with chloroform. The combined filtrate and washings were evaporated and the residue was chromatographed on silica gel (1.5 kg) with 3:1 benzene-ethyl acetate to afford **11** (41.9 g, 91%) as a colorless syrup: R_f=0.42 (2:1 benzene-ethyl acetate); $[\alpha]_D^{30}$ +15° (*c* 1.37); ^{1}H-NMR δ=1.10 (3H, d, 3-Me, *J*=7.5 Hz), 1.27 (3H, d, 5-Me, $J_{5,6}$=6.3 Hz), 1.91 (1H, d, OH, *J*=7.5 Hz), 1.90—2.30 (1H, m, H-3), 3.31 (1H, dd, H-2, $J_{1,2}$=3.0 Hz, $J_{2,3}$=6.5 Hz), 3.40 (3H, s, OMe), 3.59 (1H, dd after addition of D_2O, H-4, $J_{3,4}$=3.8 Hz, $J_{4,5}$=6.3 Hz), 3.89 (1H, dq, H-5, $J_{4,5}$=6.3 Hz), 4.55 and 4.67 (each 1H, ABq, OC<u>H</u>$_2$Ph, J_{gem}=12.0 Hz), 4.58 (1H, d, H-1, $J_{1,2}$=3.0 Hz), and 7.34 (5H, s, Ph).

Found: C, 67.65; H, 8.22%. Calcd for $C_{15}H_{22}O_4$: C, 67.64; H, 8.33%.

2-O-Benzyl-3,6-dideoxy-3-C-methyl-D-altropyranose (12). To an ice-cold stirred solution of **11** (10.0 g, 37.5 mmol) in acetic anhydride (300 ml), concd H_2SO_4 (0.30 ml) was added. After being stirred at 0 °C for 10 min, the reaction mixture was poured into a cold saturated aqueous $NaHCO_3$ solution (250 ml) and the resulting mixture was extracted with ethyl acetate (200 ml×1+100 ml×1). The extracts were washed with a saturated aqueous NaCl solution (150 ml), dried, and evaporated to give a yellow syrup (11.4 g). To a solution of this syrup in methanol (113 ml) was added dropwise 1 M† aqueous NaOH solution (113 ml) and the mixture was kept at room temperature for 3.5 h. The reaction mixture was then neutralized (pH 7) with CO_2 gas and evaporated. The residue was triturated with acetone and the insoluble matter was removed by filtration and the filter cake was washed with acetone. The combined filtrate and washings were evaporated and the residue was chromatographed on silica gel (260 g) with 1:2 toluene-ethyl acetate to afford **12** (9.06 g, 96%) as a colorless syrup: R_f=0.41 (1:2 toluene-ethyl acetate); $[\alpha]_D^{18}$ −29° (*c* 1.19, MeOH, after 2d); ^{1}H-NMR δ=1.10—1.30 (6H, m, 2×Me), 2.15—2.55 (1H, m, H-3), 2.60 (0.6H, d, α-OH, *J*=3.0 Hz), 3.19 (0.4H, br, β-OH-4), 3.44 (0.6H, d. α-OH, *J*=3.0 Hz), 3.55—4.20 (3H, m, H-2, 4, and 5), 4.04 (0.4H, d, β-OH-1, *J*=6.0 Hz), 4.55 and 4.65 (ABq, OC<u>H</u>$_2$Ph, J_{gem}=12.0 Hz), 4.56 (s, OC<u>H</u>$_2$Ph), 5.22 (0.4H, dd, β-H-1, $J_{1,2}$=4.5 Hz), 5.41 (0.6H, d, α-H-1, $J_{1,2}$=0 Hz), and 7.34 and 7.37 (each s, Ph).

Found: C, 66.92; H, 8.01%. Calcd for $C_{14}H_{20}O_4$; C, 66.64; H, 7.99%.

3-O-Benzyl-1,4,7-trideoxy-4-C-methyl-D-glycero-D-glucoheptitol (13). A solution of **12** (8.70 g, 34.5 mmol) in dry ether (25 ml) was added dropwise to an ice-cold stirred ether solution of methylmagnesium iodide [prepared from magnesium turnings (8.39 g, 345 mmol) and methyl iodide (21.5 ml, 345 mmol) in dry ether (84 ml)]. After being stirred at 35 °C for 20 h, a saturated aqueous NH_4Cl solution was carefully added to the ice-cold reaction mixture. The organic layer was separated and the aqueous layer was extracted with chloroform (300 ml×3). The combined organic layers were dried and evaporated to a syrup (9.52 g), which was chromatographed on silica gel (463 g) with 1:5 toluene-ethyl acetate to afford **13** (8.00 g, 86%) as a colorless syrup and unchanged **12** (0.72 g, 8.3%). **13**: R_f=0.33 (1:5 toluene-ethyl acetate); $[\alpha]_D^{17}$ +3°, $[\alpha]_{365}^{17}$ +18° (*c* 3.81); ^{1}H-NMR δ=0.90 (3H, d, Me, *J*=7.5 Hz), 1.14 (3H, d, Me, *J*=6.0 Hz), 1.21 (3H, d, Me, *J*=6.0 Hz), 1.70—2.00 (1H, m, H-4), 2.10—2.40, 2.40—2.70, and 2.90—3.15 (each 1H, each br, 3×OH), 3.55—4.15 (4H, m, H-2, 3, 5, and 6), 4.70 and 4.79 (each 1H, ABq, OC<u>H</u>$_2$Ph, J_{gem}=12.0 Hz), and 7.40 (5H, s, Ph).

