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Synthetic Studies of Rifamycins. IV.[1] The Synthesis of Rifamycin Ansa-chain Compound Using Carbohydrate†

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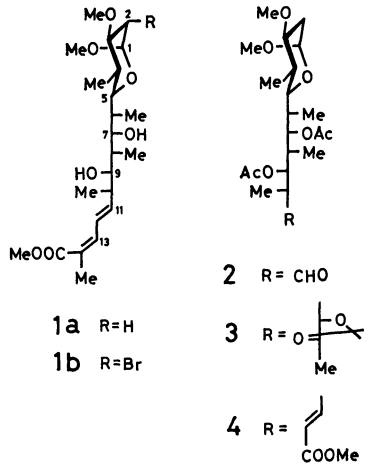
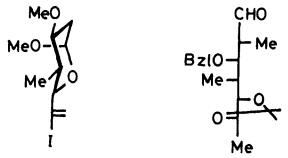
3-*O*-Benzyl-2,4,7-trideoxy-5,6-*O*-isopropylidene-2,4-di-*C*-methyl-L-*glycero*-D-*galacto*-heptose (**6**) was synthesized through 16 steps from 4,6-*O*-benzylidene-3-deoxy-3-*C*-methyl-α-D-altropyranoside (**7**). The condensation of **6** with methyl 2,4,6,7-tetradeoxy-6-lithio-4-*C*-methyl-3-*O*-methyl-α-L-*arabino*-(*E*)-6-heptenopyranoside, derived from **7**, afforded a mixture (**25**) of methyl 9-*O*-benzyl-2,4,6,8,10,13-hexadeoxy-11,12-*O*-isopropylidene-4,8,10-tri-*C*-methyl-3-*O*-methyl-6-methylene-L-*glycero*-D-*galacto*-β-D-*galacto*-tridecopyranoside and its α-L-*altro* epimer in a 61% yield. The debenzylation of **25** by hydrogenolysis with palladium black, followed by homogeneous hydrogenation with tris(triphenylphosphine)chlororhodium(I) and the chromatographic isolation of the desired diastereomer, gave, after acetylation, methyl 7,9-di-*O*-acetyl-2,4,6,8,10,13-hexadeoxy-11,12-*O*-isopropylidene-4,6,8,10-tetra-*C*-methyl-3-*O*-methyl-L-*threo*-L-*manno*-β-D-*galacto*-tridecopyranoside-(1,5) (**3**) in a 19% yield. The hydrolysis of **3** followed by periodate oxidation and Wittig condensation with (methoxycarbonylmethylene)triphenylphosphorane, affords in a 79% yield, methyl [methyl 7,9-di-*O*-acetyl-2,4,6,8,10,11,12-heptadeoxy-4,6,8,10-tetra-*C*-methyl-3-*O*-methyl-L-*manno*-β-D-*galacto*-(*E*)-11-tridecenopyranosid]uronate, which is convertible into the title compound.

In the preceding paper,[1] we described the partial synthesis of the ansa-chain compound **1a** through the degradative compound **4**, which had been derived from the naturally originating ansa compound **1b**.[2] In this paper, we wish to report the synthesis of the strategic intermediate **3**,[3] which could be converted into **4** *via* **2**. This synthesis implies the first synthesis of the ansa-chain portion of rifamycins in the form of **1a**.



The synthetic plan has been made by considering that a sterically complex intermediate like **3** will be formed by a convergence scheme comprised of two appropriate synthetic intermediates derived from hexose.[4] After many unsuccessful attempts, we succeeded in our object by the use of two intermediates, **5** and **6**. The intermediate, **5**[4] has recently been synthesized from methyl 4,6-*O*-benzylidene-3-deoxy-3-*C*-methyl-α-D-altropyranoside **7**.[4,5] The second intermediate **6** was synthesized from **7** through the route shown in Scheme 1. The treatment of **7** with *N*-bromosuccinimide (NBS),[6] followed by the lithium aluminium



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hydride reduction of the bromo derivative, **8**, afforded **9** in an 83% yield. The acetolysis of **9** with acetic anhydride in the presence of a catalytic amount of sulfuric acid gave **10** as an anomeric mixture in a 96% yield. The hydrolysis of **10** with sodium hydroxide afforded, in a 95% yield, 3,6-dideoxy-3-*C*-methyl-D-altrose, which probably exists mainly as the furanose, **11**.[7] The acetonation of **11** with iron(III) chloride[8] in acetone afforded, in a 70% yield, a sample of the furanose derivative, **12**, contaminated with a small amount of its pyranose isomer. Although the pyranose isomer could not be separated from **12** by TLC with any of the solvent systems examined, it was detected on NMR by the observation of the weak doublet (J=3 Hz) at δ=5.26 ascribed to the isomeric H-1 proton; this doublet is to be compared with the strong doublet (J=4 Hz) at δ=5.78 assigned to the H-1 proton of **12**. The sample of **12** was benzylated with sodium hydride and benzyl bromide in THF to give, in a 92% yield, a sample of **13**, accompanied by a small amount of its pyranose isomer. The hydrolysis of the sample of **13** with 70% aqueous acetic acid, followed by chromatography on silica gel, afforded 5-*O*-benzyl-3,6-dideoxy-3-*C*-methyl-D-altrofuranose (**14**) and its pyranose isomer in 82 and 11% yields respectively.

The Grignard reaction of **14** with a ten-fold excess of methylmagnesium iodide in ether provided a 6.5 : 1 mixture of the heptitol derivative, **15**, and its 6-epimer, **15'**, from which **15** and **15'** were subsequently isolated by silica gel-column chromatography in 72 and 11% yields respectively. The (6*S*)-configuration of **15** was determined by the fact that **15** was transformed into the 1,4-lactone, **22**, whose relative configuration

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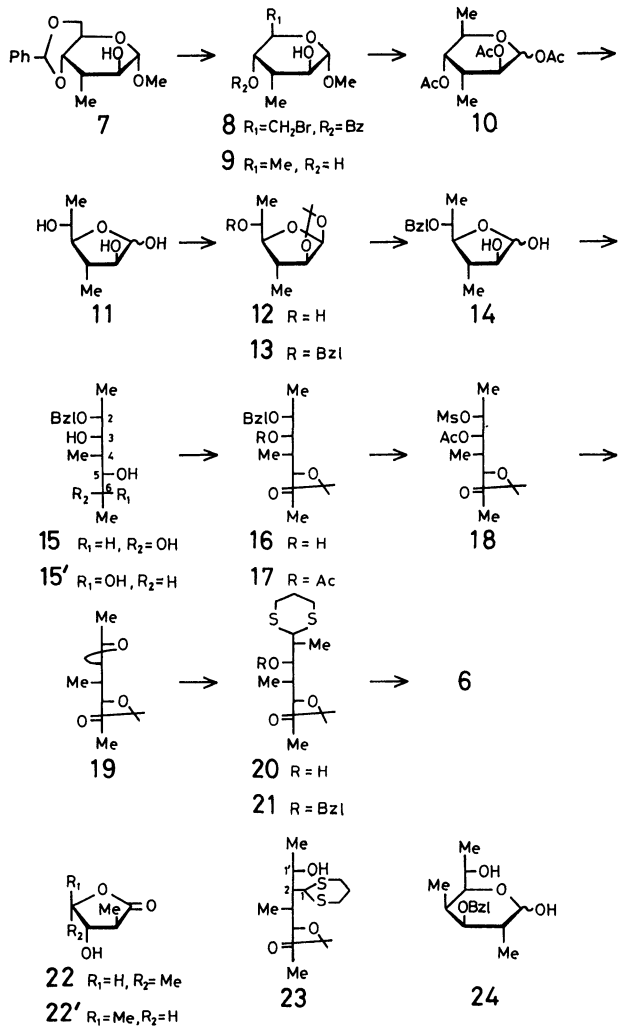
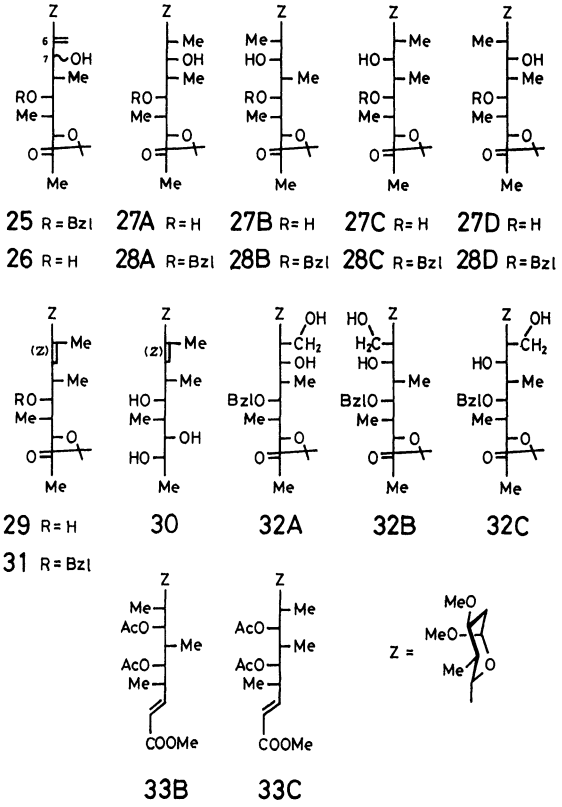


