Synthetic Studies of Rifamycins. V.[1] A Chiral Synthesis of an Ansa-chain Compound for the C-17—C-29 Portion of Rifamycin W†

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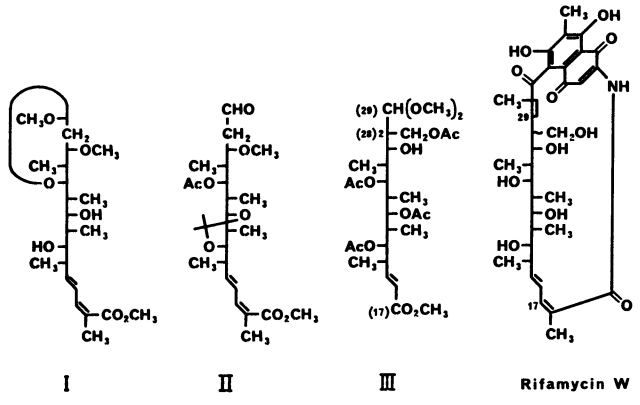
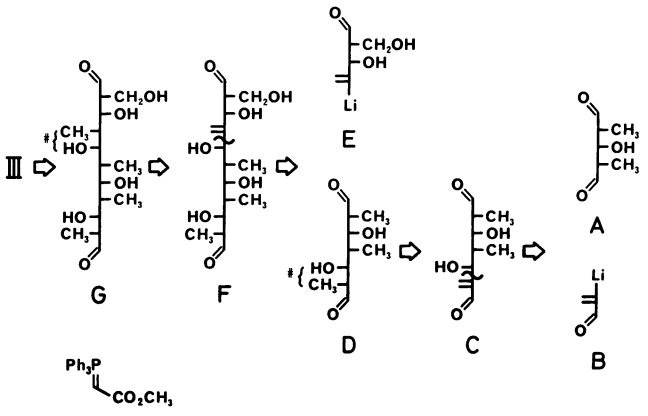
The chiral synthesis of methyl 5,7,9-tri-*O*-acetyl-2-*C*-(acetoxymethyl)-2,4,6,8,10,11,12-heptadeoxy-4,6,8,10-tetra-*C*-methyl-*aldehydo*-L-*glycero*-L-*talo*-L-*manno*-(*E*)-11-tridecenuronate 1-(dimethyl acetal) (III), a useful synthetic segment for the C-17-C-29 portion of rifamycin W, is described. The key intermediate, 3-*O*-(*t*-butyldimethylsilyl)-2,4,7-trideoxy-5,6-*O*-isopropylidene-2,4-di-*C*-methyl-*aldehydo*-D-*glycero*-D-*talo*-heptose (**28**) was synthesized in 30% yield from methyl 4,6-*O*-benzylidene-3-deoxy-3-*C*-methyl-α-D-glucopyranoside in 15 steps. The synthesis involves key steps of highly stereoselective Grignard reaction and regiospecific *cis*-epoxide ring-opening reaction. The condensation of **28** with 3,3-diethoxy-2-lithio-1-propene afforded about 1.6:1 excess of the "Cram" product (**30**, 56% yield). The desilylation of **30** followed by homogeneous hydrogenation with $(Ph_3P)_3RhCl$ gave only the *erythro* product **34**. 3,5-Di-*O*-benzyl-2,4,6-trideoxy-2,4,6-tri-*C*-methyl-L-*glycero*-L-*manno*-heptodialdose 1-(diethyl acetal) derived from **34**, condensed with the lithium reagent prepared (in ether at −95——90 °C) from butyllithium and 3-*C*-(benzyloxymethyl)-3,5,6-trideoxy-5-iodo-1,2-*O*-isopropylidene-α-D-hexenofuranose, derived from 3-deoxy-3-*C*-hydroxymethyl-1,2 : 5,6-di-*O*-isopropylidene-α-D-allofuranose, to afford a 4 : 1 mixture of the "Cram" product and its epimer in 80% yield. The homogeneous hydrogenation of the mixture followed by the debenzylation gave the diastereomerically pure major product, which could be transformed into III in 6 steps.

The first chiral synthesis of the ansa-chain portion of rifamycin S in the form of I was described in the preceding papers[1,2] from this laboratory. Recently, Nagaoka and Kishi[3] reported the highly stereocontroled synthesis of the optically active form of the ansa-chain compound II from (*S*)-(−)-3-*t*-butoxy-2-methyl-1-propanol. In this paper, we wish to report an improved convergent route for the chiral synthesis of the ansa-chain compound III, a useful synthetic segment for the C-17-C-29 portion of rifamycin W,[4] the biosynthetic progenitor of all the rifamycins.[5] Since the stereochemistry at C-28 of rifamycin W was unknown,[6] we assumed the configuration of the corresponding C-2 chiral center in III to be (*R*) by considering the facility of the synthesis. Naturally, when the opposite stereochemistry at C-2 of III was required, the chemical interchange of the acetoxymethyl and dimethoxymethyl groups at C-2 was considered feasible.

In keeping with the experimental results obtained in the synthesis of I,[1] our synthetic plan was made using the retrosynthetic analysis shown in Scheme 1. In the plan, it was expected that the starting symmetric dialdehyde **A** (a synthetic equivalent) is allowed to react successively with the lithium reagents, **B** and **E**, to afford predominantly the "Cram"[7] product **F** *via* the "Cram" product **C**, and the exo-methylene intermediates, **C** and **F**, are hydrogenated, under similar stereochemical control, to provide exclusively the *erythro*†† isomers, **D** and **G**, respectively. As the key intermediates corresponding to the synthetic equivalents, **A**, **B**, and **E**, in the planned convergence scheme, we chose the compounds, **28**, **29**, and **58**, respectively. The intermediates, **28** and **58** were obtainable by the chiral synthesis using appropriate sugar derivatives.





Scheme 1.

The key intermediate **28** was synthesized from 2-*O*-benzyl-3,6-dideoxy-3-*C*-methyl-D-glucopyranose (**6**) through the stereo- and regio-selective route. The compound **6** was prepared, through the route shown in Scheme 2, from methyl 4,6-*O*-benzylidene-3-deoxy-3-*C*-methyl-α-D-glucopyranoside (**2**),[8] which could be obtained on a large scale from methyl 4,6-*O*-benzylidene-3-deoxy-3-*C*-methyl-α-D-altropyranoside (**1**).[8,9]

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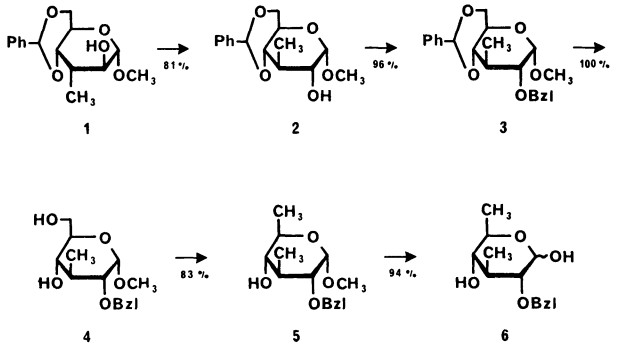
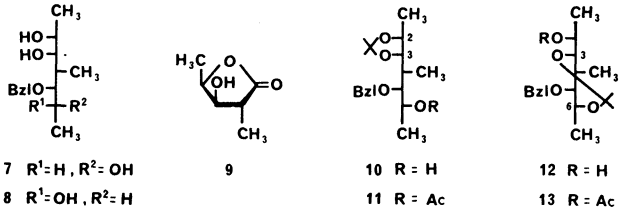
†† In this article, the substituents on the same side of the chain in a Fischer projection of acyclic molecule are prefixed as *erythro*, while those on opposite sides are prefixed as *threo*.

The *O*-benzylation of **2** followed by the debenzylidenation of the resulting **3** with methanolic hydrogen chloride afforded crystalline **4**, which was selectively 6-*O*-mesylated with 1.14 equiv. of mesyl chloride in pyridine and subsequently reduced with lithium aluminium hydride to give **5**. The acetolysis of **5** with acetic anhydride containing 0.15 equimolar amounts of sulfuric acid, followed by the hydrolysis with sodium hydroxide yielded **6** in 75% overall yield based on **2**.



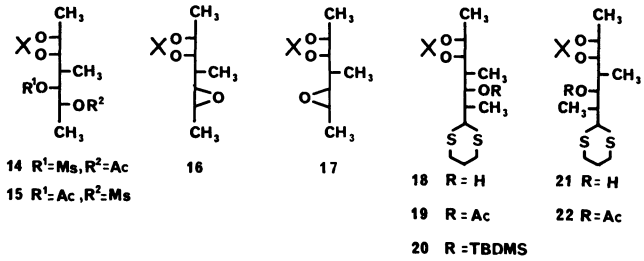
Scheme 2.

The Grignard reaction of **6** with 10 equimolar amounts of methylmagnesium iodide in ether afforded the product **7** (78%), its epimer **8** (1.5%), and the unchanged **6** (16%). The (6*R*)-configuration of the major product **7** was confirmed by the fact that **7** was transformed, through a sequence of reactions involving periodate-oxidation followed by successive debenzylation, acid hydrolysis, and bromine-oxidation, into the 1,4-lactone **9**, whose relative configuration was proved by ^{1}H-NMR analysis to be identical with that of (2*S*,3*S*,4*S*)-3-hydroxy-2-methyl-4-pentanolide[1] or its enantiomer.[10] The 2,3-acetonation of **7** with 1.5



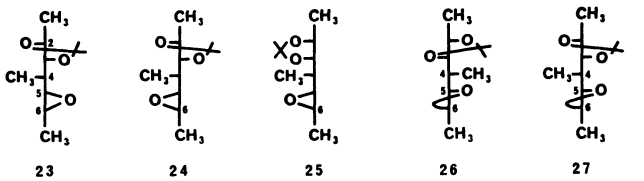
equimolar amounts of 2,2-dimethoxypropane (DMP) and 0.1 equimolar amounts of *p*-toluenesulfonic acid in DMF afforded, contrary to our expectation,[1] the mixture from which the two kinds of isomeric acetonides, **10** and **12** were isolated by column chromatography in 55% and 44% yields respectively. The structures of **10** (2,3-acetonide) and **12** (3,6-acetonide) were determined by the following facts: (i) **10** could be converted into the epoxide **16** through the sequence of reactions described later on, while **12** gave no epoxide in the same procedure as in the case of **10** and (ii) the debenzylated product obtained from **10** was cleaved with periodate reagent, while that from **12** was not affected by the same reagent. The ^{1}H-NMR spectra (250 MHz) of **10** and **12**, and of their acetates, **11** and **13**, showed signals in line with the structures as depicted. After many unsuccessful attempts, a 4.7 : 1 predominance of **10** was attained by the treatment of **7** with 2 equimolar amounts of DMP in acetone containing a catalytic amounts of concd sulfuric acid. Furthermore, **12** separated from **10** was treated with an equimolar amounts of zinc bromide in dichloromethane to give **10** in 94% isolated yield. The total yield of **10** thus amounted to 93%.

The acetylation of **10** with acetic anhydride and 4-(dimethylamino)pyridine (DMAP) in ethyl acetate afforded the 6-acetate **11** in 95% yield. The hydrogenolysis of **11** with hydrogen (palladium black) in ethanol followed by the immediate mesylation gave the 5-mesylate **14** in 92% yield after the chromatographic

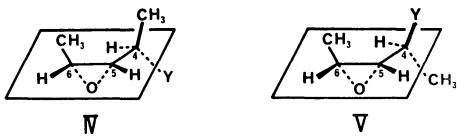


separation from the isomeric 6-mesylate **15** (5%), presumably resulted from the isomeric 5-acetate formed by the 6→5 *O*-acyl migration during the hydrogenolysis of **11**. The 5-mesylate **14** was then treated with sodium methoxide in chloroform to afford the *cis*-epoxide **16** in 81% yield after distillation. The 6-mesylate **15** also gave the diastereomeric *cis*-epoxide **17**. The reaction of **16** or **17** with 5 equiv. of 2-lithio-1,3-dithiane in THF at 5 °C afforded regiospecifically only the C-6-adduct **18** or **21** in 91% or 94% yield respectively. Since ring-opening of epoxides with nucleophiles is known to proceed with inversion at the center of addition,[11] the structures of **18** and **21** could be determined by the coupling features (double doublets) of the acetoxymethine protons in the ^{1}H-NMR spectra of their acetates, **19** and **22**.

The stereochemical control in this ring-opening process of *cis*-epoxide was truly remarkable. The analogous *cis*-epoxides, **23**,[12] **24**,[12] and **25**[13] also reacted with 2-lithio-1,3-dithiane to give only the corresponding



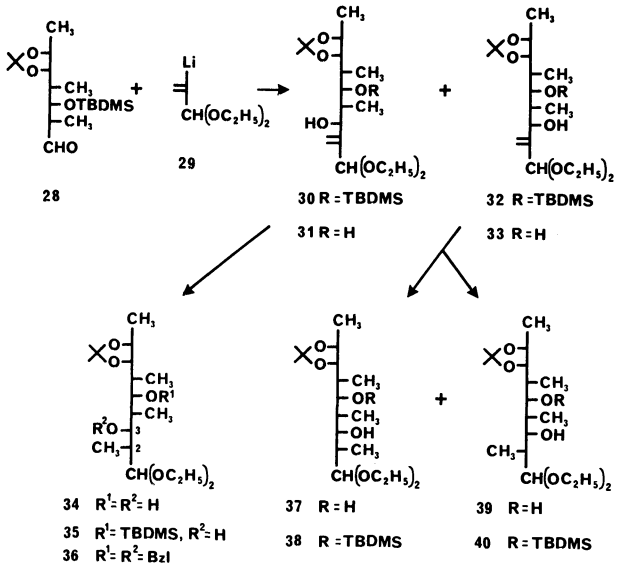
C-6-adducts in good yields. The high regioselectivity in ring-opening of these *cis*-epoxides was independent of the relative configurations at C-4 and C-5 and of the configurations of other chiral centers (C-2 and C-3). This result differed from the reported regioselectivities in the reactions of the *trans*-epoxides, **26** and **27**, with 2-lithio-1,3-dithiane. The epoxide **26** with *erythro*-configuration at C-4 and C-5 afforded a 3.1 : 1 mixture of C-6- and C-5-adducts,[1] while **27** with *threo*-configuration at C-4 and C-5 gave a 2.8 : 1 mixture of C-5- and



Scheme 3.

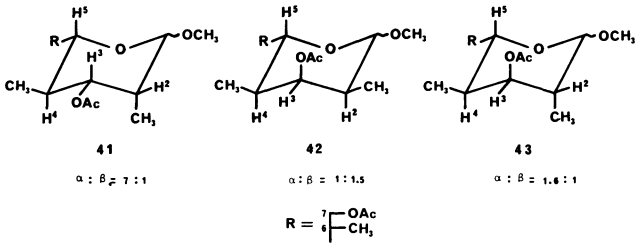
C-6-adducts.[10] Therefore, the regioselectivity of ring-opening in the *trans*-epoxides seemed to be affected by their C-4 configurations. The remarkable regioselectivity observed in the reactions of the *cis*-epoxides may be explained as follows. In the *cis* series, the free rotation of the ring-C-5-substituent ($CH(CH_3)Y$) about the C-4–C-5 bond axis should be restricted within narrow limits owing to larger nonbonding interaction of this group with the ring-methyl at C-6 than in the *trans* series. Therefore, each molecule of the *cis*-epoxides should have in the ground state a preferred conformation[14] which is rigidly held and resembles IV or V as depicted in Scheme 3. In this conformation, axial (β) attack at the C-5 position would involve the attacking group in an eclipsing interaction with the vicinal quasi axial 4-methyl group[15] or the 4-substituted Y, and addition will exclusively occur at the C-6-position, if the above-mentioned preferred reactant conformation is also favorable in the transition state of the reaction.