Found: C, 66.87; H, 8.93%. Calcd for $C_{15}H_{24}O_4$: C, 67.13; H, 9.02%.

(2S,3S,4S)-3-Hydroxy-2-methyl-4-pentanolide (14). A solution of $NaIO_4$ (82 mg, 0.38 mmol) in water (0.8 ml) was added to a solution of **13** (68.6 mg, 0.256 mmol) in acetone (0.69 ml) under ice-cooling. After being stirred for 20 min, the mixture was diluted with water and extracted with ether. The extracts were washed with a saturated aqueous NaCl solution, dried, and evaporated. The residual syrup (49.4 mg) was hydrogenolyzed in *t*-BuOH (0.98 ml) with palladium black at 28 °C for 40 min under bubbling with H_2 gas. The filtered solution was evaporated to a colorless syrup (29.2 mg), which was then oxidized with bromide (0.0148 ml, 0.287 mmol) in 50% aqueous dioxane (0.29 ml) at room temperature for 7.5 h. The reaction mixture was extracted with ethyl acetate, and the extracts were washed with saturated aqueous $Na_2S_2O_3$ and NaCl solutions, dried, and evaporated. The residue was chromatographed on silica gel (2 g) with 1:5 toluene-ethyl acetate to give **14** (13.8 mg, 46% from **13**) as a colorless oil. The ^{1}H-NMR spectrum of **14** was identical with that of the authentic sample.[5]

3-O-Benzyl-1,4,7-trideoxy-5,6-O-isopropylidene-4-C-methyl-D-glycero-D-gluco-heptitol (15). To an ice-cold stirred solution of **13** (8.00 g, 29.8 mmol) and DMP (7.30 ml, 59.6 mmol) in dry acetone (160 ml) was added dropwise concd H_2SO_4 (0.008 ml). After being stirred at 0 °C for 0.5 h, the reaction mixture was neutralized with solid Na_2CO_3. The insoluble matter was filtered and washed with acetone. The combined filtrate and washings were evaporated to afford a crude sample of **15** (8.30 g, 90%) as colorless needles. This sample was pure enough for the next step without further purification. An analytical sample was obtained after silica-gel column chromatography with 20:1 chloroform-acetone: mp 53—54 °C; R_f=0.88 (1:5 toluene-ethyl acetate); $[\alpha]_D^{15}$ +28° (*c* 0.79); ^{1}H-NMR δ=0.86 (3H, d, Me, *J*=6.6 Hz), 1.11 (3H, d,

†1M=1 mol dm^{-3}.

Me, J=6.0 Hz), 1.16 (3H, d, Me, J=6.0 Hz), 1.30 and 1.45 (each 3H, each s, CMe_2), 1.60—2.00 (1H, m, H-4), 2.47 (1H, d, OH, J=3.0 Hz), 3.61 (1H, dd, H-3, $J_{3,4}$=2.0 Hz, $J_{2,3}$=7.5 Hz), 3.77 (1H, ddd, H-2, $J_{1,2}$=6.0 Hz), 4.06 (1H, dd, H-5, $J_{5,6}$=6.0 Hz, $J_{4,5}$=10.5 Hz), 4.25 (1H, dq, H-6, $J_{6,7}$=6.0 Hz), 4.71 and 4.79 (each 1H, ABq, $OC\underline{H}_2Ph$, J_{gem}=11.7 Hz), and 7.37 (5H, s, Ph).

Found: C, 70.06; H, 9.02%. Calcd for $C_{18}H_{28}O_4$; C, 70.10; H, 9.15%.

2-O-*Acetyl-3*-O-*benzyl-1,4,7-trideoxy-5,6*-O-*isopropylidene-4*-C-*methyl*-D-glycero-D-gluco-*heptitol (16).* To a solution of the crude sample of **15** (8.30 g, 26.9 mmol) in ethyl acetate (83 ml) were added acetic anhydride (3.81 ml, 40.4 mmol) and DMAP (3.45 g, 28.2 mmol). After being stirred at room temperature for 0.5 h, the reaction mixture was diluted with ethyl acetate (83 ml) and washed with water (50 ml) and a saturated aqueous NaCl solution (50 ml), dried, and evaporated. The residue was chromatographed on silica gel (283 g) with 5:1 toluene–ethyl acetate to afford **16** (9.30 g, 89% from **13**) as colorless crystals: mp 78—78.5 °C (plates from acetone–hexane); R_f=0.78 (2:1 toluene–ethyl acetate); $[\alpha]_D^{17}$ +3°, $[\alpha]_{365}^{17}$ +14° (c 5.72); IR (KBr) 1728 cm^{-1}; ^{1}H-NMR δ=0.87 (3H, d, Me, J=7.2 Hz), 1.11 (3H, d, Me, J=6.0 Hz), 1.20 (3H, d, Me, J=6.0 Hz), 1.27 and 1.45 (each 3H, each s, CMe_2), 1.70—2.00 (1H, m, H-4), 1.92 (3H, s, OAc), 3.85 (1H, dd, H-3, $J_{3,4}$=1.5 Hz, $J_{2,3}$=9.0 Hz), 4.05—4.45 (2H, m, H-5 and 6), 4.73 (2H, s, $OC\underline{H}_2Ph$), 5.12 (1H, dq, H-2, $J_{1,2}$=6.0 Hz), and 7.30 (5H, s, Ph).