Scheme 1.

was proved by NMR analysis to be identical with that of (+)(2*R*,3*R*,4*R*)-2-butyl-3-hydroxy-4-pentanolide (blastmycinolactol-b),[7] through a sequence of reactions involving 5,6-acetonation, followed by debenzylation, periodate-oxidation, acid hydrolysis, and bromine-oxidation. By the same procedure, **15'** gave **22'**, which was shown by NMR analysis to have the same relative configuration as that of the natural blastmycinolactol.[7] Although either isomer could be used in the subsequent steps, only **15** was used here, mainly because it was produced in a higher yield. The acetonide, **16**, was prepared in a 93% yield by the use of 2,2-dimethoxypropane (DMP) and *p*-toluenesulfonic acid in DMF; it was then acetylated with acetic anhydride and 4-dimethylaminopyridine (DMAP) in ethyl acetate to give **17** in a 96% yield. The hydrogenolysis of **17**, followed by mesylation, afforded the mesylate, **18**, which was immediately treated with 1.4 equiv of sodium methoxide in chloroform to give the epoxide, **19**, in an 81% yield. The reaction of **19** with 5 equiv of 2-lithio-1,3-dithilane in THF at 0 °C furnished a 3 : 1 mixture of two positional isomeric dithiane derivatives. The isomers were separated from each other by silica gel-column chromatography. The structures of the major isomer (66%) and the minor one (24%) were identified as **20** and **23** respectively on the basis of the coupling features of the acetoxymethine protons in the NMR spectra of their acetates. The benzylation of **20** was effected with sodium hydride and benzyl bromide in DMF to give **21** in a 91% yield. The treatment of **21** with a 1 : 1 mixture of mercury(II) chloride and red mercury(II) oxide in aqueous acetone at 70 °C afforded the aldehyde **6** (62%), together with the deacetonated heptopyranose, **24** (18%).[9]



The iodide, **5** was converted into the lithium reagent[4] with 1 equiv of butyllithium in ether at −78 °C and then allowed to react with 1 equiv of **6** in ether at the same temperature to give the allylic alcohol, **25**, in a 61% yield as a mixture of 7-epimers. The acetylation of **25** gave the epimeric 7-acetates, which were shown by column chromatography on silica gel to be in the ratio 1 : 1.9. The product, **25**, was subjected to hydrogenation with palladium black to afford, at first, a debenzylated product, **26**, by hydrogenolysis. The resulting diol was shown to be a mixture of 7-epimers by TLC. On prolonged hydrogenation with a fresh catalyst, **26** changed into three products: **27B**(17%), **29**(44%), and **30**(20%). The product, **30**, could be converted into **29** by acetonation. The endo olefin structure of **29**, except for its geometry, was confirmed by NMR and elemental analysis. The catalytic reduction of allylic alcohol, **26**, resulted mainly in **29** through a hydrogenolysis reaction including the migration of the double bond, accompanied by the cleavage of the C–O bond.[10] The sole hydrogenation product, **27B**, was shown to be different from the desired isomer, **27A**, a precursor of **3** (*vide infra*). The olefin, **29**, was converted into the benzyl derivative, **31**. The hydroboration of **31**

with sodium borohydride and boron trifluoride etherate, and subsequent treatment with hydrogen peroxide, provided **28C**(20%) and **28D**(59%), which were also distinct from the desired isomer, **28A** (*vide infra*). The homogeneous hydrogenation of the debenzylated product, **26**, with a stoichiometric amount of tris-(triphenylphosphine)chlororhodium in benzene under an atmospheric pressure of hydrogen afforded **27A** (24.3%), **27B**(49.7%), and **27D**(1.5%). On the other hand, the hydroboration of **25**, followed by the mesylation of the resulting **32A**, **32B**, and **32C** and their reduction with lithium aluminium hydride, gave **28A**(12%), **28B**(3%), and **28C**(31%) respectively. The debenzylation of **28A**, **28B**, **28C**, and **28D** yielded **27A**, **27B**, **27C**, and **27D** respectively.

The acetylation of **27A** with acetic anhydride and DMAP afforded the diacetate, **3**, in a 77% yield. The selective hydrolysis of the isopropylidene group with 50% aqueous difluoroacetic acid (DFA), followed by periodate-oxidation, provided the aldehyde **2**, which was immediately condensed with (methoxycarbonylmethylene)triphenylphosphorane to afford needles of the α,β-unsaturated ester, **4**, in a 79% yield. The synthetic sample of **4** was identical in all respects with the authentic sample[1] derived from **1b**. The **27A** intermediate thus proved to be the natural type of diastereomer with the structure shown in the figure. Since the derivation of **4** to **1a** has previously been reported,[1] this work constitutes the first synthesis of the naturally originating ansa compound **1a**.

By the same transformation as was used in the case of **27A**, **27B**, and **27C** were converted into the corresponding α,β-unsaturated esters, **33B** and **33C**, which were different from **4**. The diastereomer, **27B** or **27C**, was the major isomer of the diastereomeric products in the homogeneous hydrogenation of **26**, or of the products obtained through the hydroboration of **25**, respectively. These facts reveal that **27B** or **27C** was the 6-epimeric product which was derived from the major epimer of **25** (or **26**); therefore, **27A** or **27D** was deduced as the other 6-epimer originating from the minor epimer of **25** (or **26**). The structure of **27D** (or **28D**) thus could be determined based on the known structure of **27A**. The stereochemistry of epimeric **27B** and **27C** was presumed on the basis of the following consideration. As has been described above, the hydroboration of the endo olefin **31** did not yield **28A**; this result indicates the configuration of the double bond of **31** to be *Z*, provided that the reaction proceeds by *cis*-addition. The structure of the hydroboration product, **28C**, can be deduced as depicted, based on the *Z*-geometry of **31** and on the determined **28D** structure of the other hydroboration product; therefore, the structure of the 6-epimer of **28C** must be **28B**.

These results also reveal that, although the desired epimer of **25** formed in the coupling of **5** and **6** was only half the amount of the other epimer, its homogeneous hydrogenation proceeded with a high stereoselectivity (>94%) to afford **27A**. Many attempts to improve the stereoselectivity of the desired epimer of **25** in the coupling reaction were all unsuccessful; the conversion of the vinyllithium reagent to the Grignard reagent with magnesium bromide in ether or to mixed cuprate[11] with tetrakis[iodo(triphenylphosphine)copper(I)] in ether yielded no coupling product.

Experimental

The melting points were determined on a micro hot-stage Yanaco MP-83 and are uncorrected. The specific rotations were measured with a Carl Zeiss photoelectric polarimeter. The NMR (^{1}H-NMR) spectra were determined with either a Varian A60 or EM-390 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 4-O-Benzyl-6-bromo-3,6-dideoxy-3-C-methyl-α-D-altropyranoside (8). A mixture of **7** (5.00 g, 17.8 mmol), NBS (3.56 g, 20.0 mmol), and CCl_4 (90 ml) containing $BaCO_3$ (4.70 g, 24.0 mmol) was refluxed for 2 h under stirring (argon atmosphere). Any solids were filtered off and washed with CCl_4. The filtrate and washings were washed with saturated aqueous $Na_2S_2O_3$, $NaHCO_3$, and NaCl solution successively. The dried solution was evaporated to give **8** (6.40 g, 100%) as a pale yellow syrup which was suitable for the next synthesis. A portion of this syrup was chromatographed on silica gel with 7: 3 benzene–ether to afford a pure sample: $[\alpha]_D^{20}$ +48° (*c* 1.0, $CHCl_3$); ^{1}H-NMR δ=1.18 (3H, d, 3-Me, J=6.9 Hz), 2.2—2.5 (1H, m, H-3), 3.56 (3H, s, OMe), 3.76 (1H, dd, H-2, $J_{1,2}$=4.0 Hz), 4.18 (1H, dq, H-5, $J_{4,5}$=6.1 Hz), 4.65 (1H, d, H-1), and 5.34 (1H, dd, H-4, $J_{3,4}$=4.5 Hz).