The *t*-butyldimethylsilylation of **18** provided, in 97% yield, the silyl ether **20**, whose dithioacetal group was cleaved with an 1 : 1 mixture of mercury(II)- and red mercury(II) oxide to generate the aldehyde **28** in 94% yield (or in 39.5% overall yield from **6**). The condensation of **28** with the lithium reagent **29** prepared from 3 equiv. of 2-bromo-3,3-diethoxy-1-propene[16] and 2.5 equiv. of butyllithium in THF at −110 °C was performed in THF at −110 °C to afford, after column chromatographic separation, **30** and **32** in 56 and 36% yields respectively based on **28**. The



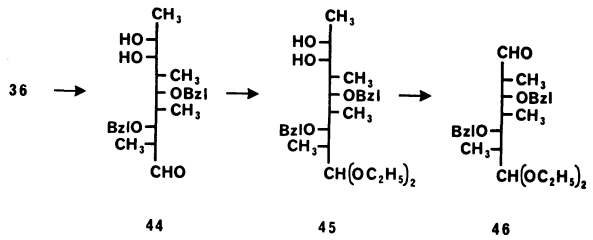
Scheme 4.

desilylation of **30** with tetrabutylammonium fluoride gave **31** in 98% yield. The homogeneous hydrogenation[1] of **31** with about 0.24 equimolar amounts of tris-(triphenylphosphine)chlororhodium (I)[17] in benzene under an atmospheric pressure of hydrogen yielded, in 93% yield, **34** as a sole hydrogenation product, whose diastereomeric homogeneity was confirmed by the TLC and 250 MHz ^{1}H-NMR analyses. The homogeneous hydrogenation of the silyl ether **30** proceeded more slowly and the reaction needed at least 1.5 equimolar amounts of the rhodium catalyst for its completion. The crude product **35** resulted in 79% yield was desilylated to afford the diastereomerically homogeneous **34**. In order to determine the configurations at C-2 and C-3 in **34**, **34** was transformed into the methyl L-heptopyranoside derivative **41** through the sequence of reactions involving deacetonation with pyridinium *p*-toluenesulfonate[18] (PPTS) in ethanol, followed by successive periodate-oxidation, sodium borohydride reduction, methanolysis with 0.5% methanolic hydrogen chloride, and acetylation. The structure shown for **41** was confirmed by the 250 MHz ^{1}H-NMR analysis

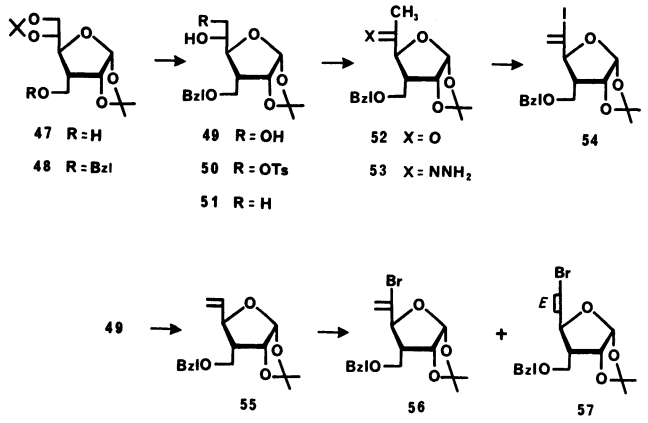


(using decoupling technique), indicating that the condensation of **28** with **29** yielded predominantly the "Cram" product **30**, which and whose desilylation product **31** were stereospecifically hydrogenated to afford the 2,3-*erythro* isomers, **35** and **34**, respectively. The minor methylene product **32** was shown to be the anti-"Cram" condensation product as follows. Unlike **31**, the desilylation product **33** from **32** afforded, on homogeneous hydrogenation, about 1 : 1 epimeric mixture of **37** and **39**, while the direct hydrogenation of **32** gave about 1 : 8 mixture of **37** and **39** *via* the corresponding mixture of **38** and **40**. The isolated **37** and **39** were transformed into the corresponding methyl L-heptopyranoside derivatives, **42** and **43**, by the procedure described in the transformation of **34** into **41**. The structures of **42** and **43** could also be well determined as depicted by the 250 MHz ^{1}H-NMR analyses.

The benzylation of **34** afforded **36** in 88% yield. The one stage deacetonation of **36** by the ethanolysis with ethanol (PPTS) or with ethanolic hydrogen chloride resulted in the low yield (≈55%) of **45**. Thus **36** was at first hydrolyzed with 75% dichloroacetic acid (DCA) and then the resulting aldehyde **44** was



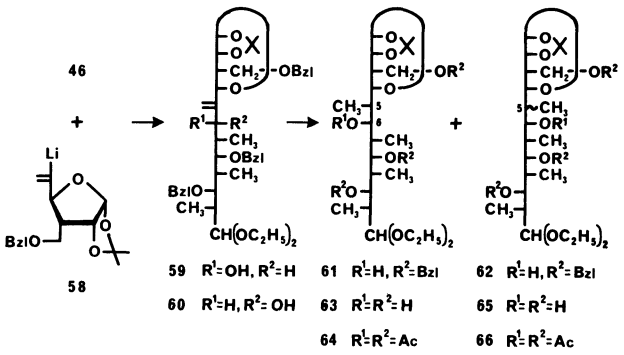
treated with ethanol in the presence of a catalytic amounts of *p*-toluenesulfonic acid to give **45** in 86% yield. The periodate-oxidation of **45** afforded the synthetic intermediate **46** in 81% yield. The lithium reagent **58** was prepared by the lithiation of the alkenyl halides, **54** and **56**, which were synthesized starting from 3-deoxy-3-*C*-hydroxymethyl-1,2:5,6-di-*O*-isopropylidene-α-D-allofuranose[19] (**47**) through the route shown in Scheme 5.



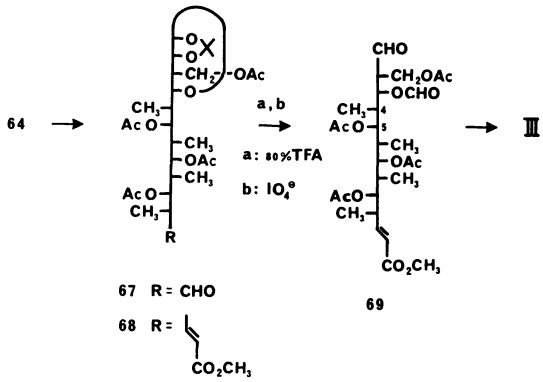
Scheme 5.

The benzylation of **47** followed by the selective hydrolysis of the resulting benzyl ether **48** with 75% acetic acid afforded the glycol **49** in 91% yield. The selective 6-*O*-tosylation of **49** followed by lithium aluminium hydride reduction gave **51** in 74% yield. The oxidation of **51** proceeded effectively with pyridinium chlorochromate (PCC) and molecular sieve 3A powder,[20] affording **52** in 92% yield. The methyl ketone **52** was converted into the alkenyl iodide **54** in 30% yield *via* the hydrazone **53**, according to the procedure of Barton *et al.*[21,8] The alkenyl bromide **56** was prepared from the 1,2-glycol **49**. The periodate-oxidation of **49** followed by the Wittig condensation with methylenetriphenylphosphorane in DMSO afforded **55** in 87% yield. The bromination of **55** with bromine in carbon tetrachloride followed by the elimination of hydrogen bromide with DBU in DMSO gave the isomeric alkenyl bromides, **56** and **57**, in 72 and 14% yields respectively after chromatographic separation.

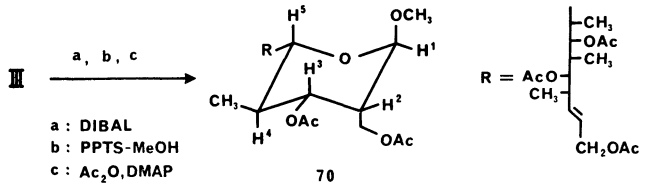
The condensation of **46** with the lithium reagent **58**, prepared from 3.1 equiv. of alkenyl iodide **54** and 3.1 equiv. of butyllithium in ether at −95——90 °C, was carried out in ether at −95——90 °C to afford a 4 : 1 mixture of **59** and **60** in 80% yield. The isomeric ratio was estimated by the 250 MHz ^{1}H-NMR analysis. On the other hand, the lithiation of the alkenyl bromide **56** had to be performed in THF at −95 °C, because **56** was virtually unreactive to butyllithium in ether at −100 °C. Thus, **46** was allowed to react in THF at −95 °C with **58**, prepared from 3.0 equiv. of **56** and 2.5 equiv. of butyllithium, to yield a mixture of **59** and **60** in 52% yield, and unchanged **46** was recovered in 29% yield. As in the case of the condensation of **28** with **29**, the major epimer **59** was anticipated to be the "Cram" product, and its structure was confirmed in the later stage of this ansa-chain synthesis. Since the preparative separation of **59** from **60** by column chromatography was impracticable in this stage, the epimeric mixture was directly hydrogenated with 2 equimolar amounts of the rhodium catalyst to give, in 82% yield, a diastereomeric mixture (**61** and **62**), which was debenzylated with lithium in liquid ammonia to afford, after column chromatographic separation, the isomerically homogeneous **63** (in 77% yield) and a minor fraction containing the isomeric mixture (**65**). The acetylation of **63** with



acetic anhydride and DMAP in ethyl acetate yielded the crystalline tetraacetate **64** in 91% yield. The acetylation product from the fraction of **65** was shown to be a 2 : 1 mixture of two C-5-epimeric acetates (**66**) by the TLC and ^{1}H-NMR analyses. The hydrolysis of **64** with 75% DCA followed by the Wittig condensation of the resulting aldehyde **67** with (methoxycarbonylmethylene)triphenylphosphorane gave **68** in 86% yield. The deacetonation of **68** with 80% trifluoroacetic acid (TFA) followed by the periodate-oxidation afforded the crystalline aldehyde **69**, which was treated with methanol containing a catalytic amounts of *p*-toluenesulfonic acid to give the target compound III in 43% yield based on **68**.



The configurations at C-4 and C-5 in **69** were determined by the following manner. The dimethyl acetal III was then reduced with a large excess of diisobutylaluminium hydride (DIBAL) in toluene at −78 °C. The methanolysis of resulting alylic alcohol with PPTS in methanol followed by the acetylation with acetic anhydride and DMAP afforded **70**, whose structure as depicted was confirmed by the 250 MHz ^{1}H-NMR analysis. Consequently, the structures shown for **64** and **59** were established. Furthermore, isomerically pure **59** and **61** were isolated by careful column



chromatography from the aforesaid condensation products and their hydrogenation products respectively, and it was confirmed that the "Cram" product **59**, as well as **30** and **31**, was stereospecifically hydrogenated to afford only the 5,6-*erythro* isomer **61**. It is interesting that, in the case of the anti-"Cram" products, **60**, **32**, and **33**, no remarkable stereoselectivity was observed.

Experimental

The melting points were determined on a micro hot-stage Yanaco MP-S3 and are uncorrected. The specific rotations were measured with a Carl Zeissphotoelectric polarimeter, using a 0.2-dm tube, in chloroform unless stated otherwise. The ^{1}H-NMR spectra were recorded with either a Varian EM-390 or a Bruker WM 250 spectrometer in $CDCl_3$ using TMS as the internal standard. The TLC was carried out on Merck TLC plates (60F-254, 0.25 mm). The column chromatography was performed on silica gel Wakogel C-200. In general, the evaporation of solvents was carried out under reduced pressure below 30 °C.

Methyl 2-O-Benzyl-4,6-O-benzylidene-3-deoxy-3-C-methyl-α-D-glucopyranoside (3). Sodium hydride (15.9 g, 55% emulsion in mineral oil) was washed free from the mineral oil with hexane and evaporated until the last traces of hexane were removed from the sodium hydride. The powdered residue was added to an ice-cooled solution of **2** (51.0 g, 0.182 mol) in dry DMF (360 ml). The mixture was stirred at room temperature for 0.5 h and then ice-cooled. Benzyl bromide (43.2 ml, 0.364 mol) was added dropwise to the stirred mixture over a period of 25 min. After the mixture had been stirred for 1.5 h at room temperature, it was poured into ice water (150 ml) and the new mixture was extracted with chloroform (200 ml × 3). The extracts were washed with a saturated aqueous NaCl solution, dried, and evaporated to a crystalline solid (102.8 g), which was chromatographed on silica gel (1.5 kg) with 15 : 1 benzene–ethyl acetate to afford a practically pure sample of **3** (64.4 g, 96%); mp 121—122.8 °C. Recrystallization from hexane gave an analytical sample as colorless needles: mp 121.7—122.1 °C; $[\alpha]_D^{27}$ +46° (c 2.14); ^{1}H-NMR δ=1.13 (3H, d, 3-Me, J=6.3 Hz), 2.0—2.5 (1H, m, H-3), 2.9—3.3 (2H, m, H-2 and 4), 3.37 (3H, s, OMe), 3.5—3.85 (2H, m, H-6 and 6′), 4.1—4.3 (1H, m, H-5), 4.5—4.6 (3H, sharp m, H-1 and OC<u>H</u>$_2$Ph), 5.41 (1H, s, C<u>H</u>Ph), and 7.2—7.5 (10H, m, 2 × Ph),

Found: C, 71.61; H, 7.11%. Calcd for $C_{22}H_{26}O_5$: C, 71.33; H, 7.08%.

Methyl 2-O-Benzyl-3-deoxy-3-C-methyl-α-D-glucopyranoside (4). A suspension of **3** (69.4 g) in dry methanol (700 ml) was stirred in an ice bath. 3.68 M HCl††† in methanol (102 ml) was then added to the suspension over a period of 10 min. After the mixture had been stirred at room temperature for 40 min, the reaction mixture was ice-cooled, neutralized (pH 6) with $NaHCO_3$ (43.5 g), and evaporated to a crystalline solid. The residue was repeatedly extracted with acetone (*ca.* 1 l) to remove insoluble matter. The acetone extracts were evaporated to afford **4** (50.0 g, 100%) as colorless crystals; mp 143.5—147 °C. Recrystallization from acetone gave a pure sample: Colorless needles, mp 143.8—144.6 °C; $[\alpha]_D^{27}$ +106° (*c* 1.20); ^{1}H-NMR δ=1.13 (3H, d, 3-Me, J=6.3 Hz), 1.8—2.2 (1H, m, H-3), 2.3—2.6 (1H, br, OH), 2.6—2.8 (1H, br, OH), 3.07 (1H, dd, H-2, $J_{1,2}$=3.3 Hz, $J_{2,3}$=9.6 Hz), 3.36 (3H, s, 1-OMe), 3.2—3.6 (2H, m, H-4 and 5), 3.6—3.8 (2H, m, H-6 and 6′), 4.5—4.6 (3H, sharp m, H-1 and OC<u>H</u>$_2$Ph), and 7.30 (5H, s, Ph).

Found: C, 63.64; H, 7.69%. 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-glucopyranoside (5). To an ice-cooled solution of the crude sample of **4** (25.4 g, mp 143.5—147 °C) in dry pyridine was added mesyl chloride (8.00 ml, 0.1035 mol) over a period of 0.5 h and stirred under ice-cooling for 3 h. The reaction mixture was then poured into a cold saturated aqueous $NaHCO_3$ solution (250 ml) and the mixture was extracted with ethyl acetate (300 ml × 3). The extracts were combined, washed successively with a saturated aqueous $KHSO_4$ solution (300 ml × 5) and a saturated aqueous NaCl solution (300 ml × 2), dried, and evaporated. The residual pale yellow crude syrup (31.9 g) of the 6-mesylate was dissolved in dry ether (480 ml), and $LiAlH_4$ (7.5 g, 0.198 mol) was added portionwise to the solution under ice-cooling over a period of 10 min. After being stirred at room temperature for 3 h, $Na_2SO_4 \cdot 10H_2O$ (62.7 g, 0.195 mol) was added to the reaction mixture, and resulting insoluble matter was filtered and washed with chloroform (80 ml × 5). The filtrate and washings were combined and evaporated to a pale yellow syrup (33.5 g), which was chromatographed on silica gel (1 kg) with 2 : 1 benzene–ethyl acetate to afford a colorless syrup of **5** (20.0 g, 83%): $[\alpha]_D^{16}$ +101° (*c* 1.41); ^{1}H-NMR δ=1.11 and 1.22 (each 3H, each d, 3-Me and H-6, J=6.3 Hz), 1.7—1.9 (1H, br, 4-OH), 1.7—2.15 (1H, m, H-3), 2.79 (1H, m, H-4, $J_{3,4}$=$J_{4,5}$=9.3 Hz), 3.07 (1H, dd, H-2, $J_{1,2}$=3.3 Hz, $J_{2,3}$=10.5 Hz), 3.35 (3H, s, 1-OMe), 3.52 (1H, dq, H-5), 4.5—4.6 (3H, sharp m, H-1 and OC<u>H</u>$_2$Ph), and 7.30 (5H, s, Ph).