Found: C, 68.48; H, 8.47%. Calcd for $C_{20}H_{30}O_5$: C, 68.54; H, 8.63%.

2-O-*Acetyl-1,4,7-trideoxy-5,6*-O-*isopropylidene-3*-O-*mesyl-4*-C-*methyl*-D-glycero-D-gluco-*heptitol (17).* A mixture of **16** (998 mg, 2.85 mmol), palladium black (freshly prepared from 1 g of palladium(II) chloride), ethyl acetate (9 ml), and methanol (1 ml) was vigorously stirred at 25 °C for 3.5 h under bubbling with H_2 gas, and the suspension was filtered. The filtrate was evaporated to a colorless syrup (741 mg, 100%), which was mesylated with mesyl chloride (0.661 ml, 8.54 mmol) in dry pyridine (7.4 ml) at room temperature for 2 h. The reaction mixture was poured into cold water (7.4 ml) and the resulting mixture was extracted with ethyl acetate (10 ml×3). The extracts were washed successively with saturated aqueous $KHSO_4$ (6 ml×5), $NaHCO_3$ (6 ml), and NaCl (6 ml) solutions, dried, and evaporated. The residue was chromatographed on silica gel (50 g) with 3:1 toluene–ethyl acetate to afford **17** (918 mg, 95%) as colorless crystals: mp 88—90 °C (needles from hexane); R_f=0.51 (3:2 toluene–ethyl acetate); $[\alpha]_D^{16}$ 0°, $[\alpha]_{365}^{16}$ −32° (c 1.48); IR (KBr) 1738 cm^{-1}; ^{1}H-NMR δ=0.93 (3H, d, Me, J=7.2 Hz), 1.14 (3H, d, Me, J=6.0 Hz), 1.27 (3H, d, Me, J=6.0 Hz), 1.33 and 1.44 (each 3H, each s, CMe_2), 1.75—2.10 (1H, m, H-4), 2.09 (3H, s, OAc), 3.04 (3H, s, OMs), 3.94 (1H, dd, H-5, $J_{5,6}$=6.0 Hz, $J_{4,5}$=10.5 Hz), 4.26 (1H, dq, H-6, $J_{6,7}$=6.0 Hz), and 5.00—5.40 (2H, m, H-2 and 3).

Found: C, 49.95; H, 7.48; S, 9.27%. Calcd for $C_{14}H_{26}O_7S$: C, 49.69; H, 7.74; S, 9.47%.

2,3-Anhydro-1,4,7-trideoxy-5,6-O-*isopropylidene-4*-C-*methyl*-D-glycero-D-allo-*heptitol (18).* To an ice-cold stirred solution of **17** (4.36 g, 12.9 mmol) in chloroform (43.6 ml) was added 3.23 M sodium methoxide in methanol (5.68 ml). After being stirred at 0 °C for 0.5 h, the reaction mixture was neutralized with CO_2 gas and poured into cold water (50 ml). The mixture was extracted with dichloromethane (30 ml×3) and the extracts were washed with a saturated aqueous NaCl solution (50 ml), dried, and evaporated. The residue was chromatographed on silica gel (75 g) with 3:1 benzene–ethyl acetate to afford oily **18** (2.32 g, 90%), which was subjected to bulb-to-bulb distillation to give a pure sample of **18** (2.09 g, 81%) as a colorless oil: bp 100—106 °C (bath temp)/8.5 Torr; R_f=0.42 (3:1 toluene–ethyl acetate); $[\alpha]_D^{15}$ +49° (c 0.77); ^{1}H-NMR δ=0.94 (3H, d, Me, J=6.0 Hz), 1.19 (3H, d, Me, J=6.0 Hz), 1.31 (3H, d, Me, J=6.0 Hz), 1.37 and 1.50 (each 3H, each s, CMe_2), 1.50—1.90 (1H, m, H-4), 2.83 (1H, dd, H-3, $J_{3,4}$=9.0 Hz, $J_{2,3}$=4.5 Hz), 3.00 (1H, dq, H-2, $J_{1,2}$=6.0 Hz), 3.98 (1H, dq, H-5, $J_{5,6}$=6.0 Hz, $J_{4,5}$=9.0 Hz), and 4.28 (1H, dq, H-6, $J_{6,7}$=6.0 Hz).

Found: C, 65.91; H, 9.87%. Calcd for $C_{11}H_{20}O_3$: C, 65.97; H, 10.07%.