Found: C, 50.14; H, 5.55; Br, 22.14%. Calcd for $C_{15}H_{19}O_5Br$: C, 50.15; H, 5.33, Br, 22.25%.

Methyl 3,6-Dideoxy-3-C-methyl-α-D-altropyranoside (9). The crude sample of **8** (2.70 g) was dissolved in dry THF (150 ml) and cooled in an ice bath. Powdered $LiAlH_4$ (2.30 g, 60.9 mmol) was then slowly stirred into the solution. After being stirred for 15 min, the mixture was refluxed for 3 h. Ethyl acetate (40 ml) and water (30 ml) were slowly added to the ice-cooled reaction mixture, and it was stirred at room temperature overnight. The mixture was then filtered, and the filter cake was washed with ethyl acetate. The filtrate and washings were washed with a saturated aqueous NaCl solution, dried, and evaporated, The residual syrup (2.20 g) was chromatographed on silica gel (100 g) with 3: 7 benzene–ethyl acetate to afford a pure sample of **9** (1.10 g, 83% based on **7**) as a colorless syrup: $[\alpha]_D^{21}$ +58° (*c* 1.0, $CHCl_3$); ^{1}H-NMR δ=1.15 (3H, d, 3-Me, J=7.2 Hz), 1.31 (3H, d, H-6, $J_{5,6}$=6.9 Hz), 1.8—2.2 (1H, m, H-3), 2.4—2.85 and 2.85—3.2 (2H, each br, 2-and 4-OH), 3.43 (3H, s, OMe), 3.4—3.65 (2H, m, H-2 and 4), 3.96 (1H, dq, H-5, $J_{4,5}$=4.8 Hz), and 4.33 (1H, d, H-1, $J_{1,2}$=4.8 Hz).

Found: C, 54.24; H, 9.09%. Calcd for $C_8H_{16}O_4$: C, 54.53; H, 9.15%.

1,2,4-Tri-O-acetyl-3,6-dideoxy-3-C-methyl-D-altropyranoside (10). To a solution of **9** (1.00 g, 5.68 mmol) in acetic anhydride (33 ml) was added concd H_2SO_4 (0.27 ml) under ice-cooling. After being kept at room temperature for 0.5 h, the reaction mixture was poured into cold water (150 ml); the mixture was neutralized with solid $NaHCO_3$ and then extracted with chloroform. The chloroform extracts were washed with a saturated aqueous NaCl solution, dried, and evaporated to give a crude sample of **10** (1.60 g, 95.8%) as a yellow syrup. A portion of this product was purified through a silica-gel column with 4 : 1 benzene–ether to afford an analytical sample of **10**: IR ($CHCl_3$) 1735 cm^{-1}; ^{1}H-NMR

δ=1.03 and 1.10 (3H, each d, 3-Me, J=6.9 and 7.1 Hz), 1.28 and 1.37 (3H, each d, H-6, J=6.2 and 6.9 Hz), 2.11 (9H, s-like, OAc×3), 2.2—2.6 (1H, m, H-3), 3.85—4.2 (1H, m, H-5), 4.8—5.1 (2H, m, H-2 and 4), 5.90 and 6.14 (1H, d and dd, β-H-1 and α-H-1, $J_{\beta\text{-}1,2}$=3.2 Hz, $J_{\alpha\text{-}1,2}=J_{\alpha\text{-}1,3}$=3.0 Hz).

Found: C, 54.03; H, 6.77%. Calcd for $C_{13}H_{20}O_7$: C, 54.16; H, 6.99%.

*3,6-Dideoxy-3-*C*-methyl-*D*-altrofuranose (11).* To a solution of the crude sample of **10** (1.30 g) in methanol (13 ml) was added an aqueous 1 M NaOH solution (14.9 ml) under ice-cooling. After being kept at room temperature for 1 h, the solution was neutralized with CO_2 gas and evaporated. The residual solid was extracted with acetone, and the acetone extracts were evaporated to afford a crude syrup of **11** (0.69 g, 91% based on **9**) as an anomeric mixture. An analytical sample of this free sugar was obtained by the silica gel-column chromatography of the crude sample with 7 : 1 benzene–ether; a colorless syrup: ^{1}H-NMR δ=1.15 and 1.19 (6H, each d, 3-Me and H-6, J=6.8 and 6.6 Hz), 1.8—2.4 (1H, m, H-3), 3.5—4.5 (3H, m, H-2,4, and 5), 5.1—5.4 (1H, m, H-1).

Found: C, 52.23; H, 7.43%. Calcd for $C_7H_{13}O_4$: C, 52.49; H, 7.55%.

*3,6-Dideoxy-1,2-O-isopropylidene-3-*C*-methyl-β-*D*-altrofuranose (12).* Anhydrous iron(III) chloride (0.42 g) was added to a stirred solution of the crude sample of **11** (1.40 g) in acetone (56 ml) under ice-cooling. The mixture was stirred at room temperature for 1 h and then poured into an ice-cooled aqueous 10% K_2CO_3 solution (14 ml) under vigorous stirring. The mixture was concentrated to remove the acetone, and the aqueous residue was extracted with chloroform. The extract was washed with a saturated aqueous NaCl solution, dried, and evaporated. The residual syrup (1.47 g) was chromatographed on silica gel (100 g) with 3 : 1 hexane–acetone to afford **12** (1.23 g, 64% based on **9**) as a colorless syrup: ^{1}H-NMR δ=1.12 (3H, d, 3-Me, J=7.5 Hz), 1.21 (3H, d, H-6, J=6.5 Hz), 1.31 and 1.54 (each 3H, each s, CMe_2), 2.1—2.8 (1H, m, H-3), 2.48 (1H, d, 5-OH, $J_{5,OH}$=3.1 Hz), 3.54 (1H, dd, H-4, $J_{3,4}$=4.1 Hz, $J_{4,5}$=6.0 Hz), 3.7—4.2 (1H, m, H-5), 4.30 (1H, dd, H-2, $J_{1,2}$=4.0 Hz, $J_{2,3}$=1.6 Hz), 5.26 (weak d, isomeric H-1, $J_{1,2}$=3.0 Hz), and 5.78 (1H, d, H-1).

Found: C, 59.21; H, 8.71%. Calcd for $C_{10}H_{18}O_4$: C, 59.38; H, 8.97%.

*5-O-Benzyl-3,6-dideoxy-1,2-O-isopropylidene-3-*C*-methyl-β-*D*-altrofuranose (13).* To a solution of **12** (1.23 g, 6.08 mmol) in dry THF (12.3 ml) was added NaH (219 mg, 9.12 mmol). After the mixture had been stirred at room temperature for 1 h, benzyl bromide (0.864 ml, 7.26 mmol) was added to the mixture and the stirring was continued for 24 h at room temperature. The reaction mixture was then poured into cold water and extracted with ethyl acetate. The extract was washed with a saturated aqueous NaCl solution, dried, and evaporated. The residual syrup (3.24 g) was chromatographed on silica gel (50 g) with 12 : 1 benzene–ethyl acetate to afford **13** (1.64 g, 92%) as a pale yellow syrup: ^{1}H-NMR δ=1.09 (3H, d, 3-Me, J=7.8 Hz), 1.28 (3H, d, H-6, J=6.0 Hz), 1.28 and 1.44 (each 3H, each s, CMe_2), 2.67 (1H, dq, H-3, $J_{3,4}$=2.7 Hz), 3.51 (1H, dd, H-4, $J_{4,5}$=8.7 Hz), 3.79 (1H, dq, H-5), 4.28 (1H, d, H-2, $J_{1,2}$=4.2 Hz), 4.48 and 4.63 (2H, each d, $PhC\underline{H}_2O$, J=12.0 Hz), 5.26 (weak d, isomeric H-1, $J_{1,2}$=3.3 Hz), 5.80 (1H, d, H-1), and 7.34 (5H, s, Ph).

Found: C, 69.90; H, 8.08%. Calcd for $C_{17}H_{24}O_4$: C, 69.83; H, 8.27%.