Found: C, 67.42; H, 8.34%. Calcd for $C_{15}H_{22}O_4$: C, 67.64; H, 8.33%.

2-O-Benzyl-3,6-dideoxy-3-C-methyl-D-glucopyranose (6). To a solution of **5** (14.8 g, 0.0556 mol) in acetic anhydride (440 ml), concd H_2SO_4 (0.46 ml) was added dropwise under ice-cooling over a period of 15 min. After being stirred at 0 °C for 15 min, the reaction mixture was poured into a cold saturated aqueous $NaHCO_3$ solution (400 ml), and then extracted with ethyl acetate (300 ml × 3). The extracts were combined, washed successively with a saturated aqueous $NaHCO_3$ (400 ml × 2) and a saturated aqueous NaCl solution (400 ml × 2), dried, and evaporated to a yellow-brown syrup (18.7 g). To a solution of this syrup in dioxane (167 ml) was added dropwise 1 M aqueous NaOH solution (167 ml) and the mixture was kept at room temperature for 5.5 h. The reaction mixture was then neutralized (pH 7) with CO_2 gas and evaporated. The residue was triturated with acetone (600 ml) and the insoluble matter was removed by filtration. The filtrate was evaporated to afford crude **6** (13.2 g, 94% from **5**); colorless crystals, mp 141—145 °C. Recrystallization from benzene gave a pure sample of **6** as colorless needles; mp 148—150 °C; $[\alpha]_D^{17}$ +55° (*c* 1.18, EtOH, after 24 h); ^{1}H-NMR δ=1.14, 1.23, and 1.29 (6H, each d, 3-Me and 3 × H-6, J=6.3 Hz), 1.4—2.2 (2H, m, H-3 and OH), 2.7—3.4 (3H, m, H-2,4, and OH), 3.80 (1H, dq, H-5, $J_{4,5}$= 9.0 Hz), 4.4—4.7 (2H, m, OC<u>H</u>$_2$Ph), 4.95 and 5.17 (1H, each d, β and α anomeric H-1, $J_{1\alpha,2}$=3.3 Hz, $J_{1\beta,2}$=11.4 Hz), and 7.36 (5H, s, Ph); α/β=5/6.

Found: C, 66.47; H, 7.97%. Calcd for $C_{14}H_{20}O_4$: C, 66.64; H, 7.99%.

††† 1 M = 1 mol dm^{-3}.

5-O-Benzyl-1,4,7-trideoxy-4-C-methyl-D-glycero-L-gulo-heptitol (7) and L-glycero Epimer (8). A solution of **6** (18.8 g, 0.0741 mol) in dry THF (56.0 ml) was added dropwise to a stirred ice-cooled ether solution of methylmagnesium iodide [prepared from magnesium turnings (18.0 g, 0.740 mol) and methyl iodide (46.1 ml, 0.74 mol) in dry ether (360 ml)] over a period of 15 min under argon. After being stirred at room temperature for 20 h, 1 M HCl (770 ml) was carefully added under ice-cooling, after which the mixture was extracted with chloroform (700 ml×1, 300 ml×2). The extracts were combined, dried and evaporated to a syrup (26.5 g), which was chromatographed on silica gel (1.6 kg) with 1 : 5 benzene–ethyl acetate to afford **7** (14.9 g, 75%), **8** (53 mg, 0.26%), a mixture of **7** and **8** (0.86 g, 4.3%), and unchanged **6** (2.9 g, 16%). The epimeric mixture (0.86 g) was again chromatographed on silica gel (130 g) with the same solvent system to give **7** (0.60 g) and **8** (0.24 g). The total isolated yields of **7** and **8** amounted to 78% and 1.5% respectively. **7** (R_f=0.34 in 1 : 5 benzene–ethyl acetate), colorless syrup; $[\alpha]_D^{21}$ −65° (*c* 1.00); ^{1}H-NMR δ=0.95 and 1.25 (3H and 6H, each d, 3×Me, J=6.7 and 6.0 Hz), 2.0—2.6 (2H, m, H-4 and OH), 3.18 (1H, dd, H-5, J=2.1 and 4.5 Hz), 3.5—4.2 (4H, m, H-2,3,6, and OH), 4.59 (2H, ABq, OC$\underline{H}_2$Ph, J_{gem}=11.2 Hz), and 7.37 (5H, s, Ph).

Found: C, 67.02; H, 8.89%. Calcd for $C_{15}H_{24}O_4$: C, 67.13; H, 9.02%.

8 (R_f=0.29 in 1 : 5 benzene–ethyl acetate), colorless syrup; ^{1}H-NMR δ=1.08 (3H, d, 4-Me, J=7.2 Hz), 1.24 and 1.28 (each 3H, each d, 2×Me, J=6.0 Hz), 2.1—2.5 (1H, m, H-4), 3.33 (1H, dd, H-5, $J_{4,5}$=3.0 Hz, $J_{5,6}$=5.8 Hz), 3.55 (1H, dd, H-3, $J_{3,4}$=2.4 Hz, $J_{2,3}$=6.7 Hz), 3.74 (1H, dq, H-2), 4.01 (1H, dq, H-6), 4.59 (2H, s, OC$\underline{H}_2$Ph), and 7.36 (5H, s, Ph).

(2R,3R,4R)-3-Hydroxy-2-methyl-4-pentanolide (9). A solution of $NaIO_4$ (90 mg) in water (0.9 ml) was added to a solution of **7** (37.5 mg) in acetone (0.75 ml) under ice-cooling. After being stirred for 20 min, the resulting insoluble matter was filtered and washed with acetone. The filtrate and washings were combined, neutralized (pH 7) with $NaHCO_3$ and then evaporated. Chloroform (2 ml) was added to the residue and the solution washed with a saturated aqueous NaCl solution, dried, and evaporated. The residual syrup (29.7 mg) was hydrogenolyzed in methanol (0.6 ml) with palladium black at room temperature for 16 min under bubbling with H_2 gas to afford methyl 2,5-dideoxy-2-*C*-methylpentofuranoside (16.2 mg, 83%) after chromatographic purification (silica gel 1.5 g, 1 : 2 benzene–ethyl acetate). The methyl furanoside (16.2 mg) was hydrolyzed with 1 : 1 mixture of 1 M hydrochloric acid and 1,4-dioxane (0.16 ml) at room temperature for 18.5 h and the acid neutralized with $NaHCO_3$. The solution was treated with bromine (7.4×10^{-6} l) for 24 h at room temperature. The reaction mixture was extracted with ethyl acetate, and the extract was washed successively with saturated aqueous $Na_2S_2O_3$ and NaCl solutions, dried, and evaporated to a pale yellow liquid, which was purified by column chromatography (silica gel 0.7 g, 1 : 3 benzene–ethyl acetate) to give the lactone **9** (7.0 mg, 42% from **7**). The ^{1}H-NMR data (90 MHz) of **9** [δ=4.10 (1H, dd, H-3, $J_{2,3}$=$J_{3,4}$=4.8 Hz) and 4.62 (1H, dq, H-4, $J_{4,Me}$=6.6 Hz)] were very similar to the reported data.[1,10]

2,3- and 3,6-O-Acetonides (10 and 12). To an ice-cooled solution of **7** (24.8 g, 0.0924 mol) and DMP (22.7 ml, 0.185 mol) in dry acetone (500 ml) was added dropwise concd H_2SO_4 (25.0×10^{-6} l) over a period of 2 min. After being kept 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 (10 ml×5). The combined filtrate and washings were evaporated to a pale yellow syrup (38.2 g), which was chromatographed on silica gel (1.6 kg) with 20 : 1 chloroform–acetone to afford **10** (21.9 g, 77%) and **12** (4.8 g, 17%): **10** (R_f=0.43 in 20 : 1 chloroform–acetone), colorless syrup; $[\alpha]_D^{17}$ 0°, $[\alpha]_{365}^{17}$ −68° (*c* 1.10); ^{1}H-NMR (250 MHz) δ=1.04, 1.16, and 1.19 (each 3H, each d, 3×Me, J=6.3, 6.3, and 7.0 Hz), 1.30 and 1.45 (each 3H, each s, CMe_2), 1.85—2.0 (1H, m, H-4), 2.95—3.0 (1H, br, 6-OH), 3.07 (1H, dd, H-5, $J_{4,5}$=2.8 Hz, $J_{5,6}$=5.3 Hz), 3.91 (1H, dq, H-6, $J_{6,7}$=6.3 Hz), 4.15—4.25 (2H, m, H-2 and 3), 4.65 (2H, s, OC$\underline{H}_2$Ph), and 7.3—7.4 (5H, m, Ph).

Found: C, 69.82; H, 8.92%. Calcd for $C_{18}H_{28}O_4$: C, 70.10; H, 9.15%.

12 (R_f=0.23 in 20 : 1 chloroform–acetone), colorless needles; mp 114.8—115.4 °C (benzene); $[\alpha]_D^{17}$ −39° (*c* 1.17); ^{1}H-NMR (250 MHz) δ=0.89, 1.15, and 1.22 (each 3H, each d, 3×Me, J=7.3 Hz), 1.31 and 1.34 (each 3H, each, s, CMe_2), 1.6—1.7 (1H, br, 2-OH), 2.35—2.45 (1H, m, H-4), 2.94 (1H, d, H-5, $J_{4,5}$=2.3 Hz, $J_{5,6}$=0 Hz), 3.73 (1H, dq, H-2, $J_{2,3}$=7.8 Hz), 3.84 (1H, dd, H-3, $J_{3,4}$=1.3 Hz), 3.98 (1H, q, H-6), 4.60 (2H, ABq, OC$\underline{H}_2$Ph, J_{gem}=12.5 Hz), and 7.25—7.45 (5H, m, Ph).

Found: C, 70.22; H, 8.97%. Calcd for $C_{18}H_{28}O_4$: C, 70.10; H, 9.15%.

A mixture of **12** (4.8 g, 15.6 mmol), $ZnBr_2$ (3.5 g, 15.6 mmol), and dichloromethane (48 ml) was stirred at 0 °C for 4 h, and then neutralized (pH 7) with Na_2CO_3. The insoluble matter was filtered and washed with dichloromethane. The combined filtrate and washings were evaporated to a yellow syrup (5.8 g), which was chromatographed on silica gel (300 g) with 20 : 1 chloroform–acetone to give **10** (4.5 g, 94%) and **12** (0.2 g, 4%).

6-O-Acetyl-5-O-benzyl-1,4,7-trideoxy-2,3,-O-isopropylidene-4-C-methyl-D-glycero-L-gulo-heptitol (11). To a solution of **10** (21.8 g, 70.7 mmol) in ethyl acetate (220 ml) was added acetic anhydride (13.4 ml, 141 mmol) and DMAP (8.6 g, 70.7 mmol). After being kept at room temperature for 15 min, the reaction mixture was poured into a cold saturated aqueous $NaHCO_3$ solution (300 ml) and the new mixture was extracted with ethyl acetate (250 ml×2). The extracts were washed with water (300 ml×2) and a saturated aqueous NaCl solution (300 ml×2), dried, and evaporated to a yellow syrup (24.6 g), which was chromatographed on silica gel (1 kg) with 10 : 1 benzene–ethyl acetate to afford **11** (23.6 g, 95%). R_f=0.48 (10 : 1 benzene–ethyl acetate), colorless syrup; $[\alpha]_D^{16}$ +15° (*c* 1.34); ^{1}H-NMR δ=1.10 and 1.11 (each 3H, each d, 4-Me and 3×H-1, J=6.7 and 5.2 Hz), 1.18 (3H, d, H-7, J=7.3 Hz), 1.25 and 1.40 (each 3H, each s, CMe_2), 1.6—2.1 (1H, m, H-4), 1.96 (3H, s, 6-OAc), 3.27 (1H, dd, H-5, $J_{4,5}$=2.9 Hz, $J_{5,6}$=7.3 Hz), 3.8—4.1 (2H, m, H-2 and 3), 4.62 (2H, ABq, OC$\underline{H}_2$Ph, J_{gem}=11.8 Hz), 5.15 (1H, dq, H-6), and 7.32 (5H, s, Ph).

Found: C, 68.78; H, 8.58%. Calcd for $C_{20}H_{30}O_5$: C, 68.54; H, 8.63%.

2-O-Acetyl Derivative (13) of 12. By the procedure described in the preparation of **11**, a sample of **12** (101 mg) was acetylated to afford **13** (111 mg, 96%): R_f=0.52 (10 : 1 benzene-ethyl acetate), colorless syrup; ^{1}H-NMR δ=0.81 (3H, d, 4-Me or H-7, J=7.5 Hz), 1.16 (3H, d, H-7 or 4-Me, J=7.1 Hz), 1.24 (3H, d, H-1, J=6.3 Hz), 1.30 and 1.33 (each 3H, each s, CMe_2), 1.8—2.2 (1H, m, H-4), 1.99 (3H, s, 2-OAc), 2.90 (1H, dd, H-5, J=0 and 2.3 Hz), 3.8—4.1 (2H, m, H-3 and 6), 4.50 (2H, ABq, OC$\underline{H}_2$Ph, J_{gem}=12.0 Hz), 4.82 (1H, dq, H-2, $J_{2,3}$=9.5 Hz), and 7.27 (5H, s, Ph).

6-O-Acetyl-1,4,7-trideoxy-2,3-O-isopropylidene-5-O-mesyl-4-C-methyl-D-glycero-L-gulo-heptitol(14) and 5-O-Acetyl-1,4,7-trideoxy-2,3-O-isopropylidene-6-O-mesyl-4-C-methyl-D-glycero-L-gulo-heptitol (15). A mixture of **11** (5.50 g, 15.7 mmol), pal-

ladium black (*ca.* 3 g), and ethanol (110 ml) was vigorously stirred at room temperature for 20 min under bubbling with H_2 gas, and the suspension filtered. The filtrate was evaporated to a colorless syrup (4.43 g), which was coevaporated with benzene (4 ml×5). The final residue (4.11 g) was immediately dissolved in dry pyridine (41 ml) and ice-cooled. Mesyl chloride (2.4 ml, 31.4 mmol) was added dropwise to the solution over a period of 10 min and the mixture was kept at room temperature for 2 h. The reaction mixture was poured into a cold saturated aqueous $NaHCO_3$ solution (50 ml), and extracted with ethyl acetate (70 ml×3). The extracts were combined, washed successively with saturated aqueous $KHSO_4$ (50 ml×5) and NaCl (50 ml×3) solution, dried, and evaporated to a crystalline residue (5.62 g). The residue was chromatographed on silica gel (560 g) with 5 : 1 benzene–ethyl acetate to afford **14** (4.89 g, 92%) and **15** (0.266 g, 5%): **14** (R_f=0.48 in 3 : 1 benzene–ethyl acetate), colorless needles; mp 78—83 °C; ^{1}H-NMR δ=1.13, 1.23, and 1.32 (each 3H, each d, 3×Me, J=6.6, 6.2, and 6.2 Hz), 1.36 and 1.47 (each 3H, each s, CMe_2), 1.8—2.2 (1H, m, H-4), 2.11 (3H, s, 6-OAc), 3.08 (3H, s, 5-OMs), 4.04 (1H, dd, H-3, $J_{2,3}$=6.0 Hz, $J_{3,4}$=7.4 Hz), 4.40 (1H, dq, H-2, $J_{1,2}$=6.2 Hz), 4.60 (1H, dd, H-5, $J_{4,5}$=2.7 Hz, $J_{5,6}$=7.8 Hz), and 5.16 (1H, dq, H-6, $J_{6,7}$=6.2 Hz): **15** (R_f=0.42 in 3 : 1 benzene–ethyl acetate), colorless syrup; ^{1}H-NMR δ=1.08, 1.23, and 1.39 (each 3H, each d, 3×Me, J=6.0, 6.4, and 6.0 Hz), 1.31 and 1.44 (each 3H, each s, CMe_2), 1.8—2.2 (1H, m, H-4), 2.13 (3H, s, 5-OAc), 2.96 (3H, s, 6-OMs), 3.72 (1H, dd, H-3, $J_{2,3}$=6.4 Hz, $J_{3,4}$=7.7 Hz), 4.26 (1H, dq, H-2, $J_{1,2}$=6.4 Hz), and 4.7—5.0 (2H, m, H-5 and 6).