2,4,7-Trideoxy-5,6-O-*isopropylidene-2,4-di*-C-*methyl*-D-glycero-D-allo-*heptose Trimethylene Dithioacetal (19).* To a cold (−40 °C) stirred solution of 1,3-dithiane 97% (4.26 g, 34.4 mmol) in dry THF (42.6 ml), 1.28 M butyllithium in hexane (26.9 ml, 34.4 mmol) was added dropwise under argon. After being stirred at −20 °C for 2 h, the mixture was recooled to −40 °C and a solution of **18** (1.38 g, 6.89 mmol) in dry THF (2.8 ml) was added dropwise to this stirred solution. After standing at 2 °C for 2 d, the reaction mixture was poured into cold water (70 ml) and the resulting mixture was extracted with chloroform (50 ml×3). The extracts were washed with water (50 ml) and a saturated aqueous NaCl solution (50 ml), dried, and evaporated. The residue was chromatographed on silica gel (200 g) with 2.5:1 hexane–ethyl acetate to afford **19** (2.05 g, 93%) as a colorless syrup: R_f=0.30 (2.5:1 hexane–ethyl acetate); $[\alpha]_D^{30}$ +16° (c 1.50); ^{1}H-NMR δ=0.91 (3H, d, Me, J=6.3 Hz), 1.12 (3H, d, Me, J=6.0 Hz), 1.14 (3H, d, Me, J=7.0 Hz), 1.30 and 1.41 (each 3H, each s, CMe_2), 1.70—2.50 (4H, m, H-2,4, and $SCH_2C\underline{H}_2CH_2S$), 2.70—3.20 (5H, m, OH and $SC\underline{H}_2CH_2C\underline{H}_2S$), 3.58 (1H, dd after addition of D_2O, J=4.5 and 7.5 Hz), 4.02 (1H, dd, H-5, $J_{4,5}$=10.0 Hz, $J_{5,6}$=6.0 Hz), 4.22 (1H, dq, H-6, $J_{6,7}$=6.0 Hz), and 4.57 (1H, d, H-1, $J_{1,2}$=3.0 Hz).

Found: m/z 320.1471. Calcd for $C_{15}H_{28}O_3S_2$: M, 320.1477.

Acetyl Derivative 20. R_f=0.53 (3:1 hexane–ethyl acetate); $[\alpha]_D^{18}$ 0°, $[\alpha]_{365}^{18}$ 0° (c 0.33); IR (KBr) 1749 cm^{-1}; ^{1}H-NMR δ=5.11 (1H, dd, H-3, J=3.0 and 9.0 Hz).

Found: C, 56.24; H, 8.15; S, 17.44%. Calcd for $C_{17}H_{30}O_4S_2$: C, 56.32; H, 8.34; S, 17.69%.

3-O-*Benzyl-2,4,7-trideoxy-5,6*-O-*isopropylidene-2,4-di*-C-*methyl*-D-glycero-D-allo-*heptose Trimethylene Dithioacetal (21).* By the procedure described in the preparation of **9**, a sample of **19** (305 mg, 0.952 mmol) afforded, after silica-gel (19.5 g) column chromatography with 50:1 toluene–ethyl acetate, **21** (357 mg, 91%) as a pale yellow syrup. An analytical sample was obtained after silica-gel column chromatography with 50:1 toluene–ethyl acetate: R_f=0.70 (5:1 toluene–ethyl acetate); $[\alpha]_D^{15}$ −20° (c 1.02); ^{1}H-NMR δ=0.96, 1.09, and 1.12 (each 3H, each s, 3×Me, J=7.2, 6.0, and 7.5 Hz), 1.30 and 1.43 (each 3H, each s, CMe_2), 1.55—3.00 (8H, m, H-2, 4, and $SCH_2CH_2CH_2S$), 3.70 (1H, dd, H-3, J=2.1 and 10.2 Hz), 4.00—4.30 (2H, m, H-5 and 6), 4.60 (1H, d, H-1, $J_{1,2}$=2.7 Hz), 4.74 (2H, s, $OC\underline{H}_2Ph$), and 7.20—7.45 (5H, m, Ph).

Found: C, 64.19; H, 8.18; S, 15.26%. Calcd for $C_{22}H_{34}O_3S_2$: C, 64.35; H, 8.35; S, 15.62%.

3-O-*Benzyl-2,4-7-trideoxy-5,6*-O-*isopropylidene-2,4-di*-C-*methyl-aldehydo*-D-glycero-D-allo-*heptose (22) and Deisopropylidenation Heptopyranose 23.* To a mixture of **21** (233 mg, 0.567 mmol) and mercury(II) oxide (540 mg, 2.49 mmol) in

aqueous 80% acetone (16.3 ml) was added mercury(II) chloride (677 mg, 2.49 mmol) at room temperature with efficient stirring. The mixture was stirred at 60 °C for 10 min, cooled, and filtered with a Celite. The filter cake was washed with acetone, and then the filtrate and washings were combined. After the subsequent removal of the acetone by concentration, the aqueous residue was extracted with chloroform (10 ml×3) and the extracts were washed with an aqueous 10% KI solution (8 ml×2) and a saturated aqueous NaCl solution (8 ml), dried, and evaporated. The residue was chromatographed on silica gel (9.1 g) with 20:1 toluene–ethyl acetate to afford **22** (118 mg, 65%) as a colorless syrup: R_f= 0.48 (20:1 toluene–ethyl acetate); ^{1}H-NMR δ=0.91, 1.11, and 1.14 (each 3H, each d, 3×Me, J=6.6, 6.0, and 7.0 Hz), 1.28 and 1.42 (each 3H, each s, CMe_2), 2.00—2.40 (1H, m, H-4), 2.60—3.00 (1H, m, H-2), 3.90—4.20 (2H, m, H-3 and 5), 4.23 (1H, dq, H-6, $J_{5,6}$=$J_{6,7}$=6.0 Hz), 4.53 and 4.63 (each 1H, ABq, $OC\underline{H}_2Ph$, J=12.0 Hz), 7.34 (5H, s, Ph), and 9.83 (1H, d, H-1, $J_{1,2}$=3.0 Hz). The elution of the silica-gel column with ethyl acetate gave **23** (42.6 mg, 27%) as a colorless syrup: R_f=0.37 and 0.46 (10:1 chloroform–methanol); ^{1}H-NMR δ=0.90—1.30 (9H, m, 3×Me), 1.40—2.00 (2H, m, H-2 and 4), 2.40—2.80 and 3.30—3.60 (each 1H, each br, 2×OH), 3.50—4.20 (3H, m, H-3, 5, and 6), 4.64 (2H, s, $OC\underline{H}_2Ph$), 4.80—5.20 (1H, m, H-1), and 7.36 (5H, s, Ph).