*5-O-Benzyl-3,6-dideoxy-3-*C*-methyl-*D*-altrofuranose (14).* A solution of **13** (1.62 g, 5.54 mmol) in aqueous 70% acetic acid (16.2 ml) was stirred at 60 °C for 1 h and then evaporated to a yellow syrup (1.76 g), which was subsequently chromatographed on silica gel (60 g) with 2: 1 hexane–acetone to afford **14** (1.15 g, 82%) and its pyranose isomer (0.15 g, 11%): **14** (syrup), R_f=0.29 (2 : 1 hexane–acetone); $[\alpha]_D^{15}$ −25° (*c* 1.47, MeOH, after 2 d); ^{1}H-NMR δ=1.1−1.3 (6H, m, 3-Me and H-6), 2.0—2.35 (1H, m, H-3), 3.11 (2H/3, d, β-2-OH, $J_{2,OH}$=10.4 Hz), 3.22 (H/3, d, α-1-OH, $J_{1,OH}$=3.0 Hz), 3.45—3.9 (10H/3, m, H-2, 4, 5, and α-2-OH), 4.07 (2H/3, d, β-1-OH, $J_{1,OH}$=9.6 Hz), 4.50 and 4.65 (2H/3, each d, α-$PhC\underline{H}_2O$, J_{gem}=11.3 Hz), 4.52 and 4.65 (4H/3, each d, β-$PhC\underline{H}_2O$, J_{gem}=11.3 Hz), 5.13 (2H/3, dd, β-H-1, $J_{1,2}$=3.8 Hz), 5.29 (H/3, d, α-H-1, $J_{1,2}$=0.0 Hz), 7.33 and 7.36 (5H, each s, Ph); ratio of α- and β-anomer, *ca.* 1: 2.

Found: C, 66.88; H, 7.88%. Calcd for $C_{14}H_{20}O_4$: C, 66.64; H, 7.99%.

Pyranose Isomer(Syrup). R_f=0.24 (2 : 1 hexane–acetone); ^{1}H-NMR δ=1.02 and 1.18 (3H, each d, α- and β-3-Me, J=7.5 and 7.8 Hz), 1.29 and 1.32 (3H, each d, β- and α-5-Me, J=7.2 and 6.0 Hz), 2.0—2.3 (1H, br, OH), 2.3—2.7 (1H, m, H-3), 2.85—4.0 (4H, m, H-2, 4, 5, and OH), 4.3—4.6 (2H, m, $PhC\underline{H}_2O$), 4.82 and 5.00 (1H, each d, β-H-1 and α-H-1, $J_{\beta\text{-}1,2}$=5.7 Hz and $J_{\alpha\text{-}1,2}$=1.5 Hz), and 7.35 (5H, s, Ph); ratio of α- and β-anomer, *ca.* 2 : 1.

*2-O-Benzyl-1,4,7-trideoxy-4-*C*-methyl-*L*-glycero-*D*-talo-heptitol (15) and *D*-glycero Epimer (15′).* A solution of **14** (1.71 g, 6.77 mmol) in dry ether (3.42 ml) was added dropwise to a stirred ice-cooled ether solution of methylmagnesium iodide [prepared from magnesium turnings (1.65 g, 67.7 mmol) and methyl iodide (4.22 ml, 67.7 mmol) in dry ether (16.5 ml)]. After 20 h under reflux, 1 M HCl (120 ml) was carefully added, after which the mixture was extracted with chloroform (120 ml×2 and 60 ml×2). The extracts were washed with a saturated aqueous NaCl solution, dried, and evaporated. The residual syrup (2.11 g) was chromatographed on silica gel (270 g) with 2 : 1 chloroform–acetone to afford **15** (1.31 g, 72%), **15′** (196 mg, 11%), and the starting free sugar **14** (103 mg, 6%): **15** (syrup), R_f=0.28 (2 : 1 chloroform–acetone); $[\alpha]_D^{16}$ −15° (*c* 0.68, MeOH); ^{1}H-NMR δ=0.90 (3H, d, 4-Me, J=7.4 Hz), 1.11 and 1.24 (6H, each d, H-1 and 7, J=5.9 and 6.0 Hz), 1.5—2.0 (1H, m, H-4), 3.15 (1H, br, OH), 3.3—3.9 (6H, m, H-2, 3, 5, 6, and OH×2), 4.48 and 4.62 (2H, each d, $PhC\underline{H}_2O$, J_{gem}=11.2 Hz), and 7.34 (5H, s, Ph).

Found: C, 66.98; H, 8.94%. Calcd for $C_{15}H_{24}O_4$: C, 67.13; H, 9.02%.

15′ (needle), R_f=0.26 (2 : 1 chloroform–acetone), mp 130.5—131.5 °C (1 : 1 acetone–hexane); $[\alpha]_D^{22}$ −19° (*c* 0.54, MeOH); ^{1}H-NMR δ=0.96 (3H, d, 4-Me, J=7.2 Hz), 1.2—1.3 (6H, m, H-1 and 7), 1.5—3.0 (4H, m, H-4 and OH×3), 3.5—3.9 (4H, m, H-2, 3, 5, and 6), 4.50 and 4.63 (2H, each d, $PhC\underline{H}_2O$, J_{gem}=11.3 Hz), and 7.35 (5H, s, Ph).

Found: C, 67.27; H, 9.08%. Calcd for $C_{15}H_{24}O_4$: C, 67.13; H, 9.02%.

*2-O-Benzyl-1,4,7-trideoxy-5,6-O-isopropylidene-4-*C*-methyl-*L*-glycero-*D*-talo-heptitol (16).* To an ice-cooled solution of **15** (2.45 g, 9.15 mmol) and DMP (1.35 ml, 11.0 mmol) in dry DMF (24.5 ml) was added anhydrous *p*-toluenesulfonic acid (158 mg, 0.915 mmol). After being stirred at room temperature for 0.5 h, the reaction mixture was neutralized with triethylamine and then evaporated. The residual syrup (3.31 g) was chromatographed on silica gel (145 g) with 8 : 1 benzene–ethyl acetate to afford **16** (2.62 g, 93%) as a colorless syrup: $[\alpha]_D^{26}$ −40° (*c* 1.24, $CHCl_3$); ^{1}H-NMR δ=0.95 (3H, d, 4-Me, J=7.1 Hz), 1.15—1.30 (6H, m, H-1 and 7), 1.38 (6H, s, CMe_2), 1.6—2.1 (1H, m, H-4), 2.73 (1H, d, OH, $J_{3,OH}$=5.0 Hz), 3.4—4.1 (4H, m, H-2, 3, 5, and 6), 4.41 and 4.66 (2H, each d, $PhC\underline{H}_2O$, J_{gem}=12.0 Hz), and 7.33 (5H, s, Ph).

Found: C, 69.86; H, 8.97%. Calcd for $C_{18}H_{28}O_4$: C,

70.10; H, 9.15%.

(2S,3S,4S)-2-Methyl-3-hydroxy-4-pentanolide (22). A solution of **16** (55 mg) in methanol (1.1 ml) was stirred with palladium black for 10 min under bubbling with hydrogen gas. The filtered solution was then evaporated to a colorless syrup (39 mg, 100%), which was subsequently dissolved in acetone (0.4 ml) and cooled in an ice bath. A solution of $NaIO_4$ (57 mg) in water (0.57 ml) was added to the solution. After being stirred for 5 min, the mixture was diluted with water and extracted with chloroform. The extract was washed with a saturated aqueous NaCl solution, dried, and evaporated. The residual aldehyde (28 mg, 91%) was hydrolyzed with 90% aqueous trifluoroacetic acid (0.28 ml) for 5 min and then neutralized with $NaHCO_3$. The reaction mixture was saturated with NaCl and extracted with ethyl acetate (10 times). The dried extracts were evaporated to afford a syrup (21 mg, 100%) of the free sugar, which was then oxidized with bromine (0.03 ml) in 50% dioxane (0.43 ml) at 25 °C for 24 h. The reaction mixture was extracted with ethyl acetate, and the extract was washed with saturated aqueous $Na_2S_2O_3$ and NaCl solutions, dried, and evaporated. The residue was chromatographed on silica gel (1 g) with 1 : 1 benzene–ethyl acetate to give **22** (12 mg, 52% from **16**). The ^{1}H-NMR data of **22** [δ=4.12 (1H, dd, H-3, $J_{2,3}=J_{3,4}$=5.0 Hz) and 4.66 (1H, dq, H-4, $J_{4,Me}$=6.6 Hz)] were very similar to those of (+)-blastmycinolactol-b.[7]