*5,6-Anhydro-1,4,7-trideoxy-2,3-*O*-isopropylidene-4-*C*-methyl-*D*-glycero-*D*-manno-heptitol (**16**).* To an ice-cooled solution of **14** (4.86 g, 14.4 mmol) in chloroform (48 ml) was added 3.6 M sodium methoxide in methanol (1.0 ml) over a period of 5 min. After being stirred under ice-cooling for 45 min the mixture was neutralized with CO_2 gas, poured into cold water (30 ml), and then extracted with dichloromethane (20 ml×3). The extracts were washed with a saturated aqueous NaCl solution (30 ml×3), dried, and evaporated to a colorless oil (2.94 g). The oil was subsequently chromatographed on silica gel (88 g) with 5 : 1 benzene–ethyl acetate to afford oily **16** (2.69 g, 93%), which was subjected to bulb-to-bulb distillation to give a pure sample of **16** (2.34 g, 81%): R_f=0.50 (5 : 1 benzene–ethyl acetate); bp 45—56 °C (bath temp)/6 Torr††††; $[\alpha]_D^{20}$ +8° (*c* 1.49); ^{1}H-NMR δ=1.08 (3H, d, 4-Me, J=6.8 Hz), 1.21 (3H, d, H-1, J=6.0 Hz), 1.30 (3H, d, H-7, J=5.7 Hz), 1.36 and 1.47 (each 3H, each s, CMe_2), 2.72 (1H, dd, H-5, $J_{5,6}$=4.2 Hz, $J_{4,5}$=9.0 Hz), 3.06 (1H, dq, H-6), 4.02 (1H, dd, H-3, $J_{2,3}$=6.0 Hz, $J_{3,4}$=7.5 Hz), and 4.34 (1H, dq, H-2).

Found: C, 65.04; H, 9.69%. Calcd for $C_{11}H_{20}O_3$: C, 65.97; H, 10.07%.

*2,3-Anhydro-1,4,7-trideoxy-5,6-*O*-isopropylidene-4-*C*-methyl-*D*-glycero-*D*-gulo-heptitol (**17**).* By the procedure described in the preparation of **16**, a sample of **15** (0.865 g) afforded, after silica gel column chromatography, **17** (0.240 g, 47%) as a colorless oil: R_f=0.44 (5 : 1 benzene–ethyl acetate); bp 78—84 °C (bath temp)/6 Torr; $[\alpha]_D^{24}$ −49° (*c* 0.92); ^{1}H-NMR δ=1.13 (3H, d, H-7, J=6.3 Hz), 1.20 (3H, d, 4-Me, J=6.0 Hz), 1.25 (3H, d, H-1, J=5.4 Hz), 1.32 and 1.45 (each 3H, each s, CMe_2), 1.4—1.8 (1H, m, H-4), 2.77 (1H, dd, H-3, $J_{2,3}$=3.8 Hz, $J_{3,4}$=8.1 Hz), 3.05 (1H, dq, H-2), 3.91 (1H, dd, H-5, $J_{5,6}$=6.3 Hz, $J_{4,5}$=5.1 Hz), and 4.26 (1H, dq, H-6).

Found: C, 65.41; H, 9.74%. Calcd for $C_{11}H_{20}O_3$: C, 65.97; H, 10.07%.

†††† 1 Torr ≈ 133.322 Pa.

*2,4,7-Trideoxy-5,6-*O*-isopropylidene-2,4-di-*C*-methyl-*D*-glycero-*D*-talo-heptose Trimethylene Dithioacetal (**18**).* A solution of 1,3-dithiane 97%, (3.95 g, 31.9 mmol) in dry THF (40 ml) was cooled to −40 °C under argon, and 1.57 M butyllithium in hexane (20.3 ml) was added dropwise. After being stirred for 2 h at −20 °C, the mixture was recooled to −40 °C. A solution of **16** (1.28 g, 6.38 mmol) in dry THF (2.6 ml) was added dropwise to this stirred solution, and stirring was continued at −20 °C for 2 h and at 5 °C for 66 h. The mixture was now poured into cold water (30 ml), and extracted with chloroform (40 ml×3). The extracts were combined, successively washed with water (50 ml×3) and a saturated aqueous NaCl solution (40 ml×2), dried, and evaporated to a crystalline solid (4.80 g), which was chromatographed on silica gel (340 g) with 5 : 1 benzene–ethyl acetate to afford **18** (1.87 g, 91%) as colorless crystals. Recrystallization of the sample (35 mg) from hexane gave a pure sample of **18** (22 mg) as plates: R_f=0.43 (5 : 1 benzene–ethyl acetate), mp 104—105 °C; $[\alpha]_D^{28}$ −40° (*c* 1.38); ^{1}H-NMR δ=1.04, 1.11, and 1.29 (each 3H, each d, 3×Me, J=6.6, 6.0, and 6.9 Hz), 1.33 and 1.48 (each 3H, each s, CMe_2), 1.7—2.2 (4H, m, H-2,4, 2×Ha), 2.7—3.1 (5H, m, 4×Hb, 3-OH), 3.41 (1H, ddd, H-3, $J_{3,OH}$=8.1 Hz, J=8.1 and 3.6 Hz), 4.1—4.5 (2H, m, H-5 and 6), and 4.66 (1H, d, H-1, $J_{1,2}$=2.4 Hz).

Found: C, 56.10; H, 8.59; S, 19.93%. Calcd for $C_{15}H_{28}O_3S_2$: C, 56.21; H, 8.81; S, 20.00%.

*Acetyl Derivative (**19**)*: Colorless syrup, R_f=0.31 (5 : 1 hexane–acetone); ^{1}H-NMR δ=4.90 (1H, dd, H-3, J=5.9 and 7.1 Hz).

*2,4,7-Trideoxy-5,6-*O*-isopropylidene-2,4-di-*C*-methyl-*D*-glycero-*D*-gulo-heptose Trimethylene Dithioacetal (**21**).* By the procedure described in the preparation of **18**, **17** (62 mg) was allowed to react with 5 equiv. of 2-lithio-1,3-dithiane in THF to afford, after silica gel column chromatography, **21** (94 mg, 94%) as a colorless crystals. A part of this sample (29 mg) was recrystallized from hexane to give a pure sample of **21** as colorless needles: R_f=0.33 (5 : 1 benzene–ethyl acetate), mp 104—105 °C; $[\alpha]_D^{28}$ −31° (*c* 1.32); ^{1}H-NMR δ=0.93, 0.94, and 1.18 (each 3H, each d, 2- and 4-Me, and 3×H-7, J=7.5, 6.9, and 6.0 Hz), 1.28 and 1.43 (each 3H, each s, CMe_2), 1.5—2.2 (4H, m, H-2,4, 2×Ha), 2.6—3.1 (5H, m, 4×Hb, 3-OH), 3.62 (1H, broad d, H-3, J=1.8 and 9.3 Hz†††††), 4.0—4.2 (1H, m, H-5), 4.27 (1H, dq, H-6, $J_{5,6}$=$J_{6,7}$=6.0 Hz), and 4.57 (1H, d, H-1, $J_{1,2}$=2.1 Hz).

Found: C, 56.44; H, 8.60; S, 20.04%. Calcd for $C_{15}H_{28}O_3S_2$: C, 56.21; H, 8.81; S; 20.00%.

*Acetyl Derivative (**22**)*: colorless syrup, R_f=0.55 (5 : 1 benzene–ethyl acetate); ^{1}H-NMR δ=5.16 (1H, dd, H-3, J=0 and 11.4 Hz).

*3-*O*-(t-Butyldimethylsilyl)-2,4,7-trideoxy-5,6-*O*-isopropylidene-2,4-di-*C*-methyl-*D*-glycero-*D*-talo-heptose Trimethylene Dithioacetal (**20**).* To a solution of **18** (907 mg, 2.83 mmol) and imidazole (936 mg, 14.2 mmol) in dry DMF (4.5 ml) at room temperature was added *t*-butyldimethylchlorosilane (2.13 g, 14.2 mmol). The resulting homogeneous solution was stirred at 60 °C for 18.5 h, after which time the reaction mixture was poured into cold water (12 ml) and extracted with ethyl acetate (15 ml×3). The extracts were successively washed with water (20 ml×3) and a saturated aqueous NaCl solution (20 ml×2), dried, and evaporated to a colorless crystalline mass (1.92 g). The solid was then chromatographed on silica gel (60 g) with 50 : 1 benzene–ethyl acetate to afford **20** (1.19 g, 97%) as colorless needles, mp 62—67 °C. Recrystallization of a portion of this product from hexane gave a pure sample: mp 65—67 °C; $[\alpha]_D^{28}$ +20° (*c* 1.48); ^{1}H-NMR

††††† Measured in $CDCl_3+D_2O$.

δ=0.83 (9H, s, *t*-Bu), 0.91, 0.97, and 1.07 (each 3H, each d, Me×3, J=6.6, 6.6, and 6.0 Hz), 1.16 and 1.30 (each 3H, each s, CMe_2), 1.6—2.1 (4H, m, 2×Ha, H-2,4), 2.55—2.9 (4H, m, 4×Hb), 3.55 (1H, dd, H-3, J=4.5 and 6.8 Hz), 3.8—4.2 (2H, m, H-5, 6), and 4.22 (1H, d, H-1, $J_{1,2}$=4.1 Hz).

Found: C, 58.15; H, 9.47; S, 14.46%. Calcd for $C_{21}H_{42}O_3S_2Si$: C, 58.01; H, 9.74; S, 14.75%.

3-O-(t-Butyldimethylsilyl)-2,4,7-trideoxy-5,6-O-isopropylidene-2,4-di-C-methyl-aldehydo-D-glycero-D-talo-*heptose(**28**).* To a mixture of **20** (1.06 g, 2.44 mmol) and mercury(II) oxide (2.34 g, 10.7 mmol) in 80% aqueous acetone (74 ml) was added mercury(II) chloride (2.93 g, 10.7 mmol) at room temperature with efficient stirring. The mixture was stirred at 60 °C for 15 min under argon, cooled, and filtered through Celite 545. The filter cake was washed with acetone (60 ml), and then the filtrate and the washings were combined. After the subsequent removal of the acetone by concentration, an aqueous 10% KI solution (50 ml) was added to the red aqueous residue. The resulting colorless solution was extracted with chloroform (30 ml×3) and the extracts were washed with a 10% aqueous KI solution (40 ml) and a saturated aqueous NaCl solution (40 ml×2), dried, and evaporated. The residual colorless syrup (0.88 g) was chromatographed rapidly on silica gel (41 g) with 40 : 1 benzene–ethyl acetate to afford **28** (0.788 g, 94%) as a colorless syrup: R_f=0.30 (40 : 1 benzene–ethyl acetate); $[\alpha]_D^{23}$ −6°, $[\alpha]_{546}^{23}$ 0°, $[\alpha]_{405}^{23}$ +15°, and $[\alpha]_{365}^{23}$ +36° (*c* 1.19); IR ($CHCl_3$, 0.15 M) 1710 cm^{-1}; ^{1}H-NMR δ=0.8—1.2 (12H, m, *t*-Bu and 1×Me), 1.14 and 1.21 (each 3H, each d, 2×Me, J=7.0 and 6.0 Hz), 1.30—1.42 (each 3H, each s, CMe_2), 1.7—2.0 (1H, m, H-4), 2.4—2.7 (1H, m, H-2), 3.78 (1H, dd, H-3, J=2.3 and 7.5 Hz), 4.00 (1H, dd, H-5, $J_{4,5}$=4.8 Hz, $J_{5,6}$=6.3 Hz), 4.22 (1H, dq, H-6, J=6.3 Hz), and 9.71 (1H, d, H-1, $J_{1,2}$=1.8 Hz).

Found: C, 62.50; H, 10.28%. Calcd for $C_{18}H_{36}O_4Si$: C, 62.74; H, 10.53%.

5-O-(t-Butyldimethylsilyl)-2,4,6,9-tetradeoxy-7,8-O-isopropylidene-4,6-di-C-methyl-2-methylene-D-erthro-L-altro-*nonose Diethyl Acetal (**30**) and* L-allo *Epimer (**32**).* To a solution of 2-bromo-3,3-diethoxy-1-propene[16] (0.925 g, 4.42 mmol) in dry THF (6.4 ml)cooled at −108——110 °C (ether and liquid nitrogen) was added 1.51 M butyllithium in hexane (2.4 ml, 3.62 mmol) over a period of 5 min under argon. After being stirred at the same temperature for 15 min, a solution of **28** (0.508 g, 1.47 mmol) in dry THF (0.5 ml) was added to the mixture over a period of 5 min, and stirring was continued at the same temperature for 15 min. The reaction mixture was quenched by adding a saturated aqueous NH_4Cl solution (3 ml) and then it was extracted with ether (4 ml×3) at room temperature. The organic layer were washed with a saturated aqueous NaCl solution, dried, and evaporated to a yellow syrup (1.08 g). The crude product was immediately chromatographed on silica gel** (110 g) with 12 : 1 benzene–ethyl acetate over a period of 5.5 h*** to afford **30** (0.394 g, 56%) and **32** (0.250 g, 36%) as colorless syrups: **30**, R_f=0.34 (15 : 1 benzene–ethyl acetate); $[\alpha]_D^{23}$ −35° (*c* 1.00); ^{1}H-NMR (250 MHz) δ=0.15 and 0.16 (each 3H, each s, $SiMe_2$), 0.92 (3H, d, 4-Me, J=7.5 Hz), 0.93 (9H, s, *t*-Bu), 1.04 (3H, d, 6-Me, J=7.3 Hz), 1.17 and 1.21 [each 3H, each t, $CH(OCH_2Me)_2$, J=7.0 Hz], 1.27 (3H, d, H-9, J=6.5 Hz), 1.33 and 1.46 (each 3H, each s, CMe_2), 1.97 (1H, ddq, H-6, $J_{5,6}$=8.0 Hz, $J_{6,7}$=3.8 Hz), 2.10 (1H, dq, H-4, $J_{3,4}\approx$0 Hz, $J_{4,5}$=2.0 Hz), 3.35—3.7 [4H, m, $CH(OCH_2Me)_2$], 3.72 (1H, dd, H-5), 3.92 (1H, s, 3-OH), 4.28 (1H, dd, H-7, $J_{7,8}$=6.5 Hz), 4.34 (1H, dq, H-8), 4.75 (1H, s, H-1), 4.80 (1H, s like, H-3), 5.35 and 5.44 (each 1H, each s like, $=CH_2$).

Found: C, 63.19; H, 10.39%. Calcd for $C_{25}H_{50}O_6Si$: C, 63.25; H, 10.61%.

32, R_f=0.26 (15 : 1 benzene–ethyl acetate); $[\alpha]_D^{24}$ −23° (*c* 1.08); ^{1}H-NMR (250 MHz) δ=0.13 and 0.14 (each 3H, each s, $SiMe_2$), 0.83 (3H, d, 4-Me, J=7.3 Hz), 0.93 (9H, s, *t*-Bu), 1.03 (3H, d, 6-Me, J=7.0 Hz), 1.22 (3H, d, H-9, J=6.8 Hz), 1.22 and 1.23 [each 3H, each t, $CH(OCH_2Me)_2$, J=7.5 Hz], 1.31 and 1.45 (each 3H, each s, CMe_2), 1.97 (1H, ddq, H-6, $J_{5,6}$=7.5 Hz, $J_{6,7}$=4.8 Hz), 2.13 (1H, ddq, H-4, $J_{3,4}$=10.0 Hz, $J_{4,5}$=2.8 Hz), 3.52 (1H, d, 3-OH, J=4.8 Hz), 3.51 and 3.69 [each 2H, each dq, $CH(OCH_2Me)_2$, J_{gem}=11.5 Hz), 3.79 (1H, dd, H-5), 4.11 (1H, dd, H-3), 4.16 (1H, dd, H-7, $J_{7,8}$=6.8 Hz), 4.34 (1H, dq, H-8), 4.95 (1H, s, H-1), 5.22 and 5.40 (each 1H, each s like, $=CH_2$).