*Transformation of **23** into **22**.* To a solution of **23** (50 mg, 0.18 mmol) in 95% ethanol (0.5 ml) was added $NaBH_4$ (13.5 mg, 0.357 mmol) and the mixture was stirred at room temperature for 24 h. The reaction mixture was neutralized with CO_2 gas and then evaporated. The residue was taken up with chroloform and an insoluble matter was filtered off. The filter cake was washed with chroloform and the combined filtrate and washings were evaporated. The residue (50.4 mg, 100%) was dissolved in dry DMF (0.5 ml) and to this were added DMP (0.044 ml, 0.36 mmol) and *dl*-10-camphorsulfonic acid (4.1 mg, 0.018 mmol). The mixture was stirred at room temperature for 3 h and poured into a cold solution of 0.1 M aqueous NaOH. The mixture was extracted with ethyl acetate and the extracts were washed with a saturated aqueous NaCl solution, dried, and evaporated. The residue was chromatographed on silica gel (3 g) with 3:1 toluene–ethyl acetate to afford an alcohol. DMSO (0.0271 ml) was added to a solution of oxalyl dichloride (0.0164 ml, 0.191 mmol) in dry dichloromethane (0.83 ml) cooled to −60 °C. After being stirred at −60 °C for 15 min, a solution of the above alcohol (41 mg) in dry dichloromethane (0.32 ml) was added to the mixture and the new mixture was stirred at −60 °C for 15 min. After being added triethylamine (0.0881 ml, 0.636 mmol), the mixture was stirred at −25 °C for 15 min. Ether (2 ml) and water (2 ml) were added and the two layers were separated. The aqueous layer was extracted with ether and the combined organic layers were washed with a saturated aqueous NaCl solution, dried, and evaporated. The residue was chromatographed on silica gel (2 g) with 20:1 toluene–ethyl acetate to afford a syrup (37 mg, 67% from **23**). The ^{1}H-NMR spectrum and TLC of this sample were identical of them of **22**.

*8-O-Benzyl-3-C-(benzyloxymethyl)-3,5,7,9,12-pentadeoxy-1,2:10,11-di-O-isopropylidene-7,9-di-C-methyl-5-methylene-*D-glycero-D-allo-L-talo-*dodecofuranose-(1,4) (**24**).* To a cooled (−90—−95 °C) solution of 3-*C*-(benzyloxymethyl)-3,5,6-trideoxy-5-iodo-1,2-*O*-isopropylidene-α-D-ribo-5-hexenofuranose[2] (0.451 g, 1.08 mmol) in dry ether (10 ml) was added 1.48 M butyllithium in hexane (0.68 ml, 1.01 mmol) over a period of 5 min under argon. After being stirred at the same temperature for 0.5 h, a solution of **22** (0.116 g, 0.361 mmol) in dry ether (0.23 ml) was added to the mixture over a period of 2 min, and stirring was continued at the same temperature for 20 min. To the reaction mixture was added a saturated aqueous NH_4Cl solution, and the separated aqueous layer was extracted with ether. The organic layers were combined, washed with a saturated aqueous NaCl solution, dried, and evaporated. The residual yellow syrup (0.553 g) was chromatographed on silica gel (83 g) with 5:1 toluene–ethyl acetate to afford **24** (0.170 g) contaminated with a small amount of impurity. This was again chromatographed on silica gel (17 g) with 2.5:1 hexane–ethyl acetate to afford a pure sample of **24** (0.134 g, 61%) as a colorless syrup: R_f=0.19 (5:1 toluene–ethyl acetate); $[\alpha]_D^{18}$ +36° (*c* 0.69); ^{1}H-NMR δ= 0.91, 0.97, and 1.11 (each 3H, each d, 3×CMe, J=6.5, 7.5, and 6.0 Hz), 1.28, 1.32, 1.41, and 1.47 (each 3H, each s, 2×CMe_2), 2.00—2.55 (3H, m, H-3, 7, and 9), 2.88 (1H, br s, OH), 3.40—4.90 (12H, m, H-2,4,6,8,10,11, $C\underline{H}_2OBzl$, and 2×$OC\underline{H}_2Ph$), 5.30 and 5.37 (each 1H, each br s, C=CH_2), 5.81 (1H, d, H-1, $J_{1,2}$=3.3 Hz), 7.33 and 7.36 (each 5H, each s, 2×Ph).

Found: C, 70.81; H, 8.15%. Calcd for $C_{36}H_{50}O_8$: C, 70.79; H, 8.25%.