(R)-4-Epimer (22'). The acetonide prepared from **15'** was transformed into **22'** by the procedure described for the preparation of **22**. The ^{1}H-NMR data of **22'** [δ=3.68 (1H, dd, H-3, $J_{2,3}$=9.0 Hz, $J_{3,4}$=7.5 Hz) and 4.21 (1H, dq, H-4, $J_{4,Me}$=6.3 Hz)] were very similar to those of natural (−)-blastmycinolactol.[7]

*3-O-Acetyl-2-O-benzyl-1,4,7-trideoxy-5,6-O-isopropylidene-4-C-methyl-*L*-glycero-*D*-talo-heptitol (17).* To a solution of **16** (1.91 g, 6.20 mmol) in ethyl acetate (19.1 ml) was added acetic anhydride (0.703 ml, 6.20 mmol) and DMAP (833 mg, 6.82 mmol). After being stirred at room temperature for 1.5 h, the reaction mixture was diluted with ethyl acetate (20 ml) and washed successively with saturated aqueous $KHSO_4$, $NaHCO_3$, and NaCl solutions, dried, and evaporated. The residue (2.26 g) was chromatographed on silica gel (80 g) with 10 : 1 benzene–ethyl acetate to afford **17** (2.09 g, 96%) as a colorless syrup: $[\alpha]_D^{26}$ +27° (*c* 0.84, $CHCl_3$); IR ($CHCl_3$); 1733 cm^{-1}; ^{1}H-NMR δ=0.96 (3H, d, 4-Me, J=7.1 Hz), 1.23 (6H, d, H-1 and 7, J=6.0 Hz), 1.37 (6H, s, CMe_2), 1.6—2.1 (1H, m, H-4), 2.11 (3H, s, OAc), 3.5—4.1 (3H, m, H-2, 5, and 6), 4.46 and 4.69 (2H, each d, $PhC\underline{H}_2O$, J_{gem}=11.5 Hz), 5.21 (1H, dd, H-3, J=4.0 and 7.5 Hz), and 7.36 (5H, s, Ph).

Found: C, 68.63; H, 8.48%. Calcd for $C_{20}H_{30}O_5$: C, 68.54; H, 8.63%.

*2,3-Anhydro-1,4,7-trideoxy-5,6-O-isopropylidene-4-C-methyl-*L*-glycero-*D*-galacto-heptitol (19).* A sample of **17** (2.06 g, 5.88 mmol) was hydrogenolyzed in methanol (41 ml) at room temperature over palladium black under bubbling with hydrogen gas for 10 min. The filtered solution was then evaporated to a colorless syrup (1.53 g), which was immediately dissolved in dry pyridine (15.3 ml), and to this mesyl chloride (0.910 ml, 11.8 mmol) was added under ice-cooling. After being kept at room temperature for 1 h, the reaction mixture was poured into cold water (75 ml) and the mixture was extracted with chloroform. The extract was washed with saturated aqueous $KHSO_4$, $NaHCO_3$, and NaCl solutions, dried, and evaporated to give a crude sample of **18** (1.99 g, 100%) as a pale yellow syrup. This sample was dissolved in dry chloroform (19.9 ml) and cooled in an ice bath, and a 4M sodium methoxide in methanol (2.09 ml) was added. After being stirred under ice-cooling for 20 min, the mixture was neutralized with CO_2 gas, poured into cold water (75 ml), and then extracted with chloroform. The extract was washed with a saturated aqueous NaCl solution, dried, and evaporated to afford a pale yellow oil (2.02 g), which was subsequently chloromatographed on silica gel (59 g) with 10:1 benzene–ethyl acetate and then distilled to give **19** (958 mg, 81% based on **17**) as a colorless oil: bp 90—95 °C (bath temp)/6 mmHg**; $[\alpha]_D^{25}$ −55° (*c* 0.95, $CHCl_3$); ^{1}H-NMR δ=1.05 (3H, d, 4-Me, J=6.0 Hz), 1.32 (3H, d, H-1, J=5.3 Hz), 1.33 (3H, d, H-7, J=5.8 Hz), 1.2—1.5 (1H, m, H-4), 1.38 and 1.42 (6H, each s, CMe_2), 2.56 (1H, dd, H-3, $J_{2,3}$=2.3 Hz, $J_{3,4}$=7.4 Hz), 2.78 (1H, dq, H-2), 3.58 (1H, dd, H-5, $J_{4,5}$=5.0 Hz, $J_{5,6}$=9.2 Hz), and 3.95 (1H, dq, H-6).

*2,4,7-Trideoxy-5,6-O-isopropylidene-2,4-di-C-methyl-*L*-glycero-*D*-galacto-heptose Trimethylene Dithioacetal (20) and Its Positional Isomer (23).* A solution of 1,3-dithiane (1.55 g, 12.5 mmol) in dry THF (15.5 ml) was cooled to −40 °C under argon. A 1.6 M butyllithium in hexane (7.80 ml, 12.5 mmol) was added to the solution dropwise under stirring . After being stirred for an additional 2 h at −20 °C, the mixture was again cooled to −40 °C. A solution of **19** (500 mg, 2.50 mmol) in dry THF (1.0 ml) was then added dropwise to this stirred solution, and stirring was continued at −20 °C for 2 h and at 0—2 °C for 4 d. The reaction mixture was poured into cold water (80 ml) and extracted with chloroform (80 ml × 2 and 40 ml × 1). The extracts were washed with a saturated aqueous NaCl solution, dried, and evaporated. The residual syrup (1.99 g) was chromatographed on silica gel (80 g) with 8 : 1 benzene–ethyl acetate to afford **20** (531 mg, 66%) and **23** (193 mg, 24%) as colorless syrups: **20**, R_f=0.31 (6 : 1 benzene–ethyl acetate); $[\alpha]_D^{22}$ −19° (*c* 0.79, $CHCl_3$); ^{1}H-NMR δ=0.90 (3H, d, 4-Me, J=7.2 Hz), 1.14 (3H, d, 2-Me, J=7.2 Hz), 1.27 (3H, m, H-7), 1.41 (6H, s, CMe_2), 1.6—2.3 (4H, m, H-2, 4, and S-$CH_2C\underline{H}_2$), 2.67 (1H, d, 3-OH, $J_{3,OH}$=5.0 Hz), 2.7—3.05 (4H, m, $SC\underline{H}_2CH_2C\underline{H}_2S$), 3.75—4.15 (3H, m, H-3,5, and 6), and 4.21 (1H, d, H-1, $J_{1,2}$=6.5 Hz).

Found: C, 56.46; H, 8.63, S, 20.22%. Calcd for $C_{15}H_{28}O_3S_2$: C, 56.21; H, 8.81; S, 20.00%.

Acetyl Derivative of 20: ^{1}H-NMR δ=2.00 (3H, s, OAc) and 5.27 (1H, dd, H-3, J=7.5 and 3.0 Hz). **23**, R_f=0.41 (6 : 1 benzene–ethyl acetate); $[\alpha]_D^{21}$ −21° (*c* 0.59, $CHCl_3$); ^{1}H-NMR δ=1.15 (3H, d, 3-Me, J=7.5 Hz), 1.27—1.43 (12H, m, CH(OH)$\underline{Me}$, H-6, and CMe_2), 1.6—2.4 (4H, m, H-2,3, and $SCH_2C\underline{H}_2$), 2.5—3.1 (4H, m, $SC\underline{H}_2CH_2C\underline{H}_2S$), 3.75—4.4 (4H, m, $C\underline{H}$(O$\underline{H}$)Me, H-5, and 6), and 4.33 (1H, d, H-1, $J_{1,2}$=3.7 Hz).

Found: C, 56.40; H, 8.64; S, 19.73%. Calcd for $C_{15}H_{28}O_3S_2$: C, 56.21; H, 8.81; S, 20.00%.

Acetyl Derivative of 23: ^{1}H-NMR δ=2.02 (3H, s, 1'-OAc) and 5.29 (1H, dq, H-1', J=6.2 and 6.2 Hz).