Found: C, 63.65; H, 10.31%. Calcd for $C_{25}H_{50}O_6Si$: C, 63.25; H, 10.61%.

2,4,6,9-Tetradeoxy-7,8-O-isopropylidene-4,6-di-C-methyl-2-methylene-D-erythro-L-altro-*nonose Diethyl Acetal (**31**) and* L-allo *Epimer (**33**).* An 1.0 M *n*-Bu_4NF in THF (1.6 ml, 1.6 mmol) was added to an ice-cooled solution of **30** (0.391 g, 0.823 mmol) in dry THF (3.9 ml), and the mixture was stirred at 0 °C for 15 min. Ice water (3 ml) was then added to the reaction mixture and it was extracted with chloroform (8 ml×3). The extracts were washed with water (5 ml×3) and a saturated aqueous NaCl solution, dried, and evaporated to a yellow syrup (0.408 g). The syrup was chromatograohed on silica gel (20 g) with 6 : 1 benzene–acetone to afford **31** (0.290 g, 98%) as a colorless syrup: R_f=0.35 (6 : 1 benzene–acetone); $[\alpha]_D^{23}$ −29° (*c* 1.02); ^{1}H-NMR (250 MHz) δ=0.97 (3H, d, 4-Me, J=7.5 Hz), 1.00 (3H, d, 6-Me, J=6.8 Hz). 1.20 and 1.22 [each 3H, each t, $CH(OCH_2Me)_2$, J=7.5 Hz], 1.26 (3H, d, H-9, J=6.3 Hz), 1.34 and 1.47 (each 3H, each s CMe_2), 2.00 (1H, ddq, H-6, $J_{5,6}$=8.5 Hz, $J_{6,7}$=5.0 Hz), 2.11 (1H, ddq, H-4, $J_{3,4}$=1.6 Hz, $J_{4,5}$=3.0 Hz), 2.98 (1H, d, 3-OH, J=2.5 Hz), 3.33 (1H, d, 5-OH, J=7.8 Hz), 3.4—3.5 (1H, m, H-5), 3.4—3.75 [4H, m, $CH(OCH_2Me)_2$], 4.32 (1H, dd, H-7, $J_{7,8}$=6.3 Hz), 4.46 (1H, dq, H-8), 4.79 (2H, s, like, H-1 and 3), 5.34 and 5.37 (each 1H, each s like, $=CH_2$).

Found: C, 63.54; H, 9.78%. Calcd for $C_{19}H_{36}O_6$: C, 63.31; H, 10.07%. By the procedure described for the preparation of **31**, **32** (0.417 g) provided **33** (0.293 g, 93%) as a colorless syrup: R_f=0.23 (6 : 1 benzene–acetone); $[\alpha]_D^{24}$ −91° (*c* 1.10); ^{1}H-NMR (250 MHz) δ=0.75 (3H, d, 4-Me, J=7.3 Hz), 1.10 (3H, d, 6-Me, J=7.3 Hz), 1.23 and 1.24 [each 3H, each t, $CH(OCH_2Me)_2$, J=7.5 Hz], 1.28 (3H, d, H-9, J=6.8 Hz), 1.35 and 1.49 (each 3H, each s, CMe_2), 1.99 (1H, ddq, H-6, $J_{5,6}$=4.0 Hz, $J_{6,7}$=2.8 Hz), 2.10 (1H, ddq, H-4, $J_{3,4}$=9.3 Hz, $J_{4,5}$=7.5 Hz), 3.4—3.8 [5H, m, H-5, and $CH(OCH_2Me)_2$], 3.80 (1H, d like, 5-OH, J=6.3 Hz), 4.20 (1H, d like, H-3, $J_{3,OH}$=0 Hz), 4.33 (1H, dd, H-7, $J_{7,8}$=6.8 Hz), 4.43 (1H, dq, H-8), 4.60 (1H, s like, 3-OH), 4.99 (1H, s, H-1), 5.25 and 5.41 (each 1H, each s like, $=CH_2$).

Found: C, 63.07; H, 9.88%. Calcd for $C_{19}H_{36}O_6$: C, 63.31; H, 10.01%.

2,4,6,9-Tetradeoxy-7,8-O-isopropylidene-2,4,6-tri-C-methyl-D-arabino-L-manno-*nonose Diethyl Acetal (**34**).* *(a)*: A solution of **31** (0.290 g, 0.803 mmol) and tris(triphenylphosphine)chlororhodium(I)[17] (0.174 g, 0.188 mmol) in benzene (14.5 ml) was stirred under an atmospheric pressure of hydrogen at room temperature for 14 h. The reaction mixture was then evaporated and the residue was passed through Florisil (100—200 mesh, 20 g)with ether and again evaporated to afford a practically pure sample of **34** (0.270 g, 93%) as a pale

** The use of Merck Kieselgel 60 instead of Wakogel C-200 resulted in decomposition of the product in large extent.

*** The elution speed was desired to be as fast as possible.

yellow syrup, which was shown to be isomerically homogeneous by TLC and ^{1}H-NMR analyses. A portion of this sample (15 mg) was chromatographed on silica gel (1 g) with 3 : 1 benzene–ethyl acetate to give a pure sample of **34** (14.4 mg): colorless syrup, R_f=0.31 (3 : 1 benzene–ethyl acetate); $[\alpha]_D^{24}$ +24° (*c* 0.72); ^{1}H-NMR (250 MHz) δ=0.82, 0.92, and 1.07 (each 3H, each d, 2,4,6-Me, J=7.0 Hz), 1.24 (3H, d, H-9, J=6.3 Hz), 1.23 and 1.25 [each 3H, each t, CH(OCH$_2$Me)$_2$, J=7.0 Hz], 1.34 and 1.46 (each 3H, each s, CMe$_2$), 1.8—2.05 (3H, m, H-2,4 and H-6), 3.31 (1H, ddd, H-5, J=3.3 and 9.0 Hz, $J_{5,OH}$=9.0 Hz), 3.5—3.9 [4H, m, CH(OCH$_2$Me)$_2$], 3.91 (1H, d, 5-OH), 4.02 (1H, dd, H-3, J=1.5 and 9.5 Hz, $J_{3,OH}$= 0 Hz), 4.25 (1H, dd, H-7, $J_{6,7}$=$J_{7,8}$=6.3 Hz), 4.44 (1H, d, H-1, $J_{1,2}$=6.0 Hz), 4.47 (1H, dq, H-8), and 4.59 (1H, s, 3-OH).

Found: C, 63.19; H, 10.27%. Calcd for $C_{19}H_{38}O_6$: C, 62.96; H, 10.57%.

(b): A sample of **30** (57.6 mg, 0.121 mmol) was hydrogenated in benzene (2.9 ml) with $(Ph_3P)_3RhCl$ (169 mg, 0.182 mmol) under atmospheric pressure of H_2 at room temperature for 20 h. The reaction product was treated with Florisil (13 g) and ether to afford crude **35** (45.7 mg, 79%) as a yellow syrup. This syrup was desilylated with 2 equimolar amounts of Bu_4NF in THF at 0 °C for 15 min and then worked up by the usual way to give a yellow syup (44.7 mg). This was chromatographed on silica gel (2.3 g) with 2 : 1 hexane–ethyl acetate to afford **34** (32.4 mg, 93% from **35**), which was isomerically homogeneous and identical with the sample of **34** obtained in *(a)*.

*2,4,6,9-Tetradeoxy-7,8-O-isopropylidene-2,4,6-tri-C-methyl-*D-arabino-L-allo-*nonose Diethyl Acetal (37) and* L-altro *Epimer (39).* *(a)*: By the procedure described in the case of the homogeneous hydrogenation of **31**, **33** (0.473 g, 1.31 mmol) was treated with $(Ph_3P)_3RhCl$ (0.284 g, 0.307 mmol) in benzene for 17 h, and the reaction mixture was worked up to afford a yellow syrup (0.475 g). The syrup was chromatographed on silica gel (50 g) with 2 : 1 hexane–ethyl acetate to give **37** (0.179 g, 38%) as colorless needles, **39** (0.173 g, 37%) as colorless syrup, and a mixture of **37** and **39** (40 mg, 8.5%): **37**, R_f=0.40 (2 : 1 hexane–ethyl acetate); mp 69.5—72 °C (from hexane); $[\alpha]_D^{24}$ −19° (*c* 1.29); ^{1}H-NMR (250 MHz) δ=0.96 (3H, d, 4-Me, J=7.0 Hz), 1.03 (3H, d, 2-Me, J=7.0 Hz), 1.07 (3H, d, 6-Me, J=6.8 Hz), 1.22 and 1.24 [each 3H, each t, CH(OCH$_2$-Me)$_2$, J=7.0 Hz], 1.26 (3H, d, H-9, J=6.3 Hz), 1.34 and 1.47 (each 3H, each s, CMe$_2$), 1.99 (1H, ddq, H-6, $J_{5,6}$=6.8 Hz, $J_{6,7}$=4.2 Hz), 2.04 (1H, ddq, H-4, $J_{3,4}$=7.0 Hz, $J_{4,5}$=7.0 Hz), 2.23 (1H, ddq, H-2, $J_{1,2}$=5.5 Hz, $J_{2,3}$=6.5 Hz), 3.44 (1H, ddd, H-5, $J_{5,OH}$=6.8 Hz), 3.53, 3.55, 3.70, and 3.76 [each 1H, each dq, CH(OCH$_2$Me)$_2$, J_{gem}=10.0 Hz], 3.60 (1H, ddd, H-3, $J_{3,OH}$=3.5 Hz), 3.87 (1H, d, 5-OH), 4.25 (1H, dd, H-7, $J_{7,8}$=6.3 Hz), 4.43 (1H, dq, H-8), 4.50 (1H, d, H-1), and 4.61 (1H, d, 3-OH).

Found: C, 62.87; H, 10.32%. Calcd for $C_{19}H_{38}O_6$: C, 62.96; H, 10.57%.

39, R_f=0.33 (2 : 1 hexane–ethyl acetate); $[\alpha]_D^{23}$ −22° (*c* 1.12); ^{1}H-NMR (250 MHz) δ=0.75 (3H, d, 4-Me, J=7.0 Hz), 0.96 (3H, d, 2-Me, J=7.0 Hz), 1.09 (3H, d, 6-Me, J= 7.0 Hz), 1.22 and 1.23 [each 3H, each t, CH(OCH$_2$Me)$_2$, J= 7.0 Hz), 1.27 (3H, d, H-9, J=6.7 Hz), 1.35 and 1.47 (each 3H, each s, CMe$_2$), 1.80 (1H, ddq, H-4, $J_{3,4}$=9.0 Hz, $J_{4,5}$=7.0 Hz), 1.88 (1H, ddq, H-2, $J_{1,2}$=6.0 Hz, $J_{2,3}$=1.0 Hz), 1.98 (1H, ddq, H-6, $J_{5,6}$=4.1 Hz, $J_{6,7}$=3.0 Hz), 3.42 (1H, ddd, H-5, $J_{5,OH}$=7.0 Hz), 3.45—3.80 [4H, m, CH(OCH$_2$Me)$_2$] 3.73 (1H, d, 5-OH), 3.95 (1H, dd, H-3, $J_{3,OH}$=0 Hz), 4.31 (1H, dd, H-7, $J_{7,8}$=6.7 Hz), 4.38 (1H, s like, 3-OH), 4.42 (1H, dq, H-8), and 4.47 (1H, d, H-1).

Found: C, 62.82; H, 10.29%. Calcd for $C_{19}H_{38}O_6$: C, 62.96; H, 10.57%.

(b): By the procedure described in the case of the hydrogenation of **30**, **32** (41 mg, 0.86 mmol) was treated with the rhodium catalyst (120 mg, 0.129 mmol) for 22 h, and the reaction mixture was worked up to afford a yellow syrup (a mixture of **38** and **40**). A solution of this syrup in THF (0.34 ml) was treated with 1.0 M *n*-Bu_4NF in THF (0.14 ml) at 0 °C for 15 min and then worked up to give a syrup, which was chromatographed on silica gel (4 g) with 2 : 1 hexane–ethyl acetate to afford **37** (1.7 mg, 6.6%), **39** (12.8 mg, 50%), and a mixture of **37** and **39** (2.3 mg).

Transformation of 34 into 41. To a solution of **34** (9.5 mg, 0.026 mmol) in dry ethanol (0.23 ml) was added a 0.026 M ethanolic PPTS solution (0.1 ml), and the mixture was stirred at 55 °C for 4 h. The reaction mixture was then neutralized with triethylamine and evaporated. The residue was chromatographed on silica gel (0.5 g) with 2 : 1 benzene–acetone to afford a colorless syrup (6.5 mg). To a solution of this syrup in acetone (0.065 ml) was added a solution of $NaIO_4$ (6.5 mg, 0.03 mmol) in water (0.065 ml) under ice-cooling. After being stirred for 20 min, the mixture was diluted with water and then extracted with ether. The extract was washed with a saturated aqueous NaCl solution, dried, and evaporated to a colorless syrup (5.4 mg). To a solution of this syrup in 95% ethanol (0.054 ml) was added $NaBH_4$ (1.8 mg, 0.048 mmol), and the mixture was stirred at room temperature for 30 min. The resulting mixture was neiutralzed with solid CO_2, concentrated, and extracted with chloroform. The extract was evaporated to a colorless syrup (5.5 mg,) which was dissolved in a 0.5% methanolic hydrogen chloride (0.055 ml). The resulting solution was kept at room temperature for 1 h, and the reaction mixture was neutralized with solid $NaHCO_4$ and evaporated. The residue was partitioned between ethyl acetate and water. The aqueous layer was saturated with NaCl and extracted with ethyl acetate. The combined organic layers were dried and evaporated to a colorless syrup (4.7 mg), which was dissolved in ethyl acetate (0.047 ml). To this solution was added acetic anhydride (0.01 ml) and DMAP (13.4 mg) and stirred at room temperature for 20 min. The reaction mixture was then diluted with ethyl acetate, and washed with a saturated aqueous NaCl solution, dried, and evaporated. The residue was chromatographed on silica gel (0.6 g) with 10 : 1 benzene–ethyl acetate to afford **41** (4.0 mg, 51% from **34**) as a colorless syrup: ^{1}H-NMR (250 MHz) δ= 0.84 and 0.86 (3H, each d, β- and α-4-Me, J=7.0 Hz), 0.90 and 0.97 (3H, each d, β- and α-2-Me, J=7.0 Hz), 1.09 and 1.12 (3H, each d, α- and β-6-Me, J=7.0 Hz), 1.95—2.05 (1H, m, H-4), 2.05 and 2.09 (0.75H, each s, 2×β-OAc), 2.06 and 2.07 (5.25H, each s, 2×α-OAc), 2.10—2.25 (2H, m, H-2 and 6), 2.98 and 3.41 (1H, each dd, β- and α-H-5, $J_{4,\beta\text{-}5}$=$J_{4,\alpha\text{-}5}$= 11.3 Hz, $J_{\beta\text{-}5,6}$=$J_{\alpha\text{-}5,6}$=2.0 Hz), 3.31 and 3.46 (3H, each s, α- and β-OMe), 3.96 and 3.99 (1H, each dd, α- and β-H-7, $J_{6,7}$= 7.5 Hz, $J_{7,7'}$=10.8 Hz), 4.31 (1H, dd, H-7′, $J_{6,7'}$=5.0 Hz), 4.29 (overlapped one of the double doublets of H-7′ proton, H-1β), 4.49 (d, H-1α, $J_{\alpha\text{-}1,2}$=1.5 Hz), and 4.59—4.93 (1H, each dd, β- and α-H-3, $J_{2,\beta\text{-}3}$=$J_{2,\alpha\text{-}3}$=5.3 Hz, $J_{\beta\text{-}3,4}$=$J_{\alpha\text{-}3,4}$= 10.5 Hz).