*8-O-Benzyl-3-C-(benzyloxymethyl)-3,5,7,9,12-pentadeoxy-1,2:10,11-di-O-isopropylidene-5,7,9-tri-C-methyl-*D-erythro-D-altro-L-talo-*dodecofuranose-(1,4) (**25**) and* D-allo *Epimer (**26**).* A solution of **24** (0.123 g, 0.201 mmol) and chlorotris(triphenylphosphine)rhodium(I) (0.0465 g, 0.0502 mmol) in benzene (6.1 ml) was stirred under an atmospheric pressure of hydrogen at room temperature for 4.5 h. The reaction mixture was then evaporated and the residue was passed through Florisil (100—200 mesh, 2.5 g) with ether and again evaporated. The residue was chromatographed on silica gel (16 g) with 4:1 toluene–ethyl acetate to afford **25** (0.117 g, 95%) and **26** (0.0047 g, 3.8%) as colorless syrups: **25**, R_f=0.29 (4:1 hexane–acetone); $[\alpha]_D^{26}$ +38° (*c* 0.75); ^{1}H-NMR (250 MHz) δ=0.78 (3H, d, 5-Me, J=6.5 Hz), 0.97 (3H, d, 9-Me, J=6.8 Hz), 0.99 (3H, d, 7-Me, J=6.8 Hz), 1.14 (3H, d, 3×H-12, J=6.5 Hz), 1.28, 1.32, 1.43, and 1.49 (each 3H, each s, 2×CMe_2), 1.70—1.80 (1H, m, H-5), 2.00—2.15 (1H, m, H-7), 2.15—2.30 (2H, m, H-3 and 9), 3.26 (1H, d, OH, J=2.3 Hz), 3.46 (1H, dd, one of $C\underline{H}_2$OBzl, J=5.3 Hz, J_{gem}=9.8 Hz), 3.71 (1H, dd, H-8, $J_{7,8}$=3.8 Hz, $J_{8,9}$=5.0 Hz), 3.79 (1H, dd, one of $C\underline{H}_2OBzl$, J=7.8 Hz, J_{gem}=9.8 Hz), 3.94 (1H, dd, H-10, $J_{9,10}$=10.5 Hz, $J_{10,11}$=5.0 Hz), 3.99 (1H, d, H-6, $J_{5,6}$=9.0 Hz, $J_{6,7}$=0 Hz), 4.22 (1H, dq, H-11), 4.37 (1H, dd, H-4, $J_{3,4}$=11.3 Hz, $J_{4,5}$=1.3 Hz), 4.46 and 4.67 (each 1H, ABq, $OC\underline{H}_2Ph$, J=12.0 Hz), 4.52 (2H, s, $OC\underline{H}_2Ph$), 4.70 (dd, H-2, $J_{1,2}$=$J_{2,3}$=3.5 Hz), 5.76 (1H, d, H-1), and 7.20—7.40 (10 H, m, 2×Ph).

Found: C, 70.05; H, 8.42%. Calcd for $C_{36}H_{52}O_8$: C, 70.56; H, 8.55%.

26, R_f=0.20 (4:1 hexane–acetone); ^{1}H-NMR (250 MHz) δ=0.94 and 1.00 (each 3H, each d, 7- and 9-Me, J=7.3 and 7.5 Hz), 1.08 (3H, d, 5-Me, J=7.3 Hz), 1.12 (3H, d, 3×H-12, J=6.5 Hz), 1.28, 1.32, 1.42, and 1.47 (each 3H, each s, 2×CMe_2), 1.90—2.05 (1H, m, H-5), 2.05—2.30 (3H, m, H-3, 7, and 9), 2.55 (1H, d, OH, J=3.8 Hz), 3.51 (1H, dd, one of $C\underline{H}_2$OBzl, J=5.3 Hz, J_{gem}=10.0 Hz), 3.62 (1H, dd, H-8, J=3.5 and 6.5 Hz), 3.68 (1H, dd, one of $C\underline{H}_2OBzl$, J=10.0 Hz, J_{gem}=10.0 Hz), 3.84 (1H, dd, H-4, $J_{3,4}$=10.0 Hz, $J_{4,5}$=3.8 Hz), 3.94 (1H, ddd, H-6, $J_{5,6}$=6.3 Hz, $J_{6,7}$=2.5 Hz), 4.03 (1H, dd, H-10, $J_{9,10}$=10.0 Hz, $J_{10,11}$=5.0 Hz), 4.17 (1H, dq, H-11), 4.39 (2H,

s, OCH_2Ph), 4.56 and 4.67 (each 1H, ABq, OCH_2Ph, J=11.3 Hz), 4.66 (1H, dd, H-2, $J_{1,2}=J_{2,3}$=4.0 Hz), 5.68 (1H, d, H-1), and 7.20—7.40 (10H, m, 2×Ph).

*6,8-Di-O-Benzyl-3-C-(benzyloxymethyl)-3,5,7,9,12-pentadeoxy-1,2:10,11-di-O-isopropylidene-5,7,9-tri-C-methyl-*D-erythro-D-altro-L-talo-*dodecofuranose-(1,4) (27).* By the procedure described in the preparation of **9**, a sample of **25** (1.05 g, 1.71 mmol) afforded, after silica-gel column chromatography with 15:1 toluene–ethyl acetate, **27** (1.16 g, 97%) as a colorless syrup: R_f=0.26 (15:1 toluene–ethyl acetate); $[\alpha]_D^{30}$ −10° (*c* 1.86); ^{1}H-NMR δ=0.85, 0.93, 0.98, and 1.07 (each 3H, each d, 4×CMe, J=7.5, 7.5, 7.0, and 6.0 Hz), 1.29, 1.33, and 1.45 (3H, 6H, and 3H, each s, 2×CMe_2), 1.70—2.40 (4H, m, H-3, 5, 7, and 9), 3.30—4.40 [7H, m, H-4, 6, 8, 10, 11, and CH_2OBzl, including dd of 3.42 (1H, J=6.0 and 9.0 Hz)], 4.51 (4H, s, 2×OCH_2Ph), 4.50 and 4.77 (each 1H, ABq, OCH_2Ph, J_{gem}=12.0 Hz), 4.69 (1H, dd, H-2, $J_{1,2}=J_{2,3}$=3.9 Hz), 5.80 (1H, d, H-1), and 7.31 (15H, s, 3×Ph).