*3-O-Benzyl-2,4,7-trideoxy-5,6-O-isopylidene-2,4-di-C-methyl-*L*-glycero-*D*-galacto-heptose Trimethylene Dithioacetal (21).* To a solution of **20** (1.07 g, 3.35 mmol) in dry DMF (10 ml) was added NaH (322 mg, 13.4 mmol) portionwise at 10 °C. After the mixture had been stirred at room temperature for 0.5 h, benzyl bromide (1.18 ml, 10.0 mmol) was added, after which the stirring was continued for 0.5 h at room temperautre. The reaction mixture was then worked-up, and the crude product (1.95 g) was chromatographed on silical gel (75 g) with 50 : 1 benzene–ethyl acetate to afford **21** (1.25 g, 91%) as a colorless syrup: $[\alpha]_D^{21}$ −6° (*c* 0.84, $CHCl_3$); ^{1}H-NMR δ=0.91 (3H, d, 4-Me, J=7.0 Hz,), 1.14 (3H, d, 2-Me, J=6.9 Hz), 1.15—1.25 (3H, m, H-7), 1.40 (6H, s, CMe_2), 1.5—2.3 (4H, m, H-2,4, and $SCH_2C\underline{H}_2$), 2.5—3.0 (4H, m, $SC\underline{H}_2CH_2C\underline{H}_2S$),

** 1 mmHg=133.322 Pa.

3.7—4.1 (4H, m, H-1,3,5, and 6), 4.8 (2H, s, PhC$\underline{H}_2$O), and 7.38 (5H, s, Ph).

Found: C; 64.05; H, 8.11; S, 15.43%. Calcd for $C_{22}H_{34}O_3S_2$: C, 64.35; H, 8.35; S, 15.62%.

*3-O-Benzyl-2,4,7-trideoxy-5,6-O-isopropylidne-2,4-di-C-methyl-*L*-glycero-*D*-galacto-heptose (6) and Deacetonated Heptopyranose 24.* To a mixture of **21** (356 mg, 0.867 mmol) and mercury(II) oxide (826 mg, 3.81 mmol) in aqueous 80% acetone (25 ml) was added mercury(II) chloride (1.03 g, 3.81 mmol) at room temperature with efficient stirring. The mixture was stirred at 70 °C for 20 min, cooled, and filtered through Celite. The filter cake was washed with acetone, and then the filtrate and the washings were combined. After the subsequent removal of the acetone by concentration, the aqueous residue was extracted with chloroform and the extract was washed with an aqueous 10% KI solution and a saturated aqueous NaCl solution, dried, and evaporated. The residue (291 mg) was chromatographed on silica gel (10 g) with 15 : 1 benzene–ethyl acetate to afford **6** (173 mg, 62%) as a colorless syrup: R_f=0.22 (30 : 1 benzene–ethyl acetate); ^{1}H-NMR δ=0.94 (3H, d, 4-Me, J=7.0 Hz), 1.18 (3H, d, 2-Me, J=7.0 Hz), 1.1—1.3 (3H, m, H-7), 1.40 (6H, s, CMe$_2$), 1.5—2.1 (1H, m, H-4), 2.4—2.9 (1H, m, H-2), 3.7—4.3 (3H, m, H-3,5, and 6), 4.56 (2H, s, PhC$\underline{H}_2$O), 7.37 (5H, s, Ph), and 9.90 (1H, d, H-1, $J_{1,2}$=0.9 Hz). The elution of the silica-gel column with ethyl acetate gave **24** (44 mg, 18%) as a syrup which crystallized on standing at room temperature for several days: R_f=0.28 (1 : 2 benzene–ethyl acetate); mp 54.0—55.5 °C (ethyl acetate–hexane); ^{1}H-NMR δ=0.8—1.5 (9H, m, 2,4, and 6-Me), 1.5—2.4 (2H, m, H-2 and 4), 3.0—4.4 (5H, m, H-3,5,6, and OH×2), 4.4—4.85 (3H/2, m, β-H-1 and PhC$\underline{H}_2$O), 5.05—5.4 (H/2, m, α-H-1), and 7.41 (5H, s, Ph); ratio of α- and β-anomer, *ca.* 1 : 1.

*Mixture, 25, of Methyl 9-O-Benzyl-2,4,6,8,10,13-hexadeoxy-11,12-O-isopropylidene-4,8,10-tri-C-methyl-3-O-methyl-6-methyl-ene-*L*-glycero-*D*-galacto-β-*D*-galacto-tridecopyranoside-(1,5) and α-*L*-altro-Epimer.* A solution of **5**[4] (171 mg, 0.54 mmol) in dry ether (1.47 ml) was cooled to −78 °C under argon. To the resulting white suspension was added slowly a 1.64 M butyllithium in hexane (0.329 ml, 0.54 mmol) *via* a syringe under stirring. The white suspension changed to a pale yellow solution, and stirring was continued at −78 °C for 1.5 h. To this a solution of **6** (173 mg, 0.54 mmol) in dry ether (0.2 ml) was slowly added *via* a syringe, and stirring was continued for 1.5 h. The reaction mixture was quenched at 0 °C by adding a saturated aqueous NH_4Cl solution, and then it was extracted with ether. The organic layers were washed with a saturated aqueous NaCl solution, dried, and evaporated to a pale yellow oil (289 mg). The crude product was purified by chromatography on silica gel (13 g) with 10 : 1 hexane–acetone to afford a colorless syrup (167 mg, 61%) of the condensation product, **25**. The TLC (silica gel, 5 : 1 hexane–acetone) of this sample revealed it to be an epimeric mixture having very similar R_f-values (0.36): ^{1}H-NMR δ=0.89 and 0.93 (9H, each d, 4,8, and 10-Me, J=7.0 Hz), 1.1—1.32 (3H, m, H-13), 1.40 and 1.42 (6H, each s, CMe$_2$), 1.55—2.50 (5H, m, H-2ax, 2eq, 4, 8, and 10), 3.1—3.5 (1H, br, OH), 3.36 and 3.41 (each 3H, each s, OMe×2), 3.5—4.66 (6H, m, H-3,5,7,9,11, and 12), 4.7—4.95 (3H, m, H-1 and PhC$\underline{H}_2$O), 5.2—5.55 (2H, m, 6-methylene), and 7.41 (5H, s, Ph).

Found: C, 68.90; H, 9.10%. Calcd for $C_{29}H_{46}O_7$: C, 68.74; H, 9.15%.

Acetylation of 25. To a solution of **25** (30.0 mg, 0.0592 mmol) in ethyl acetate (0.3 ml) was added acetic anhydride (0.017 ml, 0.18 mmol) and DMAP (8.7 mg, 0.071 mmol). After being stirred at room temperature for 3 h, the reaction mixture was worked-up as has been described in connection with the preparation of **17**. Subsequent silica gel(3.2 g)-column chromatography of the crude product with 6 : 1 benzene–ethyl acetate afforded the isomeric acetates **A** (20.3 mg, 62.5%) and **B** (10.8 mg, 33.2%): **A**, R_f=0.28 (6 : 1 benzene–ethyl acetate); ^{1}H-NMR δ=1.37 (6H, s, CMe$_2$), 1.93 (3H, s, OAc), 3.30 and 3.34 (each 3H, each s, OMe×2), 4.61 (2H, s, PhC$\underline{H}_2$O), 5.24 (2H, s, 6-methylene), and 5.58 (1H, d, H-7, $J_{7,8}$=6.0 Hz); **B**, R_f=0.21 (6 : 1 benzene–ethyl acetate); ^{1}H-NMR δ=1.39 (6H, s, CMe$_2$), 2.06 (3H, s, OAc), 3.50 (1H, dd, H-9, J=1.0 and 9.5 Hz), 3.43 and 3.35 (each 3H, each s, OMe×2), 4.41 and 4.60 (each 1H, each d, PhC$\underline{H}_2$O, J_{gem}=11.0 Hz), and 5.29 (1H, d, H-7, $J_{7,8}$=9.9 Hz), and 5.38—5.45 (2H, m, 6-methylene).