Transformation of 37 and 39 into 42 and 43. By the procedure described in the preceding paragraph, **37** (22.3 mg) and **39** (18.4 mg) were coverted into **42** (12.8 mg, 69% yield based on **37**) and **43** (9.7 mg, 63% yield based on **39**) respectively: **42**, ^{1}H-NMR (250 MHz) δ=0.83 and 0.84 (3H, each d, β- and α-4-Me, J=7.0 Hz), 0.86 (3H, d, 2-Me, J=7.0 Hz), 1.11 (3H, d, 6-Me, J=7.0 Hz), 1.73 (0.6H, ddq, β-H-2), 1.85 —2.05 (1.4H, m, α-H-2, α- and β-H-4), 2.0—2.15 (1H, m, H-6), 2.04, 2.05, 2.10, and 2.11 (6H, each s, 2×OAc), 3.33 and 3.47 (3H, each s, α- and β-OMe), 3.42 and 3.67 (1H, each dd, β- and α-H-5, $J_{4,\beta\text{-}5}$=11.0 Hz, $J_{\beta\text{-}5,6}$=2.1 Hz,

$J_{4,\alpha\text{-}5}=11.0$ Hz, $J_{\alpha\text{-}5,6}=1.9$ Hz), 3.93 and 3.98 (1H, each dd, H,α- and β-H-7, $J_{6,7}=8.0$ Hz, $J_{7,7'}=11.0$ Hz), 4.26 and 4.27 (1 each dd, α- and β-H-7′, $J_{6,7'}=6.0$ Hz), 4.23 and 4.46 (1H, each d, β- and α-H-1, $J_{\beta\text{-}1,2}=9.0$ Hz, $J_{\alpha\text{-}1,2}=3.9$ Hz), and 5.12 and 5.22 (1H, each dd, α- and β-H-3, $J_{2,\alpha\text{-}3}=J_{\alpha\text{-}3,4}=3.1$ Hz, $J_{2,\beta\text{-}3}=J_{\beta\text{-}3,4}=3.0$ Hz); **43**, ^{1}H-NMR (250 MHz) $\delta=0.83$ and 0.88 (3H, each d, β- and α-4-Me, $J=7.0$ Hz), 0.98 and 1.04 (3H, each d, β- and α-2-Me, $J=7.0$ Hz), 1.10 and 1.12 (3H, each d, α- and β-6-Me, $J=7.0$ Hz), 1.9—2.2 (3H, m, H-2,4, and 6), 2.05, 2.06, 2.07, and 2.09 (6H, each s, 2×OAc), 3.34 and 3.47 (3H, each s, α- and β-OMe), 3.43 and 3.70 (1H, each dd, β- and α-H-5, $J_{4,\beta\text{-}5}=11.0$ Hz, $J_{\beta\text{-}5,6}=2.0$ Hz, $J_{4,\alpha\text{-}5}=10.0$ Hz, and $J_{\alpha\text{-}5,6}=3.0$ Hz), 3.96 and 4.00 (1H, each dd, α- and β-H-7, $J_{6,7}=8.0$ Hz, $J_{7,7'}=11.0$ Hz), 4.31 (1H, dd, H-7′, $J_{6,7'}=5.2$ Hz), 4.38 and 4.55 (1H, each d, α- and β-H-1, $J_{\alpha\text{-}1,2}=1.8$ Hz, $J_{\beta\text{-}1,2}=2.5$ Hz), and 4.67 and 4.90 (1H, each dd, α- and β-H-3, $J_{2,\alpha\text{-}3}=J_{\alpha\text{-}3,4}=4.0$ Hz, $J_{2,\beta\text{-}3}=J_{\beta\text{-}3,4}=2.7$ Hz).

*3,5-Di-*O*-benzyl-2,4,6,9-tetradeoxy-7,8-*O*-isopropylidene-2,4,6-tri-*C*-methyl-*D*-arabino-*L*-manno-nonose Diethyl Acetal (**36**).* After a mixture of the crude **34** (0.353 g), NaH (0.119 g, 0.496 mmol) and dry DMF (3.6 ml) had been stirred at room temperature for 0.5 h, benzyl bromide (0.47 ml, 0.395 mmol) was added to the resulting solution over a period of 2 min under ice-cooling, and the mixture was stirred at 45 °C for 2 h. The reaction mixture was then poured into ice water (5 ml) and the new mixture was extracted with chloroform (8 ml×3). The extracts were washed with a saturated aqueous NaCl solution (10 ml×2), dried, and evaporated. The residual syrup (0.746 g) was chromatographed on silica gel (37 g) with 15 : 1 benzene–ethyl acetate to afford a practically pure sample of **36** (0.472 g, 88%). A part of this sample (14 mg) was chromatographed twice by using silica gel (1 g) with the same solvent system to give an analytical sample (12.5 mg) as a colorless syrup: $R_f=0.38$ (15 : 1 benzene–ethyl acetate); $[\alpha]_D^{24}=[\alpha]_{365}^{24}=0°$ (*c* 1.10); ^{1}H-NMR $\delta=0.9$—1.3 [18H, m, 2,4,6-Me, H-9, and CH(OCH$_2$Me)$_2$], 1.34 and 1.47 (each 3H, each s, CMe$_2$), 1.85—2.25 (3H, m, H-2,4, and 6), 3.2—4.0 [6H, m, H-3,5, and CH(OCH$_2$Me)$_2$], 4.2—4.8 (7H, m, H-1, 7, 8 and 2×OCH$_2$Ph), and 7.43 (10H, s, 2×Ph).

Found: C, 71.91; H, 9.02%. Calcd for $C_{33}H_{50}O_6$: C, 71.68; H, 9.22%.

*3,5-Di-*O*-benzyl-2,4,6,9-tetradeoxy-2,4,6-tri-*C*-methyl-*D*-arabino-*L*-manno-nonose Diethyl Acetal (**45**).* A mixture of crude **36** (0.390 g) and 75% DCA (11.7 ml) was stirred at 0 °C for 20 min. The resulting solution was poured into an ice-cooled saturated aqueous NaHCO$_3$ solution (60 ml). The mixture was then extracted with ethyl acetate (40 ml×3), and the extracts were washed with a saturated aqueous NaCl solution (50 ml×2), dried, and evaporated to a yellow brown syrup of **44** (0.32 g, 95%). The syrup was thoroughly dried under reduced pressure for 18 h and dissolved in dry ethanol (2.4 ml). To this solution was added dried *p*-toluenesulfonic acid (2.4 mg, 0.0139 mmol). After being kept at room temperature for 3 h, the reaction mixture was neutralized (pH 7) with triethylamine and evaporated to a yellow-brown syrup (0.42 g), which was chromatographed on silica gel (20 g) with 3 : 1 benzene–ethyl acetate to afford **45** (0.312 g, 86% based on **36**) as a colorless syrup: $R_f=0.50$ (2 : 1 benzene–ethyl acetate); $[\alpha]_D^{31}+26°$ (*c* 1.36); ^{1}H-NMR $\delta=0.98$ (6H, d, 2×Me, $J=7.3$ Hz), 1.1—1.3 (12H, m, 2×Me and 2×OCH$_2$Me), 1.5—1.65 (2H, br, 2×OH), 2.0—2.45 (3H, m, H-2,4, and 6), 3.35—4.05 (8H, m, H-3,5,7,8, and 2×OCH$_2$-Me), 4.55—4.85 (5H, m, H-1 and 2×OCH$_2$Ph), 7.34 and 7.37 (each 5H, each s, 2×Ph).

Found: C, 71.41; H, 9.09%. Calcd for $C_{30}H_{46}O_6$: C, 71.68; H, 9.22%.

*3,5-Di-*O*-benzyl-2,4,6-trideoxy-2,4,6-tri-*C*-methyl-*L*-glycero-*L*-manno-heptodialdose 1-(Diethyl acetal) (**46**).* To an ice-cooled solution of **45** (0.172 g, 0.342 mmol) in acetone (1.7 ml) was slowly added a solution of NaIO$_4$ (0.183 g, 0.856 mmol) in water (1.8 ml). After being stirred at room temperature for 2 h, the mixture was diluted with water (2 ml) and extracted with ether (5 ml×3). The combined extracts were washed with a saturated aqueous NaCl solution (5 ml×2) dried and evaporated. The residual syrup (0.16 g) was chromatographed on silica gel (8 g) with 15 : 1 benzene–ethyl acetate to afford a pure sample of **46** (0.127 g, 81%): colorless syrup, $R_f=0.41$ (15 : 1 benzene–ethyl acetate): IR (CHCl$_3$, 0.15 M) 1719 cm^{-1}; ^{1}H-NMR $\delta=0.87$ and 0.92 (each 3H, each d, 2×Me, $J=7.2$ and 7.5 Hz), 1.1—1.3 (9H, m, Me and 2×OCH$_2$Me), 1.8—2.2 (2H, m, H-2 and 4), 2.5—3.0 (1H, m, H-6), 3.1—3.9 (6H, m, H-3,5, and 2×OCH$_2$Me), 4.25—4.55 (5H, m, 2×OCH$_2$Ph and H-1), 7.23 (10H, s, 2×Ph), and 9.72 (1H, s like, H-7, $J_{6,7}=0$ Hz).

*3-C-(Benzyloxymethyl)-3-deoxy-1,2: 5,6-Di-*O*-isopropylidene-α-*D*-allofuranose (**48**).* By the procedure described in the benzylation of **2**, **47** (2.08 g, 7.57 mmol) was benzylated with NaH (22.7 mmol) and benzyl bromide (1.78 ml, 15.2 mmol) in DMF (21 ml). The crude product (3.73 g) was chromatographed on silica gel (138 g) with 20 : 1 toluene–ethyl acetate to afford **48** (2.58 g, 94%) as a pale yellow syrup: $[\alpha]_D^{15}+6°$, $[\alpha]_{365}^{15}+15°$ (*c* 1.02); ^{1}H-NMR $\delta=1.32$, 1.34, and 1.48 (total 12H, each s, 2×CMe$_2$), 2.0—2.3 (1H, m, H-3), 3.5—4.1 (6H, m, H-4,5,6, and CH$_2$OBzl), 4.51 (2H, s, OCH$_2$Ph), 4.73 (1H, dd, H-2, $J_{1,2}=J_{2,3}=3.8$ Hz), 5.75 (1H, d, H-1), and 7.34 (5H, s, Ph).

Found: C, 66.12; H, 7.77%. Calcd for $C_{20}H_{28}H_6$: C, 65.91; H, 7.74%.

*3-C-(Benzyloxymethyl)-3-deoxy-1,2-*O*-isopropylidene-α-*D*-allofuranose (**49**).* A solution of **48** (2.55 g) in 75% acetic acid (26 ml) was stirred at 33 °C for 5 h and then evaporated to a yellow syrup (3.00 g), which was subsequently chromatographed on silica gel (68 g) with 1 : 2 toluene–ethyl acetate to afford **49** (2.19 g, 97%) as a pale yellow syrup: $[\alpha]_D^{17}+6°$, $[\alpha]_{365}^{17}+10°$ (*c* 1.76); ^{1}H-NMR $\delta=1.29$ and 1.48 (each 3H, each s, CMe$_2$), 2.0—2.4 (1H, m, H-3), 3.4—4.0 (6H, m, H-4, 5,6, and CH$_2$OBzl), 4.54 (2H, s, OCH$_2$Ph), 4.64 (1H, dd, H-2, $J_{1,2}=J_{2,3}=3.7$ Hz), 5.75 (1H, d, H-1), and 7.38 (5H, s, Ph).

Found: C, 62.67; H, 7.31%. Calcd for $C_{17}H_{24}O_6$: C, 62.95; H, 7.46%.

*3-C-(Benzyloxymethyl)-3-deoxy-1,2-*O*-isopropylidene-6-*O*-tosyl-α-*D*-allofuranose (**50**).* To a solution of **49** (3.40 g, 10.5 mmol) in dry pyridine (17 ml) was added a solution of tosyl chloride (2.40 g, 12.6 mmol) in dry pyridine (4.8 ml) under ice-cooling. After being kept at room temperature for 3 h, the reaction mixture was poured into ice water (65 ml) and the mixture was extracted with ethyl acetate. The extract was washed successively with saturated aqueous KHSO$_4$, NaHCO$_3$, and NaCl solutions, dried, and evaporated to afford acrude sample of **50** (5.02 g) as a pale yellow syrup, which was suitable for the next synthesis. A pure sample of **50** was obtained by silica gel column chromatography with 9 : 1 benzene–ethyl acetate: $R_f=0.35$ (9 : 1 benzene–ethyl acetate); $[\alpha]_D^{15}+3°$, $[\alpha]_{365}^{15}+8°$ (*c* 0.63); IR (CHCl$_3$) 1177 and 1365 cm^{-1}.

Found: C, 60.20; H, 6.27; S, 6.52%. Calcd for $C_{24}H_{30}O_8S$: C, 60.24; H, 6.32; S, 6.70%.

*3-C-(Benzyloxymeihyl)-3,6-dideoxy-1,2-*O*-isopropylidene-α-*D*-allofuranose (**51**).* To an ice-cooled solution of the crude sample of **50** (5.02 g) in dry ether (50 ml) was slowly added powdered LiAlH$_4$ (0.796 g, 21.0 mmol) under stirring. The stirring was continued for 3 h under ice-cooling, and to the reaction mixture were added dropwise water (0.8 ml), 15% NaOH solution (0.8 ml), and water (2.4 ml) successively. The

resulting mixture was then filtered, and the filter cake was washed with ether. The filtrate and washings were combined, and evaporated to a syrup (3.1 g), which was chromatographed on silica gel (160 g) with 3 : 1 toluene–ethyl acetate to afford a pure sample of **51** (2.39 g, 74% based on **49**): colorless syrup, R_f=0.32 (3 : 1 toluene–ethyl acetate); $[\alpha]_D^{16}$ +7°, $[\alpha]_{365}^{16}$ +11° (*c* 2.35); ^{1}H-NMR δ=1.26 (3H, d. H-6, $J_{5,6}$=6.0 Hz), 1.28 and 1.48 (each 3H, each s, CMe_2), 1.9—2.25 (1H, m, H-3), 3.5—3.9 (4H, m, H-4,5, and $C\underline{H}_2OBzl$), 3.96 (1H, broad s, 5-OH), 4.53 (2H, ABq, $OC\underline{H}_2Ph$, J_{gem}=11.1 Hz), 4.66 (1H, dd, H-2, $J_{1,2}=J_{2,3}$=3.9 Hz), 5.74 (1H. d, H-1), and 7.35 (5H' s, Ph).

Found: C, 66.10; H, 7.70%. Calcd for $C_{17}H_{24}O_5$: C, 66.21; H, 7.85%.

3-C-(Benzyloxymethyl)-3,6-dideoxy-1,2-O-isopropylidene-α-D-allofuranos-5-ulose (52). To a stirred mixture of PCC (4.80 g, 22.3 mmol), molecular sieve 3A powder (5.57 g), and dry dichloromethane (19 ml) was added a solution of **51** (2.29 g, 7.43 mmol) in dichloromethane (4.6 ml) at room temperature. After being stirred at room temperature for 2.5 h, the reaction mixture was diluted with ether (25 ml) and filtered through a column filled with silica gel (60 g). Removal of the solvent gave almost pure sample of **52** (2.10 g, 92%) as a colorless syrup. A portion of this sample was chromatographed on silica gel with 10 : 1 benzene–ethyl acetate to afford an analytical sample of **52**: R_f=0.56 (3 : 1 toluene–ethyl acetate); $[\alpha]_D^{15}$ +3°, $[\alpha]_{436}^{15}$ +4°, and $[\alpha]_{365}^{15}$ 0° (*c* 2.09); IR ($CHCl_3$) 1720 cm^{-1}; ^{1}H-NMR δ=1.35 and 1.49 (each 3H, each s, CMe_2), 2.1—2.5 (1H, m, H-3), 2.20 (3H, s, H-6), 3.61 (1H, dd, one of the $C\underline{H}_2OBzl$, J_{gem}=9.1 Hz, J=4.6 Hz), 3.79 (1H, dd, one of the $C\underline{H}_2OBzl$, J=9.1 Hz), 4.11 (1H, d, H-4, $J_{3,4}$=9.7 Hz), 4.49 (2H, s, $OC\underline{H}_2Ph$), 4.73 (1H, dd, H-2, $J_{1,2}=J_{2,3}$=3.9 Hz), 5.90 (1H, d, H-1), and 7.34 (5H, m, Ph).

Found: C, 66.31; H, 7.12%. Calcd for $C_{17}H_{22}O_5$: C, 66.65; H, 7.24%.