*6,8-Di-O-Benzyl-3-C-(benzyloxymethyl)-3,5,7,9,12-pentadeoxy-1,2-O-isopropylidene-5,7,9-tri-C-methyl-*D-erythro-D-altro-L-talo-*dodecofuranose-(1,4) (28).* A solution of **27** (1.21 g, 1.72 mmol) in 75 (v/v)% aqueous acetic acid (24 ml) was stirred at 50°C for 1.5 h, then evaporated. The residue was chromatographed on silica gel (36 g) with 2:1 toluene–ethyl acetate to afford **28** (1.11 g, 97%) as a colorless syrup: R_f=0.31 (2:1 toluene–ethyl acetate); $[\alpha]_D^{30}$ −27° (*c* 1.50); ^{1}H-NMR δ=0.85, 0.97, 1.04, and 1.16 (each 3H, each d, 4×CMe, J=7.5, 7.5, 6.0, and 6.0 Hz), 1.27 (6H, s, CMe_2), 1.60—2.35 (4H, m, H-3, 5, 7, and 9), 3.35—4.90 (10H, m, H-2, 4, 6, 8, 10, 11, CH_2OBzl, and OCH_2Ph), 4.53 and 4.58 (each 2H, each s, 2×OCH_2Ph), 5.78 (1H, d, H-1, $J_{1,2}$=3.0 Hz), 7.30 (10H, s, 2×Ph), and 7.33 (5H, s, Ph).

Found: C, 72.20; H, 7.92%. Calcd for $C_{40}H_{54}O_8$: C, 72.48; H, 8.21%.

*6,8-Di-O-Benzyl-3-C-(benzyloxymethyl)-3,5,7,9-tetradeoxy-1,2-O-isopropylidene-5,7,9-tri-C-methyl-*D-altro-β-L-talo-*decodialdofuranose-(1,4) (29).* To an ice-cold solution of **28** (0.933 g, 1.41 mmol) in acetone (9.3 ml) was slowly added a solution of $NaIO_4$ (0.904 g, 4.23 mmol) in water (9.0 ml). After being stirred at room temperature for 5 h, the mixture was diluted with water (9.0 ml) and saturated with NaCl. The mixture was extracted with ethyl acetate (15 ml×3) and the extracts were washed with a saturated aqueous NaCl solution, dried, and evaporated. The residue was chromatographed on silica gel (15 g) with 10:1 toluene–ethyl acetate to afford **29** (0.840 g, 97%) as a colorless syrup: R_f=0.51 (5:1 toluene–ethyl acetate); ^{1}H-NMR δ=0.80, 0.83, and 1.15 (each 3H, each d, 3×CMe, J=7.5, 7.2, and 6.3 Hz), 1.25 and 1.26 (each 3H, each s, CMe_2), 1.70—2.45 (3H, m, H-3, 5, and 7), 2.70—2.95 (1H, m, H-9), 3.35—4.35 [5H, m, H-4, 6, 8, and CH_2OBzl, including dd of 3.46 (1H, J=6.6 and 9.6 Hz) and d of 4.28 (1H, J=0 and 10.2 Hz)], 4.46 and 4.50 (each 1H, two center peaks of ABq, OCH_2Ph), 4.53 (2H, s, OCH_2Ph), 4.55 and 4.85 (each 1H, ABq, OCH_2Ph, J=12.0 Hz), 4.69 (1H, dd, H-2, $J_{1,2}=J_{2,3}$=3.3 Hz), 5.82 (1H, d, H-1), 7.35 (15H, s, 3×Ph), and 9.83 (1H, s, CHO).

*6,8-Di-O-benzyl-3-C-(benzyloxymethyl)-3,5,7,9,11-pentadeoxy-1,2-O-isopropylidene-5,7,9-tri-C-methyl-11-methylene-*L-glycero-D-altro-β-L-talo-*dodecodialdofuranose-(1,4) 12-(Diethyl Acetal) (30) and* D-glycero-D-altro-β-L-talo *Epimer (31).* To a solution of 2-bromo-3,3-diethoxy-1-propene (846 mg, 4.05 mmol) in dry THF (5.7 ml) cooled at −108—−110°C was added 1.40 M butyllithium in hexane (2.41 ml, 3.37 mmol) under argon. After being stirred at the same temperature for 15 min, a solution of **29** (832 mg, 1.35 mmol) in dry THF (2.5 ml) was added to the mixture and stirring was continued at the same temperature for 0.5 h. The reaction was quenched by adding a saturated aqueous NH_4Cl solution (5 ml) and the mixture was then extracted with ether (10 ml×3) at room temperature. The organic layer were washed with a saturated aqueous NaCl solution, dried, and evaporated. The residue was chromatographed on silica gel (150 g) with 9:1 toluene–ethyl acetate to afford **30** (592 mg, 58.8%) and **31** (351 mg, 34.8%) as colorless syrups: **30**, R_f=0.32 (9:1 toluene–ethyl acetate); ^{1}H-NMR δ=0.87, 0.99, and 1.02 (each 3H, each s, 3×CMe, J=6.6, 7.5, and 7.5 Hz), 1.15—1.30 (12H, m, 2×OCH_2Me and CMe_2), 1.80—2.40 (4H, m, H-3, 5, 7, and 9), 3.30—4.40 (10H, m, H-4, 6, 8, 10, 2×OCH_2Me, and CH_2OBzl), 4.50—5.00 (8H, m, H-2, 12, and 3×OCH_2Ph), 5.30—5.50 (2H, m, C=CH_2), 5.80 (1H, d, H-1, $J_{1,2}$=4.5 Hz), and 7.32 (15H, s, 3×Ph).