Formation of 29, 27B, and 30 by Heterogenous Hydrogenation of 25. A solution of **25** (81 mg) in methanol (1.6 ml) was stirred with palladium black at room temperature for 7 min under bubbling with hydrogen gas. The filtered solution was then evaporated to afford a colorless syrup of **26** (67 mg, 100%), which was shown by TLC (3 : 1 hexane–acetone) to be a mixture of epimers with R_f-values of 0.27 and 0.25. This sample (67 mg) was again dissolved in methanol (1.4 ml) and stirred with fresh palladium black at room temperature for 20 min under bubbling with hydrogen gas. The filtered solution was evaporated, and the residue was chromatographed on silica gel (6.4 g) with 3 : 1 hexane–acetone to afford **29** (28 mg, 44%), **27B** (11 mg, 17%), and **30** (12 mg, 20%) as colorless syrup with the R_f-values of 0.43, 0.38, and 0.08 respectively on TLC (3 : 1 hexane–acetone): **29**, $[\alpha]_D^{20}$ −32° (*c* 0.93, $CHCl_3$); ^{1}H-NMR δ=1.36 (6H, s, CMe$_2$), 1.72 (3H, d, 6-Me, $J_{7,Me}$=1.5 Hz), 4.28 (1H, d, H-5, $J_{4,5}$=10.5 Hz), and 5.32 (1H, d, H-7, $J_{7,8}$=10.0 Hz). Found: C, 65.88; H, 9.92%. Calcd for $C_{22}H_{40}O_6$: C, 65.97; H, 10.07%. **27B**, ^{1}H-NMR δ=0.86, 0.93, 0.93, and 1.01 (12H, each d, 4,6,8, and 10-Me, J=7 Hz), 1.25—1.35 (3H, m, H-13), 1.40 (6H, s, CMe$_2$), 1.4—2.1 (5H, m, H-2ax, 4, 6, 8, and 10), 2.17 (1H, ddd, H-2eq, $J_{1,2eq}$=2.1 Hz, $J_{2ax,2eq}$=13.0 Hz, $J_{2eq,3}$=4.4 Hz), 3.14 (1H, ddd, H-3, $J_{2ax,3}$=$J_{3,4}$=10.5 Hz), 3.34 (6H, s, OMe×2), 3.49 and 4.12 (2H, each br, OH×2), 3.4—4.1 (5H, m, H-5,7,9,11, and 12), and 4.88 (1H, dd, H-1, $J_{1,2ax}$=2.5 Hz); **30**, ^{1}H-NMR δ=1.72 (3H, s-like, 6-Me), 3.40 and 3.42 (each 3H, each s, OMe×2), 4.32 (1H, d, H-5, $J_{4,5}$=10.5 Hz), and 5.21 (1H, d-like, H-7, $J_{7,8}$=10.5 Hz).

O-Benzyl Derivative 31 of 29. To a solution of **29** (4.9 mg, 0.012 mmol) in dry DMF (0.05 ml) was added NaH (1.2 mg, 0.049 mmol). After the mixture had been stirred at room temperature for 0.5 h, benzyl bromide (0.004 ml, 0.037 mmol) was added and the new mixture was stirred at room temperature for 1 h. The reaction mixture was then worked-up, and the crude product was chromatographed on silica gel (300 mg) with 8 : 1 benzene–ethyl acetate to afford **31** (4.9 mg, 82%) as a colorless syrup: R_f=0.31 (8 : 1 benzene–ethyl acetate); ^{1}H-NMR δ=1.70 (3H, s-like, 6-Me), 3.35 and 3.37 (each 3H, each s, OMe×2), 4.34 (1H, d, $J_{4,5}$=10.5 Hz), 4.61 (2H, s, PhC$\underline{H}_2$O), 5.50 (1H, d-like, H-7, $J_{7,8}$=9.5 Hz), and 7.32 (5H, s, Ph).

Formation of Diastereomers, 28D and 28C, by the Hydroboration of 31. $NaBH_4$ (1.1 mg, 0.03 mmol) was added to solution of **31** (4.9 mg, 0.01 mmol) in dry diglyme (0.01 ml). To this stirred mixture was added dropwise a 2M boron trifluoride etherate in dry diglyme (0.015 ml, 0.03 mmol). After being stirred at room temperature for 4 h, the reaction mixture was cooled in an ice bath, and water (0.01 ml) was added, followed by an aqueous 3 M NaOH solution (0.02 ml) and 30% H_2O_2 (0.01 ml). After being stirred at room temperature for 0.5 h, the mixture was poured into water and extracted with ether. The extract was washed with water and a saturated aqueous NaCl solution, dried, and evaporated. The residue was

chromatographed on silica gel (0.5 g) with 7 : 1 hexane–acetone to afford **28D** (3.0 mg, 59%) and **28C** (1.0 mg, 20%) as a colorless syrup: **28D**, R_f=0.41 (5 : 1 hexane–acetone); ^{1}H-NMR δ=1.39 (6H, s, CMe_2), 3.33 (each 3H, each s, OMe×2), 3.39 (1H, s, OH), 4.75 (2H, s, $PhC\underline{H}_2O$): **28C**, R_f=0.34 (5 : 1 hexane–acetone) and 0.29 (4 : 1 benzene–ethyl acetate); these R_f-values were identical with those of the sample of **28C** to be described below.

Formation of 27B, 27A, and 27D by the Homogeneous Hydrogenation of 26. A sample of **26** (33.6 mg, 0.081 mmol), prepared from **25** (41.0 mg, 0.081 mmol) by the aforesaid procedure, was dissolved in benzene (1.67 ml) and to this mixture tris(triphenylphosphine)chlororhodium(I)[12] (66.8 mg, 0.072 mmol) was added. This mixture was stirred under an atmospheric pressure of hydrogen at room temperature for 18 h. The reaction mixture was then evaporated and the residue was passed through Florisil with ether and again evaporated. The residue was chromatographed on silica gel (3.5 g) with 4 : 1 benzene–acetone to afford **27B** (16.7 mg, 49.7%), **27A** (8.2 mg, 24.3%), and **27D** (0.5 mg, 1.5%) as colorless syrup with the R_f-values of 0.35, 0.31, and 0.26 (4 : 1 benzene–acetone) respectively. **27B**: the ^{1}H-NMR data and R_f-value of this material were identical with those of the sample of **27B** obtained by the heterogeneous hydrogenation of **25**. **27A**: ^{1}H-NMR δ=0.86, 0.94, 0.94, and 1.00 (12H, each d, 4, 6, 8, and 10-Me, J=7 Hz), 1.25—1.35 (3H, m, H-13), 1.39 (6H, s, CMe_2), 1.4—2.4 (6H, m, H-2ax, 2eq, 4,6,8, and 10), 3.34 and 3.36 (6H, each s, OMe×2), 3.1—4.2 (8H, m, H-3,5,7,9,11,12, and OH×2), and 4.8—4.9 (1H, m, H-1). **27D**: on TLC this sample was found to be identical with the sample of **27D** obtained by the debenzylation of **28D** (see the following experiment).

Formation of 32A, 32B, and 32C by the Hydroboration of 25. To a stirred solution of **25** (55.8 mg, 0.11 mmol) and $NaBH_4$ 12.5 mg, 0.33 mmol) in dry THF (0.11 ml) was added a 2 M boron trifluoride etherate in dry THF (0.165 ml, 0.33 mmol). After being stirred at room temperature for 3 h, the reaction mixture was cooled in an ice bath and water (0.083 ml) was added followed by aqueous 3 M NaOH (0.15 ml) and 30% H_2O_2 (0.067 ml). Stirring was continued at room temperature for 1 h, after which the mixture was poured into water and extracted with ether. The ether extract was washed with a saturated aqueous NaCl solution, dried, and evaporated. The residue was chromatographed on silica gel (5.2 g) with 4 : 1 benzene–acetone to afford **32B** (6.1 mg, 11%) and a mixture of **32A** and **32C** (32.0 mg, 55%) as colorless syrup with the R_f-values of 0.36 and 0.26 (4 : 1 benzene–acetone) respectively.

Transformation of 32A and 32B into 28A and 28C. The mixture of **32A** and **32C** (32.0 mg, 0.067 mmol) obtained in the preceding experiment was dissolved in dry pyridine (0.32 ml), and to this mesyl chloride (0.006 ml, 0.07 mmol) was added under ice-cooling. After being stirred under ice-cooling for 1 h, the reaction mixture was poured into cold water and extracted with ether. The extract was washed with a saturated aqucous NaCl solution, dried, and evaporated. The residual syrup (36.8 mg) was dissolved in dry ether (0.74 ml) and cooled in an ice bath. $LiAlH_4$ (4.6 mg, 0.12 mmol) was then added to the solution, and stirring was continued at 0 °C for 1.5 h. Ethyl acetate and water were then added, and the mixture was stirred. The organic layer was separated and the aqueous layer was extracted with ether. The combined organic layers were washed with a saturated aqucous NaCl solution, dried, and evaporated. The residue was chromatographed on silica gel (3.1 g) with 4 : 1 benzene–ethyl acetate to afford **28A** (6.6 mg, 12% based on **25**) and **28C** (17.3 mg, 31% based on **25**) as colorless syrup having the R_f-values of 0.34 and 0.29 (4 : 1 benzene–ethyl acetate) respectively. **28A**: $[\alpha]_D^{16}$ −63° (c 1.04, $CHCl_3$); ^{1}H-NMR δ=0.82, 0.87, 0.94, and 1.12 (12H, each d, 4, 6, 8, and 10-Me, J=7 Hz), 1.15—1.25 (3H, m, H-13), 1.37 (6H, s, CMe_2), 1.5—2.4 (6H, m, H-2ax,2eq,4,6,8, and 10), 3.0—4.1 (6H, m, H-3,5,7,9,11, and 12), 3.35 and 3.39 (each 3H, each s, OMe×2), 3.48 (1H, br-s, OH), 4.70 (2H, s, $PhC\underline{H}_2O$), 4.8—4.9 (1H, m, H-1), and 7.32 (5H, s, Ph).