3-C-(Benzyloxymethyl)-3,5,6-trideoxy-5-iodo-1,2-O-isopropylidene-α-D-ribo-5-hexenofuranose (54). A mixture of **52** (1.02 g, 3.33 mmol), ethanol (10 ml), triethylamine (3.93 ml, 28.2 mmol), and 100% hydrazine hydrate (0.645 ml, 13.3 mmol) was refluxed for 10 min. The cooled reaction mixture was diluted with chloroform (33 ml), and the mixture was washed with water (20 ml). The aqueous layer was extracted with chloroform. The combined organic layers were washed with a saturated aqueous NaCl solution, dried, and evaporated to afford the hydrazone **53** (1.06 g, 100%) as a pale yellow syrup. To an ice-cooled mixture of **53** (1.06 g), dry THF (37 ml), and triethylamine (23.1 ml, 166 mmol) was added dropwise a solution of iodine (1.85 g, 7.30 mmol) in dry THF (18.5 ml). After being stirred at 0 °C for 5 min, the reaction mixture was diluted with ether (110 ml) and washed successively with 10% aqueous citric acid, saturated aqueous $Na_2S_2O_3$, and NaCl solutions, dried, and evaporated. The residual dark brown syrup (1.56 g) was chromatographed on silica gel (207 g) with 30 : 1 toluene–ethyl acetate to give colorless needles of **54** (0.407 g, 30%). Recrystallization from hexane afforded an analytical sample: R_f=0.34 (30 : 1 toluene–ethyl acetate); mp 67—67.5 °C; $[\alpha]_D^{15}$ +50° (*c* 1.25); IR (KBr) 1612 cm^{-1}; ^{1}H-NMR δ=1.35 and 1.50 (each 3H, each s, CMe_2), 2.1—2.45 (1H, m, H-3), 3.42 (1H, dd, one of the $C\underline{H}_2OBzl$, J_{gem}=9.4 Hz, J=5.5 Hz), 3.62 (1H, d, H-4, $J_{3,4}$=9.4 Hz), 3.76 (1H, dd, one of the $C\underline{H}_2OBzl$, J=9.4 Hz), 4.50 (2H, s, $OC\underline{H}_2Ph$), 4.73 (1H, dd, H-2, $J_{1,2}=J_{2,3}$=3.8 Hz), 5.88 (1H, d, H-1), 5.95 and 6.39 (each 1H, each d, C=CH_2, J=1.5 Hz), and 7.37 (5H, s, Ph).

Found: C, 48.76; H, 5.03; I, 30.66%. Calcd for $C_{17}H_{21}O_4I$: C, 49.05; H, 5.08; I, 30.49%.

3-C-(Benzyloxymethyl)-3,5,6-trideoxy-1,2-O-isopropylidene-α-D-ribo-5-hexenofuranose (55). To an ice-cooled solution of **49** (0.703 g, 2.17 mmol) in acetone (7 ml) was added a solution of $NaIO_4$ (0.695 g, 3.25 mmol) in water (7 ml). After being stirred under ice-cooling for 10 min, the mixture was diluted with water (7 ml) and extracted with ehter (7 ml×4). The combined extracts were washed with a saturated aqueous NaCl solution (7 ml), dried, and evaporated to afford a syrup of the crude aldehyde (0.614 g, 97%). A suspension of 55% NaH (0.275 g, 6.30 mmol) in dry DMSO (19 ml) was stirred at 75 °C for 45 min under argon and then cooled to room temperature. To this solution was added methyltriphenylphosphonium bromide (2.25 g, 6.30 mmol) and the mixture was stirred at room temperature for 0.5 h. A solution of the aforesaid crude aldehyde (614 mg) in dry DMSO (3.1 ml) was added dropwise to the ice-cooled resulting organge-yellow solution of the ylide over a period of 10 min. After the mixture had been stirred at room temperature for 0.5 h, it was poured into ice water (80 ml), and new mixture was extracted with ether. The extract was successively washed with water, a saturated aqueous NaCl solution, dried, and evaporated. The residue (1.55 g) was chromatographed on silica gel (31 g) with 20 : 1 benzene–ethyl acetate to afford **55** (0.544 g, 87% based on **49**) as a colorless syrup: $[\alpha]_D^{25}$ +16° (*c* 0.64); ^{1}H-NMR δ= 1.33 and 1.51 (each 3H, each s, CMe_2), 1.9—2.3 (1H, m, H-3), 3.47 (1H, dd, one of the $C\underline{H}_2OBzl$, J_{gem}=9.3 Hz, J=5.3 Hz), 3.78 (1H, dd, one of the $C\underline{H}_2OBzl$, J=9.3 Hz), 4.19 (1H, dd, H-4, $J_{3,4}$=6.8 Hz, $J_{4,5}$=10.4 Hz), 4.50 (2H, s, $OC\underline{H}_2Ph$), 4.71 (1H, dd, H-2, $J_{1,2}=J_{2,3}$=3.8 Hz), 5.15 (1H, dd, H-6(*E*), $J_{5,6}$=10.3 Hz, J_{gem}=*ca.* 1 Hz), 5.26 (1H, dd, H-6(*Z*), $J_{5,6}$= 16.5 Hz), 5.38 (2H, d and ddd, H-1 and H-5), and 7.36 (5H, s, Ph).

Found: C, 70.19; H, 7.54%. Calcd for $C_{17}H_{22}O_4$: C, 70.32; H, 7.64%.

3-C-(Benzyloxymethyl)-5-bromo-3,5,6-trideoxy-1,2-O-isopropylidene-α-D-ribo-5-hexenofuranose (56) and 3-C-(Benzyloxymethyl)-6-bromo-3,5,6-trideoxy-1,2-O-isopropylidene-α-D-ribo-(E)-5-hexenofuranose (57). To a stirred cooled (−10 °C) solution of **55** (0.541 g, 1.86 mmol) in carbon tetrachloride (5.4 ml) was added dropwise a solution of bromine (0.298 g, 1.86 mmol) in carbon tetrachloride (0.96 ml) over a period of 20 min. After being at −10 °C for 5 min, a saturated aqueous $NaHCO_3$ solution was added to the reaction mixture. The organic layer was separated and the aqueous layer was extracted with chloroform. The combined organic layers were washed with a saturated aqueous NaCl solution, dried, and evaporated. The residue was chromatographed on silica gel (25 g) with 40 : 1 toluene–ethyl acetate to afford dibromide (0.675 g, 81%) as a pale yellow syrup. The TLC (40 : 1 toluene–ethyl acetate) of this sample revealed it to be a mixture of two diastereomers with R_f=0.31 and 0.27. To a solution of the dibromide (0.674 g) in dry DMSO (4.7 ml) was added a solution of DBU (0.457 g, 3.00 mmol) in dry DMSO (2.0 ml), and the mixture was stirred at room temperature for 2 h. The reaction mixture was then diluted with water (35 ml) and extracted with ether (20 ml×4). The extracts were combined, successively washed with water and a saturated aqueous NaCl solution, dried, and evaporated. The residue (0.56 g) was chromatographed on silica gel (28 g) with 30 : 1 toluene–ethyl acetate to afford a mixture of **56** and **57**(0.496g, 90 %)and the starting dibromide (43 mg, 6.4%). The mixture of **56** and **57** was again chromatographed on silica gel (74 g) with 8 : 1 hexane–ethyl acetate to give **56** (0.401 g, 72%) and **57** (80 mg, 14%): **56** (colorless needles), R_f=0.29 (8 : 1 hexane–ethyl acetate), mp 71—72 °C (heptane); $[\alpha]_D^{17}$ +53° (*c* 1.13); IR ($CHCl_3$) 1630 cm^{-1}; ^{1}H-NMR δ=1.33 and 1.49 (each 3H, each s, CMe_2), 2.3—2.7 (1H, m, H-3), 3.47 (1H, dd, one of the $C\underline{H}_2OBzl$, J_{gem}=9.3 Hz, J=5.3 Hz), 3.77 (1H, dd, one of the

$C\underline{H}_2OBzl$, J=9.3 Hz), 4.20 (1H, d, H-4, $J_{3,4}$=10.5 Hz), 4.50 (2H, s, $OC\underline{H}_2Ph$), 4.73 (1H, dd, H-2, $J_{1,2}=J_{2,3}$=3.5 Hz), 5.64 and 5.91 (each 1H, each d, C=CH_2, J=2.1 Hz), 5.88 (1H, d, H-1), and 7.35 (5H, s, Ph).

Found: C, 55.42: H, 5.69; Br, 21.42%. Calcd for $C_{17}H_{21}O_4Br$: C, 55.30; H, 5.73; Br, 21.64%.

57 (colroless syrup), R_f=0.25 (8 : 1 hexane–ethyl acetate); $[\alpha]_D^{30}$ +30° (c 1.24); IR ($CHCl_3$) 1623 cm^{-1}; ^{1}H-NMR δ=1.32 and 1.49 (each 3H, each s, CMe_2), 2.1—2.2 (1H, m, H-3), 3.49 (1H, dd, one of the $C\underline{H}_2OBzl$, J_{gem}=9.0 Hz, J=6.3 Hz), 3.78 (1H, dd, one of the $C\underline{H}_2OBzl$, J=7.8 Hz), 4.26 (1H, dd, H-4, $J_{3,4}$=10.3 Hz, $J_{4,5}$=6.8 Hz), 4.52 and 4.53 (each 1H, each d, $OC\underline{H}_2Ph$, J_{gem}=12.5 Hz), 4.72 (1H, dd, H-2, $J_{1,2}=J=J_{2,3}$=4.0 Hz), 5.82 (1H, d, H-1), 6.24 (1H, dd, H-5, $J_{5,6}$=14.3 Hz), 6.42 (1H, d, H-6), and 7.34 (5H, s, Ph).

Found: C, 55.18; H, 5.75; Br; 21.41%. Calcd for $C_{17}H_{21}O_4Br$: C, 55.30; H, 5.73; Br, 21.64%.

*A Mixture of 8,10-Di-O-benzyl-3-C-(benzyloxymethyl)-3,5,7,9,-11-pentadeoxy-1,2-O-isopropylidene-7,9,11-tri-C-methyl-5-methylene-*L-erythro-D-altro-*α*-D-ribo-*dodecodialdofuranose-(1,4)12-(Diethyl acetal) (59) and* L-erythro-D-allo-*α*-D-ribo *Epimer (60).*

To a cooled (−90——94 °C) solution of **54** (0.588 g, 1.41 mmol) in dry ether (13 ml) was added 1.28 M butyllithium in hexane (1.1 ml, 1.41 mmol) over a period of 3 min under argon. After being stirred at the same temperature for 45 min, a solution of **46** (0.209 g, 0.458 mmol) in dry ether (0.42 ml) was added to the mixture over a period of 2 min, and stirring was continued at the same temperature for 0.5 h. To the reaction mixture was added a saturated aqueous NH_4Cl solution (3 ml), and the separated aqueous layer was extracted with ether (6 ml×2). The organic layers were combined, washed with a saturated aqueous NaCl solution, dried, and evaporated. The residual yellow syrup (0.673 g) was chromatographed on silica gel (70 g) with 20 : 1 toluene–acetone to afford the following fractions: Fr-1, a mixture of **46**, **55**, and **54** (95.7 mg); Fr-2, **55** (0.152 g); Fr-3, *ca.* 4: 1 mixture of **59** and **60** (0.272 g, 80%). The Fr-3 showed on the TLC (20 : 1 toluene–acetone) the major spot (**59**, R_f=0.29) and the minor one (**60**, R_f=0.31); ^{1}H-NMR (250 MHz) δ=0.90, 0.93, and 1.08 (each 0.6H, each d, 7,9,11-Me, J=7.0 Hz), 0.96, 1.00, and 1.02 (each 2.4H, each d, 7,9,11-Me, J=7.0 Hz), 1.15 (3H, t, $OCH_2\underline{Me}$, J=7.0 Hz), 1.18 (2.4H, t, $OCH_2\underline{Me}$, J=7.0 Hz), 1.20 (0.6H, t, $OCH_2\underline{Me}$, J=7.0 Hz), 1.34 (3H, s, CMe_2), 1.46 (2.4H, s, CMe_2), 1.50 (0.6H, s, CMe_2), 2.0—2.4 (4H, m, H-3, 7,9, and 11), 3.3—3.95 (10H, m, H-6,8,10, and 2×$OC\underline{H}_2Me$, and $C\underline{H}_2OBzl$, 6-OH), 4.04 (0.8H, d, H-4, $J_{3,4}$=10.5 Hz), 4.15 (0.2H, d, H-4, $J_{3,4}$=10.5 Hz), 4.35—4.85 (7H, m, 3×$C\underline{H}_2Ph$, and H-12), 4.77 (1H, dd, H-2, $J_{1,2}=J_{2,3}$=4.0 Hz), 5.28 and 5.29 (each 0.2H, each s, C=$C\underline{H}_2$), 5.32 and 5.44 (each 0.8H, each s, C=$C\underline{H}_2$), 5.82 (1H, d, H-1), 7.32 and 7.33 (15H, each s, 3×Ph).

*3,5,7,9,11-Pentadeoxy-3-*C-*(hydroxymethyl)-1,2-*O-*isopropylidene-5,7,9,11-tetra-*C-*methyl-*L-*erythro-*D-*altro-β-*L-talo-*dodecodialdofuranose-(1,4) 12-(Diethyl acetal) (63) and Its Isomeric Mixture (65).* A sample (0.231 g, 0.310 mmol) of the epimeric mixture (**59** and **60**) obtained in the preceding experiment was dissolved in dry benzene (12 ml). To this solution was added $(Ph_3P)_3RhCl$ (0.573 g, 0.619 mmol), and the solution stirred under an atmospheric pressure of H_2 at room temperature for 1 d. The reaction mixture was then evaporated and the residue was passed through Florisil (100—200 mesh, 40 g) with ether. The effluent was evaporated to afford a pale yellow syrup of the crude hydrogenation product (0.189 g, 82%). To a solution of this product in dry ether (3.8 ml) was added liquid ammonia (19 ml), and then lithium (0.070 g, 10 mmol) was added under cooling (−78 °C). After the mixture had been stirred at the same temperature for 50 min, the excess lithium was destroyed by addition of solid NH_4Cl. The mixture was then diluted with ether (10 ml) and allowed to concentrate spontaneously. The residue was taken with ether (10 ml), and the solution washed with a saturated aqueous NaCl solution (3 ml×2), dried, and evaporated. The residual syrup was chromatographed on silica gel (10 g) with 2 : 1 benzene–acetone to afford **63** (colorless syrup, R_f=0.25 (2 : 1 benzene–acetone), 93 mg, 77%) and a colorless syrup [R_f=0.51 (2 : 1 benzene–acetone), 17 mg] containing **65**.

*8,10-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 acetatal) (61).*

(a): A sample (60 mg) of the aforesaid crude hydrogenation product from a mixture of **59** and **60** was at first chromatographed on silica gel (6 g) with 35 : 1 chroloform–acetone to afford a pale-yellow syrup (42 mg). This was again chromatographed on silica gel (8.4 g) with 7 : 1 *s*-BuCl–ethyl acetate to give **61** (31 mg) and a product (8.4 mg) shown to be **62** by ^{1}H-NMR analysis: **61**, colorless syrup, R_f=0.31 (7 : 1 *s*-BuCl–ethyl acetate); $[\alpha]_D^{17}$ +16° (c 0.92); ^{1}H-NMR (250 mHz) δ=0.76, 0.92, 0.97, and 1.08 (each 3H, each d, 5,7,9,11-Me, J=7.0 Hz), 1.17 and 1.19 (each 3H, each t, 2×$OCH_2\underline{Me}$, J=7.0 Hz), 1.32 and 1.50 (each 3H, each s, CMe_2), 1.65—1.80, 1.90—2.05, and 2.05—2.30 (each 1H, 1H, and 3H, each m, H-3,5,7,9, and 11), 3.3—4.0 (10H, m, H-6,8,10, 2×OCH_2Me, $C\underline{H}_2OBzl$, and 6-OH), 4.4—4.75 (9H, m, H-2,4,12, and 3×$OC\underline{H}_2Ph$), 5.77 (1H,d, H-1, $J_{1,2}$=3.5 Hz), 7.32 and 7.34 (15H, each s, 3×Ph).