31, R_f=0.23 (9:1 toluene–ethyl acetate); ^{1}H-NMR δ=0.84, 0.92, and 1.04 (each 3H, each s, 3×CMe, J=6.6, 7.0, and 7.0 Hz), 1.10—1.30 (12H, m, 2×OCH_2Me and CMe_2), 1.75—2.40 (4H, m, H-3, 5, 7, and 9), 3.30—4.40 (10H, m, H-4, 6, 8, 10, 2×OCH_2Me, and CH_2OBzl), 4.50—5.00 (8H, m, H-2, 12, and 3×OCH_2Ph), 5.35—5.50 (2H, m, C=CH_2), 5.80 (1H, d, H-1, $J_{1,2}$=4.5 Hz), and 7.30 and 7.34 (10H and 5H, each s, 3×Ph).

*6,8-Di-O-benzyl-3-C-(benzyloxymethyl)-3,5,7,9,11-pentadeoxy-1,2-O-isopropylidene-5,7,9,11-tetra-C-methyl-*L-erythro-D-altro-β-L-talo-*dodecodialdofuranose-(1,4) 12-(Diethyl Acetal) (32) and* D-threo-D-altro-β-L-talo *Epimer (33).* A solution of **30** (256 mg, 0.343 mmol) and chlorotris(triphenylphosphine)-rhodium(I) (79.4 mg, 0.0858 mmol) in benzene (13 ml) was stirred under an atmospheric pressure of hydrogen at room temperature for 1 d. The reaction mixture was then evaporated and the residue was passed through Florisil (100—200 mesh, 20 g) with ether and again evaporated. The residue was chromatographed on silica gel (45 g) with 4:1 hexane–acetone to afford **32** (212 mg, 82.7%), **32**+**33** (21.7 mg, 8.4%), and **33** (9.3 mg, 3.6%) as colorless syrups: **32**, R_f=0.28 (4:1 hexane–acetone); $[\alpha]_D^{29}$ −35° (*c* 0.97); ^{1}H-NMR δ=0.82, 0.85, 0.92, and 1.05 (each 3H, each d, 4×CMe, J=7.5 Hz), 1.20 (6H, t, 2×OCH_2Me, J=7.5 Hz), 1.27 (6H, s, CMe_2), 1.60—2.40 (5H, m, H-3, 5, 7, 9, and 11), 3.35—4.40 (10H, m, H-4, 6, 8, 10, 2×OCH_2Me, and CH_2OBzl), 4.50—5.00 (8H, m, H-2, 12, and 3×OCH_2Ph), 5.80 (1H, d, H-1, $J_{1,2}$=4.2 Hz), and 7.30 and 7.33 (10H and 5H, each s, 3×Ph).

Found: C, 72.20; H, 8.43%. Calcd for $C_{45}H_{64}O_9$: C, 72.16; H, 8.61%.

33, R_f=0.19 (4:1 hexane–acetone); ^{1}H-NMR δ=0.80—1.30 (24H, m, 8×CMe), 1.70—2.40 (5H, m, H-3, 5, 7, 9, and 11), 3.25—4.40 (10H, m, H-4, 6, 8, 10, 2×OCH_2Me, and CH_2-OBzl), 4.45—4.90 (8H, m, H-2, 12, and 3×OCH_2Ph), 5.82 (1H, d, H-1, $J_{1,2}$=3.6 Hz), and 7.32 and 7.37 (10H and 5H, each s, 3×Ph).

*6,8,10-Tri-O-acetyl-3-C-(acetoxymethyl)-3,5,7,9,11-pentadeoxy-1,2-O-isopropylidene-5,7,9,11-tetra-C-methyl-*L-erythro-D-altro-β-L-talo-*dodecodialdofuranose-(1,4) 12-(Diethyl Acetal) (3).* To a solution of **32** (362 mg, 0.484 mmol) in dry ether (7.25 ml) was added liquid ammonia (36 ml), and then lithium (270 mg, 39 mmol) was added under cooling (−78°C). After the mixture was stirred at the same temperature for 4 h, the excess lithium was destroyed by adding of solid NH_4Cl. The mixture was then diluted with ether and allowed to concentrate spontaneously. The residue was taken with ether

and the solution was washed with a saturated aqueous NaCl solution, dried, and evaporated. The residual colorless syrup (231 mg, 100%) of **34** was dissolved in ethyl acetate (2.3 ml) and to this were added acetic anhydride (0.365 ml, 3.86 mmol) and DMAP (354 mg, 2.90 mmol). After being stirred at room temperature for 4 h, the reaction mixture was diluted with ethyl acetate (5 ml) and washed with a saturated aqueous NaCl solution (3 ml), dried, and evaporated. The residue was chromatographed on silica gel (30 g) with 3:2 toluene–ethyl acetate to afford **3** (280 mg, 90%) as colorless needles. The ^{1}H-NMR spectrum, R_f-value on TLC, and mp of this sample were identical with those of the authentic sample.[2)]

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