Found: C, 68.43; H, 9.37%. Calcd for $C_{29}H_{48}O_7$: C, 68.47; H, 9.51%.

28C: ^{1}H-NMR δ=0.91, 0.92, 0.94, and 1.04 (12H, each d, 4, 6, 8, and 10-Me, J=7 Hz), 1.15—1.25 (3H, m, H-13), 1.40 (6H, s, CMe_2), 1.4—2.4 (6H, m, H-2ax, 2eq,4,6,8, and 10), 2.9—4.0 (7H, m, H-3,5,7,9,11,12, and OH), 3.32 and 3.34 (each 3H, each s, OMe×2), 4.49 and 4.71 (2H, each d, $PhC\underline{H}_2O$, J_{gem}=11.7 Hz), 4.8—4.9 (1H, m, H-1), and 7.34 (5H, s, Ph).

Conversion of 32B into 28B. By the procedure described in the preceding paragraph, the aforesaid sample of **32B** (6.0 mg) was converted into crude **28B**, which was then purified by silica gel-column chromatography with 6 : 1 hexane-acetone to afford **28B** (1.5 mg, 3% based on **25**): R_f= 0.31 (5 : 1 hexane–acetone) ^{1}H-NMR δ=0.88—1.06 (12H, m, 4, 6, 8, and 10-Me), 1.2—1.3 (3H, m, H-13), 1.39 (6H, s, CMe_2), 1.5—2.4 (6H, m, H-2ax,2eq,4,6,8, and 10), 2.9—4.1 (6H, m, H-3,5,7,9,11, and 12), 3.07 (1H, br-s, OH), 3.31 and 3.34 (each 3H, each s, OMe), 4.65—4.75 (2H, m, $PhC\underline{H}_2O$), 4.8—4.9 (1H, m, H-1), and 7.34 (5H, s, Ph).

Debenzylation of 28A. A solution of **28A** (5.3 mg) in methanol (0.5 ml) was stirred with palladium black at room temperature for 5 min under bubbling with hydrogen gas. The subsequent evaporation of the filtered solution gave a syrup (4.0 mg, 92%) whose ^{1}H-NMR spectrum and TLC mobility were identical with those of **27A**.

Debenzylation of 28B and 28D. The sample of **28B** and **28D** were hydrogenolyzed by the procedsure described above for **28A**. On TLC the resulting debenzylated products showed the same mobilities as those of **27B** and **27D** obtained by the homogenous hydrogenation of **26**.

*Methyl 7,9-Di-O-acetyl-2,4,6,8,10,13-hexadeoxy-11,12-O-isopropylidene-4,6,8,10-tetra-C-methyl-3-O-methyl-*L-threo-L-manno-*β*-D-galacto-*tridecopyranoside-(1,5) (3).* To a solution of **27A** (12 mg, 0.0287 mmol) in ethyl acetate (0.12 ml) was added acetic anhydride (0.027 ml, 0.287 mmol) and DMAP (14 mg, 0.115 mmol). After being stirred at 45 °C for 20 h, the reaction mixture was worked-up as had been described in connection with the preparation of **17**. The crude product (20 mg) was chromatographed on silica gel (2.1 g) with 7 : 1 benzene–acetone to afford **3** (11 mg, 77%) as a colorless syrup: R_f=0.54 (4 : 1 benzene–acetone); IR ($CHCl_3$) 1734 cm^{-1}; $[\alpha]_D^{15}$ −83° (c 0.90, $CHCl_3$); ^{1}H-NMR δ=0.85—1.05 (12H, m, 4, 6, 8, and 10-Me), 1.22 (3H, d, H-13, J=6.9 Hz), 1.37 (6H, s-like, CMe_2), 1.4—2.6 (6H, m, H-2ax,2eq,4,6,8, and 10), 2.04 (6H, s, OAc×2), 3.05—3.9 (4H, m, H-3,5,11, and 12), 3.31 and 3.33 (6H, each d, OMe×2), 4.75—4.80 (1H, m, H-1), 4.98 and 5.19 (2H, each dd, H-7 and 9, J=8.3, 4.5 Hz and J=8.9, 1.4 Hz).

Found: C, 61.87; H, 8.97%. Calcd for $C_{26}H_{46}O_9$: C, 62.13; H, 9.22%.

*Methyl [Methyl 7,9-Di-O-acetyl-2,4,6,8,10,11,12-heptadeoxy-4,6,8,10-tetra-C-methyl-3-O-methyl-*L-manno-*β*-D-galacto-(E)-11-tridecenopyranosid]uronate (4).* A sample of **3** (9.5 mg, 0.019 mmol) was treated with aqueous 50% DFA (0.095 ml) under ice-cooling for 20 min. The reaction mixture was neutralized with solid $NaHCO_3$ and a saturated aqueous $NaHCO_3$ solution and then extracted with ether. The extract was washed with a saturated aqueous NaCl solution, dried,

and evaporated. The residual syrup [8.7 mg, 100%, R_f=0.29 (2 : 1 hexane–acetone)] was dissolved in acetone (0.08 ml) and treated with a solution of $NaIO_4$ (6.1 mg, 0.028 mmol) in water (0.06 ml) under ice-cooling for 10 min. The reaction mixture was then poured into cold water and extracted with ether. The extract was washed with a saturated aqueous NaCl solution, dried, and evaporated. The residual crude sample of **2** [7.9 mg, 100%, R_f=0.31 (3 : 1 hexane–acetone)] was dissolved in dry benzene (0.17 ml). To this, (methoxycarbonylamethylene)triphenylphosphorane (9.5 mg, 0.028 mmol) was added, after which the mixture was refluxed at 85 °C for 4 h under argon. The reaction mixture was evaporated, and the residue was chromatographed on silica gel (1.7 g) with 5 : 2 benzene–ethyl acetate to give **4** (7.0 mg, 79%) as colorless needles: R_f=0.34 (15 : 1 chloroform–acetone); mp 100—101 °C (hexane) (lit,[1] mp 100—101 °C); mixed mp 100—101 °C; The ^{1}H-NMR and IR (KBr) spectra of this sample were identical with those of the authentic sample.[1]

*Conversion of **27B** into **33B**.* A sample of **27B** was converted into the α,β-unsaturated ester, **33B**, by the procedure described in the case of **27A**. **33B**; R_f=0.37 (15 : 1 chloroform–acetone); ^{1}H-NMR δ=0.8—1.05 (12H, m, 4, 6, 8, and 10-Me), 1.2—2.35 (6H, m, H-2ax,2eq,4,6,8, and 10), 2.09 (6H, s, OAc×2), 2.9—3.5 (2H, m, H-3 and 5), 3.34 (6H, s, OMe×2), 3.74 (3H, s, COOMe), 4.7—4.95 (2H, m, H-1 and one of the two CHOAc), 5.23 (1H, d-like, one of the two CHOAc, J=8.6 Hz), 5.90 (1H, d, H-12, $J_{11,12}$=16.4 Hz), and 6.91 (1H, dd, H-11, $J_{10,11}$=9.5 Hz).

*Conversion of **28C** into **33C**.* A sample of **28C** was hydrogenolyzed by the procedure described in the case of **28A**, and the resulting debenzylation product, **27C**, was converted into **33C** by the method described in the case of **27A**. **33C**; R_f=0.42 (15 : 1 chloroform–acetone); ^{1}H-NMR δ= 0.87, 0.90, 0.92, and 1.01 (12H, each d, 4, 6, 8, and 10-Me, J=7 Hz), 1.2—2.3 (6H, m, H-2ax,2eq,4,6,8, and 10), 2.06 (6H, s, OAc×2), 3.0—3.5 (2H, m, H-3 and 5), 3.31 and 3.34 (6H, each s, OMe×2), 3.72 (3H, s, COOMe), 4.7—4.8 (1H, m, H-1), 4.82 and 5.07 (2H, each dd, H-7 and 9, J=6.8, 3.9 Hz and J=6.9, 3.9 Hz), 5.90 (1H, d, H-12, $J_{11,12}$=16.5 Hz), and 6.39 (1H, dd, H-11, $J_{10,11}$=8.7 Hz).

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