Found: C, 72.06; H, 8.43%. Calcd for $C_{45}H_{64}O_9$: C, 72.16; H, 8.61%.

62, colorless syrup, R_f=0.38 (7 : 1 *s*-BuCl–ethyl acetate); ^{1}H-NMR (250 MHz) δ=0.90, 0.92, 0.93, and 1.04 (each 3H, each d, 5,7,9,11-Me, J=7.0 Hz), 1.17 and 1.20 (each 3H, each t, 2×$OCH_2\underline{Me}$, J=7.0 Hz), 1.32 and 1.50 (each 3H, each s, CMe_2), 1.90—2.00 (1H, m, H-5), 1.95—2.25 (3H, m, H-7,9, and 11), 2.25—2.40 (1H, m, H-3), 3.15 (1H, d, 6-OH, $J_{6,OH}$=1.0 Hz), 3.3—3.65 (4H, m, one of the CH_2OBzl, and three of the 2×$OC\underline{H}_2Me$), 3.7—3.9 (2H, m, one of the $C\underline{H}_2OBzl$, and one of the 2×$OC\underline{H}_2Me$), 3.74 (1H, dd, H-6 or 8, J=2.3 and 11.0 Hz), 3.85 (1H, dd, H-6 or 8, J=0 and 9.5 Hz), 3.95 (1H, dd, H-10, $J_{9,10}$=0 Hz, $J_{10,11}$=9.0 Hz), 4.01 (1H, dd, H-4, $J_{3,4}$=10.3 Hz, $J_{4,5}$=2.3 Hz), 4.35—4.7 (6H, m, 3×$OC\underline{H}_2Ph$), 4.56 (1H, d, H-12, $J_{11,12}$=3.5 Hz), 4.69 (1H, dd, H-2, $J_{1,2}=J_{2,3}$=3.8 Hz), 5.79 (1H, d, H-1), and 7.2—7.4 (15H, m, 3×Ph).

(b): By the procedure described in the preparation of the mixture of **59** and **60**, a crude condensation product (213 mg) was obtained from **54** (155 mg) and **46** (66.1 mg). This sample was chromatographed on silica gel (32 g) with 20 : 1 toluene–acetone to afford the six fractions: Fr-1, **54** (30.1 mg); Fr-2, **54**+**46** (5.9 mg); Fr-3, **46**+**55** (11.5 mg); Fr-4, **55** (38.3 mg); Fr-5, **60** (major)+**59** (minor) (18.6 mg, 17.2% yield); Fr-6, **59** (63.5 mg, 58.7% yield). Thus obtained chromatographically pure sample (10 mg, 0.013 mmol) of **59** was hydrogenated in dry benzene (0.5 ml) with $(Ph_3P)_3RhCl$ (24.8 mg, 0.0268 mmol) at room temperature under an atmospheric pressure of H_2 for 14 h. The reaction mixture was evaporated and the residue was passed through Florisil (1 g) with ether and evaporated to a syrup whose TLC showed only one spot of **61**. The chromatographic purification (silica gel, 1 g, 3.5 : 1 hexane–ethyl acetate) gave a colorless syrup of **61** (8.6 mg, 86%).

*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) (64).*

To a mixture of **63** (81 mg, 0.169 mmol), DMAP (99 mg, 0.810 mmol), and ethyl acetate (0.81 ml) was added acetic anhydride (0.096 ml, 1.02 mmol). The mixture was stirred at room temperature for 23.5 h and then poured into a cold saturated aqueous $NaHCO_3$ solution (2 ml). The mixture was extracted with ethyl acetate (3 ml×3) and the extracts were washed with a saturated aqueous NaCl solution, dried, and evaporated. The residue was chromatographed on silica gel (10 g) with 10 : 1 benzene–acetone to afford **64** (99 mg, 91%) as colorless needles: R_f=0.38 (6 : 1 benzene–acetone); mp 100—102 °C; $[\alpha]_D^{19}$ 0°, $[\alpha]_{365}^{19}$ +60° (*c* 1.09); IR ($CHCl_3$, 0.15M) 1732 cm^{-1}; ^{1}H-NMR δ=0.9—1.3 (18H, m, 5,7,9,11-Me, and 2×$OCH_2\underline{Me}$), 1.33 and 1.46 (each 3H, each s, CMe_2), 2.00, 2.02, 2.03, and 2.08 (12H, each s, 4×OAc), 1.9—2.6 (5H, m, H-3,5,7,9,11), 3.3—4.25 (8H, m, H-4,12, $C\underline{H_2}OAc$ and 2×$OC\underline{H_2}Me$), 4.5—5.2 (4H, m, H-2,6,8, and 10), and 5.72 (1H, d, H-1, $J_{1,2}$=2.3 Hz).

Found: C, 59.12; H, 8.17%. Calcd for $C_{32}H_{54}O_{13}$: C, 59.42; H, 8.42%.

*C-5-Epimeric Actates (**66**).* The syrup (17 mg), R_f=0.51) obtained in the preparation of **63** was acetylated by the procedure described in the preparation of **64**. The crude product was purified by silica gel column chromatography with 2 : 1 toluene–ethyl acetate to afford a sample of **66** (16 mg): colorless syrup, R_f=0.50, 0.45 (1 : 1 hexane–ethyl acetate); ^{1}H-NMR (250 MHz) δ=0.9—1.05 (12H, m, 4×Me), 1.19 and 1.20 (2H and 4H, each t, 2×$OCH_2\underline{Me}$, J=6.8 Hz), 1.32 and 1.50 (each 1H, each s, CMe_2), 1.34 and 1.49 (each 2H, each s, CMe_2), 2.00, 2.05, 2.05, and 2.06 (each 1H, each s, 4×OAc), 2.01, 2.03, 2.09, and 2.10 (each 2H, each s, 4×OAc), 1.9—2.5 (5H, m, H-3,5,7,9, and 11), 3.35—3.80 (4H, m, 2×$OC\underline{H_2}Me$), 3.96 (2H/3, dd, H-4, J=5.0 and 10.0 Hz), 4.03 (1H/3, dd, H-4, J=1.0 and 10.0 Hz), 4.1—4.2 (2H, m, H-12 and one of $C\underline{H_2}OAc$), 4.29 (1H/3, dd, one of $C\underline{H_2}OAc$, J=7.8 and 10.8 Hz), 4.39 (2H/3, dd, one of $C\underline{H_2}OAc$, J=4.8 and 10.8 Hz), 4.55—4.7 (2H, m, H-2 and $C\underline{H}OAc$), 4.89 (2H/3, dd, $C\underline{H}OAc$, J=4.8 and 7.5 Hz), 5.0—5.15 (4H/3, m, 2×$C\underline{H}OAc$), 5.72 and 5.75 (1H/3 and 2H/3, each d, H-1, J=3.8 Hz).

*Methyl 6,8,10-Tri-O-acetyl-3-C-(acetoxymethyl)-3,5,7,9,11,12,-13-heptadeoxy-1,2-O-isopropylidene-5,7,9,11-tetra-C-methyl-*L*-erythro-*D*-altro-β-*L*-talo-(E)-12-tetradecenofuranuronate-(1,4) (**68**).* A mixture of **64** (86 mg, 0.133 mmol) and 75% DCA (1.7 ml) was stirred at 0 °C for 40 min. The resulting solution was poured into a cold saturated aqueous $NaHCO_3$ solution (20 ml) containing solid $NaHCO_3$. The mixture was then extracted with ethyl acetate (20 ml×2, 10 ml×1), and the extracts were washed with a saturated aqueous NaCl solution (20 ml×2), dried, and evaporated to afford colorless needles of **67** (74 mg, 97%): mp 97—102 °C. To a solution of this crystals (74 mg) in dry toluene (2.2 ml) was added (methoxycarbonylmethylene) triphenylphosphorane (90 mg, 0.27 mmol), and the mixture was stirred at 95—98 °C for 4 h under argon. The reaction mixture was concentrated to a yellow syrup which was chromatographed on silica gel (13 g) with 3 : 2 *s*-BuCl–ethyl acetate to give **68** (73 mg, 89%) as a pale yellow syrup: R_f=0.34 (3 : 2 *s*-BuCl–ethyl acetate); $[\alpha]_D^{18}$ +5°, $[\alpha]_{365}^{18}$ +15° (*c* 1.02); IR ($CHCl_3$, 0.1 M), 1725, 1650, 1220, and 984 cm^{-1}; ^{1}H-NMR (250 MHz) δ=0.90 (3H, d, 5-Me, J=7.0 Hz), 0.95 (3H, d, 7-Me, J=7.0 Hz), 0.96 (3H, d, 9-Me, J=7.0 Hz), 1.09 (3H, d, 11-Me, J=7.0 Hz), 1.32, and 1.45 (each 3H, each s, CMe_2), 1.8—2.0 (1H, m, H-5), 1.94, 2.01, 2.03, and 2.09 (each 3H, each s, 4×OAc), 2.1—2.3 (2H, m, H-3,7), 2.4—2.6 (2H, m, H-9,11), 3.71 (3H, s, COOMe), 3.84 (1H, dd, H-4, $J_{3,4}$=10.2 Hz, $J_{4,5}$=1.3 Hz), 4.13 and 4.24 (each 1H, each dd, $C\underline{H_2}OAc$, J_{gem}=11.0 Hz, J=6.1 and 8.1 Hz), 4.64 (1H, dd, H-2, $J_{1,2}$=$J_{2,3}$=3.8 Hz), 4.82 (1H, dd, H-8, $J_{7,8}$=5.3 Hz, $J_{8,9}$=8.5 Hz), 4.90 (1H, dd, H-10, $J_{9,10}$=2.0 Hz, $J_{10,11}$=9.2 Hz), 5.18 (1H, dd, H-6, $J_{5,6}$=9.9 Hz, $J_{6,7}$=0.9 Hz), 5.77 (1H, d, H-13, $J_{12,13}$=15.0 Hz), 5.77 (1H, d, H-1), and 6.75 (1H, dd, H-12, $J_{11,12}$=9.0 Hz).

Found: C, 59.43; H, 7.63%. Calcd for $C_{31}H_{48}O_3$: C, 59.22; H, 7.69%.

*Methyl 5,7,9-Tri-O-acetyl-2-C-(acetoxymethyl)-2,4,6,8,10,11,-12-heptadeoxy-4,6,8,10-tetra-C-methyl-*aldehydo-L-glycero-L-talo-L-manno-(E)-11-tridecenuronate 1-(Dimethyl acetal) (III).* A mixture of **68** (30.0 mg, 0.0477 mmol) and 75% TFA (0.3 ml) was kept in a refrigerator for 24 h. The reaction mixture was poured in to a cold saturated aqueous $NaHCO_3$ solution, and the mixture was extracted with ethyl acetate. The extract was washed with a saturated aqueous NaCl solution, dried, and evaporated toa colorless syrup, which was dissolved in acetone (0.56 ml) and ice-cooled. To this solution was added a solution of $NaIO_4$ (40.8 mg, 0.191 mmol) in water (0.5 ml), and the mixture was stirred at room temperature for 2.5 h. The reaction mixture was diluted with water, and extracted with ethyl acetate. The extract was washed with a saturated aqueous NaCl solution, dried, and evaporated to give the crude crystalline aldehyde **69**. The crude **69** was dissolved in dry methanol (0.56 ml) and to this, a 0.095 M methanolic *p*-toluenesulfonic acid (0.01 ml) was added. After being stirred at room temperature for 24 h, the reaction mixture was neutralized with triethylamine and evaporated. The residue was then chromatographed on silica gel (Kieselgel 60, 3 g) with 1 : 1 toluene–ethyl acetate to afford III (12.3 mg, 43% based on **68**) as a colorless syrup: $[\alpha]_D^{16}$ −8° (*c* 0.98); IR ($CHCl_3$), 1726 and 1652 cm^{-1}; ^{1}H-NMR (250 MHz) δ=0.89 (3H, d, 4-Me, J=7.0 Hz), 0.92 and 0.97 (each 3H, each d, 6- and 8-Me, J=7.3 and 7.0 Hz), 1.07 (3H, d, 10-Me, J=6.4 Hz), 1.65—1.85 (1H, m, H-4), 1.96, 2.00, 2.04, and 2.07 (each 3H, each s, 4×OAc), 2.1—2.2 (1H, m, H-2), 2.2—2.4 (2H, m, H-6 and 8), 2.45—2.65 (1H, m, H-10), 3.30 (1H, d, 3-OH, J=3.9 Hz), 3.41 and 3.44 (each 3H, each s, 2×OMe), 3.51 (1H, ddd, H-3, $J_{2,3}$=10.0 Hz, $J_{3,4}$=1.0 Hz), 3.71 (3H, s, COOMe), 3.98 and 4.24 (each 1H, each dd, $C\underline{H_2}OAc$, J=6.0 and 3.8 Hz, J_{gem}=11.6 Hz), 4.62 (1H, d, H-1, $J_{1,2}$=4.0 Hz), 4.85 (1H, dd, H-7, $J_{6,7}$=$J_{7,8}$=7.0 Hz), 4.98 (1H, dd, H-9, $J_{8,9}$=2.0 Hz, $J_{9,10}$=9.8 Hz), 5.02 (1H, dd, H-5, $J_{4,5}$=10.0 Hz, $J_{5,6}$=1.3 Hz), 5.79 (1H, dd, H-12, $J_{10,12}$=0.7 Hz, $J_{11,12}$=16.0 Hz), and 6.76 (1H, dd, H-11, $J_{10,11}$=9.3 Hz).

Found: C, 57.31; H, 7.72%. Calcd for $C_{29}H_{48}O_{13}$: C, 57.60; H, 8.00%.

*Transformation of III into **70**.* A solution of III (10.2 mg, 0.0169 mmol) in dry toluene (1 ml) was cooled at −78 °C and to this was added portionwise 1.76 M DIBAL in hexane (0.258 ml, 0.454 mmol) over a period of 9 h under argon. After being stirred for additional 1 h, the mixture was warmed up to room temperature and was added 50% acetic acid (0.05 ml). The precipitates formed was filtered and washed with acetone. The filtrate and washings were combined and evaporated to afford a colorless syrup (4.6 mg). To a solution of this syrup in dry methanol (0.16 ml) was added 0.022 M methanolic PPTS solution (0.05 ml), and the mixture was stirred at 55 °C for 24 h. The reaction mixture was then neutralized with triethylamine and evaporated to a colorless syrup (4.2 mg) of cyclic methyl acetal derivative. A solution of the acetal in ethyl acetate (0.1 ml) was treated with acetic anhydride (0.008 ml, 0.08 mmol), DMAP (8.2 mg, 0.067 mmol) at 24 °C for 2 h. The reaction mixture was worked up by the usual way. The crude product was chromatographed on silica gel (1 g) with 3 : 2 toluene–ethyl acetate to afford **70** (2.7 mg, 27% from III) as a colorless syrup: R_f=0.38 (3 : 2 toluene–ethyl acetate); ^{1}H-NMR (250 MHz) δ=0.82 (3H, d, 4-Me,

J=6.3 Hz), 0.93 and 0.99 (each 3H, each d, 6- and 8-Me, J= 7.5 and 7.5 Hz), 1.02 (3H, d, 10-Me, J=7.3 Hz), 1.65 —1.85 (1H, m, H-4), 1.97, 2.03, 2.05, 2.05, and 2.09 (each 3H, each s, 5×OAc), 2.05—2.25 (2H, m, H-6 and 8), 2.25—2.40 (1H, m, H-2), 2.35—2.50 (1H, m, H-10), 3.36 (3H, s, OMe), 3.49 (1H, d, H-5, $J_{4,5}$=10.0 Hz, $J_{5,6}$=0 Hz), 4.06 and 4.28 (each 1H, each dd, 2-C$\underline{H}_2$OAc, J_{gem}=11.0 Hz, J=10.0 and 83. Hz), 4.35—4.55 (2H, m, 2×H-13), 4.69 (1H, d, H-1, $J_{1,2}$= 2.0 Hz), 4.95—5.05 (2H, m, H-7 and 9), 5.05 (1H, dd, H-3, $J_{2,3}$=5.0 Hz, $J_{3,4}$=11.0 Hz), and 5.55—5.60 (2H, m, H-11 and 12).

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